

TC.
YEDİTEPE UNIVERSITY
INSTITUTE OF HEALTH SCIENCES
DEPARTMENT OF ENDODONTICS

**EPOXY RESIN BASED AND BIO CERAMIC
BASED ROOT CANAL SEALERS
RETREATABILITY AND BOND
STRENGTH**

DOCTOR OF PHILOSOPHY THESIS

DUYGU MUSTAFA PAMUK, PhD

İSTANBUL- 2022

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İSTANBUL- 2022

APPROVAL

Institute : Yeditepe University Institute of Health Sciences
Programme : Endodontics
Title of the Thesis : Epoxy Resin Based and Bioceramic Based Root Canal Sealers
Retreatability and Bond Strength in Retreatment

Owner of the Thesis : Duygu Mustafa Pamuk

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This study has approved as a Doctorate Thesis in regard to content and quality by the Jury.

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APPROVAL

This thesis has been deemed by the jury in accordance with the relevant articles of Yeditepe University Graduate Education and Examinations Regulation and has been approved by Administrative Board of Institute with decision dated and numbered

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DECLARATION

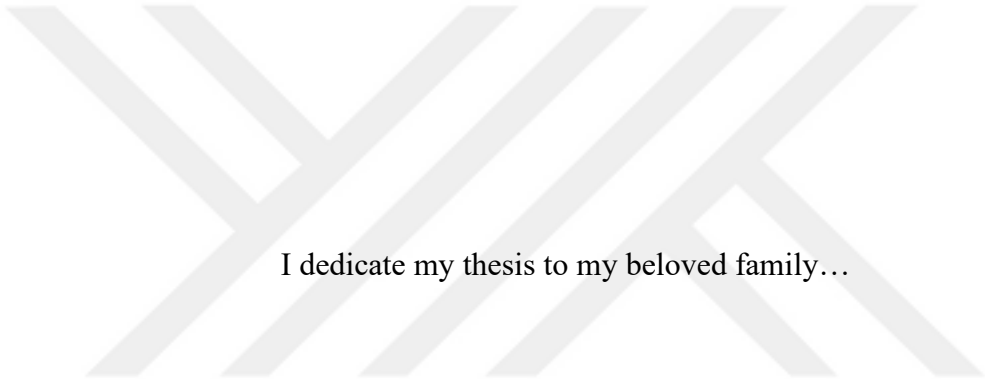
I hereby, declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

10.02.2022

Duygu Mustafa Pamuk



DEDICATION



I dedicate my thesis to my beloved family...

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LIST OF SYMBOLS AND ABBREVIATIONS

%	Percentage
°C	Celsius
Al	Aluminum
ANSI/ADA	American Nation Standard / American Dental Association
<i>C. albicans</i>	Candida Albicans
CBCT	Cone Beam Computed Tomography
Cu	Copper
<i>E. coli</i>	Escherichia Coli
<i>E. faecalis</i>	Enterococcus Faecalis
EDTA	Ethylenediaminetetraacetic Acid
<i>F. nucleatum</i>	Fusobacterium Nucleatum
hPDLSC	Human periodontal ligament stem cell
<i>K. pneumoniae</i>	Klebsiella Pneumoniae
kV	Kilowatt
<i>L. casei</i>	Lactobacillus Casei
Micro-CT	Micro Computed Tomography
Min	Minutes
mL	Milliliter
Mm	Millimeter
MPa	Megapascal
MTA	Mineral Trioxide Aggregate
N	Newton
Nano-CT	Nano Computed Tomography
NaOCl	Sodium Hypochlorite
Ni-Ti	Nickel Titanium
<i>P. gingivalis</i>	Porphyromonas Gingivalis
<i>P. intermedia</i>	Prevotella Intermedia
<i>P. micra</i>	Parvimonas Micra
<i>P. oralis</i>	Prevotella Oralis
<i>P. propionicum</i>	Propionibacterium Propionicum
<i>P. vulgaris</i>	Proteus Vulgaris
PIPS	Photon-induced photoacoustic streaming
<i>Ps. aeruginosa</i>	Pseudomonas Aeruginosa
r	Radius
<i>S. aureus</i>	Staphylococcus Aureus
<i>S. epidermidis</i>	Staphylococcus Epidermidis
<i>S. mitis</i>	Streptococcus Mitis
<i>S. mutans</i>	Streptococcus Mutans
<i>S. pneumoniae</i>	Streptococcus Pneumoniae
<i>S. salivarius</i>	Streptococcus Salivarius
<i>S. sanguis</i>	Streptococcus Sanguis
SD	Standard Deviation
SEM	Scanning Electron Microscope
μA	Microampere
μm	Micrometer

ABSTRACT

Mustafa-Pamuk, D (2022). Comparison of Epoxy Resin and Bioceramic Based Root Canal Sealers Retreatability and Bond Strength in Retreatment. Yeditepe University Institute of Health Sciences, Department of Endodontics. PhD Thesis. Istanbul.

The purpose of endodontic treatment is to prevent and heal the apical periodontitis. The success rate of root canal treatment has been found between 93-84% in the studies. According to this; even when root canal treatment performed under ideal conditions, post-treatment disease may occur. Iatrogenic errors during procedure, leakage of the coronal restoration or persistent infections can cause post-treatment disease. When post-treatment disease occurs, the infected root canal filling must be easily removed from the root canal in order to re-disinfect the root canal cavity. In this study, it was aimed to investigate retreatability and bond strength of epoxy resin based AH Plus (Dentsply Mallefier, USA, Oklahoma), calcium silicate based TotalFill BC Sealer (FKG Dentaire, Switzerland) and CeraSeal (Meta-Biomed, South Korea) canal sealers, when applied with lateral condensation and single cone methods. This study was performed on 66 extracted, single rooted, human mandibular premolars. All samples were separated from their crowns under water cooling by using a diamond separator and their root length was adjusted to 16 mm. All samples were instrumented with Protaper Next files and then randomly separated into 6 groups that contains 11 samples each. Groups were varied among the root canal sealer used and obturation techniques. Group (BC-L): TotalFill BC Sealer + Lateral Condensation, Group (BC-S): TotalFill BC Sealer + Single Cone, Group (Cera-L): CeraSeal + Lateral Condensation, Group (Cera-S): CeraSeal + Single Cone, Group (AH-L): AH Plus + Lateral Condensation, Group (AH-S): AH Plus + Single Cone. After obturation of root canals, all samples were scanned with Micro-CT device SkyScan 1172 and root canal filling volume per sample were measured. Then root canal fillings were removed with Protaper Universal Retreatment Files and the duration of the procedure was recorded in seconds, re-establishing apical patency were evaluated for each sample. Then second Micro-CT scanning were performed in order to measure residual root canal filling volumes of all samples. All teeth were re-obtured according to the group in which they were found. As final step, each sample was divided into 3 equal parts with a diamond disk and push out force applied with instron device. Finally bond strength values were

measured. Statistical analyzes were performed with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program. The results were evaluated at the significance level of $p < 0.05$. The duration of retreatment procedure (root canal filling removal only) was longer in Group (BC-L) than in Group (BC-S) ($p = 0,011$). The duration of retreatment procedure (root canal filling removal only) was longer in Group (AH-L) than in Group (AH-S) ($p = 0,001$). Group (BC-S) and Group (Cera-S) showed lower residual root canal filling volume than Group (AH-S) ($p = 0,003$, $p = 0,011$). There was no statistically significant difference between Group (BC-S) and Group (Cera-S) in terms of residual root canal filling volume. ($p = 0,412$) There were no statistically significant difference between any groups in terms of re-establishing apical patency. Bond strength of Group (BC-L) was higher than in Group (BC-S) ($p = 0,0001$) and bond strength of Group (AH-L) was higher than in Group (AH-S) ($p = 0,0001$). Bond strength of Group (Cera-S) was higher than Group (AH-S) and Group (BC-S) ($p = 0,0001$).

Keywords: Retreatability, Micro-CT, AH Plus, TotalFill BC Sealer, CeraSeal, Bond Strength.

ÖZET

Mustafa Pamuk, D. Epoksi Resin ve Biyoseramik Esaslı Kanal Patlarının Kök Kanalından Sökülebilirliklerinin ve Bağlanma Dayanımının İncelenmesi.

Endodontik tedavinin amacı apikal periodontitisi önlemek ve apikal periodontitis gerçekleştiği durumlarda da iyileştirmektir. Yapılan çalışmalarda kanal tedavisinin başarı oranı %93-84 arasında bulunmuştur. Bu sonuç; ideal koşullarda kanal tedavisi yapıldığında bile tedavi sonrası hastalık oluşabileceğini göstermektedir. İşlem sırasında gerçekleşen iyatrojenik hatalar, koronal restorasyonun sızdırması veya inatçı enfeksiyonlar kanal tedavisi sonrası hastalığa neden olabilir. Kanal tedavisi sonrası hastalık ortaya çıktığında, kök kanal boşluğunu yeniden dezenfekte edilmelidir. Bunun için de enfekte kök kanal dolgusunun kök kanalından kolayca çıkarılması gerekmektedir. Bu çalışmada, sıklıkla kullanılan epoksi resin esaslı AH Plus kanal patı ve son yıllarda piyasaya çıkmış biyoseramik esaslı TotalFill BC Sealer ve CeraSeal kök kanal patlarının lateral kondensasyon ve tek kon yöntemleri ile kullanıldıklarında kök kanalından sökülebilirliğinin ve bağlanma dayanımının karşılaştırılması amaçlanmıştır. Bu çalışmada; Yeditepe Üniversitesi Klinik Araştırmalar Etik Kurulu onayı ile 66 adet çekilmiş tek köklü insan alt küçük azı dişleri kullanılmıştır. Örnekler su soğutması altında elmas diskler ile kronlarından ayrılmıştır ve kök uzunlukları 16 mm'ye ayarlanmıştır. Tüm numuneler Protaper Next döner Ni-Ti eğeler şekillendirilmiş, ardından randomize olarak (her grupta 11 örnek olacak şekilde) 6 gruba ayrılmıştır. Gruplar kullanılan kanal patı ve kanal dolgusu tekniklerine göre oluşturulmuştur. Grup (BC-L): Totalfill BC Sealer + Lateral Kondensasyon, Group(BC-S): Totalfill BC Sealer + Tek Kon, Group(Cera-L): CeraSeal + Lateral Kondensasyon, Group(Cera-S): CeraSeal + Tek Kon, Grup(AH-L): AH Plus + Lateral Kondensasyon, Grup(AH-S): AH Plus + Tek Kon. Örneklerin kanal dolguları tamalandıktan sonra örneklerin tek tek SkyScan 1172 cihazı ile Micro-CT taraması yapılmış ve her örneğin kök kanal dolgusu hacimleri ölçülmüştür. Daha sonra Protaper Universal Retreatment döner eğeler ile kanal dolguları uzaklaştırılmıştır. Bu işlemin süresi saniye cinsinden kaydedilip, her örnek için yeniden apikal açıklığın sağlanması değerlendirilmiştir. Daha sonra tüm örneklerin kanal dolguları uzaklaştırıldıktan sonra kalan artık kök kanal dolgusu hacimlerini ölçmek için ikinci bir Micro-CT taraması yapılmıştır. Tüm dişler bulundukları gruba göre yeniden kanal

dolguları yapılmıştır. Son adım olarak her numune elmas disk ile 3 eşit parçaya bölünüp ve instron cihazı ile uygulanan itme kuvveti uygulanarak bağlanma dayanımları ölçülmüştür. Bu çalışmada istatistiksel analizler NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) paket programı ile yapılmıştır. Sonuçlar $p<0.05$ anlamlılık düzeyinde değerlendirilmiştir. Kanal dolgusunu uzaklaştırma prosedürünün süresi Grup (BC-L)'de Grup (BC-S)'ye göre daha uzun bulunmuştur ($p=0,011$). Kanal dolgusunu uzaklaştırma prosedürünün süresi Grup (AH-L)'de Grup (AH-S)'ye göre daha uzun bulunmuştur ($p=0,001$). Grup (BC-S) ve Grup (Cera-S) gruplarında artık kanal dolgusu hacimleri Grup (AH-S)'ye göre daha az olduğu görülmüştür ($p=0,003$, $p=0,011$). Grup (BC-S) ve Grup (Cera-S) arasında artık kanal dolum hacmi açısından istatistiksel olarak anlamlı fark bulunmamıştır ($p=0,412$). Apikal açıklığın yeniden oluşturulması bakımından inceleme yapıldığında altı grup arasında istatistiksel olarak anlamlı fark bulunmamıştır. Grup (BC-L)'nin bağlanma dayanımı Grup (BC-S)'ye göre daha yüksek bulunmuştur ($p=0,0001$). Grup (AH-L)'nin bağlanma dayanımı Grup (AH-S)'ye göre daha yüksek bulunmuştur ($p=0,0001$). Grup (Cera-S)'nin bağlanma dayanımı Grup (AH-S) ve Grup (BC-S)'ye göre daha yüksek bulunmuştur ($p=0,0001$).

Anahtar Kelimeler: Retreatability, Micro-CT, AH Plus, TotalFill BC Sealer, CeraSeal, Bond Strength.

1. INTRODUCTION AND PURPOSE

Odontogenic infections are inflammatory diseases caused by infected teeth. In some cases, they may extend to the alveolar bone, jaws or facial region. This inflammatory process can cause local and systemic symptoms such as abscess, swelling, fever and lymphadenopathy. The inflammation may also spread to distal areas of the body and may even cause more severe complications such as brain abscess or cavernous sinus thrombosis (1). One of the major factors that causes odontogenic infections is the infection of the root canal system of a tooth (2).

Microorganisms can enter the root canal system via caries, trauma, periodontal ligament, blood circulation or leaking coronal restorations (3). When the root canal system becomes infected, endodontic treatment must be performed in order to prevent and heal further infection and apical periodontitis (4).

Endodontic treatment is carried out by shaping, disinfecting and filling the root canals in three dimensions (5). Root canal filling is generally performed by using core gutta percha and root canal sealer combination. While gutta-percha forms the core of the root canal filling, root canal sealer fills the voids between the dentin wall and gutta-percha. Consequently, transition of microorganisms to the apical region and reinfection of the tooth are prevented (6).

The success rate of root canal treatment has been reported as 93-84% in various studies. Iatrogenic errors during root canal procedure, leakage of the coronal restoration or persistent infections can cause post-treatment disease (7). Accordingly, post-treatment disease may occur even when root canal treatment is performed under ideal conditions (8). When post-treatment disease occurs, nonsurgical retreatment must be performed (8,9). Therefore, the previous root canal filling must be removed from the root canal easily in order to perform proper disinfection of the root canal space (8).

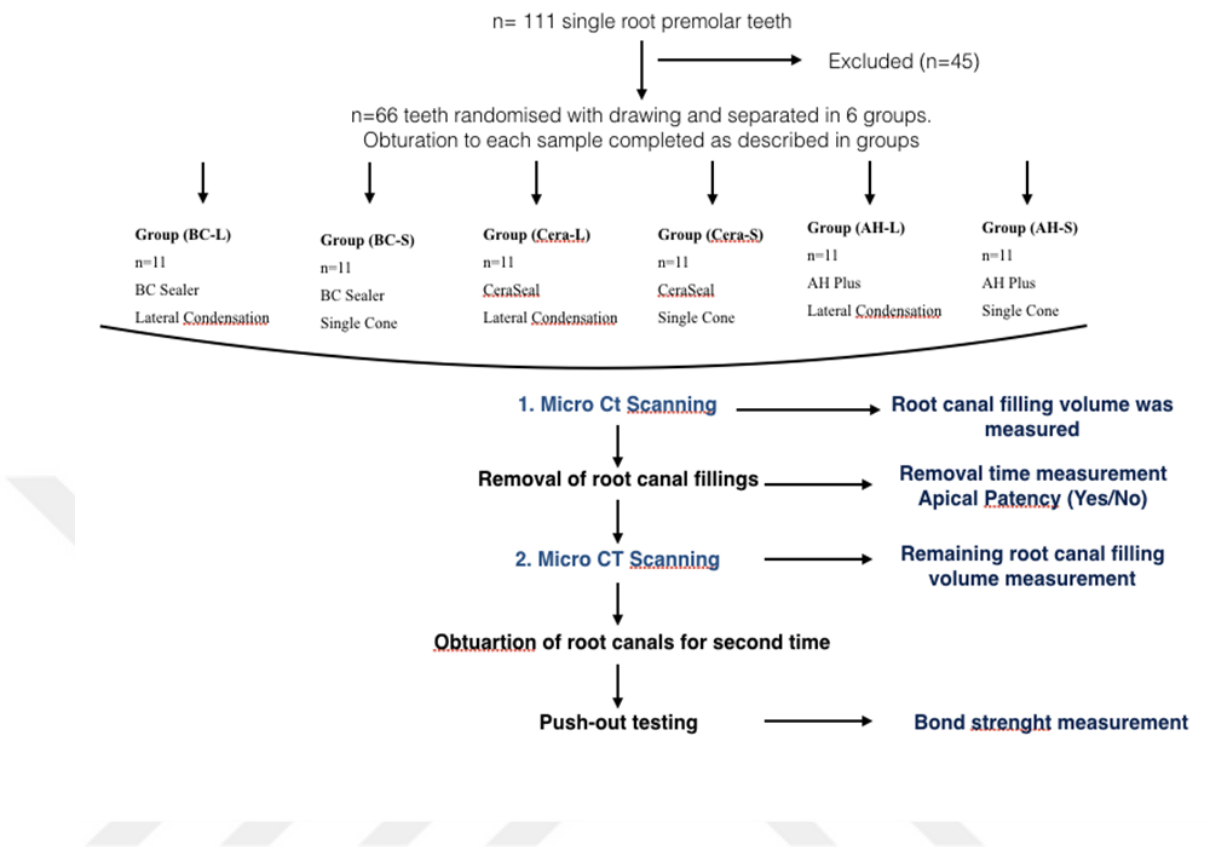
The type of sealer and root canal filling method are factors which can affect the retreatment of the root canal (10,11). There are various types of root canal sealers with different contents are available in market (5,12). Although epoxy resin-based sealers are described as the gold standard, the use of bioceramic-containing root canal sealers are also mentioned in recent years (13). Bioceramic based sealers possess favorable

characteristics such as; biocompatibility, volumetric expansion and formation of apatite like layer during polymerization and formation of a chemical bond with dentinal walls (14). Strong bond formation of the sealer to dentine is important in preventing re-infection of the root canal system. Therefore it is important in prognosis of the root canal treatment (15). However, there was concern about bioceramic sealers that the formation of chemical bond with the dentin wall would make it difficult to remove from the root canal during retreatment (16–19).

The purpose of this study is to investigate retreatability and bond strength of epoxy resin based AH Plus (Dentsply Mallefier, USA, Oklahoma), calcium silicate based TotalFill BC Sealer (FKG Dentaire, Switzerland) and CeraSeal (Meta-Biomed, South Korea) canal sealers, when applied with lateral condensation and single cone methods.

There are several methods for assessing the retreatability of the root canal filling such as; measuring residual root canal filling volumes with SEM (Scanning electron microscope) (20), digital radiography (21), confocal microscope and stereomicroscope (22), cone-beam computed tomography (CBCT) (23) and micro-computed tomography (Micro-CT) (24). Micro-CT imaging is the one method which can provide three-dimensional, high resolution images. Micro-CT imaging enables accurate measurement residual root canal filling volumes and does not damage the samples during imaging. It is also possible to repeat the scanning when it is needed (25). In this study, residual root canal filling volumes were measured with Micro-CT. In order to assess the retreatability, duration of retreatment procedure was measured and re-establishment of apical patencies during retreatment were also evaluated.

Table 1. Flow chart of the study



2. LITERATURE REVIEW

Odontogenic infections that occur in jaw bones and facial areas can reduce a person's quality of life and may even be life threatening (1). Microorganisms involved in these infections can reach the root canal system through caries, trauma, periodontal ligament, blood circulation and leakage from previous inadequate restorations (3). When microorganisms reach to the pulp-less area or the pulp tissue of root canal system, they transform the root canal into a source of infection and cause the development of apical periodontitis in the periapical region if treatment procedures are not performed. Endodontic treatment is performed in order to prevent this condition and to treat it in its presence (1). In other words, the purpose of endodontic treatment is to treat apical periodontitis or to prevent the occurrence of apical periodontitis (4).

Endodontic treatment is carried out by shaping, disinfecting and filling the root canals in three dimensions. In order to prevent the reinfection of the root canals following the completion of the disinfection process, the root canal cavity must be filled hermetically to prevent the ingress of microorganisms (5). Therefore, the effects of root canal fillings on treatment success have been the subject of hundreds of studies and they are still conducted due to the significance of the topic.

Gutta-percha forms the core of the root canal filling. Root canal sealer is used to fill the void between the core material and the canal walls (6). When gutta-percha, which is a core material, is used without root canal sealer, porous structures are formed and they adversely affect the prognosis by causing microbial leakage (26). Root canal sealer has an important role in creating a hermetic root canal filling therefore it is an important factor in the prognosis of endodontic treatment.

2.1. Overview of Root Canal Sealers

Root canal sealers are expected to form the connection between the core part of the root canal filling and the root dentine, fill the voids within the root canal filling, seal accessory canal orifices and multiple apical foramina, and provide lubrication during the placement of the core part of the root canal filling (6).

In order to accomplish these goals, root canal sealers must have ideal properties. These properties are stated by Grossman as follows:

Root canal sealers:

- Must provide hermetic covering.
- Must be radiopaque
- Must be easy to prepare and mix
- Must not shrink during polymerization
- Must form adhesion with the root canal wall.
- Must not stain dental tissues
- Must have antimicrobial effects
- working time must be long
- Must be soluble in tissue fluids, not in root canal
- Must be biocompatible or at least not irritating to periapical tissues
- Must be easily removed when it is desired to be removed from the root canal.

Today, there is no root canal sealer that meets all of these criteria (5).

According to their composition, root canal sealers are classified as:

- Zinc oxide eugenol based sealers
- Calcium hydroxide based sealers
- Non-eugenol based sealers
- Glass ionomer based sealers
- Resin based sealers
- Silicone based sealers
- Bioceramic sealers (5,27)

2.1.1. Zinc Oxide Eugenol Based Root Canal Sealers

Zinc oxide eugenol based root canal sealers were first introduced by Rikert and Dixon. They contained zinc oxide powder and eugenol oil which is an essential oil obtained from cloves (28,29). Since the original sealer was clinically successful, the initial formula was developed by different manufacturers over time and released under different names (30). For radiopacity, silver particles were added to the formula (Pulp Canal Sealer), but later the use of silver particles was discontinued because it caused discoloration of dentine (31). Later, instead of silver particles, barium sulfate was added to the formula for radiopacity and released to the market. Procosol, Tubli-Seal, Endofill, Master-Dent Root Canal Sealer, Pulpdent Root Canal Sealer are some of the barium sulfate containing zinc oxide eugenol based sealers (30). Another different formulation which stayed in the market for a period was paraformaldehyde containing zinc oxide eugenol based sealers. Root canal sealers; N2 and Endomethasone belong to this category. However, clinical use of this formulation was abandoned when it was determined that these root canal sealers cause coagulation necrosis and inflammation, delay healing in the periapical tissues and have toxic effects (32,33). In addition, it has been reported that toxic metals were isolated from different organ systems after a while due to the lead and mercury content of the N2 root canal sealer (34).

Due to the harmful effects of paraformaldehyde containing sealers mentioned above, a new root canal sealer named Endomethasone N was produced by removing the paraformaldehyde in Endomethasone and adding hydrocortisone instead. Jeanneau *et al.* observed the anti-inflammatory effects of Endomethasone N on human periodontal ligament cells due to the presence of hydrocortisone it contains (35). Zinc oxide-eugenol based sealers have favorable properties such as inhibiting neural activity at low doses, having anti-inflammatory and antimicrobial activities, providing vasodilation, resorption when extruded from the apex and a long setting time (36). On the other hand, they also have some disadvantages such as shrinkage during polymerization and high solubility (5). Saleh *et al.* compared the antimicrobial effect of Grossman paste (zinc oxide eugenol based sealer), AH plus, Ketac-Endo, Apexit, RoekoSeal Automix, RoekoSeal Automix + Primer with calcium hydroxide which is used as an intracanal medicament. In their study, a bacterial culturing method was used on powdered dentin. According to their results, Grossman sealant with zinc oxide eugenol and AH Plus sealant with epoxy resin were

found to have higher antimicrobial activity than the root canal sealers in other experimental groups (37). Long J. *et al.* observed that Pulp Canal Sealer (Zinc oxide eugenol based sealer) did not prevent biofilm formation despite its antimicrobial activity (38). Çobankara *et al.* observed the antibacterial activities of various root canal sealers against *E. faecalis* with direct contact test and agar diffusion test. As a result of this study, it was observed that zinc oxide eugenol based Sultan root canal sealer had an antibacterial effect against *E. faecalis* and this effect was higher than glass ionomer based Ketac Endo sealer (39). Dalmia *et al.* investigated the antibacterial effects of root canal sealers against *E. faecalis* with direct contact test. It was observed that TubliSeal has an antibacterial effect on *E. faecalis* and this antimicrobial activity was higher compared to MTA Fillapex (40). Because of its high antimicrobial properties; nano-sized zinc oxide eugenol particles were added to newly developed root canal sealers by investigators who aimed to benefit from this antimicrobial action (41).

One of the negative features of zinc oxide eugenol based sealers is their cytotoxic effects on the periapical tissues. Undesirable contact of a cytotoxic root canal sealer to periapical region during canal filling may cause delayed wound healing and irritation in the periapical region (42). There are various studies in literature, evaluating the cytotoxicity of root canal sealers containing zinc oxide eugenol (43–46). Jung *et al.* reported that Pulp Canal Sealer paste caused irritation on periodontal ligament cells (43). Chang *et al.* concluded that TubliSeal had a moderate cytotoxic effect in periodontal ligament-derived fibroblast cell culture (44). Willershausen *et al.* investigated the effect of several root canal sealers on cell viability using a periodontal ligament-derived fibroblast cell culture. The effect of root canal sealers on the proliferation of fibroblasts was investigated using fluorescent dyes and Petrographic Microscope. It was observed that Pulp Canal Sealer EWT (zinc oxide eugenol based) reduces the proliferation of fibroblast cells (45). Poggio *et al.* investigated the cytotoxic properties of various root canal sealers with MTT assay in immortalized human gingival fibroblast-1 HGF-1 cell culture. Pulp Canal Sealer was found to show moderate cytotoxic properties and was more cytotoxic compared to BioRoot RCS and TotalFill BC Sealer (46).

The toxic effect of zinc oxide eugenol based sealers originates from eugenol. Eugenol alters the immune response in the periapical region, causing periapical inflammation and pain (47).

Another reason why zinc oxide eugenol based sealers are not included in today's routine endodontic practice is their high solubility (48). The reason for high solubility is the leakage of the excess eugenol that remains without polymerization and the hydrolysis reaction of the polymerized zinc oxide eugenolate (49).

2.1.2. Calcium Hydroxide Based Root Canal Sealers

Calcium hydroxide was used as a root canal filling material for the first time in 1940, by Rhoner. Since calcium hydroxide possesses osteogenic, cementogenic and antibacterial properties, its use as a root canal sealer has been considered. Sealapex, Apexit, CRCS are some of the calcium hydroxide sealers (5,50,51).

Antibacterial property of calcium hydroxide is achieved by dissociation of calcium hydroxide into calcium and hydroxyl ions which leads to an increase in pH (50). High pH neutralizes lactic acid released from osteoclasts and activates alkaline phosphatase. This activation induces hard tissue formation (50). Another mechanism involved in the formation of hard tissue is the adenosine triphosphate reaction initiated by calcium ions (50). In order for these positive properties to take place, calcium and hydroxyl ions must be dissociated (5).

There are various studies evaluating the solubility and leakage of calcium hydroxide sealers (52–57). Sleder *et al.* investigated the solubility of Sealapex and Tubli Seal using the dye penetration method. According to the results of Sleder *et al.*, no statistically significant difference observed between Tubli Seal and Sealapex (calcium hydroxide sealer) in terms of dye leakage. Shetty *et al.* investigated the leakage of Tubli Seal using dye penetration. According to this study, Tubli Seal was found to be more impermeable than Sealapex (53). Siquera *et al.* investigated the leakage of various root canal sealers with bacterial infiltration. In their study, Sealapex root canal sealer caused more bacterial leakage than AH 26 root canal sealer (54). Ersahan *et al.* observed the total weight loss of various root canal sealer samples which were kept in distilled water for 14 days. Sealapex showed the highest solubility compared to other experimental groups (iRoot SP, AH Plus, EndoRez) (55). Lone *et al.* evaluated the leakage of root canal fillings performed with Sealapex and AH Plus using the warm vertical condensation method on 70 extracted, single-rooted, human teeth with the dye penetration method. They observed

that the Sealapex caused more leakage compared to the AH Plus group (56). Da Costa Michelotto *et al.* investigated the leakage of Sealapex, AH Plus and Epiphany sealers with high performance liquid chromatography-tandem mass spectrometry method for 60 days. According to the results of their study; Epiphany group showed the highest leakage followed by Sealapex (57). Despite the differences in studies in terms of material and methodology; a general finding was that calcium hydroxide sealers tend to show more leakage compared to other root canal sealers (53–57).

There are various studies evaluating the antimicrobial properties of calcium hydroxide based sealers (39,40,58). According to Çobankara *et al.*, Sealapex showed greater antimicrobial activity against *E. faecalis* compared to other canal sealers with different contents (zinc oxide eugenol, glass ionomer, epoxy resin) in direct contact test. However, there was no statistically significant difference observed between Sealapex and other canal sealers in terms of antimicrobial activity when agar diffusion test was used (39).

Shantiaee *et al.* investigated the antibacterial activity of Apexit, AH 26 and pure zinc oxide eugenol by using the direct contact test and agar diffusion test. Apexit (calcium hydroxide sealer) showed antimicrobial effect on *S. mutans*, but this effect was found to be less than that of resin based AH 26 and pure zinc oxide eugenol (58). According to Dalmia *et al.*, Sealapex showed greater antimicrobial effect on *E. faecalis* than AH plus, Tubliseal and MTA Fillapex in agar diffusion test (40).

The high antimicrobial activity of calcium hydroxide based sealers depends on the amount of dissociation into ions (59). Dissolution of the root canal sealer in the root canal does not meet the above-mentioned criteria defined for ideal sealers. Schafer *et al.* investigated the solubility of the root canal sealers with various contents. In their study, the samples were kept in artificial saliva solutions created at different pH values for 28 days and the average weight losses were measured. According to the results of the study, the solubility of the calcium hydroxide based sealers (Apexit and Sealapex) were found to be higher than the other root canal sealers containing epoxy resin, silicone and polyketone (48). McMichen *et al.* observed the total weight loss of Apexit, Roth 801, Tubli-Seal EWT, AH Plus and Endion samples after they were kept in distilled water for 3 months. The highest weight loss was found in the Apexit group (60). Grga *et al.* observed the weight loss of Apexit, Acroseal and AH Plus. The samples were weighed

after keeping them in Hank's solution for 28 days. According to this study, the group showing the highest weight loss was Apexit (61).

2.1.3. Root Canal Sealers with Non-Eugenol Content

The toxic effect of zinc oxide eugenol based sealers originates from the eugenol they contain. For this reason, a new root canal sealer was produced by removing the eugenol in its formula. Non-eugenol root canal sealer was inspired from the periodontal paste that does not contain eugenol. It contains zinc oxide, barium sulfate and bismuth oxychloride (5). Mattison *et al.* investigated the leakage of Nogenol, N2, Procosol and Diaket sealers with the electrochemical microleakage method. According to their results, Nogenol sealer showed more leakage than N2 and Procosol sealer, and less leakage than Diaket sealer. Nogenol has been reported to cause moderate leaching (62). Von Fraunhofer *et al.* investigated the physical properties of root canal sealers in their study and concluded that Nogenol sealer volumetrically expanded during polymerization. Owing to this feature, it has been reported that to have positive effects in terms of leakage in the long term (63).

2.1.4. Glass Ionomer Based Root Canal Pastes

Glass ionomer cements, first introduced by Wilson and Kent, have also been suggested to be used as root canal sealers because of their ability to form chemical bond with dentin tissue resulting in a successful adhesion (64,65). High fluidity and polymerization in the presence of moisture are among the positive features of these pastes (66). Glass ionomer based sealers are available in the market under brand names Ketac Endo, Activ GP Sealer and Endion.

Glass ionomer based sealers have limited antimicrobial properties (37,39,67). Neelakantan *et al.* observed the antimicrobial effect of various root canal sealers against *E. faecalis* and *C. albicans* with agar diffusion test. Ketac Endo reached a peak level of its antimicrobial activity in the first 24 hours, then antimicrobial activity decreased by the end of 24 hours and completely disappeared at the end of 72 hours. It was observed that

the antimicrobial activity of Ketac Endo was higher than AH Plus, Epiphany and RoekoSeal (67). Çobankara *et al.* showed that the antimicrobial activity of Ketac Endo decreased at the end of the 19th hour and was less than AH plus, Sealapex and Sultan canal sealers (39). Saleh *et al.* observed the antibacterial effect of Ketac Endo, AH Plus and Grossman Paste on extracted human teeth infected with *E. faecalis*. According to the results of their study; antimicrobial activity of Ketac Endo was found to be lower than AH Plus and Grossman paste (37). This limited antimicrobial effect was attributed to the low pH value and fluorine ion release (68–70).

There are various studies in the literature, evaluating the biocompatibility of glass ionomer based sealers (71). Kolokuris *et al.* observed the immune reactions caused by Ketac Endo canal sealer. In this study, samples of Ketac Endo canal sealer were placed in subcutaneous tissues of rats within Teflon carriers and immune reactions of the rats were observed for 120 days. According to this study; Ketac Endo initiated a moderate immune reaction at the end of the 5th day (71).

According to studies which evaluate the physical properties of root canal sealers; glass ionomer based sealers tend to show greater leakage and dissolution than other root canal sealers with different ingredients (48,72). It is stated that this is due to shrinkage during polymerization. Polymerization shrinkage causes stress at the bonding interface. As a result, adhesion is adversely affected (72–74). Carvalho-Júnior *et al.* compared the solubility of Ketac Endo with root canal sealers with different contents. In their study, root canal sealers were prepared in Teflon molds and kept in distilled water for 1 week, then subjected to drying and weighed and the resulting weight loss was calculated. The authors concluded that Ketac Endo showed greater weight loss than Endofill, N-Rickert, and Sealer 26 sealants (72). Schafer *et al.* investigated the solubility of various root canal sealers (AH 26, AH Plus, RoekoSeal Apexit, Sealapex, Aptal-Harz, Ketac-Endo, Diaket). In their study, samples were kept in artificial saliva solutions prepared at various pH values for 28 days and the average weight loss of each canal sealer was calculated. In this study, Ketac Endo showed high resolution (48). Flores *et al.* investigated the physicochemical properties of root canal sealers with different contents. They evaluated AH Plus, GuttaFlow, RoekoSeal and Activ GP in their study. In order to compare solubility; samples from all four root canal sealers were kept in distilled water for 7 days. Samples were taken from the water in which they were kept, and solubility of root canal sealers were measured with atomic absorption spectrometry. According to the results,

Active GP sealer showed high solubility. Other tests revealed that Active GP sealer showed low radiopacity and low setting time. Although the setting time complies with ANSI/ADA criteria, it was found to be lower than AH Plus, GuttaFlow and RoekoSeal (74). Glass ionomer based sealers are not preferred in today's routine endodontic practice due to their high leakage, dissolution in the root canal and impractical use.

2.1.5. Resin Based Root Canal Sealers

2.1.5.1. Epoxy Resin Based Root Canal Sealers

Epoxy resins, which were first introduced by P. Castan in 1938 and were used in restorations and posts in dentistry, later started to be used as root canal sealers. AH 26 is the first epoxy resin-containing root canal sealer in the market (30). AH 26 shows a successful bonding and adhesion to the dentine (75). Lee *et al.* evaluated the bond strength of different sealers to dentine by using the tensile test method. According to their results, the bond strength of AH 26 was found to be greater than glass ionomer, calcium hydroxide and zinc oxide based sealers (75).

Gee *et al.* investigated the physical properties of AH 26 and Ketac Endo with the push out test and liquid filtration method. According to their results, AH 26 showed less microleakage and less polymerization shrinkage than Ketac Endo (76).

One of the positive features of AH 26 is its antimicrobial effect. Monajemzadeh *et al.* investigated the antimicrobial effects of AH 26, zinc oxide eugenol and MTA with agar diffusion test. AH 26, zinc oxide eugenol and MTA were prepared at different concentrations and exposed to *S. mutans*, *S. sanguis*, *S. salivarius*, *C. albicans*, and *L. casei* cultures for 3 days. The inhibition zones were evaluated after 3 days. According to the results; AH 26 was found to have an antimicrobial effect against *Streptococcus mutans*, *Lactobacillus casei* and *Candida Albicans* (77). Jafari *et al.* investigated the antimicrobial activity of AH 26 and MTA Fillapex with direct contact test. In their study, AH 26 and MTA Fillapex were brought into direct contact with microorganisms for 7 days. At the end of the 1st, 2nd, 3 and 7 days, the proliferating microorganisms were measured using a spectrophotometer. According to the results, AH 26 was found to have an antifungal effect against *Candida glabrata* and *Candida krusei* (78).

AH 26 also has some negative features such as cytotoxicity and discoloration (79–81). It has been shown to have cytotoxic effects on V79 mammalian cells. Formaldehyde formation during the setting reaction of AH 26 was found to be the reason for this cytotoxic effect (79). Cytotoxic effects due to formaldehyde release were also reported by Koulaouzidou *et al.* Their study was performed on rat subcutaneous fibroblast cell culture and rat pulp cell culture. The effects of AH 26, AH Plus and Topseal sealers on cell viability were investigated. According to their results, AH 26 caused a decrease in the number of viable cells more than the other experimental groups (80). The cytotoxicity of AH 26 is thought to be harmful to the periapical tissues when it is extruded beyond the apex of the root canal. Barkhordar *et al.* reported a case of paresthesia in the lower premolar region caused by apical extrusion of the root canal filling performed using the AH 26 sealer (81). There are similar cases in the literature on this issue (82,83). Spielman *et al.* reported a case in which a 37-year-old female patient reported loss of sensation in the mandibular region right after the root canal treatment of tooth no.35. The root canal filling material was apically extruded and AH 26 was used as the root canal sealer (82). Another case was reported by Tamse *et al.* After the root canal treatment of tooth no.35 in a 28-year-old female patient using AH 26 sealer, the patient reported complaints of itching and partial numbness in the lower lip area. It was reported that the paresthesia complaint in this case resolved spontaneously after 1 year (83).

Another negative feature of AH 26 root canal sealer is that it causes discoloration on the teeth. Jahromi *et al.* reported that AH 26 caused more tooth discoloration compared to Dorifill (DoriDent Dr. Hirschberg GmbH, Wien, Austria) which contains zinc oxide eugenol (84). A new formulation, AH Plus, has been introduced to the market in order to eliminate the negative properties such as cytotoxicity and discoloration.

AH Plus is an epoxy resin containing root canal sealer similar to AH 26 sealer. Unlike AH 26, it does not cause formaldehyde release during polymerization (85). Dentine bonding of the AH Plus sealer is very successful (86). Silva *et al.* investigated the bond strength of AH Plus, Endoseal MTA and MTA Fillapex with the push out test. According to results, AH Plus showed higher bond strength compared to Endoseal MTA and MTA Fillapex which contained calcium silicate (87). Nagas *et al.* compared the bond strength of AH Plus, MTA Fillapex, iRoot SP and Epiphany sealers using the push out test on 80 extracted single-rooted human teeth. According to their results; iRoot SP showed the highest bond strength, followed by AH Plus (88) Dem *et al.* investigated the

bond strength of AH Plus, Guttaflow Bioseal and Guttaflow 2 using the push out test. According to their results, AH Plus showed the highest bond strength (89). In other push out studies in which the bond strength of sealers to dentin was tested, the dentin bonding of AH Plus generally revealed successful results (86–90).

AH Plus has a short-term antimicrobial effect due to bisphenol-A diglycidyl ether formation during polymerization reaction (91). Kapralos *et al.* reported that AH Plus had a strong antibacterial effect in the first 24 hours on *E. faecalis*, *S. mutans*, *S. epidermidis* and *S. aureus* in the planktonic state. However, this effect gradually decreased after 24 hours. AH Plus showed strong antibacterial effect in the first 1 hour on monoclonal biofilms of *E. faecalis* and *S. epidermidis*. It showed stronger antibacterial activity on monoclonal biofilms of *S. mutans* and *S. aureus* compared to the TotalFill BC Sealer (92). Faria-Júnior *et al.* also showed that AH Plus had an antibacterial effect on the *E. faecalis* biofilm in the first 15 hours (93). In similar studies, it has been observed that AH Plus has a strong antibacterial effect, especially during the polymerization process, and this effect decreases over time (39,94). Zang *et al.* investigated the antibacterial effects of root canal sealers with different contents using the direct contact test on *E. faecalis* culture for 6 days. According to their results, AH Plus showed a strong antibacterial effect in the first 5 minutes and did not show any antibacterial properties after 1 day (94). Çobankara *et al.* observed the antibacterial effects of various root canal sealers on *E. faecalis* with direct contact test and agar diffusion test. According to their study; AH Plus had an antibacterial effect for 19 hours and this effect was found to be stronger than RoekoSeal and Ketac-Endo (39).

AH Plus has a successful dentine covering feature (95). It is possible to increase this feature by removing the smear layer with irrigation activation methods (96). Gu *et al.* investigated the effects of different irrigation activation methods on the penetration depth of AH Plus into dentine using extracted human teeth. AH Plus was marked with a fluorescent isocyanide molecule and used in root canal obturation with gutta-percha by using continuous wave method. In the final irrigation, activation was performed with conventional syringe method, sonic activation method, ultrasonic activation method, V clean and ND Yap laser methods in different groups of the study. According to the results, the deepest penetration of AH Plus was observed in the group activated with the Nd Yap laser. In the groups where other irrigation methods were used, a greater depth of penetration was achieved compared to the conventional syringe method (97).

The mechanical properties of AH Plus are also favorable. It has a high radiopacity, low polymerization shrinkage and low solubility. Urban *et al.* evaluated the solubility of AH Plus, BioRoot RCS and MTA Fillapex sealers. In their study; weight loss was measured after the samples were stored in distilled water for 6 months. According to their results, AH Plus canal sealer showed the lowest solubility (98). Zhou *et al.* investigated fluidity, film thickness, working time, solubility, volumetric change and pH change of various root canal sealers including AH Plus. According to the results of their study, the fluidity of AH Plus was compatible with ISO standards and was higher than GuttaFlow. Furthermore, film thickness was found to be thinner than MTA Fillapex, Thermaseal and BC Sealer. Working time was found to be longer compared to GuttaFlow and MTA Fillapex. The solubility of AH Plus was compatible with ISO standards with 3% loss of weight and was lower compared to Pulp Canal Sealer, MTA Fillapex and BC Sealer. The polymerization shrinkage of AH Plus was also compatible with ISO standards (less than 1.0%) (99). Malka *et al.* observed the radiopacities of various root canal sealers by using a photoshop program. According to this study, the radiopacity of AH Plus was found to be higher than MTA Fillapex and Endo CPM (100).

Studies evaluating the solubility of AH Plus show that AH Plus displays less solubility compared to many root canal sealers (48,60). Schafer *et al.* evaluated the solubility of different root canal sealers. In their study, the sealers were kept in artificial saliva solutions which were prepared at different pH values for up to 28 days and the average weight loss was calculated for each root canal sealer. The results showed that the solubility of AH Plus was lower than silicon, polyketone, glass ionomer, calcium hydroxide and zinc oxide eugenol based sealers (48). McMichen *et al.* investigated the solubility of different root canal sealers. In their study, sealer samples were kept in distilled water for 2 days, then dried for 3 days and this process was repeated for 12 weeks. Average loss of weight was calculated after 12 weeks. AH Plus was found to exhibit less solubility than Apexit, Endion, Roth 801, Tubli-Seal EWT root canal sealers (60).

Although AH Plus has physically superior properties, it is not an ideal root canal sealer (60). AH Plus has cytotoxic effects on vital tissues, but these cytotoxic effects are not as high as AH 26 (80). Alsubait *et al.* investigated the cytotoxicity of root canal sealers on human bone marrow mesenchymal stem cells. Alamar blue was used to determine the cytotoxicity of root canal sealers. The cytotoxic effects of AH Plus were found to be higher than that of bioceramic sealers (101). Koulaouzidou *et al.* observed the cytotoxic

effects of AH Plus and AH 26 on rat skin cells and rat pulp cells. Sulforhodamine B staining and cell viability methods with hemocytometry were used to determine cytotoxicity. The results showed that AH Plus had a cytotoxic effect even though it was less than AH 26 (80).

2.1.5.2. Methacrylate Resin Based Root Canal Sealers

First Generation

In 1975, methacrylate resin based root canal sealer was produced for the first time under the name Hydron. The main ingredient of this root canal sealer was poly-2-hydroxyethyl methacrylate, poly-HEMA, which is a hydrophilic gel (5). While using Hydron sealer; it was recommended that Gutta-percha should not be used and root canal filling should only be performed with Hydron. In this way, a single monoblock connection is formed in the root canal (102). Although Hydron drew attention with its antimicrobial properties and biocompatibility, there are various studies which showed the opposite (103–105). Tanzilli *et al.* observed the tissue reaction to Hydron placed in the subcutaneous tissue of the rats for 3 months. It was observed that Hydron formed calcification in living tissues and caused macrophage activation in the long term (103). Reid *et al.* observed the immune reaction to Hydron and AH 26 in Guinea pigs. In their study, teflon carriers containing Hydron and AH 26 canal sealer were placed in the mandible of Guinea pigs and tissue reaction was monitored for 26 weeks. Both sealers showed similar reactions in living tissues. It was observed that both sealers induced lymphocyte infiltrations and fibro-adipose capsule formation around themselves (104). McNamara *et al.* investigated the biocompatibility of Hydron, AH 26, and Tubliseal sealers using L929 cell culture. According to their results, Hydron suppressed cell division and decreased cell functions and biosynthesis. These harmful effects were found to be greater than AH 26 and similar to Tubliseal (105).

Kronman *et al.* investigated the antibacterial effects of Poly-HEMA on bacterial cell culture and it was shown that Poly-HEMA has antibacterial effects on *S. mitis*, *S. aureus*, *P. vulgaris*, *Ps. aeruginosa*, *E. faecalis*, *S. pneumoniae*, *K. pneumoniae* and *C.*

albicans (106).

Hydron's sealing ability was not as good as expected, and it was found to be less than the combination of Gutta-percha and Grossman sealer (107).

Second Generation

Urethane dimethacrylate based root canal sealer EndoRez is a hydrophilic and dual cure root canal sealer. Its use does not require the application of a dentine adhesive or etching. However, it is recommended by the manufacturer to use EDTA in the final irrigation right before root canal obturation. By removing the smear layer with EDTA, EndoRez penetrates into the dentinal tubules and accessory canals better and ensures the formation of resin tags (5,108).

EndoRez can be used with its own resin-coated gutta-percha or conventional gutta-percha. Although it is stated that using EndoRez with resin-coated gutta-percha enables to create triple monoblock connection with the root canal wall, some push out studies show that bond strength of EndoRez and resin coated gutta-percha combination was not higher than root canal sealers with different contents (102,109,110).

Sungur *et al.* investigated the bond strength of EndoRez, Activ GP, Smart Seal, AH 26 with the push out test. According to their results, the bond strength of EndoRez was the lowest (109).

Similarly, Patil *et al.* determined that the bond strength of EndoRez was lower than the bond strength of gutta-percha-AH Plus and Resilon-Epiphaney combinations (110).

EndoRez is known to cause less discoloration compared to other root canal sealers (111,112). Ekici *et al.* investigated the dentine discolorations caused by various root canal sealers in 60 extracted human teeth. Dentin discolorations formed by Endorez, AH 26, Pulpispad and MTA Fillapex were followed for 3 years and measured with fotospectrometer. According to the results of this study, it was observed that all root canal sealers caused some discoloration. In the first month, EndoRez and MTA Fillapex caused less discoloration than the other two root canal sealers. However, after 3 years, there was no significant difference between EndoRez, MTA Fillapex and AH 26. These three sealers were found to cause less discoloration than Pulpispad (111). Gürel *et al.* compared the

dentine bleaching ability of the extracted human teeth samples which were obturated with AH 26, MTA Fillapex and EndoRez. It was observed that the most bleached teeth samples belonged to the group filled with EndoRez (112).

Eldeniz *et al.* observed the *S. Mutans* leakage of various root canal sealers in 144 extracted human single-rooted teeth for 40 days. According to their results, Epiphany showed less leakage than GuttaFlow, Apexit and EndoRez (113). Schafer *et al.* compared the radiopacities and solubility of EndoRez, AH Plus and RealSeal SE sealers. Samples were formed from root canal sealers, kept in distilled water for 28 days and average weight losses were measured. Their results showed that EndoRez had higher solubility and less radiopacity than AH Plus and RealSeal SE sealants (114).

EndoRez root canal sealer has negligible antibacterial properties (115,116). Queiroz *et al.* investigated the antimicrobial effects of different sealers with direct contact test. According to their results, EndoRez did not show antimicrobial properties against *E. faecalis*, *S. mutans* and *E. coli* (115). Eldeniz *et al.* observed the antibacterial effects of various root canal sealers against *E. faecalis*, *S. aureus* and *P. aeruginosa* by using direct contact and agar diffusion tests. It was observed that EndoRez has no antibacterial effect on these bacteria (116).

Another negative feature of EndoRez is related to biocompatibility (117–119). Eldeniz *et al.* investigated the cytotoxic effects of different sealers on periodontal ligament cell culture. In their study, EndoRez caused more DNA double-strand breaks in periodontal ligament cells compared to bioceramic based MTA Fillapex, iRoot SP and BioRoot RCS sealers. However EndoRez showed less cytotoxic effects compared to Hybrid Root SEAL, Acroseal, RealSeal SE and AH Plus Jet sealers (117). Suzuki *et al.* observed the immune response in the periapical tissues caused by EndoRez sealer in two mongrel dogs. In their study, mild immune response was observed in the periapical region even when the canal filling terminated behind the apical foramen. When root canal filling created with EndoRez sealer was beyond the apical foramen, thickening of the periodontal ligament, migration of giant inflammatory cells and increasing of the chronic inflammatory cells in periapical area were observed (118).

Diomedea *et al.* investigated the cytotoxic effects of EndoRez on dental pulp stem cells, fibroblast derived stem cells, osteoblast and fibroblast cell cultures. According to their results, EndoRez caused inhibition of proliferation of stem cells and increased pro-

inflammatory cytokines (119).

López-García *et al.* investigated the effects of AH Plus, Bio-C Sealer and TotalFill BC Sealers on cell viability (MTT assay), mineralization (Alizarin red dye), cell migration, and cell attachment, using hPDLSC cell culture. Their results showed that AH Plus caused reduction of viable cells and inhibited the cell migration and its effect on mineralization was found to be less than the other two root canal sealers. Cell attachment on the sealers' surface was also less than the other two root canal sealers (120).

Third Generation

Third generation methacrylate sealers consist of self-etching primer and dual cure composite. Self-etching primer provides superficial demineralization in dentin due to its acidic structure. Thanks to this demineralized layer, it is aimed to form micro-mechanical adhesion on root canal walls (5). Third generation methacrylate sealers are commercially available under the names Fibrefill R.C.S., RealSeal and Epiphany and contain 2-acrylamido-2-methyl-propanesulfonic acid (AMPS). Resilon; a dimethacrylate containing polycaprolactone, is generally used as the core material with these third generation root canal sealers (5,121).

Resin-containing canal sealers were produced to create a tight connection with dentin, but there is no consensus in the literature on this subject (122,123). Shrinkage occurs during polymerization in resin-containing sealants. The amount of polymerization shrinkage increases as the bonding surface increases. Polymerization shrinkage is directly related with the C-factor. The C factor is obtained by dividing the bonded surface by the non-bonding surface. When resins are used as root canal sealers, the bonding area on the root canal wall surface is very large, so polymerization shrinkage is expected to be very high. This may cause the formation of voids inside the root canal filling and improper covering of dentinal tubules and subsequent leakage (124). Souza *et al.* observed the microleakage of the root canal fillings created with AH Plus–Gutta Percha and Epiphany-Resilon using dye penetration in 44 extracted human single-rooted lower teeth. Their results showed that root canal filling with Epiphany-Resilon caused more leakage (123). Economides *et al.* compared the leakage of third generation FibreFill and Calcebiotic Root Canal Sealer (CRCS) on 60 extracted single-rooted human teeth by using fluid filtration

model. According to the authors, FibreFill caused more leakage than Calciobiotic Root Canal Sealer (CRCS) and removing the smear layer increased the sealing ability of Fibrefill (122). Saleh *et al.* observed the sealing ability of AH Plus, Apexit, RealSeal in 100 extracted human teeth with the fluid filtration method. According to the authors, these sealers were not statistically superior to each other and all root canal sealers showed leakage. Removal of the smear layer increased the leakage of RealSeal and Apexit (125). There are various studies in the literature, evaluating the bond strength of Third Generation sealers (126,127). Gogos *et al.* observed the bond strength of Fibrefill, CRCS, Topseal and Endion with shear load test. According to Gogos *et.al.* the bond strength of Fibrefill was higher than CRCS and Topseal. There was no statistically significant difference found between Fibrefill and epoxy resin based Endion (126). Stiegemeier *et al.* investigated the dentine bond strength of Resilon-RealSeal, Resilon-MetaSEAL and Gutta-percha-Kerr EWT combinations using the push out test in 40 extracted human teeth. According to their results, bond strength of Resilon-RealSeal was lower than the 4th generation Resilon-MetaSEAL and there was no statistically significant difference found with Gutta-percha-Kerr EWT (127).

In the cytotoxicity studies which investigate 3rd generation methacrylate based sealers, initiation of various tissue reactions are usually observed (128–130). Martinho *et al.* investigated the cytotoxicity of AH Plus, Apexit and EndoRez on human pulp-derived stem cell culture. According to the authors, AH Plus was more cytotoxic compared to Apexit and EndoRez. It was observed that AH Plus increased IL-6, IL-8 and TNF- α in SV40 cells obtained from pulp (128). Gambarini *et al.* evaluated the biocompatibility of Fibrefill, Bioseal and AcroSeal sealers in mouse fibroblast culture. According to their results, Fibrefill showed more cytotoxic effects than Bioseal and AcroSeal (129). Xu *et al.* evaluated the biocompatibility of RealSeal and AH Plus on osteoblast-like MG63 cell culture. According to their results, RealSeal showed more toxic effects than AH Plus (130). Al-Hiyasat *et al.* investigated the cytotoxic effects of root canal sealers with different contents on fibroblast cell culture. According to their results, Epiphany was more cytotoxic than AH Plus and EndoRez and less cytotoxic than the fourth generation MetaSEAL (131).

It was reported that root canal sealers in this group generally have a mild antibacterial effect. Mohammadi *et al.* observed the antibacterial effects of various root canal sealers with direct contact test. The inhibition zones of root canal sealers were

investigated in cultures of *S. aureus* and *S. mutans*. The antibacterial properties of RealSeal were found to be less than AH 26 and did not show a statistically significant difference with the antibacterial effect of GuttaFlow (132). Huang *et al.* investigated the antibacterial effects of different sealers on *E. faecalis*, *C. albicans*, and *E. coli* with direct contact and agar diffusion test. According to their results, antimicrobial activities of RealSeal and AH Plus were higher than GuttaFlow 2 and ProRoot MTA (133).

Fourth Generation

The acidic primer of third generation methacrylate is incorporated into the resin structure in the fourth generation methacrylate sealers. For this reason, there is no need for acid and primer application steps in canal sealers (5). Due to their acidic nature, the fourth generation methacrylate sealers form a hybrid layer on the dentin wall and form micromechanical adhesion with the dentinal walls (5). MetaSEAL and RealSeal SE are 2 sealers which represent the fourth generation in the market.

According to some bond strength studies, MetaSEAL showed better bond strength compared to RealSeal SE (another brand from fourth generation) and lower generation of methacrylate based resin sealers (134,135). Babb *et al.* investigated the bond strengths of MetaSEAL, RealSeal SE and EndoRez in extracted human teeth using the push out test. MetaSEAL showed higher bond strength than the fourth generation RealSeal SE and the second generation EndoRez. EndoRez was reported to be the sealant with the lowest bond strength among these three sealants (135). Stelzer *et al.* observed the bond strength of AH Plus and RealSeal SE. The bond strength of AH Plus was found to be higher than that of RealSeal SE. In their study, the effects of irrigation solutions used in the final irrigation were also investigated. According to the results; final irrigation solutions did not affect the bond strength of AH Plus. The use of 17% EDTA + 0.9% saline during final irrigation decreased the bond strength of RealSeal SE. The bond strength was higher only when 0.9% saline solution was used (136). Mai *et al.* reported that MetaSEAL has minimal demineralization effect on smear free dentin. This may result in the absence of hybrid bonding layer when EDTA is used as the final wash solution, resulting in low bond strength. Usage of EDTA solution as the final irrigating solution may result in the absence of hybrid bonding layer, therefore causes a low bond strength (137).

Some studies examining the cytotoxicity of fourth-generation sealants showed that these sealers have cytotoxic and neurotoxic effects (131,138–140). Ruparel *et al.* investigated the neurotoxic effects of these canal sealers on the trigeminal nerve fiber of rats. In their study, RealSeal SE showed less neurotoxic effects than AH Plus and zinc oxide eugenol (138). According to Garza *et al.*, MetaSEAL had cytotoxic effects on L929 rat fibroblasts (139). Yamanaka *et al.* observed the cytotoxic effects of methacrylate based sealers by placing the samples of those sealers into subcutaneous tissue of rats. It was observed that Epiphany SE, MetaSEAL and Super-Bond RC sealer increased inflammation initiating cells and inflammatory molecules (140). Al-Hiyasat *et al.* observed the effect of various root canal sealers on cell viability with MTT assay on Balb C 3T3 fibroblast cell culture. In this study, MetaSEAL showed more cytotoxic effects compared to AH Plus ,Epiphany and EndoRez (131).

2.1.6. Silicone Based Root Canal Sealers

Silicone based root canal sealers are available in the market under the names RoekoSeal, GuttaFlow and GuttaFlow 2 (5). GuttaFlow contains gutta percha powder, poly dimethylsiloxane and nano-sized silver particles (141). Most of the root canal sealers show shrinkage during polymerization reaction but Gutta-flow's volume slightly increases with polymerization. Owing to this feature, leakage is expected to be minimized (142).

De-Deus *et.al.* investigated the leakage caused by AH Plus, GuttaFlow and Roekoseal using the polymicrobial leakage test. According to the authors, GuttaFlow and RoekoSeal caused less leakage than AH Plus and Pulp Canal Sealer (142). Another microleakage study concluded that GuttaFlow caused more leakage than the combination of Epiphany + Resilon and AH Plus + Thermafil. However, in this study, single cone obturation method was used in the GuttaFlow group, warm vertical compaction method was used in the Epiphany+ Resilon group, and the warm filling method was used in the AH Plus + Thermafil group (143). Özok *et al.* investigated the leakage of AH 26, RoekoSeal and GuttaFlow sealers with the glucose leakage model. In their study, root canal filling methods differed between groups. The AH 26 group was obturated with the lateral condensation and the other two sealer groups were obturated with the single cone

method. According to their results, AH 26 group showed the least leakage, whereas no statistically significant difference was found between GuttaFlow and Roekoseal (144). Hwang *et al.* investigated the bacterial leakage of GuttaFlow, AH Plus, and Endoseal MTA. In their study, obturation techniques differed between groups. In the GuttaFlow group, the single cone method was used. There were also two groups that included AH Plus. Continuous wave technique was used in one of these groups and Guttacore system was used in the other AH Plus group. In the EndoSeal MTA group, canal filling was performed by ultrasonic vibration method. In their study, the Guttacore group was found to show the highest leakage (145).

Vasiliadis *et al.* investigated the leakage of GuttaFlow and AH Plus by using a liquid filtration model. In their study, lateral condensation method was used in both groups and there was no statistically significant difference between GuttaFlow and AH Plus in terms of leakage (146).

Antimicrobial properties of silicone based sealers were investigated in many studies and different results were obtained (147–149). Ruiz-Linares *et al.* investigated the antibacterial effect of GuttaFlow and AH Plus by using direct contact and confocal laser scanning microscope. According to their results, GuttaFlow showed antibacterial effect on *E. faecalis* and biofilm formation for 4 weeks (147). Pawińska *et al.* observed the antimicrobial effects of various sealers on cultures of *Actinomyces israelii* and *Actinomyces viscosus* by direct contact test. The zones of inhibition created by the root canal sealers on the culture were evaluated. According to the results, RoekoSeal Automix and GuttaFlow were found to have no antimicrobial effect against these two bacteria (148). Özcan *et al.* investigated the antifungal properties of various root canal sealers on *Candida albicans* culture using the direct contact test. According to their results, GuttaFlow showed no antifungal effect (149).

Rodríguez-Lozano *et al.* evaluated the biocompatibility of GuttaFlow, GuttaFlow 2, MTA Fillapex and AH Plus on hPDLSC culture. According to their results, the biocompatibility of GuttaFlow and GuttaFlow 2 were higher than that of MTA Fillapex and AH Plus. It was observed that GuttaFlow induces the differentiation of cementoblasts. At the same time, these two canal sealers increased the cell migration and wound healing (150). Szczurko *et al.* investigated the biocompatibility of various root canal sealers on stem cell culture derived from human periodontal ligament. In their study, Gutta Flow

caused less cell necrosis than AH Plus, Apexit Plus and Tubli-Seal (151). Taraslia *et al.* investigated the effect of GuttaFlow 2, MTA-Fillapex, TotalFill BC Sealer, BioRoot RCS, AH Plus and Roth's 801 root canal sealers on cell viability using a human periodontal ligament cell culture. It was observed that the highest number of viable cells was found in the GuttaFlow 2 group (152). Saygılı *et al.* investigated the biocompatibility of GuttaFlow, GuttaFlow 2, AH Plus and MTA Fillapex using fibroblast cell culture. In their study, MTT assay was used to determine cell viability, and TUNEL assay, which detects breaks in the DNA helix, was used to evaluate cytotoxic properties. It was observed that both sealants of GuttaFlow were found to be less cytotoxic than MTA Fillapex and AH Plus (153). Collado-González *et al.* evaluated the biocompatibility of GuttaFlow, GuttaFlow 2, MTA Fillapex and AH Plus. Human-periodontal ligament derived stem cells were placed on sealer samples and attachment, viability and morphology of the cells were examined. According to their results, GuttaFlow and GuttaFlow 2 promoted the formation of cell attachments and spread more than other root canal sealers (154).

2.1.7. Bioceramic Based Root Canal Sealers

Bioceramic materials are divided into two groups as bioactive and bioinert materials. Bioactive substances interact with the surrounding tissues to form more durable tissues. Calcium phosphate and glass are examples of these materials. There are also degradable and non-degradable types of bioactive materials. Bioinert materials do not have any biological or physiological effect on the surrounding tissues. Examples of these materials are zirconia and alumina (155). These highly biocompatible materials started to be included in the content of root canal sealers.

The first stage of the bonding mechanism of bioceramic sealers to dentin is the diffusion of the sealer into dentinal tubules. In this way, tags in the dentinal tubules are formed (156). In the second stage, a mineral infiltration layer is formed due to the alkaline nature of bioceramics. Alkaline pH of bioceramics exerts a caustic effect on collagen and this results in denaturation of the collagen. Calcium, carbonate and hydroxyl ions begin to precipitate in this denatured area. In this way, a mineral infiltration area is formed. Then, the reaction of phosphate, calcium silicate hydrogel and calcium hydroxide forms the hydroxyapatite crystals (157). The general features of bioceramic sealers are;

- High biocompatibility due to their similar structure to hydroxyapatite
- Osteoinductive properties
- Successful dentine covering.
- Chemical bond formation with dentin and hydroxyapatite formation at the bonding interface
- Good radiopacity
- Volumetric expansion when polymerized
- Antimicrobial properties
- Supporting regeneration
- Hydrophilic properties
- Fluidity and chemical stability
- Solubility in tissue fluids and being insoluble in the root canal (157–159).

Bioceramic canal sealers are classified according to their contents.

- Calcium silicate Based Bioceramic Sealers
- MTA Based Bioceramic Sealers
- Calcium Phosphate Based Bioceramic Sealers (157)

Calcium Silicate Based Bioceramic Sealers

Bioceramic based calcium silicate sealers; contain zirconium oxide, calcium silicate, calcium phosphate, calcium hydroxide, hydroxyapatite, filling and thickening agents (157). They are commercially available as iRoot SP, Bio-C Sealer, BioRoot RSC, Endosequence BC Sealer, TotalFill BC Sealer and CeraSeal (160). TotalFill BC Sealer and Endosequence BC Sealer have the same formulation. TotalFill BC Sealer is one of the canal sealers used in the present study.

Calcium silicate based sealers have antimicrobial properties due to their alkaline pH (91,160–162). Zordan-Bronzel *et al.* investigated the antimicrobial effects of TotalFill BC Sealer and AH Plus with direct contact and modified direct contact test methods. It was observed that TotalFill BC Sealer has antimicrobial activity against *E. faecalis* and *C. albicans*, and this effect was found to be greater than AH Plus canal sealer. In addition, it was observed that TotalFill BC Sealer has an antimicrobial effect on *E. faecalis* biofilm (161). Alsubait *et al.* examined the antibacterial activity of various root canal sealers on *E. faecalis* biofilm. *E. faecalis* bacteria were marked with SYT9 molecule, which gives a red fluorescent color when the membrane integrity is broken and contacted with the root canal sealers. The viability of the bacteria was observed with a confocal laser scanning microscope for 30 days. The antibacterial effect of Bioroot RCS on *E. faecalis* biofilm was found to be greater than AH Plus and TotalFill BC Sealer (160). Bukhari *et al.* investigated the antibacterial effects of various root canal sealers on *E. faecalis* biofilms that were marked with fluorescent molecules. Antibacterial effects were observed with a confocal laser scanning microscope after the sealants were contacted with the biofilm. As a result of their study, it was observed that Endosequence BC Sealer had an antibacterial effect on *E. faecalis* biofilm and this effect was higher than AH Plus (162).

Calcium silicate based sealers have high biocompatibility properties (120,163,164). López-García *et al.* investigated the biocompatibility of different root canal sealers on hPDLSC cell culture by using the MTT viability assay and Alizarin red method. It was observed that TotalFill BC Sealer and Bio-C Sealer have the potential to induce mineralization. At the same time, these two sealers showed lower cytotoxic properties compared to AH Plus (120). Zhu *et al.* investigated the expressions of the genes that induce the secretion of inflammatory mediators in macrophage cells that were in

contact with different root canal sealers. It was observed that iRoot SP sealer and MTA repair material increased the expression of genes that secrete proinflammatory cytokines. However, it was observed that both materials were not cytotoxic (163). Zhang *et al.* investigated the biocompatibility of iRoot SP and AH Plus on osteoblast-like human MG63 cell culture. Cytotoxicity and changes in gene expressions of the proteins that support hard tissue mineralization were observed with MTT assay and PCR method. According to this study, iRoot SP did not show any cytotoxic properties. In addition, it increased the expression of osteocalcin and the gene expression of proteins that support mineralization (164).

Calcium silicate based sealers form a chemical bond with dentin as described above. Ersahan *et al.* observed the dentine bonding of iRoot SP and AH Plus with the push out test. According to Ersahan *et al.* there was no statistically significant difference between the bond strengths of iRoot SP and AH Plus. However, the bond strength of these two root canal sealers were higher than Endorez and Sealapex (165). Unlike the study by Tuncel *et al.*, the bond strength of iRoot SP was found to be higher than AH Plus (166).

Akçay *et al.* investigated the penetration depth of root canal sealers into dentinal tubules. According to their results, the activation method of the final irrigation significantly affected the penetration depth of the root canal sealers. Conventional needle, passive ultrasonic and Pips irrigation activation methods were used in the study. AH Plus, iRoot SP, MTA Fillapex, and GuttaFlow were used as root canal sealers. The penetration depth was measured with a confocal microscope. It was observed that the iRoot SP root canal sealer group, which was activated with PIPS in the final irrigation, reached the deepest penetration into the dentinal tubules (96).

Calcium silicate based root canal sealants have good sealing properties (167,168). Zhang *et al.* compared the leakage of iRoot SP and AH Plus with the fluid filtration method. According to their results, there was no statistically significant difference between the leakage of iRoot SP and AH Plus (167). Gandhi *et al.* investigated the bacterial leakage of iRoot SP root canal sealer and perforation repair material ProRoot MTA. According to their results, iRoot SP showed superior sealing ability compared to ProRoot MTA (168).

Forghani *et al.* investigated the discoloration of dentine caused by iRoot SP, MTA Fillapex and AH Plus root canal sealers. In their study, root canal sealers were applied on

extracted human premolars and the discolorations were measured with an intraoral spectrophotometer. There was no statistically significant difference between the discoloration of these three root canal sealers. It was observed that all three root canal sealers caused maximum discoloration in the first three months right after their application. After 3 months, the discolorations slightly decreased (169).

MTA Based Bioceramic Sealers

In the early 1990s, Mineral Trioxide Aggregate (MTA) cement was introduced as a perforation repair material developed by Torabinejad (170). It contains tricalcium silicate, dicalcium silicate, tricalcium aluminate, bismuth oxide and gypsum. Calcium hydroxide is formed when MTA comes into contact with tissue fluids and then the calcium hydroxide molecule dissociates into calcium and hydroxyl ions, raising the pH of the environment (170). MTA has positive features such as biocompatibility, stimulation of hard tissue formation, ability to cover dentinal tubules, alkaline structure and insusceptibility to moisture (5). Due to these positive features, MTA was included in the content of root canal sealers. MTA Fillapex, Endo CPM Sealer, ProRoot Endo Sealer are root canal sealers containing MTA (157).

Although MTA is a material known for its high biocompatibility, the formulas produced as root canal sealer have not been as successful as expected (153,154). Collado-González *et al.* observed the effect of MTA Fillapex, AH Plus, GuttaFlow and GuttaFlow root canal sealers on cell viability and compared the adhesion of stem cells to the surface of these root canal sealers. At the end of 24 hours, while viability was not observed in cells seeded on MTA Fillapex, viable stem cells were observed in the GuttaFlow and GuttaFlow2 group (154). Similar results were found by Saygılı *et al.* who investigated the cytotoxicity of MTA Fillapex, AH Plus, GuttaFlow and GuttaFlow on L929 rat fibroblast cell culture. In their study, the effects of MTA Fillapex, AH Plus, GuttaFlow and GuttaFlow 2 sealers on the viability of these cells were investigated with MTT assay and TUNEL assay. MTA Fillapex showed more cytotoxic effects than GuttaFlow, GuttaFlow 2 and AH Plus sealer. The cells that underwent apoptosis were observed the most in the MTA Fillapex group (153).

Shakya *et al.* investigated the antibacterial effects of MTA Fillapex and other root canal sealers (AH Plus, CRCS, Gutta Flow 2) against *E. faecalis* by using direct contact and agar diffusion test. There was no statistically significant difference between the antibacterial effect of MTA Fillapex and AH Plus. The antimicrobial effect of MTA Fillapex was found to be higher than the silicone based sealers (171). Dalmia *et al.* investigated the antimicrobial effect of MTA Fillapex, AH Plus, Tubliseal and Sealapex on *E. faecalis* by using agar diffusion test. The antibacterial effect of MTA Fillapex was found to be lesser than Sealapex, AH Plus and Tubliseal (40). Chávez-Andrade *et al.* investigated the bond strength of MTA Fillapex, Sealapex and AH Plus with the push out test. The bond strength of MTA Fillapex was found to be similar to Sealapex and lower than AH Plus (172). Silva *et al.* investigated the bond strength of MTA Fillapex, Endoseal and AH Plus on 18 dentin sections which were obtained from 6 human maxillary teeth. According to their results, MTA Fillapex showed lower bond strength compared to Endoseal and AH Plus (173). Akçay *et al.* observed the penetration depth of MTA Fillapex, AH Plus, iRoot SP and GuttaFlow Bioseal into the dentinal tubules of 156 human mandibular premolars using a confocal microscope. The penetration depth of MTA Fillapex into dentinal tubules was found to be lower than iRoot SP (96).

MTA based bioceramic root canal sealers were generally found unsuccessful in the studies conducted in terms of leakage and solubility (174,175). Sönmez *et al.* investigated the leakage of MTA Fillapex, AH Plus and ProRoot MTA in 51 extracted human single-rooted incisors with the dye penetration method. It was observed that MTA Fillapex showed more leakage than AH Plus and ProRoot MTA (174). Ahuja *et al.* investigated the leaking properties of MTA Fillapex, Adseal, ProRoot MTA with the dye penetration test on 75 extracted single-rooted human teeth. Leakage of MTA Fillapex was found to be higher than ProRoot MTA and Adseal Sealer (175).

Urban *et al.* evaluated the solubility of MTA Fillapex, BioRoot RCS and AH Plus. In their study sealer samples were kept in distilled water for 6 months and weight loss at the end of 6 months were observed. According to the results; weight loss in the MTA Fillapex group was greater than BioRoot RCS and AH Plus (98). Torres *et al.* observed the solubility of AH Plus, MTA Fillapex and Endofill. In their study, sealer samples were kept in distilled water for 30 days, and the volume and mass losses were investigated. The resulting volume loss was measured with Micro-CT. It was reported that MTA Fillapex showed higher solubility and porosity than AH Plus and Endofill sealers (176). Silva *et*

al. measured the weight loss of MTA Fillapex and AH Plus sealers after they were soaked in deionized water for 28 days. The weight loss of MTA Fillapex was found to be higher than AH Plus group (177). Tanomaru-Filho *et al.* observed the solubility of MTA Fillapex, Sealapex and AH Plus. Sealer samples were kept in distilled water for 30 days, and the weight and volume loss at the end of 30 days were measured. Micro-CT was used for volume loss measurement. As a result of the study, it was stated that MTA Fillapex showed the highest amount of loss in terms of mass and volume (178).

Calcium Phosphate Based Bioceramic Sealers

Calcium phosphate based root canal sealers in the market are found under the experimental names of Sankine Apatite Root Canal Sealer 1-2-3, Apatite Root Sealer and Capseal 1-2-3 (157). Sankine Apatite root canal sealer contains calcium phosphate, iodoform and hydroxyapatite (179). The content of Capseal1 consists of tetracalcium phosphate, dicalcium phosphate anhydrous, zirconium oxide and portland cement. In Capseal 2, white Portland cement is used instead of gray Portland cement (180).

Chang *et al.* investigated the cytotoxicity and osteogenic activities of Apatite Root Canal Sealer, Sealapex, MTA Fillapex, and iRoot SP on stem cell culture originating from the human periodontal ligament. MTT assay was used for cytotoxicity analysis, alkaline phosphatase activity, alizarin red staining and RNA isolation was performed for observing osteogenic activity. According to the results, none of the canal sealers showed cytotoxic properties, but Apatite Root Canal Sealer activated more proinflammatory cytokines on cells compared to other canal sealers. However, it was observed that Apatite root canal sealer stimulated the differentiation of stem cells into osteoblasts. In addition, it caused the formation of less reactive oxygen products compared to Sealapex (179). Bae *et al.* investigated the osteogenic properties and effects on cell viability related with AH Plus, Pulp Canal Sealer EWT, Capseal 1, 3 and Sankin root canal sealers using stem cells derived from human periodontal ligament. It was observed that Capseal 1, 3 and Sankin root canal sealer have cytotoxic effects, but this effect was found to be lower than Pulp Canal Sealer EWT and AH 26. It was observed that Capseal 1 and 3 stimulated osteoblastic differentiation more than other canal sealers and provided the formation of more mineralized nodules at the end of the 14th day. Intracellular reactive oxygen

products were observed less in Capseal 1 and 3 compared to other canal sealers (181). Kim *et al.* investigated the biocompatibility of various canal sealers in subcutaneous tissue of rats. At the end of the first week, Apatite Root Canal Sealer 2 and Pulp Canal Sealer EWT caused severe inflammation and this effect was found to be more severe than the inflammation created by Capseal 1 and 2 (182). According to these studies, calcium phosphate based sealers showed mild cytotoxic properties, but still supported mineralization and were more biocompatible compared to root canal sealers with different contents such as zinc oxide eugenol and epoxy resin. In addition, Capseal, one of the canal sealers containing calcium phosphate, was generally found to be more successful than the others (181,182).

According to studies investigating the dentin sealing and leakage of calcium phosphate based sealers, Capseal exhibited more successful results compared to Sankine Apatite and Apatite root canal sealers (180,183). Yang *et al.* examined the leakage of various sealers with the P. Nigrescens leakage method. It was observed that Sankine Apatite sealer showed leakage within the first 15 days. On the other hand, Capseal showed 40% leakage in the first 30 days and 86.7% in the 60 days. In addition, it was observed that Sankine Apatite sealer could not penetrate the dentinal tubules as deep as AH Plus, Sealapex and Capseal, and it was easily separated from the dentin surface (180). Al-Haddad *et al.* observed the voids inside root canal fillings performed with Sankine Apatite sealer, Endosequence BC Sealer, MTA Fillapex and AH Plus using 60 extracted human premolars. All root canal sealers were marked with Rhodamine B dye for confocal laser microscope observation. It was observed that more voids were formed than the AH Plus group in the Sankine Apatite group. There was no statistically significant difference between the voids inside the root canal fillings in the Sankine Apatite, MTA Fillapex and Endosequence BC sealer groups (183). Jafari *et al.* investigated the leakage properties of MTA Fillapex, Apatite Root Canal Sealer and AH 26 sealers by using the bacterial infiltration method. It was observed that Apatite canal sealer caused more leakage than AH 26 (184).

Bae *et al.* observed the pH and calcium ion releases of Capseal I, Capseal II, Sankine Apatite Root Sealer III and Sealapex canal sealers. The pH values of Capseal 1 and 2 were found to be more alkaline and calcium ion release was higher than Sankine Apatite canal sealer (185).

2.2. Root Canal Sealers Used in This Study

2.2.1. AH Plus

AH Plus (Dentsply Mallefier, USA, Oklahoma) canal sealer, which contains epoxy resin, is mentioned in detail in Section 2.1.5.1.

2.2.2. TotalFill BC Sealer

TotalFill BC Sealer (FKG Dentaire, Switzerland) which was mentioned in Chapter 2.1.7, is a root canal sealer that stands out with its successful biocompatibility (46,120,161,186). The effects of TotalFill BC Sealer, AH Plus and Bio-C Sealer on cell viability (MTT assay), migration and mineralization were investigated by Lopez-Garcia *et al.* This study was performed on stem cells derived from human periodontal ligament. It was observed that TotalFill BC Sealer produced more cell attachments than other root canal sealers. It was also stated that TotalFill BC Sealer supports mineralization of stem cells (120). Zordan-Bonzel *et al.* also stated that TotalFill BC Sealer has biocompatible and mineralization-supporting properties (161). Rodríguez-Lozano *et al.* evaluated the effect of TotalFill BC Sealer, MTA Fillapex and AH Plus on cell viability, cell migration and DNA damage using hPDLSC cell culture. It was observed that TotalFill BC Sealer supported the cell migration and cell attachment to type 1 collagen and had less cytotoxic effects compared to other root canal sealers (186). Poggio *et al.* observed the effect of TotalFill BC Sealer, BioRoot RCS, MTA Fillapex, Sealapex, AH Plus, EasySeal, Pulp Canal Sealer and N2 root canal sealer on viability of the cells using immortalized human gingival fibroblast type-1 cell culture (ATCC CRL-2014). The cytotoxic effects were evaluated with the DMEM assay. It was observed that TotalFill BC Sealer and BioRoot RCS did not show cytotoxic effects in the first 24 hours and had moderate cytotoxic effects in 48 hours and later. It was observed that this cytotoxic effect was less than the other root canal sealers (46).

Although TotalFill BC Sealer showed more solubility than other root canal sealers,

its solubility still does not exceed the determined standards (178,187,188). Torres *et al.* kept TotalFill BC Sealer, AH Plus, Bio-C Sealer and Sealer Plus BC sealers in distilled water for 1 week and observed the resulting volume loss with Micro-CT. It was observed that the volume loss of TotalFill BC Sealer, Bio-C Sealer and Sealer Plus BC sealer were greater than that of AH Plus (187). Poggio *et al.* observed the solubility of MTA Fillapex, Sealapex, AH Plus, EasySeal, Pulp Canal Sealer and TotalFill BC Sealer. In their study, sealer samples were kept in distilled water for 24 hours and weight losses were evaluated. It was observed that the solubility and the pH of TotalFill BC Sealer were higher than MTA Fillapex, Sealapex TM, AH Plus, EasySeal and Pulp Canal Sealer. However, the solubility of TotalFill BC Sealer was not above 3%. Therefore, it complies with the ISO standards (188). Tanomaru-Filho *et al.* investigated the solubility of TotalFill BC Sealer, GuttaFlow Bioseal and AH Plus. In their study, sealers were kept in distilled water for 30 days and the resulting loss of volume was measured by Micro-CT. The results showed that TotalFill BC Sealer had the highest solubility (178).

The adhesion of TotalFill BC Sealer to dentin is very successful. Al-Hiyasat *et al.* the investigated bond strength of TotalFill BC Sealer, AH Plus on the palatal root of 60 extracted maxillary molars. It was observed that the bond strength of TotalFill BC Sealer was higher than AH Plus, regardless of canal filling techniques (189).

Turkel *et al.* investigated the penetration depths of TotalFill BC Sealer and AH Plus sealers into the dentinal tubules by using a scanning electron microscope. The bond strength of these root canal sealers were evaluated with the push out test on 142 extracted single-rooted human teeth. In this study, the effect of activation methods used in the final irrigation on the penetration depth were also investigated. EndoVac, PIPS laser and conventional syringe methods were used as irrigation methods. It was observed that the group with the deepest penetration was the combination of TotalFill BC sealer and PIPS, and it was found to be significantly superior to the combination of AH Plus and PIPS (190). Yap *et al.* investigated the bond strength of TotalFill BC Sealer, EndoRez and AH Plus using 60 extracted anterior human teeth. It was observed that while the bond strength of TotalFill BC Sealer did not statistically differ from AH Plus, it was found to be higher than EndoRez (191).

Kapralos *et al.* observed the antibacterial effects of AH Plus, TotalFill BC sealer, RoekoSeal and GuttaFlow 2 sealers to the planktonic and biofilm states of *E. faecalis*, *S.*

epidermidis, *S. aureus* and *S. mutans*. It was observed that TotalFill BC Sealer has an antibacterial effect on planktonic *E. faecalis* for 7 days. In addition, its antibacterial effect on planktonic *S. mutans*, *S. epidermidis*, *S. aureus* and *E. faecalis* was found to be higher than AH Plus, Roekoseal and Gutta-flow2. TotalFill BC Sealer also showed antibacterial effects on the biofilm versions of *S. mutans*, *S. epidermidis*, *S. aureus* and *E. faecalis* (92). Zordan-Bonzel *et al.* investigated the antimicrobial effects of TotalFill BC Sealer and AH Plus on the planktonic and biofilm forms of *E. faecalis* and *C. albicans* by using the direct contact test method. It was observed that TotalFill BC Sealer has antimicrobial effects on planktonic and biofilm forms of *E. faecalis*. It also had an antifungal effect against *Candida Albicans* (161). Poggio *et al.* investigated the antibacterial effects of eight different root canal sealers (BioRoot RCS, TotalFill BC Sealer, MTA Fillapex, Sealapex Root Canal Sealer, AH Plus, EasySeal, Pulp Canal Sealer, N2) on *E. faecalis* with the agar diffusion and direct contact test. According to the results, TotalFill BC Sealer showed a bactericidal effect on *E. faecalis* (192).

2.2.3. CeraSeal

CeraSeal (Meta-Biomed, South Korea) is a newly released calcium silicate based root canal sealer. It contains calcium silicate, zirconium oxide and thickening agents. The features specified by the manufacturer are high dentin coverage, superior biocompatibility, antimicrobial properties depending on alkaline pH and dimensional stability. When this hydrophilic root canal sealer interacts with water, calcium aluminate hydrate gel and calcium silicate hydrate gel are formed. It is stated by the manufacturer that CeraSeal can also be used with a single cone obturation method (193). López-García *et al.* investigated the effect of Endosequence BC Sealer, CeraSeal and Endoseal root canal sealers on cell viability (MTT), cell migration and wound healing potential (wound healing assay) in hPDLSC cell culture. In their study, CeraSeal and Endosequence BC Sealer provided more cell adhesion than EndoSeal and increased the expression of ALP, CAP, CEMP-1 genes, which support the mineralization (194).

Oh *et al.* investigated the effects of CeraSeal, AH Plus and EndoSeal TCS on the cell viability and osteogenic effects on stem cells derived from periodontal ligament. According to their results, the root canal sealer with the least cytotoxicity was CeraSeal,

and the highest was found as AH Plus. It was stated that the root canal sealer with the greatest effect on mineralization was EndoSeal TCS, followed by CeraSeal (195).

Kharouf *et al.* examined the physical and antibacterial properties of CeraSeal and BioRoot RCS root canal sealers in 20 extracted human mandibular first premolars. In their study, root canal sealers were used with the single-cone obturation technique and the voids inside the root canal fillings were examined with a scanning electron microscope. In the CeraSeal group, void structures were observed less than the BioRoot RCS group. Samples were kept in distilled water for 168 hours and pH measurements were made intermittently. As a result of this analysis, pH of both root canal sealers were alkaline and BioRoot RCS had higher pH values. To evaluate the solubility, the samples were soaked in distilled water for 72 hours, 3 times for 14 days. According to the results, CeraSeal showed lower solubility. There was no statistically significant difference between the two sealants in the compression test. Antibacterial activities on *E. faecalis* were evaluated with the agar diffusion test and direct contact test. In the first 3 hours, both canal pastes did not show antibacterial activity. At the end of 24 hours, BioRoot RCS showed more bactericidal effects. At the end of 72 hours, both root canal sealers showed a bactericidal effect of more than 95% (196). Lee *et al.* investigated the voids inside the root canal fillings performed with CeraSeal using plastic tooth models. Root canal fillings were performed by using single cone and continuous heat methods and the void structures which occurred in 2 different obturation techniques were observed with Micro-CT. According to the results, more voids were observed in the single cone group (197).

Park *et al.* investigated the physical and biocompatibility properties of CeraSeal, Bright Endo MTA, One-Fil, and AH Plus sealers. In their study, the samples were kept in distilled water for 30 days to evaluate the dimensional stability, and then the resulting volumetric change was calculated. As a result of this analysis, CeraSeal showed the most expansion, and Bright Endo MTA was the root canal sealer with the least dimensional change. Cell viability was investigated in hPDLSC cells to examine their biocompatibility properties. At the end of the 7th day, CeraSeal and EndoSeal TCS were found to be the most biocompatible groups as they had the highest number of viable cells. It was stated that the AH Plus group was the group with the lowest number of viable cells for 7 days. When the radiopacities were examined, it was observed that the most radiopaque group was AH Plus followed by CeraSeal and Bright Endo MTA. In the fluidity test, it was observed that all root canal sealants met the ISO 6876/2012 standards, and One-Fil was

the sealant with the highest fluidity (198).

2.3. Root Canal Obturation Methods

In endodontic treatment of infected teeth, microorganisms and their products are removed from the root canal with chemo-mechanical preparation and adequate disinfection is ensured. The better the root canal system is isolated from the external environment, the better the prognosis of the tooth is. Therefore, sealing the root canal plays an important role in the success of root canal treatment (11).

Different methods have been developed for creating hermetic root canal filling in three dimensions. These methods are;

- Lateral Condensation
 - Cold Lateral Condensation
 - Warm Lateral Condensation
- Warm Gutta-Percha Methods
 - Warm Vertical Compaction
 - Compaction with Continuous Wave
 - Thermoplastic Injection
 - Thermomechanical Compaction
- Gutta Percha Carrier Systems
- Single Cone Method
- Other Methods
 - Solvent Methods
 - Filling with Sealer
 - Immediate Obturation (5,199)

2.3.1. Lateral Condensation

2.3.1.1. Cold Lateral Condensation Method

The cold lateral condensation method is one of the most widely used methods in endodontic practice (5). With this method, there is no need for an extra device during obturation and the control of the working length can be easily achieved (11).

In the lateral condensation method, gutta-perchas with a standard conicity of 2% are used. The master gutta-percha cone is measured and positioned to tuck into the working length. At this point, it is important to get the tug back feeling. It is necessary to try the master gutta-percha one size smaller if the master cone cannot reach the working length, and one size larger if the master cone goes beyond the working length. If necessary, gutta-percha can be cut from its tip and adapted to the root canal. After selecting the appropriate master cone, periapical radiography should be taken in order to observe the fitting of the master cone. Afterwards, root canal sealer is applied to the canal walls and the master gutta-percha is placed in the root canal. A slight pressure is applied in the lateral direction, with the spreader 1-2 mm behind the working length to make room for the auxiliary gutta-percha cones (5).

Pressure at this stage is important because excessive pressure can cause fractures or cracks in the root (200,201). Usage of a finger spreader enables pressure control more easily than hand spreader, so the use of a finger spreader is recommended (202). The alloy of the spreader used is also important. Ni-Ti spreaders are more flexible and can penetrate deeper and transmit less pressure to the root. Stainless steel spreaders are not as flexible as Ni-Ti (203).

After creating space with the spreader, the auxiliary cone is placed in this space. This process is continued until the filling of the canal is completed. When the spreader starts to penetrate a distance of maximum 1-2 mm from the canal orifice, it is considered that the root canal obturation is completed and the gutta-percha is removed with a heated hand tool 1 mm below the canal orifice (5).

The advantage of this method is that the working length control is enabled more easily. The disadvantage is that it is difficult to fill the irregularities in the root canal (5).

2.3.1.2. Warm Lateral Condensation

Endotec2 device was produced in order to obturate the root canal with the warm lateral condensation. The gutta-percha cones are heated and homogenized with the electrically heated tip of the Endotec 2 (Medidenta) device. The advantage of this method is that it is easier to provide working length control compared to the warm vertical condensation method (5). Another device that can be used in this method is the Endo Twin (Hu-Friedy). The heat and vibration tip of this device is suitable for use in both lateral condensation and vertical compaction methods. The DownPak (Hu-Friedy) device is also suitable for the warm lateral compaction method (5).

2.3.2. Warm Gutta-Percha Methods

2.3.2.1. Warm Vertical Compaction

In the warm vertical compaction technique, it is aimed to obturate the root canal tightly in three dimensions and create a root canal filling consisting of a minimum amount of sealer and maximum amount of gutta-percha. In this technique, the gutta-percha in the root canal is softened and brought to a homogeneous consistency with the help of an equipment that provides heat. By applying pressure in the vertical direction, it is adapted to the structure of the root canal cavity and the root canal is filled (108). Touch 'n Heat (SybronEndo), DownPak (Hu-Friedy), and System B (SybronEndo) devices are the devices used in this method (5).

2.3.2.2. Compaction with Continuous Wave

It is a different version of the warm vertical compaction method. In this method, System-B device is used to obturate the root canal (5). This device provides the application of heat for a certain time. Vertical pressure can be applied with the same tip that gutta-percha is heated. System B has temperature settings of 200°C, 250°C and

300°C. It is known that a temperature increase of 10°C around the dental tissues has a detrimental effect on the periodontal ligament (108). During the use of this device, the temperature increase in the periodontal ligament was found to be 4.1°C (5).

2.3.2.3. Thermoplastic Injection

It is a root canal filling technique based on the principle that gutta-percha is thermoplasticized with heat and applied to the root canal. When gutta-percha is thermoplasticized and applied to the root canal, voids may occur inside the root canal filling and gutta percha may shrink during cooling down. To prevent this situation, thermoplasticized gutta-percha should be condensed (108).

Obturation of a root canal only with thermoplastic injection method creates a risk of extrusion of the root canal filling from the root apex. For this reason, it is safer to use the thermoplastic injection method as a backfill obturation method. In the backfill obturation method, the apical 1/3rd of the root canal is obturated with lateral condensation or single cone method. Later, the middle 1/3rd and coronal 1/3rd are obturated with the thermoplastic injection. The control of working length can thus be easily assured and root canal filling can be adapted easily to the irregularities of the root canal system (108).

There are various devices for root canal obturation using the thermoplastic injection method. The systems are Obtura III (Obtura Spartan), Ultrafill 3D (Coltène/ Whaledent), Calamus (DENTSPLY Tulsa Dental Specialties), Elements (SybronEndo), and HotShot (Discus Dental).

2.3.2.4. Thermomechanical Compaction Method

“McSpadden Compactor” is used to obturate the root canal with thermomechanical compaction method. The McSpadden Compactor is a low-speed device and it has the design of the opposite structure of the H file. The compactor generates frictional heat and this heat softens the gutta-percha. The advantage of this system is the practicality of use and its ability to fill irregular structures in the root canal due to the heat generation. As a disadvantage, there is a risk of separation of the instrument and the risk of extrusion of

the root canal filling. It is produced from Ni-Ti alloy to make the compactor more resistant and flexible against breakage (5).

2.3.3. Gutta Percha Carrier Systems

It is a root canal filling method in which heated gutta-percha is placed into the root canal with the help of a carrier. There are various gutta-percha carrier systems. These are Thermafil, SimpliFill and GuttaCore. Thermafil consists of a metal core covered with gutta-percha. It is applied to the root canal after softening with heat. Although it is very easy to apply, root canal treatment repetition and post space opening are very difficult (108). In the GuttaCore system, the carrier core part is made of gutta-percha instead of metal. By this way, the disadvantages mentioned in Thermafil are attempted to be eliminated (5).

2.3.4. Single Cone Method

Single cone is a method of obturation of the root canal by using a single gutta-percha which is compatible with the taper of the Ni-Ti files used in root canal shaping (204). This method is preferred by clinicians because of its practicality compared to other canal filling methods (205). root canal fillings obturated with the single cone method, the amount of root canal sealer is higher than the amount of gutta-percha. Therefore, in the single cone method sealing ability of root canal sealers plays an important roll in the prognosis of the endodontic treatment (204). It is thought that the volumetric expansion feature of bioceramic root canal sealers can form less voids than root canal fillings, therefore can eliminate the risk of leakage in the single cone method (157). Celikten *et al.* examined the void structures inside the root canal fillings obturated with various root canal sealers using the Micro-CT. There was no statistically significant difference observed between epoxy resin, glass ionomer and bioceramic sealants in terms of void formation. Void structures were observed in all canal fillings (206). Huang *et al.* observed the void structures inside the root canal fillings with the nano-CT. It was observed that the volumetric expansion feature of bioceramic sealers caused less void formation than

epoxy resin based sealers (207). Wang *et al.* observed the void structures of the root canal fillings obturated with iRoot SP and AH Plus sealers using a laser confocal microscope. This study was performed in 42 extracted human lower incisors and the root canal fillings of the samples were obturated with single cone and warm vertical compaction methods. According to this study, root canal obturation method did not affect the amount of the void structures inside root canal fillings (208). Similarly, Keleş *et al.* concluded that there was no statistically significant difference between the single cone method and the warm vertical compaction method in terms of void formation as a result of their micro-CT study (209). There are also studies showing the opposite of these results. Celikten *et al.* showed that structures with the highest number of voids were observed in root canal fillings of the single cone group, followed by the lateral condensation group, and the structures with the lowest number of voids occurred in the warm vertical compaction group (210).

2.3.5. Other Methods

2.3.5.1. Solvent Methods

In the solvent method, gutta percha is softened with the help of solvents and applied to the root canal. Usually, Chloroform, Xylol and Eucalyptol are used as solvents. When the solvent is used on gutta-percha, shrinkage occurs after evaporation of the solvent and voided structures are formed. However, it is very difficult to provide working length control in this method. For these reasons, this method is not frequently used today (5).

2.3.5.2. Filling with Sealer

Obturation of the root canal only by using root canal sealer for complex anatomies was also considered. However, this methodology is not preferred because of many disadvantages such as difficulty of controlling the working length, risk of apical extrusion and formation of voids (5).

Immediate Obturation

In cases such as teeth with open apex that have not completed their development or external root resorption at the apex, this area should be closed with a barrier to prevent extrusion of the root canal filling. Materials such as dentin chips, calcium hydroxide, demineralized dentin, lipolyzed bone, tricalcium phosphate, hydroxyapatite and collagen are used as barriers (5).

While calcium hydroxide shows successful results in the long term, there are also disadvantages such as a long treatment period, difficulty of patient compliance, and the tendency of the tooth to break. For this reason, biomaterials are currently used to create an apical barrier. MTA is frequently used in the treatment of teeth that require such an apical barrier and is preferred in endodontic practice due to its high dentin coverage, insusceptibility to moisture, superior biocompatibility, osteogenic properties, high pH and antibacterial properties (5).

2.4. Overview of Retreatment

The success rate of endodontic treatment was found between 93-84% in the clinical study performed by Farzaneh *et al.* In this study, the absence of periapical lesions (teeth with a pai index less than 3) and the absence of clinical symptoms were accepted as success (211). However in case of failure, post treatment disease occurred.

Post treatment disease can occur as “emergent”, “persistent” or “recurrent”. Post treatment disease is defined as “emergent” if the symptoms occur immediately after endodontic treatment is completed, “persistent” if the symptoms do not disappear despite the tooth was endodontic treated, and “recurrent” if the symptoms reoccur after healing is completed (8).

There are various reasons for post-treatment disease to occur. These are iatrogenic errors that may occur during root canal treatment, leakage of the coronal restoration and persistent infections (7). In addition to these reasons, due to the complex root canal anatomy, it is possible to encounter reinfection, and therefore post treatment disease in

cases where the disinfection and obturation of the root canals cannot be performed adequately (212). When the root canal instrument separates inside the root canal, microorganisms and their products, pulp tissue or infected root canal filling cannot be eliminated and cleaned properly. In this case, the prognosis of treatment is adversely affected (212). Perforations are another iatrogenic factor that adversely affect the prognosis and they can occur during access cavity preparation or mechanical preparation of the root canal. If the perforation area is not repaired properly, microorganism leakage will occur and the root canal system becomes reinfected (212). If flexible root canal instruments are not used during mechanical preparation of the root canal, ledge formation can happen inside the root canal. This formation may cause insufficient cleaning of the apical 1/3 of the root canal and secondary infection. Due to ledge formation, it is not possible to obturate the root canal until working length. Therefore, root canal filling terminates short of the anatomical apex and this situation negatively affects the prognosis of endodontic treatment (212).

Peter *et al.* investigated the contact of Protaper Universal Ni-Ti rotary instrument to the root canal walls using Micro-CT. According to their study, these instruments did not contact all the canal walls (213). Similarly, Thomas *et al.* investigated the contact of WaveOne Gold, TRUShape, EdgeCoil, and XP-3D Shape rotary canal instruments to the root canal walls with the Micro-CT. It was reported that none of the rotary file systems used could contact the entire root canal walls (214). Walls that are not in contact with canal instruments can cause reinfection if the root canal is not cleaned adequately by irrigation. Missing root canals that are left untreated during endodontic treatment also cause reinfection of the tooth and post treatment disease (8).

Apically extruded root canal fillings or other foreign materials that are extruded from the root canal may cause foreign body reactions in periapical tissues, apical radiolucencies and cause apical periodontitis symptoms to persist (215). Insufficient isolation during root canal treatment can cause microorganisms to enter inside the root canal system and cause reinfection. Microorganisms originating from the carious lesion, saliva or biofilm on the tooth crown may cause insufficient infection control in the root canal system. Even if infected irrigation solutions or infected root canal instruments are used in root canal treatment, adequate disinfection cannot be achieved (216).

Falling of the temporary restoration between root canal treatment sessions,

intentionally leaving the endodontic cavity open, or leakage of the temporary restoration can cause reinfection of the root canal system (216). After the root canal treatment is completed, the formation of new caries in the crown or the leakage of the coronal restoration may cause secondary infection (216).

It has been reported that post-treatment disease is observed in 5-15% of the teeth with preoperative apical periodontitis even if teeth have received endodontic treatment in accordance with the standards (8). Another factor that causes disease after root canal treatment is persistent infection.

According to the treatment guideline of the American Endodontic Society:

- In cases where periradicular pathology continues with symptoms,
- In the presence of persistent symptoms,
- In cases where the root canal system is contaminated with saliva and bacterial leakage is occurred,
- If the restorative treatment plan includes an endodontically treated tooth that has radiographically inadequate root canal filling.
- If there is a possibility that the planned restoration will cause infection of the root canal system of the endodontically treated tooth.
- In the presence of insufficient root canal filling on the radiograph and accompanying apical pathological image or symptoms,

Non-surgical retreatment is indicated (9).

2.4.1. Microorganisms Involved in Post Treatment Disease

In the case of post treatment disease (secondary infection), the structure of the microbial flora in the root canal is different from the primary infection. Microorganisms seen in secondary infection are usually resistant to irrigation solutions and intracanal medicaments used in root canal treatment. Gram-negative bacteria are frequently seen in primary endodontic infections, and Gram-positive bacteria are seen in secondary

infections. Thick peptidoglycan layers in the cell wall of gram positive bacteria provide protection against antimicrobial agents used during the root canal treatment. *E. faecalis*, actinobacteria, *Candida albicans*, *P. aeruginosa*, *E. coli*, enteric rods and staphylococcus are microorganisms frequently seen in secondary infections (216).

The remaining root canal filling after the retreatment procedure creates a barrier between the antimicrobial agents applied during the treatment and the infected dentin (217).

For this reason, it is very important to adequately remove the infected root canal filling which contains resistant microorganisms and to provide an effective disinfection in order to achieve success in the retreatment.

One of the reasons for post treatment disease is persistent infections. Persistent infections may develop due to endodontic infection or they can occur due to non-endodontic reasons. If the persistent infection is caused by endodontic infection, it is usually seen as an acute abscess. Acute abscess is a polymicrobial infection in which microorganisms with low virulence create a synergistic effect and overcome the host's defense barrier. In this type of infection, *Actinomyces*, *P. Acnes*, *P. Propionicum*, *P. Gingivalis*, *P. Oralis*, *P. Intermedia*, *P. Micra* and *F. Nucleatum* are frequently seen (216). In persistent infections that are not caused by endodontic infection, the infection occurs due to bacteria which are settled on the root surface. These bacteria form a biofilm layer and actinomycotic colonies outside the surface of the root apex. *Actinomyces* and *P. propionicum* species are usually responsible for these infections (216).

Biofilm is a complex and dynamic structure in which a group of microorganisms adhere to various surfaces and each other. These microorganisms multiply and at the same time produce a polymerized matrix consisting of proteins, polysaccharides and residues (218).

In endodontic infections, biofilm structures can be seen inside the root canal, outer surface of the root apex, in the periapical region or around the biomaterials. The biofilm seen inside the root canal is usually composed of spirochetes, cocci, rods and filamentous bacteria. The bacteria characterized with biofilm formation in endodontic infections is *E. faecalis* (219).

Biofilms outside of the root surface and in the periapical region can be seen even

in the absence of endodontic infection. If the biomaterials used in endodontic treatment or materials such as gutta-percha are extruded from the root apex, Gram positive facultative cocci may settle on the surface of these materials (216). Nair *et al.* observed the biofilm structures with light and electron microscopy in the root canal of 21 infected extracted human teeth for the first time (220). Caldwell *et al.* described 4 characteristic features of biofilm. These are expressed as autopoiesis, homeostasis, synergy, and communality. These are autopoiesis which is the ability to self-organize, homeostasis which is the ability to resist environmental harsh conditions, synergy which is the ability to be more effective in a group than alone, communality which is the ability to collectively respond to changes in environmental conditions (219,221).

The communality feature is also referred to as quorum sensing (222). In addition to all these features, microorganisms in the biofilm have the ability to form extracellular barriers such as capsules and secrete extracellular secretions. In this way, they become more resistant to the effects of antimicrobial agents and sudden changes in environmental factors compared to their planktonic phase (222). Kalfas *et al.* mentioned a case of apical periodontitis that did not heal for 7 years and occasionally went into acute phase. In this case report, apical resection was performed after root canal treatment. Resected root dentine was subjected to microbiological examination and Actinomyces microorganisms which are responsible for persistent non-root infections were observed (223). Souza *et al.* investigated the apically resected root dentine of 20 teeth that received orthograde root canal treatment and did not heal with SEM. Teeth with chronic apical abscess, acute symptoms or apical lesion that did not reduce in size in the 5-year follow-up period were included in this study. Biofilm formation was observed in the outer surface of the root tip in all of the samples. Multiple apical foramina were observed in 50%, microcracks in 80%, resorption cavities in 50% of the samples. It is known that multiple apical foramina and microcracks are convenient sites for the retention of microorganisms. Biofilm formation also suggests persistent extraradicular infection (224). Biofilm formation also indicates persistent extraradicular infection.

2.4.2. Root Canal Instruments Used in Retreatment

Retreatment procedure consists of 3 stages that are; chemo-mechanical preparation, disinfection and canal filling (9). In the chemo-mechanical preparation stage, the infected root canal filling is removed from the root canal and the root canal system is disinfected again. Hand files or nickel-titanium rotary instrument systems are used to remove the infected root canal filling (225). The use of nickel-titanium rotary instrument systems reduces the procedure time and provides convenience to physicians (226). Rotary instruments which are used in retreatment remove the infected root canal filling with rotary or reciprocating motion. Examples of retreatment sets working with continuous rotation are: Protaper Universal Retreatment, R-Endo, D-Race, Mtwo Retreatment file, and for those working with reciprocating motion: Resiproc, Wave One, Wave One Gold systems (226).

Mtwo retreatment files is a system consisting of two instruments working with continuous rotation. Instruments R15 and R25 have 05 tapers and are 16 mm long. Mtwo retreatment files remove the root canal filling owing to their active cutting tip and fixed helical angle (227). The R-ENDO system is a system designed specifically for root canal filling removal, consisting of a handpiece and 4 rotary instruments. A glidepath is opened in the gutta-perchas with a hand file called Rm file, then the root canal filling in the coronal 3mm is removed with an instrument named Re. Other instruments of the system are R1, R2, R3. These instruments are used in the coronal 1/3, middle 1/3 and apical 1/3, respectively (228). Protaper Universal Retreatment system consists of 3 files that work with continuous rotation, specially designed for root canal filling removal. The instruments in the system are: D1, D2, D3 respectively. Taper of D1: 09, D2: 08, D3: 07. The apical diameters of the instruments are #30, #25, #20 and the lengths are 16mm, 18mm, and 22mm, respectively. D1 instrument is used for the removal of coronal 1/3 root canal filling, D2: middle 1/3, D3: apical 1/3. The D1 has an active cutting edge design, while the D2 and D3 instruments do not have active edges (229). D-Race system works with continuous rotation and is specifically designed for the removal of root canal filling. D-Race system consists of 2 instruments which are DR1 and DR2. DR1 is an instrument with an apical diameter of #30, taper of 10 and 15mm length and produced for the removal of coronal 1/3rd of root canal filling. DR2 is used for the removal of the middle and apical 1/3rd of the root canal filling. DR2 has an apical diameter of 25, 04 taper and a length of

25mm (230). The Reciproc system is a single file system that works with the reciprocal movement. This system includes 3 instruments: R25, R40, R50. R25 has a taper of 08, R40 has a taper of 06 and R50 has a taper of 05. With R25, removal of the root canal filling is performed with a single file which has #25 apical diameter. When the apical diameter is desired to be expanded more, other files of the system can be used (231). The Reciproc system has an S-shaped design and active cutting surfaces. This system is created for primary root canal treatment. However it is used in retreatment in some studies (23,226,232,233). Wave One is a reciprocating, single file system, which has variable pitch flutes, convex triangular cross-section design in the coronal part and modified convex triangular design in the apical part. Although this system was produced for mechanical shaping in primary root canal treatment, it has also been used in retreatment studies (234). There are 3 instruments in this system, which allows mechanical shaping in different apical radius. These instruments are; #21 apical diameter with 0.6 taper instrument, #25 apical diameter with 0.8 taper, #40 apical diameter with 0.8 taper (235). WaveOne Gold is also a single file system that provides shaping with reciprocal motion. It is an instrument with inverted helix design, semi-active tip with parallelogram section. It is produced with gold wire technology. It is 80% more durable and 50% more flexible than the old version of Wave One. There are options with #20 apical diameter and 07 taper, #25 apical diameter and 07 taper, #35 apical diameter and 06 taper and #45 apical diameter and 05 taper (236). It is produced for mechanical preparation in primary root canal treatment, but has also been used in retreatment studies (234).

Comparin *et al.* investigated the level of post-operative pain in patients after retreatment, performed with Mtwo retreatment file working with continuous rotation and Reciproc systems working with reciprocal motion in 65 patients. At the end of this study, no statistically significant difference was found between treatments using these 2 systems (237). Das *et al.* observed the retreatment ability of ProTaper retreatment files, Mtwo retreatment and R-Endo systems with a stereomicroscope in 60 extracted human teeth. As a result of this study, it was observed that the Protaper group removed more root canal filling in the coronal and middle part than the other canal files, and the Mtwo system removed the least amount of canal filling (22).

Raj *et al.* investigated the retreatment efficiency of D-Race, Protaper Universal Retreatment files and H-type hand files with SEM in 63 extracted central incisors. As a

result of their study, Protaper Universal Retreatment files were found to be more efficient than D-Race and H type files (238). De Siqueira Zuolo *et al.* investigated the efficacy of Trushape and Reciproc systems in removing the root canal filling using Micro-CT in 64 extracted lower human canines. There was no statistically significant difference between the 2 systems, however the procedure time was found to be shorter in the Reciproc retreatment group compared to the Trushape group (23). Canali *et al.* investigated the efficiency of Wave One and Wave One Gold systems in the removal of root canal filling using Micro Ct in 20 extracted human mandibular first molars. They found no statistically significant difference between the performances of the 2 systems (234).

2.4.3. Irrigation in Retreatment

While chemo-mechanical preparation is performed for removing the infected root canal fillings from root canals, irrigation should also be performed to ensure disinfection of the root canal system. With irrigation, infected root canal filling residues, infected tissue residues, microorganisms and by-products are removed from the areas where root canal instruments are unable reach, and lubricity is enabled for the instruments (239). NaOCl has been accepted as the gold standard in irrigation solutions (240). Sodium hypochlorite dissociates into ions in the form of Na and OCl, and when the pH of the environment is between 4-7, the chlorine (OCl) ion turns into hypochlorous acid (HOCl). Hypochlorous acid has a strong antibacterial effect by inhibiting oxidative phosphorylation and membrane activities. It inhibits mitochondrial activities and DNA synthesis of microorganisms. Sodium hypochlorite has a dissolution effect on organic tissues and on the organic part of dentin. For this reason, it is used for the disinfection of the root canal space in endodontic treatment and retreatment (239).

After mechanical preparation of the dentin tissue, a 2-5µm thick mineralized layer is formed, consisting of organic residues such as microorganisms, their by-products and necrotic tissue residues. This layer is defined as the "smear layer". Residual products in the smear layer can cause reinfection of the root canal system. The smear layer may cause microorganisms to penetrate into the deep layers of the dentin and prevents the irrigation solutions from penetration to deep dentine. Therefore, smear layer creates a barrier between the root canal filling and the dentin wall, preventing the root canal filling from

penetrating to the dentine. Therefore, it must be removed (241). The smear layer consists of organic and inorganic components. With the use of NaOCl, it is possible to remove the organic part; however it is necessary to use chelation agents or organic acids in order to remove the inorganic part. The chelating agent frequently used in endodontic practice is EDTA. Organic acid solutions that are used in endodontic practice are citric acid, tannic acid, lactic acid and polyacrylic acid. Apart from these solutions, MTAD solution created with a mixture of detergent acid and tetracycline isomer and mixtures called Qmix are also used to remove the smear layer (241).

Qmix was first released in 2011. It contains EDTA, chlorhexidine, and N-acetyl-N,N,N-trimethylammonium bromide (CTAB) (242). Nogo-Živanović *et al.* investigated the smear layer removal efficiency of Qmix, MTAD and 17% EDTA with the SEM in 40 extracted maxillary human incisors. There was no statistically significant difference between the smear layer removal efficiency of Qmix and MTAD, but it was reported that the smear layer removal efficiency of these two solutions was higher than 17% EDTA. It was also observed that MTAD caused more mineral loss in root dentin than other irrigation solutions (242).

Irrigation activation methods also help the removal of the smear layer and they are classified as manual activation methods, irrigation methods applied with devices and methods that assist root canal disinfection. In manual activation methods, side-perforated irrigation needles and canal brushes are used. Irrigation methods applied with devices include rotary brushes, continuous irrigation systems, sonic and ultrasonic systems and systems working with pressure change. Lasers and ozone are used in methods that assist root canal disinfection. Zang *et al.* observed the remaining root canal filling volumes after retreatment with Micro-CT and they also observed the remaining root canal filling volumes after activation with XP-Endo Finisher R. According to their study, activation reduced the remaining root canal filling volumes (232). Similarly Alsubait *et al.* and Crozeta *et al.* showed that irrigation activation methods reduce the remaining root canal filling volume (24,243).

Chlorhexidine is another irrigation solution that is frequently used in root canal treatment. Chlorhexidine has a long-lasting antibacterial effect. It has antibacterial activity on *E. faecalis*, which is often isolated in secondary apical periodontitis and resistant to most irrigation solutions (244).

If NaOCl and chlorhexidine are mixed, during the final wash protocol, a brown-colored carcinogenic precipitate which is called Para-chloroaniline is formed. In order to avoid this situation, irrigation with sterile saline should be done between NaOCl and chlorhexidine in the final irrigation protocol (245).

In the retreatment procedure, intracanal medicaments are also frequently used for root canal disinfection, as there are more resistant microorganisms in the microbial flora than in primary endodontic infection. After disinfecting the root canal, the root canal filling must be completed hermetically as in primary endodontic treatment.

2.5. Evaluation of the Retreatability of the Root Canal Filling

There are several methods for assessing the retreatability of the root canal filling. In the studies carried out; SEM (Scanning electron microscope) (20), digital radiography (21), confocal microscope and stereomicroscope (22) Optical microscope, cone-beam computed tomography (CBCT) (23) and micro-computed tomography (Micro-CT) (24) are among the evaluation methods used for this purpose. Each of these methods have advantages and disadvantages over each other.

Samples must be divided in order to perform imaging with the SEM. Therefore, it becomes more difficult to perform further analysis on the samples (20). In the digital radiography method, the samples are not damaged, but it is possible to observe the samples only in two dimensions (21,246).

Cone beam computed tomography has been used frequently in recent years. De Siqueira Zuolo *et al.* investigated the retreatability of Pulp Canal Sealer EWT and Endosequence BC Sealer using the cone beam computed tomography (23). Cone-beam computed tomography provides three-dimensional imaging of teeth and surrounding tissues with less radiation dose than conventional computed tomography (247). CBCT contains more radiation dose than classical two-dimensional radiographic methods. In this method, multiple images are obtained by irradiating the area to be imaged, from different directions and a three-dimensional image is obtained by reconstructing these images with the help of various software programs (247).

Nowadays, cone beam computed tomography is clinically used to detect situations that are difficult to diagnose in two-dimensional radiography, such as procedural errors, difficult anatomies, root resorptions or root fractures (248). The advantages of this method are providing three-dimensional observation, not damaging the samples and the possibility to repeat scanning (249). However, there is also the view that CBCT is less successful than periapical radiography in detecting voids in the root canal filling (250).

The imaging method with micro computed tomography was developed in the 1980s. It provides a three-dimensional, *in vitro* observation without damaging the samples. Image obtained with Micro-CT consists of cubic image units called voxels. The size of a voxel is 1 million times smaller than conventional computed tomography image units (25). In this method, higher resolution images are obtained compared to CBCT and conventional computed tomography. In conventional computed tomography, image observations are performed at 1-2mm cross-section intervals while Micro-CT imaging has the opportunity to observe the image sections in 5-50 micrometers (251,252). In Micro-CT, the x-ray source is smaller than in conventional computed tomography. This results in sharper images. In addition, in Micro-CT, the x-ray source is fixed and the object to be imaged is rotated while in computed tomography it is the opposite. Moving the X-ray source causes vibration and therefore reduces the resolution (25).

Similar to computed tomography, Micro-CT does not damage the samples during imaging and the scan can be repeated. Unlike computerized tomography, it provides a clearer image and measurement. The disadvantage is that it cannot be used *in vivo* due to the high radiation level (25). Micro-CT is used in Endodontics to evaluate root canal anatomy, root canal shaping, quality of the root canal filling, the accumulated debris and residual root canal filling in retreatment (25).

2.6. Methods for Evaluating Bond Strength of Root Canal Filling

There are several methods for evaluating the bond strength of root canal sealers to the dentinal wall. These are; shear bond test, pull-out test, microtensile test(stretching) and push out test (253).

Shear bond test: In this test method, the force is applied parallel to the bonding

surface in order to test the bond strength (253). The width of the bonding area and the head by which the force is applied (such as wire knot, knife tip) can change the results (254).

Pull-out test: In this method, two surfaces are bonded with the help of adhesive and force is applied until separation occurs. The force at which the separation occurs is recorded. This method is generally used for the bond strength measurement of endodontic posts (254).

Macro-tensile test: In this method, force is applied to the test material from two directions. In this way, the force is more evenly distributed compared to the shear test. This method is used for testing the bond strength of cements (254).

Push out test: This method was used in 1973 to test orthopedic implants (255). Later, Haller *et al.* used it in their studies to examine the bond strength of restorative materials (255).

The push out test is frequently used to measure the bond strength of root canal sealers. In this method, cross-sections are taken from the endodontically treated samples and these samples are fixed in the piston. The force is applied through the piston with a universal testing machine, parallel to the bonding surface. It is important that the force applying head must not touch the canal walls (254). The maximum force is obtained in Newtons (N). The resulting N value is divided by the bonding surface. The bonding surface is calculated with the formula $\pi (r_1 + r_2).h$. The r_1 value represents the apical radius of the dentin disc, the r_2 value represents the coronal radius of the dentin disc, and the h value represents the thickness of the dentin disc. When the N value is divided by the bond surface, the bond strength value in Megapascal (MPa) is obtained (256).

3. MATERIALS AND METHODOLOGIES

3.1. Selection of Sample Teeth

This study was performed on 66 extracted human premolars. Inclusion criteria for the extracted teeth used in the study were;

- teeth with single and straight root canal
- teeth with no cracks
- teeth having fully formed apices
- absence of calcification in the root canal
- the width of all teeth at a distance of 5 and 10 mm from the apical should be close to each other
- teeth with root canal curvature below 10 degrees
- teeth with oval root canal structure.

In order to meet all these criteria, the extracted teeth were examined under Zeiss Opmi Pro (Oberkochen, Germany) operation microscope (*Figure 1a*), and cracked teeth were excluded from the study. All teeth were visualized by digital radiography in bucco-lingual, mesio-distal direction (*Figure 1b*). Teeth with a configuration other than Vertucci 1 or calcification in the root canal were excluded from the study and replaced with new ones. The degree of curvatures was measured with the Image J program using Schneider's technique (*Figure 1c*), and teeth with a curvature above 10 degrees were excluded from the study (257). The specimens were measured with calipers 5 and 10 mm from the apical in mesio-distal and bucco-lingual directions, and teeth with oval root canals with similar values were included in the study. (*Figure 1d*) Specimens which have apical diameter higher than #25 were excluded from the study and replaced with new ones.

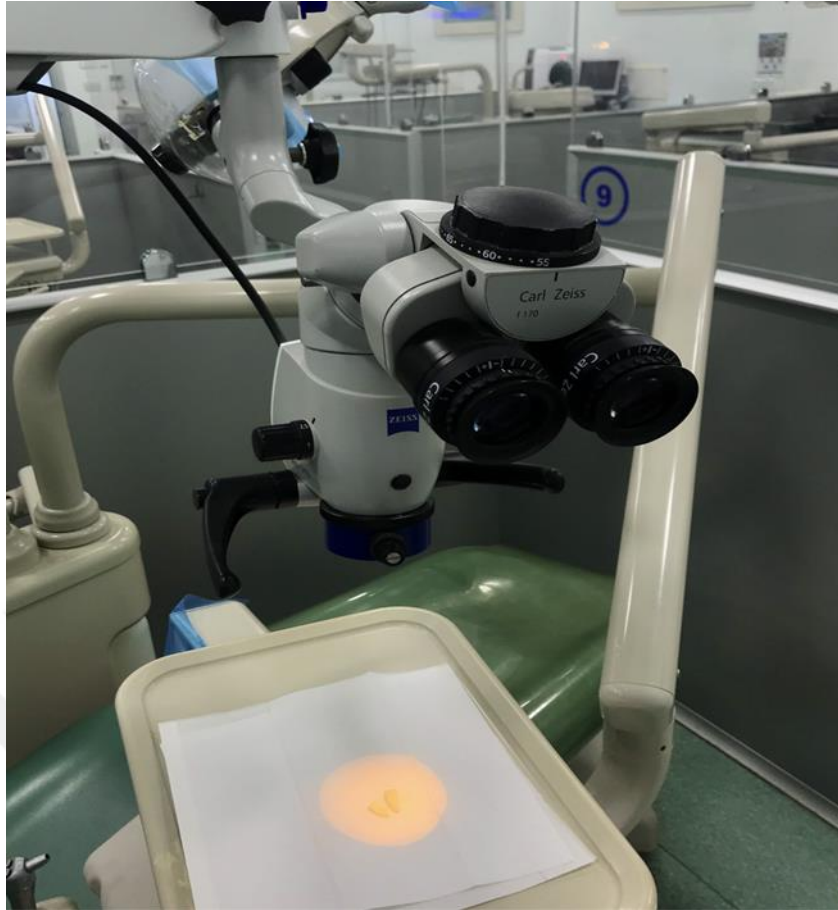


Figure 1a: Observation of samples in operation microscope to detect cracks.

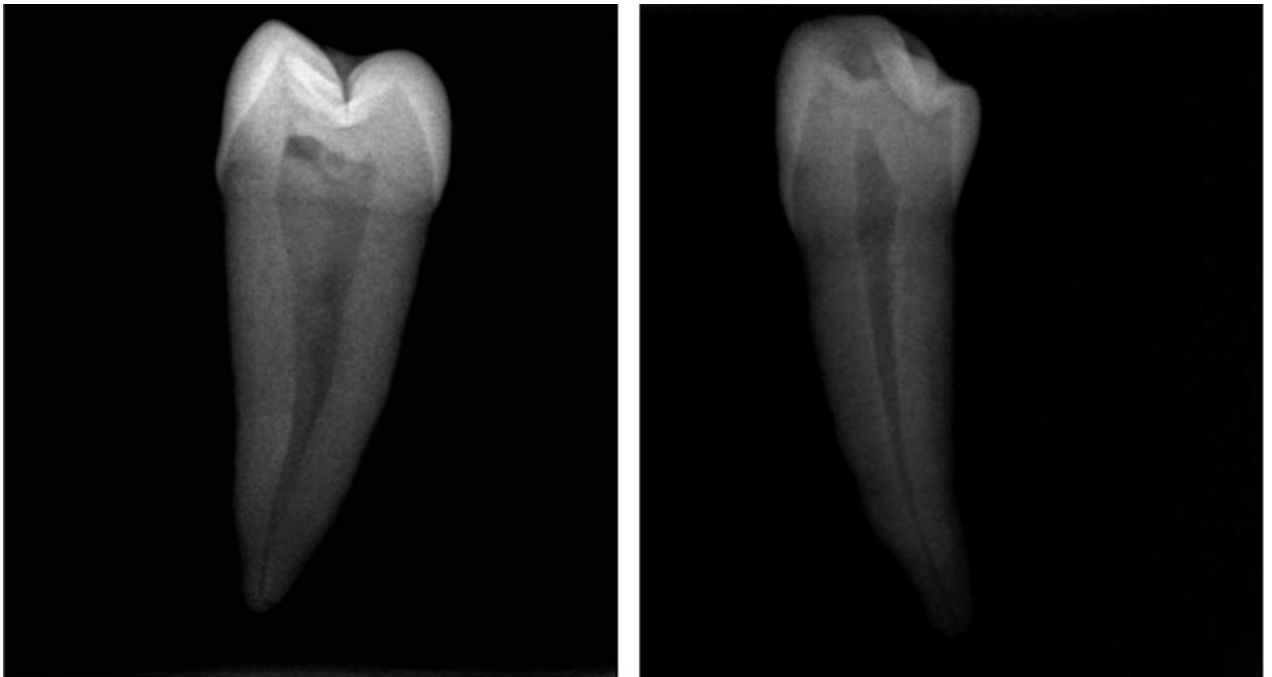


Figure 1b: Digital radiography of a sample in bucco-lingual, mesio-distal direction.

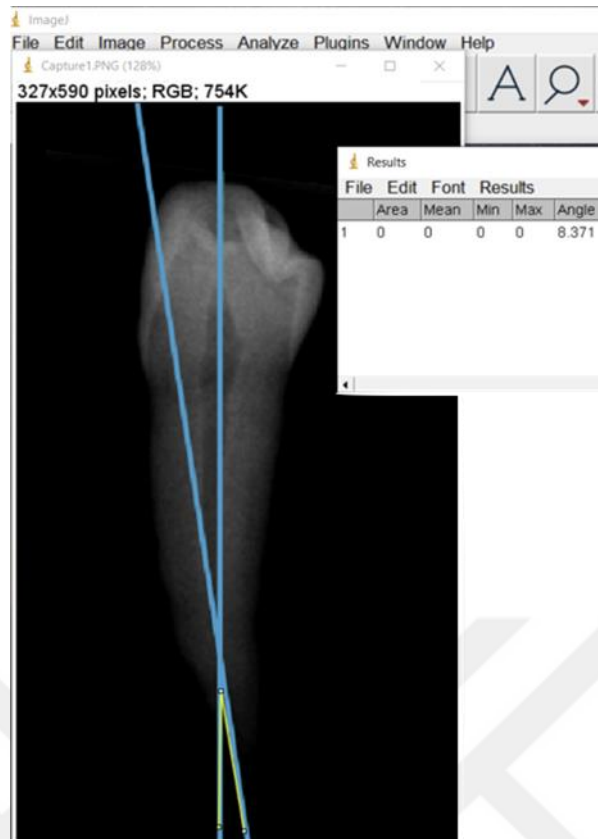


Figure 1c: The degree of curvatures was measured with the Image J program using Schneider's technique.



Figure 1d: All samples were measured 5 and 10 mm from the apical in mesio-distal and bucco-lingual directions.

3.2. Preparation of Sample Teeth

Residual periodontal tissues on the root surfaces were cleaned with the help of periodontal curettes and ultrasonic instruments. All teeth were kept in isotonic saline solution until the beginning of the study. 66 teeth, meeting the above-mentioned criteria were separated from their crowns under water cooling by using a diamond separator (*Figure. 2a*) (Horico, HOPF, RINGLEB & CO. GMBH & CIE, Germany) and their root length was adjusted to 16 mm. (*Figure. 2b*)



Figure 2a: Separation of crowns from sample teeth.



Figure 2b: Sample lengths were adjusted to 16mm.

3.3. Chemo-Mechanical Shaping of Sample Teeth

First access to root canal, done with 10 no K files (Dentsply Maillefer, North America) and a glidepath was created. Working length determined as 15mm, 1mm behind the apex. (*Figure 3a*) Root canals were shaped with Protaper Next (Dentsply Maillefer, Ballaigues, Switzerland) with nickel-titanium rotary instruments; X1, X2, X3, respectively. (*Figure 3b*) During shaping, the X-Smart Plus (Dentsply Maillefer, North America) endodontic motor was used, adjusting to 300 rpm and 2.0 torque values. (*Figure 3c*) After each instrument 2 mL of 5% sodium hypochlorite (Wizard, Chemical Directory, Turkey) irrigation was done with 2mm from behind the work length (258). (*Figure 4a*)

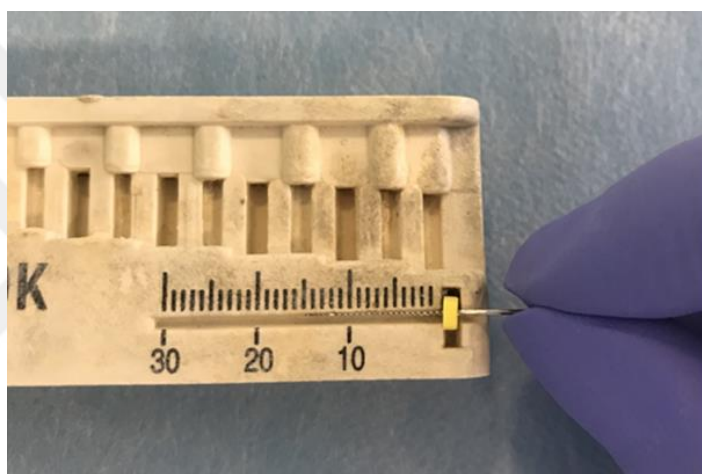


Figure 3a: Adjustment of working length to 15mm.



Figure 3b: Protaper Next System (Dentsply Maillefer, North America) was used in chemo-mechanical preparation of all samples.



Figure 3c: Endodontic motor Dentsply x-smart plus (Dentsply Maillefer, North America) adjusted to: 300rpm speed, 2.0 torque for chemo-mechanical preparation of the samples.

30 gauge laterally perforated irrigation needle (KerrHawe SA, Switzerland) was used in the irrigation process. (*Figure 4b*) As final irrigation protocol; to remove the smear layer 5mL 17% EDTA (Ethylenediaminetetraacetic acid), 2ml sterile saline solution, 2mL sodium hypochlorite 5% (Microvem, Turkey, Turkey) and finally 2mL sterile saline (to prevent the harmful effects of the solutions) were used (259). (*Figure 5a, 5b*) Root canals were dried using #35 paper cones (Diadent, Korea). Chemo mechanical preparation of all samples were completed.



Figure 4a: Irrigation needle adjusted 2mm behind working length.



Figure 4b: 30 gauge irrigation needle was used in irrigation of samples. (KerrHawe SA, Switzerland)



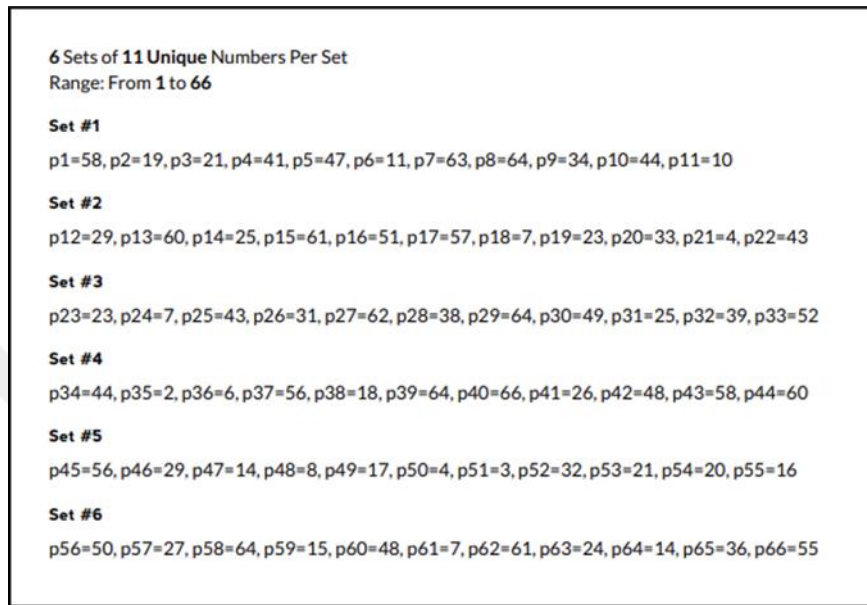
Figure 5a: %5 Sodium Hypochlorite solution (Microvem, Turkey) used in irrigation between endodontic instruments. %17 EDTA (Wizard, Chemical Directory, Turkey) solution used in final irrigation protocol of the samples.



Figure 5b: Irrigation of a sample.

3.4. Creating the Groups

All samples were numbered and randomly separated into 6 groups with the software of randomizer.org. (243). (*Figure 6*)



6 Sets of 11 Unique Numbers Per Set
Range: From 1 to 66

Set #1
p1=58, p2=19, p3=21, p4=41, p5=47, p6=11, p7=63, p8=64, p9=34, p10=44, p11=10

Set #2
p12=29, p13=60, p14=25, p15=61, p16=51, p17=57, p18=7, p19=23, p20=33, p21=4, p22=43

Set #3
p23=23, p24=7, p25=43, p26=31, p27=62, p28=38, p29=64, p30=49, p31=25, p32=39, p33=52

Set #4
p34=44, p35=2, p36=6, p37=56, p38=18, p39=64, p40=66, p41=26, p42=48, p43=58, p44=60

Set #5
p45=56, p46=29, p47=14, p48=8, p49=17, p50=4, p51=3, p52=32, p53=21, p54=20, p55=16

Set #6
p56=50, p57=27, p58=64, p59=15, p60=48, p61=7, p62=61, p63=24, p64=14, p65=36, p66=55

Figure 6 Samples were numbered and randomized with the software program of randomizer.org.

1.Group (BC-L): TotalFill BC Sealer + Lateral Condensation

2. Group (BC-S): TotalFill BC Sealer + Single Cone

3.Group (Cera-L): CeraSeal + Lateral Condensation

4. Group (Cera-S): CeraSeal + Single Cone

5.Group (AH-L): AH Plus + Lateral Condensation

6.Group (AH-S): AH Plus + Single Cone

Group 1 (BC-L): Obturation of the Samples

In this group samples were obturated with TotalFill BC Sealer (FKG Dentaire, Switzerland) with Lateral Condensation method. TotalFill BC sealer (FKG Dentaire, Switzerland) is a pre-mixed obturation material. (Figure 7a, Figure 7b) In this group it was placed onto mixing paper. 30# gutta percha (Diadent, Korea) was tested by controlling tug back feeling at 1mm behind the working length. With the help of 30# paper point, the prepared canal sealer was applied to the canal walls 2 mm shorter than the root tip. The tip of the master cone 30# gutta percha was covered with canal paste and placed in the root canal. After applying lateral pressure with 25# spreader and making space, 20# gutta percha was placed in the root canal as lateral cone. Placement of the lateral cones in the root canal was continued until the spreader entered the root canal less than 2 mm. (Figure 7c) After the filling of the canal was completed, the gutta perchas were cut with the help of an excavator heated with a torch.



Figure 7a: Group BC-L: Samples in this group were obturated with TotalFill BC Sealer and Lateral Condensation.



Figure 7b: TotalFill BC Sealer (FKG Dentaire, Switzerland).



Figure 7c: Lateral condensation example from the Group (BC-L)

Group 2 (BC-S): Obturation of the Samples

In this group samples were obturated with TotalFill BC Sealer (FKG Dentine, Switzerland) with Single Cone method. (Figure 8a,) Protaper Universal gutta percha points (Dentsply Mallefier, USA, Oklahoma) were used which are compatible with Protaper Next System. (Figure 8b) TotalFill BC sealer is applied with the help of #40 paper point, to the canal walls 2mm behind the working length. 06 tapered # 30 gutta-percha was inserted into the root canal. (Figure 8c) With the aid of the torch-heated excavator, the guttas were cut.

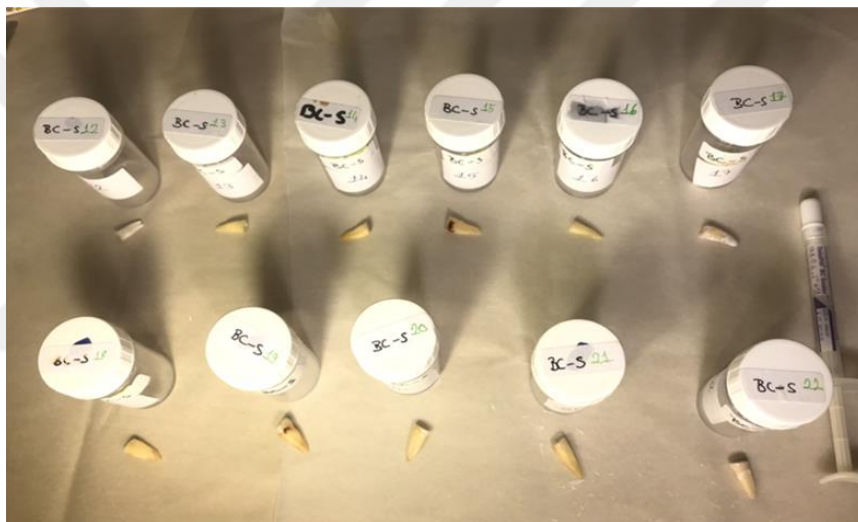


Figure 8a: Samples of Group (BC-S) were obturated with TotalFill BC Sealer (FKG Dentine, Switzerland) and single-cone method.

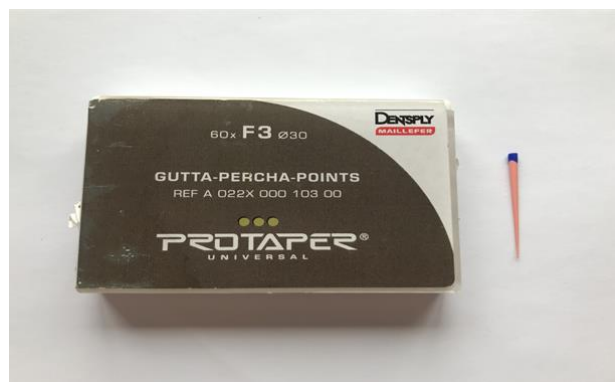


Figure 8b: Protaper Gutta Percha Points (Dentsply Mallefier, USA, Oklahoma) used in single-cone method.

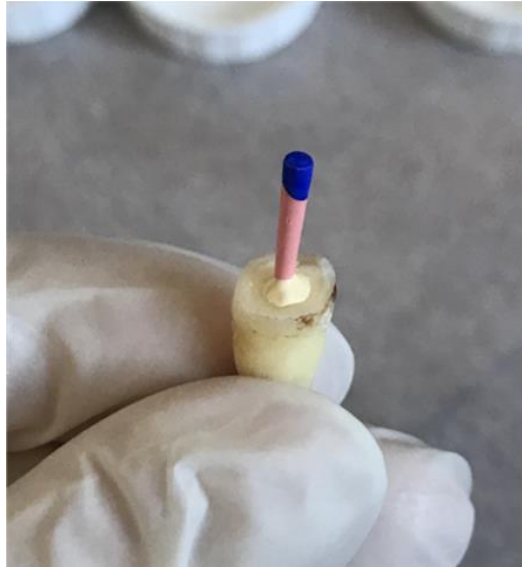


Figure 8c: Obturation of a sample from Group (BC-S) with single-cone method.

Group 3 (Cera-L): Obturation of the Samples

In this group samples were obturated with CeraSeal (Meta-Biomed, South Korea) with Lateral Condensation method. (*Figure 9a*) CeraSeal (Meta-Biomed, South Korea) is a pre-mixed root canal obturation material (*Figure 9b*) Samples were obturated with lateral condensation method as explained in group 1.



Figure 9a: Samples of Group (Cera-L) were obturated with CeraSeal (Meta-Biomed, South Korea) and lateral condensation method.

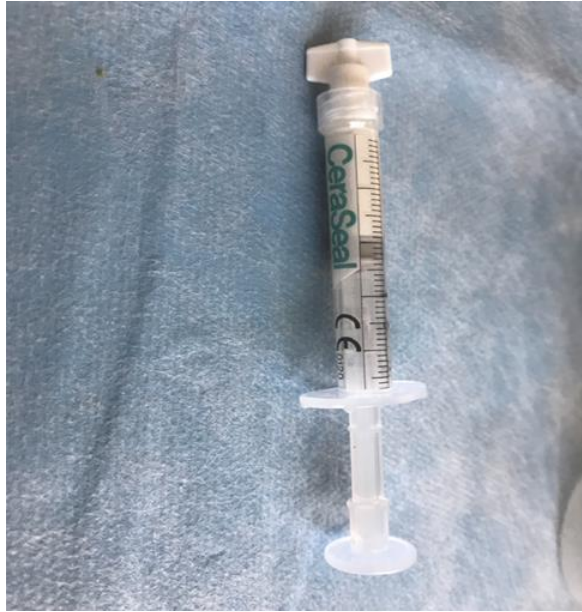


Figure 9b: CeraSeal Bioceramic Sealer (Meta-Biomed, South Korea).

Group 4 (Cera-S): Obturation of the Samples

In this group samples were obturated with CeraSeal with Single Cone method. CeraSeal applied to root canal walls as described in group 2. (*Figure 10*) Root canal filling was carried out using the single cone method as described in the second group.



Figure 10: Samples of Group (Cera-S) were obturated with CeraSeal (Meta-Biomed, South Korea) root canal sealer and Single Cone method.

Group 5 (AH-L): Obturation of the Samples

In this group samples were obturated with AH Plus Sealer (Dentsply Mallefier, USA, Oklahoma) (*Figure11a, Figure11b*) with Lateral Condensation method. Equal amounts from both tubes of AH Plus canal sealer were mixed on paper. As in the first group, canal filling was carried out using the lateral condensation method.



Figure 11a: Samples of Group (AH-L) were obturated with AH Plus sealer (Dentsply Mallefier, USA, Oklahoma) and lateral condensation method.

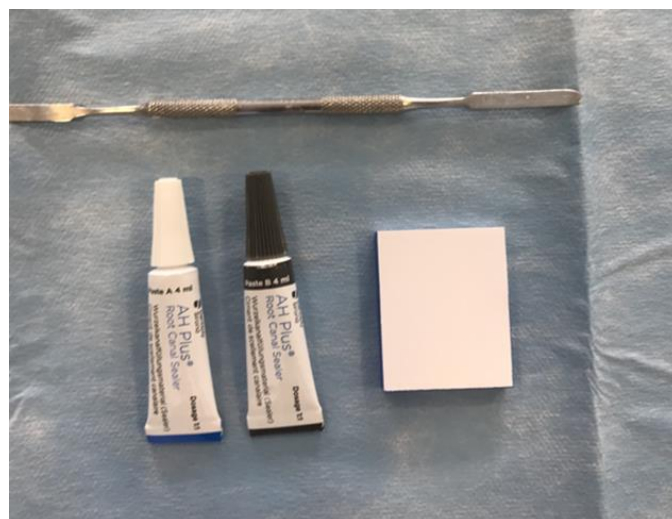


Figure 11b: AH Plus Sealer (Dentsply Mallefier, USA, Oklahoma).

Group 6 (AH-S): Obturation of the Samples

In this group samples were obturated with AH Plus Sealer (Dentsply Mallefier, USA, Oklahoma) with Single Cone method. (*Figure12*) Equal amounts from both tubes of AH Plus canal sealer were mixed on paper. As in the second group, root canal filling was carried out using the lateral condensation method.



Figure 12: Samples of Group (AH-S) were obturated with AH Plus sealer (Dentsply Mallefier, USA, Oklahoma) and single-cone method.

The cavities of all sample teeth were closed with Coltosol F (Coltene Whaledent, Switzerland) and kept in the oven at 37 degrees 100% humidity for 7 days (260). (Figure13)



Figure 13: After obturation of the samples were completed, all samples were stored in 37 degrees 100% humidity for 7 days.

3.5. First Micro CT Scanning

After obturation of all samples were completed, Micro CT scanning was performed in order to measure total root canal filling volume for each sample and data were recorded. (Figure 15) Each sample were placed in the SkyScan 1172 (Bruker-microCT, Kontich, Belgium) Micro-CT device. (Figure 14) Scanning were done with 100 kV power and 100 μ A current.

From each sample: 13.68 μ m size and a resolution of 2000x1330 pixels were obtained with the help of 11 MP camera. Al+Cu filter was used in scanning. The scans were performed with 180° rotation angle on the vertical axis, 0.5° rotation range and 2300

ms camera exposure time. The images obtained were reconstructed in NRecon (v.1.6.4, Bruker-MicroCT) software with 70% beam-hardening correction, 2 smoothing and 0-0.35 attenuation coefficient values and ring artifact corrections.



Figure 14: First Micro Ct scanning of all samples were performed with Bruker-Micro-CT device.

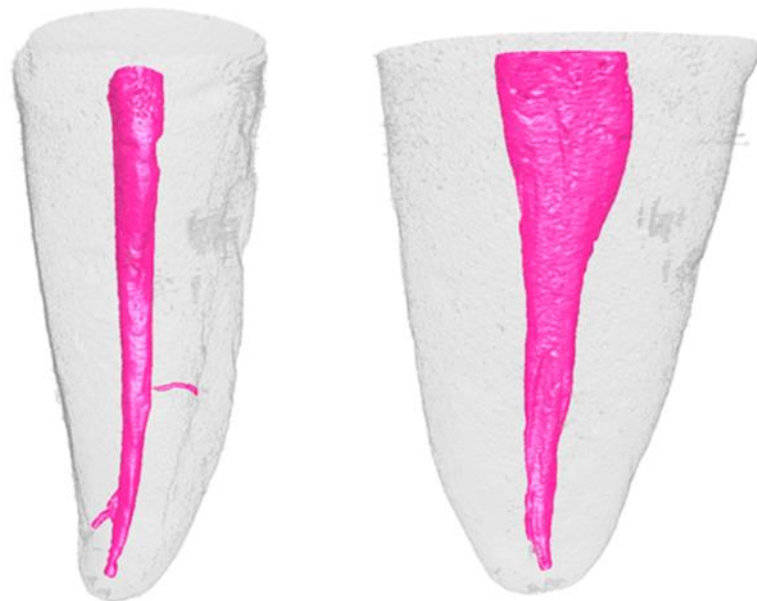


Figure 15: Initial Micro-CT scanning of a sample.

3.6. Retreatment of All Samples

All samples were went through the same retreatment protocol. Root canal fillings were removed with Protaper Universal Retreatment Files (Dentsply Mallefier, USA, Oklahoma) at 500 rpm and 2.0 torque settings (261). (Figure16)



Figure 16: Protaper Universal Retreatment set (Dentsply Mallefier, USA, Oklahoma) was used in order to remove root canal fillings.

The coronal 1/3 of the root canal filling was removed using the instrument D1 of the series, the middle 1/3 removed by using the instrument numbered D2, and the apical 1/3 removed by using the instrument numbered D3. #25 H-files were also used at the points where it is felt that the rotary instruments are strained inside root canal. Between all instruments, samples were irrigated with 2 mL %5 NaOCl solution. All samples irrigated with total 10 mL NaOCl solution. As the final irrigation protocol; 5mL 17% EDTA to remove the smear layer then 2mL sodium hypochlorite 5% and finally 2mL saline to prevent the harmful effect of the solutions were used.

Time elapsed during retreatment procedure were recorded for each sample with a digital chronometer. Recording was initiated with the introduction of D1 instrument to root canal and terminated when retreatment procedure was completed. During irrigation and instrument change, recording was paused. Retreatment procedure continued until no

residual canal sealant was visible in the threads of the instrument (262). Each sample was evaluated in terms of working length accessibility and formation of apical patency with #10 K file and data were saved.

3.7. Second Micro CT Scanning

After the root canal filling removal procedure, the samples were re-scanned and reconstructed for the second time by using the first scanning and reconstruction principles. (*Figure 17*) The data which obtained from the first and second scans of the samples was overlapped in three dimensions using DataViewer v.1.5.6 (Bruker-MicroCT, Belgium) software. Images were transferred to CTAn (v.1.18.8, Bruker-MicroCT) software in order to make measurements. For each sample, volumetric measurements of canal filling and canal filling residues were made. Three-dimensional models were created and analyzed with CTVol (v.2.2.3, Bruker-microCT) software. The calculation of residual root canal filling percentage was done by dividing the volumetric result obtained in the second scan to the volumetric result in the first scan. Data were presented as percentages.

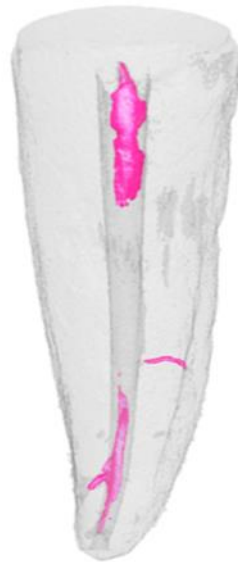


Figure 17: Image of a sample after root canal filling removal procedure.

3.8. Obturation of Root Canals for Second Time

After Micro-CT scanning, all samples were chemo mechanically instrumented with the same protocol described in Chapter 3.3. As the final irrigation protocol, 5mL 17% EDTA to remove the smear layer then 2mL sodium hypochlorite 5% and finally 2mL saline to prevent the harmful effect of the solutions were used. All teeth were re-obtured according to the group in which they were found (with the same protocol described in Chapter 3.4). Each sample was kept in 20 mL distilled water for 24 hours, 37 degrees, 100% humidity in the oven.

3.9. Push Out Test

Each sample were placed inside plastic tubes and fixed with acrylic resin. (Imicryl, Konya Turkey) (*Figure18a, Figure18b*).

Dentine discs were sliced with 0.6 mm diamond disc, under water cooling by using Isomet device. (*Figure18c*) Each dentine disc was obtained from the middle 1/3 of the specimens and was prepared in 1mm thickness. (*Figure 18d*) In order to replace the damaged dentin discs during the slicing process, 3 dentin discs were obtained from each tooth sample. During sectioning procedure if a dentine disc is damaged new section were taken from middle 1/3. *Figure19 a,b,c,d,e,f*. Each disc were placed into Instron device (Lloyd LRX; Lloyd Instruments Ltd, Fareham, UK) for push out test. (*Figure18e, Figure18a*) Push out force was applied with 0.5 mm thick stainless steel tip. Force of 1mm/min was applied until a sudden decrease in the load/time curve was observed on the computer connected to the Instron device. (*Figure 20c*) Maximum force values were recorded in N and bond strength calculated in MPa with the formula:

Bond Strength (MPa) = Maximum Force (N) / Bonding area of root canal filling (mm²)

Bonding area of root canal filling (mm²) is calculated with: $\pi (r_1 + r_2) \cdot h$ formula. r_1 value stands for apical radius of root canal filling, r_2 value stands for coronal radius of root canal filling, h value stands for thickness of dentine disc (256).

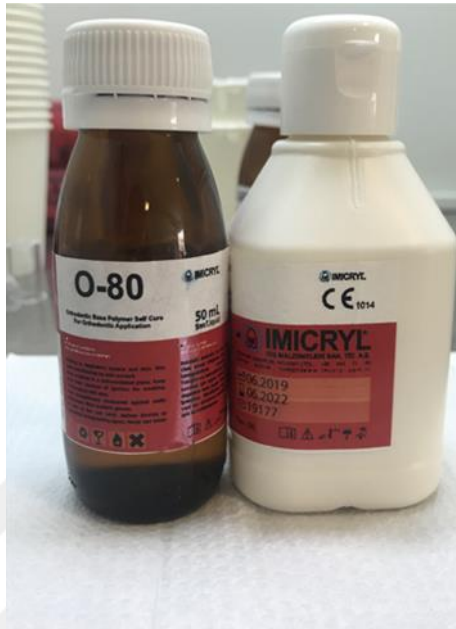


Figure 18a: Imicryl Acrylic used in order to fix samples inside plastic tubes.



Figure 18b: Samples were fixed with acrylic inside plastic tubes.



Figure 18c: 1mm thick dentine discs were obtained with the help of Isomet device.

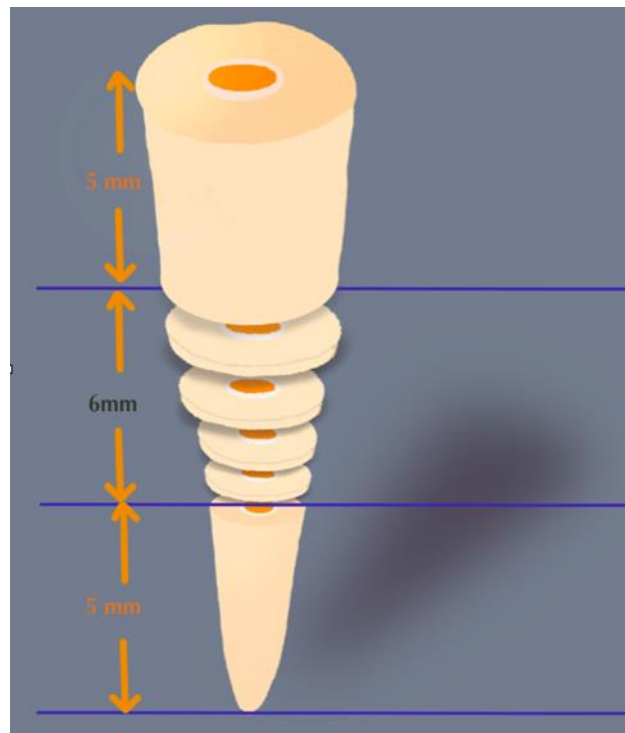


Figure 18d: Dentine discs were obtained from the middle 1/3 of every sample.



Figure 18e: Universal Testing Machine, Instron (Lloyd LRX; Lloyd Instruments Ltd, Fareham, UK); that used in push out testing in order to calculate bond strength of samples.



Figure 19a: 1mm thick dentin discs were prepared from the samples of Group (BC-L)



Figure 19b: 1mm thick dentin discs were prepared from the samples of Group (BC-S)



Figure 19c: 1mm thick dentin discs were prepared from the samples of Group (Cera-L)



Figure 19d: 1mm thick dentin discs were prepared from the samples of Group (Cera-S)



Figure 19e: 1mm thick dentin discs were prepared from the samples of Group (AH-L)



Figure 19f: 1mm thick dentin discs were prepared from the samples of Group (AH-S)

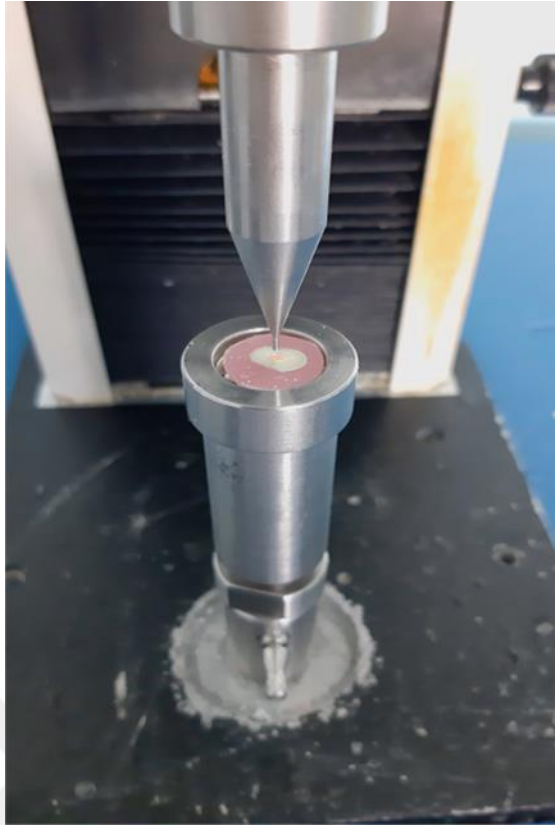


Figure 20a: A sample placed inside universal testing machine, ready for push out testing.

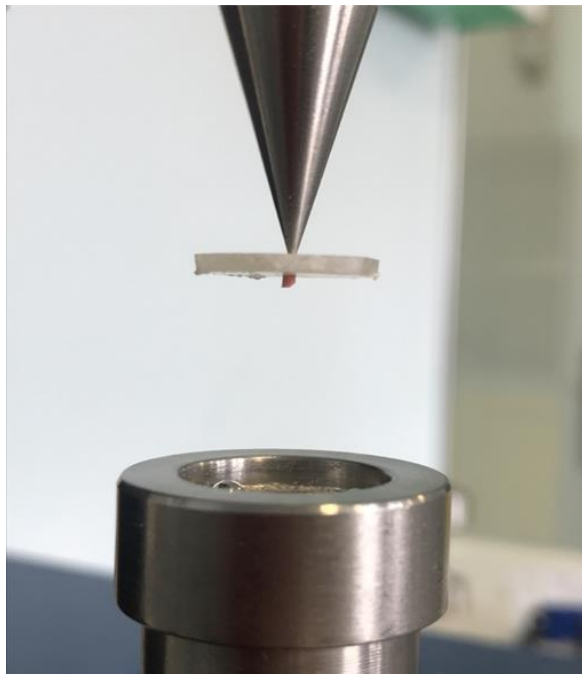


Figure 20b: Image of a sample right after push out testing.

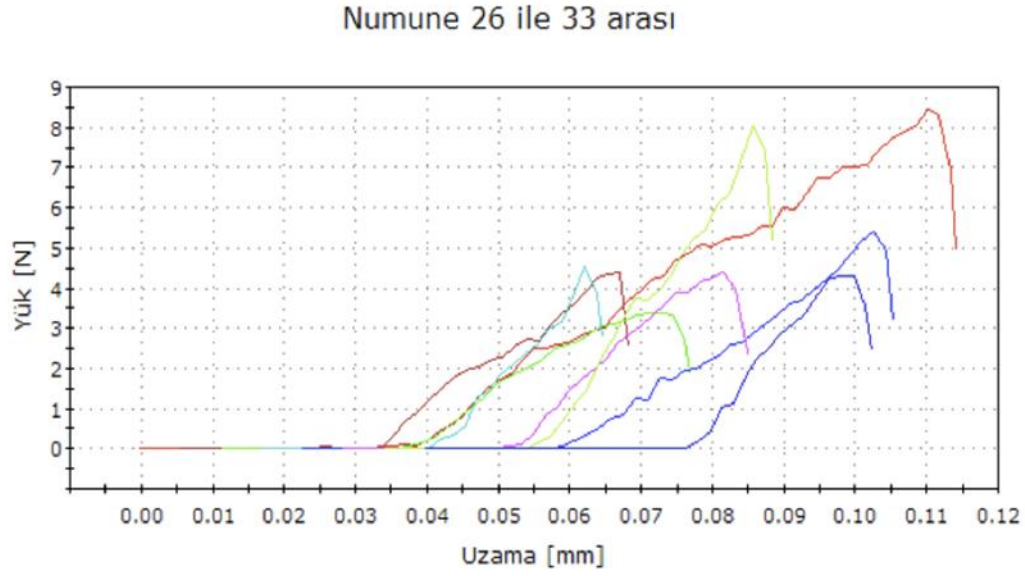


Figure 20c: Sudden decrease in the load/time curve was observed on the computer.

3.10. Statistical Analyzes

In this study, statistical analyzes were performed with NCSS (Number Cruncher Statistical System) 2007 Statistical Software (Utah, USA) package program.

In addition to descriptive statistical methods (mean, standard deviation, median, interquartile range) in the evaluation of the data, the distribution of the variables was examined with the Shapiro – Wilk normality test, the Kruskal Wallis test for the intergroup comparisons of the variables that did not show normal distribution, the Dunn's multiple comparison test for the subgroup comparisons, the Dunn's multiple comparison test for the comparison of the paired groups. Mann Whitney U test and chi-square test were used to compare qualitative data. The results were evaluated at the significance level of $p < 0.05$.

4. RESULTS

In this study, it was aimed to compare TotalFill BC Sealer, CeraSeal and AH Plus root canal sealers retreatability and bond strength with two different obturation techniques; lateral condensation and single cone. In terms of evaluating retreatability;

- Volume of the residual root canal fillings were measured with Micro-CT scanning.
- Duration of the retreatment procedure were calculated.
- Re-establishing of apical patency were evaluated.

In order to evaluate bond strength of TotalFill BC Sealer, CeraSeal and AH Plus root canal sealer; push out test was performed.

Power Analysis

Power analysis made with the G*power 3.1 program. The effect size of the study groups for Retreatability was found to be 0.48 (alpha error probability=0.05). The sample size analysis performed with a power value of 0.80 and the total number of samples was found to be 66 (11 teeth for each group).

The effect size for the bond strength of the study groups was found to be 0.48 (alpha error probability=0.05); The sample size analysis performed with a power value of 0.80, the total number of samples was found to be 60 (10 teeth for each group).

In order to meet the criteria for both retreatability and bond strength analyses; total number of samples were taken as 66. (n=11)

Design of the Groups

Groups were designed as in Table 2.

Table 2. Design of the Groups

1.Group (BC-L):	Totalfill BC Sealer + Lateral Condensation
2. Group (BC-S):	Totalfill BC Sealer + Single Cone
3.Group (Cera-L):	CeraSeal + Lateral Condensation
4. Group (Cera-S):	CeraSeal + Single Cone
5.Group (AH-L):	AH Plus + Lateral Condensation
6.Group (AH-S):	AH Plus + Single Cone

4.1. Retreatability of the Groups

4.1.1. Volume of the Residual Root Canal Fillings

As mentioned in Chapter 3.7; the calculation of residual root canal filling percentage was calculated by dividing residual root canal filling volume to the initial root canal filling volume (Table 3, Table 4). Initial root canal filling volume was measured in first Micro-CT scanning. Residual root canal filling volume was measured in second Micro-CT scanning right after removal of root canal fillings of the samples.

Table 3. Initial root canal filling volume and residual root canal filling volume of all samples.

		Initial root canal filling volume	Residual root canal filling volume
Group (BC-L)	1	26.2495	4.2096
Group (BC-L)	2	10.7344	1.1943
Group (BC-L)	3	8.0639	2.4062
Group (BC-L)	4	7.8585	0.3811
Group (BC-L)	5	10.7164	2.8860
Group (BC-L)	6	23.1795	2.3872
Group (BC-L)	7	10.8741	1.9720
Group (BC-L)	8	17.3509	1.2255
Group (BC-L)	9	10.0485	1.0006
Group (BC-L)	10	12.7450	1.8580
Group (BC-S)	11	12.7795	1.3902
Group (BC-S)	12	7.1387	1.9619
Group (BC-S)	13	7.6019	1.0729
Group (BC-S)	14	9.2796	0.7202
Group (BC-S)	15	10.8903	0.5446
Group (BC-S)	16	7.9290	0.7990
Group (BC-S)	17	10.7556	0.9873
Group (BC-S)	18	8.5287	1.1194
Group (BC-S)	19	13.8570	1.9495
Group (BC-S)	20	8.5358	0.7279
Group (BC-S)	21	12.8276	0.7020
Group (Cera-L)	22	9.6034	4.9878
Group (Cera-L)	23	24.2022	10.1092
Group (Cera-L)	24	16.2171	1.0983
Group (Cera-L)	25	9.3601	0.7615
Group (Cera-L)	26	7.2386	0.7770
Group (Cera-L)	27	10.0043	1.5686
Group (Cera-L)	28	13.3130	0.5184
Group (Cera-L)	29	14.2457	2.8886
Group (Cera-L)	30	12.8925	4.2226
Group (Cera-L)	31	8.6497	1.9841
Group (Cera-L)	32	15.3356	7.5186
Group (Cera-S)	33	13.1746	3.7461
Group (Cera-S)	34	8.0783	0.2686
Group (Cera-S)	35	7.7264	0.1035
Group (Cera-S)	36	9.1929	0.7039
Group (Cera-S)	37	6.8372	0.5729
Group (Cera-S)	38	10.3287	0.4332
Group (Cera-S)	39	9.6431	2.0046
Group (Cera-S)	40	8.7881	1.7774
Group (Cera-S)	41	10.9159	2.2404
Group (Cera-S)	42	8.4371	2.8220
Group (Cera-S)	43	10.9717	0.3579
Group (AH-L)	44	7.2794	0.2479
Group (AH-L)	45	5.8823	1.9392
Group (AH-L)	46	18.0646	0.8555
Group (AH-L)	47	11.4710	4.6388
Group (AH-L)	48	7.0854	1.2833
Group (AH-L)	49	14.9529	6.1617
Group (AH-L)	50	11.6398	3.7842
Group (AH-L)	51	14.6381	0.8428
Group (AH-L)	52	12.2670	2.5852
Group (AH-L)	53	25.3386	9.6576
Group (AH-L)	54	7.3027	0.9255
Group (AH-S)	55	6.7205	0.2176
Group (AH-S)	56	12.5578	2.8309
Group (AH-S)	57	12.0356	4.7922
Group (AH-S)	58	16.9827	6.0998
Group (AH-S)	59	10.4297	2.4927
Group (AH-S)	60	10.9074	2.0099
Group (AH-S)	61	16.6135	5.8731
Group (AH-S)	62	14.0035	8.1930
Group (AH-S)	63	8.3684	1.5687
Group (AH-S)	64	10.2803	0.8980
Group (AH-S)	65	10.8931	1.0424
Group (AH-S)	66	11.5111	1.8710

Table 4. Volume percentages of residual root canal fillings.

	Group (BC-L)	Group (BC-S)	Group (Cera-L)	Group (Cera-S)	Group (AH-L)	Group (AH-S)
1	16.04%	27.48%	41.77%	3.32%	32.97%	22.54%
2	11.13%	14.11%	6.77%	1.34%	4.74%	39.82%
3	29.84%	7.76%	8.14%	7.66%	40.44%	35.92%
4	4.85%	5.00%	10.73%	8.38%	18.11%	23.90%
5	26.93%	10.08%	15.68%	4.19%	41.21%	18.43%
6	10.29%	9.18%	3.89%	20.79%	32.51%	35.35%
7	18.14%	13.13%	20.28%	20.23%	5.76%	58.51%
8	7.06%	14.07%	32.75%	20.52%	21.07%	18.75%
9	9.96%	8.53%	22.94%	33.45%	38.11%	8.74%
10	14.56%	5.47%	49.03%	3.26%	12.67%	9.57%
11	10.88%	5.47%	28.43%	3.41%	3.24%	16.25%

Table 5. Remaining root canal filling volumes of all groups.

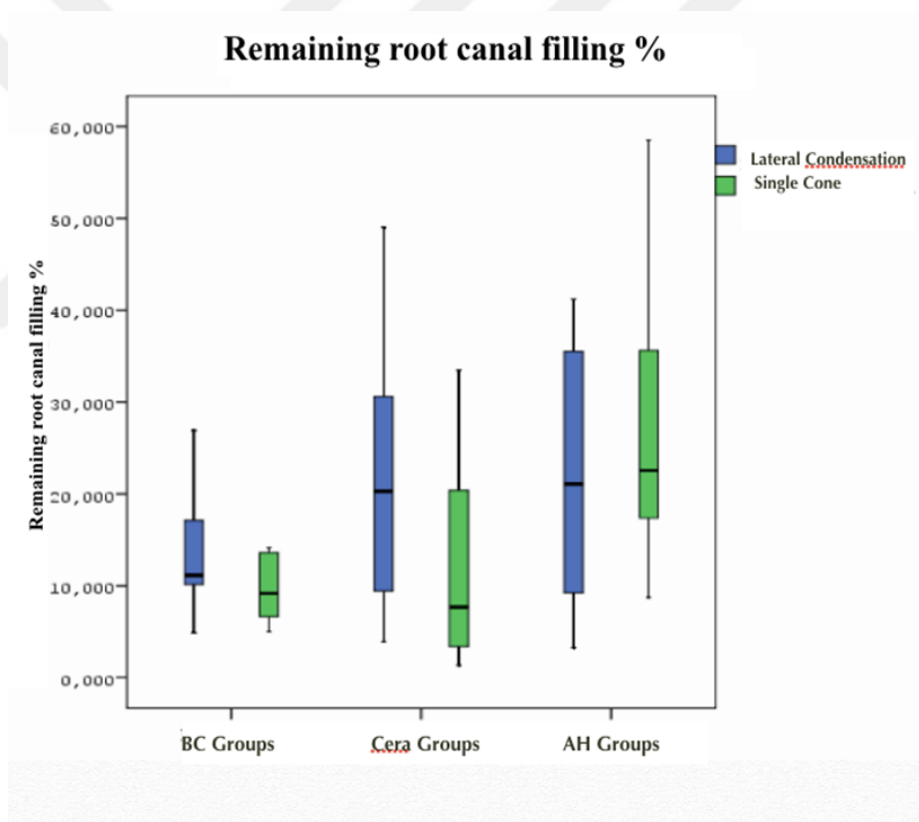


Table 6. Comparison of the root canal filling methods between same sealer groups in terms of remaining root canal filling volumes.

Remaining root canal filling %			
	Mean±SD	Median (IQR)	p*
Group (BC-L)	14,52±7,85	11,13 (9,96-18,14)	0.178
Group (BC-S)	10,93±6,43	9,18 (5,47-14,07)	
Group (Cera-L)	21,86±14,83	20,28 (8,14-32,75)	0.061
Group (Cera- S)	11,5±10,52	7,66 (3,32-20,52)	
Group (AH-L)	22,8±14,86	21,07 (5,76-38,11)	0.622
Group (AH-S)	26,16±14,91	22,54 (16,25-35,92)	
*Mann Whitney U testi			

There was no statistically significant difference found between Group (BC-L) and Group (BC-S) in terms of residual root canal filling volumes (p=0,178). There was no statistically significant difference found between Group (Cera-L) and Group (Cera-S) in terms of residual root canal filling volumes (p= 0,061). There was no statistically significant difference found between Group (AH-L) and Group (AH-S) in terms of residual root canal filling volumes (p= 0.662). (Table 6)

Table 7. Comparison of the root canal sealers among lateral condensation groups in terms of remaining root canal filling volumes.

		Group (BC-L)	Group (Cera-L)	Group (AH-L)	p*
Remaining root canal filling (%)	Mean±SD	14,52±7,85	21,86±14,83	22,8±14,86	0.449
	Median (IQR)	11,13 (9,96-18,14)	20,28 (8,14-32,75)	21,07 (5,76-38,11)	
*One-Way Analysis of Variance					

There was no statistically significant difference found between laterally condensed groups; Group (BC-L), Group (Cera-L) and Group (AH-L) in terms of remaining root canal filling volumes (p=0,449). (Table 7)

Table 8. Comparison of the root canal sealers among single cone groups in terms of remaining root canal filling volumes.

		Group (BC-S)	Group (Cera-S)	Group (AH-S)	p*
Remaining root canal filling (%)	Mean±SD	10,93±6,43	11,5±10,52	26,16±14,91	0.006
	Median (IQR)	9,18 (5,47-14,07)	7,66 (3,32-20,52)	22,54 (16,25-35,92)	
*One-Way Analysis of Variance					

A statistically significant difference was observed between the single cone groups; Group (BC-S), Group (Cera-S), Group (AH-S) (p=0.006). (Table 8)

Table 9. Multiple comparison between single cone groups in terms of remaining root canal filling percentages.

Remaining root canal filling (%)	p*
Group (BC-S) / Group (Cera-S)	0.412
Group (BC-S) / Group (AH-S)	0.003
Group (Cera-S) / Group (AH-S)	0.011
Dunn's Multiple Comparison test	

The remaining root canal filling volume percentage of the Group (AH-S) were found to be statistically significantly higher than the Group (BC-S) and Group (Cera-S) (p=0.003, p=0.011). There was no statistically significant difference found between Group (BC-S) and Group (Cera-S) (p=0.412). (Table 9)

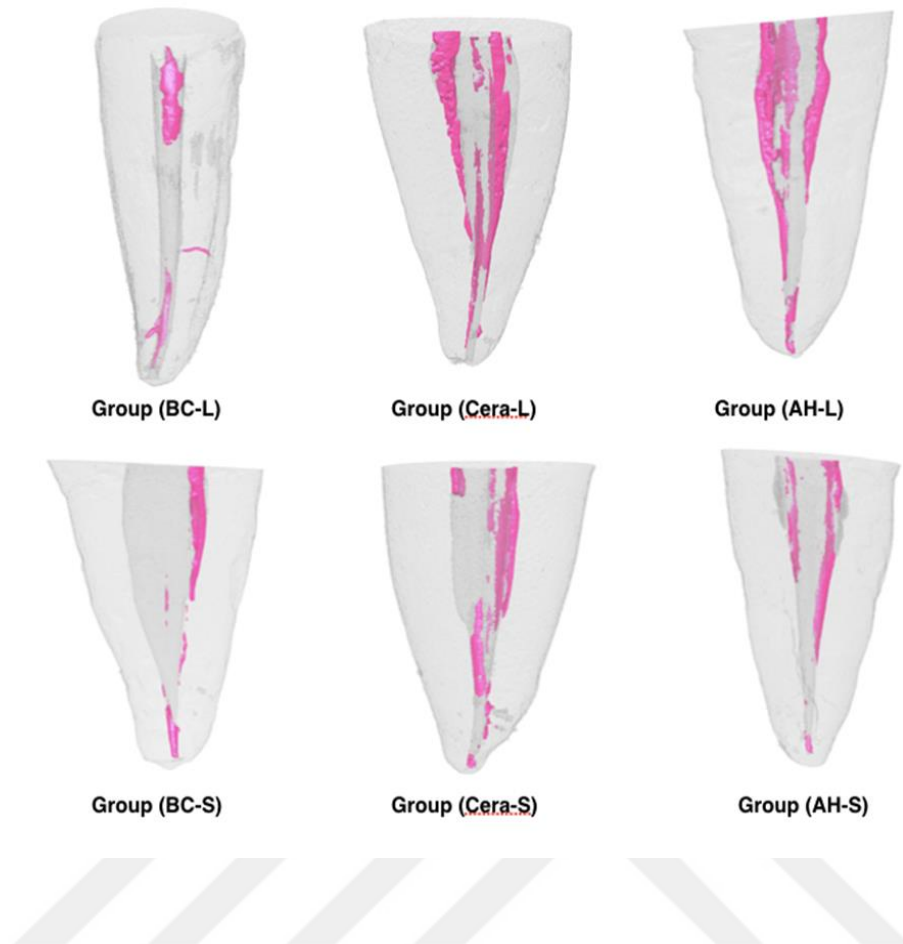


Figure 21 Examples of Micro-CT images, showing the remaining root canal filling volumes for each group.

4.1.2. Duration of the Retreatment Procedure

Time elapsed during retreatment procedure were recorded for each sample with a digital chronometer, as explained in Chapter 3.6. (Table 10, Table 11)

Table 10. Duration of the retreatment procedure in minutes of all samples.

	Group (BC-L)	Group (BC-S)	Group (Cera-L)	Group (Cera-S)	Group (AH-L)	Group (AH-S)
1	12:03.87	03:16.28	09:20.41	11:42.46	05:49.21	01:57.09
2	10:32.38	05:18.09	07:34.14	11:53.23	27:21.93	01:28.66
3	06:25.14	01:25.15	01:06.19	19:25.00	15:34.26	03:56.91
4	02:57.91	00:38.49	02:15.94	01:13.76	10:30.46	03:25.73
5	03:04.73	01:35.47	04:53.90	02:12.34	07:05.30	00:47.32
6	04:37.37	07:09.23	03:10.45	01:18.97	05:39.36	01:28.83
7	04:41.98	01:34.97	06:59.12	03:11.83	09:35.85	08:18.32
8	02:51.46	01:48.96	03:40.40	09:25.70	05:25.89	01:03.47
9	25:54.50	02:09.46	03:37.40	01:52.14	07:56.96	00:23.50
10	08:10.98	03:42.42	04:37.84	02:17.60	03:48.37	00:12.00
11	02:02.56	01:30.00	05:06.42	00:56.24	05:28.26	03:26.37

Table 11. Duration of the retreatment procedure in minutes of each group.

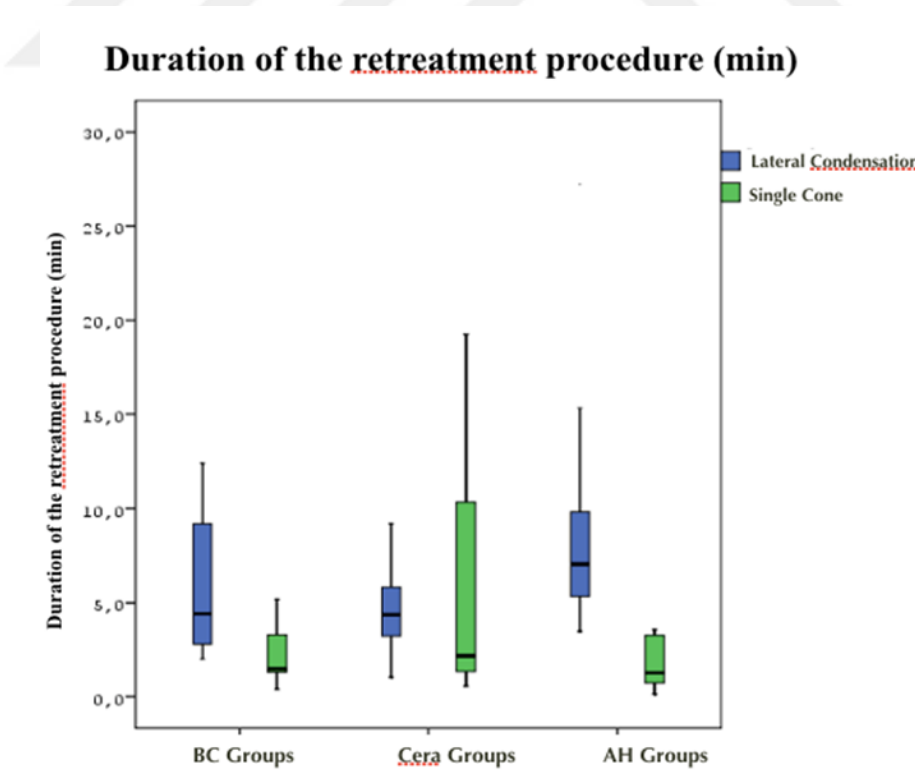


Table 12. Comparison of the root canal filling methods between same sealer groups in terms of duration of the retreatment procedure.

	Duration of the retreatment procedure (min)		
	Mean±SS	Median (IQR)	p*
Group (BC-L)	7,41±6,91	4,41 (2,57-10,3)	0.011
Group (BC-S)	2,55±2,02	1,49 (1,3-3,42)	
Group (Cera-L)	4,56±2,38	4,37 (3,1-6,59)	0.652
Group (Cera- S)	5,75±6,16	2,18 (1,19-11,42)	
Group (AH-L)	9,25±6,8	7,05 (5,28-10,3)	0.001
Group (AH-S)	2,21±2,33	1,29 (0,47-3,27)	
*Mann Whitney U testi			

A statistically significant difference was observed between Group (BC-L) and Group (BC-S) in terms of duration of the retreatment procedure. Retreatment procedure of Group (BC-L) were found to be statistically significantly longer than the Group (BC-S) (p=0.011). There was no statistically significant difference found between the retreatment procedure of Group (Cera-L) and Group (Cera-S). (p=0.652) A statistically significant difference was observed between Group (AH-L) and Group (AH-S) in terms of duration of the retreatment procedure. Retreatment procedure of Group (AH-L) were found to be statistically significantly longer than the Group (AH-S) (p=0.001). (Table 12)

Table 13. Comparison of the root canal sealers among lateral condensation groups in terms of duration of the retreatment procedure in minutes.

		Group (BC-L)	Group (Cera-L)	Group (AH-L)	p*
Duration of the retreatment procedure (min)	Meant±SD	7,41±6,91	4,56±2,38	9,25±6,8	0.056
	Median (IQR)	4,41 (2,57-10,3)	4,37 (3,1-6,59)	7,05 (5,28-10,3)	
*One-Way Analysis of Variance					

There was no statistically significant difference found between laterally condensed groups; Group (BC-L), Group (Cera-L) and Group (AH-L) in terms of duration of the retreatment procedure. (p=0.056) (Table 13)

Table 14. Comparison of the root canal sealers among single cone groups in terms of duration of the retreatment procedure in minutes.

		Group (BC-S)	Group (Cera-S)	Group (AH-S)	p*
Duration of the retreatment procedure (min)	Mean±SD	2,55±2,02	5,75±6,16	2,21±2,33	0.314
	Median (IQR)	1,49 (1,3-3,42)	2,18 (1,19-11,42)	1,29 (0,47-3,27)	
*One-Way Analysis of Variance					

There was no statistically significant difference found between single cone groups; Group (BC-S), Group (Cera-S) and Group (AH-S) in terms of duration of the retreatment procedure (p=0.314). (Table 14)

4.1.3. Re-establishing Apical Patency

Re-establishing of apical patencies were evaluated for each sample and shown in (Table 15). “1” stands for apical patency is re-established, “0” stands for apical patency could not be achieved.

Table 15. Re-establishing of apical patencies were evaluated for each sample. (1: Apical patency re-established. 0= Apical patency could not be re-established.)

	Group (BC-L)	Group (BC-S)	Group (Cera-L)	Group (Cera-S)	Group (AH-L)	Group (AH-S)
1	0	1	1	0	1	1
2	0	0	1	1	1	1
3	1	1	1	1	1	0
4	1	1	1	1	1	1
5	1	1	1	1	1	1
6	1	0	1	1	1	0
7	1	1	0	1	1	0
8	1	1	1	0	1	1
9	1	1	1	1	1	1
10	1	1	1	1	1	1
11	1	1	1	1	1	1

Table 16. Evaluation of re-establishing apical patencies of all groups.

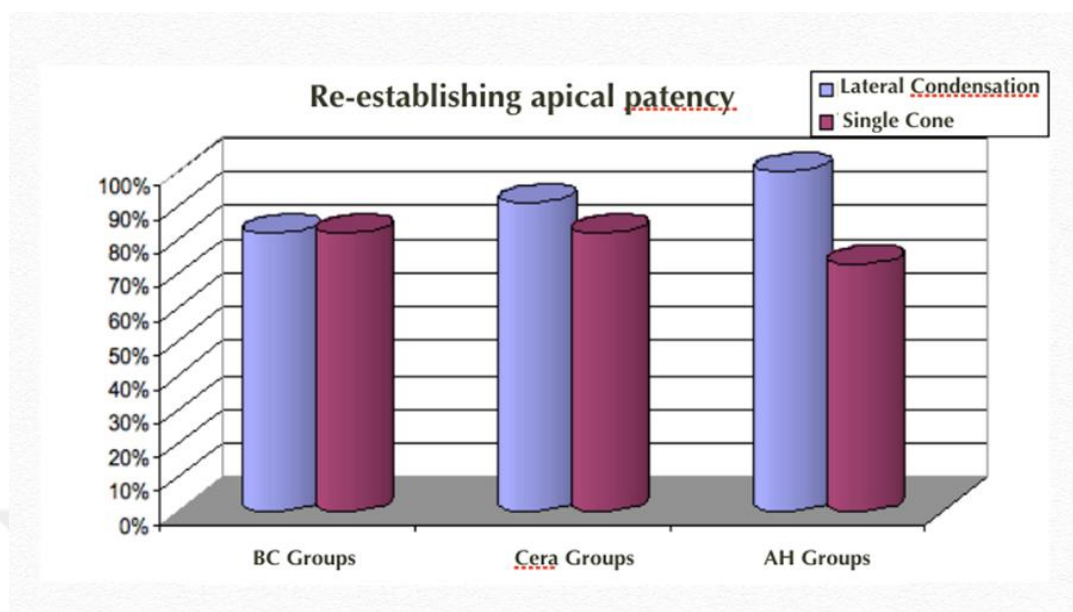


Table 17. Comparison of all groups in terms of re-establishing apical patencies with chi square test.

Re-establishing Apical Patency								
		BC Groups		CERA Groups		AH Groups		p+
Lateral Condensation	Not established	2	18,18%	1	9,09%	0	0,00%	0.144
	Established	9	81,82%	10	90,91%	11	100,00%	
Single Cone	Not established	2	18,18%	2	18,18%	3	27,27%	0.608
	Established	9	81,82%	9	81,82%	8	72,73%	
p+		1		0.759		0.214		
+Chi Square Test								

There was no statistically significant difference found between laterally condensed groups; Group (BC-L), Group (Cera-L), Group (AH-L) ($p=0.144$). There was no statistically significant difference found between single cone groups; Group (BC-S), Group (Cera-S), Group (AH-S) ($p=0.608$). There was no statistically significant difference found between BC Sealer groups; Group (BC-L) and Group (BC-S) ($p=1$). There was no statistically significant difference found between CeraSeal groups; Group (Cera-L) and Group (Cera-S) ($p=0.759$). There was no statistically significant difference found between AH Plus Sealer groups; Group (AH-L) and Group (AH-S) ($p=0.214$). (Table 17)

4.2. Bond Strength of the Root Canal Fillings

Bond strength values were measured with push-out test as described in Chapter 3.9 and data were recorded in Table 18.

Table 18. Bond strength values of all samples in MPa.

Bond strength in MPa						
	Group (BC-L)	Group (BC-S)	Group (Cera-L)	Group (Cera-S)	Group (AH-L)	Group (AH-S)
1	6.54	1.75	2.6	3.48	11.15	1.02
2	14.92	1.21	9.9	11	7.89	1.83
3	6.18	0.78	11.57	4.75	11.46	1.2
4	8.18	1.23	8.84	4.28	11.79	2.58
5	6.41	1.46	5.22	9.78	7.06	2.39
6	8.58	1.79	9.9	11.62	9.55	1.05
7	4.24	2.05	13.55	6.27	6.37	1.57
8	1.72	0.62	4.93	3.73	8.32	0.45
9	4.66	1.32	8.41	5.64	7.38	2.25
10	4.72	0.49	7.28	2.58	14.56	1.27
11	11.03	0.55	8.72	0.86	4.34	0.93
12	4.54	1.48	1.21	3.18	6.32	1.85
13	5.96	0.44	9.19	6.6	8.56	1.09
14	7.88	2.26	4.74	3.16	12.65	1.02
15	10.62	1.39	4.22	4.12	7.8	0.93
16	10.84	0.68	6.41	6.61	5.45	1.36
17	9.2	0.63	14.02	9.94	7.15	1.85
18	9.54	1.81	8.55	3.05	12.39	0.95
19	3	1.9	1.26	5.97	12.25	0.96
20	9.9	2.14	4.06	7.8	3.8	0.91
21	10.4	1.58	9.87	4.11	9.53	1.19
22	7.54	1.95	12.1	13.06	3.17	0.55
23	8.32	1.88	13.02	8.91	1.62	0.72
24	13.47	1.21	5.92	9.63	4.88	0.87
25	8.21	1.39	9.44	4.51	8.63	1.45
26	4.89	0.92	0.56	3.07	9.16	2.22
27	2.87	0.61	2.32	9.41	3.49	1.26
28	3.81	1.54	14.05	9.54	9.52	1.09
29	0.56	1.75	4.28	3.71	7.11	1.46
30	10.38	1.66	6.54	2.91	6.79	1.74
31	8.77	1.97	2.98	3.28	8.93	1.25
32	8.97	2.27	0.46	4.12	9.24	2.12
33	11.2	0.54	5.24	9.32	9.12	1.39

Table 19. Bond strength values of all groups.

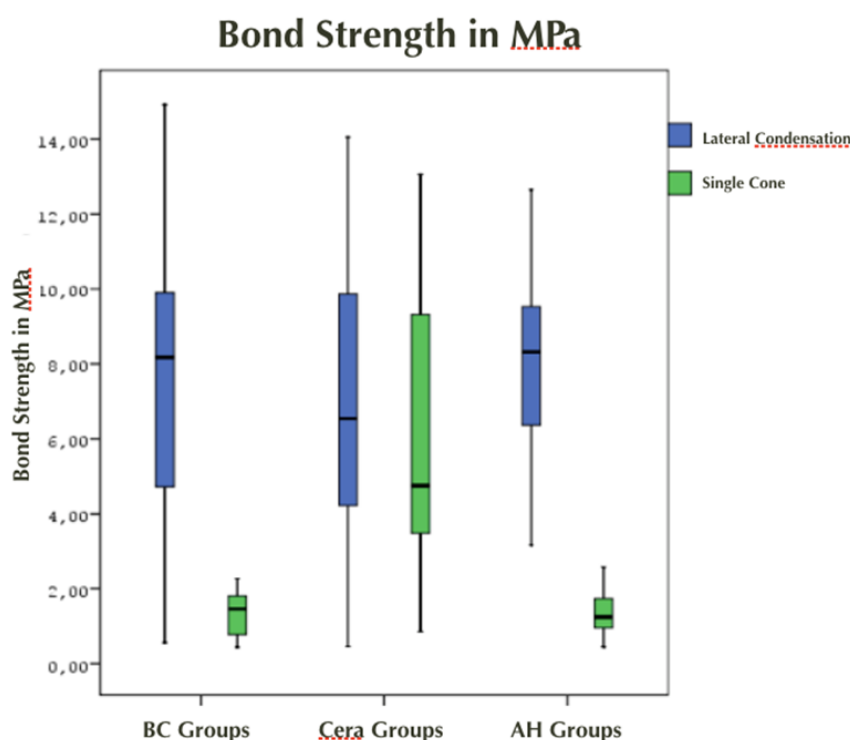


Table 20. Comparison of the root canal filling methods between same sealer groups in terms of duration of the bond strength.

Bond Strength (Mpa)			
	Mean±SD	Median (IQR)	p*
Group (BC-L)	7,52±3,35	8,18 (4,69-10,14)	0.0001
Group (BC-S)	1,37±0,57	1,46 (0,73-1,84)	
Group (Cera-L)	7,01±4,03	6,54 (4,14-9,88)	0.349
Group (Cera- S)	6,06±3,16	4,75 (3,38-9,36)	
Group (AH-L)	8,10±3,02	8,32 (6,34-9,54)	0.0001
Group (AH-S)	1,36±0,53	1,25 (0,95-1,78)	
*Kruskal Wallis Testi *Mann Whitney U testi			

A statistically significant difference was observed between Group (BC-L) and Group (BC-S) in terms of bond strength. Bond strength of Group (BC-L) were found to be statistically significantly higher than the Group (BC-S) ($p=0.0001$). There was no statistically significant difference found between Group (Cera-L) and Group (Cera-S) in terms of bond strength ($p=0,349$). (Table 20)

A statistically significant difference was observed between Group (AH-L) and Group (AH-S) in terms of bond strength. Bond strength of Group (AH-L) were found to be statistically significantly higher than the Group (AH-S) ($p=0.0001$). (Table 20)

Table 21. Comparison of the root canal sealers among lateral condensation groups in terms of bond strength.

Bond Strength (MPa)		Group (BC-L)	Group (Cera-L)	Group (AH-L)	p‡
	Meant±SD	7,52±3,35	7,01±4,03	8,10±3,02	0.506
	Median (IQR	8,18 (4,69-10,14)	6,54 (4,14-9,88)	8,32 (6,34-9,54)	
‡Kruskal Wallis Testi *Mann Whitney U testi					

There was no statistically significant difference found between laterally condensed groups; Group (BC-L), Group (Cera-L), Group (AH-L) in terms of bond strength ($p=0,506$). (Table 21)

Table 22. Comparison of the root canal sealers among single cone groups in terms of bond strength.

Bond Strength (MPa)		Group (BC-S)	Group (Cera-S)	Group (AH-S)	p*
	Meant±SD	1,37±0,57	6,06±3,16	1,36±0,53	0,0001
	Median (IQR)	1,46 (0,73-1,84)	4,75 (3,38-9,36)	1,25 (0,95-1,78)	
*Kruskal Wallis Testi *Mann Whitney U testi					

A statistically significant difference was observed between single cone groups; Group (BC-S), Group (Cera-S), Group (AH-S) in terms of bond strength. Bond strength of Group (Cera-S) were found to be statistically significantly higher than the Group (BC-S) and Group (AH-S) ($p=0.0001$). (Table 22)

Table 23. Multiple comparison of single cone groups in terms of bond strength.

Bond Strength of single cone groups	p*
Group (BC-S) / Group (Cera-S)	0.0001
Group (BC-S) / (AH-S)	0.696
Group (Cera-S) / Group (AH-S)	0.0001
Dunn's Multiple Comparison	

A statistically significant difference was observed between Group (BC-S) and Group (Cera-S). Bond strength of Group (Cera-S) were found to be statistically significantly higher than the Group (AH-S) ($p=0.0001$). There was no statistically significant difference found between Group (BC-S) and Group (AH-S) in terms of bond strength ($p=0.696$). A statistically significant difference was observed between Group (Cera-S) and Group (AH-S). Bond strength of Group (Cera-S) were found to be statistically significantly higher than the Group (AH-S) ($p=0.0001$). (Table 23)

5. DISCUSSION

The aim of endodontic treatment is to prevent the infection in the root canal from spreading to the periapical tissues, and when it does, to heal the infection in this area (4). After the disinfection step is completed, the canal space must be hermetically sealed to prevent reinfection of the root canal system (11). The success rate of endodontic treatment was found to be between 93-84% in studies (211). In other words, 7-16% of endodontically treated teeth may show apical periodontitis symptoms again. The majority of these failed cases can be retained in the mouth with retreatment. Factors such as iatrogenic errors that occur during root canal treatment, leakage of the coronal restoration, and persistent infections can cause post treatment disease (7). In case of post treatment disease, the previous root canal filling should be removed from the root canal and the root canal cavity should be disinfected again (8). One of the ideal root canal sealer properties defined by Grossman is that the sealant should be easily removed from the root canal when retreatment is required (5).

The retreatability of bioceramic-based sealers, which have been used frequently in endodontic practice in recent years, continues to be a subject of interest due to the necessity of planning studies on newly introduced bioceramic based products in the market. In this study, retreatability and bond strength of epoxy resin based AH Plus, calcium silicate based TotalFill BC Sealer and CeraSeal canal sealers, when applied with lateral condensation and single cone methods, were investigated.

This study was planned on 66 extracted human single-rooted premolars and ethical approval was taken from Yeditepe University Clinical Research Ethics Committee with the decision number Kaek no: 1509. Samples in our study were divided into 6 groups in order to evaluate the effects of both root canal sealers and obturation methods on retreatability and bond strength. These groups were created as; Group (BC-L): TotalFill BC Sealer + Lateral Condensation, Group (BC-S): TotalFill BC Sealer + Single Cone, Group (Cera-L): CeraSeal + Lateral Condensation, Group (Cera-S): CeraSeal + Single Cone, Group (AH-L): AH Plus + Lateral Condensation, Group (AH-S): AH Plus + Single Cone.

Power analysis was performed with the G*power 3.1 program to determine the sample size. The effect size of the study groups for retreatability was found to be 0.48

(alpha error probability=0.05); The sample size analysis performed by taking the power value of 0.80, the total number of samples was found to be 66 teeth (n= 11). The power analysis performed with the G*power 3.1 program related to our study and the effect size for the bond strength of the study groups was found to be 0.48 (alpha error probability=0.05); When the sample size analysis was performed by taking the power value of 0.80, the total number of samples were determined as 60 teeth (n=10). Since both methods were used, the number of samples included in each group was determined as 11.

In this study, extracted human single-rooted premolars were used to mimic clinical conditions. The reason for choosing the premolar group was the wide and smooth root canal anatomy of premolar teeth. Since the amount of root canal filling will be relatively higher in large root canals, it was thought that the comparison between groups would be easier. There are many studies in the literature evaluating the retreatability of root canal fillings on premolars (16,24,232,263–266).

Premolar teeth with oval canal structures were included in this study. Crozeta *et al.* stated that it is more challenging to create a hermetic root canal filling in oval root canals and the obturation method has important effects on dentin bonding as well as the root canal sealer (243). Baranwal *et al.* stated that they prefer premolars with oval canals for similar reasons (266). For these reasons, oval-shaped premolars were used in this study, considering that the bond strength and retreatability of canal sealers can be better observed in these challenging anatomical structures.

Detailed examination in the determination of sample teeth is important in terms of standardization and elimination of tooth-related differences. For this reason, a detailed study was carried out for the selection and preparation of the experimental materials. To ensure the standardization of the groups; inclusion criteria of extracted premolars were as follows:

- Vertucci 1 anatomy
- Oval canal structure
- No cracks
- Fully formed apical foramen
- No calcification in the root canal

- Apical widths close to each other, 5mm and 10mm from the apex
- Root canal curvatures less than 10 degrees

One hundred and eleven single rooted premolars were collected and kept in 0.1% thymol solution until use (267). Sample teeth were examined under Zeiss Opmi Pro (Oberkochen, Germany) operating microscope, and teeth with broken or cracked surfaces were not included in the study (16).

In order to ensure the standardization of the samples, all samples were observed by digital radiography from bucco-lingual and mesio-distal directions, and those samples having canal configuration other than Vertucci 1 were excluded from the study. Root curvature was calculated with the Schneider technique in the Image J program and those samples which had a curvature above 10 degrees were excluded from the study (257).

The widths of the sample teeth were measured 5mm and 10mm from the apical foramen with a digital caliper, and the teeth with the closest values to each other were included in the study (268). During the control of the canal opening, the teeth in which a No.25 K file could reach the working length without difficulty as the initial file were considered as having an open apex and those teeth were excluded from the study (269).

Regarding the selection of the sample teeth, 4 teeth with open apices, 9 teeth with round root canal structure, 21 teeth with configurations other than Vertucci 1 canal structure, 4 teeth with cracks on the root surface and 7 teeth which were too wide due to the measurements made at 5mm-10mm from the apical were excluded from the study because they did not comply with the above-mentioned criteria. As a result of detailed examinations, 66 sample teeth that fulfilled all the criteria were randomly divided into groups with the randomizer.org program.

In terms of retreatability, it was thought that the length of the root may affect the volume of filling residues remaining on the root canal walls after retreatment. For this reason, in order to ensure standardization among the samples in terms of working lengths, all teeth were standardized at 16 mm length and their crowns were removed with the help of a diamond separator.

The working length of the samples with a root length of 16mm was established as 15mm. Chemo-mechanical preparation of samples was performed by a single operator.

As a result, operator-related changes were prevented (270).

Chemo-mechanical preparation of root canals was performed with the Protaper Next nickel titanium rotary file system. This provided a standardization in the preparation of root canals. Protaper Next is a 5th generation endodontic instrument produced with the M-Wire technology. It shapes the root canal with an off-center, sinusoidal movement with its 2 sharp surfaces (271). The reason for using the Protaper Next system is that it has been involved in such studies and to ensure the elimination of file-related differences when it is necessary to make comparisons with similar studies (18,272,273).

It can be speculated that the use of nickel titanium rotary instrument systems used in preparation of oval root canals may cause insufficient preparation due to the large root canal diameter, especially in the coronal region. This may constitute one of the limitations of the present study. However, in the present study, preparation was completed with the #30 of the Protaper Next system and this diameter was thought to be sufficient for shaping the apical $\frac{1}{3}$ rd. Since gutta-percha cones with compatible taper with the Protaper Next system were used, preparation did not include wider files. As mentioned before, since one of the goals of the present study was to evaluate the bond strength of sealers to dentin, oval root canals were preferred and these limitations were attempted to be minimized by measuring the canal diameters meticulously and not including teeth with very wide root canals. The availability of tapered gutta-percha cones compatible with the Protaper Next system enabled the ideal application of both filling methods in the study.

The manufacturer's recommendation for the use of the Protaper Next rotary instrument system is to use one file per root canal. However when the literature is examined, it is observed that files were used up to 5 samples in similar studies (16). Accordingly, in our study, the preparation of 5 samples was completed with a set of ProTaper next system. No instrument separation was observed during the chemo-mechanical preparation.

NaOCl solution is accepted as the gold standard in endodontic treatment due to its strong antimicrobial properties, dissolving effects on organic tissues and organic part of dentin (239,240). Concentrations of 0.5%-6% are generally used in endodontic treatment. Studies have shown that there is a relationship between the concentration of the solution and its tissue dissolving effect. High concentrations of NaOCl can dissolve organic tissues in a shorter period (274). Elimination of the organic part of the smear layer covering the

dentinal tubules and the organic remnants on the root canal walls are important in the penetration of canal sealers to dentinal tubules. For this reason, the use of NaOCl solution with 5% concentration was preferred in our study. Each canal was irrigated with a total of 10 mL of NaOCl solution, using 2 mL after each instrument (16).

Although NaOCl is successful in removing organic tissues, it has no effect on removing the inorganic part of the smear layer (241). As already known, the smear layer makes it difficult for irrigation solutions to contact the dentinal walls and prevents the root canal filling from penetrating the dentinal tubules (241). For this reason, the bond strength of root canal fillings to dentin and their removal from the root canal were examined. It was thought that the removal of the smear layer would provide the opportunity to make a more accurate examination.

Morago *et al.* reported that the combined use of NaOCl with 17% EDTA removed the smear layer more successfully than using NaOCl alone (275). It has been shown by many researchers that the combination of NaOCl and EDTA is effective in removing the smear layer (241,276).

In studies examining the bond strength of canal fillings to dentin, it is an important issue to promote sealer penetration by removing the smear layer. Therefore, in our study, we tried to ensure complete elimination of the smear layer by using 17% EDTA solution after the canal preparation was completed with 5% NaOCl.

Niu *et al.* indicated that the use of NaOCl after EDTA in the final irrigation protocol may cause more dentin erosion than the use of EDTA alone. However they also reported that this application provides more effective removal of the smear layer (276).

According to this information, 5 mL of 17% EDTA was applied in the final irrigation and root canal irrigation was completed using 2 mL of NaOCl solution. In this way, it is aimed to effectively provide the debridement of the dentinal tubules with NaOCl after removing the smear layer as mentioned above.

It has been reported that the pH and efficacy of NaOCl decreases and chlorine gas is released as a result of the sequential use of NaOCl and EDTA solutions (277). Therefore, in our study, 2 mL saline solution was used between NaOCl and EDTA solutions in order to prevent the solutions from interacting with each other. Finally, irrigation was completed using 2 mL of saline solution in order to eliminate the harmful

effects of NaOCl (278).

Hess *et al.* used a similar final irrigation protocol in their study in which they investigated the retreatability of root canal sealers (259).

The use of laterally-perforated endodontic needles during irrigation provides more effective removal of debris by increasing the depth of penetration, especially in curved root canals (279). the same time, the use of laterally perforated endodontic needles significantly reduces the risk of extrusion of the irrigation solution from the apical foramen. Due to these advantages, endodontic needles are frequently used in endodontic practice. In this study, 30 gauge, closed-end, side-perforated needles were used during the chemo-mechanical preparation of the samples. In this way, clinical conditions were imitated and similar conditions were obtained with other studies in the literature (233,243,280).

Epoxy resin containing AH Plus root canal sealer has many advantages such as dentin covering (90) and successful bonding to dentin, low solubility and polymerization shrinkage (98), and clinically successful outcomes (211). All these positive features have rendered AH Plus root canal sealer a widely preferred material in endodontic practice which is accepted as the gold standard (13).

Therefore, in this study, bioceramic sealers were compared with AH Plus canal sealer. In addition to these favorable properties, AH Plus root canal sealer shows low amount of polymerization shrinkage (5,98). It is not an ideal root canal sealer because it does not have a moderate cytotoxic effect on vital tissues and does not support hard tissue healing (120). These missing features have led to the continuation of the search to develop new root canal sealers and bioceramic based sealers.

Bioceramic-based sealers, which have been on the market in recent years; have many advantages such as biocompatibility, stimulation of hard tissue formation (164), volume expansion during polymerization (12), hydrophilic properties, stimulation of regeneration, and superior dentine sealing properties.

All these positive properties of bioceramic sealers are promising for their widespread clinical use. However, these advantages still need to be supported by independent researchers. Therefore, in our study, the retreatment and bond strength of TotalFill BC Sealer, which has been in use for a while, and CeraSeal sealer, which is a

newly produced bioceramic-based sealer were investigated and compared with AH Plus.

TotalFill BC Sealer is a root canal sealer that does not show polymerization shrinkage, that is biocompatible (46,120,186) has ability to form chemical bonds with dentin (189,281), and has antibacterial effect (91,162,192).

Chybowski *et al.* observed 307 patients who received root canal treatments between 2009 and 2015. In this retrospective cohort study, root canal fillings were performed with Endosequence BC sealer, which has the same content as TotalFill BC Sealer, using the single cone method. These cases were followed for an average of 30 months. According to this study, the success rates of primary root canal treatments and retreatment cases, which were completed using bioceramic sealers, were found to be close to each other (282). Therefore, the clinical use of TotalFill BC Sealer seems promising for the future and stands out among bioceramic based sealers. However, Chybowski *et al.* did not give any information about the sealers used in the initial root canal treatment of teeth that underwent retreatment.

According to a survey conducted by Guivarc'h *et al.* in a population of 2335 consisting of general dentists and endodontists, it was observed that 55.6% of the population were concerned that they might have problems in re-establishing the apical patency during retreatment when bioceramics are used (283). As Guivarc'h *et al.* stated, the retreatability of bioceramic-based sealers is still being investigated and clinicians wonder whether it is a problem. For this reason, bioceramic based TotalFill BC Sealer and CeraSeal have been included in the study groups.

Another root canal sealer used in our study is CeraSeal. CeraSeal canal paste contains calcium silicate and has healing-supporting properties on hard tissues (194). It is stated by the manufacturer that CeraSeal does not cause polymerization shrinkage (284). CeraSeal is hydrophilic and has a high pH value. Since CeraSeal is a newly released root canal sealer, there are few studies in the literature with this root canal sealer. (195–197) CeraSeal also has a price advantage compared to other bioceramic sealers, and its clinical use can be expected to become widespread after its physical and technical properties are tested. For this reason, CeraSeal sealer was also included in our study and it was aimed to compare it with AH Plus, which is accepted as the gold standard and TotalFill BC Sealer, which is a candidate to become the gold standard among bioceramics.

Various studies have been conducted comparing the retreatability of AH Plus with different canal sealers. Alsubait *et al.* compared AH Plus and BioRoot RCS sealers, Neelakantan *et al.* compared AH Plus, MTA Fillapex and MTA Plus sealants and Agrafioti *et al.* compared AH Plus, TotalFill BC Sealer and MTA Fillapex root canal sealers in terms of retreatment (24,285,286).

There are also studies in the literature investigating the retreatability of TotalFill BC Sealer. Kakoura *et al.* investigated the retreatability of TotalFill BC Sealer, BioRoot RCS and AH 26 sealants. Agrafioti *et al.* investigated the retreatability of TotalFill BC Sealer, AH Plus and MTA (20,286).

Although there is no study in the literature evaluating the retreatability of CeraSeal; There are no studies evaluating the retreatability and bond strength of AH Plus, TotalFill BC Sealer and CeraSeal. In the present study, we aimed to make a contribution to the existing literature by investigating the retreatability of these sealers and their bond strength after obturating with the same canal sealer.

The methods used to obturate the root canals also affect the removal of the canal filling from the root canal (10,11). Various root canal filling methods have been proposed in order to obtain appropriate and desired root canal filling until now. The lateral condensation method is a root canal filling method that is widely used in endodontic practice due to its advantages such as not requiring the use of extra devices, easy control of the working length, and good adaptation of the root canal filling to the dentin walls (199). Freidman *et al.* observed and evaluated the prognosis of 450 teeth with the Periapical index (PAI). In this cohort study, root canal fillings were performed with lateral condensation and AH Plus. The success rate of endodontic treatment was found as 92% in teeth without apical periodontitis and 81% in all cases (211). The lateral condensation method, which is frequently preferred in clinical practice due to its practicality and positive contributions to the success of root canal treatment, was chosen as one of the filling techniques of this study.

In the single cone method, which is another preferred canal filling method in this study, a gutta-percha is produced in accordance with the taper of the instruments used in preparation (204). Since root canals can be filled with a single piece of gutta-percha, root canal filling can be completed within a short time (206).

In the single cone method, no condensation is performed to adapt the root canal filling to the root canal walls. In this case, the task of sealing is mostly provided by root canal sealer. For this reason, it is important that the root canal sealer does not shrink during polymerization, but rather expands. The volumetric expansion properties of bioceramic-based sealers cause them to be preferred in the single-cone method (282).

A success rate of 90.9% was achieved by Chybowski *et al.* in the endodontic treatment of 307 patients. In the present study, endodontic treatments were performed with the single-cone method (282). Due to the practical application of the single-cone method and the successful clinical results, it was preferred to test the single cone method with newly produced bioceramic sealers. Briefly, single cone method was used as the other obturation method in this study.

Another common obturation method in endodontics is thermoplastic methods, in which the adaptation of gutta-percha to the root canal is enhanced by heat (10,287,288). Karatekin *et al.* and Wolf *et al.* reported that more successful root canal fillings were performed with thermoplastic techniques rather than lateral condensation in tooth models with difficult canal anatomy and C-shaped and accessory canal structures (287,288). Although thermoplastic methods provide high adaptability, they adversely affect the physical properties of bioceramic sealers (289). Viapiana *et al.* showed that changes in the physical properties of bioceramic sealers occur due to high temperature (289). Therefore, in the present study, thermoplastic canal filling methods were not preferred due to the bioceramic contents of TotalFill BC Sealer and CeraSeal.

After the canal fillings were completed, the samples were kept in an oven at 37 degrees for 7 days in 100% humidity. This environment has the heat and humidity that mimics the oral environment, allowing the root canal fillings to harden completely. Similar environmental conditions were also provided in the study by Osiri *et al* (290).

When the need for retreatment arises in endodontic treatment, hand files, retreatment sets specially produced for this process (22,238), some of the reciprocal Ni-Ti files used in shaping (23,234) and file combinations are used (259).

In the present study, Protaper Universal Retreatment set was used during the retreatment of the samples. Since the Protaper Next system was used in preparation, it was thought that it would be appropriate to use the Protaper Universal Retreatment Set,

which is compatible with this system, during the retreatment process. Protaper Universal Retreatment was also used in a similar study by Uzunoğlu *et al.* which evaluated the retreatability of different sealers (16). Similarly, Kakoura *et al.* investigated the removal of BioRoot RCS, TotalFill BC Sealer and AH 26 from the root canal during retreatment. Retreatment was performed using the Protaper Universal Retreatment set (20). Alsubait *et al.* investigated the retreatability of Bioroot RCS and AH Plus canal sealers with the Micro-CT. They used the Protaper Universal Retreatment set for root canal filling removal (24).

Retreatment of 5 samples was performed with each Protaper Universal Retreatment set. According to the user instructions of Protaper Universal retreatment set, the instruments should be used in a maximum of 8 canals with a curvature of less than 10 degrees (291). Since retreatment sets were used in 5 canals in similar studies, this approach was also applied in our study (20).

During the retreatment process, the D1-D2-D3 instruments of the Protaper Universal Retreatment set were used successively, and irrigation was performed with 2 mL of 5% NaOCl between each instrument. #25 H type hand files were also used at the points where the rotary instruments are felt to be stuck in root canal filling. In some samples, complete removal of canal fillings was observed with only D1 instruments or only D1 and D2 instruments. Although the root canal filling was removed in these samples, irrigation was continued until 10 mL. The removal of the root canal filling was considered to be complete when there was no residual canal filling on the retreatment instruments (16).

Gutta-percha solvents are also used to remove root canal fillings during retreatment procedure. These solvents can facilitate retreatment (292). Oltra *et al.* investigated the retreatability of Endosequence BC Sealer and AH Plus in the presence and absence of gutta-percha solvent and reported that there was no statistically significant difference between retreatability of the groups. The use of chloroform in the groups in which BC Sealer was used significantly increased the reestablishment of the apical patency (269). Athkuri *et al.* reported that gutta solvents can cause root canal residue deposition in anatomically challenging areas of the root canal system (264). The main reason for not using gutta-percha solvents in this study was the emphasis that gutta solvents may cause the softening of the root canal filling and therefore accumulate in the root canal. In

addition, usage of gutta-percha solvents may cause shortening of the duration of retreatment procedure and may facilitate the reestablishment of apical patency. It was thought that these effects, which may facilitate the treatment, might adversely affect the evaluation of the sealer factor, which forms the basis of the study.

Irrigation activation methods which reduce the amount of residual canal filling can also be used in retreatment procedures (232). In most of the studies, the amount of residual root canal filling was evaluated prior to activation (24,232,243). In order to evaluate the effects of the activation methods, a third Micro CT scan was performed right after the irrigation activation procedure. These studies show that irrigation activation reduces the remaining canal filling volume (24,232,243).

In this study, activation methods were not used in order to clearly examine the difference between the residual canal filling volumes in different sealer groups. Based on the results of the present study, further studies can be planned with using similar sealers and retreatment supported by activation methods.

There are several methods for assessing the residual of root canal filling volumes from the root canal, as detailed in Section 2.5. Scanning electron microscopy (SEM), digital radiography, confocal microscope, stereomicroscope, Optical microscope, cone-beam computed tomography (CBCT) and micro-computed tomography (Micro-CT) are among the evaluation methods used for this purpose.

In this study, for assessing the residual of root canal filling volumes, Micro CT scanning was preferred because it provides the opportunity to measure three-dimensionally and clearly without damaging the samples. There is also the possibility of repeating the measurements using in this methodology (25). Due to these advantages, this method has been preferred to determine the volumes of residual root canal fillings.

In this study, Micro CT scans were performed twice on the samples to compare the residual canal filling volumes. The first scan was performed immediately after the root canal fillings were completed and the total volume of the canal filling was calculated. The second Micro CT scan was performed right after the removal of the root canal filling and the volume of the residual root canal filling was measured. The volume found at the end of the second scan was divided by the volume in the first scan, and the percent values of the residual canal filling were calculated for each sample. There are many studies which

also utilize this protocol (24,243,269).

One of the features expected from a proper root canal sealer is to provide the connection between the dentin wall and the gutta-percha. There are several methods for assessing the strength of this connection. These are shear bond test (shearing), pull-out test (pull out), Macro-tensile test (stretching) and push out (push) test (253–255).

The most commonly used method to evaluate the bond strength of root canal fillings is the push-out test (254). The advantage of this method over shear bond test and tensile bond test is that it is possible to measure the bond strength of the sealer when there is dentin tissue all around the root canal filling being tested (293). There are many studies that investigated the bond strength of the sealers to dentine. Donnermeyer *et al.* investigated the bond strength of TotalFill BC Sealer, AH Plus and Endo CPM using the push out test (15). Dem *et al.* investigated the bond strengths of AH Plus, Guttaflow and Guttaflow 2 with the push out test (89). Khalil *et al.* examined the bond strength of Guttaflow and Zical canal sealers using the same methodology (294). Silva *et al.* also investigated the bond strength of EndoSeal MTA, MTA Fillapex and pozzolan based root canal sealer sealers with push out test (87).

Because the push-out test is a frequently preferred system in the literature, it was also used in the present study to evaluate the bond strength. A search of the literature reveals that there is yet no study which evaluates the bond strength of AH Plus, TotalFill BC Sealer and CeraSeal. Meanwhile, there is no study which investigates the bond strength of these sealers after retreatment. This study was carried out in order to fill this gap in the literature.

In studies investigating the bond strength, the resistance of sealers to pushing forces can be examined in sections which are taken from different parts of the root. In order for the push out test to be applied effectively and accurately on dentine discs obtained from different sections, push out force must be applied with the appropriate tip for that section (295).

In a meta-analysis, Silva *et al.* stated that the samples taken from the middle 1/3rd portion showed higher bond strengths compared to the apical and coronal sections (296). In the push out studies performed by Amin *et al.*, Olivera *et al.*, Razmi *et al.*, cross-sections were taken from the middle 1/3rd (297–299). Similarly, Carvalho *et al.* examined

the bond strength of Endosequence BC Sealer and AH Plus sealers. In their study, the sections were taken from the middle 1/3rd (300).

In the present study, similar to the studies by Carvalho *et al.*, Amin *et al.*, Olivera *et al.* and Razmi *et al.*, 3 different root sections were taken from the middle 1/3rd for the push out test (297,299,300). Although sections were taken only from the middle third, it was aimed to evaluate the bond strength accurately by keeping the sample size as large as possible. During sectioning procedures, 19 dentin discs were fragmented. Fragmented dentin discs were replaced with new dentin discs which were taken from the middle 1/3rd of the same sample. One of the limitations of the study is the inability to obtain cross-sections from the coronal and apical regions. However, it is possible to plan different studies based on the results obtained from the middle 1/3rd, where the best evaluations can be made.

In retreatment cases, the excessive amount of residual root canal filling is important because it can cause reinfection of the root canal system. In many studies, it has been reported that the old root canal filling cannot be completely removed from the root canal and the residual filling pieces remain in the root canal walls (16,19,243). In this study, it was observed that the root canal fillings could not be completely removed from the root canals in all experimental groups, and this finding was compatible with other studies (16,19,243). The fact that the root canal fillings could not be completely removed has directed the attention of the studies to the examination of the amount of residual filling. It has been reported that hydroxyapatite-like crystal structures occur between the dentin and the material interface of bioceramic sealers (12,156). For this reason, in the studies examining the retreatability of bioceramic sealers, it was investigated whether this chemical connection has an effect on the volume of residual canal filling (16,18,19,269,285). According to some studies investigating the retreatability of root canal fillings which were created with the single-cone method, more residual canal filling is left in the groups obturated with epoxy resin sealers (24,233,243,301). Crozeta *et al.* evaluated the retreatability of AH Plus and Endosequence BC Sealer on 28 extracted mandibular molars (distal root) with Micro-CT. In that study single cone method was used as obturation method. According to their results, AH Plus group left more residual filling than Endosequence BC Sealer group (243). Alsubait *et al.* observed the retreatability of AH Plus and BioRoot RCS 34 extracted human mandibular premolars with Micro-CT.

Single cone method was preferred in their study and according to their findings AH Plus group showed higher volume of root canal filling compared to BioRoot RCS (24). Rajda *et al.* observed the retreatability of AH Plus and TotalFill BC Sealer on 40 extracted single rooted human teeth with Micro-CT. In this study single cone obturation method was used with Bioceramic gutta-percha. According to Rajda *et al.* TotalFill BC Sealer group caused less amount of residual root canal filling (301). Donnermeyer *et al.* observed teeth in which root canal fillings were performed with BioRoot RCS, MTA Fillapex, Endo C.P.M. and AH Plus sealers following retreatment using the light microscope. The residual root canal filling volumes were measured with the ImageJ program. The samples were obturated with the single cone method in all groups. In this study, 3 different rotary retreatment instruments and H type hand files were used during the retreatment process. Among the residual root canal fillings, the AH Plus+H type file group had the highest residual canal filling volume, and there was no statistically significant difference between the other groups (including sealers and retreatment instruments) (233).

In the present study, it was found that the residual root canal filling volume was lower in the bioceramics (Group (BC-S) and Group (Cera-S) groups compared to the AH Plus (Group (AH-S)) group among single-cone groups ($p=0.006$). Chemical bond formation of bioceramic sealers suggest that the retreatment of bioceramic sealers may be difficult. But in our study the result was the opposite of that. Therefore, the results of our study are fully consistent with the results of Crozeta *et al.*, Alsubait *et al.*, Donnermeyer *et al.*, Rajda *et al.* (between single cone groups) (24,233,243,301). Rajda *et al.* explained this situation with the usage of reciprocating retreatment instruments (301). However in this study continuously rotating retreatment instruments were used. Unlike Rajda *et al.*; Crozeta *et al.*, Alsubait *et al.*, Donnermeyer *et al.* explained this situation with the weakening of the chemical bond between bioceramics and root dentin due to the removal of calcium from dentin by the use of EDTA (24,233,243).

Unlike our study, Uzunoglu *et al.* investigated the residual root canal filling volume after retreatment of AH 26, iRoot SP add MTA Fillapex sealers used with different obturation methods (AH 26 single cone, AH 26 Lateral condensation, iRoot SP-single cone and MTA Fillapex-single cone) using the stereomicroscope (16). The volume of residual root canal filling in the iRoot SP-single cone group was found to be higher than the AH 26-single cone and AH 26 lateral condensation groups (16). This difference may

because of AH 26 usage instead of AH Plus. Therefore, observation methods (stereomicroscope usage) of these studies are also differed from each other which also may cause different results. Oltra *et al.* investigated the retreatability of Endosequence BC Sealer and AH Plus with the Micro-CT. In their study the effects of Chloroform are also observed. According to their findings, less residual root canal filling was observed in the AH Plus group which was retreated with Chloroform (269). This different result is thought to be caused by Chloroform usage.

In our study, there was no statistically significant difference between lateral condensation groups (Group (AH-L), Group (BC-L), Group (Cera-L)) in terms of residual canal filling volumes. Similarly, in the study by Baranwal *et al.*, the retreatability of AH Plus and BioRoot RCS from the root canal was investigated by CBCT. In this study, lateral condensation method was preferred as the obturation method. As a result, there was no statistically significant difference between the residual volumes of AH Plus and BioRoot RCS groups (266). Despite the difference in the observation methods used by Baranwal *et al.*, similar results were obtained with our study.

In the present study, when the duration of the retreatment process was examined, it was found that there were differences when the same canal sealer was applied with different obturation techniques. The duration of the retreatment process took longer in the lateral condensation groups than single cone groups for TotalFill BC sealer and AH Plus. ($p=0.011$, $p=0.001$) There was no statistically significant difference between lateral condensation and single cone in the groups in which CeraSeal was used. ($p=0.652$) When the groups using lateral condensation were compared within themselves, no statistically significant difference was found between the duration of retreatment procedure of the 3 sealers. ($p=0.056$) When the groups using the single cone method were compared among themselves, no significant difference was found between the 3 sealers. ($p=0.314$) In particular; In the AH Plus and TotalFill BC Sealer groups, the obturation method was found to be determinative on the retreatment time. It is thought that the reason why the procedure time was similar in both lateral condensation and single-cone methods in the CeraSeal group may be due to the strong chemical bond it forms with dentin.

Hess *et al.* investigated the duration of retreatment process of AH Plus and BC Sealer. AH Plus groups were obturated with the single cone and BC Sealer groups were obturated with the continuous wave method. There were two AH Plus and BC Sealer

groups in the study. In one of these groups, the root canal filling was terminated at the working length, while in the other group it was terminated 2 mm behind the apex. The duration of the procedure was found to be the longest in the BC Sealer group filled until the working length. The group with the shortest procedure time was found to be the AH Plus group which was filled until the working length. No statistically significant difference was found between the other two groups which were filled behind 2mm of the apex (259). The statistically significant difference resulting from this study can be attributed to the different obturation technique therefore which can be consistent with our study.

Athkuri *et al.* compared the duration of retreatment procedures of the root canal fillings created with BioRoot RCS and AH Plus. Lateral condensation, thermoplastic injection and warm vertical condensation techniques were used in the subgroups of the study. When the duration of retreatment procedures were examined, there was no statistically significant difference between the sealers, but a significant difference was observed between obturation methods. Regardless of the sealer, it was observed that duration of the treatment procedure was shorter in the lateral condensation groups compared to the warm techniques (264). The results of the study of Athkuri *et al.* are also in agreement with our study.

Uzunoğlu *et al.* investigated the duration of retreatment procedures of the groups filled using AH 26+single cone, AH 26+Lateral condensation, iRoot SP+single cone and MTA Fillapex+single cone. The group with the shortest retreatment period was found to be MTA Fillapex. There was no statistically significant difference between iRoot SP (calcium silicate) and AH 26 groups (epoxy resin content). According to this study, calcium silicate content of iRoot SP did not cause the extension of the duration of retreatment process (16). Similarly, in our study; there was no statistically significant difference between the retreatment durations of TotalFill BC Sealer, CeraSeal and AH Plus sealer in the single cone groups.

In some studies, it has been observed that the calcium silicate contents of sealers affect the duration of retreatment procedures (24,233,286). Different results have been obtained in studies which investigated the duration of retreatment procedures of different root canal sealers and used the single cone obturation method. For example, Donnermeyer *et al.* investigated the duration of the retreatment procedure of BioRoot RCS, MTA

Fillapex, Endo C.P.M. Sealer and AH Plus by using three different retreatment instruments and hand files. According to their study; among hand file groups, AH Plus had the longest retreatment duration compared to other sealers. Contrary to this result, Alsubait *et al.* indicated that the duration of retreatment procedure of BioRoot RCS was longer than AH Plus (24,233). In our study, however, no statistically significant difference was found between TotalFill BC Sealer, CeraSeal and AH Plus among single cone groups and lateral condensation groups. It was thought these differences between studies may be due to the different rotary instrument systems used during the retreatment process. Although the retreatment period was not included in the study by Alsubait *et al.*, there was a methodological difference as irrigation activation is used. It was thought that this might have an effect on the results. Agrafioti *et al.* compared the duration of retreatment procedure of AH Plus, TotalFill BC Sealer and MTA Fillapex and they used the study continuous wave technique. Different from our study, it was observed that the duration of the retreatment procedure in root canal sealers containing calcium silicate was longer than that of AH Plus (286). This difference may be due to the usage of different obturation methods in the studies.

Reestablishment of apical patency positively affects the endodontic prognosis of teeth with periapical lesions (302). In our study, reconstruction of apical patency was evaluated using a #10 K type hand file. Apical patency was re-established in the groups between 72.73% and 100% on average. There was no statistically significant difference found between the six groups.

Oltra *et al.* investigated the effect of chloroform on reestablishing the apical patency of Endosequence BC Sealer and AH Plus in retreatment. Apical patency was achieved less in the group in which BC Sealer was retreated without chloroform compared to the other groups (269). Unlike our study; Oltra *et al.* used gutta-percha solvent in some groups during the retreatment process. We think that the reason for the different results obtained is due to the use of gutta-percha solvents. Hess *et al.* investigated the reestablishment of apical patency in the retreatment of Endosequence BC Sealer and AH Plus. AH Plus groups were obturated with single cone method whereas BC Sealer groups were obturated with continuous heat method. There were two AH Plus and BC Sealer groups in the study. In one of these groups, the canal filling was performed at the working length, while in the other group, it was filled 2 mm behind the apex. According to the

results of the study, the apical patency was found to be the least in the group where BC Sealer was filled 2 mm. Short of the apex, and there was no statistically significant difference between the other groups (259). In this study, the fact that the gutta-percha was positioned 2 mm behind the apical foramen in some groups may have allowed the apical region to be filled with sealer only. This may have caused the long duration of the retreatment process. Baranwal *et al.* investigated the reestablishment of apical patency of BioRoot RCS and AH Plus. There was no statistically significant difference between the two root canal sealers (266). Yang *et al.* investigated the reestablishment of the apical patency of Endosequence BC Sealer HiFlow, iRoot SP and AH Plus when they were obturated with the single-cone and continuous heat methods. In their study, apical patency could be established in all samples (18). Agrafioti *et al.* investigated the reestablishment of apical patency in the retreatment of AH Plus, MTA Fillapex and TotalFill BC Sealer sealers. Apical patency was reestablished in all samples (286). Yang *et al.* and Agrafioti *et al.* reported that 100% apical patency was achieved. In our study, while apical patency was 100% in some groups, these rates differ up to 73% in some groups. However, this difference was not statistically significant.

In our study, as a result of the push out test of the 6 groups, there was no statistically significant difference between the three sealers among the lateral condensation groups. In the single cone groups, the bond strength of Group (Cera-S) was found to be higher than Group (AH-S) and Group (BC-S) ($p=0,0001$). It can be speculated that when the single cone method is used, a thicker sealer layer is formed compared to the lateral condensation groups and this result may be caused by difference in thickness. Setya *et al.* observed the sealer thickness of the sealers when they were used with different obturation methods, using the stereomicroscope. As a result of the study, when the single cone method is used, the thickness of the sealer was found to be thicker than the lateral and vertical condensation methods (303).

As a result of the pairwise comparisons; only Group (Cera-S) and Group (Cera-L) groups did not show a statistically significant difference in terms of bond strength. TotalFill BC Sealer and AH Plus groups showed higher bond strength when obturated with lateral condensation compared single cone. This result is in agreement with the results in which the duration of retreatment procedure were examined. Duration of retreatment procedure was found to be longer in the TotalFill BC Sealer and AH Plus

groups when obturated with lateral condensation compared to the single cone method. There was no statistically significant difference between Group (Cera-S) and Group (Cera-L) in terms of duration of the retreatment procedures. This shows the strength of the chemical bond formed by CeraSeal with dentin in the single cone method. During the experiment, our personal experience was that the bond of CeraSeal to dentin is stronger.

Al Hiyasat *et al.* investigated the bond strength of AH Plus and TotalFill BC Sealer with push out test. In this study, lateral condensation, single cone and warm vertical condensation methods were used in subgroups. When the results of the study are examined; while the bond strength of AH Plus is affected by obturation methods used, obturation method used in BC Sealer groups does not affect the bond strength. When the groups obturated with single cone were compared, the bond strength of BC Sealer was found to be higher than that of AH Plus (189). Since warm gutta-percha methods were not used in our study, a direct comparison is not possible. Therefore, the results of our study differ from the study of Al Hiyasat *et al.* In addition, in our study, the bond strength of the BC Sealer group was found to be slightly higher than the AH Plus group among single cone groups, however this result was not reflected in the statistical analysis.

Carvalho *et al.* investigated the bond strength of AH Plus and Endosequence BC Sealer using the push out test. In their study, the sealer was applied to the root canal without gutta-percha. In this study, AH Plus showed higher bond strength compared to BC Sealer (300). The results of our study differ from Carvalho *et al.* This difference may be due to the application of canal sealers without gutta-percha.

Silva *et al.* selected 17 studies (about the bond strength of sealants with different contents) out of 1704 studies and evaluated the bond strength of sealants in a meta-analysis. The authors stated that there was no statistically significant difference between the bond strength of epoxy resin-containing sealants and the bond strength of bioceramic sealants (296). The results of Silva *et al.* and the results of our Laterally Condensed groups are in agreement.

6. CONCLUSION

This study planned to investigate the retreatability and bond strengths of TotalFill BC Sealer, CeraSeal and AH Plus. In order to evaluate the retreatability, remaining root filling volumes were evaluated with Micro-CT, duration of the retreatment procedure was measured and reestablishment of apical patency were evaluated. In order to evaluate the bond strength to dentine of the sealers, push out test was conducted.

- According to Micro-CT, it was observed that the root canal fillings could not be completely removed in any of the groups.
- When laterally condensed groups were evaluated, there was no statistically significant difference observed between TotalFill BC Sealer, CeraSeal and AH Plus in terms of remaining root filling volumes.
- When the root canals obturated with the single-cone were evaluated, Bioceramics (CeraSeal and TotalFill BC Sealer) had less remaining filling than epoxy resin based sealer (AH Plus).
- The obturation method did not affect the remaining root filling volumes of the same sealers.
- In AH Plus and TotalFill BC Sealer groups; duration of the retreatment procedure took longer in the lateral condensation compared to single cone groups. However, there was no statistically significant difference observed between the retreatment procedure of single-cone and lateral condensation groups of CeraSeal.
- Apical patency was re-established in the groups between %100 and %73.7. Therefore, there were no statistically significant difference between bioceramics and epoxy resin based sealers.
- AH Plus and TotalFill BC Sealers showed higher bond strength to dentine when lateral condensation method was used (compared to single cone obturation). However, obturation method did not affect the bond strength of CeraSeal.
- When laterally condensed groups were observed, there was no statistically significant difference observed between the three sealers in terms of bond

strength. However, when the single cone method was used, bond strength of CeraSeal was higher than TotalFill BC Sealer and AH Plus.



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8. APPENDICES

8.1. Ethical Approval



Sayı : 37068608-6100-15- 2226
Konu: Klinik Araştırmalar
Etik Kurul Başvurusu hk.

14/10/2021

İlgili Makama (Duygu Mustafa)

Yeditepe Üniversitesi Diş Fakültesi Endodonti AD. Prof. Dr. Rabia Figen Kaptan'ın sorumlu araştırmacı olduğu “**Epoksi Rezın ve Biyoseramik Esaslı Kök Kanal Patlarının Kök Kanalından Sökülebilirlikleri ve Bağlanma Dayanımlarının İncelenmesi**” isimli araştırma projesine ait Klinik Araştırmalar Etik Kurulu (KAEK) Başvuru Dosyası (2280) kayıtlı Numaralı KAEK Başvuru Dosyası, Yeditepe Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından 13.10.2021 tarihli toplantıda incelenmiştir.

Kurul tarafından yapılan inceleme sonucu, yukarıdaki isim belirtilen çalışmanın yapılmasının etik ve bilimsel açıdan uygun olduğuna karar verilmiştir (KAEK Karar No: 1509)

Prof. Dr. Hasan AYDIN

Yeditepe Üniversitesi
Klinik Araştırmalar Etik Kurul Başkan Yrd.

9. CURRICULUM VITAE

Personal Information

Name	DUYGU	Surname	MUSTAFA PAMUK
Place of Birth		Date of Birth	
Nationality		TC number	
e-mail		Phone	

Educational Background

Degree	Field of study	Graduated Institution	Graduation Year
PhD	Endodontics	Yeditepe University Institute of Health Sciences	
Postgraduate			
Undergraduate		Yeditepe University Faculty of Dentistry	2016
High School	-	Niřantaşı Nuri Akın Anadolu Lisesi	2009