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MEANDROS
MEDICAL AND DENTAL JOURNAL

# CONTENTS

99 Low Level Laser Therapy in Orthodontics
*Düşük Doz Lazerlerin Ortodonti Alanında Kullanımı*
Serpil Çokakoğlu, Filiz Aydoğan, Burcu Aydın; Isparta, Amsterdam, Turkey, Netherlands

106 Vitamin D Level and Infertility
*Vitamin D Düzeyi ve İnfertilite*
Özgür Deniz Turan; Aydın, Turkey

111 The Morphological Changes in the Mandible Bone: The Effects of Age, Gender and Dental Status
*Mandibular Morfolojik Değişiklikler: Yaş, Cinsiyet ve Diş Durumunun Etkileri*
Güldane Mağat, Sevgi Özcan Şener; Konya, Turkey

121 Comparison of Hierarchical and Non-hierarchical Fuzzy Models with Simulation and an Application on Hypertension Data Set
*Aşamalı ve Aşamalı Olmayan Bulanık Modellerin Simülasyon ve Hipertansiyon Veri Seti Üzerinde Bir Uygulama ile Karşılaştırılması*
Fulden Cantaş, İmran Kurt Ömürlü, Mevlüt Türe; Aydın, Turkey

130 Distribution of Some Risk Factors Related to Soft Tissue Injuries in Dentoalveolar Traumas
*Dento Alveolar Travmalarda Görülen Yumuşak Doku Yaralanmalarıyla Bağlantılı Risk Faktörlerinin Dağılımı*
Fatih Şengül, Hüseyin Şimşek; Erzurum, Ordu, Turkey

136 Apical Extrusion of Debris and Irrigant Using XP-Endo Finisher, EndoActivator, Passive Ultrasonic Irrigation or Syringe Irrigation
*XP-Endo Finisher Eğesi, EndoActivator, Pasif Ultrasonik İrrigasyon veya İğne İrrigasyonu Sırasında Meydana Gelen Debris ve İrrigant Ekstrüzyonunun Değerlendirilmesi*
Evren Sarıyılmaz, Cangül Keskin; Ordu, Samsun, Turkey

141 Evaluation of Different Root Canal Filling Methods in Primary Teeth
*Süt Dişlerinde Farklı Kök Kanal Dolum Yöntemlerinin Değerlendirilmesi*
Sezin Özer, Emine Şen Tunç, Elif Kalyoncuoğlu, Banu Gülcan; Samsun, Kocaeli, Turkey

147 Evaluation of Complications Following Impacted Mandibular Third Molar Extraction in Patients with Different Hand Preference
*Farklı El Tercihi Olan Hastalarda Mandibular Gömülü Üçüncü Molar Çekim Sonrası Oluşan Komplikasyonların Değerlendirilmesi*
Utkan Kamil Akyol, Neziha Keçecioğlu; Rize, Turkey

153 Effects of Polishing on Color Stability and Surface Roughness of CAD-CAM Ceramics
*Polisajın CAD-CAM Seramiklerin Renk Stabilitesi ve Yüzey Pürüzlülüğüne Etkileri*
Işıl Sarıkaya, Yeliz Hayran; Tokat, Turkey

160 Biostimulatory Effects of Diode Laser and Ozone on Wound Healing in Rats
*Ratlarda Yara İyileşmesinde Ozon ve Diod Lazerin Biyostimülatör Etkisi*
Hilal Alan, Çiğdem Güler, Ümit Yolcu, Mahmut Koparal, Ebru Çakır, Pınar Demir; Malatya, Ordu, Adıyaman, İzmir, Turkey

MEANDROS
MEDICAL AND DENTAL JOURNAL

# CONTENTS

168 A Case of Acute Lymphoblastic Leukemia with Isolated Orbital Relapse
*İzole Orbita Tutulumu ile Relaps Olan Akut Lenfoblastik Lösemi Olgusu*
Aziz Polat, Funda Özgürler Akpınar, Yasemin Işık Balcı, Semra Acer, Ali Koçyiğit, Havva Evrengül; Denizli, Turkey

171 A Rare Cause of Embolism: Cardiac Papillary Fibroelastoma
*Nadir Görülen Bir Embolizm Nedeni: Kardiyak Papiller Fibroelastom*
Mehmet Boğa, Selim Durmaz, Tünay Kurtoğlu, Uğur Gürcün, Nil Çulhacı, Melek Yılmaz; Aydın, Malatya, Turkey

175 Shprintzen-Goldberg Syndrome: Case Report
*Shprintzen-Goldberg Sendromu: Olgu Sunumu*
Sinem Yalçıntepe, Özge Özalp Yüreğir, Sevcan Tuğ Bozdoğan, Hüseyin Aslan; Adana, Mersin, Eskişehir, Turkey

178 Extracranial Meningioma: A Case Report
*Ekstrakraniyal Meningiom: Bir Olgu Sunumu*
Özlem Erdal Özdemir, Tuğba Özbek, Canten Tataroğlu, Sevilay Gürcan, Ayşe Gül Örmeci; Aydın, Turkey

182 A Rare Complication Occurring Years After Thyroid Surgery: A Cutaneous Fistula
*Tiroit Cerrahisinden Yıllar Sonra Ortaya Çıkan Nadir Bir Komplikasyon: Deri Fistülü*
Mustafa Ünübol, Ahmet Orhan Çelik, Adem Maman, Çiğdem Kalaycık Ertugay; Aydın, Tokat, Turkey

Review / Derleme

# Low Level Laser Therapy in Orthodontics

## *Düşük Doz Lazerlerin Ortodonti Alanında Kullanımı*

Serpil Çokakoğlu[1], Filiz Aydoğan[1], Burcu Aydın[2]

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**Abstract**

Lasers are widely used in most of the fields in dentistry for many years and they have recently gained popularity in orthodontic practice. Most common procedures with laser applications in orthodontics could be summarized as acceleration of tooth movement, pain reduction after force application, bone regeneration in the median palatal suture area during maxillary expansion or consolidation phase after distraction osteogenesis, enamel etching during bonding procedure, reduction of enamel decalcification, debonding of ceramic brackets, soft tissue applications such as gingival recontouring and attachment placement for impacted teeth. In this review, biostimulation effect or low level laser therapy in orthodontics will be exclusively evaluated.

**Öz**

Lazerler genellikle yıllardır diş hekimliğinin birçok alanında kullanılmaktadır ve son yıllarda ortodonti pratiğinde popülarite kazanmıştır. Ortodontide lazerin en yaygın kullanım alanları; diş hareketinin hızlandırılması, kuvvet uygulanmasını takiben ağrının azaltılması, maksiller genişletme esnasında veya distraksiyon osteogenezisin konsolidasyon safhasında midpalatal sütur alanında kemik rejenerasyonu, bonding prosedürü esnasında minenin pürüzlendirilmesi, mine dekalsifikasyonunun azaltılması, seramik braketlerin debonding işlemi esnasında kullanımı, diş eti konturlaması ve gömülü dişler için ataçman yerleştirmeyi içeren yumuşak doku uygulamaları şeklinde özetlenebilir. Bu derlemede ortodontide lazerin biyostimülasyon etkisi veya düşük doz lazer tedavisi detaylı bir şekilde değerlendirilecektir.

**Keywords**
Biostimulation, low level laser, orthodontics

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Biyostimülasyon, düşük doz lazer, ortodonti

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### Introduction

Laser is an acronym for "light amplification by stimulated emission of radiation", which is one of the greatest technological advances of the 20th century. Introduction of lasers to medical world was in 1963. One year later, the first laser applications in the field of dentistry were performed with the use of ruby laser on the hard tissues (1). A laser is a single wavelength (or color) of light, travelling through a collimated tube delivering a concentrated source of energy (2). Laser light has some exclusive properties such as monochromaticity (the same color), coherence (all the light waves are in phase both spatially and temporally) and collimation (all rays are parallel to each other and do not diverge significantly even over long distances) (3). When laser

wavelengths reach the target area, depending on the optical characteristics of the applied tissue different interactions such as reflection, absorption, scattering, transmission can occur (4). Additionally, various photobiological effects including photothermal, photochemical, fluorescence, photoacoustic or biostimulation have been produced by the use of a dental laser. By changing the laser parameters such as beam diameter, energy, exposure time, different formed of photothermal laser-tissue interactions (e.g. incision/excision, ablation, hemostasis/coagulation) can be used for dissimilar procedures (5).

Currently, the most popular types of lasers used in dentistry are the argon, carbon dioxide ($CO_2$), diode, neodymium-doped yttrium aluminum garnet (Nd:YAG) and the erbium lasers (6). Dental lasers can be categorized as soft and hard tissue lasers according to their applicability of tissues. For example, erbium and $CO_2$ lasers are effective on both tissues. However, soft tissue applications with erbium lasers have less coagulation and hemostasis capacities on target tissues than $CO_2$ lasers (7). Not only $CO_2$ lasers but also Nd:YAG and diode lasers stimulate the natural healing process in the cells. Soft lasers that can be used in nonsurgical mode for biostimulation, for more rapid wound healing, pain relief, increased collagen growth and general anti-inflammatory effects (8). At the same time, this group can be termed as low-level lasers, low level laser therapy (LLLT) and laser-phototherapy (9).

## Effects of Low Level Laser Therapy on Tooth Movement

Tooth movement induced by a physical stimulus/force consists of a series of phenomena involving physiological and pathological reactions of the alveolar bone, periodontal ligament, gingiva, vascular and neural networks (10). According to the limited research available, it is assumed that LLLT is dose-dependent and can stimulate or inhibit biological processes depend on physical features and parameters of laser device (e.g., wavelength, output power, frequency, irradiation dose, type of probe size), irradiation protocol, and properties of target tissue (e.g., absorption coefficient, density, depth, thickness).

Many studies evaluated the influences of LLLT with the various mediators such as the receptor activator of nuclear factor kappa B (RANK)/RANK ligand (RANKL) (11), the macrophage colony-stimulating factor/its receptor (12), tartrate-resistant acid phosphatase (13), matrix metalloproteinase-9, cathepsin K, and alpha(v) beta(3) [a(v)b3] integrin (14), and consequently suggested that low level therapy had an influence on the acceleration of the tooth movement by supporting the alveolar bone remodeling.

In the literature, the effects of LLLT on the tooth movement were evaluated with both clinical (15-20) and animal studies (14,21-24). Numerous studies on human subjects demonstrated that LLLT stimulated the velocity of tooth movement (15,17-20). At that point, it is emphasized that the effects of laser application on biostimulation depend on the irradiation dose (25). In previous studies, the preferred dose of irradiation was extended from 0.71 J/cm$^2$ to 8 J/cm$^2$ with diode laser and increased the tooth movement in human subjects (15,17-19). Cruz et al. (15) applied low level diode laser gallium-aluminum-arsenide (wavelength of 780 nm, output power of 20 mW, energy dose of 5 J/cm$^2$) for 10 seconds on 0, 3, 7, 14 day intervals of each two month and showed significant higher acceleration of the canine retraction on the irradiated side when compared to the control. Similarly, Youssef et al. (17) evaluated the effect of the different GaAlAs diode laser parameters (809 nm, 100 mW) with the increased dose of irradiation energy (8 J/cm$^2$) with the same time intervals applied by Cruz et al. (15) during the canine retraction. Later, Sousa et al. (18) evaluated the effect of diode laser (780 nm, 20 mW) for 10 seconds with the same dose of energy (5 J/cm$^2$) used by Cruz et al. (15) during three days of each three month during canine retraction. They demonstrated significantly an increased rate of movement (approximately 1.49 mm) in irradiated group when compared to non-irradiated group in accordance with the previous studies (15,17,19).

Contrary to these, Genc et al. (20) applied very low amount of irradiation with a dose of 0.71 J/cm$^2$ using semiconductor GaAlAs diode laser (808 nm, 20 mW) with an application time of 10 seconds on the day 0, and the 3$^{rd}$, 7$^{th}$, 14$^{th}$, 21$^{st}$, and 28$^{th}$ days. They reported that the application of LLLT accelerated the orthodontic tooth movement significantly.

On the other hand, many researchers found that the laser stimulation influenced the tooth movement rate neither positively or negatively. In a study published by Limpanichkul et al. (16), no significant

differences were determined in the rate of orthodontic tooth movement with the application of GaAlAs laser (860 nm, 100 mW) between irradiated and control groups. Nonetheless, these authors suggested that energy density of LLLT at the level of 25 J/cm$^2$ was incompetent for accelerating tooth movement.

From clinical point of view, different laser parameters have been used and controversial results have been reported in previous studies depending on doses of laser energy and irradiation times. Clinical results have been supported by ongoing animal experiments at the same time. Altan et al. (21) studied the effects of LLLT on osteoclastic and osteoblastic cell proliferation-activity and RANKL/osteoprotegerin release during orthodontic tooth movement. In this metrical and histological investigation, they concluded that low-level GaAlAs diode laser (820 nm, 100 mW) with different irradiation doses (54 and 15 joules) accelerated the bone remodeling process by stimulating osteoblastic and osteoclastic cell proliferation and function in rats. However, there were some contradictory findings in this issue. Seifi et al. (22) evaluated the effects of two different types of low level laser wavelength (630 nm continuous and 850 nm pulsed, output powers of 10 and 5 mW, respectively) on rate of tooth movement in rabbits. The results of this study showed the inhibitory effect of LLLT, with other words, the amount of orthodontic tooth movement was decreased. In another study, Marquezan et al. (23) evaluated the influence of different irradiation protocols (daily irradiations and irradiations on the first two days of tooth movement) on the velocity of tooth movement. They used GaAlAs diode laser (830 nm, 100 mW) a with a total energy of 54 J and reported that laser irradiation increased the number of blood vessels but was not able to accelerate the orthodontic tooth movement on rats. In a recent study, Salehi et al. (24) investigated the effect of LLLT on the rate of movement and the amount of relapse during rotational tooth movement in dogs. For this purpose, GaAlAs diode laser (810 nm, 200 mW, 2J/session) was preferred for irradiation after the beginning of force application. However, the total energy dose of laser (2J/session: 32 J/cm$^2$/point) was reported as insufficient to accelerate the rotational tooth movement, although this dose reduced the relapse up to 3 months after force application and laser irradiation.

In summary, some researchers reported that LLLT has an accelerating effect on tooth movement, while others suggested no positive effects. These controversial results may be influenced the applied laser parameters and treatment protocols. For that reason, additional randomized clinical studies to determine the optimal dose or energy density for accelerating the orthodontic tooth movement must be performed.

## Pain Relief by Low Level Laser Therapy

Pain during orthodontic therapy is a common clinical symptom, as well as a reason for patients to discontinue to treatment. To eliminate the patient complaints and have a comfortable orthodontic treatment process, it is necessary to find new methods for pain control. Several different methods such as transcutaneous nerve stimulation (25,26), induction of periodontal ligament by vibration (27), chewing or biting stimulating compression of ligament area and recently, use of analgesics (28) have been developed to control pain. Side effects of the use of analgesics including reduction in amount on tooth movement led the clinicians to find other methods (29). One of these methods is the LLLT, which is claimed as an efficient method to relieve pain in orthodontic therapy.

Mechanisms of pain reduction by the effect of LLLT during orthodontic treatment have been explained by several hypothesis; such as suppression of cyclooxygenase-2 mRNA expression (30,31), an alteration in the transmission (32), induction of stimulating action potentials in peripheral nerves stimulate a reduction in endogenous endorphins (33).

A wide range of laser types (GaAlAs diode, HeNe, $CO_2$ lasers) with different wavelengths and energy doses to reduce pain during orthodontic treatment are described in literature. Researchers have evaluated the different stages of orthodontic treatment with using lasers to have a better understanding of their effect on pain relief; after application of elastomeric separators, after initial arch wire placement, during canine retraction (17,19,34-40). Lim et al. (34) presented that LLLT could not provide immediate pain relief, whereas it was found to be effective in reducing pain about 24 to 48 hours after application of elastic separators with GaAlAs laser (830 nm, 30 mW, 59.7 mW/cm$^2$) irradiation. These data also corroborated

by Bicakci et al. (37) that used LLLT (820 nm, 50 mW, 7.96 J/cm$^2$). As a result of this study, there were significantly increased mean prostaglandin E2 (PGE2) levels in control group, whereas a gradual decrease occurred in laser group. The differences in PGE2 levels at both 1 hour and 24 hours were statistically significant between the groups.

With contradiction to these studies above, Fujiyama et al. (35) found that pain sensation was significantly lower with $CO_2$ laser treatment from immediately through 4 days, but after that, there was no significant difference between the study groups. This result was confirmed by another study (38) in which pain intensity was found significantly lower in the laser treated quadrant than in the placebo treated quadrant. The researchers suggested that LLLT at the parameters (830 nm laser, 100 mW, 5 J/cm$^2$) reduced pain in patients following placement of orthodontic rubber separators.

In a recent meta-analysis (39) that evaluated pain relief with laser irradiation (varies between 635- 910 nm, 6-160 mW, 2- 4 J/cm$^2$ per point) after application of elastomeric separators, they found that LLLT had good analgesic effect at 6 hours, 1 day, 2 days, 3 days after placement of separators. The evaluated six studies in this meta-analysis applied LLLT in several times regarding the study design. While at 2 hours, 4 days, 5 days after the placement, the results tend to support LLLT, but found statistically insignificant (39). Some studies evaluated the effect of lasers in pain relief after application of initial arch wire during fixed orthodontic therapy (36,40). Tortamano et al. (36) found lower mean numeric rating scale scores' in the LLLT group for intensity and duration of pain, as well as for oral pain. However, they concluded that there was not any significant effect of GaAlAs diode laser (830 nm laser, 30 mW, 2,5 J/cm$^2$) neither at start nor in the alteration of pain. On the other hand, Turhani et al. (40) reported that there was a significant difference at 6 and 30 hours after LLLT (670 nm, 75 mW). However, there was no significant difference at 54 hours after application.

Moreover, different studies assessed the efficiency of laser treatment on reduction of pain during canine retraction and it was found that pain was decreased in the irradiated sides (17,19).

## Bone Regeneration in the Midpalatal Suture

Expansion of the midpalatal suture, a common procedure in orthodontic practice produced an increase in the transverse width of the maxillary basal bone (41). In the literature, it is emphasized that the velocity and quality of new bone formation in the midpalatal suture affect post-expansion relapse. Histological studies on animal (42-44) and human subjects (45-48) with maxillary expansion procedures demonstrated that LLLT stimulated the increased fibroblast proliferation and amount of osteoid tissue, faster ossification and increased bone mineral density when compared with non-irradiated group.

Saito and Shimizu (42) investigated the effects of GaAlAs laser (830 nm, 100 mW, 35.3 J/second/cm$^2$) during the expansion of midpalatal sutures using different treatment protocols and found that late irradiation (4–6 days) had no effect on expansion but that radiation within 0–2 days was effective in the 3-day irradiation groups. In another study, Amini et al. (43) evaluated the efficiency of GaAlAs laser (810 nm, 4J/cm$^2$) on rats after expansion of midpalatal suture in three different time intervals (7,14 and 30 days) and reported that the highest extent of bone regeneration was occurred in the first 7 days, the highest efficacy of laser was observed in 3$^{rd}$ and 4$^{th}$ weeks by conforming the late effects of laser. In a recent study, Rosa et al. (44) applied the increased energy density with diode laser irradiation (780 nm, 70 mW, 18 J/cm$^2$) and demonstrated increased hydroxyapatite deposition in the midpalatal suture after rapid maxilla expansion on rats.

In regard to this, the positive effect of LLLT on bone regeneration during maxillary expansion procedures was clarified with the clinical studies. Angeletti et al. (45) evaluated the effects of LLLT in the midpalatal anterior suture after surgically assisted rapid maxillary expansion using GaAlAs laser (830 nm, 100 mW) with the total energy of 25.2 J at an energy density of 420 J/cm$^2$. In this study, LLLT accelerated bone regeneration with an approximately 30% higher mineralization rate in laser group when compared to the control group.

In another clinical study, Cepera et al. (46) applied diode laser (780 nm, 40 mW, 10 J/cm$^2$) to evaluate the effects of LLLT on bone regeneration in patients treated with rapid maxillary expansion. They reported that LLLT provided efficient opening of the midpalatal

suture and influenced the bone regeneration by accelerating the healing process. Similarly, Ferreira et al. (47) used GaAlAs (780 nm, 70 mW) and found that LLLT had a positive influence on bone regeneration of the midpalatal suture by stimulating the repair process.

Although most of the studies demonstrated the efficacy of diode lasers with different parameters and application procedures on bone regeneration, Moawad et al. (48) used Er:YAG laser by applying mucosal-bony perforations along the midpalatal suture every month for three consecutive months. These authors observed significant differences in the laser group after rapid maxillery expansion phase, but no significant differences with retention or total treatment duration.

According to most studies that evaluated the effects of low level laser treatment on the expansion of a midpalatal suture, LLLT stimulated the regeneration process based on the total amount of irradiation, frequency, and duration of application.

## Effects of Low Level Laser Therapy in Distraction Osteogenesis

Over the last few years, distraction osteogenesis (DO) has become an effective treatment method for facial bone reconstruction (49), for the patients with several congenital (hemifacial macrosomia) or acquired dentofacial deformities (oncologic surgery) (50).

The aim of DO is to generate new bone on the treated side where adjacent bone segments are separated by distraction (49). The distraction devices (distractors) necessary to perform osteodistraction are also crucial for stabilization after accomplishing the distraction needed. The rather complicated distraction appliances can become discomfortable and unpleasant for the patients functionally, esthetically and psychologically (51). The use of LLLT seems to have a positive effect on osteoblastic activity, the repair of bone and soft tissues in this way reducing the retention time (51,52).

In the literature, several studies with different designs evaluated the effect of LLLT on animal subjects (51-54). Miloro et al. (51) aimed to determine the effects of LLLT (820 nm, 400 mW) for acceleration of bone regeneration and diminish the length of the consolidation phase of DO. They concluded that LLLT advanced the bone regeneration process during the consolidation phase. Hübler et al. (52) evaluated the effect of LLLT (GaAlAs; 830 nm, 40 mW, 10 J/cm$^2$) in an animal experiment on bone at the distraction site in terms of chemical composition, crystallinity as well as crystalline structure. They found a positive effect on the percentage of newly formed bone on the chemical composition according to the Ca/P ratios, and on the crystallinity and crystalline structure according to the detection of hydroxyapatite phases. Kreisner et al. (53) evaluated the efficacy of LLLT using the same laser parameters on newly formed bone with DO during the consolidation phase and suggested the positive effect of LLLT on the amount of newly formed bone with better quality. This could allow earlier removal of the distractors and resulting in reduction of total treatment time. On the other hand, Mayer et al. (54) evaluated the area of bone neoformation after DO through histological analysis and also with measurement of the amount of neoformed bone after LLLT (830 nm laser, 40 mW, 10 J/cm$^2$) performing the irradiation protocol immediately after activation of the distractor. They found significantly higher amount of neoformed bone in the laser treated group (62.68%) than in the control group (43.09%). Recently, Medeiros et al. (55) evaluated the effects of laser therapy (808 nm laser, 100 mW, 6 J/cm$^2$) and ultrasound on animal subjects after the 2-day latency period. Although the greatest effects were observed with combined ultrasound and laser treatment, bone healing was accelerated with the application of laser irradiation. The studies that evaluated the effects of LLLT in DO had limited information due the several facts including absence of power analysis, different study designs, limited numbers of subjects. In the framework of our knowledge, the reported findings could not be clarified with human subjects. On the other hand, despite of these limited information, most of the studies used the same laser parameters (830 nm, 40 mW) with the same type of laser (GaAlAs) due to its improved tissue penetration profile (52-54).

## Conclusion

Low level laser therapy may be effective especially in orthodontic clinical practice in order to reduce total treatment duration and increase patient comfort during treatment. Although laser systems have higher costs and require intensive safety instructions in

clinical conditions, LLLT will be frequently preferred in future by converting disadvantages into advantages.

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**Ethics**

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**Authorship Contributions**

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Review / Derleme

# Vitamin D Level and Infertility

## *Vitamin D Düzeyi ve İnfertilite*

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**Abstract**

Infertility is one of the major health problems of our time. In fact, infertility is caused by many factors. Among these factors the effect of vitamin D levels of infertility are overlooked. The prevalence of vitamin D deficiency varies between 20% and 66.8% in different countries. In fact, vitamin D deficiency can lead to infertility both women and man. Lack of vitamin D in women with polycystic ovary syndrome in the study, uterine fibroids, as well as has been demonstrated over a relationship with a decrease in reserves. In males it has been suggested to affect sperm count and morphology. At the same time vitamin D levels may play a role in facilitating implantation. Even in studies in vitro fertilization has been shown to increase the success rate with the support of vitamin D. In this article, vitamin D deficiency and infertility issues were revised in light of the current articles.

**Öz**

İnfertilite çağımızın önemli sağlık sorunlarından biridir. Aslında infertiliteye birçok faktör neden olmaktadır. Bu faktörler arasında D vitamini düzeyinin infertiliteye olan etkisi gözden kaçmaktadır. Vitamin D eksikliğinin görülme sıklığı değişik ülkelerde %20 ile %66,8 arasında değişmektedir. Aslında D vitamini eksikliği hem erkeklerde, hem de kadınlarda infertiliteye neden olabilmektedir. Çalışmalarda kadınlarda D vitamini eksikliğinin polikistik over sendromu, uterin miyom yanı sıra over rezervinin azalması ile ilişkisi ortaya konmuştur. Erkeklerde ise sperm sayısını ve morfolojisini etkilediği öne sürülmüştür. Bununla birlikte vitamin D düzeyi implantasyonu kolaylaştırıcı rol oynayabilmektedir. Hatta çalışmalarda in vitro fertilizasyon başarı oranlarının D vitamini desteği ile arttığı gösterilmiştir. Bu yazıda, D vitamini eksikliği ve infertilite konusu güncel makaleler eşliğinde gözden geçirilmiştir.

**Keywords**
Vitamin D, infertility, in vitro fertilization

**Anahtar Kelimeler**
D vitamini, infertilite, in vitro fertilizasyon

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### Introduction

It has been known for centuries that the human body needs many vitamins. Vitamin D is known as a steroid hormone produced mainly by ultraviolet B. Only about 10-20% of this vitamin can be taken by diet. Some genetic and environmental factors can cause this vitamin deficiency. These include high latitude living, traditional outdoor clothing, dark skin color, old age, inadequate vitamin D intake by diet, parenchymal diseases of kidney and liver, genetic defects preventing vitamin D synthesis and function, drugs and sunscreen use (1,2).

### Epidemiology

Vitamin D deficiency first appeared in the 17th century by the German pathologist G. Pommer. The first scientific publication on vitamin D

deficiency was published in 1966 by Ramser et al. (3), who identified in six patient rib biopsies consistent with vitamin D deficiency. Studies conducted after these years have revealed the real effect of vitamin D on bone mineralization (2). Vitamin D deficiency of incidence ranges between 20% to 66.8% in different countries (4-6) has been reported, in a study conducted in Turkey 74.9% (7). Studies showing lack of vitamin D in different countries reported in the literature are shown in Table 1.

## Vitamin D and Systemic Diseases

Recent epidemiological studies suggest that low levels of vitamin D are associated with several diseases such as certain cancers, hypertension, autoimmune and infectious diseases (8,9). It also has been reported that vitamin D protects DNA from oxidative stress through nuclear mechanisms and prevents telomeric shortening (9). A meta-analysis reported a 7% reduction in the risk of five-year mortality with an average intake of 528 IU/day vitamin D (10).

Vitamin D has been shown to prevent hypertension by suppressing the renin gene. Observational studies have shown that low vitamin D levels correlate with blood pressure, coronary artery calcification, and the presence of cardiovascular disease. Research suggests that suboptimal vitamin D levels are associated with an increased risk of cardiovascular disease (9). The recent studies on animal models and humans have shown that vitamin D regulates glucose metabolism, and may play an important role in the development of type 1 and type 2 diabetes mellitus (DM). In particular, it is known that there is a link between infantile vitamin D deficiency and type 1 DM development (11). Breast, colon, prostate cancer cells and leukemic cells also have vitamin D reseptors (VDR). Calcitriol is known to be an inhibitory effect on these cells. Although its mechanism is not fully understood, vitamin D is thought to be involved in cellular regulation, induction of differentiation, impaired growth stimulation, inhibition of angiogenesis and increased apoptosis of malignant cells (12). It is known that the phagocytic activity of macrophages is increased in the presence of vitamin D (13). In addition, VDR activation increases gene expression of cathelicidin, a bacteriocidal protein known to be lethal for tuberculosis and other infective agents (14).

Several studies have shown that vitamin D affects the growth and differentiation of immune system-regulating cells such as macrophages, dendritic cells, T and B lymphocytes. Vitamin D may be used in the treatment of autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, type 1 DM, inflammatory bowel diseases and multiple sclerosis (MS) (15). Studies support that lower levels of vitamin D are associated with greater severity in patients with MS (16). Vitamin D deficiency is associated with depression and decreased cognitive function (17). In short, vitamin D affects many systems and deficiencies cause disorders in these systems. Table 2 shows the effects of D vitamins.

## Vitamin D and Infertility

Vitamin D deficiency can actually cause many gynecological problems. These are mentioned below.

**Vitamin D Deficiency and Polycystic Over Syndrome**

Although many gynecological diseases are associated with vitamin D deficiency, polycystic ovarian syndrome (PCOS) is the most commonly studied and described. This syndrome is known as the most common endocrine disorder in the reproductive ages. The prevalence of the syndrome has been reported to be approximately 6-8%. Infertility can be seen in this syndrome, which is diagnosed by oligo-anovulation, clinical and/or biochemical hyperandrogenism findings and ultrasonographic polycystic ovaries.

It has been suggested that sex hormone-binding globulin decreases with vitamin D deficiency. Thus, androgen levels are increasing and providing the basis for PCOS (18).

**Table 1. Studies on the D vitamin deficiency in different countries**

| | Country | Time | Season | Number | Vitamin D deficiency rate |
|---|---|---|---|---|---|
| Maghbooli et al. (4) | Iran | 2002 | Winter | 552 | 66.8% |
| Weiler et al. (5) | Canada | 2002-2004 | All year | 183/146 | 32%/30.4% |
| Nanri et al. (6) | Japan | 2010-2011 | Summer-winter | 529 | 9.3%-46.7% |
| Hekimsoy et al. (7) | Turkey | 2007 | Winter | 209 | 74.9% |

| Table 2. Effects of vitamin D |
|---|
| Cell differentiation |
| Calcium and phosphorus balance in skeletal system |
| Antiproliferative effect |
| Anti-inflammatory effect |

In a prospective cohort study of 91 patients with PCOS, less follicular development was observed after 50 mg of clomiphene citrate treatment in the group with vitamin D deficiency (19). In another study, it was reported that 60 PCOS-diagnosed infertile patients were divided into 3 groups, metformin in the first group, vitamin D in the second group, and vitamin D and metformin in the last group, resulting in higher number of dominant follicles in the combination therapy group (20).

In a recent study, vitamin D levels were associated with decreased insulin resistance. Patients with PCOS have been reported to have improved insulin resistance, androgen levels, folliculogenesis, and menstrual irregularities with the addition of vitamin D to treatments (21). In Reyman et al.'s (22) study, it was noted that supplementation of vitamin D, a disease with PCOS deficiency of vitamin D, improves menses and follicular developmental abnormalities, thus increasing pregnancy rates.

In other studies, it has been shown that fat patients with PCOS is treated with vitamin D deficiency, resulting in increased weight loss and improved menstrual cycle rhythms. Similarly, adolescent obese persons were observed to be thinner when vitamin D deficiency was eliminated (23,24).

In another study of 127 patients with PCOS but not treated and 117 normal subjects, 25-hydroxy-D [25(OH) D] vitamin levels below 50 nM/mL were defined as vitamin D deficiency and those above 75 nm/mL were normal. In this study, there was no significant difference between the vitamin D levels of the two groups when there was a negative correlation between metabolic syndrome and vitamin D level (25). In a 24-week study of 57 policystic over patients with vitamin D deficiency, the patient was given 20.000 IU of vitamin D per week and reported a 50% improvement in oligomenorrhea and anovulation, as well as a marked decrease in fasting blood glucose (26).

## Vitamin D Level and Over Reserve

Reduced over-reserves is one of the important causes of infertility. Anti-Müllerian hormone (AMH) is accepted as the laboratory test that shows the best over reserve. As is known, AMH reduces oocyte loss rate. There was a positive correlation between serum vitamin D level and serum AMH level. When vitamin D deficiency was eliminated, estradiol (9%), estrone (21%) and progesterone (9%) production from over, in addition the amount of insulin-like growth factor binding protein was increased. It has been shown that there is a positive correlation between levels of serum AMH and vitamin D in women in the premenopausal period (27). Serum AMH levels are 18% lower in the winter months than those in the summer months, but there is no such seasonal fluctuation seen in AMH when vitamin D deficiency is eliminated (28).

All this information with low AMH levels should be considered vitamin D deficiency. However, there are few studies in the literature regarding low AMH and vitamin D deficiency. For this reason, randomized controlled trials are needed for vitamin D replacement therapy.

## Vitamin D Level and Uterine Myom

Vitamin D has a regulatory role in the development of uterine fibroids. Patients with myomas with low levels of vitamin D were observed to have a higher risk of myoma formation and more myomas, they were larger than the control group (29). Another study reported a decrease in the rate of myomas in patients with D-vitamin supplementation. Vitamin D3 has been shown to reduce myoma cell proliferation *in vitro*, and *in vivo* animal models to decrease tumoral myoma growth. These results support that vitamin D3 is effective and safe in the medical treatment of myoma (29,30).

## Vitamin D Level and In Vitro Fertilization

In vitro fertilization (IVF) rates are influenced by many factors in our time, and as days go by, we become aware of the majority of these factors. Some of them look like vitamin D. Patients with serum vitamin D level <30 ng/mL were found to have a low pregnancy rates (31). In a study conducted, the serum and follicular fluid also had a positive correlation with the measurement of 25(OH)D levels and IVF ratios.

However, follicular fluid 25(OH)D levels were recorded inversely proportional to body mass index. As a result, follicular fluid 25(OH)D vitamin levels were predicted to be an independent predictor of IVF success. In study conducted by Ozkan et al. (32), it was observed that with 1 ng/mL vitamin D increase in follicular fluid, 6% increase in live pregnancy was observed.

Contrary to these views, the follicular fluid with high levels of vitamin D is found in studies showing that the number of enucleated oocytes and embryo quality are reduced. One of them has found that the high D vitamin levels have been impaired the developmental properties of the embryo and the IVF success has been adversely affected (33).

In addition to studies showing increased vitamin D and IVF ratios, there are studies suggesting that there is no relationship. Among them, 517 patients were studied by Franasiak et al. (34), and vitamin D was reported to be unrelated to pregnancy outcomes after embryo transfer. As a result, it was emphasized that serum 25OH vitamin level failed to predict the implanted blastocyst.

Vitamin D levels may play a role in facilitating implantation. Calcitriol reduces T cell function. Calcitriol reduces cytokines released from endometrial cells. During the calcitriol treatment, in natural killer cells the secretion rates of cytokines such as colony-stimulating factor 2, interleukin (IL)-1, IL-6 and tumor necrosis factor decreased. For this reason, vitamin D deficiency may play a role in the habitual abortus (31).

## Vitamin D Level and Male Infertility

Low levels of vitamin D may cause infertility in males as well as infertility in females. There was a positive correlation between the number of motile sperm and progressive motile sperm and the serum level of 25(OH)D vitamin. *In vitro* studies have shown that vitamin D increases sperm motility and induces acrosome reaction (35). Contrary to this view, it has been found to correlate with high vitamin D content and sperm count and normal morphological deterioration (36).

Two recent large-scale studies have shown a positive correlation between serum D-vitamin levels and serum testosterone levels (37,38). The enzyme that metabolizes vitamin D is CYP24A1. This enzyme has been found in the human testis, the ejaculatory duct, the mature spermatozoa and the Leydig cells (39). In a study of 77 infertile men and 50 healthy men, CYP24A1 expression was measured and there was a significant decrease in CYP24A1 expression in infertile men (40). As a result, it has been shown that changes in vitamin D levels affect infertility through several mechanisms. For this reason, it is also necessary to consider examining the level of vitamin D when following a routine infertility patient.

**Ethics**

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Original Article / Özgün Araştırma

# The Morphological Changes in the Mandible Bone: The Effects of Age, Gender and Dental Status

## *Mandibular Morfolojik Değişiklikler: Yaş, Cinsiyet ve Diş Durumunun Etkileri*

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**Keywords**
Gonial angle, antegonial angle and depht, ramus height and width, dentate, age

**Anahtar Kelimeler**
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### Abstract

**Objective:** This present study aimed to analzye the impact of age, gender and dental condition on remodeling of gonial and antegonial, condylar and ramus regions. We evaluated the changes in the antegonial angle (AGA), gonial angle (GA), antegonial depht (AGD), condylar height (CH), ramus width (RW) and ramus height (RH) in different age and dental groups on both genders.

**Materials and Methods:** Approximately nine hundred and ten panoramic radiographs that were gathered were arranged into groups of age, dental status and gender. An evaluation of the GA, AGA, AGD, CH, RW, and RH was made.

**Results:** There were no differences for CH in regard to gender, dental status and age groups on both sides ($p>0.05$). Age influenced RW in females and on AGD in males ($p<0.05$). Dental status influenced RW and AGA in females and on GA and RW in males ($p<0.05$). Gender also effected the GA, RH, AGA and AGD ($p<0.05$).

**Conclusion:** The results of this study demonstrated that age, gender, and dental status influenced the remodeling of the gonial, antegonial, and ramus regions. This remodeling influenced specific regions in the mandible. A conclusion can be made to say that the differences that are related to gender, age and dental status can be linked with the variance in the masticatory activity throughout this region of the mandible. Since age, gender and dental status do not affect the CH, the significant changes in the length of CH can be considered to be signs of an abnormal situation.

### Öz

**Amaç:** Bu çalışmanın amacı yaş, cinsiyet ve diş durumunun gonial ve antegonial, kondil ve ramus bölgelerine etkilerini araştırmaktır. Her iki cinsiyette farklı yaş ve diş gruplarında gonial açı (GA), antegonial açı (AGA), antegonial derinlik (AGD), kondil yüksekliği (KY), ramus yüksekliği (RY) ve ramus genişliği (RG) değişikliklerini değerlendirdik.

**Gereç ve Yöntemler:** Dokuz yüz on panoramik radyografi elde edildi ve bunlar yaş, diş durumu ve cinsiyete göre gruplandırıldı. GA, AGA, AGD, KY, RY ve RG analiz edildi.

**Bulgular:** KY, her iki tarafta cinsiyet, yaş grupları ve diş durumuna göre fark göstermemekteydi ($p>0,05$). Yaşın kadınlarda RG, erkeklerde ise AGD üzerine etkili olduğu bulundu ($p<0,05$). Diş durumu kadınlarda AGA ve RG'yi etkilerken, erkeklerde GA ve RG üzerine etkili olduğu saptanmıştır ($p<0,05$). Ayrıca cinsiyetin GA, RY, AGA ve AGD'yi etkilediği tespit edildi ($p<0,05$).

**Sonuç:** Bu çalışmanın sonuçları, gonial ve antegonial ve ramus bölgelerinin yaş, cinsiyet ve diş durumundan etkilendiğini (remodeling) göstermektedir. Bu

remodeling, mandibuladaki spesifik bölgeleri etkilemektedir. Yaş, cinsiyet ve diş durumu ile ilişkili farklılıkların çene kemiğinin bu bölgesindeki çiğneme aktivitesindeki varyansla ilişkili olduğu sonucuna varılabilir. Yaş, cinsiyet ve diş durumu KY üzerinde bir etkisi olmadığından, KY uzunluğundaki önemli değişiklikler bazı anormal durumların bulguları olarak düşünülebilir.

## Introduction

Bone remodeling is an endless and a combination of complicated procedures which happen throughout our life (1). Mandibular stimuli which exist throughout the development phase to adulthood can alter the growth of the mandible and also effect its bone remodeling. Some of the evident changes that have been suggested are the change in the antegonial, gonial, condylar, ramus regions (2-5).

Long-term studies have shown that remodeling of the mandibular bone happens in relation to age (6,7). Casey and Emrich reported that (8), the average mandibular angle stayed the same throughout the time of adulthood to until at least the 7$^{th}$ decade of life with the exception of considerable tooth loss. They stated that gender had no effect on gonial angle (GA). Ohm and Silness (3) implied that differences in gender did not have much importance and age was not connected to the size of the GA. Futhermore, Dutra et al. (9) stated that age, gender and dental condition did not alter GA.

The cause of this remodeling is thought to be related to the absence and the presence of the teeth. The general organization of the remodeling fields in adolescents with a growing mandible has noticeable differences from edentate mandibles (10). In a report by Enlow et al. (1), it was stated that specific responses of remodeling happen due to tooth loss and alterations of the structural and functional relationships of the whole adult mandible takes place. These changes include modified mandibular rotation and occlusal relationships, remodeling and transformation of the mandibular body, changes in the muscle-bone alignment and alteration and reduction in the areas for muscle connection. Huumonen et al. (11) proposed that, morphological changes of the mandible in adults are associated with the person's occlusal relationship and age. Xie et al. (12) approved that long-term edentulousness and the probability of reduced masticatory forces may be associated with the changes to the angle of the mandible. Ghosh et al. (5) reflected that this is possible because the activities of masticator muscles are associated to the dimensions of the facial skeleton. The bone remodeling in these regions, however, have received little attention and the interaction of gender, age and dental status have not been subjected to detailed analysis.

This present study aims to investigate the influence of age, gender and dental status on remodeling of antegonial and gonial, condylar and ramus regions. We evaluated the changes in the GA, antegonial depth (AGD) and antegonial angle (AGA), ramus height (RH), ramus width (RW) and condylar height (CH) in different age and dental groups of both genders.

## Materials and Methods

Nine hundred and ten panoramic radiographs which were taken from patients over the age of 18 years who applied for routine dental examination to the oral and maxillofacial radiology department of dentistry faculty were analyzed between the years of 2012 and 2013 (Table 1). The Ethics Committee of Selçuk University Faculty of Dentistry approved the research protocol (decision no: 2012/33). The

**Table 1. The distribution of sample is presented as number (n) and percentage (%) by gender, age group and dental status**

| Characteristics | n | % |
|---|---|---|
| **Gender** | | |
| Male | 445 | 48.9 |
| Female | 465 | 51.1 |
| **Age (years)** | | |
| 18-40 | 154 | 16.9 |
| 41-55 | 104 | 11.4 |
| 56-69 | 449 | 49.3 |
| 70 and above | 203 | 22.3 |
| **Dental status** | | |
| 18-40 years old dentate | 150 | 16.5 |
| Above 40 years old dentate | 154 | 16.9 |
| Above 40 years old partially dentate | 150 | 16.5 |
| Above 40 years old maxillary edentulous | 150 | 16.5 |
| Above 40 years old mandibular edentulous | 156 | 17.1 |
| Above 40 years old totally edentulous | 150 | 16.5 |

same panoramic machine was used to gather all the panoramic images (Kodak® 8000 Rochester, New York, USA) by the same technician according to the manufacturer's reference guide.

Only the radiographs that were clear with a higher quality and with no signs of distortion were chosen. Criteria for the selection of the radiographs were based on the tympanic plate, mental foramen, condyle, the lower and the posterior border of the mandible to be precise and explicit on the radiograph to be able to evaluate the structures on both sides. This study excluded the panoramic radiographs that belonged to patients who had orthognathic surgery, fractures and facial asymmetry. Only a single experienced radiologist observed all the panoramic radiographic for the evaluation that was performed on the two sides of the mandible. Adobe Photoshop CS4 was used after the adjustment of a 27% magnification for an improved simulation of the clinical condition. The ruler tool of Adobe Photoshop CS4 was used to measure the SP.

Evaluations of the measurements were made at two different times by a single observer that was professionally experienced for a period of 3 years in the department of oral and maxillofacial radiology. To determine the intra-observer dependability, a random selection of 50 samples was made for the measurements which were repeated at an interval of one month.

The GA was evaluated by using a line that followed alongside the lower border of the mandible and a similar line which was alongside the distal border of the ramus on both sides. These lines intersected to form the mandibular angle (Figure 1) (13). Two lines which were parallel to the lower cortical border of the mandible bone were traced and the angle that they intersected at the deepest point throughout the antegonial notch was used to measure the AGA (Figure 1) (9). AGD was measured as the distance along a perpendicular line from the deepest point of antegonial notch concavity to a line which was parallel to the inferior cortical border of the mandible (Figure 2) (9).

A tracing line was drawn on the outer borders of the condyles and the ascending rami on the two sides of the mandible. The most lateral points of the condylar image and the ascending ramus were connected with a line that was traced between them. A line that was perpendicular to this line which is also known as the ramus tangent was traced from the most superior points of the condylar image. The vertical distance between the line on the ramus tangent and the most lateral point of the condyle that was projected on the ramus tangent was measured. This distance was referred to as CH (Figure 2) (14). The distance that was primarily marked between the most lateral points on the image was referred to as RH and was measured (Figure 2) (14).

The RW was measured as the distance between the posterior and anterior borders of the ramus on the line that was perpendicular to the ramus tangent which passes through the points that corresponds to the middle of the inferior border of the mandibular foramen (Figure 2) (15).

The following criteria were used for assessing dental status (third molars were excluded):

(1) 18-40 years old dentate,

(2) Above 40 years old dentate,

(3) Above 40 years old partially dentate (maximum 15 teeth),

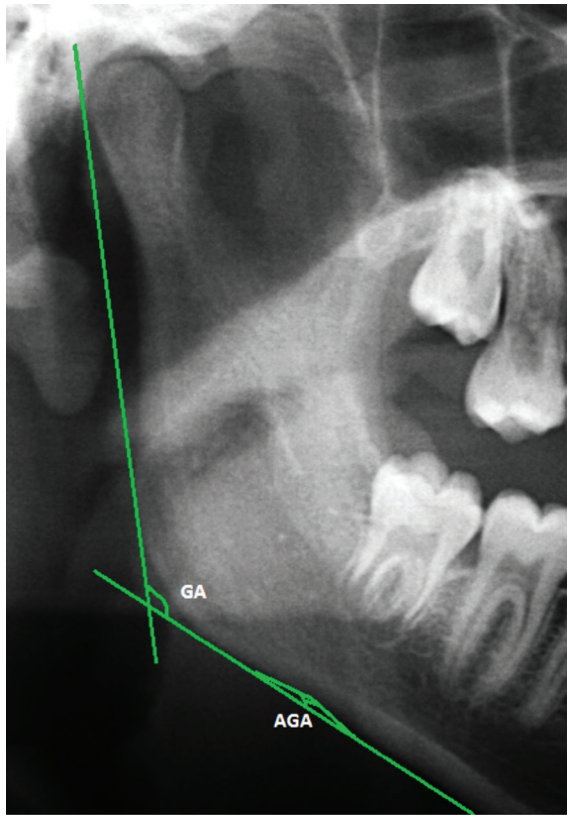


**Figure 1.** The presentation of anguler measurements
GA: Gonial angle, AGA: Antegonial angle

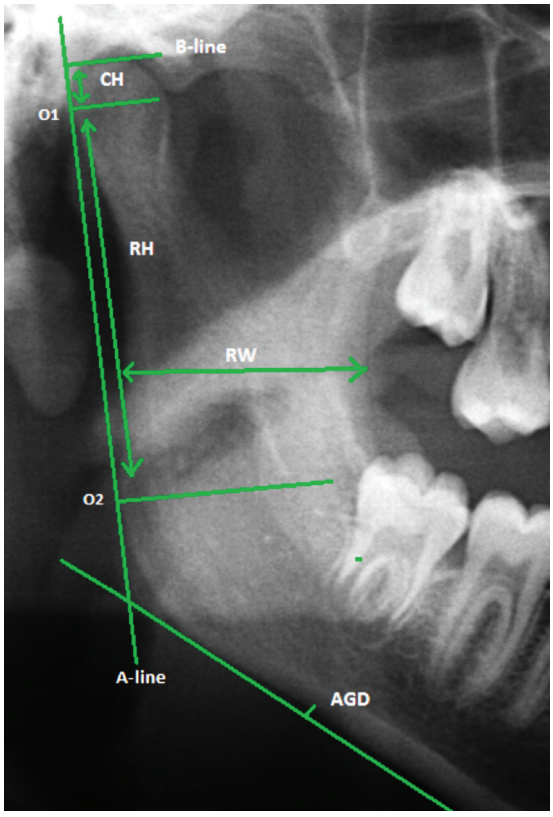


**Figure 2.** The presentation of linear measurements
RH: Ramus height, RW: Ramus width, AGD: Antegonial depth
CH: Condylar height

(4) Above 40 years old maxillary edentulous,
(5) Above 40 years old mandibular edentulous,
(6) Above 40 years old totally edentulous.

The age was based on four age groups as following: 18-40 years, 41-55 years, 56-69 years and 70 and above years of age.

**Statistical Analysis**

Software packages SPSS 21.0 was used for the statistical analysis of the data. Descriptive statistics for each variable were calculated. The intraclass correlation coefficient (ICC) was calculated for GA, AGA, AGD, CH, RH, RW. The Kolmogorov-Smirnov test, Wilcoxon test, Mann-Whitney U test, Kruskal Wallis, and chi-square test was used. The significant level was set at 5%.

## Results

The present study consisted of all the available observations which were readable. The calculations of the distances were performed on both sides. For right and left ICC values were 0.879, 0.828, 0.891, 0.925, 0.935, 0.943, 0.962, 0.914, 0.882, 0.897, 0.927 and 0.916 (nearly perfect) for GA, AGA, AGD, CH, RH and RW, respectively.

The mean values of right and left measurements of lengths and angles are presented in Table 2 for both

**Table 2. Mean measurement values in milimeters and angle by gender, quadrant and lineer (antegonial depth, condylar height, ramus height, ramus width) and anguler (gonial angle and antegonial angle) measurements. Standard error values for each measure are also included**

| | Female | | Male | | Total | |
|---|---|---|---|---|---|---|
| | Mean | SE | Mean | SE | Mean | SE |
| Right GA | 122.39 | 6.34 | 119.58 | 6.90 | 121.02 | 6.77 |
| Left GA | 123.14 | 6.32 | 120.86 | 7.47 | 122.03 | 6.99 |
| Right AGA | 168.25 | 9.38 | 160.52 | 12.62 | 164.47 | 11.73 |
| Left AGA | 167.85 | 9.97 | 161.36 | 12.14 | 164.68 | 11.54 |
| Right AGD | 1.02 | 0.79 | 1.67 | 1.05 | 1.34 | 0.98 |
| Left AGD | 1.08 | 0.87 | 1.71 | 1.18 | 1.39 | 1.08 |
| Right CH | 8.17 | 1.79 | 7.88 | 1.80 | 8.03 | 1.80 |
| Left CH | 7.92 | 1.86 | 8.06 | 2.09 | 7.99 | 1.98 |
| Right RH | 46.91 | 6.36 | 51.99 | 7.16 | 49.39 | 7.22 |
| Left RH | 47.07 | 6.24 | 51.50 | 6.93 | 49.23 | 6.95 |
| Right RW | 31.84 | 4.84 | 32.34 | 4.97 | 32.08 | 4.91 |
| Left RW | 33.30 | 4.99 | 33.87 | 5.38 | 33.58 | 5.19 |

GA: Gonial angle, AGA: Antegonial angle, AGD: Antegonial depth, CH: Condylar height, RH: Ramus height, RW: Ramus width, SE: Standard error

genders. There was a statistical variation between left and right sides ($p<0.05$) in the values of RW and GA calculations. The measurements of right side were significantly lower than left side's.

The mean and standard error values corresponding to gender, age groups and dental status were presented in Tables 2, 3, 4.

For bilateral GA, there weren't any statistical differences found in age groups. But, above 40 years dentate males had significantly smaller GA on both sides than the other dental groups ($p<0.01$). Also, females had significantly wider GA on both sides than males ($p<0.05$) (Table 5).

No significant difference was found for AGA in regard to age groups in both sexes ($p>0.05$). But females had significantly greater AGA than males ($p<0.05$). Also, above 40 years totally edentulous females had smaller AGA than the other dental groups ($p<0.05$) (Table 5).

For AGD, there were no significant differences in regard to dental status on both sides in both sexes ($p>0.05$). Significant differences were observed between females and males ($p<0.05$). Males had significantly greater AGD than females ($p<0.05$). Also, males in 41-55 age group had significantly higher AGD than the other age groups ($p<0.05$) (Table 5).

For bilateral CH, no significant differences were found as to gender, age groups and dental status on both sides ($p>0.05$) (Table 5).

For bilateral RH, both sexes did not have any differences to age groups and dental status on both sides ($p>0.05$). Yet, the measurements of males had significantly larger RH than females's ($p<0.05$) (Table 5).

There was not any significant difference in regard to gender for RW on both sides ($p>0.05$). Females in the 41-55 age group had smaller RW than the other age groups ($p<0.05$) (Table 5). The more prominent decline was seen for RW due to the decreased number of teeth in females. Totally edentulous males that were above 40 years of age had significantly smaller RW than the other dental groups.

## Discussion

There were not any radiographic and medical criteria for the selection of the study group of patients. Also, patients were not chosen from any specific dental specialty. All of the calculations were made on panoramic radiographs which were obtained during the patient's routine dental examination. To guarantee consistency and reliability, evaluation of each image was managed by a single dentomaxillofacial

**Table 3. Mean measurement values in milimeters and angle by age group, quadrant and lineer (antegonial depth, condylar height, ramus height, ramus width) and anguler (gonial angle and antegonial angle) measurements. Standard error values for each measure are also included**

| | 18-40 | | 41-55 | | 56-69 | | Above and 70 | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| Right GA | 120.53 | 6.96 | 121.71 | 8.08 | 121.32 | 6.29 | 121.32 | 6.29 |
| Left GA | 121.24 | 7.04 | 122.54 | 8.4 | 122.3 | 6.7 | 122.3 | 6.7 |
| Right AGA | 166.38 | 11.47 | 162.31 | 12.09 | 164.28 | 11.53 | 164.28 | 11.53 |
| Left AGA | 165.96 | 11.11 | 161.97 | 12.07 | 165 | 11.28 | 165 | 11.28 |
| Right AGD | 1.34 | 1.02 | 1.5 | 1.05 | 1.33 | 0.97 | 1.33 | 0.97 |
| Left AGD | 1.4 | 1.06 | 1.72 | 1.21 | 1.33 | 1.02 | 1.33 | 1.02 |
| Right CH | 8.16 | 1.81 | 7.81 | 1.96 | 8 | 1.64 | 8 | 1.64 |
| Left CH | 7.98 | 1.77 | 7.78 | 1.86 | 8.09 | 2.02 | 8.09 | 2.02 |
| Right RH | 50.52 | 7.48 | 48.48 | 7.48 | 49.03 | 6.62 | 49.03 | 6.62 |
| Left RH | 50.52 | 7.16 | 48.34 | 7.32 | 48.96 | 6.71 | 48.96 | 6.71 |
| Right RW | 33.71 | 5.25 | 30.82 | 5.29 | 31.7 | 4.35 | 31.7 | 4.35 |
| Left RW | 35.05 | 5.36 | 32.62 | 5.9 | 33.3 | 4.76 | 33.3 | 4.76 |

GA: Gonial angle, AGA: Antegonial angle, AGD: Antegonial depth, CH: Condylar height, RH: Ramus height, RW: Ramus width, SE: Standard error

**Table 4. Mean measurement values in milimeters and angle by dental status, quadrant and lineer (antegonial depth, condylar height, ramus height, ramus width) and anguler (gonial angle and antegonial angle) measurements. Standard error values for each measure are also included**

| | 18-40 Aged dentate | | | | Above 40 years old dentate | | | |
|---|---|---|---|---|---|---|---|---|
| | Female | | Male | | Female | | Male | |
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| Right GA | 121.36 | 6.38 | 119.46 | 7.33 | 121.43 | 5.64 | 116.43 | 6.22 |
| Left GA | 122.06 | 6 | 120.09 | 7.71 | 122.56 | 6.12 | 118.11 | 6.78 |
| Right AGA | 171.05 | 8.55 | 161.84 | 12.22 | 169.87 | 9.7 | 159.42 | 13.11 |
| Left AGA | 171.05 | 9.1 | 162.56 | 11.91 | 167.37 | 11.27 | 159.98 | 12.78 |
| Right AGD | 0.92 | 0.83 | 1.73 | 1.03 | 0.98 | 0.95 | 1.8 | 1.09 |
| Left AGD | 1 | 0.83 | 1.78 | 1.12 | 1.02 | 0.88 | 1.76 | 1.19 |
| Right CH | 8.49 | 1.91 | 7.83 | 1.67 | 8.21 | 1.87 | 7.87 | 1.61 |
| Left CH | 8.24 | 1.83 | 7.73 | 1.72 | 7.73 | 1.75 | 7.98 | 1.78 |
| Right RH | 48.27 | 7.78 | 52.78 | 6.51 | 47.25 | 6.12 | 52.19 | 6.77 |
| Left RH | 48.56 | 7.29 | 52.6 | 6.46 | 46.93 | 6.16 | 51.26 | 6.82 |
| Right RW | 33.98 | 5.34 | 33.64 | 5.16 | 33.02 | 4.63 | 33.45 | 4.82 |
| Left RW | 35.12 | 5.09 | 35.2 | 5.53 | 34.15 | 5.04 | 34.23 | 4.73 |
| | Above 40 years old partial dentate | | | | Above 40 years old inferior edentulous | | | |
| | Female | | Male | | Female | | Male | |
| | Mean | SE | Mean | SE | Mean | SE | Mean | SE |
| Right GA | 124.06 | 7.6 | 120.42 | 6.87 | 124.06 | 7.6 | 119.87 | 7.33 |
| Left GA | 124.86 | 6.77 | 122.73 | 7.78 | 124.86 | 6.77 | 119.98 | 8.75 |
| Right AGA | 169.98 | 8.05 | 160.53 | 11.92 | 169.98 | 8.05 | 159.59 | 12.33 |
| Left AGA | 167.56 | 9.56 | 160.74 | 9.73 | 167.56 | 9.56 | 160.68 | 14.54 |
| Right AGD | 2.87 | 0.75 | 1.75 | 0.94 | 0.99 | 0.75 | 1.65 | 1.05 |
| Left AGD | 1.25 | 0.88 | 2 | 1.19 | 1.25 | 0.88 | 1.58 | 1.28 |
| Right CH | 7.98 | 1.74 | 8.04 | 1.81 | 7.98 | 1.74 | 7.72 | 1.83 |
| Left CH | 8.47 | 1.65 | 7.76 | 1.73 | 7.68 | 1.65 | 7.73 | 2.14 |
| Right RH | 46.35 | 6.56 | 53.6 | 8.89 | 46.35 | 6.56 | 51.33 | 6.63 |
| Left RH | 46.23 | 6.32 | 52.65 | 8.34 | 46.23 | 6.32 | 50.3 | 6.7 |
| Right RW | 31.37 | 4.8 | 33.23 | 5.39 | 31.37 | 4.8 | 31.56 | 4.61 |
| Left RW | 33.1 | 5.29 | 34.9 | 5.79 | 33.1 | 5.29 | 32.76 | 5.31 |
| | Above 40 years old superior edentulous | | | | Above 40 years old totally edentulous | | | |
| | Female | | Male | | Female | | Male | |
| | Mean | SE | Mean | SD | Mean | SE | Mean | SE |
| Right GA | 122.61 | 5.64 | 121.29 | 6.57 | 122.11 | 5.75 | 120.25 | 6.13 |
| Left GA | 123.49 | 5.57 | 122.64 | 6.51 | 123.39 | 6.61 | 121.88 | 6.1 |
| Right AGA | 167.39 | 9.38 | 165.15 | 10.87 | 163.56 | 8.27 | 156.73 | 13.76 |
| Left AGA | 169.1 | 9.77 | 161.96 | 12.99 | 165.01 | 8.65 | 162.15 | 10.37 |

radiologist for the distinction of the radiographs that were of the highest quality. The ICC values were nearly flawless. This indicated that the method of indexes for evaluation is very dependable.

In some studies, the magnification values for the panoramic machines were roughly 15-30% (16-21). In the present study, all calculated values were scaled down to the original size of the mandibular features, which was a magnification of 27% used by the panoramic machine according to the manufacturer. This compensation gave the possibility of comparison with other studies because every panoramic machine has unique magnification factors. Regardless, this context has indicated that a common global magnification factor cannot reflect the complex magnification and distortion principle in panoramic radiographs that are theoretically well-understood. But even so, the use of indexes compensates considerably for the unknown local magnification in the image.

In the literature, morphometric evaluations were performed with panoramic radiographs by most authors who have researched mandibular remodeling (3-5,9,11,22-25). In the present study, it was used to obtain these measurements, too.

In this study, the analysis made on the left and right RW and GA measurements showed statistical variations. These variations may be due to the shape of the mandibular base, specifically the gonial region, which have correlations with the function and shape of the muscles of mastications (26). Furthermore, this difference may be the result of an increased function based on a favored chewing side. The effect of the

**Table 4. Continued**

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Right AGD | 1.04 | 0.7 | 1.3 | 1.01 | 1.2 | 0.62 | 1.72 | 1.07 |
| Left AGD | 0.94 | 0.83 | 1.56 | 1.32 | 1.28 | 0.8 | 1.55 | 0.94 |
| Right CH | 8.06 | 1.53 | 7.86 | 1.95 | 8.35 | 2 | 7.95 | 1.91 |
| Left CH | 8.25 | 2.06 | 8.48 | 2.58 | 8.18 | 1.99 | 8.67 | 2.31 |
| Right RH | 47.85 | 6.07 | 51.5 | 7.3 | 45.58 | 5.93 | 50.52 | 6.49 |
| Left RH | 47.49 | 5.93 | 51.22 | 7.04 | 46.41 | 6.62 | 50.91 | 6.03 |
| Right RW | 31.33 | 3.54 | 31.58 | 4.77 | 31.11 | 5.77 | 30.45 | 4.23 |
| Left RW | 33.07 | 3.93 | 33.86 | 5.08 | 32.03 | 5.57 | 32.18 | 5.3 |

GA: Gonial angle, AGA: Antegonial angle, AGD: Antegonial depth, CH: Condylar height, RH: Ramus height, RW: Ramus width, SE: Standard error

**Table 5. The differences between age groups, gender and dental status**

| | Aged group | | Dental status | | Gender |
|---|---|---|---|---|---|
| | Female | Male | Female | Male | |
| Right GA | 0.13 | 0.804 | 0.34 | 0.001* | 0.000* |
| Left GA | 0.296 | 0.306 | 0.155 | 0.000* | 0.000* |
| Right CH | 0.171 | 0.747 | 0.588 | 0.787 | 0.562 |
| Left CH | 0.235 | 0.247 | 0.062 | 0.071 | 0.443 |
| Right RH | 0.619 | 0.618 | 0.056 | 0.176 | 0.000* |
| Left RH | 0.24 | 0.146 | 0.449 | 0.258 | 0.000* |
| Right RW | 0.000* | 0.092 | 0.000* | 0.000* | 0.063 |
| Left RW | 0,001* | 0.056 | 0.001* | 0.008* | 0.091 |
| Right AGA | 0.063 | 0.095 | 0.000* | 0.068 | 0.000* |
| Left AGA | 0.232 | 0.145 | 0.029* | 0.742 | 0.000* |
| Right AGD | 0.435 | 0.014* | 0.15 | 0.067 | 0.000* |
| Left AGD | 0.323 | 0.010* | 0.052 | 0.073 | 0.000* |

*p<0.05, GA: Gonial angle, AGA: Antegonial angle, AGD: Antegonial depth, CH: Condylar height, RH: Ramus height, RW: Ramus width, SE: Standard error

unilateral chewing on RW and GA measurements should be analyzed in the studies which other related parameters are fixed (27).

In correlation with the results of other studies (4,9,23), bilateral GA did not differ according to age groups in our study. Two papers were not in consistent with our results (3,28). The difference may result from using different radiographic method in their study (cephalometric radiography). Because the main disadvantage of lateral cephalometric radiography is the superimposition of images to the contralateral side (29).

In the present study, the influence of gender was statistically significant on the GA value on both sides and this observation showed similarity to the other reports (8,11,22,30), but there were also studies defending otherwise (3,4,9,31). These differences could be due to the unequal distribution of genders in sample of their studies. Females had wider GA than males in our study. The presence of strong activity of masticatory muscle would give rise to a small GA (24). According to the previous suggestion, females may have wider GA than male because the masticatory activity of females is lower.

It was reported in prior publications that results showed variation in regard to GA and dental status. It was concluded that GA was not affected by dental status (6,8,9,31-33), but it was also reported that GA also decreased and the GA increased and decreased with the tooth loss (3,7,7,11,22,28,34,35). In the present study, only in males, it was observed that the GA is shown changes according to the dental status on both sides. Above 40 years dentate males had significantly smaller GA on both sides than the other dental groups in males. In this dentate age group, the effect of bruxism should be investigated in males.

Dutra et al. (9) and Ghosh et al. (5) did not indicate any significant variations between age groups in measurements of AGA and AGD. They showed that the AGA in females was significantly larger than in males and that the AGD in females was significantly smaller than in males. They also indicated that edentulous patients had a smaller AGA than dentate and partially dentate patients. Tozoğlu and Cakur (31) found that there was a significant difference comparing the AGA with regards to dental status. Furthermore, they did not find any differences between dental groups for the AGD.

In this study, there wasn't any significant difference found among age groups in measurements of AGA on both sides of both genders. In males, 41-55 age-group had significantly greater AGD than the other age groups. This finding is contrast to some reports (5,9). In the study of Dutra et al. (9), the distribution of gender was not homogenous and above 40 years old individuals were not included. The age range of sample of Ghosh et al. (5) was also different from our sample. The present study showed that males had lower values of AGA as compared to females. With regards to AGD, males had larger values as compared to females. Our findings were similar to those obtained in different studies by other investigators (5,9,25,31). In this study, a statistically significant decline in the AGA value with a decreasing number of teeth in only females was observed. There were not any significant differences regarding AGD value in both sexes related to dental status. There are different findings about the effect of teeth number on AGA and AGD (5,9,31). However, the reliable comparison of the previous results between the findings of this study can't be possible due to many important differences such as grouping of dental status, radiographic method used and sample size. Differences related to gender, age and dental status can be considered to be due to masticatory activity and biting force for GA, AGA and AGD. Also, bruxism should be investigated as an effective clinical factor by new studies. It was kept in mind that the prevalence of bruxism was higher in women (36).

Prior publications have indicated varying results with respect to the relationship between age, gender, dental status and CH (4,11,22,33). In our study, age, gender, and dental status did not have any statistically significant impact on the CH on neither of the sides. These findings are different from the results of Huumonen et al. (11). The discrepancy may be due to differences in their sample age range (between 60 and 78 years). According to results of present study, CH can be accepted as relatively autonomous structure from gender, age and dental status.

Furthermore, in this study, no significant differences in RH were observed in regard to age and dental status on both sides. But, gender had a statistically significant impact on the RH on both sides. This outcome was consistent with the literature (4,11,22,33,37). However, this finding differed from

the outcome of Huumonen et al. (11) and Okşayan et al. (33) studies for dental status. This could be due to differences of age range and dental grouping.

There is a single article in the literature which evaluated the RW (15). They indicated that gender had statistically significant impact on the RW on both sides. In this study, significant differences were observed regarding RW according to age (only females) and dental status (both gender) on both sides. But, gender did not have any statistically significant impacts on the RW on neither of the sides. The difference may be the cause of the differences in sample size. According to the results of this study, RW shows a decline due to the decrease in the number of teeth in females and total loss of teeth in males. This difference between genders also may be due to the fact that women inherently have a lower bone density than men (38).

Since the methods that were used in this study were identical to many studies, the conclusions were also similar. To present significant results, a lot of images were included and evaluated in this study with the use of the proper exclusion criteria. Furthermore, various indexes of the change in the mandible's morphology were used with the purpose of determining changes in regard to age, gender, and dental status (tooth loss).

## Conclusion

As a result of this study, it has been indicated that gender, age, and dental status are factors that are connected to the remodeling that happens in the gonial, antegonial and ramus regions. Particular regions in the mandible may be affected by this remodeling. The analysis showed noticeable differences for people that were aged 40 or above. Aside from age, tooth loss which is more considerable for this age group may also be an effective additional factor. Furthermore, hormonal factors may be effective in this age group. CH is not affected by gender, age and dental status. Signs of situations that are abnormal can be considerably connected to the significant changes of CH. In conclusion, it can be said that the differences associated with gender, age and dental status can be connected to the variance in the masticatory activity in this region of the mandible. Future studies which were evaluated by different clinical parameters such as the duration of use and type of prosthesis, occlusion type, and habit of chewing, bruxism may give obvious information about the changes of mandibular bone. Radiographic findings should be supported by electromyographic results in future studies to clarify the relationship between masticatory activity and mandibular remodeling in this region. To determine the specific role of age and dental status in remodeling process of mandible, longitudinal studies can also be necessary for both genders separately.

### Ethics

**Ethics Committee Approval:** The Ethics Committee of Selçuk University Faculty of Dentistry approved the research protocol (decision no: 2012/33).

**Informed Consent:** For this type of study, formal consent is not required.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: G.M., Concept: G.M., S.Ö.Ş., Design: G.M., S.Ö.Ş., Data Collection or Processing: G.M., Analysis or Interpretation: G.M., S.Ö.Ş., Literature Search: G.M., S.Ö.Ş., Writing: G.M., S.Ö.Ş.

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Original Article / Özgün Araştırma

# Distribution of Some Risk Factors Related to Soft Tissue Injuries in Dentoalveolar Traumas

## *Dento Alveolar Travmalarda Görülen Yumuşak Doku Yaralanmalarıyla Bağlantılı Risk Faktörlerinin Dağılımı*

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### Abstract

**Objective:** Treatment failures in soft tissue injuries may result in economic, psychological, and esthetic problems. The aim of this study was to investigate the presentation of soft tissue injuries in dento-alveolar traumas.

**Material and Methods:** The data were obtained from 268 children aged 1-15 years who were referred to a pedodontics clinic within one week of experiencing dental trauma during 2010-2015. The criteria used to categorize the data obtained from the dental trauma records were gender, age, localization (lips, gingiva, cheeks, tongue, and perioral tissues), wound type (abrasion, laceration, contusion, and mixed), time elapsed to treatment of the injury, and classification of the dento-alveolar trauma.

**Results:** Soft tissue trauma was noted in 90 (33.6%) children. There was no statistically significant difference between the patients according to gender, age, and the time elapsed between the injury and treatment. With regard to the type of soft tissue trauma, 18.9% were contusions, 7.8% were abrasions, 43.3% were lacerations, and 30% were mixed injuries. Soft tissue injuries were frequently (64.4%) accompanied by periodontal injuries.

**Conclusion:** Soft tissue injuries are occasionally seen in dento-alveolar traumas. Within the limits of this study, the type, localization, and classification of the trauma were more important factors than gender in soft tissue injuries.

**Keywords**
Tooth injuries, soft tissue injuries, child

### Öz

**Amaç:** Yumuşak dolu yaralanmalarında görülen tedavi başarısızlıkları ekonomik, psikolojik ve estetik problemlerle sonuçlanabilmektedir. Biz bu çalışmayla diş-alveol travmalarında görülen yumuşak doku yaralanmalarını incelemeyi amaçladık.

**Gereç ve Yöntemler:** Veriler 2010-2015 yılları arasında diş travmasından dolayı 1 hafta içerisinde pedodonti kliniğine başvuran 1-15 yaş arasındaki 268 çocuk hastadan elde edildi. Diş travmasından elde edilen veriler cinsiyet, yaş, lokalizasyon (dudak, diş eti, yanak, dil ve periodontal dokular), yaralanma tipi (abrazyon, laserasyon, kontüzyon ve karışık), yaralanma ve tedavi arasında geçen zaman ve diş travma sınıflaması kriterleri kullanılarak kategorize edildi.

**Bulgular:** Tüm hastalardan 90 (%33,6) hastada yumuşak doku yaralanması görüldü. Hastalarda yaş, cinsiyet, yaralanma ve tedavi arasında geçen zaman açısından istatistiksel olarak bir farklılık gözlenmedi. Yumuşak yaralanma tipine bakıldığında

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Diş yaralanmaları, yumuşak doku yaralanmaları, çocuk

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kontüzyon %18,9, abrazyon %7,8, laserasyon %43,3 ve karışık %30 oranında görüldü. Yumuşak doku yaralanmaları sıklıkla (%64,4) periodontal yaralanmalarla birlikte görüldü.
**Sonuç:** Dental travmalarda yumuşak doku yaralanmaları sıklıkla görülmektedir. Bu çalışma sınırları içerisinde yumuşak doku yaralanmalarının lokasyonu, tipi ve travma sınıflaması gibi kriterler cinsiyete göre daha önemli bulunmuştur.

## Introduction

The oral region accounts for as little as 1% of the total body size. However, injuries to this region account for 5-33% of all injuries among all ages (1,2). Traumatic dental injuries often result in soft tissue injuries. Osunde et al. (3) observed soft tissue injuries in 70% of all patients with maxillofacial traumas. Díaz et al. (4) reported that 39% of dento-alveolar traumas were accompanied by soft tissue injuries. In spite of this fact, the soft tissue injuries might be exposed to ignorance by the dentists who primarily focus on the patients' traumatized teeth.

Soft tissue traumas are usually seen as abrasion (rubbing or scraping of the mucosa), contusion (a bruise caused by a blunt object), laceration (tear in mucosa), and rarely seen as penetration (produced by sharp object) and avulsion (loss of tissue) (2).

Inadequate emergency care of soft tissue injuries in dento-alveolar traumas may cause economic, psychological, and aesthetic problems (5). There is limited research on the relationship between soft tissue injuries and dento-alveolar traumas (3,6). Although soft tissue injuries in children decrease with age, Osunde et al. (3), found out that this was not the case in dento-alveolar injuries (3).

The null hypothesis was that the soft tissue injuries in children, who referred to a pedodontics clinic with dento-alveolar traumas have no difference according to gender, age, localization (lips, gingiva, cheeks, tongue, and perioral tissues), wound type (abrasion, laceration, contusion, and mixed), time elapsed before treatment, and the relationship of these factors to the trauma classification.

## Material and Methods

The study protocol was approved by the Ethics Committee of the Atatürk University Faculty of Medicine (reference number: 2013/40). A retrospective study was conducted in eastern Anatolia region, Turkey. The study included 268 records of patients (166 boys and 102 girls) aged 1-15 [8.19±3.90 standard deviation (SD)] with dento-alveolar traumas who were examined and treated for different injuries in the university dental clinic between April 2010 and July 2015. Of these 268 patients, only 90 had soft tissue injuries.

The inclusion criteria for this study were patients with dento-alveolar traumas who had presented to the clinic within seven days of the injury and who had not sought any dental treatment earlier. The exclusion criteria were dento-alveolar fractures with severe skeletal deformities in the head and neck region, and patients who had injured themselves after receiving local anesthesia.

The dento-alveolar trauma records included the patient's gender, age, affected dentition and localization (lips, gums, cheeks, palate, floor of the mouth, and tongue), classification of soft tissue injury (abrasion, laceration, contusion, and mixed), and the time interval between trauma and treatment. The dento-alveolar trauma was classified as injuries to the hard dental tissues and pulp, root fracture, injuries to the supporting tissues, and multiple injuries (7).

### Statistical Analysis

Data analyses were carried out using SPSS software (SPSS for Windows, version 20.0, SPSS Inc., Chicago, IL, USA). Comparisons were performed with $X^2$ tests and the Mann-Whitney U test, where appropriate, to investigate the association between various factors related to the dental trauma and the characteristics of the trauma. The comparisons were followed by logistic regression analyses of the dento-alveolar traumas impact on soft tissue injury types. The statistical significance level was set at $p<0.05$.

## Results

In total, 268 children with dento-alveolar traumas presented to our clinic within one week of the injury [males, n=166 (61.9%); females, n=102 (38.1%)]. The percentage of soft tissue injuries in traumatic dental injuries experience was 31.9% in males and 36.3% in females. Therefore, females were found to be more prone to experience soft tissues injury in case of

dento-alveolar trauma. Despite the numerical and proportional differences in the soft tissue traumas, there was no difference according to gender ($X^2$=0.53, p=0.46).

There was no statistically significant difference (p=0.32) in the mean age of the patients with soft tissue traumas (7.87±3.69 SD) and the mean age of the remaining 178 children (8.35±4.0 SD).

The null hypothesis was rejected. Soft tissue injuries were increased in the mixed dentition period (6-12 years) (n=47), reaching the highest between the ages of 8 and 10 (Figure 1). The primary dentition period (0-6 years) was the next most common time of the injuries (n=32). The incidence of soft tissue traumas decreased after the age of 12 ($X^2$=17, p=0.36). The ratio of soft tissue injuries in the dento-alveolar traumas ranged between 21% and 83% according to age (Figure 2). The ratio was generally between 21-42% whereas, it was more than 50% for the ages of 4-6 years.

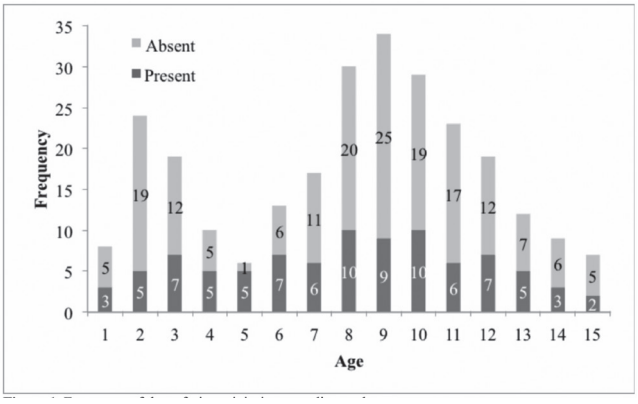


**Figure 1.** Frequency of the soft tissue injuries according to the age

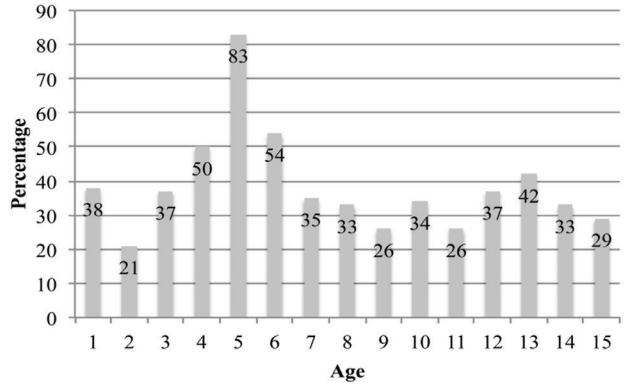


**Figure 2.** Distribution of the soft tissue injuries according to the age

The localization of the soft tissue injury types is shown in Figure 3. The frequencies of soft tissue injuries in children were 43.3% for lacerations, 30% for the mixed (more than one type of soft tissue injuries), 18.9% for contusions, and 7.8% for abrasions. Only, four patients with lacerations had penetration injuries. There was a statistically significant difference between the frequencies of abrasions and those of the other soft tissue injury types ($X^2$=20.79, p=0.008). Most of the soft tissue injuries were in the maxilla (n=78, 86.7%), followed by the mandible (n=5, 5.6%) and both jaws (n=7, 7.8%). Also, the distribution of soft tissue injuries in the maxilla and mandible fits that of the injuries to the teeth ($X^2$=3.84, p=0.045).

Figure 4 depicts the treatment times of the patients. Twenty-two (24.4%) children with soft tissue injuries received treatment on the same day, 47 (52.2%) in 2-3 days, and 21 (23.3%) within 4-7 days. There was no statistically significant difference in the arrival times of the children with and without soft tissue injuries (p=0.401).

Figure 5 shows the association between the dento-alveolar trauma and the resultant wounds. Among

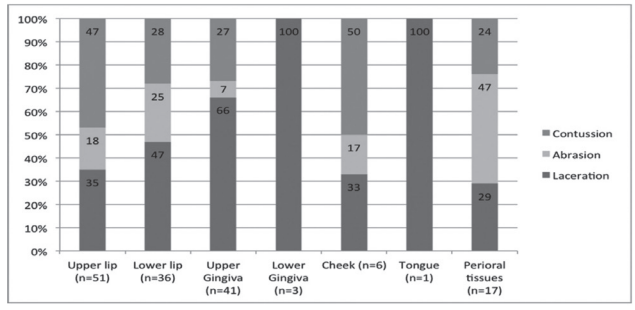


**Figure 3.** Distribution of the soft tissue injuries according to the localization

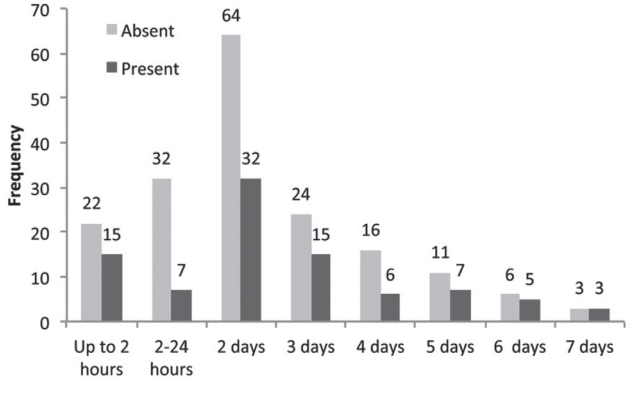


**Figure 4.** Time elapsed between the accident and seeking dental treatment

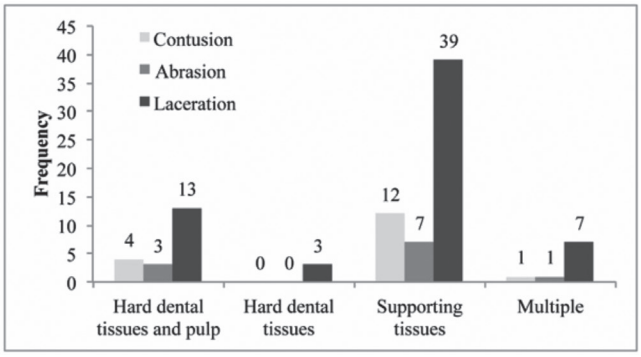


**Figure 5.** Distribution of the dento alveolar traumas according to wound type

the 90 patients with soft tissue injuries, 58 (64.4%) had injuries to the supporting tissues, 20 (22.2%) had hard dental tissue and pulp injuries, 9 (10%) had multiple injuries, and 3 (3.3%) had hard dental tissue injuries. There was a statistically significant difference in the soft tissue injuries, resulting from supporting tissue injuries ($p=0.001$ $X^2=15.72$). Soft tissue injuries in the primary dentition were the consequence of supporting tissue injuries (84.8%). And in the permanent dentition soft tissue injuries originated from supporting tissue injuries (52.6%) and hard dental tissues and the pulp injuries (31.6%).

## Discussion

Traumatic dental injuries are usually accompanied by soft tissue injuries. In this study the soft tissue injuries in children were evaluated according to various factors. The null hypothesis was rejected. In our study, the frequency of soft tissue injuries was 33.6%, which is similar to the distribution of dental injuries reported to be 30-50% in other studies (1,4,8,9). Similar to our findings, many studies showed that males are more prone than females to dento-alveolar trauma (10,11). However, we found no statistically significant difference in soft tissue injuries according to gender in common with other studies (12-15).

Although there was no statistically significant difference in age, the patients with soft tissue injuries were younger (7.87±3.69 SD) than those without soft tissue injuries (8.35±4.0 SD). Severe trauma as a result of poorly developed defense mechanisms, muscle coordination, and motor skills may affect the frequency of soft tissue injuries in younger children (14-17). In our study, soft tissue injuries and dento-alveolar injuries were common in mixed dentition, with the highest frequency found in children aged 8-10 years. As reported in the literature, children aged 1-4 years are most susceptible (among all ages) to accidents and have the highest number of soft tissue injuries (3,6,12,14,16,18). Studies have also reported that younger children who have a higher cranial vs. facial skeletal size, softer and more elastic bones, and protective thick soft tissues are more likely to be exposed to minor injuries, such as soft tissue injuries, whereas older children tend to be more susceptible to serious injuries (6,17,19). Vuletić et al. (20), found that soft tissue injuries peaked among preschool children aged two years (18). After the preschool period, the superego develops, and the child is exposed to disciplined training at school (19,21). As reported in the literature, such training can decrease injury rates among those aged 4-6 years, even among children from disorganized families (19,21). Nevertheless, in the present study, the highest percentage of soft tissue injuries in dento-alveolar traumas was observed among the children aged 4-6 years and particularly among those aged five years.

In dento-alveolar trauma, soft tissue injuries are seen most frequently in the maxilla, especially in the upper lip (20,22). As reported in the literature, the high incidence of such injuries may be due to the protrusive structure of the maxilla (4,11,13,21,23). In the present study, soft tissue injuries were most frequently found in the maxilla as previous studies.

Fractures of the molar teeth may be associated with traumatic injuries to the chin (22,24). In our study only one patient had extrusive luxation and laceration on his permanent maxillary left first premolar caused by facial collision into a doorknob following slippage.

In studies of soft tissue injuries in maxillofacial and dento-alveolar trauma patients, lacerations accounted for 37.5-83.4%, contusions accounted for 8.4-32.8%, and abrasions accounted for 1.6-29.7% (4,6,13,15,23,25). Similarly, the frequency of lacerations in our study of soft tissue injuries was 43.3%, whereas the frequency of mixed injuries, contusions, and abrasions was 30%, 18.9%, and 7.8%, respectively.

Abrasions are observed more commonly in perioral than intraoral tissues and are therefore less common than other types of injuries. A traumatic force with a high intensity, which could lead to dento-alveolar injury, may cause lacerations as the most frequent

type of soft tissue injury (24,26). Many lacerations resulting in swellings may be due to a combination of crushing and tearing of tissue. As noted in the literature, special attention should be paid to children with such injuries because healing occurs faster than in adults, resulting in the rapid formation of hypertrophic scars and keloids (25,27).

In Eastern Anatolia Region, most emergency management of children's tooth injury trauma is undertaken by pediatric dentistry department. The most important principle in the treatment of soft tissue injuries is debridement of the wound and thorough cleaning with saline (20,22). Lacerations were treated with suture. Antibiotics were prescribed, depending on the severity of the injury. If the patient has not received tetanus prophylaxis in the previous five years, patients were referred to hospital for additional doses (25,27).

After the occurrence of soft tissue injury, new tissue formation lasts between 4-30 days (10,26). Meanwhile, relatively simple soft tissue injuries, including contusion, heals within one week (11,27). For this reason, the dento-alveolar trauma patients who were admitted within one week, were included in this study. Also, there was a statistically significant difference in the arrival time of the children with and without soft tissue injuries. Vuletić et al. (20) reported that children with soft tissue injuries presented earlier for dental treatment (18). However, there was no difference in the presentation time of those with soft tissue injuries in our study. With regard to the presentation time for dental treatment, the majority of the children with soft tissue injuries presented on the second day after the injury, followed by the first and third post-injury days. Among the patients who sought treatment within the first 24 hour, the frequency of those who presented within 2 hour of the injury may be explained by the sensitivity of parents to soft tissue injuries. Delays in the initial treatment might be due to a large number of the referred patients living some distance from the clinic, the absence of an after-hours dentist, unawareness of the after-hours service, giving a low priority to dental injuries, and not considering emergency management of dental injuries a priority.

According to a previous study, the most common type of dento-alveolar trauma was hard dental tissue and pulp injuries in permanent dentition and supporting or hard dental tissue and pulp injuries in primary dentition (28). A literature search revealed no relationship between soft tissue injuries and dento-alveolar trauma. In our study, we observed soft tissue injuries more frequently in injuries to the supporting tissues (64.4%) than injuries to the hard dental tissues and pulp (22.2%). With regard to tooth injury mechanisms, one study found that a low-velocity direct force, usually cushioned by the lips or cheek, was responsible for damage caused to the supporting structures (24,26). Another study found that the presence of cartilage in the skeletal system in children and a greenstick fracture pattern may help both soft and hard tissues absorb a traumatic force (29). In this study, high supporting tissue injury rates was responsible for the high incidence of soft tissue injuries in primary dentition.

Although soft tissue injuries are self-healing, inadequate primary treatment may result in unsightly scarring. It is important to educate primary health care providers on the proper emergency management of soft tissue injuries to reduce the long-term consequences and to educate parents about the necessity of seeking immediate treatment. Future studies of the treatment of such injuries and the patients' prognoses might be useful to provide additional information on the consequences and management of soft tissue trauma.

## Conclusion

Soft tissue injuries are occasionally seen in dento-alveolar traumas. The severity, type, and localization of the trauma seem to be more important factors than gender and age in the occurrence of soft tissue injuries. Soft tissue injuries were frequently seen in the maxillary region, and they were accompanied by supporting tissue injuries. The most common soft tissue injuries were lacerations, and abrasions were common in perioral tissues.

**Ethics**

**Ethics Committee Approval:** The study protocol was approved by the Ethics Committee of the Atatürk University Faculty of Medicine (reference number: 2013/40).

**Informed Consent:** The written informed consent was obtained from all patients.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Concept: F.Ş., H.Ş, Design: H.Ş., F.Ş., Data Collection or Processing: F.Ş., Analysis or Interpretation: H.Ş., Literature Search: H.Ş., Writing: F.Ş.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Original Article / Özgün Araştırma

# Apical Extrusion of Debris and Irrigant Using XP-Endo Finisher, EndoActivator, Passive Ultrasonic Irrigation or Syringe Irrigation

## *XP-Endo Finisher Eğesi, EndoActivator, Pasif Ultrasonik İrrigasyon veya İğne İrrigasyonu Sırasında Meydana Gelen Debris ve İrrigant Ekstrüzyonunun Değerlendirilmesi*

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**Keywords**
XP-Endo Finisher, passive ultrasonic irrigation, sonic irrigation, apical extrusion

**Anahtar Kelimeler**
XP-Endo Finisher, pasif ultrasonik irrigasyon, sonik irrigasyon, apikal ekstrüzyon

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### Abstract

**Objective:** Extrusion of irrigant and debris into the periapical tissues is a potential risk for flare-ups during root canal treatment. The aim of this study was to evaluate the apically extruded debris and sodium hypochlorite during XP-Endo Finisher (XP-Endo) file use and compare with final irrigation techniques. The tested null hypothesis in this study was that there was no difference among the irrigation techniques.

**Materials and Methods:** An agar gel model was prepared for 80 extracted single rooted human mandibular premolar teeth, which were prepared up to the apical size of #40. The samples were divided into four groups according to the final irrigation regime: conventional syringe irrigation, XP-Endo, passive ultrasonic irrigation (PUI), and EndoActivator (EA). The test apparatus was weighed before and after the experiment, and the amount of apically extruded debris and irrigant was calculated.

**Results:** There was minimal irrigant and debris extrusion in all groups. No significant difference among the tested groups was detected ($p>0.05$).

**Conclusion:** Using the PUI, XP-Endo file, or EA according to the manufacturers' instruction does not increase the extrusion risk.

### Öz

**Amaç:** Kanal tedavisi esnasında irrigantların ve debrisin periapikal dokulara taşması akut alevlenme açısından potansiyel bir risk teşkil etmektedir. Bu çalışmanın amacı XP-Endo Finisher (XP-Endo) kullanımı esnasında apikalden taşan debrisi ve sodyum hipokloriti değerlendirmek ve final irrigasyon teknikleri ile karşılaştırmaktır. Çalışmanın sıfır hipotezi, test edilen sistemler arasında fark olmadığıdır.

**Gereç ve Yöntemler:** Bir agar jel model, apikal boyutları 40 numaraya kadar prepare edilmiş 80 adet çekilmiş tek köklü insan mandibular premolar dişi kullanılarak hazırlandı. Örnekler final irrigasyon protokolüne göre dört gruba ayrıldı: Geleneksel iğne irrigasyonu, XP-Endo, EndoActivator (EA) ve pasif ultrasonik irrigasyon (PUI). Test düzeneği deneyden önce ve sonra tartıldı ve apikalden taşan debris ve irrigant hesaplandı.

**Bulgular:** Her grupta minimal irrigant ve debris ekstrüzyonu saptandı. Test edilen gruplar arasında anlamlı fark bulunamadı (p>0,05). **Sonuç:** PUI, XP-Endo ve EA üretici firma talimatlarına uyarak kullanıldığında apikal ekstrüzyon riskini artırmamaktadır.

## Introduction

Endodontic treatment utilizes irrigants to achieve chemomechanical preparation to remove tissue remnants, debris, microorganisms and their byproducts from the root canal systems (1). Extrusion of irrigants, dentinal chips, debris, and microorganisms to periapical tissues is inevitable during root canal treatment. These extruded substances may lead to inflammation, postoperative pain, and/or delay in periapical healing (2,3). Many irrigation systems have been developed to deliver and activate irrigants during endodontic treatment. Besides these objectives, ensuring safety during irrigation activation should be considered while using these systems (4).

EndoActivator (EA) (Dentsply, York, PA, USA), which has a handpiece and various disposable polymer activator tips (yellow 15/02, red 25/04, blue 35/04) that do not cut dentin, is a sonic irrigation activation system (5). EA is recommended for irrigant agitation, after flushing root canals using conventional syringe irrigation (SI), as final step of chemomechanical root canal preparation (6). The polymer tips, which should passively fit in the root canal, are activated by a battery-operated handpiece at 10000 cycles/min for 30-60 seconds. EA has been reported as a safe irrigation agitation procedure when compared to manual activation (4). XP-Endo Finisher (XP-Endo) (FKG Dentaire SA, La Chaux-de-Fonds, Switzerland) was designed as a final canal irrigation protocol to enhance cleaning. XP-Endo is a non-tapered instrument (size #25) and was developed to both respect the original root canal anatomy and effectively clean those irregular areas due to its reputed increased flexibility and ability to expand to adapt to the root canal three dimensionally (7). Its ability to remove hard tissue debris and smear layer effectively has been reported in previous studies (7,8). However, to our knowledge, there is no study on the amount of apically extruded debris and irrigant during the use of the XP-Endo.

Several *in vitro* techniques have been used to calculate the amount of apical extrusion of irrigants and debris (9,10). Most studies utilized the empty tube model, but this model does not simulate *in vivo* clinical conditions because, unlike periodontal ligament, empty tube does not provide a back pressure (9,10). Lu et al. (11) developed a 1.5% agar gel model to provide back pressure for apically extruded materials and reported that the model simulates clinical conditions more accurately than the empty tube model. The aim of this study was to compare the amount of apically extruded debris and irrigant during the use of the XP-Endo file, EA, passive ultrasonic irrigation (PUI), and SI. The null hypothesis that tested in this study was that there is no difference among these final disinfection steps.

## Materials and Methods

The study protocol of this study was approved by the Ordu University Clinical Researches Ethics Committee (2016/70). This study was performed in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from all participants. Sample size calculation revealed that a minimum 12 specimens per group would suffice to show a 5% difference in amount of apically extruded debris with a power of 90%. Eighty freshly extracted human mandibular premolar teeth that fulfilled following criteria were selected: single straight root, fully formed apex, no resorption, and no calcified root canals. The canal curvatures, which were determined according to Schneider's method, were less than 10° (12). The root lengths were standardized as 14 mm (14±0.85 mm) using sterile diamond disks under water-cooling by removing the crown. A #20 broach was used to extirpate the pulp tissue. The working length (WL) of each root canal was determined to be 1 mm short of the length of a #10 K file (VDW GmbH, Munich, Germany) that was visible at the apical foramen. The root canals were prepared with the Reciproc system up to the file R40 under copious 5.25% sodium hypochlorite (NaOCl) irrigation (5 mL). Canal patency was maintained by inserting a #10 K-file 1 mm beyond the apical foramen. Following the completion of root canal mechanical preparation, the canals were flushed with 2 mL distilled water and 2.5 mL of 17% ethylenediaminetetraacetic acid, respectively. The specimens were numbered and then weighed three times using an analytical balance with

10-4 g accuracy (Precisa XB 220A, Precisa Instruments, Dietikon, Switzerland).

An agar gel model was prepared as described by Lu et al. (11). A 1.5% agar solution was prepared and then injected into Eppendorf tubes, which were inverted for gel to seal the cling film-coated root surfaces. Following the congelation of agar, the test apparatus was reweighed three times. The weight of the apparatus without the specimens, which was recorded as the initial weight, was calculated by subtracting the specimen weight from the test apparatus's weight. The specimens were randomly divided into four groups as follows (n=20): SI (group 1), XP-Endo (group 2), EA (group 3), and PUI (group 4).

**Group 1:** SI. The tip of the 30-gauge side-vented needle (Ultradent, South Jordan, UT, USA) was placed 2 mm short of the WL, and 5.25% of NaOCl solution was delivered passively at a rate of 6 mL/minute, moving with the amplitude of 2 mm for 60 seconds. For WL control, a stopper was placed on the needle.

**Group 2:** XP-Endo. The instrument was placed in a torque-controlled endodontic motor (VDW Gold, Munich, Germany), cooled down (Chloraethyl, Dr. Georg Henning GmbH, Germany), and then removed from the plastic tube by applying a slight lateral movement. The XP-Endo file was inserted into the root canal, which was irrigated with 6 mL of 5.25% NaOCl without rotation. The instrument was operated at 800 rpm speed and 1 N.cm torque value for 60 seconds with vertical movements of 7-8 mm to the full WL, which was recommendation of the manufacturer.

**Group 3:** EA. The canals were irrigated 6 mL of 5.25% NaOCl using a 30-gauge side-vented needle and then 25/04 polymer tip, which mounted on EA device, was inserted into the NaOCl-filled root canal (2 mm shorter then WL). The device was activated at 10,000 cycles per minute with vertical strokes with the amplitude of 2 mm for 60 seconds.

Group 4: PUI. The canals were irrigated 2 mL of 5.25% NaOCl using a 30-gauge side-vented needle. Then it was ultrasonically activated with a 15.02 ultrasonic tip (Irrisafe) mounted on a piezoelectric ultrasonic unit with the power setting at 10%. The tip was placed 2 mm short of the WL and operated with the amplitude of 2 mm for 20 seconds without touching the root canal walls. The root canals were flushed with 2 mL of 5.25% NaOCl then it was ultrasonically activated for 20 seconds again. NaOCl was activated by a total of three cycles of 20 seconds.

One experienced endodontist (C.K.) performed all procedures. During the experiment, the test apparatus was secured in an opaque glass vial to prevent any movement and contact of fingertips. The tooth was removed from the Eppendorf tube. The test apparatus with extruded irrigant and debris was weighed again. The weight of the extruded debris and irrigant was calculated by subtracting the initial weight from the final weight. All measurements were made three times, and the mean values were calculated. Weight measurements and analysis were performed by one clinician (E.S.) who was blinded to the study groups.

### Statistical Analysis

SPSS 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The normality of the data distribution was confirmed with the Shapiro-Wilk test, and the data was analysed by One-Way Analysis of Variance and Bonferronni post-hoc test with the level of significance of 95%.

## Results

The standard deviation and median values of the weighed apically extruded irrigant and debris of each experimental group are presented in Table 1. Based on the statistical analysis, no significant differences were found among the experimental groups (p>0.05).

**Table 1. The mean mass of extruded debris and irrigant (g)**

| | Mean value (SD) | Minimum | Maximum | n |
|---|---|---|---|---|
| **Group 1 (SI)** | $385.10^{-5}$ ($9.10^{-4}$) | $20.10^{-5}$ | $901.10^{-5}$ | 20 |
| **Group 2 (XP-Endo)** | $581.10^{-5}$ ($6.10^{-4}$) | $30.10^{-5}$ | $673.10^{-5}$ | 20 |
| **Group 3 (EA)** | $579.10^{-5}$ ($8.10^{-4}$) | $60.10^{-5}$ | $700.10^{-5}$ | 20 |
| **Group 4 (PUI)** | $429.10^{-5}$ ($13.10^{-4}$) | $80.10^{-5}$ | $690.10^{-5}$ | 20 |

SD: Standard deviation, SI: Syringe irrigation, XP-Endo: XP-Endo Finisher, EA: EndoActivator, PUI: Passive ultrasonic irrigation

## Discussion

Irrigation is an indispensable phase of root canal treatment that is necessary for disinfection, lubrication, and removal of inorganic and organic tissue remnants from the root canal system due to the solutions' chemical and flushing effects (1). SI is the most widely used irrigation method because of the technique's simple usage manner, which provides needle depth and irrigant volume control (13). However, previous studies revealed that conventional SI is usually inadequate to achieve these goals (14). Several irrigation devices, instruments, and methods were introduced to overcome the limitations of SI (15). The common aim of these irrigation devices is to clean the root canal system more effectively by enhancing the irrigation solution's flow and distribution within the irregularities of the root canal system (16). The results of this study revealed that apical irrigant and debris extrusion occurred regardless of the final irrigation regime used, and no significant difference was observed among the SI, PUI, XP-Endo, and EA. Therefore, the null hypothesis was accepted. The amount of extruded debris produced during PUI or EA activation was investigated by many studies; however, to the authors' knowledge, there has not yet been a study regarding the amount of apically extruded debris and irrigant produced during the use of the XP-Endo file.

XP-Endo is a novel NiTi file that is recommended for the removal of debris, intracanal medication, and residual obturation materials from root canals. The XP-Endo has a unique characteristic which allows the file to be straight in the Martensitic phase at the room temperature; however, the phase and the shape of file change when inserted into the root canal to adapt to the three-dimensional root canal anatomy to access and clean the irregularities of root canals (7). According to the results of this study, the supplementary use of the XP-Endo file does not increase the risk of extrusion and could be suggested as a safe supplementary method.

Ultrasonic devices oscillate files at 25-30 kHz, producing nodes and antinodes along the file, whereas sonic devices such as EA operate at lower frequencies of about 1000 to 6000 Hz, so only one node and antinode occur near the tip (17,18). In EA, the irrigant's streaming velocity is lower when compared with ultrasonics (17). However, sonic irrigation produces higher amplitude and tip movement (18). In the present study, no significant difference was detected between EA and PUI. The results of this study are in line with a previous study that reported no significant association between the irrigation technique (PUI, EA, and SI) and the apically extruded material, although there were methodological differences between these studies regarding the test models (19). The present study utilized the test apparatus described by Lu et al. (11) to simulate the back pressure of periapical tissues. In clinical conditions, the presence of periapical structures and granulation tissues might provide resistance to apically extruded irrigant and debris (20). The density of 1.5% agar gel is 1045 kg-3, whereas the density of human periapical tissues is 1000-1100 kg-3. Because of this similarity, the agar gel model was used in the present study to represent clinical situations better (11). Extruded irrigant was not distinguished from the debris because extruded irrigant can also trigger flare-up and provoke foreign body reactions (21).

The use of NaOCl might cause the precipitation of sodium crystals and interfere with the amount of apically extruded debris. This is why previous apical extrusion studies used distilled water as an irrigant (22,23). Tanalp and Güngör (24) stated in their literature review that the use of routinely used irrigation solutions in apical extrusion studies seems logical to reflect clinical conditions. In the present study, 6 mL of 5.25% NaOCl was used for the irrigation of the specimens of each experimental group to standardize the amount of irrigation solutions.

### Study Limitations

All the factors could not be standardized in the present study since the microhardness of experimented teeth might also affect the amount of apically extruded material, which presents a limitation to the present study (24).

## Conclusion

Within the limitations of this study, supplementary use of the XP-Endo file, PUI, or EA do not increase the risk of irrigant extrusion beyond the apex. Further clinical studies on postoperative pain and flare-up incidences following the use of this file are needed.

**Ethics**

**Ethics Committee Approval:** The study protocol of this study was approved by the Ordu University Clinical Researches Ethics Committee (2016/70).

**Informed Consent:** Written informed consent was obtained from all participants.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Concept: E.S., C.K., Design: E.S., C.K., Data Collection or Processing: E.S., Analysis or Interpretation: C.K., Literature Search: E.S., Writing: E.S., C.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Original Article / Özgün Araştırma

# Evaluation of Different Root Canal Filling Methods in Primary Teeth

## *Süt Dişlerinde Farklı Kök Kanal Dolum Yöntemlerinin Değerlendirilmesi*

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**Objective:** To compare the efficacy of 5 different methods for filling primary teeth root canals by digital radiography.

**Materials and Methods:** A total of 50 extracted primary anterior teeth with no more than 25% root resorption were prepared using Mtwo® NiTi rotary instruments to a standard apical file size. Teeth were randomly divided into 5 groups, as follows according to the sealer application method. Group 1: Metapex® syringe (control); group 2: Metapex® syringe and Endoactivator® (sonic activation); group 3: Metapex® syringe and indirect ultrasonic activation; group 4: Endodontic irrigation needle; group 5: Lentulo spiral. Photostimulated phosphor radiographs of canals were evaluated for length of filling (underfilled, suboptimally filled, optimally filled, overfilled) and quality of filling (presence, localization and total sum of voids). Data was statistically analyzed using Kruskal-Wallis and Bonferroni-corrected Mann-Whitney U tests.

**Results:** For the both length and the quality of the filling the worse results were seen in the endodontic irrigation needle group (group 4) ($p<0.05$). However, there were no significant differences between the other groups ($p>0.05$).

**Conclusion:** Based on the results of this study apart from the endodontic irrigation needle group, all the tested methods could be used for obturation of primary teeth.

**Keywords**
Digital radiography, root canal obturations, Metapex®, ultrasonic aid

**Anahtar Kelimeler**
Dijital radyografi, kök kanal dolgusu, Metapex®, ultrasonik aktivasyon

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## Öz

**Amaç:** Süt dişleri kök kanallarının dolumu için kullanılan beş farklı metodun etkinliğinin dijital radyografi yöntemiyle karşılaştırılmasıdır.

**Gereç ve Yöntemler:** Çalışmada kök rezorpsiyonu %25'ten fazla olmayan toplam 50 adet çekilmiş süt ön diş kullanıldı. Dişler, Mtwo® NiTi döner aletler kullanılarak standart bir apikal genişlik elde edilecek şekilde hazırlandı. Dişler rastgele 5 gruba ayrıldı: grup 1: Metapex® şırınga (kontrol); grup 2: Metapex® şırınga ve Endoaktivatör® (sonik aktivasyon); grup 3: Metapex® şırınga ve indirekt ultrasonik aktivasyon grup 4: Endodontik irrigasyon iğnesi; grup 5: Lentulo spiral. Kanalların fosfor plakla alınmış radyografik görüntüleri ile kanal dolgusunun uzunluğu (yetersiz, ideale yakın, ideal ve taşkın dolgu) ve kalitesi (boşlukların varlığı, lokalizasyonu ve toplam alanı) değerlendirildi. Veriler istatistiksel olarak Kruskal-Wallis ve Bonferroni-düzeltmeli Mann-Whitney U testleri kullanılarak analiz edildi.

**Bulgular:** Kök kanal dolumları hem uzunluk hem de kalite anlamında

değerlendirildiğinde en kötü sonuçlar endodontik irrigasyon iğnesi grubunda elde edildi (grup 4) ($p<0,05$). Bununla birlikte diğer gruplar arasında istatistiksel olarak anlamlı bir fark bulunamadı ($p>0,05$).
**Sonuç:** Çalışmanın sonuçlarına göre; endodontik irrigasyon iğnesi grubu dışında tüm test edilen yöntemler süt dişlerinin kanal dolgusu sırasında kullanılabilir.

## Introduction

Pulpectomy treatment is one option for maintaining primary teeth diagnosed with pulpal tissue inflammation involving radicular or nonvital pulp until normal exfoliation (1). The treatment consists of extirpation of the infected pulp tissue, removal of debris from the canal and obturation with resolvable antibacterial paste (2). The success of primary teeth root canal pulpectomy depends on several factors, including the adequacy of biochemical preparations, the material used in obturation, and a hermetic seal with minimal voids. How the obturating material is mixed and the technique used for obturation also significantly affects the success of primary teeth root-canal treatment (3,4).

The most popular root-canal filling materials for primary teeth have been zinc oxide eugenol, calcium hydroxide and iodoform-based pastes (2,5). In addition, pastes containing a mixture of calcium hydroxide and iodoform have recently come into more frequent use as a primary root-canal filling material and have demonstrated good clinical and radiographic success (6,7).

A variety of methods can be used to deliver paste into primary teeth root canals, including an endodontic pressure syringe (8), a disposable tuberculin syringe, a local anesthetic syringe (2) and a NaviTip syringe (9). Endodontic pluggers may also be used, especially in long straight canals and a Lentulo spiral mounted on a slow-speed handpiece can be used in both straight and curved narrow canals (10).

Ultrasound has been used extensively in dentistry for many years, mainly for its ability to enhance polishing and plaque and tartar removal from tooth surfaces (11). Its effects on viscosity and voids have also made it useful in restorative dentistry (12), and its use in endodontics has become more frequent in recent decades, particularly in applications such as gaining access to canal openings, cleaning and shaping, obturation of root canals, removal of intracanal materials and obstructions, and endodontic surgery (13).

The ideal root canal filling technique must provide complete filling of the canal, with no overfill and with minimal or no voids (14). While there is currently no agreement as to which technique provides the best sealing of root-canal filling material in primary teeth, it may be hypothesized that ultrasonic and sonic aid can improve condensation and adaptation of root-canal filling pastes in primary anterior teeth. Therefore, the aim of this study was to compare using digital radiography the sealing ability of Metapex®, a mixture of calcium hydroxide and iodoform, applied using 5 different techniques: 1. Metapex® syringe (control); 2. Metapex® syringe and EndoActivator® (sonic activation); 3. Metapex® syringe and indirect ultrasonic activation; 4. Endodontic irrigation needle; and 5. Lentulo spiral.

## Materials and Methods

The study was approved by the Ondokuz Mayıs University Human Research and Ethics Committee (approval no: 2014/682). The study was conducted with 50 extracted primary anterior teeth. Teeth with more than 25% root resorption, signs of root-canal obstruction or root anomalies, or previous endodontic treatment were excluded. Moreover, in order to standardize samples, only teeth whose canals had a curvature of less than 15 degrees, as determined by Schneider's method (15) were included. Teeth were immersed in 5.25% sodium hypochlorite (NaOCl) for 24 hours and stored in saline solution until use.

### Root Canal Preparation

All canals were prepared and filled by a single operator. A standard access cavity was prepared in each tooth, a #10 K file (Mani Co, Tokyo, Japan) was introduced into the canal until the tip was just visible at the apical foramen, and working length was determined as 1.0 mm short of the apical foramen. Root canals were instrumented with Mtwo® NiTi rotary files up to size 35/0.06 at working length. Canals were irrigated between each instrument with 1 mL of 2.5% NaOCl using a 21-gauge needle attached to a 10 mL syringe. After instrumentation was complete, canals were flushed with 1 mL of 17%

ethylenediaminetetraacetic acid, followed by 5 mL of 2.5% NaOCl to remove the smear layer, and then dried (16).

The apexes of the prepared roots were covered with red wax to prevent any extrusion of the filling material. The roots were mounted in 1x1 cm cold-cured acrylic resin blocks from 1 mm below the cemento-enamel junction (17).

**Root Canal Filling**

Root canals were filled with, Metapex® (Meta Biomed Co., Ltd, Korea), a commercially available iodoform-calcium hydroxide paste. Specimens were randomly divided into five groups (n=10) according to sealer application method, as follows:

**Group 1 (control):** Prepared canals were filled with paste using the Metapex® syringe. The procedure was repeated at least twice until back fill was observed in the orifice.

**Group 2:** Prepared canals were filled with paste using the Metapex® syringe and EndoActivator® (Dentsply Tulsa Dental Specialties, Tulsa, OK, USA). The Metapex® syringe was placed in the canal, and the paste was injected. The EndoActivator® tip (25/04) was then inserted into the canal 2 mm short of working length, and the paste was spread for 1 s using the EndoActivator handpiece set at 10.000 cycles/min. The procedure was repeated at least twice until back fill was observed in the orifice.

**Group 3:** Prepared canals were filled with paste using the Metapex® syringe and indirect ultrasonic activation. The Metapex® syringe was placed in the canal, and the paste was injected. During injection, an ultrasonic diamond tip (Suprasson® P-Max, Satelec Acteon Group, France) was placed in contact with the Metapex® syringe for 1 second. The procedure was repeated at least twice until back fill was observed in the orifice.

**Group 4:** Prepared canals were filled with Metapex® paste using an endodontic irrigation needle (KerrHawe SA, Bioggio, Switzerland). The sealer was transferred into a local anesthetic syringe cartridge, and the paste was placed in the canal using a 30-gauge endodontic needle. The procedure was repeated at least twice until back fill was observed in the orifice.

**Group 5:** Prepared canals were filled with Metapex® paste using a lentulo spiral (Size 30) mounted in a low- speed handpiece (W&H Company, Bürmoos, Austria). The lentulo spiral was inserted into the canal, rotated in a clockwise direction and withdrawn gently from the canal while still rotating. The procedure was repeated at least twice until the canal orifice appeared filled with paste.

For all groups, a rubber stop was placed around the filling instrument 1 mm short of the working length, and when the canal was assumed to be completely filled, a wet cotton pellet was used to lightly tamp the material into the canal.

**Radiographic Evaluation**

Digital radiographs of the root canals were taken in the buccolingual direction using a paralleling technique with both receptor and tooth aligned in the same direction. Photo stimulated phosphor radiographs were exposed with a dental X-ray unit (Evostyle NG, New life radiology, Torino, Italia) at 60 kVp, 6 mA for 0.25 seconds with a target-film distance of 15 mm. Digital images were recorded as TIFF files and evaluated on a 19-inch monitor set at a 32-bite resolution in a darkened room using the ImageJ software analysis program. Root canals were assessed by two blinded, calibrated observers. Length of fill was scored as follows: 1=Underfilled: less than or equal to half the root-canal length filled; 2=Sub-optimal filling: more than half the root-canal length filled but filling less than optimal; 3=Optimal filling: canal filled to the radiographic apex or up to 1.5 mm short of the apex; 4=Overfilling: filling material extended beyond the root apex (Figure 1a-d). Quality of filling was evaluated based on the presence, localization, and total amount (%) of voids. The number of voids in each third of the root canal (coronal, middle, apical) was also calculated.

**Statistical Analysis**

Statistical analysis was performed using Kruskal-Wallis and Bonferroni-corrected Mann-Whitney U tests, with the level of significance set at $p<0.05$.

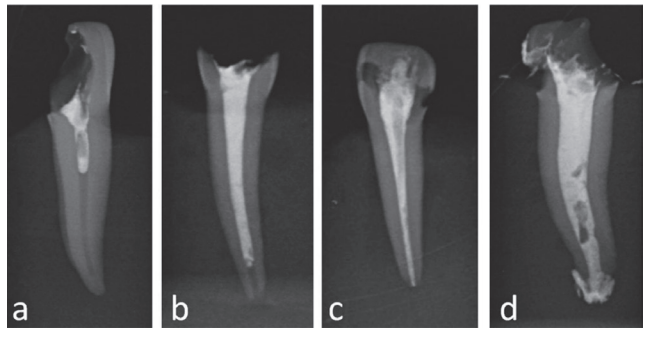


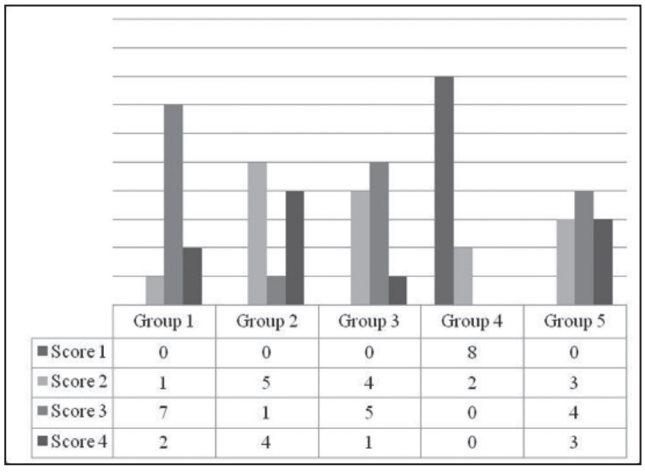

**Figure 1 (a-d).** Scores for root filling in all groups

## Results

Figure 2 shows the frequencies of each root filling score by group. The groups were rank in order according to acceptable scores (score 2 and 3) as group 3 > group1 > group5 > group 2 > group 4. For acceptable filling scores no statistically significant differences were observed between the test methods accept group 4 ($p<0.05$).

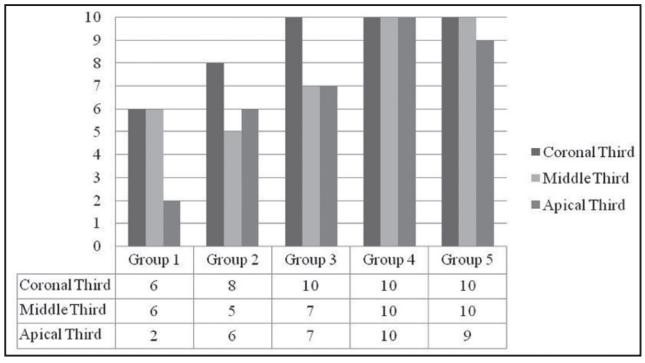
Voids were detected in all groups. The sum of voids (%) was highest in group 4 (55.75%), followed by group 3 (16.6%), group 2 (13.3%), group 5 (11.9%) and group 1 (6.94%). The difference between group 4 and the other groups was statistically significant ($p<0.05$); however, the differences among the remaining groups were not statistically significant ($p>0.05$).

Figure 3 shows the distribution of voids in each third of the root canal (coronal, middle, apical). It was observed that the voids were localized generally the coronal and the middle thirds of the canals for all tested methods.



| | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---|---|---|---|---|---|
| Score 1 | 0 | 0 | 0 | 8 | 0 |
| Score 2 | 1 | 5 | 4 | 2 | 3 |
| Score 3 | 7 | 1 | 5 | 0 | 4 |
| Score 4 | 2 | 4 | 1 | 0 | 3 |

**Figure 2.** Frequency distribution of each score in all experimental groups




| | Group 1 | Group 2 | Group 3 | Group 4 | Group 5 |
|---|---|---|---|---|---|
| Coronal Third | 6 | 8 | 10 | 10 | 10 |
| Middle Third | 6 | 5 | 7 | 10 | 10 |
| Apical Third | 2 | 6 | 7 | 10 | 9 |

**Figure 3.** Frequency distribution of voids in all experimental groups

## Discussion

Conventional primary root-canal filling essentially involves placing filling material into the pulp chamber using a plastic instrument or lentulo and packing it into the canal with a root canal plugger or lentulo, followed by a cotton pellet (18). Despite the apparent simplicity of the technique, it remains difficult to master. Air entrapment can cause underfilling, voids and failure to create a hermetic seal, resulting in ultimate failure. Conversely, uncontrolled, excessive pressure can cause overfilling (19). Different root canal sealer systems have been introduced to overcome these disadvantages. While these systems all use their own syringes to obturate root canals with light pressure (20), according to the literature, they share a common defect: overfilling.

Despite numerous studies evaluating and comparing success rates of different techniques used to fill primary-teeth root canals (4,17,21), none of the techniques described consistently provide optimal results. Therefore, the present study examined several new endodontic technologies, including EndoActivator® and a new endodontic needle, in terms of performance in primary teeth root canal obturation.

Root filling quality can be assessed by a variety of techniques, including radioisotopes, dyepenetration, fluidfiltration, bacterialleakage, microscopicanalysis, radiographic examination and clearing techniques (22-24). This study evaluated filled root canals using photo stimulated phosphor radiographs, which have been shown to perform better than conventional radiographic techniques in detecting small voids compared (24).

Determination of working length is one of the most important steps in primary teeth pulpectomy treatment due to continuing resorption. Because the apical foramen may not correspond to the anatomic root apex, but may be coronal to it, as the course of resorption progresses, it is advisable to maintain a working length 2-3 mm short of the radiographic working length in order to prevent overextension through the apical foramen, especially in teeth exhibiting signs of apical root resorption. In the present study, the length of the filling was assumed as acceptable when the score 2 and score 3 was observed.

Various endodontic irrigation needles have been developed to improve the effectiveness of root canal irrigation, and it was hypothesized that the characteristic side openings would enable these needles to perform better in filling the full diameter of the root canal. However, the study findings showed the specimens filled using an endodontic irrigation needle (group 4) were the least adequately filled in terms of both filling length and percentage of voids. This may be due to the small gauge of the needle, which is incompatible with the relatively stiff Metapex® paste. Needle displacement during injection could also have affected the results.

Recently, ultrasound technology has regained its popularity as a tool in dentistry. One study used indirect ultrasound to improve the compaction of glass ionomer cement, and another study using direct ultrasound to agitate root canal during irrigation also found it helped in the compaction of root-end filling material (25,26). In the present study, ultrasonic and sonic support groups (groups 2 and 3) showed similar acceptable scores to the Metapex® syringe alone for the length and the quality of primary teeth root canal fillings.

The lentulo spiral has been and continues to be the instrument most commonly used as a root-canal paste carrier (14). However, lentulo instruments suffer from difficulties in terms of fitting the rubber stop, instrument fracture, and a tendency towards extrusion beyond the apex (4,27). The extrusion of the filling material and the high percentage of voids observed with the lentulo spiral is in line with the findings of previous studies (14,17).

The survival of root canal treatment is affected by voids (28), the presence of which encourage the possibility of microorganism and toxin retention that may be associated with post-treatment disease (29). In clinical practice, the number, location and size of voids depends upon the material and technique used to fill the root canal as well as the skill of the operator (30). Voids located in the apical and middle third of the root have been shown to greatly affect the survival time of root canal treatment of permanent teeth; however, void location is less important in primary teeth due to their large apexes (31). In the present study, all groups, including the control group, showed similar results in terms of amounts and locations of voids.

**Power Analysis**

For 5 study groups to be evaluated at the study capitals, the number of patients required to take each group with 80% power was calculated as 10. In the calculations; Joe Rebellato et al. (32), 1997 "Lower arch perimeter preservation using the lingual arch" named study was taken as reference.

[t-tests - means: Difference between two independent means (two groups)

Analysis:

A priori: Compute required sample size

Input: Tail(s)=One

Effect size d=0.9262547

α err prob=0.05

Power (1-β err prob)=0.90

Allocation ratio N2/N1=1

Output: Noncentrality parameter δ=3.0014083

Critical t=1.6838510

Sample size groups=7

Total sample size=35

Actual power=0.9040840]

## Conclusion

Within the limitations of the present study apart from the endodontic irrigation needle group, all of the tested methods could be used for obturation of primary teeth but not perfect and so new technologies and techniques are needed to improve primary root canal fillings.

**Ethics**

**Ethics Committee Approval:** The study was approved by the Ondokuz Mayıs University Human Research and Ethics Committee (approval no: 2014/682).

**Informed Consent:** Consent form was filled out by all participants.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: E.K., B.G., S.Ö., Concept: E.Ş.T., E.K., S.Ö., Design: E.Ş.T., E.K., Data Collection or Processing: S.Ö., E.K., Analysis or Interpretation: E.K., S.Ö., Literature Search: E.Ş.T., E.K., S.Ö., Writing: E.Ş.T., S.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Original Article / Özgün Araştırma

# Comparison of Hierarchical and Non-hierarchical Fuzzy Models with Simulation and an Application on Hypertension Data Set

## *Aşamalı ve Aşamalı Olmayan Bulanık Modellerin Simülasyon ve Hipertansiyon Veri Seti Üzerinde Bir Uygulama ile Karşılaştırılması*

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**Keywords**
Hierarchical, non-hierarchical, fuzzy model, classification, simulation, hypertension

**Anahtar Kelimeler**
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## Abstract

**Objective:** The aim of this study is to compare the classification performances of hierarchical and non-hierarchical fuzzy models built by using different membership functions.

**Materials and Methods:** In this study, normally distributed data sets containing different number of independent variables (p=3 and p=6) were generated. Besides, the classification performances of hierarchical and non-hierarchical fuzzy models built by using the data set which contained body mass index, fasting blood glucose and triglyceride values of hypertensive (n=206) and control (n=113) people were compared.

**Results:** It was found that there was a significant difference between the fuzzy models (p<0.001). According to the result of both simulation and hypertension data set application, non-hierarchical fuzzy models were found to have better classification performance than hierarchical fuzzy models according to sensitivity, specificity, accuracy and root mean square criteria. Moreover, when number of independent variables was increased, performances of the models increased too and approached to each other.

**Conclusion:** In fuzzy logic methods, data structure, distributions of the variables and correlation between them, how to divide independent variables into categories and which of the fuzzy logic methods is to choose should be examined by taking an expert support.

## Öz

**Amaç:** Bu çalışmanın amacı farklı üyelik fonksiyonları ile oluşturulan aşamalı ve aşamalı olmayan bulanık modellerin sınıflandırma performanslarının karşılaştırılmasıdır.

**Gereç ve Yöntemler:** Bu çalışmada farklı sayıda (p=3 ve p=6) bağımsız değişkenler içeren normal dağılıma uygunluk gösteren veri setleri türetildi. Ayrıca hipertansif (n=206) ve kontrol (n=113) bireylerine ilişkin beden kitle indeksi, açlık kan şekeri ve trigliserid değerlerini içeren veri seti kullanılarak oluşturulan aşamalı ve aşamalı olmayan bulanık modellerin sınıflandırma performansları karşılaştırıldı.

**Bulgular:** Bulanık modeller arasında ileri düzeyde farklılık olduğu bulundu (p<0,001). Hem simülasyon hem de hipertansiyon veri seti sonuçlarına göre, aşamalı

olmayan bulanık modellerin duyarlılık, özgüllük, doğruluk ve hata kareler ortalamasının karekökü kriterlerine göre aşamalı bulanık modellerden daha iyi sınıflandırma performansı gösterdiği tespit edildi. Bunun yanı sıra, bağımsız değişken sayısı artırıldığında modellerin performansları arttı ve birbirine yaklaştı.

**Sonuç:** Bulanık mantık yöntemlerinde veri yapısı, değişkenlerin dağılımı ve değişkenler arasındaki ilişki, bağımsız değişkenlerin kategorilere nasıl ayrılacağı ile hangi bulanık mantık yönteminin seçileceği uzman desteği alınarak irdelenmelidir.

### Introduction

In scientific researches, examined events are defined by mathematical models. The mathematical models that are formed enable to interpret in which state the examined event will be in time. Since the statistical events cannot be interpreted absolutely, the case of transition of events from one to another occurs. In the study of this kind of problems fuzzy logic approach may be used (1).

Fuzzy logic structure is developed by an article entitled "Fuzzy Sets" written by Zadeh (2). While classical logic is dichotomous as {0,1} and there is not any uncertainty; fuzzy logic enables the membership of an element to a fuzzy set to be any value in [0,1] interval. Human thought structure utilizes events with approximate terms such as "a few", "many", "more" instead of the crisp terms such as "present", "absent" (3,4). When viewed from this aspect, fuzzy logic represents the real world and human thought structure in a good way.

While non-hierarchical fuzzy models (NHFMs) are built by adding all independent variables to the model at the same time; HFMs are created by combining fuzzy sub-models having lower dimensions. In NHFM approach; as the number of independent variables increases, the number of rules that are used to make decision about dependent variable increases exponentially in knowledge base, which causes "curse of dimensionality" due to the fact that the number of adaptive parameters increases so much especially when there are too many independent variables (5). In order to overcome this problem, HFMs are suggested since the number of rules are linearly increases (5-8). The aim of this study is to compare the classification performances of HFMs and NHFMs using different membership functions.

## Materials and Methods

### Adaptive Neuro-fuzzy Inference System (ANFIS)

ANFIS is a non-hierarchical hybrid network structure which represents Sugeno fuzzy inference system (9-16). The rules of ANFIS structure are as follows (8,11,17-21):

Rule 1: If $X_1=A_1$ and $X_2=B_1$ then $\hat{Y}_1=f_1(X_1,X_2)=p_1X_1+q_1X_2+r_1$
Rule 2: If $X_1=A_1$ and $X_2=B_2$ then $\hat{Y}_2=f_2(X_1,X_2)=p_2X_1+q_2X_2+r_2$
Rule 3: If $X_1=A_2$ and $X_2=B_1$ then $\hat{Y}_3=f_3(X_1,X_2)=p_3X_1+q_3X_2+r_3$
Rule 4: If $X_1=A_2$ and $X_2=B_2$ then $\hat{Y}_4=f_4(X_1,X_2)=p_4X_1+q_4X_2+r_4$

ANFIS structure consists of 5 layers (Figure 1) (22-24):

**1st layer, fuzzification layer:** Each node in this layer is adaptive and outputs of the nodes consist of a membership degree depending on the membership function used and values of independent variables. The output $O_{1,i}$ of this node is calculated as follows:

$O_{1,i} = \mu_{Ai}(X_1)$, i = 1,2

$O_{1,i} = \mu_{Bi-2}(X_2)$, i = 3,4

To predict the parameters of this layer with the least error, backpropagation algorithm is used (9,25,26).

**2nd layer, rule layer:** None of the nodes in this layer is adaptive and they are expressed as Π. Each node corresponds to the rules written according to Sugeno fuzzy inference system and the number of them. Outputs of each rule nodes $O_{2,i}$ show rule weights calculated by (27,28):

$O_{2,i}=\mu_{Ai}(X_1) * \mu_{Bj}(X_2)$, i =1, j = 1,2

$O_{2,i}=\mu_{Ai}(X_1) * \mu_{Bj}(X_2)$, i =2, j = 1,2

**3rd layer, normalization layer:** All of the nodes in this layer are fixed. Each node gives normalized value of each rule (29,30):

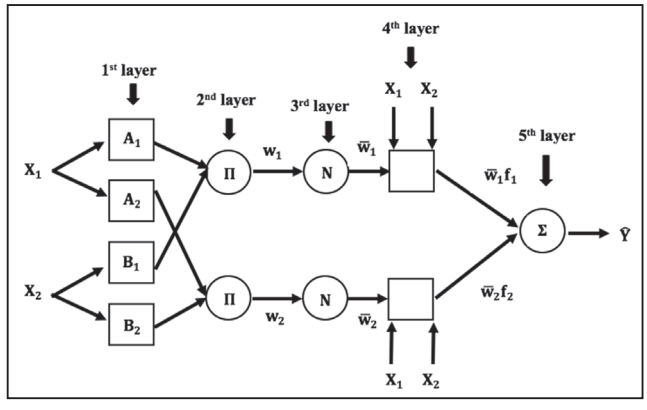


**Figure 1.** Adaptive neuro-fuzzy inference system structure

$$O_{3,i} = \bar{w}_i = \frac{w_i}{\sum_i w_i}, i = 1,2,3,4$$

**4th layer, weighting layer:** Each of the nodes $O_{4,i}$ in this layer, are adaptive and weighted output values of each rule are calculated. To predict the output parameters set $[p_i,q_i,r_i]$ of $i^{th}$ rule with minimum error, least squares estimation method is used (16,31):

$$O_{4,i} = \bar{w}_i f_i = \bar{w}_i(p_i X_1 + q_i X_2 + r_i), i = 1,2,3,4$$

**5th layer, aggregation layer:** There is only one node in this layer and the node is fixed. Outputs of weighting layer are gathered in this layer and the real value of ANFIS system is obtained (11,24):

$$\hat{Y} = O_{5,i} = \sum_i \bar{w}_i f_i = \frac{\sum_i w_i f_i}{\sum_i w_i}, i = 1,2,3,4$$

**Hierarchical Fuzzy Model Structure**

Use of NHFMs in complex and high dimensional systems causes curse of dimensionality problem. HFMs are suggested to overcome this (5,7).

The number of rules exponentially increases as the number of independent variables increases in NHFMs while it increases linearly in HFMs. Supposing that there are m independent variables and each of these variables has v membership functions, then the number of rules equals to $v^m$ in NHFMs while there are $[(m – 1) * v^2]$ rules in HFMs (6,7,32,33). Examining the HFM that has v fuzzy sets and m independent variables (Figure 2), it is seen that intermediate outputs ($U_1$,$U_2$,... $U_{m-2}$) and dependent variable $\hat{Y}= U_{m-1}$ are calculated by adding independent variables ($X_1$,$X_2$,...,$X_m$) to the model hierarchically.

**Simulation**

In simulation, normally distributed data sets were generated and the number of units was set to n=1000.

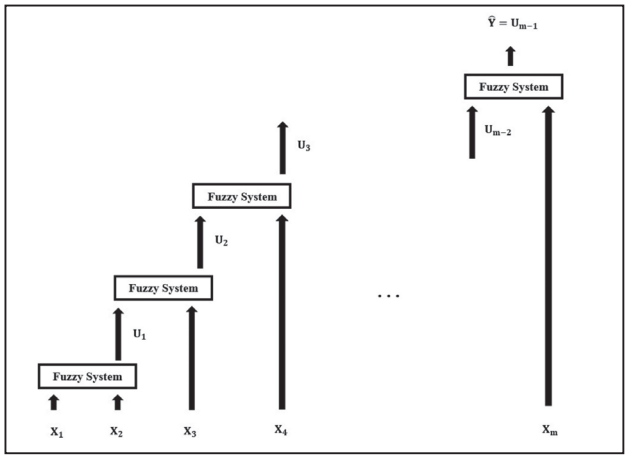


**Figure 2.** A hierarchical fuzzy model structure consisting of (m-1) fuzzy sub-models and m independent variables (32)

The data sets were randomly divided into 70% (700 units) training and 30% (300 units) test sets.

**Simulation with Three Independent Variables**

Independent variables were derived from normal distributions as being $X_1$~N(200,45), $X_2$~N(130,30), $X_3$~N(60,14) and correlated to one another ($r_{12}$=0.704, $r_{13}$ =0.553, $r_{23}$=0.372).

In training set, the most correlated independent variables $X_1$ and $X_2$ were added to a layer by creating a Sugeno fuzzy model (SFM) in both training and test sets, then intermediate output $U_1$ was obtained. After this, HFM was built by using $U_1$ and $X_3$. In this way, class prediction of dependent variable in test set was done.

When building NHFM, all the independent variables were used in ANFIS structure. Then the class prediction of dependent variable in test set was done running the created model.

**Simulation with Six Independent Variables**

Independent variables were generated as being $X_1$~N(150,35), $X_2$~N(110,25), $X_3$~N(130,30), $X_4$~N(100,15), $X_5$~N(85,20), $X_6$~N(50,10) and correlated to one another ($r_{min}$ =0,400 – $r_{max}$ = 0.900).

First, the most correlated independent variable pairs $X_1 – X_2$, $X_3 – X_4$ and $X_5 – X_6$ were layered and the intermediate outputs $U_1$, $U_2$ and $U_3$ of each layer were obtained both in training and test sets. By compounding intermediate outputs, the HFM was constructed and class prediction of dependent variable in test set was done.

**Table 1. Fuzzification of body mass index, triglyceride, fasting blood glucose and descriptive statistics (mean ± standard deviation) of sub-groups**

| Independent variables | Sub-groups | Mean ± SD | Min-Max |
|---|---|---|---|
| BMI (kg/m²) | Normal | 22.90±1.58 | 18.10-24.80 |
| | Overweight | 27.46±1.45 | 25-29.80 |
| | Obese | 32.36±1.92 | 30-37.10 |
| TG (g/dL) | Normal | 103.74±26.39 | 36-149 |
| | High at limit | 173.02±13.97 | 150-199 |
| | High | 269.29±69.93 | 200-478 |
| FBG (mg/dL) | Hypoglycaemia | 65.56±2.18 | 60-69 |
| | Normal | 88.5±10.75 | 70-110 |
| | Hyperglycaemia | 114.67±2.86 | 111-120 |

SD: Standard deviation, BMI: Body mass index, TG: Triglyceride, FBG: Fasting blood glucose, Min: Minimum, Max: Maximum

All independent variables were used in ANFIS structure to construct NHFM and classes of each unit were predicted.

**Hypertension Data Set**

In order to construct fuzzy models, the variables fasting blood glucose (FBG) (mg/dL), body mass index (BMI) (kg/m$^2$) and triglyceride (TG) (g/dL) which showed significant difference between hypertension and control groups, were correlated to each other and had fuzziness in their distributions were chosen as independent variables (34).

Each of the independent variables of hypertension data set was fuzzified by being divided into three subgroups. Mean ± standard deviation and minimum-maximum values (minimum-maximum) of each of the groups were calculated to predict fuzzy models (Table 1).

In the first step of hypertension data set application, data set was randomly separated into 70% (223 units) training and 30% (96 units) test sets. The correlation coefficients between independent variables were $r_{BMI–TG}$ = 0,842, $r_{TG–FBG}$ = 0.210 and $r_{BMI–FBG}$ = 0.113. In training set, SFM was constructed by using the most correlated variable pairs BMI-TG in the first layer of HFM. Then by using intermediate output $U_1$ of SFM and FBG as the independent variables of ANFIS structure, HFM was constructed.

In order to build NHFM structure, all the independent variables of training set and descriptive statistics (Table 1) of these variables were used in ANFIS structure.

Then classes of each unit of both training and test sets were predicted by adapting initial membership values of fuzzified variables to obtain minimum classification error.

## Results

**Simulation**

The results showed that there was a significant difference ($p<0.001$) between classification performances of NHFMs and HFMs based on sensitivity (%), specificity (%), accuracy (%) and root mean square error (RMSE) (%).

Comparison results of simulation with three independent (Table 2) and six independent (Table 3) variables showed that the sensitivity, specificity and accuracy rates of NHFMs were higher while RMSE was lower than HFMs in test set.

**Hypertension Data Set Application**

It was found in hypertension data set application that different membership functions resulted in different classification results. In test set, sensitivity (%), specificity (%) and accuracy (%) rates were higher and RMSE (%) was lower NHFMs than HFMs constructed by Gaussian membership function (Table 4).

Rule basis of hierarchical and NHFMs are as follows:

**Rule Base in Non-hierarchical Fuzzy Models**

**Rule 1:** If $BMI_{normal}$ and $TG_{normal}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$

**Rule 2:** If $BMI_{normal}$ and $TG_{normal}$ and $FBG_{normal}$ then $GROUP_{control}$

**Rule 3:** If $BMI_{normal}$ and $TG_{normal}$ and $FBG_{hyperglycaemia}$ then $GROUP_{control}$

**Rule 4:** If $BMI_{normal}$ and $TG_{high\ at\ limit}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$

**Rule 5:** If $BMI_{normal}$ and $TG_{high\ at\ limit}$ and $FBG_{normal}$ then $GROUP_{control}$

**Rule 6:** If $BMI_{normal}$ and $TG_{high\ at\ limit}$ and $FBG_{hyperglycaemia}$ then $GROUP_{control}$

**Rule 7:** If $BMI_{normal}$ and $TG_{high}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$

**Rule 8:** If $BMI_{normal}$ and $TG_{high}$ and $FBG_{normal}$ then $GROUP_{control}$

**Rule 9:** If $BMI_{normal}$ and $TG_{high}$ and $FBG_{hyperglycaemia}$ then $GROUP_{control}$

**Rule 10:** If $BMI_{overweight}$ and $TG_{normal}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$

**Rule 11:** If $BMI_{overweight}$ and $TG_{normal}$ and $FBG_{normal}$ then $GROUP_{control}$

**Rule 12:** If $BMI_{overweight}$ and $TG_{normal}$ and $FBG_{hyperglycaemia}$ then $GROUP_{control}$

**Rule 13:** If $BMI_{overweight}$ and $TG_{high\ at\ limit}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$

**Rule 14:** If $BMI_{overweight}$ and $TG_{high\ at\ limit}$ and $FBG_{normal}$ then $GROUP_{control}$

**Rule 15:** If $BMI_{overweight}$ and $TG_{high\ at\ limit}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$

**Rule 16:** If $BMI_{overweight}$ and $TG_{high}$ and $FBG_{hypoglycaemia}$ then $GROUP_{hypertension}$

**Rule 17:** If $BMI_{overweight}$ and $TG_{high}$ and $FBG_{normal}$ then $GROUP_{hypertension}$

**Rule 18:** If $BMI_{overweight}$ and $TG_{high}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$

**Rule 19:** If $BMI_{obese}$ and $TG_{normal}$ and $FBG_{hypoglycaemia}$ then $GROUP_{hypertension}$

**Rule 20:** If $BMI_{obese}$ and $TG_{normal}$ and $FBG_{normal}$ then $GROUP_{hypertension}$

**Rule 21:** If $BMI_{obese}$ and $TG_{normal}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$
**Rule 22:** If $BMI_{obese}$ and $TG_{high\ at\ limit}$ and $FBG_{hypoglycaemia}$ then then $GROUP_{hypertension}$
**Rule 23:** If $BMI_{obese}$ and $TG_{high\ at\ limit}$ and $FBG_{normal}$ then $GROUP_{hypertension}$
**Rule 24:** If $BMI_{obese}$ and $TG_{high\ at\ limit}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$
**Rule 25:** If $BMI_{obese}$ and $TG_{high}$ and $FBG_{hypoglycaemia}$ then $GROUP_{hypertension}$
**Rule 26:** If $BMI_{obese}$ and $TG_{high}$ and $FBG_{normal}$ then $GROUP_{hypertension}$

**Table 2. Descriptive statistics [median ($25^{th}$-$75^{th}$ percentiles)] of sensitivity, specificity, accuracy and root mean square error of hierarchical fuzzy models and non-hierarchical fuzzy models and their comparison results with three independent variables in test set**

| Function | Model | Sensitivity | Specificity | Accuracy | RMSE |
|---|---|---|---|---|---|
| Bell* | NHFM | 97.78 (96.15-98.66) | 97.45 (96.43-98.63) | 97.33 (96.67-98.00) | 16.33(14.14-18.26) |
| | HFM | 90.85 (88.96-92.93) | 90.57 (88.56-92.67) | 90.67 (89.33-92.00) | 30.55 (28.28-32.66) |
| Gauss* | NHFM | 98.04 (96.88-99.27) | 98.04 (96.91-99.26) | 98.00 (97.33-98.33) | 14.14 (12.91-16.33) |
| | HFM | 91.16 (89.14-93.06) | 90.85 (88.89-92.89) | 91.00 (89.67-92.00) | 30.00 (28.28-32.15) |
| Triangular* | NHFM | 98.11 (97.11-99.31) | 98.12 (97.08-99.31) | 98.00 (97.33-98.67) | 14.14 (11.55-16.33) |
| | HFM | 91.56 (89.64-93.38) | 91.29 (89.40-93.29) | 91.33 (90.33-92.67) | 29.44 (27.08-31.09) |
| Trapezoidal* | NHFM | 97.90 (96.56-98.70) | 97.90 (96.60-98.69) | 97.67 (97.00-98.33) | 15.28 (12.91-17.32) |
| | HFM | 90.88 (88.89-92.86) | 90.34 (88.31-92.59) | 90.67 (89.33-91.67) | 30.55 (28.87-32.66) |

*: p<0.001, RMSE: Root mean square error, HFM: Hierarchical fuzzy models, NHFM: Non-hierarchical fuzzy models

**Table 3. Descriptive statistics [median ($25^{th}$-$75^{th}$ percentiles)] of sensitivity, specificity, accuracy and root mean square error of hierarchical fuzzy models and non-hierarchical fuzzy models and their comparison results with six independent variables in test set**

| Function | Model | Sensitivity | Specificity | Accuracy | RMSE |
|---|---|---|---|---|---|
| Bell* | NHFM | 98.00 (97.01-98.70) | 98.04 (96.90-98.74) | 98.00 (97.33-98.33) | 14.14 (12.91-16.33) |
| | HFM | 95.24 (93.71-96.60) | 95.54 (94.00-96.75) | 95.33 (94.33-96.00) | 21.60 (20.00-23.80) |
| Gauss* | NHFM | 97.95 (96.86-98.70) | 97.97 (96.92-98.72) | 98.00 (97.00-98.33) | 14.14 (12.91-17.32) |
| | HFM | 95.74 (94.24-96.90) | 96.00 (94.63-97.18) | 95.67 (95.00-96.33) | 20.82 (19.15-22.36) |
| Triangular* | NHFM | 97.39 (96.13-98.58) | 97.40 (96.27-98.60) | 97.33 (96.67-98.00) | 16.33 (14.14-18.26) |
| | HFM | 96.05 (94.78-97.33) | 96.39 (95.12-97.44) | 96.33 (95.33-97.00) | 19.15 (17.32-21.60) |
| Trapezoidal* | NHFM | 97.93 (96.76-98.68) | 97.99 (96.97-98.71) | 97.67 (97.00-98.33) | 15.28 (12.91-17.32) |
| | HFM | 94.56 (92.74-96.15) | 95.10 (93.42-96.50) | 94.67 (93.67-95.67) | 23.09 (20.82-25.17) |

*: p<0.001, RMSE: Root mean square error, HFM: Hierarchical fuzzy models, NHFM: Non-hierarchical fuzzy models

**Table 4. Sensitivity, specificity, accuracy and root mean square error values of hierarchical fuzzy models and non-hierarchical fuzzy models in test set of hypertension data set**

| Function | Model | Sensitivity | Specificity | Accuracy | RMSE |
|---|---|---|---|---|---|
| Bell | NHFM | 91.53 | 27.03 | 66.67 | 57.74 |
| | HFM | 81.36 | 32.43 | 62.50 | 61.24 |
| Gauss | NHFM | 94.92 | 16.22 | 64.58 | 59.51 |
| | HFM | 94.92 | 10.81 | 62.50 | 61.24 |
| Triangular | NHFM | 84.75 | 35.14 | 65.63 | 58.63 |
| | HFM | 86.44 | 24.32 | 62.50 | 61.24 |
| Trapezoidal | NHFM | 93.22 | 29.73 | 68.75 | 55.90 |
| | HFM | 81.36 | 32.43 | 62.50 | 61.24 |

RMSE: Root mean square error, HFM: Hierarchical fuzzy models, NHFM: Non-hierarchical fuzzy models

**Rule 27:** If $BMI_{obese}$ and $TG_{high}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$

**Rule Base in Hierarchical Fuzzy Models**

$U_{1i}$ (i=1,2,3) is to be the $i^{th}$ sub-category of the intermediate output $U_1$ then rules of HFMs are as follows:

**Rule 1:** If $BMI_{normal}$ and $TG_{normal}$ then $U_{11}$
**Rule 2:** If $BMI_{normal}$ and $TG_{high\ at\ limit}$ then $U_{11}$
**Rule 3:** If $BMI_{normal}$ and $TG_{high}$ then $U_{11}$
**Rule 4:** If $BMI_{overweight}$ and $TG_{normal}$ then $U_{12}$
**Rule 5:** If $BMI_{overweight}$ and $TG_{high\ at\ limit}$ then $U_{12}$
**Rule 6:** If $BMI_{overweight}$ and $TG_{high}$ then $U_{12}$
**Rule 7:** If $BMI_{obese}$ and $TG_{normal}$ then $U_{13}$
**Rule 8:** If $BMI_{obese}$ and $TG_{high\ at\ limit}$ then $U_{13}$
**Rule 9:** If $BMI_{obese}$ and $TG_{high}$ then $U_{13}$
**Rule 10:** If $U_{11}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$
**Rule 11:** If $U_{11}$ and $FBG_{normal}$ then $GROUP_{control}$
**Rule 12:** If $U_{11}$ and $FBG_{hyperglycaemia}$ then $GROUP_{control}$
**Rule 13:** If $U_{12}$ and $FBG_{hypoglycaemia}$ then $GROUP_{control}$
**Rule 14:** If $U_{12}$ and $FBG_{normal}$ then $GROUP_{hypertension}$
**Rule 15:** If $U_{12}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$
**Rule 16:** If $U_{13}$ and $FBG_{hypoglycaemia}$ then $GROUP_{hypertension}$
**Rule 17:** If $U_{13}$ and $FBG_{normal}$ then $GROUP_{hypertension}$
**Rule 18:** If $U_{13}$ and $FBG_{hyperglycaemia}$ then $GROUP_{hypertension}$

## Discussion

There are a lot of researches on classification problems in which fuzzy models have been used. As being in many research fields, there are a lot of works on classification with fuzzy models built by health data sets in medicine literature too.

Resulting of examination of literature, it is seen that in most of the classification problems NHFMs are used. Karahoca et al. (22) aimed to compare the classification performances of non-hierarchical fuzzy logic and multinomial logistic regression methods by using age, waist/hip and glucose ratio variables. They divided 390-unit-data set into training (300 units) and test (90 units) sets. In order to build ANFIS structure they fuzzified age and glucose ratio variables that were crisp valued by dividing into three and five sub-categories, respectively. They reported that RMSE of assigning diabetic individuals into "hypoglycaemic", "hypoglycaemia at low risk", "healthy", "diabetes at low risk" or "diabetic" classes with NHFM was 17.45% while this value was found to be 23.43% in multinomial logistic regression. In this way, they determined that non-hierarchical fuzzy logic method made better classification than multinomial logistic regression method. Ankişhan and Ari (23) aimed to make snore-related sound classification by non-hierarchical fuzzy logic method. For this aim, they divided sounds which were normal and related to sleep apnea into pieces, then calculated the entropy and energy of those sounds as independent variables of the model. They reported that the ANFIS structure they created constituted 97.08% of the accuracy of allocating individuals to 'snoring', 'sleeping' or 'silent' classes. Mahmoudi et al. (31) aimed to compare the performances of the ANFIS structure in classification of individuals into cancer types using a total of six microchip gene expression data sets for breast, blood, colon, prostate, lung and lymphoma cancers and the performance of the support vector machine, k-nearest neighborhood and classification and regression trees methods. They found that the highest classification performance among the models they created separately for all cancer data sets was mostly due to the non-hierarchical fuzzy logic method. In another study, Uçar et al. (24) aimed to use a shorter data mining method as an alternative to the medical diagnostic test for the diagnosis of tuberculosis disease and stated that they preferred ANFIS to estimate in what probability individuals carry the bacterial cause of tuberculosis in their body. They classified dependent variables as 0, 0.25, 0.50, 0.75 or 1.00 probability classes for this and reported that 97% of the classification success of the NHFM using the 20 most important variables among the 30 risk factors of the disease was found. Yang et al. (35) performed a classification study on brain signals, a total of 200 brain signals were recorded from electrical status epilepticus in sleep (ESES) patients and control subjects in 8-second segments with a 16-channel electroencephalogram device. In the study where each channel was used as an independent variable, two different entropies were calculated from 8-second segments and two NHFMs were constructed by building ANFIS structure. With these models created by using bell membership function, the individuals were divided into ESES or control classes with 89% and 82% accuracy respectively. Ziasabounchi and Askerzade (16) aimed to classify individuals with a NHFM using the Gaussian membership function according to their degrees of having cardiac disease. They selected age, chest pain

type, cholesterol, maximum heart rate, resting blood pressure, glucose and electrocardiographic variables among independent variables in the Cleveland heart disease data set from the University of California artificial intelligence database, which consists of 303 units and 13 independent variables. In the fuzzification step of the HFM, they divided age, blood pressures at rest, cholesterol variables into three; and the maximum heart rate into two sub-categories. They then divided the data set into 80% (243 units) training and 20% (60 units) test data and reported that they classified the test data set with 15% error and 92.3% accuracy with the classification model built in training set with 1% error. In our study, by using simulation and hypertension data set and different membership functions, HFMs as well as NHFMs were created and the classification performances of these models were compared according to sensitivity, specificity, accuracy, and RMSE criteria. By this comparison, it was found that NHFMs were better than HFMs.

In cases where the number of independent variables is large, hierarchical fuzzy logic method is proposed, which is achieved by combining smaller sized fuzzy sub-models. Since in the process of constructing fuzzy model with the best classification; the number of parameters that need to be adapted in the most appropriate way, which is also called the "dimension problem", increases as the number of independent variables increases. This causes both parameter complexity and time loss in the classification phase in the fuzzy inference process (5-8).

There are not many studies that use HFMs in the health field. Akbarzadeh-T and Moshtagh-Khorasani (36) conducted a test which was consisted of thirty questions and measured the ability of repeating the sentences, comprehending and matching names, written language qualification of 265 individuals who were aphasic. Because of the large number of independent variables, they pointed out that they aimed to classify aphasia species with an HFM. From the thirty independent variables in the first layer of the HFM, they constructed a fuzzy model with four rules using six interrelated variables that best described disease types, on the other hand; in the second layer using the outputs of the first layer and the four independent variables that they chose among thirty independent variables they created the second fuzzy model and classified aphasia types with 92% accuracy. Amouzadi and Mirzaei (37) aimed to build HFM to make classification of the data sets whose dependent variables were categorical by using "breast cancer" data set which consisting of nine independent variables with 699 units; "pima" data set containing eight independent variables with 768 units, "wine" data set with thirteen independent variables and 178 units, "haberman" data set with three independent variables and 306 units and lastly "iris" data set with four independent variables with 150 units.

They reported that they preferred the hierarchical fuzzy logic method as the classification method in order to avoid the curse of dimensionality caused by a large number of independent variables and the length of the classification process time. They used as many layers as sub-categories that each independent variables had in the study and divided the membership functions they used in each layer into two to form the rule base. At the end of the study, they reported that they achieved a correct classification of 96% in the "breast cancer" data set, 76% in the "pima" data set, 95% in the "wine" data set, 77% in the "haberman" data set and 95% in the "iris" data set. Shaeiri and Ghaderi (38) aimed to classify patients into types of cancers using gene expression data sets for blood, prostate and colon cancers. In order to do this, they first divided the cancer data set which consisted of 7129 genes of 72 patients into training (38 units) and test (34 units) sets and then classified patients in test data set into "acute myeloblastic leukemia" or "acute myeloid leukemia" classes with accuracy of 100%; in addition to this, they used prostat data set which consisted of 12600 genes of 102 patients and classified patients into "tumor" or "normal" classes with 99.21% accuracy. They also reported that they had 98.84% accuracy of classification of patients into "normal" or "tumor" classes by creating a fuzzy model from the data set which contained 2000 genes of 62 units after dividing it into training and test sets. In our study, the effect of the number of independent variables used in both HFMs and NHFMs on the classification performance of the model was examined. For this purpose, it was observed that the performance of the classification of the model increases with the increase of the number of independent variables as a result of simulation using three and six independent variables. In addition, the classification performances of the models were found to approximate each

other. However, with the increase in the number of independent variables, it was observed that the rule base expanded in both models. In simulation, when the number of independent variables increased from 3 to 6; the number of rules increased accordingly from 8 to 64 in NHFM; from 8 to 27 in HFM. In hypertension data set application, 18 rules were obtained in HFM while this number was 27 in NHFM. As a result of the analyses, it was determined that the classification performances of the fuzzy models depend on the distribution of data, the number of sub-categories of each of the independent variables has, the type of membership function to be used, the number of the independent variables to be modelled and correlation between them. Accordingly, histogram graphs of independent variables should be used in the fuzzification step. In cases where the distributions are highly intertwined, the model should be further refined by increasing the number of sub-categories, and the fuzziness should be tried to be eliminated. The extent to which fuzziness is eliminated should be determined from the overlapping regions in the drawn membership function graphs, and a model should be created using the membership function that gives the most appropriate result. Moreover, if the number of independent variables is too large, the variables associated with each other should be included in the same layer, then these layers must be combined to form an HFM. However, loss of information in transitions between layers of HFMs is a limitation of this method. It is predicted that increasing the number of independent variables and modelling the independent variables with high correlation level can prevent the loss of information due to the layers and thus the classification performance of the model will be better.

## Conclusion

Health data contain many factors that cause diseases. When the diagnosis of a disease is made, which sub-category the values of the factors that cause diseases belong is and the interaction between the sub-categories are important. In this kind of data structures, fuzzy logic methods should be used, which is a method that allows the estimation of the output values by using the factors whose categories are transitive and the interactions of sub-categories of them. Particularly in data sets with large number of factors, HFM which allows the creation of smaller rule base by gathering highly correlated factors into the same layer should be used. In cases that the inference of which sub-categories of the factors interacted to each other are important for classification of the individuals as patient or control, then a NHFM should be used. It should be noted, however, that the number of factors or the number of sub-categories of them should be chosen so as not to constitute an extremely large rule base.

**Ethics**

**Ethics Committee Approval:** It was not taken.

**Informed Consent:** It was not taken.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Concept: İ.K.Ö., M.T., Design: F.C., İ.K.Ö., M.T., Data Collection or Processing: F.C., İ.K.Ö., Analysis or Interpretation: F.C., İ.K.Ö., M.T., Literature Search: F.C., Writing: F.C., İ.K.Ö.

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Original Article / Özgün Araştırma

# Evaluation of Complications Following Impacted Mandibular Third Molar Extraction in Patients with Different Hand Preference

## *Farklı El Tercihi Olan Hastalarda Mandibular Gömülü Üçüncü Molar Çekim Sonrası Oluşan Komplikasyonların Değerlendirilmesi*

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**Anahtar Kelimeler**
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### Abstract

**Objective:** Individual preference of using right or left hand for doing various hand workings, is the most easily observable form of the cerebral lateralization. It was stated that, among the right or left hand dominant individuals, there is an immunological asymetry, and a difference in motor control, visuospatial skills, and in the incidence of a number of disease. The aim of the study was to investigate pain, edema, trismus following the mandibular third molar extraction in patients with different hand preference.

**Materials and Methods:** Forty-three patients who were indicated for bilateral surgical extraction of impacted mandibular third molars were included in the study. The interval between the extraction of the right and left molars of the patient was 30 days. The patients were divided into four groups; 1) left handed-right (right third molar), 2) left handed-left, 3) right handed-right, and 4) right handed-left. Measurements were made for comparison of pain, edema and trismus before and after operation.

**Results:** The statistical significance was not observed between the groups regarding the pain, edema and trismus ($p>0.05$).

**Conclusion:** The results suggest that severity of pain, edema and trismus may not be related to the hand preference following the right and left mandibular third molar extraction. Extended studies demonstrating an extent of an influence of hand preference in the complications of oral surgery, could be useful for planning the surgical interventions as well as for treatment results in maxillofacial surgery.

### Öz

**Amaç:** Bireyin çeşitli el işlerini yapmak için sağ veya sol elini tercih etmesi serebral lateralizasyonun en kolay gözlenebilen şeklidir. Sağ veya sol eli dominant olan kişiler arasında motor kontrol, vizyospasyal görevleri yerine getirmede, çeşitli hastalıkların görülme insidansında farklılıklar ve immün asimetri olduğu söylenmiştir. Bu çalışmada, mandibular 3. molar çekimini takiben görülen ağrı, ödem, trismusun el tercihi farklı olan hastalarda değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntemler:** Çalışmaya, sağ ve sol mandibular gömülü 3. molar dişlerin çekiminin gerekli olduğu 43 hasta dahil edildi. Aynı hastadan sağ ve sol mandibular gömülü diş çekimi 30 gün arayla yapıldı. Dört hasta grubu oluşturuldu: 1) el tercihi sol-sağ (sağ mandibular 3. molar dişi çekilen), 2) el tercihi sol-sol, 3) el tercihi sağ-sağ, 4) el tercihi sağ-sol. Ağrı, ödem ve trismusun operasyondan önce ve sonra karşılaştırılması için ölçümler yapıldı.
**Bulgular:** Gruplar arasında ağrı, ödem, trismus açısından istatistiksel bir fark görülmedi (p>0,05).
**Sonuç:** Sonuçlar, sağ ve sol mandibular üçüncü molar ekstraksiyonu sonrası ağrı, ödem ve trismus şiddetinin el tercihi ile ilişkili olmayabileceğini düşündürmektedir. Fonksiyonel serebral lateralizasyon olan el tercihinin oral cerrahi komplikasyonlarında ne kadar etkin olduğunu ortaya çıkaracak daha kapsamlı araştırmaların gerek maksillofasiyal cerrahi girişimlerinin planlanmasında gerekse tedavi sonuçlarında faydalı olabileceği kanaatine varılmıştır.

## Introduction

Extraction of impacted mandibular third molars is among the commonly performed procedures in oral surgery. Complications such as pain, edema, and trismus may occur after extraction. The severity of these complications depends on how embedded the extracted tooth is, its anatomical position, its adjacencies, and gum inflammation, in addition to the patient's systemic diseases, pre-and postoperative oral hygiene, and immune resistance (1-5).

Hand preference is defined as choosing the right or left hand to perform various manual tasks such as writing and using a fork and knife. Cerebral lateralization is the anatomical and functional differentiation between the right and left hemispheres of the brain. The right and left hemispheres have separate functions, and the dominant hemisphere performs these functions better than the other (6-9). There is a direct relationship between hand preference and right- or left-hemisphere dominance. Hand preference is functional cerebral lateralization and is the most easily observed manifestation of cerebral lateralization (8,9). Studies have revealed differences in motor control, performance of visuospatial tasks, and the incidence of various diseases between right-handed and left-handed individuals (10-12).

Several studies have evaluated the complications that occur following impacted mandibular third molar extraction in different patient groups (13,14). In this study, complications of impacted mandibular third molar extraction, such as pain, edema, and trismus, were compared in patients with different hand preferences.

## Materials and Methods

A total of 43 patients between 17 and 43 years old with a mean age of 21.6 years were included in the study. The group comprised 11 (25.5%) males and 32 (74.4%) females. All patients included in the study required extraction of both left and right mandibular third molars [class 2, position B, vertically impacted according to the Pell and Gregory Classification System (15)] with bone removal. Patients who were pregnant or had systemic disease, smoking habit, allergy to any of the drugs to be used postoperatively, history of antibiotic or analgesic use in the last month, or infection, acute pericoronitis, and severe periodontal disease at the operation site were not included.

All patients were informed about the surgical procedure and possible complications. The study protocol was reviewed and approved by the Recep Tayyip Erdoğan University Faculty of Medicine Clinical Research Ethics Committee (meeting date: 23.10.2015, decree no: 37). Panoramic radiographies of all patients were obtained preoperatively. Each patient's name, age, gender, and the classification of impacted teeth were recorded in a patient follow-up form. Patients provided informed consent by signing a volunteer consent form which including brief information about the study.

The procedures were performed under mandibular and buccal local anesthesia. Following an L-type incision, a full-thickness flap was lifted. The bone tissue around the tooth was removed under flow of a physiological saline solution. Also, after extraction of the tooth, the cavity was irrigated with physiological saline solution. The wound was closed with a primary 3-0 silk suture. All the extractions were done by the same surgeon. Forty-three patients with different hand preferences whose impacted mandibular right and left third molars needed to be extracted were included in the study. Eleven of the patients were left-handed and 32 were right-handed. For data analysis, 4 groups were created: 1) Left hand preference-right extraction (n=11); 2) Left hand preference-left extraction (n=11); 3) Right hand preference-right

extraction (n=32); 4) Right hand preference-left extraction (n=32). For all patients, there was a 30-day interval between extractions of the right and left impacted mandibular third molars, and a total of 86 teeth were extracted.

An antibiotic (amoxicillin 500 mg twice daily), analgesic (paracetamol 500 mg 3 times daily), and mouthwash (2% chlorhexidine gluconate 3 times daily) were prescribed postoperatively. Patients were advised by a physician postoperatively to not eat or drink for 2 hours after surgery, to avoid hot food and drinks within the first 24 hours, to not chew with the area involved in the operation, to eat soft and warm foods, to brush normally in the unoperated areas, to avoid touching the teeth, stitches, and gums in the surgery area while brushing, to use the prescribed mouthwash twice a day, after brushing their teeth in the morning and evening, and to not eat or drink anything for 1 hour after using the mouthwash. For all patients, sutures were removed on the 7th postoperative day.

**Collection of Data Before and After Extraction**

The visual analogue scale (VAS) was used to assess pain in the study. VAS scores (0-10 points) were evaluated at postoperative 2, 6, and 12 hours and 2, 4, and 7 days.

We modified the method described by Schultze-Mosgau et al. (16) to assess edema in the jaw and the face: 6 fixed points and 5 surgical baselines were marked on the patient's face while the mouth was closed, and the distances between the points were measured using a string. Measurements were made immediately before surgery and at 2nd and 7th days postoperatively. The sum of all measurements was taken as face size. The amount of edema at 2nd and 7th days was calculated for each patient by subtracting the preoperative face size (sum of preoperative facial measurements) from the postoperative face size (sums of facial measurements taken at postoperative 2 and 7 days, respectively).

To evaluate trismus, the distance between the lower and upper right central teeth were measured using a millimetric ruler before the surgery and at 2nd and 7th days after surgery. The difference between preoperative and postoperative measurements was recorded as the amount of trismus on the given day.

Hand preference was determined using the Edinburgh Handedness Inventory (8). Those with handedness scores lower than zero were considered as left-handed and those with scores higher than zero were considered right-handed.

**Statistical Analysis**

The Mann-Whitney U and Wilcoxon tests were used for statistical analysis of the data. P value of less than 0.05 was considered statistically significant.

## Results

According to VAS scores, all patients had similar high levels of pain at 2 hours, 6 hours, and 2 days after extraction. VAS scores decreased at 4 days and were lowest on day 7. There was no statistically significant difference between groups in terms of postoperative VAS values ($p>0.05$).

There was no statistically significant difference ($p>0.05$) between groups when postoperative 2 and 7 day edema and trismus values were compared.

## Discussion

Pain, edema, and trismus after the extraction of impacted third molars are expected outcomes and these complications adversely affect the daily life of patients (17-19). Many studies have suggested that corticosteroids, different anesthetics, pain killers, and anti-inflammatory drugs may reduce the severity of these complications (20,21). It has been claimed that post-extraction pain reaches maximum intensity within 2-4 hours or, according to some studies, within 12 hours, and that the pain level decreases on postoperative day 6 (17-21). We did not find any studies on oral surgery in patients with different hand preferences in the literature. In our study, we found that pain was high in all groups at 2 hours, 6 hours, and 2 days after extraction, decreased on day 4, and reached its lowest level on day 7. There was no statistically significant difference between the groups in terms of VAS scores ($p>0.05$). Furthermore, there was no statistical difference in the VAS values after impacted right and left mandibular third molar tooth extraction, regardless of hand preference. In their study on cerebral lateralization, Pauli et al. (22) stated that right hemisphere hyperactivity causes increased pain sensitivity and that pain sensitivity may vary according to hemisphere dominance. The level of pain after the removal of an impacted tooth may vary from patient to patient. Therefore,

we conducted our study in patients undergoing extraction of symmetrical impacted third molars with similar difficulty level to allow the comparison of postoperative pain on both sides in the same patients. Our study group also included patients with different hand preference. As hand preference known to be a functional cerebral lateralization, we concluded that cerebral lateralization does not create a difference in terms of pain intensity after impacted mandibular third molar extraction.

Pain is one of the most important causes of trismus after mandibular third molar extraction. Other causes of trismus include postoperative edema, inflammation, hematoma, muscle and tendon trauma, and psychological components (19-21). Trismus reaches its maximum level 2 days after extraction and may last for 7-10 days (21). It has been claimed that the duration and severity of this complication varies from patient to patient (17-21). In our study, there was no statistically significant difference between groups when the levels of trismus at postoperative 2 and 7 days were compared. We observed that trismus was severe on day 2 in all groups and decreased on day 7, consistent with the results of other studies in the literature (17-21) Similarly, no statistically significant difference was found between groups in edema at postoperative 2 and 7 days.

Severe trismus can cause secondary infection by making the maintenance of oral hygiene difficult after extraction, thus increasing the development of postoperative complications (23). Moreover, poor oral hygiene after extraction can also increase the severity of trismus. The superiority of right- or left-handed patients in maintaining oral hygiene is a subject of debate. In a study of patients with different hand preferences, it was reported that right-handed patients practiced better oral hygiene and had a lower incidence of decay compared to left-handed patients (24). There are also studies that state the opposite (25-27). Herrmann and van Dyke (28) found that left-handed subjects were faster than the right-handed subjects in evaluating the same or different sensory patterns presented in various orientations. Studies have focused on the possibility that patient motivation, manual dexterity, and tooth brushing efficiency may differ in right-handed and left-handed individuals and, therefore, have lead to differing conclusions regarding whether postoperative inflammation and the maintenance of oral hygiene are associated with handedness (29).

There are also studies in the literature showing that there is a relationship between hand preference and various diseases. Type 2 diabetes and autoimmune and inflammatory diseases are some of the diseases whose incidence differs between right- and left-handed individuals (30,31). Some studies have reported that the immune system is stronger on the left side of the body and in left-handed people (32-34). There is a direct relationship between the immune system and inflammation. The mediators released during inflammation target immune and inflammatory cells (35). The severity of complications such as pain, edema, and trismus after extraction is affected by the severity of inflammation at the site of extraction (19-21). Severe inflammation may increase the development of complications after extraction (19-21). In our study, there was no statistical difference in the pain, edema, and trismus values after extraction between the right-handed groups 3 and 4 and the left-handed groups 1 and 2, suggesting that there was also no difference in inflammation in the extraction areas. Recent studies have focused on whether the number, size, and ultrastructural features of lymph nodes on the left and right sides of the body are different in individuals with different hand preferences (36-38).

One study stated that cerebral lateralization influences facial structure, with the right craniofacial region being larger than the left in right-handed people, and the left craniofacial region being larger than the right in left-handed people (39). The authors of another study emphasized that facial asymmetry was less pronounced in left-handed individuals compared to right-handed individuals (40). Research is also being conducted on whether this asymmetry influences chewing strength and whether there is a right or left chewing side preference in individuals with different hand preferences (41).

## Conclusion

Our results show that the severity of complications such as pain, edema, and trismus that occur after mandibular third molar extraction may not be related to hand preference. There was no statistically significant difference in pain, edema, and trismus severity after impacted mandibular right and left third molar extraction between patients with different hand

preferences. More extensive research elucidating the impact of hand preference, which is a functional measure of cerebral lateralization, on oral surgery complications may be beneficial both in the planning of maxillofacial surgical interventions and in achieving favorable treatment outcomes.

**Ethics**

**Ethics Committee Approval:** The study protocol was reviewed and approved by the Recep Tayyip Erdoğan University Faculty of Medicine, Clinical Research Ethics Committee (meeting date: 23.10.2015, decree no. 37).

**Informed Consent:** Informed consent was obtained from all patients.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: U.K.A., Concept: U.K.A., Design: U.K.A., Data Collection or Processing: U.K.A., N.K., Analysis or Interpretation: U.K.A., Literature Search: U.K.A., N.K., Writing: U.K.A.

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Original Article / Özgün Araştırma

# Effects of Polishing on Color Stability and Surface Roughness of CAD-CAM Ceramics

## *Polisajın CAD-CAM Seramiklerin Renk Stabilitesi ve Yüzey Pürüzlülüğüne Etkileri*

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**Keywords**
Color stability, surface roughness, polishing, CAD-CAM ceramic

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## Abstract

**Objective:** The purpose of this study is to determine the effects of polishing techniques on color stability and surface roughness of lithium disilicate glass ceramic (LDC) and zirconia-reinforced lithium silicate ceramic (ZLS).

**Materials and Methods:** Two hundred forty disks of LDC and ZLS were prepared. Glazing with the ceramics' own glazing procedure, a series of sof-lex polishing discs and abrasive stones were used as the different polishing groups. Color differences (ΔE*) was evaluated by spectrophotometer, initial and after 48 hours of immersion in various solutions (n=10). Surface roughness (Ra) was evaluated by profilometer (n=10). Data were analyzed by Two-Way ANOVA, and Mann-Whitney U test.

**Results:** No significant difference in ΔE* values was observed between the sof-lex groups and abrasive stone groups ($p>0.05$) on LDC. ΔE* values were significantly different with glazed, and abrasive stone groups than sof-lex groups ($p<0.05$) on ZLS. Within the staining solutions for LDC specimens decreasing ΔE* values were observed in coffee to coke, and then tea and water. However, within the staining solutions for ZLS specimens the highest ΔE* values were observed in coffee, and then equal ΔE* values in coke and tea and the lowest ΔE* values were observed in water. Within the CAD-CAM ceramic materials ΔE* values of ZLS specimens were higher than LDC specimens ($p<0.05$). Both of ZLS and LDC specimens, the lowest Ra values were observed in glazing groups, which were not statistically different from each other ($p>0.05$). The highest Ra value in ZLS was observed in group sof-lex. No significant difference was observed among group abrasive stone and sof-lex in LDC specimens ($p>0.05$).

**Conclusion:** The amount of staining in the polished ZLS samples was more than the LDC samples. The coffee was determined as the most colorant solution. Abrasive stone may be used instead of sof-lex for polishing of LDC specimens.

## Öz

**Amaç:** Bu çalışmanın amacı, polisaj tekniklerinin lityum disilikat cam seramik (LDC) ve zirkonya ile güçlendirilmiş lityum silikat seramiklerin (ZLS) renk stabilitesi ve yüzey pürüzlülüğüne etkilerini belirlemektir.

**Gereç ve Yöntemler:** LDC ve ZLS'den 240 disk hazırlanmıştır. Farklı polisaj grupları olarak seramiklerin kendi glaze prosedürü, sof-lex polisaj diskleri ve aşındırıcı taşlar kullanılmıştır. Renk farklılıkları (ΔE*), 48 saat çeşitli solüsyonlarda bekletilme öncesinde ve sonra spektrofotometre ile değerlendirilmiştir (n=10). Yüzey

pürüzlülüğü (Ra) profilometre ile değerlendirilmiştir (n=10). Veriler çift-yönlü ANOVA ve Mann-Whitney U testi ile analiz edilmiştir.
**Bulgular:** LDC için sof-lex grupları ve aşındırıcı taş gruplarının ΔE* değerleri arasında anlamlı fark bulunmamıştır (p>0,05). ZLS için gleyz ve aşındırıcı taş gruplarının ΔE* değerleri sof-lex gruplarından anlamlı fark göstermiştir (p<0,05). Boyayıcı solüsyonlar arasında LDC örnekler için kahveden kola, çay ve suya doğru azalan ΔE* değerleri gözlenmiştir. Bununla birlikte boyayıcı solüsyonlar arasında ZLS örnekler için en yüksek ΔE* değerleri kahvede, ardından eşit ΔE* değerleri kola ve çayda ve en düşük ΔE* değerleri ise suda gözlenmiştir. CAD-CAM seramik materyalleri arasında ise ZLS örneklerin ΔE* değerleri LDC örneklerden daha fazladır (p<0,05). ZLS ve LDC örneklerin her ikisi için de en düşük Ra değerleri gleyz gruplarında gözlenmiş olup istatistiksel olarak birbirinden farklı değildir (p>0,05). ZLS için en yüksek Ra değeri sof-lex grubunda gözlenmiştir. LDC örnekler için aşındırıcı taş ve sof-lex grupları arasında önemli fark gözlenmemiştir (p>0,05).
**Sonuç:** Polisaj yapılmış ZLS örneklerdeki boyanma miktarı LDC örneklerden fazla bulunmuştur. Kahve en boyayıcı solüsyon olarak tespit edilmiştir. LDC örneklerin polisajında aşındırıcı taş, sof-lex yerine kullanılabilir.

## Introduction

High-performance restorative materials are able to obtain with industrially produced CAD-CAM blocks. Besides excellent esthetic properties with good polishing characteristic and high refiring stability industrially produced and secondary milled materials are more homogeneity in comparison with hand-built materials. Today, industrially produced CAD-CAM materials are recognized as high reliable materials. IPS e.max CAD (Ivoclar, Vivadent, Liechtenstein) is the lithium disilicate glass ceramic (LDC) block which has been designed for CAD-CAM technique and is indicated veneers to twelve-unit bridges with its high strength. Also, high translucent blocks especially are used with ceramic inlay and onlay restorations exhibit a chameleon effect in oral environment. Vita suprinity (Vita Zahnfabrik, Germany) glass ceramic is the first zirconia-reinforced lithium silicate ceramic (ZLS) which is fortified with zirconia (approximately 10% by weight) to provide superior durability. Moreover ZLS was adopted glass ceramic properties aesthetically.

The surface texture of dental restorative material is very important because of longevity and aesthetics. When the surface texture is irregular, many negative effects occur of such as loss of esthetic qualities, wear of the occlusal surface of tooth on the opposite arch, decrease of strength of restoration material (1-5). Smooth surfaces do not mean perfect aesthetically but can be mean that more suitable biologically. Moreover, both of the wear of the tooth on the opposite arch can be minimum level and longevity of restoration can be prolonged (1,2,6,7).

Glaze surfaces may deformate during contour adjustments of the restoration's surfaces. Due to clinical adjustments of the ceramic restoration, some aesthetic problems may occur with patients' visual perception. Intraoral finishing and polishing sets can be used alternatively that have sufficient properties to obtain clinically acceptable surface roughness (6,7).

Furthermore, staining of the ceramic restorations with colorant inside the frequently consumed drinks requires extra efforts from the clinicians. Several studies are avaliable on the efficiency of various polishing techniques instead of glazing about color stability (2-4).

The aim of this *in vitro* study was to investigate the effects of staining solutions and different polishing techniques on color stability and surface roughness of CAD-CAM ceramics. The null hypotheses of the study were that various staining solutions and polishing techniques would be not correlated with the stainability and surface roughness of CAD-CAM ceramics.

## Materials and Methods

LDC and ZLS materials used in the study are listed in Table 1. Specimens were obtained with cutting of the high translucent-CAD/CAM blocks with 1.2-mm-thick, and 14-mm-diameter specimens at low speed (150 rpm) in a precision saw machine (Micracut 201, Bursa, Turkey). A2-color were chosen for all of the specimens in accordance with the scale of Vitapan Classical shade guide (Vita Zahnfabrik, Germany).

Twelve groups consisting of 10 specimens were created for both LDC and ZLS (totally 240) as listed in Table 2. Distilled water served as the control group in groups I1a, I2a, I3a, S1a, S2a and S3a. The LDC and ZLS specimens were roughened on both sides with a fine diamond instrument (Dega Medical Instrument, Wanchai Hong Kong) for smoothing out the surface structure created by the CAD/CAM procedure before glazing. Staining and glazing were made with IPS e.max CAD Stains (Ivoclar, Vivadent, Liechtenstein), IPS e.max CAD Glaze Paste and Liquid

(Ivoclar, Vivadent, Liechtenstein) in one step to the manufacturer's recommendations in LDC groups I1a, I1b, I1c, I1d. ZLS specimens were made stains and glaze firing with Vita Akzent Plus effect stains (Vita Zahnfabrik, Germany) and Vita Akzent Plus powder materials (Vita Zahnfabrik, Germany) following the manufacturer's recommendations in S1a, S1b, S1c and S1d. The specimens in the I2a, I2b, I2c, I2d, S2a, S2b, S2c and S2d groups were polished with a series of 12.7-mm-diameter sof-lex polishing discs (3M Espe, MN, USA) on an hand piece set at a speed of 10.000 rpm for coarse and medium discs, and 30.000 rpm for fine and superfine discs, according to the manufacturers' instructions. The specimens were polished with a low-speed hand piece at 10.000 rpm with an abrasive stone (Dura Green Stones; Shofu Inc, Kyoto, Japan) and with coarse silicon carbide polisher (Ceramaster Coarse; Shofu Inc, Kyoto, Japan), and silicon carbide polisher (Ceramaster; Shofu Inc, Kyoto, Japan) in the groups I3a, I3b, I3c, I3d, S3a, S3b, S3c and S3d. Both sides of the specimens were polished with a low-speed rotating hand piece (Kavo Ewl 4990; KaVo Dental Gmbh, Germany). Allpolishing process were conducted by the same investigator.

All the specimens were ultrasonically cleaned in deionized water (Pro-Sonic 600; Sultan Healthcare, NJ, USA) for ten minutes and then dried with compressed air. Also thickness of the specimens were controlled with a digital caliper (Absolute Digimatic, Mitutoyo, Japan).

Mean surface roughness (Ra) of the specimens were analyzed by a tactile profilometer (Taylor Hobson Surtronic 25, Leicester, UK) initially and after polishing with a 0,25 mm cut-off value. The constant measuring speed of 0.5 mm/sec was used to determine an average roughness profile (Ra) in µm. The profilometer calibrated before measurements of each group (n=10). All surface roughness records were made at the sample center.. For each specimen, three measurements were made and the mean was obtained as the parameter Ra. When the Ra value falls, the surface becomes smoother.

Baseline color measurements were performed with a clinical spectrophotometer (Vita Easy Shade Advance, Vita Zahnfabrik, Germany) using CIE L*a*b* and recorded before exposure to the staining solution. All measurements were performed onto the white, black and neutral gray surfaces under

**Table 1. Materials tested**

| Material | Code | Composition | Translucency/shade | Lot no. | Manufacturer |
|---|---|---|---|---|---|
| IPS e.max CAD | LDC | Lithium disilicate glass ceramic | HT/A2 | S50172 | Ivoclar Vivadent |
| Suprinity | ZLS | Zirconia reinforced lithium disilicate ceramic | HT/A2 | 45000 | Vita Zahnfabrik |

LDC: Lithium disilicate glass ceramic, ZLS: Zirconia-reinforced lithium silicate ceramic

**Table 2. Materials, surface finishing and groups**

| Materials | Surface finishing and groups | | | |
|---|---|---|---|---|
| LDC IPS e-max CAD (I) | Glaze+water I1a | Glaze+coke I1b | Glaze+tea I1c | Glaze+coffee I1d |
| | Sof-lex+water I2a | Sof-lex+coke I2b | Sof-lex+tea I2c | Sof-lex+coffee I2d |
| | Abrasive stone+water I3a | Abrasive stone+coke I3b | Abrasive stone+tea I3c | Abrasive stone+coffee I3d |
| ZLS Suprinity (S) | Glaze+water S1a | Glaze+coke S1b | Glaze+tea S1c | Glaze+coffee S1d |
| | Sof-lex+water S2a | Sof-lex+coke S2b | Sof-lex+tea S2c | Sof-lex+coffee S2d |
| | Abrasive stone+water S3a | Abrasive stone+coke S3b | Abrasive stone+tea S3c | Abrasive stone+coffee S3d |

LDC: Lithium disilicate glass ceramic, ZLS: Zirconia-reinforced lithium silicate ceramic

standard illuminant D65. Measurements were repeated 3 times for each specimen and the mean values of the L*, a*, and b* data were calculated. According to the CIE L*a*b* color differences (ΔE*) formula, L* demonstrates lightness, a* demonstrates the chromaticity coordinate for red-green, and b* demonstrates the chromaticity coordinate for yellow-blue (6).

After baseline color measurements were made the specimens were stored in various solutions. The tea solution 2g-tea bag (Lipton, Unilever, Turkey) with adding into 200 mL boiling water was prepared. And the coffee solution was prepared with 3.6g-coffee (Nescafe Classic; Nestle, Bursa, Turkey) was dissolved in 300 mL of boiling distilled water. After 10 min of stirring, the solution was filtered through a filter paper. Among coffee drinkers, the average consumption of coffee is 3.2 cups per day. When the average time for consumption of one cup of a drink is thinking is 15 min, the 48 hours storage time simulated consumption over a two-month period (2,7). The solution was stirred every 8±1 hours. Distilled water served as control group. Cola solution was represented by a can of 330-mL coke (The Coca-Cola Company, Turkey). All specimens were stored at 37 °C for 48 hours in 100 mililiters of solution. After the storage time the specimens were rinsed with distilled water for 5 min, and dried.

At this point, color measurements were performed with spectrophotometer in the same manner described for baseline readings. The calculation of the color differences ΔE* between the two color measurements (after 48-hour storage and baseline) were made using the following formula.

$\Delta E^* = [(\Lambda_1^* - \Lambda_2^*)^2 + (\alpha_1^* - \alpha_2^*)^2 + (\beta_1^* - \beta_2^*)^2]^{1/2}$

In this study, average color acceptability threshold of ceramics were accepted as ΔE*=2.7 (8).

**Statistical Analysis**

A statistical analysis was performed with SPSS 20.0 System (SPSS Inc., Chicago IL, USA) for Windows. ΔE* data were analyzed by Two-Way ANOVA, and Mann-Whitney U test. Ra data were analyzed by Two-Way ANOVA. The relationship between the polishing techniques and color stability was evaluated with the Pearson rank correlation test. The level of significance was set at 5% ($p<0.05$).

## Results

The Two-Way ANOVA test results and the means and standard deviations of ΔE* values are shown in Table 3. No significant difference in ΔE* values was observed between the groups I1a, I2a, I3a, S1A, S2a and S3a, which distilled water served as control group ($p>0.05$). Also no significant difference in ΔE* values was observed between the sof-lex groups (I2a, I2b, I2c, I2d) and abrasive stone groups (I3a, I3b, I3c, I3d) ($p>0.05$) on LDC. But these two polishing groups were significantly different with glazed groups (I1a, I1b, I1C, I1d) ($p<0.05$) on LDC. ΔE* values were significantly different with glazed (S1a, S1b, S1C, S1d), and shofu

**Table 3. Mean and standard deviation of ΔE* values and differences between groups**

| | | Distilled water | Coke | Tea | Coffee |
|---|---|---|---|---|---|
| **LDC IPS e-max CAD (I)** | **Glaze** (n=10) | 0.027±0.004 A,x,p | 0.65±0.16 B,x,p | 1.01±0.07 C,x,p | 1.60±0.15 D,x,p |
| | **Sof-lex** (n=10) | 0.035±0.006 A,x,p | 1.27±0.14 B,x,q | 1.43±0.20 C,x,q | 2.48±0.29 D,x,q |
| | **Abrasive stone** (n=10) | 0.030±0.006 A,x,p | 1.19±0.16 B,x,q | 1.35±0.12 C,x,q | 2.28±0.27 D,x,q |
| **ZLS Suprinity (S)** | **Glaze** (n=10) | 0.030±0.008 A,x,p | 1.19±0.11 B,y,p | 1.16±0.12 B,y,p | 1.98±0.22 C,y,p |
| | **Sof-lex** (n=10) | 0.035±0.004 A,x,p | 1.61±0.22 B,y,q | 1.73±0.21 B,y,q | 2.96±0.28 C,y,q |
| | **Abrasive stone** (n=10) | 0.030±0.007 A,x,p | 1.45±0.28 B,y,p,q | 1.57±0.25 B,y,p,q | 2.63±0.26 C,y,p,q |

Different latters indicate statistically significant difference between groups ($p<0.05$), *A,B,C,D intra-group comparisons, **x,y between-group comparisons column, ***p,q,z column-group comparisons, LDC: Lithium disilicate glass ceramic, ZLS: Zirconia-reinforced lithium silicate ceramic

**Table 4. Mean and standard deviation of Ra values and differences between groups**

| | Glazing | Abrasive stone | Sof-lex |
|---|---|---|---|
| LDC | 0.39±0.09 A,x | 0.81±0.21 B,y | 0.79±0.14 B,y |
| ZLS | 0.30±0.14 A,y | 0.85±0.25 C,y | 1.07±0.32 B,x |

Different laters indicate statistically significant difference between groups ($p<0.05$), *A,B,C intra-group comparisons, **x,y between-group comparisons column, LDC: Lithium disilicate glass ceramic, ZLS: Zirconia-reinforced lithium silicate ceramic

groups (S3a, S3b, S3c, S3d) than sof-lex groups (S2a, S2b, S2c, S2d) ($p<0.05$) on ZLS.

Within the staining solutions, decreasing ΔE* values were observed in coffee to coke, and then tea and water for LDC specimens. However within the staining solutions for ZLS specimens the highest ΔE* values were observed in coffee, and then equal ΔE* values in coke and tea and the lowest ΔE* values were observed in water. Also, ΔE* values of ZLS specimens were higher than ΔE* values of LDC materials ($p<0.05$).

The Two-Way ANOVA test results and the means and standard deviations of Ra values are shown in Table 4. Comparing the Ra values of ZLS and LDC ceramics at baseline, no statistically significant differences were found among all groups ($p>0.05$). Both of LDC and ZLS specimens, the lowest Ra values were observed in glazing groups, which were not statistically from each other ($p>0.05$). The highest Ra value in ZLS was observed in group abrasive stone (1.07±0.32). No significant difference was observed among group abrasive stone (0.81±0.21) and sof-lex (0.79±0.14) in LDC specimens ($p>0.05$). For ZLS specimens the group abrasive stone (0.85±0.25) differed significantly from the group sof-lex (1.07±0.32) ($p<0.05$).

The result of Pearson correlation analysis, the coefficient of correlation between Ra and ΔE values was found to be statistically significant ($p<0.01$, $r^2=0.74$), indicating that these two variables were correlated, in a portion of 74%, with each other. For both ceramic types, smoother surfaces showed more color stability than rough surfaces.

## Discussion

According to the results of the study, the null hypotheses that staining solutions and polishing techniques are not correlated with the stainability and surface roughness of CAD-CAM ceramics were rejected.

Extra laboratory procedures have to be applied for additional firings thus these procedures are time-consuming. And additional firings can cause color changes and porcelain devitrification. For these reasons, mechanical finishing methods have been recommended instead of reglazing (5,9-11). Clinicians can obtain good aesthetic and acceptable surface smoothness if mechanical finishing methods are applied in the direction of the manufacturer's proposal (12,13). In the investigations it has been detected that silicon carbide points obtain better surface roughness than polishing paste and disks (2,14).

Many studies have reported that several chairside polishing systems recommended for ceramic restorations have created smooth surfaces as glazing (1,5,13). However, type of surface treatment was a significant factor in color stability (3,4,9). Because the different ceramic materials, and polishing systems are now available, which polishing system yields the smoothest surface on a prefered ceramic material should have been determined.

In the present study, it was concluded that polishing with abrasive stone created smooth surfaces as well as glazing on zirconia-reinforced lithium disilicate ceramic.

Some of the *in vitro* studies have shown that surface of ceramic restoration which applies glazing ensures adequate surface smoothness (1,5,9), and however there are studies which have demonstrated mechanical surface finishing methods such as rubber abrasives and rotary instruments shown acceptable surface smoothness (1,5,13).

Johnston and Kao (15) reported average color acceptability threshold of ceramics is ΔE*=3.7. A large number of ΔE* value is considered to be the reference value which varies ΔE*=2 to 4 in the different studies based on dental ceramics (3,8,16,17). O'Brien (16), limited ΔE* values between 0 and more than 3.5 (ΔE*=0, perfect; ΔE*=0.5 to 1, is accepted excellent; ΔE*=1 to 2, is accepted good; ΔE*=2 to 3.5, is accepted clinically acceptable; and ΔE*>3.5, is accepted inconsistent). Also, color perception is related to multiple factors such as illuminant conditions, difference in perception of color, selected material's properties, and measurement differences of color matching (17).

Clinical evaluation degrees of color differences have classified by some of the authors. Goldstein and Schmitt (18) proposed that experienced clinicians or technicans can detect when ΔE* values more than 0.4. On the other hand, another study states that color differences of dental restoration can be acceptable when ΔE* value was less than 2.6 (19).

In this study, average threshould value of color difference was accepted ΔE*=2.7 like previous studies (8). Also, there is a contentious about the accepted ΔE* limit as a threshould until the present day. In the study, only ΔE* values of the ZLS specimens' polished with sof-lex and stored in coffee were over the accepted threshold of 2.7 (Group S2d, ΔE*=2.96).

In a previous study (20), evaluated the effects of tea, coffee, and cola on the color of composite resins and porcelain, it was reported that staining of porcelain was not noticeable (ΔE*=1.2 to 1.4). In another study (21), glazed ceramic material's staining after immersion in coffee was found less than composite resin.

Coffee was used as a staining solution that followed by tea, and coke in the most color studies (3,4,7,8). In our study, within the staining solutions the highest ΔE* values were observed in coffee for LDC and ZLS specimens.

Some of the authors have used tea, coffee and coke to evaluate discoloration of dental restorative materials (2,3,20,21). In this study, four different staining solutions were used to evaluate color changes (3,7).

In the present study, LDC has shown lower ΔE* values than ZLS in all staining solution groups. The fact remains that coffee solution groups have shown higher ΔE* values than tea and coke (22).

As the color stability became better the surface roughness is decreased. In the present study, no significant difference was observed with Ra parameter among group abrasive stone and sof-lex in LDC specimens. It was also determined that correlated with the results of ΔE* values of abrasive stone and sof-lex groups of LDC specimens. Also ΔE* and Ra values of abrasive stone and sof-lex groups of LDC were determined that correlated with each other.

Most of the investigators have studied to get better surface smoothness and so they have investigated a lot of various finishing methods on ceramic surfaces. But there is no consensus about how to get greater surface via finishing method among investigators (23).

Usually, some of the factors such as grain size, crystalline mold, pigment types, size of crystalline and distribution of porosity can affect the translucency of dental ceramics. The most studied chemical structure among dental ceramics is LDC.

ZLS ceramics are produced with three different translucency. Also it was thought that color of oral tissues may absorb by high translucent ZLS blocks with chameleon effect. But presinterised zirconia-reinforced glass ceramic ZLS contain lithium metasilicate (Li2SiO3) crystals. Contraction of the material during the transformation of lithium metasilicate (Li2SiO3) crystals to lithium disilicate crystals may be responsible of the lower color stability of ZLS ceramics than lithium disilicate ceramics.

Although there are many materials that can be tested, IPS e.max CAD and Vita Suprinity have been choosen because clinicians preferred. On the other hand, little knowledge can be found about IPS e.max CAD and there was no information about Vita Suprinity.

In the present there is little knowledge about the efficiency of polishing materials and polishing techniques of CAD/CAM ceramics. Also further investigations should necessary to evaluate the color stability and surface roughness of different types of CAD/CAM ceramics.

**Study Limitations**

The main limitation of the present study is that the study is carried out *in vitro*. Another limitation is that only three of various chairside polishing techniques were applied. Although the coffee was found to be the most colorant drink in previous studies (3,4,7,8), only four different solutions were used in the present study. In addition, Atomic Force Microscopy or Scanning Electron Microscopy analyzes of samples may be performed to support surface roughness measurements with profilometer.

## Conclusion

1. Within the CAD-CAM ceramic materials ΔE* values of ZLS were higher than LDC materials.

2. The coffee was determined as the most colorant solution.

3. Polishing with abrasive stone and sof-lex creates a similar polished surface on the surface of LDC material.

**Ethics**

**Ethics Committee Approval:** Human subjects, human material, or human data, have not been used in this research article. So, the Declaration of Helsinki, and an ethics committee consent have not been referring provided.

**Informed Consent:** Human subjects, human material, or human data, have not been used in this research article. So, any informed constent have not been referring provided.

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**Authorship Contributions**

Surgical and Medical Practices: I.S., Concept: I.S., Y.H., Design: I.S., Y.H., Data Collection or Processing: I.S., Analysis or Interpretation: I.S., Y.H., Literature Search: Y.H., I.S., Writing: I.S.

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Original Article / Özgün Araştırma

# Biostimulatory Effects of Diode Laser and Ozone on Wound Healing in Rats

## *Ratlarda Yara İyileşmesinde Ozon ve Diod Lazerin Biyostimülatör Etkisi*

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### Abstract

**Objective:** Diode laser and ozone can be used to healing of skin wounds. The aim of this study is to evaluate the biostimulatory effects of diode laser and ozone on the healing of sutured skin wounds in rats.

**Materials and Methods:** In this study, 21 adult males Wistar albino rats were used. Three 1-cm-longs, full-thickness incisions were applied to the back of each animal and closed with sutures. Diode laser treatment, irrigation with 0.9% saline solution and ozone therapy was applied to the wounds through 7 days. Animals were euthanized on the 3rd, 7th, and 14th days after treatment, and all wounds were surgically removed for histopathological evaluation.

**Results:** According to histological results, a statistically significant difference was found among the three treatment methods in acute inflammatory reactions on 3rd day ($p<0.05$). Ozone treatment reduced the intensity of acute inflammatory reactions by the 3rd day ($p<0.05$). In addition, a statistically significant difference was found between the follow-up periods in all treatment groups for fibrosis ($p<0.01$).

**Conclusion:** It was found that ozone treatment was more effective when compared to the other treatments for reducing the intensity of acute inflammatory reactions on the healing of sutured skin wounds.

**Keywords**
Ozone, diode laser, wound healing, rat, therapy, soft tissue

### Öz

**Amaç:** Diod lazer ve ozon deri yaralarının iyileşmesinde kullanılan yöntemlerdendir. Bu çalışmanın amacı sütüre edilmiş deri yarasında diod lazer ve ozonun biyostimülatör etkisinin değerlendirilmesidir.

**Gereç ve Yöntemler:** Bu çalışmada; 21 erkek Wistar albino rat kullanılmıştır. Hayvanların sırtına üç adet 1 cm uzunluğunda tam kalınlıkta insizyon yapıldı ve sütüre edildi. Yaralara 7 gün diod lazer tedavisi, %0,9 salin solüsyonla irrigasyon ve ozon tedavisi uygulandı. Hayvanlar tedaviden sonra 3., 7., ve 14. günlerde sakrifiye edildi ve histopatolojik değerlendirme için yara bölgesi cerrahi olarak çıkarıldı.

**Bulgular:** Histolojik sonuçlara göre, 3. günde akut enflamatuvar reaksiyon açısından üç tedavi yöntemi arasında istatistiksel olarak anlamlı farklılık vardır ($p<0,05$). Ozon tedavisi akut enflamasyon yoğunluğunu 3. günde düşürmüştür ($p<0,05$). Ayrıca, takip periyotlarında bütün tedavi gruplarında fibroziste istatistiksel olarak anlamlı fark bulunmuştur ($p<0,01$).

**Anahtar Kelimeler**
Ozon, diod lazer, yara iyileşmesi, rat, yumuşak doku tedavisi

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**Sonuç:** Sütüre edilmiş deri yarasının iyileşmesinde akut enflamatuvar reaksiyonun azalmasında diğer tedavilerle karşılaştırıldığında ozon tedavisinin daha etkili olduğu bulunmuştur.

## Introduction

Wound healing is one of the most challenging difficulties in today's medical issues especially in surgery field. Several methods have been recommended for acceleration of wound-healing over decades. Chemical materials, electro-stimulation of wound, low-level laser therapy (LLLT), negative pressure wound therapy and also ozone ($O_3$) are among these methods (1).

The healing of soft tissue wounds is an extremely organized process (2). The healing process includes phases such as inflammatory cell immigration, granulation tissue synthesis, collagen and proteoglycan deposition, and scar maturation (3).

Different kinds of lasers can be used in dentistry for cavity preparation, soft-tissue surgery, caries prevention, caries diagnosis, and endodontic treatment. The laser therapy is one of the techniques used to accelerate the improvement of soft tissue functionality in the management of injured soft tissue. Lasers are recommended for the healing process of skin incisions due to the healing of the tissue by causing collagen synthesis and vessel dilatation, and by rising tissue oxygenation (4). Enwemeka et al. (5) reported that laser treatments positively impact all stages of the healing period. The wavelength and energy density of the laser are crucial factors in successful treatment (6). Several kinds of laser have been tried in order to improve the quality of healing of soft tissue wounds (7). Diode lasers have been used in dentistry for numerous indications, such as periodontics, endodontics, bleaching, or LLLT (8). The biostimulatory effects of LLLT on the healing process of tissues have attracted considerable attention. Various researches have studied the effect of LLLT on the normal and damaged wound healing process in clinical and experimental. The generality of researchers stated enhanced blood vessel endothelium enhanced, wound closure, enhanced tensile strength, increased fibroblasts, induction of collagen synthesis, and reduced inflammatory reaction (9). However, there has been little training on the effects of LLLT on the healing of sutured skin wounds (10).

$O_3$ is generally accepted as one of the best antifungal, bactericidal, and antiviral agents (11). Therefore, it is empirically used as a clinical therapeutic agent for chronic wounds (12).

It has been systematically shown that LLLT is able to modify the morphology of scar tissue in soft tissue wounds because of its positive effect on the proliferation and differentiation of fibroblasts, synthesis of collagen, and neoangiogenesis, and the positive impacts of $O_3$ on wound healing could be supposed to be owing to reduced bacterial infection, amelioration of decreased cutaneous wound healing, or enlarged oxygen tension by $O_3$ exposure in the wound area (13). However, a comparison of the effects of $O_3$ and LLLT on the healing of sutured skin wounds has not been studied yet.

The aim of this study was to evaluate and compare the impact of diode laser and $O_3$ on the healing of sutured skin wounds in rats. The null hypothesis was that there would be differences in the healing process of sutured skin wounds treated with diode laser or $O_3$ in rats.

## Materials and Methods

İnönü University's Experimental Animal Ethics Committee (protocol no: 2013/A-14) approved to this study's experimental procedures.

Twenty-one adult males Wistar albino rats with an average weight of 270-300 g and age of 3-5 months were used in this study. All of the subjects were kept in a room with a cycle of twelve hours of light and twelve hours of dark. Temperature of the room was 21 °C and the rats were fed ad libitum. All trial processes followed the guidelines of the Animal Care and Use Committee of the İnönü University Faculty of Medicine's Experimental Animal Center.

The experiment was designed with 21 rats. Three 1-cm-long, full-thickness incisions were applied to the back of each animal. The three incisions on each rat were closed with sutures (Figure 1) (14).

LLLT with diode laser was then applied to the first wound every day after surgery through 7 day (laser group). The second wound was irrigated with 0.9% saline solution (control group). $O_3$ therapy was

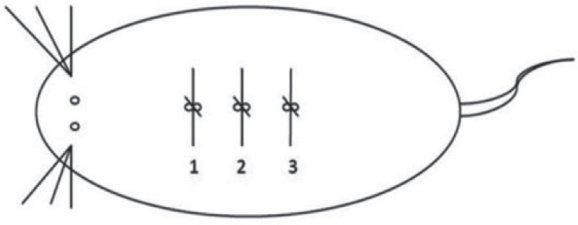


**Figure 1.** Three 1-cm-long, full-thickness incisions were applied to the back of each rat. For suturing, a single knot was made in the middle of the incision. 1: low-level laser therapy with diode laser (laser group), 2: 0.9% saline solution (control group), 3: ozone (ozone group)

applied to the third wound after surgery through 7 day ($O_3$ group). Seven of the animals were sacrificed after 3 days, 7 were sacrificed after 7 days, and 7 were sacrificed after 14 days. Amoxicillin were injected to all rats intramuscularly (50 mg/kg) for 4 days every 24 hours, starting one day before the surgery and after the operation they were injected an intramuscular analgesic every 24 hours through 3 days. All operations were achieved paying attention to sterilization. Anesthesia was carried out with 2% xylazine (0.1 mL/100 g) and 10% ketamine (0.1 mL/100 g). After general anesthesia, the dorsal skin of the rats was shaved and the cutaneous surface was disinfected before the surgery. Three 1-cm-long incisions were made using a scalpel. After the treatment procedure, the wounds were sutured with absorbable 3-0 polyglactin 910 sutures (Vicryl; Ethicon, Somerville, NJ, USA).

The LLLT (CHEESE Dental Laser System, DEN4A) procedure was started following surgery on the first sutured wound of each rat through 7 days, for 90 seconds with continuous output with a potency of 0.3 W and wavelength of 810 nm. The laser array was placed directly over the animal at a vertical distance of 1 cm from the wound. The second sutured wound was not treated and served as a control, only irrigated with 0.9% saline solution.

The $O_3$ application device was a portable $O_3$ delivery system (OzoneDTA generator, APOZA, Taiwan). $O_3$ was applied to the third sutured wound of each rat through 7 days according to the manufacturer's instructions. During $O_3$ therapy, oxygen was converted on the surface of the sutured skin wound. $O_3$ devices were used for 90 seconds with a 3 number flat probe and output power of 12 for sutured wound disinfection.

Seven animals were sacrificed with an overdose of general anesthesia on 3rd day, 7th day, or 14th day after surgery. Tissue specimens were fixed in 10% neutral-buffered formalin, and 3 samples including the incisions were obtained for histologic examination. The samples were embedded in paraffin blocks. Sections measuring 5 µm were stained with hematoxylin and eosin for histopathologic evaluation. For each specimen, acute inflammation, chronic inflammation, granulation tissue, ulcer, fibrosis, crust, and hyperkeratosis were assessed. The severity of acute and chronic inflammation, fibrosis, and granulation tissue were scored with a grade of 0 to 3 as follows: 0, none; 1, mild; 2, moderate; and 3, severe. Crust, ulcer, and hyperkeratosis were assessed as present or absent.

**Statistical Analysis**

Statistical analysis of the data was performed using SPSS version 22.0 (IBM SPSS, Turkey). The Kruskal-Wallis test was applied to compare between the groups for assessment of acute inflammation, chronic inflammation, fibrosis, and granulation tissue. The Bonferroni correction and the Mann-Whitney U test were applied for the determination of the group's differences. Fisher, Freeman-Halton, and chi-square tests were applied to compare between the groups for assessment of crust, ulcer and hyperkeratosis, a significance level of $p<0.05$ was chosen.

## Results

There was no statistically significant difference among the treatment groups for chronic inflammation, fibrosis, and granulation tissue. There was a statistically significant difference between the treatment groups on 3rd day for acute inflammation. In the $O_3$ group, acute inflammation on 3rd day was lower than in the other treatment groups ($p<0.017$). Histological views of acute inflammatory reactions on 3rd day for the three treatment methods are shown in Figure 2.

Although there was no statistically significant difference among the treatment groups for fibrosis, there was a greater amount of fibrosis in the $O_3$ group on 14th day and the differences between the follow-up periods in all treatment groups were statistically significant on 7th day and 14th day (Table 1).

Histological views of fibrosis on 7th day for the three treatment methods are shown in Figure 3.

The lowest chronic inflammation rate was in the $O_3$ group on 7th day and in the laser group on 14th day, but there was no statistically significant difference. Granulation tissue was lower in the $O_3$ group than in the laser group on 3rd and 7th day but was higher on 14th day. Crust formation and ulceration was higher in the $O_3$ group than in the other groups on 3rd and 7th days but this difference was not statistically significant (Table 2).

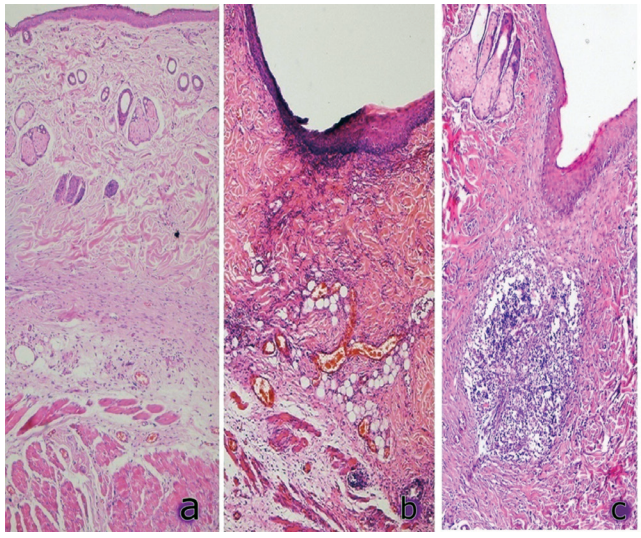


**Figure 2.** Acute inflamation at 3rd day; a: ozone group, b: laser group, c: control group

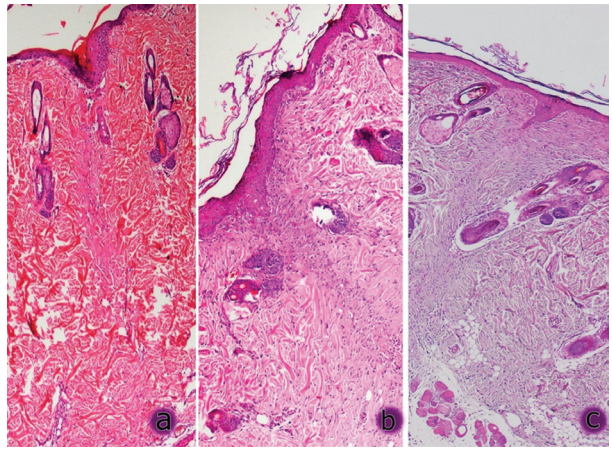


**Figure 3.** Fibrosis at 7th day; a: ozone group, b: laser group, c: control group

**Table 1. Distribution of acute inflammation, chronic inflammation, fibrosis and granulation tissue according to groups**

| | | Control | Ozone | Laser | p |
|---|---|---|---|---|---|
| | | Mean ± SD (Median) | Mean ± SD (Median) | Mean ± SD (Median) | |
| **Acute inflammation** | **Day 3** | 2.2±0.84 (2)[a] | 1.0±0 (1)[b] | 1.4±0.55 (1)[ab] | **0.034*** |
| | **Day 7** | 2.2±1.1 (3) | 1.0±0 (1) | 1.0±0.71 (1) | **0.089** |
| | **Day 14** | **0.6±0.55 (1)** | **2.0±1.0 (2)** | 1.0±1.0 (1) | **0.097** |
| | p | 0.030* | 0.031* | 0.649 | |
| **Chronic inflammation** | **Day 3** | 1.8±0.45 (2) | 1.6±0.55 (2) | 1.6±0.55 (2) | **0.756** |
| | **Day 7** | 2.2±0.84 (2) | 1.4±0.55 (1) | 1.6±0.55 (2) | **0.217** |
| | **Day 14** | 1.8±0.45 (2) | 2.0±0.71 (2) | 1.2±0.84 (1) | 0.226 |
| | p | 0.502 | 0.330 | 0.627 | |
| **Fibrosis** | **Day 3** | 0±0 (0) | 0±0 (0) | 0±0 (0) | **1.000** |
| | **Day 7** | **1.4±0.55 (1)** | **1.8±0.45 (2)** | **1.8±0.45 (2)** | 0.326 |
| | **Day 14** | 2.0±1.0 (2) | 2.4±0.55 (2) | 2.2±0.84 (2) | 0.792 |
| | p | 0.005** | 0.003** | 0.005** | |
| **Granulation tissue** | **Day 3** | 0.8±0.45 (1) | 1±0.71 (1) | 1.6±0.55 (2) | **0.111** |
| | **Day 7** | 1.2±0.45 (1) | 1.4±0.55 (1) | 1.8±0.84 (2) | **0.378** |
| | **Day 14** | 0.8±0.45 (1) | 1.8±0.45 (2) | 1.6±1.14 (2) | **0.085** |
| | p | 0.288 | 0.141 | 0.941 | |

*p<0.05, **p<0.01, SD: Standard deviation

[a,b]Different superscripts represent the difference between the groups at each line (Kruskal-Wallis test)

Bold characters in each column represent the differences between the measurement periods in the relevant working groups (Bonferroni correction and Mann-Whitney U test)

| Table 2. Distribution of hyperkeratosis, crust and ulcer according to groups | | | | | |
|---|---|---|---|---|---|
| n (%) | | Control | Ozone | Laser | p |
| | | n (%) | n (%) | | |
| Hyperkeratosis | Day 3 | 4 (80%) | 4 (80%) | 2 (40%) | **0.500** |
| | Day 7 | 2 (40%) | 3 (60%) | 3 (60%) | **1.000** |
| | Day 14 | 0 (0%) | 2 (40%) | 2 (40%) | **0.451** |
| | p | 0.036* | 0.800 | 1.000 | |
| Crust | Day 3 | 4 (80%) | 5 (100%) | 4 (80%) | **1.000** |
| | Day 7 | 0 (0%) | 4 (80%) | 2 (40%) | **0.036*** |
| | Day 14 | 1 (20%) | 0 (0%) | 0 (0%) | **1.000** |
| | p | 0.020* | 0.006** | 0.036* | |
| Ulcer | Day 3 | 2 (40%) | 3 (60%) | 1 (20%) | **0.800** |
| | Day 7 | 0 (0%) | 2 (40%) | 1 (20%) | **0.725** |
| | Day 14 | 0 (0%) | 0 (0%) | 0 (0%) | - |
| | p | 0.286 | 0.251 | 1.000 | |

*p<0.05, **p<0.01, Fisher, Freeman-Halton, and chi-square tests

## Discussion

In this study, the effects of diode laser and $O_3$ on wound healing in rats were histopathologically evaluated. $O_3$ treatment was the more-effective treatment when compared to LLLT for reducing the intensity of acute inflammatory reactions on 3rd day. However, the effects of diode laser and $O_3$ on skin wound healing were found to be similar over 14 days.

Wound healing is a natural reaction to tissue damage. Specific cells move into the wound area for this extremely organized healing process, to provide the main signaling actions that are compulsory for a new blood supply and the arrival of connective tissue cells (15). Wound healing involves inflammation, tissue formation, and tissue remodeling phases and begins with acute inflammation during which increased vascular permeability and vasodilatation occurs (14,16). Although its long-term continuity is regarded as one of the most significant reasons for delays in the healing process, this inflammation is certainly obligatory to provide wound healing (10). Throughout the inflammatory phase, macrophages, platelets, lymphocytes, and neutrophils migrate to the wound area. The acute-phase reactants decrease and the macrophages and fibroblasts proliferate during the proliferative phase. Lastly, throughout the remodeling phase, fibroblasts support and restructure the deposited collagen and the extracellular matrix (17).

Mester et al. (18) introduced LLLT for therapeutic application. Subsequently, numerous studies have shown that LLLT is helpful in regulating various biological events, for example analgesic, anti-inflammatory, and trophic regenerative effects (15). However, some investigators have reported that LLLT has not shown positive effects on wound healing and that it could even have antagonistic effects on this process (19,20). The positive effects of appropriate treatment protocols for LLLT on wound healing may be explained by its ability to stimulate certain biological reactions responsible for activating several phases of soft-tissue healing, such as induction of cytokines and expression of growth factors. In contrast, when LLLT has been used with inappropriate treatment protocols, the healing process may result in negative responses because of an inappropriate interaction between laser light and tissue components (15).

At this time, there is no universal agreement regarding how LLLT affects wound healing. The energy emitted by LLLT has shown healing, anti-inflammatory, and analgesic properties, and it has been extensively used in the process of wound healing because its wavelength and the low densities of energy can penetrate tissues (21).

Clinically, LLLT has been used to stimulate the healing of different varieties of wounds, such as open skin wounds, soft-tissue injuries, tendinitis, acne, and psoriasis (14). LLLT affects the inflammatory reaction

in the early days after injury, with enhancement of the amount of mast cells and polymorphonuclear neutrophils, enlargement of blood vessels, and vasodilatation; in this way, the inflammatory process accelerates and the healing of the wound occurs more quickly (16). The influence of LLLT depends on numerous factors, including spot size, wavelength, repetition rate, total treatment time, and power (22). The optimal parameters for LLLT are still not defined. In the literature, daily exposure of LLLT is recommended, which is predicted to provide more noticeable effects than single or weekly treatments (23). Therefore, we applied LLLT daily.

There have been conflicting results regarding the appropriate energy density of LLLT. Although Kana et al. (24) reported that 4 J/cm$^2$ is the optimum energy density of LLLT, Meirelles et al. (25) reported that LLLT with 20 J/cm$^2$ energy density improved collagen maturation on the 21$^{st}$ day. It has been suggested that LLLT stimulates proliferation with low doses such as 2 J/cm$^2$, while high doses of LLLT such as 16 J/cm$^2$ are suppressive (23). Mendez et al. (26) showed that the gallium-aluminium-arsenide laser (λ 830 nm) at 50 J/cm$^2$ stimulated intense collagen maturation in soft-tissue wounds in rats. However, Gonçalves et al. (27) recommended that the highest energy density (90 J/cm$^2$) demonstrated positive effects on the healing process. These contradictory results are likely due to limitations in the experimental models and variations in treatment factors, the absence of control groups, and lack of comparison to heterogeneous clinical wounds, and limited or no blinding of researchers (28).

Although it has previously been suggested that LLLT has possible systemic effects, in several earlier studies in which experimental and control conditions were applied on the same animal, it was observed that LLLT had a significantly positive effect. Therefore, it may be theorized that the main effect of LLLT on soft-tissue wound healing is local. Consequently, the question of systemic effects of LLLT needs more investigation (29).

The medical use of $O_3$ was initiated in the nineteenth century. $O_3$ has numerous beneficial effects in soft tissue healing owing to its nascent oxygen release feature, stimulate antioxidant enzymes and have bactericidal capabilities (30). There are numerous known effects of $O_3$ on the body, for example analgesic, immunostimulating, detoxicating, anti-hypoxic, antimicrobial, biosynthetic, and bioenergetic effects (31). It has recently been shown that although $O_3$ does not infiltrate the cells, it responds instantly through polyunsaturated fatty acids to form reactive oxygen species such as hydrogen peroxide, which, via the activation of redox transcription factors such as NF-kappaB, can induce the synthesis of growth factors and accelerate the cell cycle (32). Studies have revealed that $O_3$ treatments increase the secretion of transforming growth factor-ß1, platelet-derived growth factor, and cytokines, such as interleukin-8 (33). Koca et al. (34) showed that oxidative stress and inflammatory cytokines were reduced after both $O_3$ and hyperbaric oxygen therapies.

Kim et al. (33) proved that $O_3$ might improve acute cutaneous wound healing. Although they emphasized that topical treatment with $O_3$ could impact granulation tissue development in the wound healing process instead of affecting the early development of blood clots and improvement of inflammatory cells while the inflammation phase, these results were inconsistent with ours.

Zhang et al. (35) reported that the oxygen-$O_3$ treatment significantly stimulated the early effective rate of wound healing at day 20 in diabetic foot-ulcer patients. Valacchi et al. (32) demonstrated that a specific level of ozonated sesame oil can accelerate the first stage of wound healing in SKH1 mice. These findings are consistent with our results.

## Conclusion

According to our study, it seems that LLLT and $O_3$ therapy accelerate wound healing in some phases of the healing process. However, based on the present results, acute inflammatory reactions were statistically reduced in $O_3$-treated wound tissues when compared to the LLLT group on 3$^{rd}$ day post-incision.

**Ethics**

**Ethics Committee Approval:** The experimental protocol was approved by the İnönü University's Experimental Animal Ethics Committee (protocol no: 2013/A-14).

**Informed Consent:** This study was a animal study.

**Peer-review:** Externally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: H.A., Ç.G., P.D., Concept: H.A., Ç.G., Ü.Y., M.K., Design: H.A., Ç.G., Ü.Y.,

M.K., Data Collection or Processing: H.A., Ç.G., P.D. Analysis or Interpretation: E.Ç. Literature Search: P.D., M.K., Writing: H.A., C.G., Ü.Y., M.K.

**Financial Disclosure:** Purchasing of chemicals and animals.

**Conflict of Interest:** The authors declare that they have no conflict of interest.

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Case Report / Olgu Sunumu

# A Case of Acute Lymphoblastic Leukemia with Isolated Orbital Relapse

## *İzole Orbita Tutulumu ile Relaps Olan Akut Lenfoblastik Lösemi Olgusu*

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### Abstract

Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood. Central nervous system is the most frequent place of both at the onset and relapse of the disease, but orbital involvement is rarely seen. A seven-year-old girl diagnosed with high risk ALL and Turkish ALL-Berlin Frankfurt Münster (BFM)-2000 high risk group treatment was given. However, after induction and consolidation treatments, before the maintenance treatment she had blindness in her right eye. Ophthalmologic examination her visual acuity was fingers to count in two meters. In her right eye there was exudative retinal detachment and her orbital magnetic resonance imaging (MRI) showed that, there was a mass lesion in the posterior of right orbital globe, on the neighbourhood of optic disc, consistent with metastasis. After ALL-REZ-BFM-2002 relapse protocol treatments and radiotherapy her visual acuity was increased to 6/10. In control orbital MRI regression of mass lesion size was established. Bone marrow transplantation was planned. Orbital involvement is rarely seen in leukemia, but it is responsive to chemotherapy and radiotherapy combination.

### Öz

Akut lenfoblastik lösemi (ALL) çocukluk çağının en sık görülen malignitesidir. Tanı anında ve relaps olgularda santral sinir sistemi tutulumu sık görülmesine karşın orbital tutulum nadiren görülmektedir. Yedi yaşında kız hasta kliniğimizde yüksek risk ALL tanısı alarak Türk ALL-Berlin Frankfurt Münster (BFM)-2000 yüksek risk grubu protokol tedavisini almakta iken; indüksiyon ve konsolidasyon tedavileri ardından, idame tedavisi öncesi sağ gözde görememe şikayeti ile başvurdu. Hastanın oftalmolojik muayenesinde görme keskinliği iki metreden parmak sayma şeklindeydi. Hastanın sağ gözünde retinal dekolman mevcuttu ve orbital manyetik rezonans görüntülemesinde (MRG) sağ orbita arkasında metastaz ile uyumlu kitle lezyonu saptandı. Hastaya ALL-REZ-BFM-2002 relaps protokol tedavisi ve radyoterapi uygulandıktan sonra hastanın görme keskinliği 6/10 olarak saptandı ve kontrol MRG görüntülemesinde kitle lezyonda küçülme gözlendi. Hastaya kemik iliği nakli yapılması planlandı. Lösemide orbital tutulum nadiren görülmektedir, ancak bu durum kemoterapi ve radyoterapi kombinasyonuna yanıt vermektedir.

**Keywords**
Orbita, relapse, acute lymphoblastic leukemia

**Anahtar Kelimeler**
Orbita, relaps, acute lymphoblastic leukemia

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This case was presented as poster presentation at 9th National Pediatric Hematology Congress at 24-28 May 2013 in Van.

## Introduction

Acute lymphoblastic leukemia (ALL) is the most common malignancy of childhood, which could be curable in 80% with intensive chemotherapy protocols (1). Central nervous system is the most frequent place of both at the onset and relapse of the disease (2). Orbital involvement is rarely seen. In literature, with 25 isolated orbital relapse case series it is indicated that isolated relapse cases were treated successfully with chemotherapy and radiotherapy combination (3). We report a high risk ALL case with isolated orbital relapse that was treated with Turkish ALL-Berlin Frankfurt Münster (TRALL-BFM)-2000 protocol.

## Case Report

A seven-year-old girl administered to our clinic with the symptoms of fever and abdominal pain. In her physical examination, there were widespread lymphadenopathy, gingival hypertrophy, hepatomegaly with 6 cm and splenomegaly with 5 cm. Laboratory results were as follow; hemoglobin: 6.5 g/dL, platelet: 139 K/UL, white blood cell count: 611 K/UL, lactate dehydrogenase: 1961 U/L, uric acid: 13.6 mg/dL. There was L1 type lymphoblast in peripheral smear 98% and in bone marrow aspiration 85%. With flow-cytometry results, she was diagnosed with pre B cell ALL. BCR/ABL fusion was detected in cytogenetic analysis. She was diagnosed with high-risk group due to high white blood cell count and Philadelphia chromosome positivity. TRALL-BFM-2000 high risk group treatment was started. There was not any lymphoblast in her cerebrospinal fluid (CSF).

After induction and consolidation treatments, before the maintenance treatment blindness developed in her right eye. Ophthalmologic examination her visual acuity was fingers to count in two meters. In her right eye there was exudative retinal detachment and metastatic lesion around optic nerve. Bilaterally intraocular pressure and ophthalmologic examination of left eye were normal (Figure 1). Cranial magnetic resonance imagining (MRI) was normal, but orbital MRI showed that there was a mass lesion in the posterior of right orbital globe, on the neighbourhood of optic disc with dimensions of 6x1 cm consistent with metastasis. Her CSF and bone marrow aspiration, which were done for relapse, were normal. Biopsy could not be performed

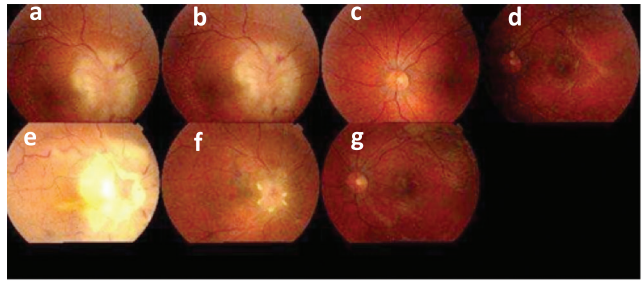


**Figure 1.** a, b) Right optic nerve invasion cause retinal detachment c, d) Left eye (normal) e) Serous retinal detachment of right eye f) Right eye, after treatment g) Left eye (normal)

from mass lesion. Patient age and primary sickness were considered and diagnosed as ALL relapse. After ALL-REZ-BFM-2002 relapse protocol F1, F2 and R2 block treatments; radiotherapy and bone marrow transplantation from unrelated donor was planned. At the end of R2 block chemotherapy, her visual acuity was increased to 6/10 and in her ophthalmologic examination decrease in retinal detachment was detected. In control orbital MRI regression of mass lesion size was established.

Informed consent was taken from patient family.

## Discussion

In ALL patients, like our case, hyperleukocytosis at administration, Philadelphia chromosome positivity show poor prognosis. The most frequent extramedullary involvement is seen in central nervous system (2). Orbital involvement is rarely seen in leukemia patients. In differential diagnosis of exudative detachment there are uveal fusion syndrome, choroidopathy, Harada syndrome, choroid detachment, choroidal neovascularisation, and severe intraocular hypotonic but with consideration of patients age and primary illness it was thought with orbital relapse. In ALL patients who were in remission period, 25 isolated case series were reported. In the 10 of patients were on treatment, 15 of patients after completion of treatment. They administered with orbital symptoms. Their age was between 1 to 13. An average of 29 months after diagnosis, ocular relapse was detected, and long-term survival was long in the group who took both chemotherapy and radiotherapy. In one patient who took low dose local radiotherapy, resistance of leukemic cells was developed, and enucleation was performed. In this case series, it was reported that with local radiotherapy and systemic

chemotherapy treatment was successfully achieved. Also, after treatment prognosis was reports as better in isolated orbital relapse group than central nervous system and bone marrow relapse groups (3). First case with isolates orbital ALL relapse administered with unilaterally retinal detachment and unresponsive to medical treatment painful glaucoma. Patient was treated successfully with systemic and intrathecal chemotherapy (4). A 17-year-old patient, who was followed as leukemia, administered with retinal detachment and choroidal haemorrhage. Patient was treated with prednisolone, topical steroid and atropine but while when she administered her CSF and bone marrow was clean, after five months bone marrow relapse was seen (5). In our country, Azık et al. (6) reported an eight-year-old ALL patient, who had sudden visual loss in remission period. In this case there was also isolated orbital relapse was detected without bone marrow and central nervous system relapse. Retinal detachment resulted with sudden visual loss (6). Our case was high risk ALL patient and isolated orbital relapse was seen. From 10 months of diagnosis, orbital involvement was seen. After systemic chemotherapy leukemic infiltration and retinal detachment decreased.

As a result, orbital involvement is rarely seen in leukemia, but it is responsive to chemotherapy and radiotherapy combination. Leukemia patients, especially high-risk ones, should be screened with ophthalmologic examinations both at diagnosis and after treatment.

**Ethics**

**Informed Consent:** Informed consent was taken from patient family.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: A.P., Concept: S.A., Design: Y.I.B., Data Collection or Processing: A.K., Analysis or Interpretation: H.E., Literature Search: F.Ö.A., Writing: F.Ö.A.

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Case Report / Olgu Sunumu

# A Rare Cause of Embolism: Cardiac Papillary Fibroelastoma

## *Nadir Görülen Bir Embolizm Nedeni: Kardiyak Papiller Fibroelastom*

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**Abstract**

Cardiac tumors are rarely encountered pathologies, but they may have versatile and different clinical implications. Cardiac papillary fibroelastomas are the third most common primary heart tumors and these are often diagnosed incidentally. When these tumors cause symptoms, they often emerge with cerebral embolic events or myocardial ischemia. Surgical resection of the tumor is recommended to eliminate the risk of embolism and sudden death for symptomatic cases and when the tumor originates from the left side of the heart and mobile. In this case report, we present valve-sparing complete resection of a cardiac papillary fibroelastoma arising from aortic valve which causes neurological symptoms.

**Keywords**
Cardiac tumors, papillary fibroelastoma, embolism

**Öz**

Kalp tümörleri nadir olarak karşılaşılan bununla birlikte çok yönlü değişik klinik yansımalara sahip olabilen patolojilerdir. Kardiyak papiller fibroelastomlar tüm kalp tümörleri arasında üçüncü en sık görülen primer tümörleridir ve bu tümörlere çoğunlukla rastlantısal olarak tanı konulmaktadır. Kardiyak papiller fibroelastomlar semptom verdiğinde, sıklıkla embolizme bağlı serebral olaylar veya miyokardiyal iskemi ile karşımıza çıkmaktadır. Semptomatik olgularda ve özellikle kitlenin kalbin sol tarafından köken aldığı ve mobil olduğu durumlarda emboli ve ani ölüm riskini ortadan kaldırmak için tümörün cerrahi rezeksiyonu önerilmektedir. Bu olgu sunumunda nörolojik semptomlar ile kliniğe yansıyan, aort kapağı üzerinde yerleşimli bir kardiyak papiller fibroelastomun kapak koruyucu tam rezeksiyon ile tedavi edilmesi sunulmaktadır.

**Anahtar Kelimeler**
Kalp tümörleri, papiller fibroelastom, embolizm

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It was presented as an e-poster at the 11th National Cardiovascular Surgery Congress.



### Introduction

Cardiac tumors are rare pathologies with a frequency of 0.02% in the large autopsy series. Fibroelastomas are the third most common primary tumors after myxomas and lipomas and constitute 8-10% of benign heart tumors (1). The majority of the cases are asymptomatic and usually diagnosed by incidental echocardiographic examinations. However, cardiac papillary fibroelastomas may have variable clinical reflections. They may cause cerebral events due to systemic embolism and myocardial ischemia due to embolism in coronary arteries or tumor

prolapse (1-3). Surgical resection is recommended in symptomatic cases and for mobile tumors originating from the left side of the heart to eliminate the risk of embolism and sudden death (4).

In this paper, we present a case of cardiac papillary fibroelastoma located on the aortic valve causing neurologic symptoms. The tumor was resected surgically by preserving the aortic valve. The surgical techniques used in such cases are discussed and the literature is reviewed.

## Case Report

A 37-year-old female patient with no previous history of neurological symptoms or transient ischemic attack admitted to the emergency service with left hemiparesis after syncope. Neurological status improved during the clinical follow-up. Routine blood tests, electrocardiograms, and direct chest X-ray were observed to be normal.

Cranial magnetic resonance imaging (MRI) and carotid doppler ultrasonography examinations did not reveal any pathology. Transesophageal echocardiography showed smooth, sessile, (1.4 x 1.2 cm) mobile mass on the aortic surface of the aortic valve, located between the left coronary and the non-coronary leaflets. The mass was moving in accordance with the heart cycle. There was no aortic valve dysfunction and intracardiac thrombus and other valvular structures were found to be normal. Cardiac MRI was performed to delineate the anatomy of the mass, detect the concomitant pathologies and to plan the surgical strategy. On imaging, the presence of supra-aortic left coronary fissure was confirmed (Figure 1). Considering the risk of recurrent embolism early surgical resection was planned because of the unknown pathology of the mass and the cerebrovascular event that the patient had experienced. Informed consent was obtained from the patient.

After median sternotomy cardiopulmonary bypass was initiated with ascending aorta and right atrium cannulation and the left atrial vent cannula was placed. Following the aortic cross-clamping, diastolic cardiac arrest was maintained via antegrade cardioplegia administration from the aortic root. Transverse aortotomy was performed immediately proximal to the aortic root. On the left coronary leaflet, approximately 1x1 cm sized tumor mass in close proximity to the non-coronary leaflet was observed (Figure 2). The tumor was macroscopically bright and had a soft, gelatinous structure. The tumor was completely resected by preserving the basal area which is held by the leaflet tissue. Post-resection aortic valve coaptation was normal. The postoperative period was uneventful. Pathologic examination of the

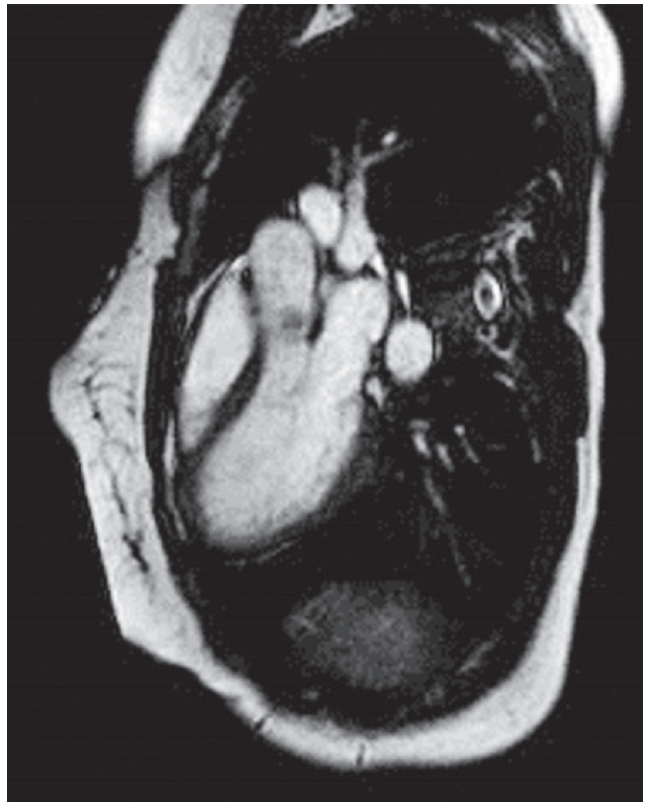


**Figure 1.** Appearance of the mass on the aortic valve on cardiac magnetic resonance examination

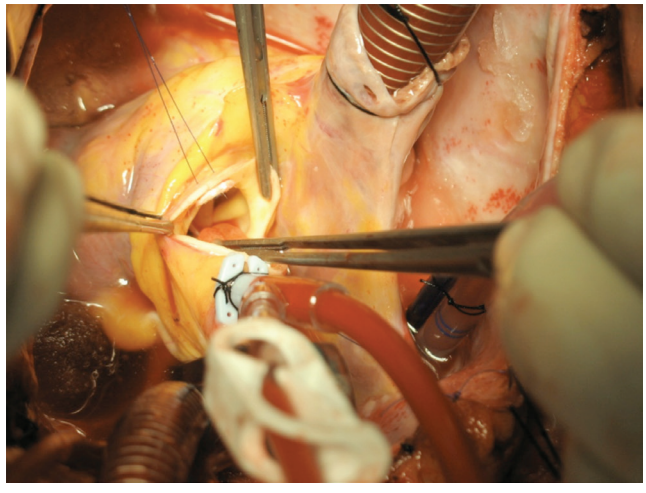
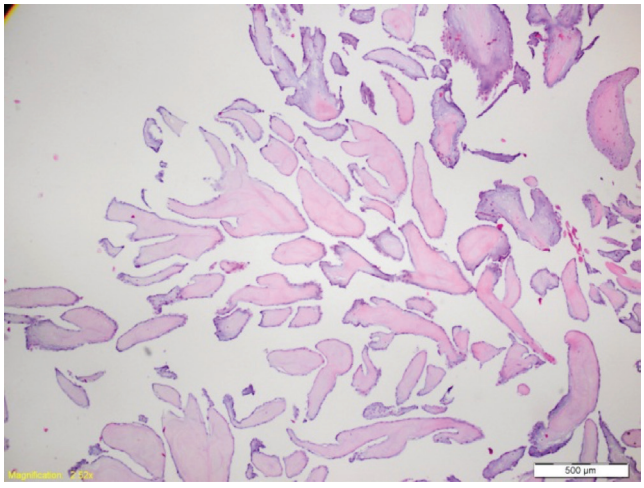


**Figure 2.** Surgical exposure of the tumor

mass revealed papillary proliferation and hyperplastic endothelial cells containing fibroblast, collagen and elastic fibers, confirming the diagnosis of cardiac papillary fibroelastoma (Figure 3).




**Fiure 3.** Papillary proliferation and hyperplastic endothelial cells containing fibroblast, collagen and elastic fibers detected on histopathologic examination of the resected mass (hematoxylin eosin staining, x40 magnification)

## Discussion

Cardiac papillary fibroelastomas are avascular tumors originating from fibrous tissue, elastic fibers and smooth muscle cells (5). These tumors, usually less than 1 cm in diameter, are held with a short stem in the endocardium. Although the pathogenesis of fibroelastomas is not known precisely, it is suggested that these tumors may be due to mechanical damage to the endothelium or to hamartomatous disease associated with organized thrombus (6). Macroscopically, the appearance of papillary fibroelastomas resembles a marine anemone, typically with extensions in the water (2).

Cardiac papillary fibroelastomas may be diagnosed at any age but are frequently detected in the seventh and eighth decades. Although the incidence of these tumors is not known precisely, it does not differ in terms of gender (1,4). The most commonly affected valve is the aortic valve (44%) however, the papillary fibroelastomas can also be located in the mitral (35%), tricuspid (15%) or pulmonary valves (8%) (7). In symptomatic patients, the clinical picture shows a broad spectrum depending on the location, size, and growth rate and embolization tendency of the tumor. Papillary fibroelastomas which are located in left heart generally manifest with embolic neurological complications. In our case, papillary fibroelastoma on the aortic valve was also accompanied by history of syncope and hemiparesis.

The mechanisms of thromboembolism in cardiac papillary fibroelastomas involve tumor embolization and thrombus formation on the tumor. For this reason, there may be significant changes in tumor size at short time intervals (8). Since these tumors are usually located on the outflow tract of the left ventricle and exposed to high-velocity blood flow, the risk of thromboembolism is higher than the benign atrial myxomas which are more common heart tumors. Thus, tumor size may not be an indicator for the risk of thromboembolism in cardiac papillary fibroelastomas (9).

There is a consensus on surgical resection for symptomatic cardiac papillary fibroelastomas (10). The management in asymptomatic cases is controversial. Large, mobile tumors originating from the left side of the heart are suggested to be surgically removed to prevent sudden death and embolism. Serial echocardiography examinations and anticoagulation therapy can be adequate in the follow up of small and non-mobile tumors but surgical resection becomes mandatory if there is an increase in tumor size, tumor gets mobile or symptoms occur (4). However, there are no long-term and comprehensive studies evaluating the outcome of non-surgical treatments for cardiac papillary fibroelastomas. For this reason, some authors recommend surgical resection of all cardiac papillary fibroelastomas taking into account the potential risks (9).

In a majority of cases, surgical treatment of cardiac papillary fibroelastomas can be performed with low risk allowing complete removal of tumor tissue. As these tumors are usually pedicellate, simple excision of the tumor with preservation of the valve texture is often sufficient. The stalk and the endocardium to which the tumor is attached must be completely removed. If the defect formed in the tissue is too large, the repair can be performed by direct suture or it may be closed by means of a pericardial or Dacron patch. Replacement of the valve may be necessary in cases of severe mechanical damage to the valve structures or in cases where the tumor is widespread on the leaflet. Care should be taken to avoid fragmentation of the tumor during operation to prevent intraoperative

embolization. All heart cavities should be examined to notice additional tumor masses that may not have been detected before surgery (8).

In our case, the stalked tumor located on the left coronary leaflet of the aortic valve was excised by preserving the valve structure. There was no complication in the early postoperative period and no tumor recurrence was detected in one year follow up.

In conclusion, although cardiac papillary fibroelastomas are rare tumors, they are being more commonly detected with the development of diagnostic tools. Even though these tumors are benign and usually asymptomatic, their natural course is still unknown. Cardiac papillary fibroelastomas can cause embolization and mortality and therefore should be kept in mind in the differential diagnosis of cardiac masses. Early surgical resection is curative in symptomatic cases.

**Ethics**

**Informed Consent:** Patient informed consent form was received.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: M.B., S.D., U.G., Concept: S.D., M.B., Design: S.D., T.K., M.Y., Data Collection or Processing: S.D., M.Y., Analysis or Interpretation: N.Ç., Literature Search: S.D., M.Y., Writing: S.D., T.K.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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Case Report / Olgu Sunumu

# Shprintzen-Goldberg Syndrome: Case Report

## *Shprintzen-Goldberg Sendromu: Olgu Sunumu*

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**Abstract**

Shprintzen-Goldberg syndrome is a rare syndrome with craniosynostosis of coronal, sagittal or lambdoidal sutures, dolichocephaly, typical craniofacial features, skeletal abnormalities, scoliosis, joint hyperextensibility or contractures, neurological findings and brain malformations. Fifteen months old male patient with hydrocephalus and dysmorphic facial appearance was referred to our clinic for genetical evaluation. In his dysmorphic examination, the findings were dolichocephaly, prominent forehead and glabella, hypertelorism, prominent eyes, proptosis, depressed nasal root, anteverted nostrils, small nose, low-set and posteriorly rotated, dysplastic ears, microretrognathia, short philtrum, fish mouth of mouth, plump cheeks, high and narrow palate, secondary alveolar arch, pectus carinatum. Hands were small and he had arachnodactyly. Toes were thin. He had also hypotonia and umbilical hernia. With these findings, he was clinically diagnosed as Shprintzen-Goldberg syndrome. This is the first reported case of Shprintzen-Goldberg syndrome from Turkey according to literature review.

**Keywords**
Shprintzen-Goldberg syndrome, dolichocephaly, craniosynostosis

**Öz**

Shprintzen-Goldberg sendromu koronal, sagital ya da lambdoid sütürlerin kraniyosinostozu, dolikosefali, tipik kraniofasiyal özellikler, iskelet anomalileri, skolyoz, eklem hiperekstansibilitesi veya kontraktürleri, nörolojik anomaliler ve beyin anomalileri ile karakterize nadir görülen bir sendromdur. On beş aylık erkek hasta, hidrosefali nedeniyle genetik inceleme amacıyla polikliniğimize yönlendirildi. Hastanın dismorfik muayenesinde, dolikosefali, belirgin alın ve glabella, hipertelorizm, makroftalmik-proptotik görünüm, basık burun kökü, antevert burun delikleri, küçük burun, düşük, geriye yerleşimli ve displastik kulaklar, mikroretrognati, kısa filtrum, balık ağzı görünümü, dolgun yanaklar, yüksek ve dar damak, sekonder alveolar kemer, pektus karinatum mevcuttu. Ayrıca eller küçüktü ve araknodaktili görünümündeydi. Ayak parmakları da inceydi. Olguda hipotoni ve umblikal herni mevcuttu. Hasta mevcut bulgularla değerlendirildiğinde; klinik olarak Shprintzen-Goldberg sendromu tanısı konuldu ve takibe alındı. Literatür taramalarında Türkiye'den bildirilen ilk olgu olduğunun görülmesi ve nadir görülen bir olgu olması nedeniyle sunulmaktadır.

**Anahtar Kelimeler**
Shprintzen-Goldberg sendromu, dolikosefali, kraniosinostoz

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## Introduction

Shprintzen-Goldberg syndrome (SGS), is a syndrome characterized by typical dysmorphic features, craniosynostosis and marfanoid

features, skeletal and neurological abnormalities. Craniosynostosis, dolichostenomelia, proptosis, low-set ears, arachnodactyly, camptodactyly, pes planus, pectus excavatum or carinatum, scoliosis, joint hyperextensibility or contractures, hydrocephalus, dilatation of lateral ventricles, Chiari 1 malformation may be seen in this syndrome. Cardiovascular anomalies like prolapse of mitral valve, mitral regurgitation, aortic regurgitation and aortic root dilatation may accompany. Minimal increasing of adipose tissue, abdominal wall defects, myopia and cryptorchidism are also rarely seen in SGS. The weight of patients generally tends to increase with age, while their weights are generally below the third percentile (1).

Craniosynostosis is seen in 40% of SGS patients. The anterior fontanel is large and often has a wider secondary alveolar arch. Hydrocephalus is seen in 40% of cases. Umbilical hernia is among the commonly identified findings in patients (1).

Diagnosis is based on clinical and radiological findings (C1-C2 anomalies, large anterior fontanel, thin ribs, square shaped vertebrae and osteopenia) and the *SKI* gene is known to be only gene associated with this syndrome (1).

Nutritional problems, cyanosis due to respiratory problems, obstructive apnea are frequently seen during the infantile period. The linear growth rate is increasing with age.

## Case Report

A 15-month-old male patient was referred to our genetics diagnosis center for genetic screening by the department of pediatric neurology where he was followed up for hydrocephalus.

A healthy 24-year-old father and a 24-year-old healthy mother, who were not consanguineous; told that antenatal follow-ups of the mother regularly performed and developmental retardation was detected in the prenatal follow up of baby. The case was the first pregnancy of the mother and was delivered with spontaneous vaginal birth at the hospital, weighing 2.500 g. The family did not remember birth height and head circumference.

Postnatal physical examination was found to be normal. The patient was taken to the pediatrics department by the family with the complaint of failure to thrive at the age of 2.5 months. After the examination, the child was followed up for further examination and treatment by the department of pediatric neurology and brain surgery due to hydrocephalus.

On physical examination, body weight was 9200 g (10-25 p), height was 72 cm (3-10 p), head circumference was 45 cm (25-50 p). On the dysmorphic examination, dolichocephaly, large anterior fontanel, prominent forehead and glabella, hypertelorism, macrophthalmic-proptotic appearance, flattened nasal root, antevert nostrils, small nose, low, posterior and displaced ears, microretrognatia, short philtrum, fish mouth, high and narrow palate, secondary alveolar arch, pectus carinatum (Figure 1). We found also, his hands were small and associated with arachnodactyly and his toes were thin. Hypotonia and umbilical hernia were present in the patient.

Developmental milestones were retarded. He did not say a meaningful word at the age of 15 months.

In brain magnetic resonance imaging (MRI), cerebellar tonsillar ectopia and supratentorial hydrocephalus (Arnold Chiari syndrome); in cervical-thoracal-lumbar MRI cerebellar tonsillar ectopia and pectus carinatum were detected.

The case was diagnosed as SGS because of dolichocephaly, large anterior fontanel, hypertelorism, ocular proptosis, posteriorly located, low-set ears, microretrognatia, pectus carinatum, umbilical hernia and hydrocephalus.

The patient's family and ethics committee have been granted permission for this study. There was no statistical analysis in this study.

**Figure 1.** Dysmorphic appearance of Shprintzen-Goldberg syndrome patient

## Discussion

SGS is a syndrome characterized by marfanoid habitus, dolichocephaly, craniosynostosis, mental retardation, ocular proptosis, hypertelorism, down slanting palpebral fissures, strabismus, low-set ears, micrognathia, arachnodactyly, camptodactyly. Mental retardation is a frequent finding, patients are hypotonic and developmental milestones are retarded. Findings such as thin and sparse hair, Chiari malformation, bifid uvula, choanal atresia/stenosis, vocal cord paralysis, dental malocclusion, aortic root dilatation, mitral valve prolapse, inguinal hernia, hyperelastic skin, hypospadias have also been described less frequently in the patients.

SGS was first presented by Sugarman and Vogel in a 17-year-old boy with plagiocephaly, multiple craniofacial, vertebral and skeletal anomalies, umbilical and inguinal hernia, hypotonia and mental retardation. Shprintzen and Goldberg, 1982, described this syndrome as a separate clinical form (1). In our case, hydrocephalus, dolichocephaly, large anterior fontanel, hypertelorism, ocular proptosis, low-set, posteriorly located ears, microretrognatia, pectus carinatum, umbilical hernia were present.

Phenotypic characters can be variable and differential diagnosis must be done carefully. In a few cases localized *fibrillin-1 (FBN1)* mutation has been identified in the 15q21.1 region. However, *SKI* is the only gene which is reported as associated with SGS (1). The E3692A mutation of the *FBN1* gene (C1221Y) was described by Kosaki et al. (2) in a Japanese case whom clinical findings were consistent with SGS. Pauliks et al. (3) described complex congenital heart disease in a new SGS patient. Elmistekawy et al. (4) reported the first double-valve surgery in a patient with severe mitral and tricuspid regurgitation with SGS. Pavone et al. (5) in a 16-year-old case, after 12 years of follow-up, was found to have dental malformations among the various clinical features of SGS. Because of the compatibility of clinical findings, we did not have the opportunity to perform molecular analysis of the patient diagnosed with SGS.

Although SGS has typical findings, it has similar clinical features with Loeys-Dietz syndrome (LDS) and Marfan syndrome (MFS). Hypotonia and mental retardation are more common in SGS, but they are rare in LDS and MFS. Some radiologic findings (C1/C2 anomalies, 13 pairs of ribs, square shaped vertebra, Chiari 1 malformation) are more common in SGS than LDS and MFS. Aortic root dilatation is common in LDS and MFS, although it is rare in SGS, it can be a very serious clinical entity (6). Aortic aneurysm is also more common in LDS. Congenital contractural arachnodactyly, frontometaphyseal dysplasia, Melnick-Needles syndrome, Idaho syndrome and Antley-Bixler syndrome should also be considered in the differential diagnosis. When all the differential diagnoses are considered, our patient complies with the SGS clinic with dysmorphic features and other clinical findings.

This is the firstly reported case of SGS from Turkey. It is an example in terms of clinically encountered patients because it carries typical clinical findings.

**Ethics**

**Informed Consent:** Informed consent form was taken.

**Peer-review:** Internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: S.Y., Ö.Ö.Y., Concept: Ö.Ö.Y., H.A., Design: S.Y., S.T.B., Data Collection or Processing: Ö.Ö.Y., S.T.B., Analysis or Interpretation: S.T.B., H.A., Literature Search: S.Y., Writing: S.Y., Ö.Ö.Y.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

# Extracranial Meningioma: A Case Report

## *Ekstrakraniyal Meningiom: Bir Olgu Sunumu*

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**Abstract**

Extracranial meningiomas are rare tumors that occur in soft tissue or skin on the scalp and along the vertebral axis. The etiology of extracranial meningiomas is unknown, although four hypotheses have been postulated according to World Health Organization: (i) meningothelial cells carried along nerve sheaths as they exit the skull or vertebral column; (ii) ectopic arachnoidal cap cells; (iii) meningothelial cells displaced during trauma, and (iv) pluripotent mesenchymal cells capable of under going meningothelial differentiation or metaplasia. Extracranial meningiomas can be presented at all ages, with bimodal peaks occurring in the second decade of life and in the fifth to seventh decades. There is a slight female predominance.

Located swelling in the neck for almost a year, 46-year-old female patient was made mass excision. Macroscopically the mass was 1 cm in greatest dimension, nodular in appearance, cross-sectional face-cream-white color and solid. In microscopic examination, tumor, composed of large oval-round nucleated cells and hyaline stroma were observed. Tumor surrounding thin fibrous pseudocapsule and a plurality of peripheral nerve sections were observed around it. In the stroma psammom body like calcifications were observed. Tumor cells were positive for vimentin, S100, progesterone receptor, cytokeratin and focally epithelial membrane antigen; and negative for glial fibrillary acidic protein, and actin. Based on these findings the patient was diagnosed as extracranial meningioma. Slow growing and with very good prognosis of these tumors, surgical excision is the treatment of choice and do not require further treatment. In the differential diagnosis of soft tissue tumors, extracranial meningiomas should always be considered. It can be skipped because it is rare, so we have found the value to present this case.

**Keywords**
Extracranial meningioma, scalp, tumor

**Anahtar Kelimeler**
Ekstrakraniyal meningiom, skalp, tümör

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**Öz**

Ekstrakraniyal meningiomlar, vertebral aks boyunca, skalpte yumuşak doku ya da deride oluşan, nadir görülen tümörlerdir. Etiyolojisi çok iyi bilinmemesine rağmen patogenezlerinde Dünya Sağlık Örgütü'ne göre 4 hipotez öne sürülmektedir: (i) meningotelyal hücrelerin sinir kılıfları boyunca taşınarak kafatası ve vertebranın dışına çıkması; (ii) ektopik araknoid kap hücreleri; (iii) travma esnasında meningotelyal hücrelerin yer değiştirmesi; ve (iv) pluripotent mezenkimal hücrelerin meningotelyal farklılaşma ya da metaplazi göstermesi. Tüm yaşlarda görülebilmesine rağmen yaş dağılımı bimodaldir, 2. dekatta ve 5-7. dekatlar arasında daha sık görülür. Hafif bir kadın cinsiyet baskınlığı gösterir. Yaklaşık bir yıldır ense bölgesinde şişlik şikayeti bulunan 46 yaşındaki kadın hastaya kitle eksizyonu yapılmıştır. Kitlenin makroskopik değerlendirmesinde en büyük boyutu 1 cm olan, nodüler görünümde, kesit yüzü krem-beyaz renkli, solid, yumuşak doku materyali izlenmiştir. Mikroskopik incelemede ise arada lenfositik hücreler içeren hyalinize stromaya sahip, iri oval-yuvarlak nükleuslu hücrelerden oluşan tümör

izlenmiştir. Tümör çevresinde ince, fibröz bir psödokapsül ve bu kapsül çevresinde çok sayıda periferik sinir kesitleri gözlenmiştir. Tümöral alanlarda yer yer psammom cismi benzeri kalsifikasyonlar dikkat çekmiştir. Tümör hücreleri vimentin, S100, progesteron reseptörü, sitokeratin ve yer yer de epitel membran antijeni ile boyanmış, glial fibriler asidik protein ve aktin ile boyanmamıştır. Hastanın klinik olarak incelenmesinde intrakraniyal meningioma rastlanmamıştır. Bu bulgularla hastaya ekstrakraniyal meningiom tanısı konulmuştur. Yavaş büyüyen ve prognozları çok iyi olan bu tümörlerin tedavisinde cerrahi eksizyon tercih edilir ve ileri bir tedavi yöntemine ihtiyaç duyulmaz. Yumuşak doku tümörlerinde ayırıcı tanıya giderken ekstrakraniyal meningiom mutlaka düşünülmelidir. Ancak nadir görüldüğünden sıklıkla atlanır. Nadir görülen bir tümör olması sebebiyle biz bu olguyu sunulmaya değer bulduk.

## Introduction

Meningiomas are second most common benign tumors of the central nervous system. 20% of intracranial meningiomas spread to extracranial areas (1). Primer extracranial meningiomas are rare tumors of scalp, soft tissue or skin along the vertebral axis. By definition, they are not associated with a meningioma of the underlying neuroaxons, and it should always be kept in mind that there may be an extracranial extension of an intracranial meningioma before it is accepted as a soft tissue or skin primary tumor. Primary extracranial meningiomas constitute less than 2% of all meningiomas (2,3). Two categories are examined: primary and secondary extracranial meningioma. Primary type is independent of intracranial meningioma. Secondary type is developed by direct release of the intracranial mass. The differential diagnosis includes various benign and malignant neoplasms, such as epithelial, neurogenic, vascular and mesenchymal tumors (4).

## Case Report

A 46-year-old woman was admitted to the hospital for complaints of swelling in the nape region for approximately one year. Mass excision was applied. In the macroscopic evaluation of the mass, 1x0.6x0.4 cm nodular appearance, cross-section cream-white colored, solid, soft tissue material was observed. A well-defined nodular lesion was observed on microscopic examination. The cells forming the lesion were composed of solid islands and occasionally trabecularized in a hyalinized stroma. Lymphocytic cells were observed in the stroma between the islands. Psammom bodies were noticed in places (Figure 1). Tumor cells are large, oval-round nucleus and contain small nucleoli (Figure 2). A thin fibrous pseudocapsule around the lesion and numerous peripheral nerve sections around the capsule caught attention. Tumor cells were immunohistochemically stained by vimentin (Dako, Glostrup, Denmark), S100 (Dako, Glostrup, Denmark), progesterone receptor (Dako, Glostrup, Denmark), cytokeratin (Dako, Glostrup, Denmark), and occasionally epithelial membrane antigen (EMA) (Dako, Glostrup, Denmark). Glial fibrillary acidic protein (GFAP) (Dako, Glostrup, Denmark) and actin (Dako, Glostrup, Denmark) did not showed expression (Figures 3, 4). Ki-67 (Dako,

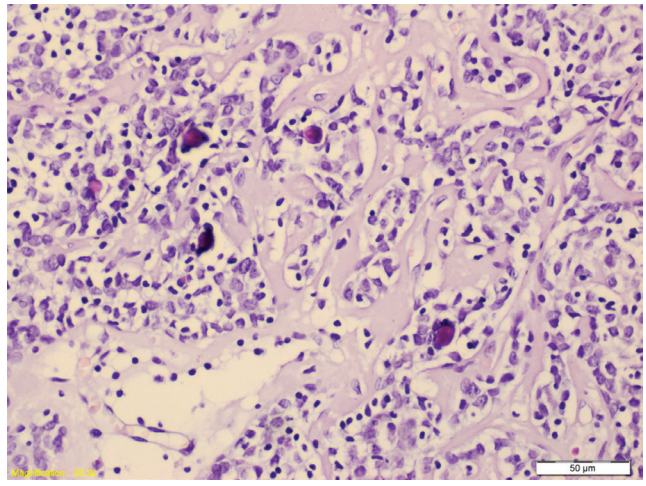


**Figure 1.** Psammom bodies among the tumoral islands (x400, hematoxylin and eosin)

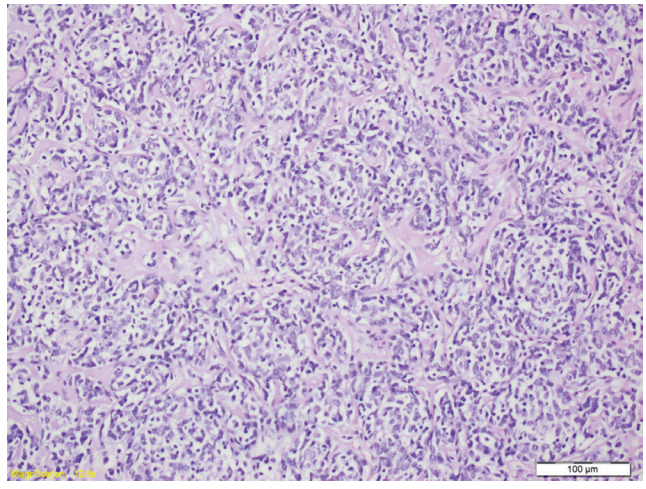


**Figure 2.** Tumor cells forming islands in the hyalinized stroma (x200, hematoxylin and eosin)

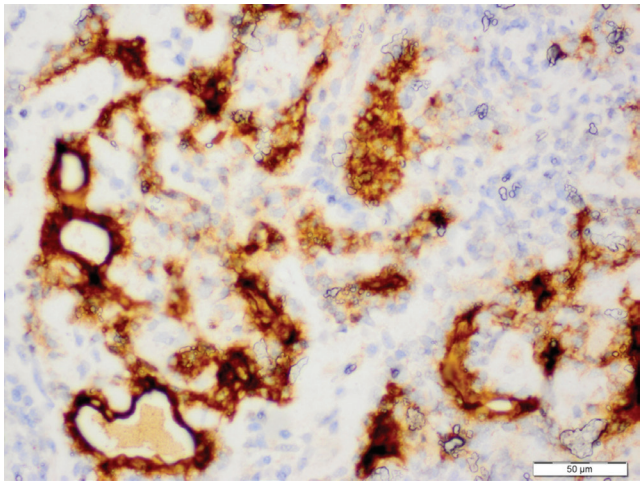


**Figure 3.** Tumor cells showing focal staining with EMA (x400, EMA)

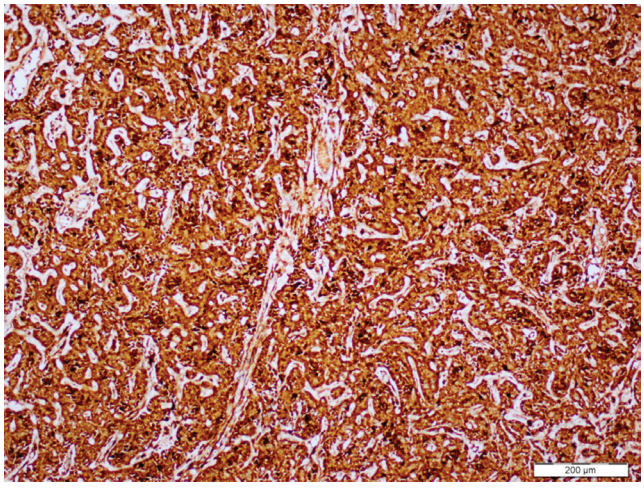


**Figure 4.** Tumor cells showing diffuse staining with S100 (x100, S100)

Glostrup, Denmark) was stained 2% of tumor cells. With these findings, the patient was diagnosed with extracranial meningioma.

Informed consent was not necessary because the case report was a retrospective study.

## Discussion

Meningiomas are slow-growing, relatively common tumors arising from arachnoid cap cells of the meninges and constitute 13-18% of adult intracranial neoplasms. They are more frequent in women and appear more frequently in middle age (5). They are divided into 3 types according to their malignancy degree: benign [World Health Organization (WHO) grade 1], atypical (WHO grade 2), and anaplastic (WHO grade 3). Approximately 80% of meningiomas are benign. The most common histologic variants are meningothelial, fibrous, and transitional (1). Extracranial meningiomas are less common and constitute less than 2% of all meningiomas. Although it can be seen at all ages, the age distribution is bimodal, they are more common in 2$^{th}$ and 5$^{th}$-7$^{th}$ decades. There is a slight female gender dominance. They occur more frequently in the vertebrae, neck, thorax, shoulder and peritoneum (3). In many cases, orbita is shown as the most common region, but tumors that have no connection with the optic nerve should be considered extracranial. Meningiomas with intracranial and intraspinal components should be excluded by definition. For example, en plaque meningiomas are usually invasive to the skull, and these tumors should not be evaluated as pure intraosseous. Although the etiology is not well known, 4 hypotheses are suggested in pathogenesis according to the WHO: (i) meningothelial cells moving out of the skull and vertebra along the nerve sheaths; (ii) ectopic arachnoid cap cells; (iii) displacement of meningothelial cells during trauma; and (iv) meningothelial differentiation or metaplasia of pluripotent mesenchymal cells. Tumor-related symptoms are associated with tumor size, location, and growth rate. They are usually seen as painless, slow growing masses.

Although macroscopically like intracranial meningiomas, the spread to the surrounding tissue is more common in these tumors. The color and consistency properties vary depending on the cellularity, collagen accumulation, and tumor grade (6).

Histologically, these tumors are indistinguishable from normal intracranial meningiomas (7). In the literature, extracranial meningiomas are divided into various histological types and grades, such as those with intracranial location (5,8,9). Solid meningiothelial cell nests are layered or coiled and occasionally contain psammom bodies. Generally, the tumors are irregular and composed of neoplastic, epithelioid cell lobules and folds. The nuclei are usually round-oval, contains thin nuclear chromatin and occasionally intranuclear pseudoinclusions. Although intranuclear inclusions are not always obvious and can not be easily detected, they are present in 71% of tumors (5). There are various hypotheses about the formation of psammom bodies. They are thought to be derived

from endothelial cells of obliterated vessels or may be formed by the secretion of arachnoid vessel cells and the calcification of necrotic cells (10).

Immunoprofiles of extracranial meningiomas are the same as meningiomas located in the central nervous system. They all express EMA and vimentin, while some express S100 protein (28%). Progesterone receptor positivity is also frequently seen (6). GFAP is negative. The Ki-67 index is below 5% and supports the slow progress of this clinical course (5,7-9).

Clinically, the differential diagnosis is extensive and includes nevi, fibroma, glioma, hemangioma, lipomas and many other benign or epithelial tumors and many malignant entities such as neurogenic tumors, melanoma, olfactory neuroblastoma, vascular tumors, mesenchymal tumors (4). Another entity that needs attention in differential diagnosis is psammomatous melanocytic schwannoma. This entity is seen as a finding of the Carney complex. For this reason, the patient needs to be investigated for myxoma, pigmentation or endocrine disorders that might suggest the Carney complex. These two tumors can be separated based on their histopathological characteristics. Extracranial meningioma does not have melanin pigment as well as areas of Antoni A and Antoni B expected to be seen in psammomatous melanocytic schwannoma. Careful microscopic examination and selection of appropriate immunohistochemical stain helps to confirm the diagnosis when cutaneous meningiomas is in the differential diagnosis. Nevertheless, more frequent tumors should be considered in differential diagnosis and the diagnosis should be based on histopathologic examination (7,8).

Depending on tumor grade and resection width, the prognosis of these slow-growing tumors is generally excellent (1,6). It is more likely to recur in intraosseous areas. Surgical excision provides complete cure and no further treatment is required. Distant metastases have been reported in only 6% of cases, frequently in anaplastic variants (6). It is important to note that these tumors have the potential to appear in places we have never expected. This, in turn, removes the potential difficulties associated with diagnosis and treatment management (5,8). As a result, extracranial meningiomas are tumors that cause diagnostic difficulties from time to time because of their abundant entity in their differential diagnosis. However, the prognosis is very good because of the slow growth and complete cure with complete surgical excision.

**Ethics**

**Informed Consent:** Informed consent was not necessary because the case report was a retrospective study.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: C.T., Ö.E.Ö., Concept: Ö.E.Ö., C.T., Design: Ö.E.Ö., Data Collection or Processing: Ö.E.Ö., C.T., Analysis or Interpretation: Ö.E.Ö., S.G., T.Ö., A.G.Ö., Literature Search: Ö.E.Ö. Writing: Ö.E.Ö., S.G., T.Ö., A.G.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

# A Rare Complication Occurring Years After Thyroid Surgery: A Cutaneous Fistula

## *Tiroit Cerrahisinden Yıllar Sonra Ortaya Çıkan Nadir Bir Komplikasyon: Deri Fistülü*

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**Keywords**
Thyroid surgery, cutaneous fistula, complication

**Anahtar Kelimeler**
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This case was presented as poster presentation at 36th Turkey Endocrinology and Metabolism Diseases Congress at 21-25 May 2014 in Antalya.



### Abstract

The mortality and morbidity of thyroid surgery are low. The complications after thyroid surgery include bleeding, wound site infection, keloid formation, recurrent laryngeal nerve and superior laryngeal nerve injury, temporary and permanent hypocalcemia, and injury to surrounding structures such as esophagus, artery, vein and the cervical sympathetic trunk.
Other much rare complication includes cutaneous fistula formation. In this report, we describe a patient who underwent thyroid surgery and developed cutaneous fistula in the late postoperative period, a complication that has never been reported previously following thyroid surgery.

### Öz

Tiroid cerrahisi düşük mortalite ve morbiditeye sahiptir. Tiroid cerrahisi sonrası görülen komplikasyonlar; kanama, yara yeri enfeksiyonu, keloid oluşumu, rekürren laringeal sinir ve süperior laringeal sinir hasarı, geçici ve kalıcı hipokalsemi, özofagus, arter, ven ve servikal sempatik zincir gibi çevre yapılarda zedelenmedir. Deri fistülü gelişmesi çok nadir bir komplikasyondur. Bu makalede, tiroid cerrahisi uygulanmış ve geç postoperatif dönemde tiroid cerrahisi sonrası daha önce bildirilmemiş bir komplikasyon olarak deri fistülü gelişmiş bir olgu tanımlanmıştır.

### Introduction

Thyroid surgery is a safe procedure with low mortality and morbidity (1). The most common complications after thyroid surgery are post-operative hypocalcemia and recurrent laryngeal nerve injury (2). Cutaneous fistula developing from thyroidectomy incision scar is not among the known complications (3). We observed that a 57-year-old female patient developed cutaneous fistula from the incision scar 21 years after the thyroid surgery she had undergone. This case is being reported because it is an unexpected late complication following thyroid surgery.

## Case Report

The 57-year-old female patient had undergone thyroid surgery 21 years ago. The patient presented with yellow-colored discharge that was spontaneous and occurred without trauma, from an area about 1.5 cm in diameter on the thyroidectomy incision scar. A tract covering an area of about 1.5 cm was seen to have developed on the patient's thyroidectomy scar (Figure 1). There was no discharge. Ultrasonography was performed and demonstrated a hypoechoic nodule, 5 mm in diameter, in the right in a heterogeneous internal structure, sized 7x9x18 mm, in the left and 16x16x38 mm in the right, as well as a residual thyroid tissue with heterogeneous internal structure containing coarse calcifications in an approximately 8 mm area in the right. There was an approximately 1.5 cm fistulized tract in the skin in the midline. It was considered that the tract ended in a blind end, and echogenicities with air values were determined in it. Neck magnetic resonance imaging was taken and demonstrated an area that was 1 cm in diameter which showed peripheral contrast substance uptake in post-contrast analyses, which was hypointense in the T1A sequence and hyperintense in the T2A sequence with no apparent association with trachea, thyroid gland and other anatomical bodies located in the subcutaneous fatty tissue at the level of the isthmus location in the thyroid. This area was extending to the skin. Thyrotrophin-stimulating hormone, sT4, sedimentation, C-reactive protein and white blood cells in whole blood count were normal. Patient's follow up demonstrated no persistent discharge, but two black suture materials came out of a 1.5 cm area on day 7 (Figure 2). The tract closed spontaneously without requiring any surgical intervention and the patient is currently under follow up with no problems.

Written consent regarding publication of the findings and photos was received from the patient.

**Figure 1.** Cutaneous fistula on the thyroidectomy incision scar

**Figure 2.** Two black suture materials coming out of the cutaneous fistula

## Discussion

Bleeding, wound site infection and keloid formation are general complications following surgery. Specific complications after thyroid surgery are injury of recurrent laryngeal nerve and the outer branch of the superior laryngeal nerve, transient and permanent hypocalcemia, and injury to the surrounding tissue (3). In a large series including 14.934 cases evaluating complications following thyroid surgery, transient hypoparathyroidism was reported in 8.3%, permanent hypoparathyroidism in 1.7%, recurrent permanent injury of the laryngeal nerve in 1%, transient injury in 2%, superior laryngeal nerve injury in 3.7%, diplegia, dysphagia, bleeding, and wound site infection very rare (4). Cutaneous fistula was not observed in this series. Likewise, a study by Bergenfelz et al. (5) which evaluated 3.660 cases did not report cutaneous fistula following thyroid surgery. A literature search revealed that different complications than anticipated occurred following thyroid surgery. Hypopharyngeal fistula (6), Horner's syndrome, chylous leakage fistula (7,8), flap edema (7) and seroma (8) are rare complications following thyroidectomy. With literature search,

there was no report of suture material spontaneously causing fistula in the skin years after thyroid surgery. Non-absorbable multifilament sutures are black, and was used in cutaneous, subcutaneous and fascia repairs in the past. It is, however, not preferred much currently. It may result in fistula tract, hypertrophic scar and infection if left for a long time in the skin (9). In our patient, we thought that the black suture material coming out of the cutaneous fistula was a non-absorbable multifilament suture. We believe that this suture material was used in the thyroid surgery performed 21 years ago and was left under the skin.

Development of a fistula and suture material coming out of the fistula years after thyroid surgery was considered to be a very rare late complication. With this case, we report for the first time in the literature that cutaneous fistula can be seen as a late complication of thyroid surgery. In addition, we would like to emphasize that suture material left under the skin could be one of the causes when fistula develops from a thyroidectomy scar years after the procedure and that the fistula can close spontaneously without surgical intervention.

**Ethics**

**Informed Consent:** Was obtained from patient who participated in this case.

**Peer-review:** Externally and internally peer-reviewed.

**Authorship Contributions**

Surgical and Medical Practices: M.Ü., Ç.K.E., A.O.Ç., A.M., Concept: M.Ü., Design: M.Ü., Data Collection or Processing: M.Ü., Analysis or Interpretation: M.Ü., Ç.K.E., Literature Search: M.Ü., Ç.K.E., Writing: M.Ü., Ç.K.E.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The author declared that this study has received no financial support.

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