Comparison of biological efficacy of two mineral trioxide aggregate based materials: *in vivo* study

Myeongyeon Lee

The Graduate School

Yonsei University

Department of Dentistry

Comparison of biological efficacy of two mineral trioxide aggregate based materials: *in vivo* study

A Dissertation Thesis
Submitted to the Department of Dentistry
and the Graduate School of Yonsei University
in partial fulfillment of the requirements
for the degree of Master of Dental Science

Myeongyeon Lee

June 2016

This certifies that the dissertation of Myeongyeon Lee is approved.

Thesis Supervisor: *Choi, Hyung-Jun*

Thesis Committee Member: *Choi, Byung-Jai*

Thesis Committee Member: *Song, Je Seon*

The Graduate School

Yonsei University

June 2016

연세대학교
YONSEI UNIVERSITY

감사의 글

본 논문이 완성되기까지 지도와 격려해주신 최형준 지도 교수님께 감사를 드립니다. 실험의 기틀에서 완성까지 모든 과정을 지도해주신 송제선 교수님, 논문 심사에 수고해주시며 지도해주신 최병재 교수님께도 깊은 감사를 드립니다. 아울러 관심있게 지켜봐주신 손흥규 교수님, 이제호 교수님, 강정민 선생님과 김승혜 교수님, 이효설 교수님께도 진심으로 감사드립니다.

또한 같이 실험 진행한 전미정 연구원, 이다선 위생사, 신영섭 선생과 바쁜 생활 속에서도 동료로서 연구에 힘이되어준 소아치과 의국원 여러분께도 감사드립니다.

마지막으로 변함 없는 사랑으로 바라봐 주시는 어머님, 의지가 되는 동생 중연이에게 감사의 말씀 전합니다.

2016년 6월

이명연 드림

Table of contents

List of Figures

List of Tables

Abstract

Comparison of biological efficacy of two mineral trioxide aggregate based materials: *in vivo* study

Myeongyeon Lee

Deptartment of Dentistry,
The Graduate School, Yonsei University
(Directed by professor Hyung-Jun Choi, D.D.S., M.S., Ph.D.)

Mineral trioxide aggregate (MTA) is considered a suitable material for vital pulp therapy, but has the limitations of causing tooth discoloration, having a long setting time, and presenting handling difficulties. Therefore, much effort has been focused on overcoming these problems by modifying the chemical composition of MTA-based materials used in pulp therapy. And newly developed products have been introduced to the market. The aim of this study was to compare the biocompatibility of Endocem Zr® and ProRoot MTA® by histopathologic analysis in a dog model of pulpotomy.

This study utilized 39 teeth of two beagle dogs. The exposed pulp tissues were treated by pulpotomy using ProRoot MTA (n=19) or Endocem Zr (n=20). After 8 weeks, the teeth were extracted and processed with hematoxylin-eosin staining for histologic evaluation. Development of a calcific barrier, the inflammatory response, and formation of an odontoblast layer were evaluated and scored from 1 to 4 in order of decreasing biological efficacy.

Most of the ProRoot MTA and Endocem Zr specimens developed a calcific barrier at the pulp amputation site and formed an odontoblast layer. However, some of the Endocem Zr specimens showed less calcific barrier formation with a greater inflammatory response and less odontoblast layer formation when compared with the ProRoot MTA specimens.

ProRoot MTA and Endocem Zr specimens developed a calcific barrier; however, ProRoot MTA was more biocompatible than Endocem Zr.

Keywords: MTA, pulpotomy, ProRoot MTA, Endocem Zr

Comparison of biological efficacy of two mineral trioxide aggregate based materials: *in vivo* study

Myeongyeon Lee

Deptartment of Dentistry,
The Graduate School, Yonsei University
(Directed by professor Hyung-Jun Choi, D.D.S., M.S., Ph.D.)

I. Introduction

In recent years, there have been considerable developments in vital pulp therapy following introduction of mineral trioxide aggregate (MTA). The purpose of vital pulp therapy is to maintain pulp viability and function. In cases of mechanical or traumatic pulp exposure, vital pulp therapies, including direct pulp capping, partial pulpotomy, and full pulpotomy, are recommended, especially when immature permanent teeth are involved (Cohenca et al., 2013; Fuks, 2008; Witherspoon, 2008).

Pulpotomy is a common procedure for maintaining pulp viability (Fuks, 2008). It is performed on primary molar teeth with extensive dental caries but without clinical or radiological evidence of pulp degeneration, and on permanent teeth with traumatic pulp exposure requiring apexogenesis (Cohenca et al., 2013; Fuks, 2008). For pulpotomy to be successful, the dressing material should ideally be bactericidal, harmless to the pulp and surrounding structures, and effective for healing the radicular pulp. Additionally, it should not interfere with physiologic root resorption (Sonmez et al., 2008).

To satisfy the above conditions, calcium hydroxide (CH) has traditionally been the material of choice for a pulpotomy procedure involving an immature permanent tooth (Farhad and Mohammadi, 2005). CH has antibacterial properties due to its high pH and can stimulate mineralization (Foreman and Barnes, 1990). However, despite the widespread use of CH in vital therapy for permanent teeth, MTA is increasingly recommended nowadays as a substitute for CH because of its low solubility and ability to form a strong calcific barrier (Witherspoon, 2008).

Although, there have been several reports on the good biocompatibility and favorable physicochemical properties of MTA (Camilleri and Pitt Ford, 2006; Rao et al., 2009), some reports discuss the limitations associated with clinical application of MTA, such as tooth discoloration, long setting time and handling difficulty (Islam et al., 2006). Therefore, much effort has been made to modify the chemical composition of MTA-based materials used in pulp therapy.

Endocem Zr® (Maruchi, Wonju, Korea) is a newly developed MTA-based material, the composition of which is shown in Table 1. According to previous research, tooth discoloration can be reduced by replacement of the radiopacifier (Kang et al., 2015), so the radiopacifier in Endocem Zr has been changed from bismuth oxide to zirconium oxide. Endocem Zr® has relatively a shorter final setting time (4 minutes ± 30 seconds) than

ProRoot MTA® (261 minutes ± 21 minutes) (Choi et al., 2013). However, Chung et al, in an in vitro study of the cytotoxicity of these materials, reported that Endocem Zr was more cytotoxic and associated with lower expression of vascular endothelial growth factor and angiogenin (Chung et al., 2015). However, further in vivo study is needed to evaluate the biocompatibility of this new material. The aim of this study was to compare the response of dental pulp to Endocem Zr with the response to ProRoot MTA by histopathologic analysis in a dog model of pulpotomy.

Table 1. Compositions of ProRoot MTA® and Endocem Zr®.

Material	Manufacturer	Composition	Content (wt%)
ProRoot MTA®	Densply, Tulsa, OK	Calcium oxide (CaO)	44.2
		Silicon dioxide (SiO_2)	21.2
		Bismuth oxide (Bi_2O_3)	16.1
		Aluminium oxide (Al_2O_3)	1.9
		Magnesium oxide (MgO)	1.4
		Sulphur trioxide (SO_3)	0.6
		Ferrous oxide (FeO)	0.4
Endocem Zr®	Maruchi, Wonju, Korea	Calcium oxide (CaO)	27-37
		Silicon dioxide (SiO_2)	7-11
		Aluminium oxide (Al_2O_3)	3-5
		Magnesium oxide (MgO)	1.7-2.5
		Ferrous oxide (Fe_2O_3)	1.3-2.3
		Zirconium oxide (ZrO_2)	43-46

II. Materials and Methods

1. Animal Model

Thirty-nine teeth from two beagle dogs (age 18–24 months) were used in this study. Incisors, canines, and first and second premolars of the maxilla and mandible were selected. All animal procedures conformed to the Institutional Animal Care and Use Committee, Yonsei Medical Center, Seoul, Korea (certification #2013-0317-4).

The teeth were divided into two groups on the basis of the pulp capping materials used in the cervical pulpotomy procedure as follows: Endocem Zr (n=20) and ProRoot MTA (n=19). Table 1 shows the composition of these materials.

2. Pulpotomy Procedure

Local anesthetic was delivered with using lidocaine (2% lidocaine hydrochloride with epinephrine 1:100,000; Kwangmyung Pharmaceutical Co., Seoul, Korea). The pulp was mechanically exposed via occlusal cavities using a high speed carbide bur No. 330 (H7 314 008, Brasseler, Germany) with water spray. After coronal accessment, the coronal portion of pulp was removed at the level of the cementoenamel junction. Bleeding was controlled by application of a sterile cotton pellet with light pressure and irrigation with sterile saline. The remaining pulp was covered with the experimental material, and cotton pellets moistened with saline were used to adapt MTA onto the pulp wound area. The cavities were restored with conventional glass-ionomer cements (Ketac-Molar, ESPE Platz, Seefeld, Germany). The whole procedures were carried out under general anesthetic condition and the animals were euthanized 8 weeks after the procedure.

3. Histological Analysis

The teeth were extracted with forceps and the apical third of each root was removed with a high-speed bur. The specimens were fixed in 10% buffered formalin (Sigma-Aldrich, St Louis, MO, USA) for 48 hours, demineralized in ethylenediaminetetraacetic acid (pH 7.4; Fisher Scientific, TX, USA) for 6 weeks, and then embedded in paraffin. For each specimen, 3-μm serial sections were made in the buccolingual direction and stained with hematoxylin-eosin. The specimens were observed with a BX40 optical microscope (Olympus Optical Co Ltd, Tokyo, Japan), and imaged using an Infinity 2.0 CCD digital camera (Lumenera Co, Ottawa, ON, Canada) and InnerView 2.0 image analyzer software (Innerview Co Ltd, Seongnam-Si, Gyeonggi-do, Korea).

The sections were examined by five investigators (YS, JK, HL, JH, and ML) blinded to the groups. Histopathologic analysis of the specimens included calcific barrier formation (continuity, morphological aspects, and thickness), extent of the inflammatory reaction (chronic or acute, number of cells, and extension of the reaction), hyperemia, and formation of an odontoblast layer. All findings were scored 1 to 4 using a modified version of the scoring system devised by Nowicka et al (H. Lee et al., 2015; Nowicka et al., 2013) (Table 2). The final score was determined by agreement of more than three observers.

Table 2. Scores Used during Histological Analysis of Calcific Barriers and Dental Pulp

Scores	Calcific barrier continuity
1	Complete dentin bridge formation
2	Partial/incomplete dentin bridge formation extending to more than one-half of the exposure site but not completely closing the exposure site
3	Initial dentin bridge formation extending to not more than one-half of the exposure site
4	No dentin bridge formation
Scores	**Calcific barrier morphology**
1	Dentin or dentin associated with irregular hard tissue
2	Only irregular hard tissue deposition
3	Only a thin layer of hard tissue deposition
4	No hard tissue deposition
Scores	**Tubules in calcific barrier**
1	No tubules present
2	Mild (tubules present in less than 30% of calcific barrier)
3	Moderate to severe (tubules present in more than 30% of calcific barrier)
4	No hard tissue deposition
Scores	**Inflammation intensity**
1	Absent or very few inflammatory cells
2	Mild (an average of <10 inflammatory cells)
3	Moderate (an average of 10–25 inflammatory cells)
4	Severe (an average >25 inflammatory cells)

Scores	Inflammation extensity
1	Absent
2	Mild (inflammatory cells next to dentin bridge or area of pulp exposure only)
3	Moderate (inflammatory cells observed in one-third or more of the coronal pulp or in the midpulp)
4	Severe (all of the coronal pulp is infiltrated or necrotic)
Scores	**Inflammation type**
1	No inflammation
2	Chronic inflammation
3	Acute and chronic inflammation
4	Acute inflammation
Scores	**Dental pulp congestion**
1	No congestion
2	Mild (enlarged blood vessels next to dentin bridge or area of pulp exposure only)
3	Moderate (enlarged blood vessels observed in one-third or more of the coronal pulp or in the midpulp)
4	Severe (all of the coronal pulp is infiltrated with blood cells)
Scores	**Odontoblastic cell layer**
1	Palisade pattern of cells
2	Presence of odontoblast cells and odontoblast-like cells
3	Presence of odontoblast-like cells only
4	Absent

III. Results

Histopathological evaluation was performed for 18 ProRoot MTA and 14 Endocem Zr specimens. The remaining specimens were excluded from analysis because of extraction or failed histopathologic processing. Each specimen of both groups was excluded from inflammation and odontoblast layer evaluation due to pulpal tissue amputation respectively. Tables 3, 4, and 5 show the percentages of scores for each material. In general, ProRoot MTA had better scores than Endocem Zr (Fig. 1).

1. Calcific Barrier Formation

The percentages of scores given for calcific barrier formation using each material are shown in Table 3. In total, 77.68% of ProRoot MTA and 57.14% of Endocem Zr specimens formed a calcific barrier that completely obliterated the pulp amputation site. Notably, formation of hard tissue was not observed in one Endocem Zr specimen. In terms of tubular defects in the calcific barrier, ProRoot MTA displayed a higher rate of score 1 and 2 than Endocem Zr.

2. Inflammatory response

In total, 47.06% of ProRoot MTA® and 30.77% of Endocem Zr ® specimens were found to be free of inflammation. Mild dental pulp congestion was observed in both groups, with the majority of specimens having a score of 2 (Table 4).

3. Odontoblastic Cell Layer

In the ProRoot MTA group, 23.53% of specimens had a score of 1 (indicating a palisading odontoblast pattern) and 53.95% had a score of 2 (indicating the presence of odontoblasts and odontoblast-like cells). However, the Endocem Zr group displayed distinct tendency compared with the ProRoot MTA group. The majority of specimens in the Endocem Zr group had scores of 2 (30.77%) or 3 (46.15%) (Table 5).

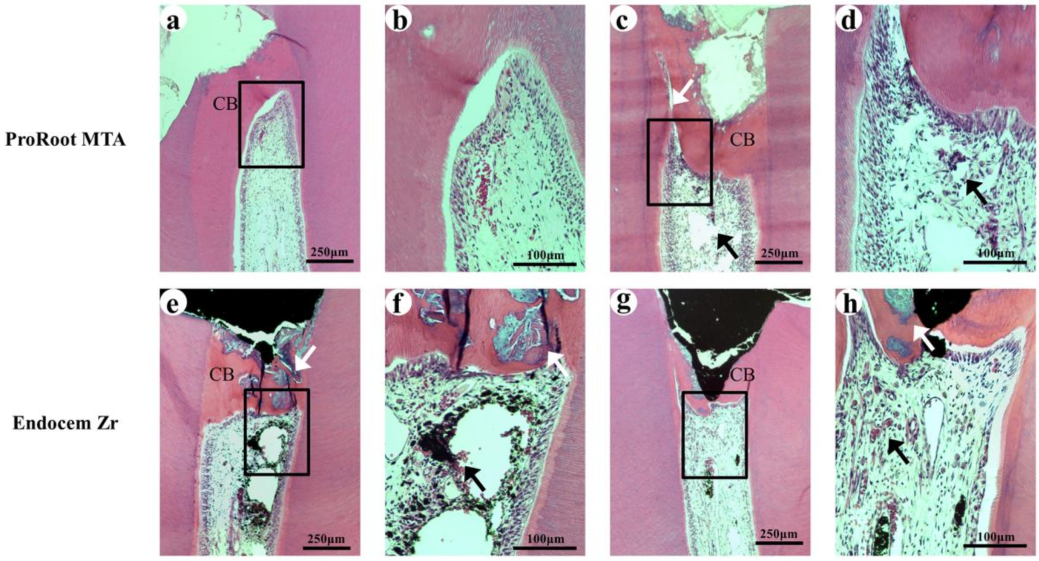

Figure 1 Formation of the CB in the ProRoot MTA® and Endocem Zr® groups after 8 weeks. (a-d) show features associated with ProRoot MTA (a, c: scale bar = 250 μm, b, d: scale bar = 100 μm) and (e-h) show features associated with Endocem Zr (e, g: scale bar = 250 μm, f, h: scale bar = 100 μm). Black arrows indicate the presence of inflammatory cells and white arrows indicate the presence of tubular defect in the CB (hematoxylin eosin staining, 40× magnification). Abbreviation: CB, calcific barrier.

Table 3. Score Percentages for Calcific Barriers

Groups	Scores			
	1	2	3	4
Calcific barrier continuity (%)				
ProRoot MTA®	77.68 (14/18)†	16.67 (3/18)	5.56 (1/18)	—
Endocem Zr®	57.14 (8/14)	28.57 (4/14)	7.14 (1/14)	7.14 (1/14)
Calcific barrier morphology (%)				
ProRoot MTA®	33.33 (6/18)	61.11 (11/18)	5.56 (1/18)	—
Endocem Zr®	14.29 (2/14)	64.29 (9/14)	14.29 (2/14)	7.14 (1/14)
Tubules in calcific barrier (%)				
ProRoot MTA®	16.67 (3/18)	55.56 (10/18)	27.78 (5/18)	—
Endocem Zr®	—	50.00 (7/14)	42.86 (6/14)	7.14 (1/14)

†(number of teeth receiving the score/total number of teeth evaluated)

Table 4. Score Percentages for Inflammatory Responses

Groups	Scores			
	1	2	3	4
Inflammation intensity (%)				
ProRoot MTA®	41.18 (7/17) †	41.18 (7/17)	11.76 (2/17)	5.88 (1/17)
Endocem Zr®	30.77 (4/13)	46.15 (6/13)	23.08 (3/13)	—
Inflammation extensity (%)				
ProRoot MTA®	47.06 (8/17)	41.18 (7/17)	11.76 (2/17)	—
Endocem Zr®	30.77 (4/13)	53.85 (7/13)	15.39 (2/13)	—
Inflammation type (%)				
ProRoot MTA®	47.06 (8/17)	52.94 (9/17)	—	—
Endocem Zr®	30.77 (4/13)	69.23 (9/11)	—	—
Dental pulp congestion (%)				
ProRoot MTA®	23.53 (4/17)	52.94 (9/17)	23.53 (4/17)	—
Endocem Zr®	23.08 (3/13)	61.54 (8/13)	15.39 (2/13)	—

†(number of teeth receiving the score/total number of teeth evaluated)

Table 5. Score Percentages for the Odontoblastic Cell Layer

Groups	Scores			
	1	2	3	4
Odontoblastic cell layer (%)				
ProRoot MTA®	23.53 (4/17) †	52.94 (9/17)	17.65 (3/17)	5.88 (1/17)
Endocem Zr®	15.38 (2/13)	30.77 (4/13)	46.15 (6/13)	7.69 (1/13)

†(number of teeth receiving the score/total number of teeth evaluated)

IV. Discussion

The aim of this study was to evaluate the biological efficacy of Endocem Zr using a dog model of pulpotomy. ProRoot MTA was used as a positive control. Both materials induced formation of a complete calcific barrier at the pulp amputation site with controlled inflammation of the pulp tissue. However, the ProRoot MTA specimens showed better calcific barrier morphology and fewer tubular defects than their Endocem Zr counterparts.

Endocem Zr is a pozzolan-based, white-colored MTA material developed to overcome the long setting time and tooth discoloration found with conventional MTA. Endocem® was the previously introduced pozzolan-based MTA material, and has been reported to have biocompatibility and mineralization potential comparable with that of ProRoot MTA (Choi et al., 2013; Song et al., 2014). However, in spite of the decreased setting time of Endocem, use of MTA for vital pulp therapy involving the anterior teeth is limited by its propensity to cause tooth discoloration (Yun et al., 2015). Bismuth oxide, which is used as a radiopacifier in MTA cement, interacts with the collagen in dentin, so could be the cause of tooth discoloration (Marciano et al., 2014). Therefore, the radiopacifier was replaced with zirconium oxide in the Endocem Zr formulation. Some authors have reported on the propensity for discoloration (Kang et al., 2015), biocompatibility (Chung et al., 2015), and physicochemical properties (Han et al., 2015; K. S. LEE et al., 2015) of Endocem Zr, but clinical use of this new material needs to be supported by in vivo research.

To evaluate the response of the dental pulp to each material, we used a modified version of the scoring system devised by Nowicka et al (Nowicka et al., 2013). This scoring system includes evaluation of the calcific barrier, inflammation of the dental pulp, dental pulp congestion, and formation of an odontoblast layer. We considered formation of a calcific barrier to be a beneficial pulp reaction after a pulpotomy procedure. However, formation of a calcific barrier could be interpreted either as a healing process or as a reaction to irritation (Al-Hezaimi et al., 2011; Schröder, 1985). Further, the dental pulp tissue could come into contact with the coronal aspects of the calcific barrier via tubular defects therein (Goldberg et al., 1984). Therefore, we included criteria for evaluation of the dental pulp, i.e., inflammation, congestion, and patterns of odontoblast-like cells.

Although both materials showed a capacity to form a calcific barrier, the ProRoot MTA specimens developed a better barrier in terms of quality and quantity. MTA produces calcium ions via a hydration procedure (Camilleri, 2008). Calcium ions stimulate the dental pulp cells at the amputation site to synthesize fibronectin dose-dependently (Mizuno and Banzai, 2008). Fibronectin plays a role in the differentiation of odontoblast-like cells and formation of the hard tissue barrier (Yoshiba et al., 1996). According to one in vitro study, the calcium ion concentration in Endocem Zr is less than that in ProRoot MTA (Han et al., 2015). An increased concentration of extracellular calcium induces the biological response of dental pulp cells and contributes to formation of the calcific barrier (Mizuno and Banzai, 2008). Therefore, the low extracellular calcium ion concentration achieved using Endocem Zr could explain the deficient calcific barrier formation found when this material is used.

The major component of Endocem Zr is zirconium oxide, which substitutes for bismuth oxide to reduce tooth discoloration. Zirconium oxide is a radiopacifier with the characteristics of biocompatibility (Dion et al., 1994) and radiopacity (Húngaro Duarte et al., 2009), and an ability to accelerate hydration (Li et al., 2013). In a previous study of radiopacifier replacement in Portland cement, zirconium oxide was reported not to participate in the hydration reaction (Camilleri et al., 2011) and not to affect its physical properties (Cutajar et al., 2011). However, the atomic number of zirconium is half that of bismuth, so the proportion of zirconium oxide in Endocem Zr needs to be higher than the proportion of bismuth oxide in ProRoot MTA to show a similar degree of radiopacity (Húngaro Duarte et al., 2009). According to the manufacturer's specifications, 43–46 wt% of Endocem Zr consists of zirconium oxide (Table 1) and this has been shown to have adequate radiopacity On the other hand, a decreased amount of calcium silicate in cement indicates the possible of shortcomings in terms of calcium ion release (Hungaro Duarte et al., 2012; K. S. LEE et al., 2015). Calcium ion release from Portland cement has been reported to decrease on addition of a radiopacifying agent (Camilleri et al., 2011; Hungaro Duarte et al., 2012). This could be a reason for the lower extracellular calcium ion concentration and calcific barrier formation found with Endocem Zr.

Sealing ability is another reason for the less favorable histologic result achieved using Endocem Zr. Coronal microbial leakage could cause reinfection of the pulp cavity (Madison and Wilcox, 1988), so the sealing ability of the capping material is essential for the clinical success of vital pulp therapy. It appears that MTA provides good sealing ability and marginal adaptation (Torabinejad and Parirokh, 2010). It has been reported that Endocem, the earlier pozzolan-based MTA material, has sealing ability comparable with that of ProRoot MTA (Choi et al., 2013). In contrast, Endocem Zr was found to have less favorable sealing ability than other MTA-based materials in a dye penetration study (K. S. LEE et al., 2015). However, the results of dye penetration studies do not necessarily reflect bacterial invasion (Barthel et al., 1999), and there are no reports on the mechanical properties of Endocem Zr. Thus, further studies are needed to evaluate the physicochemical properties of Endocem Zr.

In terms of biocompatibility, the only study published to date on cell viability with Endocem Zr reported initial transient cytotoxicity in the fresh mixed state and lower levels of angiogenic factors, such as vascular endothelial growth factor, angiogenin, and basic fibroblast growth factor-2 than ProRoot MTA (Chung et al., 2015; Song et al., 2014). Endocem is reported to be associated with less cell viability than ProRoot MTA and Angelus MTA®, especially in the fresh mixed state (Song et al., 2014). Chung et al considered the higher concentration of aluminum in pozzolan-based cement to be a cause of the initial transient cytotoxicity associated with this material (Chung et al., 2015). In spite of the initial transient cytotoxicity of Endocem Zr, inflammatory response and dental pulp congestion scores were comparable with those of ProRoot MTA. These data imply that Endocem Zr could be concerned in vital pulp therapy.

In the present study, ProRoot MTA achieved a better histologic result than Endocem Zr, especially in terms of formation of a calcific barrier. However, Endocem Zr has the advantages of a shorter setting time and not causing tooth discoloration Moreover, previous clinical studies have shown that the histologic findings for vital pulp therapy do not always coincide with clinical signs and symptoms (Caicedo et al., 2006; Iwamoto et al., 2006). Therefore, further clinical studies using human teeth may be required for evaluation of the biological efficacy of this material.

V. Conclusion

In conclusion, this in vivo study described the comparing of dental pulp response after pulpotomy procedure with ProRoot MTA® and Endocem Zr®. Endocem Zr® showed inferiority especially in calcific barrier formation. However, both materials were observed comparable result with inflammatory response of dental pulp tissue.

Reference

Al-Hezaimi K, Salameh Z, Al-Fouzan K, Al Rejaie M, Tay FR: Histomorphometric and micro–computed tomography analysis of pulpal response to three different pulp capping materials. *Journal of endodontics* 37(4): 507-512, 2011.

Barthel C, Moshonov J, Shuping G, Orstavik D: Bacterial leakage versus dye leakage in obturated root canals. *International Endodontic Journal* 32(5): 370-375, 1999.

Caicedo R, Abbott P, Alongi D, Alarcon M: Clinical, radiographic and histological analysis of the effects of mineral trioxide aggregate used in direct pulp capping and pulpotomies of primary teeth. *Australian dental journal* 51(4): 297, 2006.

Camilleri J: Characterization of hydration products of mineral trioxide aggregate. *International Endodontic Journal* 41(5): 408-417, 2008.

Camilleri J, Cutajar A, Mallia B: Hydration characteristics of zirconium oxide replaced Portland cement for use as a root-end filling material. *Dental Materials* 27(8): 845-854, 2011.

Camilleri J, Pitt Ford T: Mineral trioxide aggregate: a review of the constituents and biological properties of the material. *International Endodontic Journal* 39(10): 747-754, 2006.

Choi Y, Park S-J, Lee S-H, Hwang Y-C, Yu M-K, Min K-S: Biological effects and washout resistance of a newly developed fast-setting pozzolan cement. *Journal of endodontics* 39(4): 467-472, 2013.

Chung C, Kim E, Song M, Park J-W, Shin S-J: Effects of two fast-setting calcium-silicate cements on cell viability and angiogenic factor release in human pulp-derived cells. *Odontology*: 1-9, 2015.

Cohenca N, Paranjpe A, Berg J: Vital Pulp Therapy. *Dental Clinics of North America* 57(1): 59-73, 2013.

Cutajar A, Mallia B, Abela S, Camilleri J: Replacement of radiopacifier in mineral trioxide aggregate; characterization and determination of physical properties. *Dental Materials* 27(9): 879-891, 2011.

Dion I, Bordenave L, Lefebvre F, Bareille R, Baquey C, Monties J-R, et al.: Physico-chemistry and cytotoxicity of ceramics. *Journal of Materials Science: Materials in Medicine* 5(1): 18-24, 1994.

Farhad A, Mohammadi Z: Calcium hydroxide: a review. *International dental journal* 55(5): 293-301, 2005.

Foreman PC, Barnes IE: A review of calcium hydroxide. *International Endodontic Journal* 23(6): 283-297, 1990.

Fuks AB: Vital pulp therapy with new materials for primary teeth: new directions and treatment perspectives. *Journal of endodontics* 34(7): S18-S24, 2008.

Goldberg F, Massone EJ, Spielberg C: Evaluation of the dentinal bridge after pulpotomy andcalcium hydroxide dressing. *Journal of endodontics* 10(7): 318-320, 1984.

Húngaro Duarte MA, de Oliveira El Kadre GDa, Vivan RR, Guerreiro Tanomaru JM, Filho MT, de Moraes IG: Radiopacity of Portland Cement Associated With Different Radiopacifying Agents. *Journal of Endodontics* 35(5): 737-740, 2009.

Han L, Kodama S, Okiji T: Evaluation of calcium-releasing and apatite-forming abilities of fast-setting calcium silicate-based endodontic materials. *International endodontic journal* 48(2): 124-130, 2015.

Hungaro Duarte MA, Minotti PG, Rodrigues CT, Zapata RO, Bramante CM, Filho MT, et al.: Effect of Different Radiopacifying Agents on the Physicochemical Properties of White Portland Cement and White Mineral Trioxide Aggregate. *Journal of Endodontics* 38(3): 394-397, 2012.

Islam I, Chng HK, Yap AUJ: Comparison of the physical and mechanical properties of MTA and Portland cement. *Journal of Endodontics* 32(3): 193-197, 2006.

Iwamoto CE, Adachi E, Pameijer CH, Barnes D, Romberg E, Jefferies S: Clinical and histological evaluation of white ProRoot MTA in direct pulp capping. *American journal of dentistry* 19(2): 85, 2006.

Kang S-H, Shin Y-S, Lee H-S, Kim S-O, Shin Y, Jung I-Y, et al.: Color changes of teeth after treatment with various mineral trioxide aggregate–based materials: an ex vivo study. *Journal of endodontics* 41(5): 737-741, 2015.

Lee H, Shin Y, Kim S-O, Lee H-S, Choi H-J, Song JS: Comparative Study of Pulpal Responses to Pulpotomy with ProRoot MTA, RetroMTA, and TheraCal in Dogs' Teeth. *Journal of endodontics* 41(8): 1317-1324, 2015.

LEE KS, KIM JS, LEE DY, KIM RJY, SHIN JH: In vitro microleakage of six different dental materials as intraorifice barriers in endodontically treated teeth. *Dental materials journal* (0), 2015.

Li Q, Deacon AD, Coleman NJ: The impact of zirconium oxide nanoparticles on the hydration chemistry and biocompatibility of white Portland cement. *Dental* *materials journal* 32(5): 808-815, 2013.

Madison S, Wilcox LR: An evaluation of coronal microleakage in endodontically treated teeth. Part III. In vivo study. *Journal of endodontics* 14(9): 455-458, 1988.

Marciano MA, Costa RM, Camilleri J, Mondelli RFL, Guimarães BM, Duarte MAH: Assessment of Color Stability of White Mineral Trioxide Aggregate Angelus and Bismuth Oxide in Contact with Tooth Structure. *Journal of Endodontics* 40(8): 1235-1240, 2014.

Mizuno M, Banzai Y: Calcium ion release from calcium hydroxide stimulated fibronectin gene expression in dental pulp cells and the differentiation of dental pulp cells to mineralized tissue forming cells by fibronectin. *International endodontic journal* 41(11): 933-938, 2008.

Nowicka A, Lipski M, Parafiniuk M, Sporniak-Tutak K, Lichota D, Kosierkiewicz A, et al.: Response of human dental pulp capped with biodentine and mineral trioxide aggregate. *Journal of endodontics* 39(6): 743-747, 2013.

Rao A, Rao A, Shenoy R: Mineral trioxide aggregate—a review. *Journal of Clinical Pediatric Dentistry* 34(1): 1-8, 2009.

Schröder U: Effects of calcium hydroxide-containing pulp-capping agents on pulp cell migration, proliferation, and differentiation. *Journal of Dental Research* 64: 541-548, 1985.

Song M, Yoon T-S, Kim S-Y, Kim E: Cytotoxicity of newly developed pozzolan cement and other root-end filling materials on human periodontal ligament cell. *Restorative dentistry & endodontics* 39(1): 39-44, 2014.

Sonmez D, Sari S, Çetinbaş T: A Comparison of Four Pulpotomy Techniques in Primary Molars: A Long-term Follow-up. *Journal of Endodontics* 34(8): 950-955, 2008.

Torabinejad M, Parirokh M: Mineral Trioxide Aggregate: A Comprehensive Literature Review—Part II: Leakage and Biocompatibility Investigations. *Journal of Endodontics* 36(2): 190-202, 2010.

Witherspoon DE: Vital Pulp Therapy with New Materials: New Directions and Treatment Perspectives—Permanent Teeth. *Journal of Endodontics* 34(7, Supplement): S25-S28, 2008.

Yoshiba K, Yoshiba N, Nakamura H, Iwaku M, Ozawa H: Immunolocalization of fibronectin during reparative dentinogenesis in human teeth after pulp capping with calcium hydroxide. *Journal of dental research* 75(8): 1590-1597, 1996.

Yun D, Park S, Lee S, Min K: Tooth discoloration induced by calcium-silicate-based pulp-capping materials. *European Journal of Dentistry* 9(2): 165, 2015.

국문요약

개의 치수절단술을 이용한 두 MTA재료의 생체효능 비교

연세대학교 대학원 치의학과

이 명 연

지도교수: 최형준

Mineral trioxide aggregate (MTA) 는 뛰어난 생체적합성으로 생활치수치료시 우선적으로 고려되는 재료이다. 그러나, MTA는 치아 변색, 긴 경화 시간, 조작의 어려움과 같은 재료적 한계가 있다. 따라서 이러한 단점을 극복하기 위해 화학적 조성을 변화시킨 새로운 MTA 기반 재료의 개발이 이루어지고 있다. 본 실험의 목적은 개에서의 치수절단술 시행을 통해 새로운 재료인 Endocem Zr와 기존 ProRoot MTA의 생체적합성을 조직학적 분석으로 비교하였다.

2마리의 비글견에서 39개의 치아를 선택하였다. ProRoot MTA (n=19), Endocem Zr(n=20) 두개의 실험군으로 나누어 치수절단술을 시행하였으며, 8주 뒤 해당치아를 발거하여 조직학적 분석을 시행하였다.

실험 결과 두 재료 모두 대부분의 시편에서 석회화된 경조직 벽의 형성이 관찰되었다. 그러나, 일부 Endocem Zr의 시편은 ProRoot MTA에 비해 더

적은 양의 경조직 벽 형성과 상아모세포층 형성 및 더 심한 염증반응을 관찰할 수 있었다.

본 연구를 통해 Endocem Zr와 ProRoot MTA의 생체효능을 비교한 결과 두 재료 모두에서 치수절단부위의 경조직 벽 형성을 관찰 할 수 있었으나, Endocem Zr의 생체친화성이 ProRoot MTA에 비해 떨어짐을 알 수있었다.

핵심되는 말: MTA, 치수절단술, ProRoot MTA, Endocem Zr