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PREOPERATIVE FACTORS AFFECTING THE CONTROL OF MTA PLUG LENGTH PLACEMENT IN NON-VITAL TEETH WITH OPEN APICES

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REVIEW OF THE LITERATURE

1. Introduction

Treatment of permanent immature teeth with necrotic pulp has always been an endodontic challenge. Deep carious lesions, trauma or anatomical conditions may lead to pulp necrosis before the root development is complete. As a result, the root is left with a wide apex without an apical stop, which makes obtaining a tight apical seal hard, and thin dentinal walls, which leave the tooth prone to fracture.

In the past, a variety of techniques has been proposed in order to manage teeth with open apices, including the use of pastes as filling material (Friend 1967), apical surgery and the use of custom fitted gutta-percha cones (Stewart 1963, Friend 1966, Kerezoudis et al 1999). All of these techniques pose significant difficulties and have seen limited success (Rafter 2005).

As a result of the ongoing advances in dentistry, new techniques have emerged to deal with this type of teeth. Apexification with the use of calcium hydroxide, apexification with the use of an artificial barrier and regenerative endodontic procedures are the ones commonly used in recent years. The breakthrough that made these treatment options viable was the incorporation of novel dental materials into clinical practice, and especially the introduction of mineral trioxide aggregate (MTA) by Lee et al in 1993.

2. Mineral Trioxide Aggregate

2.1 Introduction

MTA was first described in the literature in 1993 as an aggregate of mineral oxides added to trioxides of tricalcium silicate, tricalcium aluminate and tricalcium oxide silicate oxide (Lee et al 1993). Initially, it was of grey color (GMTA) but in 2002 a white version (WMTA) was introduced in the market. The WMTA has been shown to contain lower amounts of iron, aluminum and magnesium (Asgary et al 2005, Song et al 2006). MTA consists of approximately 75% Portland cement, 20% bismuth oxide and 5% calcium sulfate dihydrate or gypsum. Additional minor trace elements may also be present.

2.2 Portland cement

Portland cement is manufactured by crushing the individual raw materials to acquire a smaller particle size and then mixing them to create a specific composition. The mixture is ground and blended together and heated to 1430-1650°C. This process fuses the materials together after a series of reactions which include evaporation of water, dehydration of the clays and decarbonation of the calcium carbonate. The mixture produced is called clinker and after it cools, it is ground to a fine powder size and is then considered Portland cement.

The Portland cement component in MTA consists of tricalcium silicate ($3CaO{\cdot}SiO_2$ or Ca_3SiO_5, also known as alite), dicalcium silicate ($2CaO{\cdot}SiO_2$ or Ca_2SiO_4, also known as belite), and tricalcium aluminate ($3CaO{\cdot}Al_2O_3$ or $Ca_3Al_2O_6$). These are found in both grey and white MTA, although less tricalcium aluminate is contained in the white versions (Asgary et al 2005). Tetracalcium aluminoferrite ($4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$) is present in the grey MTA, but not in white MTA.

In a typical Portland cement, tricalcium silicate and dicalcium silicate are in greatest proportion and are estimated to be roughly 75-80% of the cement, while tricalcium aluminate and tetracalcium aluminoferrite at about 10% each. In MTA, tricalcium aluminate is found in lower amounts (Belío-Reyes et al 2009), which led to the suggestion that MTA is produced in a laboratory environment (Camilleri 2007), although others have stated that it is manufactured in the same way as Portland cement (Darwell & Wu 2011).

2.3 Bismuth oxide and Gypsum

Bismuth oxide is added in MTA to increase the radiopacity of the material, as Portland cement is not sufficiently radiopaque for dental use. It may also play a minor role in the setting of MTA, as it is present in the calcium silicate hydrate structure (Camilleri 2007). Moreover, the addition of bismuth oxide to Portland cement seems to decrease its compressive strength and increase its porosity (Coomaraswamy et al 2007).

Gypsum is added in order to modify the setting time of the material. It mainly influences the reactions of the tricalcium aluminate. MTA contains approximately half the amount of calcium sulfate as found in Portland cement.

2.4 Physical properties of MTA

Hydration of MTA results in a colloidal gel that solidifies into a hard structure. Many factors have been identified to play a significant role in the characteristics of the set MTA, such as the powder-to-liquid ration, the mixing method, the pressure used for condensation, the pH of the environment etc. It has been stated that some of these factors cannot be easily controlled and therefore different results on the physical properties of MTA may be obtained during one study (Fridland & Rosado 2003).

2.4.1 Setting time

MTA is prepared by mixing its powder with sterile water in a 3 to 1 powder to liquid ratio. Its setting time has been found to be approximately 165 minutes (Torabinejad et al 1995a). GMTA exhibits longer setting times than the WMTA (Chng et al 2005). Moisture is a critical component for the setting of MTA, however deficient or excessive moisture may have a detrimental effect on MTA's properties (Walker et al 2006). The material's long setting times have been considered an important drawback, especially in 1-visit clinical applications, and many investigators have proposed different additives in order to overcome this.

2.4.2 Setting expansion

In vitro studies showed that mineral trioxide aggregate cements exhibit slight expansion (0,04 – 0,77%) when immersed in water-based solutions. The expansion appeared to be a water-dependent mechanism, as it did not occurred in cements immersed in oil-based solutions (Gandolfi et al 2009). This property of MTA may be one of the reasons of its excellent sealing ability. There are conflicting results regarding the setting expansion of different types of MTA. Although early studies showed that WMTA expands slightly more than GMTA (Chng et al 2005, Islam et al 2006), others reported that GMTA expanded significantly more than WMTA or Portland cement (Storm et al 2008).

2.4.3 pH

In chemistry, pH is the measure of the solvated hydrogen ion. Pure water has a pH close to 7. Solutions with a pH lower than 7 are acidic and those with a pH higher than 7 are alkaline.

The pH of MTA immediately after mixing is highly alkaline, approximately 10,2, and rises to 12,5 after 3 hours (Torabinejad et al 1995a). Fridland & Rosado (2003) have reported that the pH of MTA continues to exhibit high values even after 78 consecutive days. WMTA has been reported to display higher pH values for an extended period of time when compared to GMTA. The high pH values of the material are caused by the precipitation of calcium hydroxide after the hydration of MTA (Bozeman et al 2006).

2.4.4 Solubilty

Solubility is defined as the maximum amount of a substance that will dissolve in a given amount of solvent at a specific temperature. It is apparent from the definition that the solubility of a substance greatly depends on the solvent, as well as the temperature and pressure.

The solubility of MTA is still a matter of debate. Most studies report low or no solubility for the material (Torabinejad et al 1995a, Danesh et al 2006), but other researchers reported high solubility over a long period of time (Fridland & Rosado 2005). As mentioned before, the water-to-powder ratio affects the solubility of the MTA, as higher ratios increase the solubility and the porosity of the material (Fridland & Rosado 2003).

2.4.5 Compressive strength

Compressive strength is defined as the capacity of a material to withstand loads tending to reduce its size. MTA exhibits significantly lower compressive strength than other dental materials, like amalgam, IRM and Super-EBA after the first 24 hours. However, after 3 weeks there is no significant difference between the same materials in terms of compressive strength (Torabinejad et al 1995a). One possible explanation for this finding is the different hydration rates of tricalcium and dicalcium silicate (Dammaschke et al 2005). As a result, MTA's compressive strength peaks several days after mixing.

2.4.6 Flexural and push-out strength

Flexural strength is defined as the ability of a material to withstand bending forces applied perpendicular to its longitudinal axis. Push-out strength determines the extent of resistance to the dislodgement of a filling material when applied to root canal dentin. Both of these physical properties are improved when the material receives enough moisture after placement, usually by placing a moist cotton pellet in direct contact with MTA (Walker et al 2006, Gancedo-Caravia & Garcia-Barbero 2006).

2.4.7 Radiopacity

Torabinejad et al (1995a) reported that the mean radiopacity for MTA was at 7,17mm of an equivalent thickness of aluminum. This value is higher than the ones reported for Super EBA or IRM. However, a study that directly compared the radiopacity of these materials reported that MTA was less radiopaque than both Super EBA and IRM (Laghios et al 2000). Interestingly, WMTA has been reported to be more radiopaque than GMTA (Chng et al 2005, Islam et al 2006), despite the fact that both of them contain similar amounts of bismuth oxide. The presence of other substances in WMTA might be the reason for its higher radiopacity.

2.4.8 Particle size

The size of the Portland cement particles in WMTA ranges from less than 1 to 30 µm and the bismuth oxide particles from 10 to 30 µm (Camilleri 2007). WMTA particles appear to be more homogenously sized than those of GMTA (Komabayashi & Spångberg 2008), with fewer larger particles (Camilleri et al 2005), which may explain its better handling properties. In comparison to Portland cement, Dammanschke et al (2005) reported that WMTA has more uniform and smaller sized particles, but their shape is very similar (Komabayashi & Spångberg 2008). As a result, the particles contained in the hydrated WMTA are smaller than both the GMTA and the industrial Portland cement (Asgary et al 2004, Asgary et al 2005).

2.4.9 Porosity

Porosity is a measure of the void spaces within a material. Many studies have evaluated this property of the MTA and the amount of porosity in mixed cement depends on the amount of the water added to the material, the entrapment of air bubbles during the mixing procedure and the acidic pH of the environment (Namazikhah et al 2008, Saghiri et al 2008).

2.4.10 Microhardness

Microhardness or indentation hardness is the hardness of a material exposed to low applied loads. This property of MTA can be influenced by the pH of the environment, the thickness of the material, the condensation pressure, the amount of the entrapped air in the mixture, humidity, acid etching of the material and temperature. An acidic environment can have a negative effect on the microhardness of both WMTA and GMTA (Namazikhah et al 2008). Lee et al (2004) investigated the effect of the environmental conditions on the hydration behavior of MTA and reported that the material consists of needle-like and dominant cubic crystals. When the environment had an acidic pH, the needle-like crystals were absent and that was deemed the reason why the material exhibited decreased microhardness.

The thickness of material is another factor that may affect the microhardness of the MTA. A study compared the micorhardness of 2mm and 5mm-thick GMTA and WMTA plugs and regardless the type of the material and the placement technique, a 5mm-thick plug was harder that a 2mm-thick plug (Matt et al 2004).

2.5 Physicochemical properties of MTA

In 2005, Sarkar et al immersed MTA slurry samples into a synthetic tissue fluid for 3 days and used inductively coupled-plasma atomic spectroscopy to analyze the precipitates found in the solution. They reported high concentration of calcium as well as the presence of other cations in lower concentrations, that leached from MTA into the synthetic tissue fluid. They suggested that this release of calcium in large quantities from MTA triggers a chain of physicochemical reactions in biological environments that result in the formation of hydroxylapatite in a diffusion-controlled reaction between hydroxylapatite and dentin. This formation leads to a strong chemical bond between material and dentin thus filling any possible gap in between the two. The afore-mentioned activity may be considered responsible for the favorable sealing ability, biocompatibility and dentinogenic dynamic of the MTA.

3. Apexification with calcium hydroxide

3.1 Calcium hydroxide

Calcium hydroxide was first used in Endodontics as a direct pulp-capping material in 1920 by Hermann. It is an odourless white powder with low solubility in water. The pure powder has a high pH, approximately 12,5-12,8 (Farhad & Mohammadi 2005). The material is chemically classified as a strong base and its main properties are a result of the ionic dissociation of Ca^{2+} and OH^{-} and their effect on vital tissues (Siqueira & Lopes 1999).

The release of hydroxyl ions in an aqueous environment and the high pH are responsible for the antimicrobial activity (Siqueira 2001) and the mineralizing action of calcium hydroxide (Estrella et al 1995). Due to these properties, calcium hydroxide has been used extensively in various applications in Endodontics: as an intracanal medicament, as a base for root canal sealers, as a pulp-capping agent and in apexification treatment (Mohammadi & Dummer 2011).

3.2 Apexification with calcium hydroxide

The apexification technique with the use of calcium hydroxide mixed with camphorated parachlorophenol was first introduced in 1964 by Kaiser. In 1966, Frank proposed a step-by-step procedure and described four types of apical closure commonly observed with this technique. A number of researchers studied different mixtures of calcium hydroxide to reduce cytotocixty. Cresatin, saline, sterile or distilled water and methylcellulose have been used together with calcium hydroxide and have demonstrated similar clinical success (Rafter 2005).

3.3 Technique

The first phase of treatment consists of debriding the canal by minimal instrumentation of the thin dentinal walls and abundant irrigation with sodium hypochlorite. It is advisable to confirm the working length radiographically as the electronic apex locator does not give reliable readings due to the wide apical foramen (Hulsmann and Pieper 1989). Overinstrumentation should be avoided in order not to damage the periapical tissues (Torneck et al 1973, Cooke & Rowbotham 1988). Regarding the sodium hypochlorite, care must be taken to avoid extrusion beyond the apex. Furthermore, low concentrations are preferable to minimize the possible adverse effects to the periapical tissues. The high volume of the irrigant used should compensate for the lower concentration (Del Caprio-Perochena et al 2015). The canal is then dried out with sterile paper points and calcium hydroxide paste is applied for 1-3 weeks.

The technique of the hard tissue barrier formation is similar to the one used in vital pulp therapy. Calcium hydroxide is packed initially against the apical tissue with a plugger or a thick paper point and then additional is added in order to fill the rest of the canal up to the point of the orifice. In clinical practice, it is advisable to use a preparation of calcium hydroxide without a radiopacifier in order to be able to evaluate the wash out of the medicament throughout the treatment, as it is possible that the radiopacifier will not wash out as readily as the calcium hydroxide itself (Metzger et al 2001). Proper placement of pure calcium hydroxide makes the root appear as obliterated on the x-ray, since the medicament exhibits similar radiopacity to dentin (Pires de Souza et al 2010).

Evaluation of the hard tissue barrier formation and the possibility of calcium hydroxide wash out is performed every 3 months by radiographic examination. If the root canal becomes well visible in the x-ray, wash out of the intracanal medicament is assumed and a fresh calcium hydroxide mixture should be placed inside the canal. Otherwise, the medicament can be left in place for another 3 months. Despite the common practice of replenishing the calcium hydroxide dressing every 3 months, there has been a number of researchers advocating single application of calcium hydroxide. Chawla (1986) was the first to suggest that one-time placement of the medicament suffices for the barrier formation. He reported that 24 out of 26 non-vital teeth with open apices developed a calcified apical barrier after a single placement of calcium hydroxide medication, while the rest 2 teeth required repeated dressings. Subsequent studies confirmed that there are no significant clinical benefits from the scheduled periodic changes of the calcium hydroxide dressing (Chosack et al 1997). On the contrary, repeated applications may hinder the healing process because of the initial toxicity of the calcium hydroxide (Lengheden et al 1991). As a result, it has been proposed that the intracanal dressing should be replaced only when the tooth becomes symptomatic or wash out is evident (Cvek 1972, Feiglin 1985). On the other hand, Abbott (1988) suggested that regular replacement of the calcium hydroxide medicament may lead in faster hard tissue barrier formation with subsequent shorter treatment time and fewer complications. These conclusions were based on the results of previous studies by Cvek (1972) and Yates (1988), who applied the calcium hydroxide dressing once and multiple times respectively. Cvek reported that complete formation of the apical hard tissue barrier was observed in 18,2 months on average, while Yates reported that a mean time period of 9 months was needed. Moreover, Abbott pointed out that an additional advantage of multiple dressings is the opportunity to directly evaluate the formation of the apical barrier during the session when calcium hydroxide is replaced.

Hard tissue barrier completion may take anywhere from 3 to 24 months (Kleier & Barr 1991, Sheehy & Roberts 1997, Finucane & Kimirons 1999). It was found that a younger age as well as absence of apical pathology may decrease the time for apexification (Cvek 1972, Walia et al 2000), even though other researchers dispute that claim (Kleier & Barr 1991). When the barrier formation is indicated radiographically and can be confirmed clinically by probing against it gently with an instrument or a paper point, the canal is considered to be ready for filling with gutta-percha and sealer. It is important not to use excessive force vertically while condensing the gutta-percha as it may cause dislodgement of the apical barrier (Abbott 1988).

3.4 Biological mechanism

Mitchell and Shankwalker (1958) were the first to demonstrate the potential of calcium hydroxide to promote heterotopic bone formation when implanted in the connective tissue of rats. The healing process of the periapical tissues after the application of calcium hydroxide is similar to that of the pulp tissue (Holland et al 1977). Calcium hydroxide generates a multilayered necrosis that acts as a low-grade irritation for the underlying tissue, creating the base of a matrix that is capable of mineralization (Dylewski 1971, Schröder & Granath 1971).

The pattern of the hard tissue barrier created by the use of calcium hydroxide has been described as a cap, bridge or ingrown wedge (Ghose et al 1987) and the mineralized tissue has been identified as cementum (Steiner & van Hassel 1971), dentin, bone, osteodentin (Dylewski 1971) or osteocementum (Mohammadi & Dummer 2011). The hard tissue is porous (Walia et al 2000) and appears to form from the periphery to the center of the apex in decreasing concentric circles (Steiner & van Hassel 1971). Histologic analysis and scanning electron microscopy revealed that the apical barrier consists of different layers. The outer surface displayed irregular topography with indentations and convexities and appeared similar to cementum. The central layer consisted of a mix of irregular dense, fibrocollagenous connective tissue, with areas of highly mineralized dystrophic calcifications (Baldassari – Cruz et al 1998).

3.5 Outcome

A number of studies regarding the outcome of calcium hydroxide apexification has been conducted, reporting comparable results. Many of them have not set strict criteria for success or failure. Commonly, successful cases are considered those without any signs or symptoms of periapical disease. Specifically, the absence of pain, swelling, sinus tract, pathological mobility, tenderness to percussion and internal or external root resorption are usually recorded (Mendoza et al 2010, Bezgin et al 2012). In calcium hydroxide apexification cases, another criterion that needs to be fulfilled in order to consider a case successful is the formation of an apical barrier (Yates 1988). The barrier formation can be confirmed either radiographically or by tactile sensation (El-Meligy & Avery 2006, Bezgin et al 2012). El Meligy and Avery used the term "radiographic success" in order to distinguish the absence of clinical signs and symptoms from the apical barrier formation, but most researchers take both of criteria into consideration in order to classify a case as successful. The findings of those studies are summarized in **Table 1.**

Table 1. Reported outcome of the apexification technique with calcium hydroxide.

Study	***N***	***Follow Up Period***	***Success Rate***	***Apical Barrier Formation***
Ghose et al, 1987	51	NR	88,2%*	96,0%
Yates, 1988	22	NR	77,3%	100,0%
Kleier & Barr, 1991	48	NR	95,8%, remaining 2 could not be followed up	100,0%
Walia et al, 2000	15	24m	100,0%	100,0%

Dominguez Reyes et al, 2005	26	NR	100,0%	100,0%
Pradhan et al, 2006	10	NR	100,0%	100,0%
El Meligy & Avery, 2006	15	12m	87,0%	87,0%
Mendoza et al, 2010	28	24m	92,9%	100,0%
Yassen et al, 2012	23	3-36m	78,26% helaed, rest healing	100,0%
Bezgin et al, 2012	10	6-15m	100,0%	100,0%
Jeeruphan et al, 2012	22	NR	77,3%	NR
Damle et al, 2012	15	3-12m	93,3%	93,3%
Ghosh et al, 2014	51	3-12m	86,3%	72,5%
Alobaid et al, 2014	7	22m	100,0%	NR
Bonte et al, 2015	16	12m	75,0%	50,0%
Lee et al, 2015	20	NR	100,0%	100,0%
Lin et al, 2017	34	12m	100,0%	82,4%
Kandemir Demirci et al, 2019	34	12-48m	79,4% + 11,8% healing	91,0%
Pereira et al, 2021	22	12-24m	86,4%	NR

3.6 Disadvantages

The apexification technique using calcium hydroxide demands multiple visits over a long period of time. The patients' failure to return for future appointments or the possibility of a fracture between the scheduled appointments that would deem the tooth unrestorable are the main drawbacks of this technique.

In 1992, Cvek reported a higher than expected incidence of cervical fractures on immature teeth that had been treated with long-term calcium hydroxide dressing. Andreasen et al (2002), based on the previous findings, hypothesized that the calcium hydroxide may alter the mechanical properties of dentin. To test their hypothesis, they applied a calcium hydroxide dressing to intact immature sheep mandibular incisors and recorded the fracture strength of the teeth after 14 days, 1, 2, 3, 6, 9 and 12 months. They concluded that calcium hydroxide has a detrimental effect on the mechanical properties of dentin, that is increased over time. They suggested that a possible mechanism for the changes in dentin is the denaturation of the organic matrix due to the pH changes after calcium hydroxide placement. In 2008, Hatibović-Kofman et al repeated a similar experiment on mature sheep mandibular incisors after cutting off the last 3mm of the root. Their sample consisted of three groups, the control group with teeth that were left untreated and two experimental groups, with teeth filled with either calcium hydroxide or MTA. The fracture strength of the teeth of each group was measured after 2 weeks, 2 months and 1 year. They reported that after 1 year there was no significant difference between the control group and the calcium hydroxide group, but the teeth filled with MTA required a statistically significant larger force to fracture. Hawkins et al (2015) tested the effect of three different calcium hydroxide formulations on immature deciduous sheep teeth, using similar methods with the previous studies. After evaluating the teeth at 1, 3 and 6 months intervals, they reported that there were not any statistical significant differences in the fracture resistance between either the experimental groups or between any of the experimental and the negative control groups. They attributed their findings to the use of commercial formulations instead of pure calcium hydroxide. Three years later, Kahler et al (2018) studied the fracture resistance of 330 sheep mandibular incisors after dressing the canals with 3 different commercial formulations of calcium hydroxide. Untreated teeth were used as negative controls and teeth filled with pure calcium hydroxide as positive controls. They recorded the fracture resistance of each group after 3, 6 and 9 months and concluded that there were no statistical differences between any of the groups. They concluded that calcium hydroxide treatment is not associated with a reduction in the fracture strength of the teeth. Instead, based on Cvek's (1992) findings, they stated that the increasing frequency of fractures in immature teeth is associated with decreasing stage of root development.

4. Apexification with an artificial barrier

4.1 Introduction

The treatment of permanent teeth with necrotic pulps and open apices in one visit is not a novel approach. Koenings et al published an article in 1975 using a tricalcium phosphate resorbable ceramic material to induce apical closure in permanent teeth of adult primates. Four years later, Coviello and Brilliant (1979) proposed an one-visit technique using calcium hydroxide or tricalcium phosphate as apical barriers to condense gutta-percha against. Since then, a variety of different materials have been used as artificial barriers: resorbable oxidized cellulose in combination with amalgam, freeze-dried cortical bone, freeze-dried dentin and dentinal shavings (Morse et al 1990).

In 1999, Torabinejad and Chivian included apexification as a potential clinical application for mineral trioxide aggregate (MTA), which had been used as a retrograde filling in apical surgery and as a repairing material for perforations. Early research had already shown that MTA exhibited high biocompatibility (Torabinejad et al 1995b) and good sealing ability (Torabinejad et al 1993), and the first animal study using MTA as an apical barrier reported promising results (Shabahang et al 1999).

Following the advances in dental materials, new bioceramic materials, like Biodentine, calcium-enriched mixture cement and EndoSequence/TotalFill BC Root Repair Material, have been used as substitutes of MTA in artificial barrier apexification. The newer bioceramic materials possess similar characteristics to MTA, but also present a few different properties, such as shorter setting time, higher mechanical strength (Guo et al 2016) and reduced discoloration potential (Kahler & Rossi-Fedele 2016), in an attempt to improve their clinical use in endodontic applications. Despite the promising early clinical results of these materials, MTA is still considered the gold standard in terms of the artificial barrier apexification technique.

4.2 Technique

As mentioned before, disinfection of the root canal is of paramount importance in every technique applied. Mechanical and chemical preparation of the canals is similar to what was described in the calcium hydroxide section. Despite apexification with an artificial barrier being described as an one-visit technique in the literature, short-term calcium hydroxide dressing may still be placed inside the canal until the tooth becomes asymptomatic (Torabinejad & Chivian 1999, Giuliani et al 2002).

After the canal is clean and dry, the MTA mixture is transferred to the apical 3 to 5mm of the canal with an appropriate carrier and is condensed using suitably sized pluggers. Sterile paper points may be used for better adaptation of the material to the canal walls and to remove the excess moisture (Ree & Schwartz 2017). Correct placement of the plug is confirmed radiographically. In the past, at this point a wet cotton pellet was placed on top of the apical plug for at least a few hours or a few days (Torabinejad & Chivian 1999, Giuliani et al 2002). Nowadays, with the introduction of fast-setting bioceramic putties, this step is not considered necessary as long as the bioceramic material does not dry out (Shokouhinejad et al 2016). Thermoplasticized gutta-percha is then injected inside the canal and the tooth is ready to be restored permanently.

Due to the difficulty in MTA handling, a variety of techniques has been proposed in order to condense the apical plug, like the use of customized gutta-percha points (Günes & Aydinbelhe 2012) and different sizes of Thermafil carriers (Giovvaruscio et al 2013). In addition, in vitro studies have demonstrated that ultrasonic agitation can be used to enhance the mixing and placing techniques in order to improve the marginal adaptation and bond strength of the material to the dentinal walls (Parashos et al 2014, Ghasemi et al 2017, Aguiar et al 2019).

4.3 Biological mechanism

MTA is a bioactive material which is mainly composed of calcium silicate (Camilleri et al 2005). As such, it can conduct and induct hard tissue formation when it is in contact with human tissues. This property seems to be related to the release of calcium hydroxide in the form of calcium ions upon the setting of the material (Reyes-Carmona et al 2009). The concentration of calcium ions enhances osteoblastic viability and modulates cell attachment and proliferation (Maeno et al 2005). In 2005, Sarkar et al described the creation of a white layer in the interface between MTA and dentin in vitro and they were the first to suspect that it was hydroxyapatite. Previously, the calcified tissue in association with MTA had been described as dentinal bridge, osteodentin or reparative dentin. A few years later, Reyes-Carmona et al identified the hard tissue in contact with the MTA to be carbonated apatite. More studies have demonstrated the high potential of MTA to induce the formation of apatite on its surface (Gandolfi et al 2010, Han et al 2015).

MTA also exhibits a highly alkaline pH, due to the release of hydroxyl ions (Eldeniz et al 2006). High pH contributes to hard tissue precipitation (Sarkar et al 2005), as well as the creation of an environment unfavorable for bacterial growth (Eldeniz et al 2006). MTA appears to preserve the alkaline pH for an extended period of time. Fridland and Rosado (2005) reported high pH, ranging between 11 and 12, for 78 cumulative days.

4.4 Outcome

As MTA gained popularity, more research has been conducted regarding the outcome of artificial barrier apexification with the use of this material. There is an agreement across the literature that MTA plug treatment exhibits comparable outcomes to the calcium hydroxide apexification. Calcified tissue barrier formation has not been considered essential in the success of this technique, and only few researchers reported its creation in their results. Although it seems that apical calcified tissue is present in less artificial barrier apexification cases, the inability to assess the situation clinically, unlike the calcium hydroxide cases, should be taken into consideration. **Table 2** reports the findings of the literature regarding the outcome of MTA apexification.

Table 2. Outcome of MTA apexification treatment

Study	***N***	***Follow Up Period***	***Success Rate***	***Apical Barrier Formation***
El Meligy & Avery, 2006	15	12m	100,0%	NR
Simon et al, 2007	43	6-36m	62,8% (81% relative success)	25,6%
Witherspoon et al, 2008	78	6m – 4,87 yrs	75,6% (92,2% relative success)	NR
Holden et al, 2008	20	12-44m	85% (90% relative success)	NR
Moore et al, 2011	22	18m minimum	90,9%	63,6%
Damle et al, 2012	15	12m	100,0%	93,3%
Jeeruphan et al, 2012	19	NR	68,0%	NR
Mente et al, 2013	252	12-128 m	90,1%	NR
Nagy et al, 2014	9	18m	100,0%	NR
Pace et al, 2014	16	10 yrs	93,8%	NR
Bonte et al, 2015	15	12m	82,4%	76,5%

Ree & Schwartz, 2017	69	5-15 yrs	96,0%	NR
Silujjai & Linsuwanont, 2017	29	12-96m	80,8%	NR
Kandemir Demirci et al, 2019	39	12-48m	74,4% (92,3% relative success)	74,0%
Tek & Keskin, 2021	14	12m	57,1%	NR
Caleza-Jimenez et al, 2022	9	6-66m	100,0%	NR

4.5 Fracture resistance

Catastrophic fractures are a common mode of failure for immature teeth treated with an apexification technique (Cvek 1992). It has been speculated that MTA obturation can increase the fracture resistance of immature teeth. Bortoluzzi et al (2007) studied the effect of MTA plug on the fracture resistance of standardized bovine teeth and reported higher values for teeth treated with MTA plug and restored with a metal post. As described previously (see section 3.5), Hatibović-Kofman et al (2008) found that MTA filled teeth showed increased fracture resistance after 1 year compared to untreated and calcium hydroxide filled teeth. They also performed immunofluorescence staining on one tooth of each group and reported that MTA induced the expression of Tissue Inhibitor of Metalloproteinases 2 (TIMP-2) in dentin matrix. They suggested that the MTA-induced TIMP-2 upregulation and the subsequent suppression of the degenerative activity of Matrix Metalloproteinases 2 and 14 (MMP-2 and MMP-14) may explain their findings, but could not propose a mechanism for TIMP-2 expression.

However, it is still unclear whether the thickness of the apical plug affects the fracture resistance of the root. Girish et al (2017) reported better results for the completely obturated teeth in comparison to those with a 5mm-thick apical plug. In contrast, Çiçek et al (2017) found that teeth with 3mm and 6mm-thick apical plugs fractured under higher loads. Finite element analysis of teeth filled with MTA plugs of different thickness supports their findings (Eram et al 2020). More specifically, the researchers generated a 3D finite element analysis model using a simulated immature maxillary central incisor and created 7 different models representing the immature tooth without any reinforcement material, the same tooth with a 4mm MTA apical plug, a 4mm Biodentine apical plug, a 4mm Bioaggregate apical and the tooth completely filled with 8,5mm of MTA, Biodentine and Bioaggregate. They concluded that the 4mm MTA apical plug exhibited higher fracture resistance than the 8,5mm MTA obturation, as well as that the latter led to higher loads at the cervical area of the tooth. Moreover, the stress increased when the 4mm MTA apical plug was replaced by either Biodentine or Bioaggregate, although the reported differences were not statistically significant.

The restoration of the apexification-treated teeth plays a key part in the survival of these teeth and research shows that the application of intracoronal bonded restorations can increase their fracture resistance (Desai & Chandler 2009). In addition, laboratory studies have reported that the use of fiber posts can further improve the fracture resistance of immature teeth (Schmoldt et al 2011, Brito-Junior et al 2014).

4.6 Disadvantages

Despite the excellent physical and biological properties of MTA, a number of drawbacks has been reported in the literature. One of its main disadvantages is the potential discoloration of the teeth treated with MTA. Despite the introduction of white MTA in clinical practice, it still produces a darkening effect on dentin (Moore et al 2011, Ioannidis et al 2013). Considering that the MTA plug technique is commonly applied on anterior traumatized teeth, it is understandable why tooth discoloration is such an important drawback. Internal bleaching has been used successfully on teeth previously treated with MTA apexification (Ree & Schwartz 2017), but new materials have been proposed in order to minimize dentin discoloration, such as Biodentine, EndoSequence Root Repair Material and other (Możyńska et al 2017).

MTA apexification cannot promote the strengthening of the thin dentinal walls in teeth with open apices, thus leaving them prone to fracture. Whether MTA in combination with a proper restoration can enhance the fracture resistance of an immature tooth is still questionable.

Another disadvantage is the difficulty in retreating a tooth obturated with MTA. Removal of the material can be achieved in straight canals with the use of ultrasonics, but is extremely challenging beyond the curvature in curved canals (Boutsioukis et al 2008).

Lastly, MTA is a material with difficult handling properties. As a result, the placement of the material at the radiographic apex may prove challenging. Unintentional extrusion of MTA in the periapical tissues has been described in the literature and its role on periapical healing has been examined. Studies agree on the deleterious effect of MTA extrusion on the time needed to complete periapical healing, but its role on success rate of MTA apexification is still debatable. Mente et al (2013) reviewed the outcome of 252 teeth treated with apexification with MTA apical plug for 12-128 months. In 43 of the teeth, extrusion of the material was present. The recorded success rate for the teeth with MTA extrusion was 86%, while the teeth without extrusion exhibited a success rate of 91%. The difference was found to be borderline statistically significant. Other studies do not support this finding (Demiriz & Haraz-Bodrumlu 2017, Roy et al 2021). Demiriz & Haraz-Bodrumlu (2017) reviewed the outcome of 55 maxillary central incisors treated with MTA apexification for 3 years, with 21 of them presenting unintentional extrusion of MTA. The researchers reported a 100% absolute success rate for the teeth without the extrusion, while 19 out the 21 teeth that presented unintentional extrusion of MTA were completely healed within 3 years. One tooth with extruded MTA showed incomplete healing and the other one was deemed a failure. The authors also reported a significant reduction of the extruded MTA in 85% of the teeth, while in 10% it was almost absent. Finally, Roy et al (2021) reviewed 75 maxillary central incisors treated with MTA plug for 3 years. They reported that 28 teeth presented material extruded in the periapical tissues. Complete periapical healing was observed in 89,2% of the teeth with extruded MTA and in 100% of the teeth without extrusion, although the reported differences were not statistically significant. The amount of the extruded material was reduced in only 16% of the teeth. In addition, the teeth in the extrusion group showed complete healing later than the teeth in the control group and the differences were statistically significant.

A summary of the current literature concerning the extrusion of MTA and its possible effect on periapical healing is found in **Table 3**.

Table 3. Cases in the literature with reported extrusion of MTA in the periapical tissues.

Study	*Type*	*N*	*Gender*	*Age*	*Tooth*	*Dental History*	*Apical Diameter*	*Periapical Lesion (Size)*	*Follow Up*	*Outcome*	*Notes*
Tahan et al, 2010	Case Report	1	F	17yo	21	Trauma	NR	Present (Large)	12m	Healing	
Tezel et al, 2010	Case Report	1	M	9yo	11	Trauma	>80	Present (Large)	24m	Healed	
Asgary & Ehsani, 2011	Case Report	1	F	22yo	11	Previously Treated	NR	Present (Small)	7yrs	Healed	Complete resorption of extruded MTA
Britto-Junior et al, 2012	Case Report	1	F	30yo	11	Previously Treated	>80	Present (Large)	6m	Failed	Partial resorption of extruded MTA / Surgical retreatment, healed in the 2yrs follow up
Nosrat et al, 2012	Case Reports	3	M	18yo	21	Trauma	>80	Present (Large)	4yrs	Healed	Parital resorption of extruded MTA
			M	15yo	21	Trauma, unsuccessfully treated with CH apexification for 28m	>100	Present (Medium)	27m	Failed	Surgical retreatment, healed in the 12m follow up
			F	50yo	21	Previous periradicular surgery	60	Present (Small)	12m	Healed	The extruded MTA was found directly under the mucosa and caused tenderness to palpation, was removed surgically

Chang et al, 2013	Case Reports	3	M	15yo	11	Trauma	>140	Present (Large – 20mm in diameter)	36m	Healing	Extruded MTA shifted position and was completely surrounded by bony tissues on the last recall
			M	36yo	11	Previously Treated	55	Present (Large – 11x15mm)	54m	Healed	
			F	16yo	21	Trauma	>140	Present (Large – 15mm in diameter)	48m	Healed	Radiolucent halo around the extruded MTA until the 24m follow up
Mente et al, 2013	Prospective Cohort Study	43	-	-	-	-	-	-	12-128m	86% healed	Univariate analysis identified apical extrusion of MTA as a statistically significant variable
Nagmnonde et al, 2016	Case Reports	3	F	29yo	12	Previously Treated	>50	Present (Small)	6m	Healed	Slight resorption of the extruded MTA
			F	30yo	21	Trauma	NR	Present (Medium)	6m	Healing	
			M	17yo	11	Trauma	NR	Present (Medium)	6m	Healing	Gradual resorption of the extruded MTA
Demiriz & Haraz-Bodruml ul, 2017	Retrospective Cohort Study	21 (extrusion)	-	-	-	-	-	-	3yrs	19 Healed, 1 Healing, 1 Failed	The extruded MTA does not prevent periapical healing but it may be a delaying factor. The resorption of the extruded material was not eseential for periapical healing.
		34 (no extrusion)	-	-	-	-	-	-	3yrs	34 Healed	

Roy et al, 2021	Retrospective Cohort Study	28 (extrusion)	-	-	-	-	-	-	3yrs	25 Healed, 2 Healing, 1 Failed	MTA extrusion does not have a major effect on periapical healing, but may lead to a delay in complete healing. Resorption of the material takes time and needs to be followed-up.
		47 (no extrusion)	-	-	-	-	-	-	3yrs	47 Healed	

5. Regenerative Endodontic Procedures

5.1 Introduction

Regenarative endodontics is a relatively new treatment option for immature teeth with necrotic pulps. Its main goals are the elimination of the root canal infection and the resolution of apical periodontits, as well as the reinforcement of the remaining dentinal walls and the continuation of root development.

In 1961, Nygaard Ostby, in order to study the potential role of the blood clot in endodontic treatment, provoked bleeding from the periapical tissues through the apical foramen in both animal and human teeth and then extracted them after various time periods, ranging from 13 days to 3,5 years. Histological findings reported the presence of granulation tissue inside the canal that transformed into fibrous tissue more apically and the deposition of cellular cementum on the root canal walls. He was the first to propose that the creation of an apical blood clot can be used in teeth with necrotic pulps and open apices, although his protocol did not lead to complete regeneration.

Interest in pulp regeneration had subsided, until Iwaya et al reported a successful case of revascularization of an immature mandibular second premolar with apical periodontitis and sinus tract in 2001. Three years later, Banchs and Trope (2004) presented a case report of a new regenerative technique using MTA as a matrix to promote tissue growth. Since then, research on regenerative endodontics has been increased and both the American Association of Endodontists and the European Society of Endodontology have published position statements with proposed clinical protocols in order to integrate this treatment modality in daily practice (Galler et al 2016).

5.2 Technique

According to the statements of both the American Association of Endodontists and the European Society of Endodontology, the proposed clinical protocol is based on the elimination of bacteria with the use of common endodontic medicaments and the introduction of stem cells inside the root canal by provoking bleeding from the periapical tissues.

Disinfection of the root canal is achieved with the use of sodium hypochlorite in low concentrations of 1,5-3%. It has been shown that high concentrations of sodium hypochlorite can have an adverse affect on the survival and differentiation of the stem cells of the apical papilla (Martin et al 2014). Minimal instrumentation of the dentinal walls is advised as they are already thin and prone to fracture and the generation of a smear layer that can occlude the dentinal tubules should be avoided.

At the end of the first visit, the canals are dried with sterile paper points and an antibacterial dressing is placed. Initially a triple antibiotic paste was used, containing ciprofloxacin, metronidazole and minocycline (Banchs & Trope 2004). However, in order to avoid the staining effects of minocycline on dentin (Kim et al 2010), the triple antibiotic paste was replaced by either a double antibiotic paste (ciprofloxacin, metronidazole) or calcium hydroxide (Kahler & Rossi-Fedele 2016).

The second appointment should be scheduled 2-4 weeks later. Any signs of infection present at the first visit should be resolved, otherwise the antibacterial treatment should be repeated. The use of an anesthetic solution without a vasoconstrictor, like mepicavaine 3%, has been proposed by researchers, as adrenaline may hinder the bleeding from the apical tissues. On the other hand, it is important to achieve adequate anesthesia, and depending on patient's compliance and sensation of pain, the clinician may opt for using an anesthetic with a vasoconstrictor (Galler et al 2016). The intracanal dressing is removed using small handfiles and irrigation with low concentration sodium hypochlorite or EDTA. The use of EDTA 17% as the last irrigant in cases of regeneration is significant, as it promotes attachment, proliferation and odontoblastic differentiation of stem cells (Dos Reis-Prado et al

2022). Ultrasonic activation seem to enhance the EDTA-induced release of growth factors (Widbiller et al 2017).

After the excess moisture is dried using paper points, bleeding is provoked with the use of a pre-bent 40 Hëdstrom file by lacerating the apical tissues. The canal is then filled with blood, preferably until 2mm below the gingival margin and is left for 15 minutes to form a blood clot (Galler et al 2016). Usually a collagen matrix is placed upon the blood clot to condense the bioactive hydraulic cement against without displacing the material inside the canal. Although Banchs and Trope proposed MTA as a suitable material for regenerative endodontic procedures, the material's potential for crown discoloration led to the use of alternatives, like Biodentine and EndoSequence/Total Fill putty (Kahler & Rossi-Fedele 2016).

Follow-up appointments should be scheduled after 6, 12, 18 and 24 months and after that annually for 5 years (Galler et al 2016).

5.3 Biological mechanism

Regenerative Endodontic Procedures (REPs) are based on tissue engineering techniques and require the delivery of appropriate stem cells and growth factors embedded within a scaffold. Research on the best source of stem cells and the required growth factors for their differentiation towards odontoblast-like cells, as well as the possible scaffolds that would allow the correct spatial position of those cells is ongoing.

The apical papilla is the main provider of mesenchymal stem cells (MSCs) for REPs. It contains a large number of undifferentiated MSCs which exhibit great proliferative and odontogenic differentiation capacity (Huang et al 2008). Furthermore, due to the proximity of the apical papilla to the apex of the tooth, it is convenient to transfer the MSCs inside the root canal space without the need of harvesting and manipulating them exogenously. Due to the mechanical irritation of the periapical tissues during REPs, other types of MSCs may also be considered as potential candidates for these procedures. Inflammatory periapical progenitor cells (iPAPCs), periodontal ligament stem cells (PDLSCs) and bone marrow stem cells (BMSCs) can also be transferred inside the root canal during the application of a regenerative protocol, depending on the status of the periapical tissues (Friedlander et al 2009).

Bioactive molecules such as growth and transcription factors play an important role in the differentiation of MSCs. During the mineralization of dentin in primary dentinogenesis, growth factors and proteins secreted by odontoblasts become embedded into the dentin matrix. Based on that, dentin can act as a growth factor reservoir for REPs. In fact, the treatment of dentin with the use of EDTA 17% and the subsequent demineralization of the dentin matrix liberates growth factors which control the stimulation of progenitor cells and the differentiation of stem cells (Dos Reis-Prado et al 2022).

A physical scaffold is necessary in order to provide a spatially correct position of cell location, promote proliferation, differentiation and metabolism of the cells and enable their nutrient and gaseous exchanges. A variety of natural and synthetic scaffolds have been proposed for REPs, like collagen, hyaluronic acid, demineralized dentin matrix, platelet rich plasma, alginate, polyglycolic acid, bioceramics and hydrogels (Kim et al 2018, Jazayeri et al 2020, Noohi et al 2022). The one that is most commonly used in current REP protocols is the blood clot. Although the blood clot offers the advantage of not requiring ex vivo manipulation, it poses some serious challenges, as it lacks a few properties of an ideal scaffold. It is often difficult to achieve and it exhibits poor mechanical properties (Galler et al 2011, Noohi et al 2022). In addition, the cell death of hematopoietic cells may negatively affect the stem cell survival. Nevertheless, an ideal scaffold that fulfills all the criteria is yet to be found.

Histological studies on human teeth treated with REPs which were later extracted for various reasons have shown that a fibrous connective tissue is formed inside the canal (Shimizu et al 2013, Becerra et al 2014, Meschi et al 2016, Nosrat et al 2019). In most of the reported cases no odontoblast-like cells have been reported (Becerra et al 2014, Nosrat et al 2019), so the newly formed soft tissue cannot be characterized as pulp-like tissue, but there have been reports of odontoblast-like cells lining the newly formed dentin similarly to a mature tooth (Austah et al 2018). Dense collagen bundles and blood vessels were found throughout the connective tissue along with fibroblasts (Becerra et al 2014). Occasional globular and malformed cementum as well as dystrophic calcifications, encasing dentinal chips or necrotic tissue, were also seen (Nosrat et al 2019).

The newly formed hard tissue in association with the dentinal walls has been described as a cementum-like tissue, both cellular and acellular (Becerra et al 2014), but without the presence of tubules within it (Shimizu et al 2013). In some areas, the newly formed mineralized tissue was clearly discernible from the dentinal walls by a dark line, when stained with hematoxylin-eosin (Becerra et al 2014). The presence of necrotic tissue remnants between the new tissue and dentin has also been described (Meschi et al 2016). Collagen bundles from the connective tissue were inserted into the cementum-like tissue (Becerra et al 2014). It has been reported that this mineralized tissue was partially detached from the dentinal walls (Yamauchi et al 2011, Becerra et al 2014), leaving the strength of the junction between cementum-like tissue and dentin questionable.

5.4 Outcome

The treatment outcome of endodontic procedures is based on strict criteria concerning the absence of symptoms and radiographic findings. However, the goals of REPs extend beyond the classic goals of endodontic treatment, as described by Diogenes et al in 2016.

At the first level, there are the patient-centered outcomes. Patients’ expectations of a treatment outcome can be very different from those of the dentist. The main patient-centered outcomes include the absence of signs and symptoms of inflammation, the resolution of disease and the tooth survival. Esthetic concerns should also be taken into consideration as the intracanal dressing and the materials used as coronal barrier in REPs may cause discoloration of the treated tooth.

At the second level, there are the clinician-based outcomes. They include the radiographic resolution of the periapical lesion, the radiographic signs of continued root development and the positive response to vitality testing. Clinicians use objective and subjective testing in order to ascertain the clinical success of the applied treatment.

Finally, there are the scientist-based outcomes that focus on important scientific questions, like the histologic nature of the newly formed tissue inside the root canal and whether complete regeneration of the pulp-dentin complex can be achieved. These outcomes are not directly related to the patient's well-being or the clinical success of the treatment, but can pave the way for future advances.

In **Table 4,** the clinician-based outcomes of REPs, as reported in the literature, are summarized.

Table 4. Clinician-based outcomes of regenerative endodontic procedures as reported in the literature.

Study	***N***	***Follow Up Period***	***Success Rate***	***Continued Root Development***	***Positive Response to Vitality Testing***	***Complete Apical Closure***
Jeeruphan et al, 2012	20	NR	80% healed and 20% healing	NR	NR	NR
Alobaid et al, 2014	19	6-23m	79,0%	NR	NR	NR
Bezgin et al, 2015	20	18m	95,0%	90,0%	35,0%	65,0%

Chen et al, 2016	17	12m	70,6% healed and 23,5% healing	NR	NR	NR
Alagl et al, 2017	30	12m	100,0%	73,0%	63,3%	73,3%
Shivashankar et al, 2017	54	12m	85,2% strict, 96,3% loose	NR	14,7%	NR
Jiang et al, 2017	43	7-28m	100,0%	100,0%	25,6%	30,2%
Lin et al, 2017	69	12m	100,0%	81,2%	NR	65,2%
Silujjai et al, 2017	17	12-93m	76,5%	NR	NR	NR
Lv et al, 2018	10	12m	100,0%	80,0%	40,0%	80,0%
Rizk et al, 2019	26	12m	100,0%	NR	NR	NR
Ragab et al, 2019	22	12m	75,4%	NR	NR	54,5%
Ulusoy et al, 2019	73	10-49m	97,3%	78,0%	86,0%	73,9%
ElSheshtawy et al, 2020	30	12m	90,0%	NR	NR	NR
Chreppa et al, 2020	51	1-8,2yrs	84,3%	91,4%*	54%*	NR
Meschi et al, 2021	23	7-54m	91,3%	47,8%	43,4%	52,2%
Pereira et al, 2021	22	12-30m	95,5%	NR	0,0%	NR
Caleza-Jimenez et al, 2022	9	6-66m	100,0%	100,0%	NR	NR

5.5 Disadvantages

Like every other treatment modality, regenerative endodontic procedures present some disadvantages. Firstly, one major drawback is the potential discoloration of the teeth treated with REPs (Kahler & Rossi-Fedele 2016). Either the intracanal dressing or the material of the coronal barrier can have a darkening effect on coronal dentin. Taking into consideration that most of the immature teeth presenting with apical periodontitis are anterior teeth, esthetic demands are high. Different techniques have been proposed in order to overcome this shortcoming. As mentioned before, minocycline-containing intracanal dressings have been replaced by calcium hydroxide or double antibiotic pastes and newer materials exhibiting minimal risk of coronal discoloration have been introduced in daily practice (Kahler & Rossi-Fedele 2016). In addition, flowable composite has been used to seal the dentinal tubules and minimize the risk of discoloration (Reynolds et al 2008).

Secondly, the teeth treated with REPs cannot be restored with the use of a post, due to the presence of the coronal barrier. This drawback becomes even more prominent considering the fact that trauma is one of the main reasons for which immature teeth require endodontic intervention. Songtrakul et al (2019) have proposed a modified apexification procedure that could potentially offer the advantages of continued root development and possibly allow the placement of an intraradicular post. At the first appointment, they prepared the access cavity and determined the root canal length using an apex locator and a periapical radiograph. The canal was debrided with K-files and was irrigates with copious amounts of 3% sodium hypochlorite. At the end of the first appointment, a calcium hydroxide dressing was applied and the access cavity was closed with a cotton pellet and Intermediate Restorative Material (IRM). At the second appointment, which was scheduled 2 weeks later, the access cavity was reopened and the calcium hydroxide was removed by copious irrigation with 3% sodium hypochlorite. They did not use EDTA as an irrigant and no bleeding from the periapical tissues was provoked. A 3mm thick biocompatible resorbable collagen matrix was placed 1-2mm short of the apex. A 3mm thick MTA or Biodentine apical plug was placed above the collagen matrix with the use of MAP system. The rest of the coronal space was obturated with warm gutta-percha and the access cavity was restored with a composite resin filling. The researchers applied this technique in 10 teeth and reviewed them over a period of 2-4 years. Initially, all teeth presented with a periapical lesion and by the end of the follow-up period, all teeth showed complete healing. Seven teeth exhibited increased thickness of the apical root canal walls, increased apical root length and apical closure. One tooth showed increased thickness and apical closure, but not increased length, another showed increased apical length but not increased thickness or apical closure, and one tooth did not show any radiographic changes of the dentinal walls.

Last but not least, histological studies are in agreement that the newly formed tissue cannot be characterized as pulp-like. Current knowledge and techniques lead towards a repairing process that is promising in terms of periapical healing and root maturation, but cannot achieve complete regeneration of the pulp-dentin complex (Digka et al 2020). As a result, tissue engineering-based strategies are being researched in order to develop novel protocols.

EXPERIMENTAL

PART

Introduction

Endodontic management of teeth with necrotic pulp and open apices can be quite challenging. Mechanical preparation should be kept to a minimum to prevent further weakening of the tooth. Chemical debridement is usually performed with low concentration of sodium hypochlorite, in order to minimize the side effects of an accidental extrusion to the periapical tissues. Finally, the obturation of teeth with open apices is very difficult with the conventional techniques.

Nowadays, there are three different treatment modalities that are advocated for treating this type of teeth: apexification with calcium hydroxide, apexification with an artificial barrier and regenerative endodontic procedures (REPs). All of them have exhibited very good results in terms of outcome and predictability.

Mineral trioxide aggregate (MTA) is a material that has been used either as an artificial apical barrier in apexification or as a cervical barrier in REPs due to its excellent biological properties. However, one of the main disadvantages of MTA is its difficult handling properties, which may hinder the correct placement of the material at the desired position.

Accidental extrusion of MTA in the periapical tissues has been reported in numerous case reports in the literature. Mente et al (2013), after reviewing 252 teeth treated with MTA apexification, concluded that MTA extrusion was a borderline significant prognostic factor for the treatment outcome, but they underlined the importance for further evaluation of their findings on the basis of larger sample sizes. However, two more recent studies by Demiriz & Hazar Bodrumlu (2017) and Roy et al (2021) reported that the presence of extruded MTA in the periapical tissues did not affect the outcome of the treatment, but could delay the healing process.

Aim

The aim of the present study is the **identification of the prognostic pre-operative factors** that could affect the **ideal placement of MTA** in the canals of teeth with necrotic pulp and open apices which will receive treatment with MTA apexification. Furthermore, the **radiographic outcome** of the teeth treated with MTA apexification in the Postgraduate Clinic of Endodontics was also evaluated.

Materials & Methods

The study was approved by the Research & Ethics committee of the Dental School of the National and Kapodistrian University of Athens (Number: 512/24.06.2022) A search was conducted in the archives of the Postgraduate Clinic of Endodontics of NKUA to identify the cases that were treated with the technique of MTA plug from January 2000 to December 2021. To consider a case as eligible for inclusion in the study, the availability of a preoperative and a postoperative radiograph of good quality was mandatory. Cases in which the original root canal anatomy could not be addressed due to procedural errors were excluded from the present study. The data that were collected from patients' files and the preoperative and postoperative radiographs were the following:

1. age,
2. sex,
3. tooth position (maxilla/mandible and anterior/posterior),
4. the type of treatment (endodontic treatment or retreatment),
5. the reason why the MTA plug technique was selected (immature root/external resorption/iatrogenic enlargement of the apical foramen),
6. the presence of a periapical lesion and its size,
7. the size of the apical foramen based on the preoperative radiograph and finally
8. the position of MTA apical plug, based on the classification described by Moore et al (2011):
    i. ideal,
    ii. overfilled (MTA extruded into the periapical tissues) and

iii. underfilled (MTA plug placed 2mm or more short of the radiographic apex).

Moreover, for the cases that were treated after the implementation of the Digital Patients Records from the Dental School (October 2016), the presence of follow up radiographs was used to record the outcome of the treatment.

Digitization of the analogue radiographs

As the radiographs in the patients' files before the October 2016 were stored in analogue form (x-ray films), a conversion to digital images was needed in order to perform radiometric analysis. To digitize the radiographic films, a portable x-ray illuminator was used to provide the necessary lighting and a digital camera to capture the image. A black and white filter was applied to minimize the effect of exogenous colouring from the light source.

Measurement of the size of the apical foramen on the digital radiographs

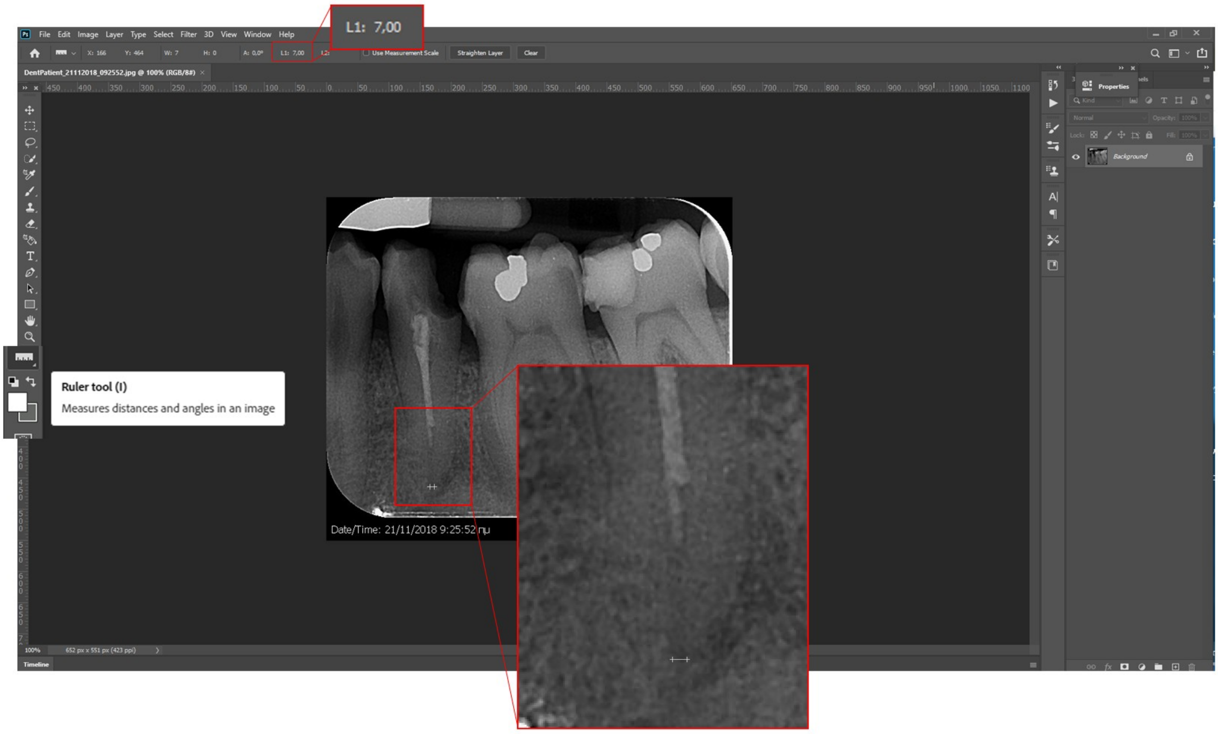
In order to perform the measurements of the diameter of the apical foramen an image editing software was used (Adobe Photoshop 2020, Adobe, San Jose, CA). The method was based on the paper by Ahmed et al in 2021. Firstly, the pixel density of each image was calculated. For that, the number of pixels for a known length was measured for every radiograph. The known length used was the size of the film. The length for analogue films and the digital size 2 phosphor plates is the same, namely 41mm. Then, the number of the pixels for the diameter of the apical foramen was measured, as shown in **Figure 1**. Consequently, the size of the apical foramen on the radiograph in millimetres can be given by the following ratio:

$$ApicalDiameter = \frac{FilmLength \times ApicalDiameterPixels}{FilmLengthPixels} = \frac{41 \times ApicalDiameterPixels}{FilmLengthPixels}$$

Instead of recording the diameter of the apical foramen in millimetres, we opted to record it in hundredths of a millimetre, which is more relatable to clinical practice as it is directly comparable to the ISO standardized endodontic files. So in the end, the ratio used was:

$$ApicalDiameter = \frac{41 \times ApicalDiameterPixels}{FilmLengthPixels} \times 100$$

Figure 1. Using the Ruler Tool of Adobe Photoshop to measure the pixels of the apical diameter on a mandibular premolar.



Measurement of the maximum size of the periapical lesion

In a similar way, the size of the periapical lesions (when present) was measured. For the calculation of lesion size, the maximum diameter of the lesion, as it appeared on the radiograph, was measured in pixels. The ratio used was the following:

$$LesionDiameter = \frac{41 \times LesionDiameterPixels}{FilmLengthPixels}$$

Radiographic outcome

For the cases that were treated after the October of 2016 and the Digital Records contained follow up radiographs, the radiographic outcome was also recorded. In order to determine the radiographic success rate, the Periapical Index (PAI) that was introduced by Orstavik et al in 1986 was used. Each follow up radiograph was given a PAI score from 1 to 5 and the follow up period was noted. Based on the paper of Orstavik et al in 2004, the classification for the treatment outcome was as follows:

- Healed: $PAIScore \leqslant 2$
- Not Healed: $PAIScore \geqslant 3$

Statistical analysis

Basic sample characteristics are summarised using descriptive statistics. For categorical variables, frequencies (n) and percentages (%) are reported. For continuous variables, normality was firstly examined using Kolmogorov-Smirnov and Shapiro-Wilk tests. Since none of the continuous variables was normally distributed, median, interquartile range (IQR) and minimum and maximum values are reported instead of mean and standard deviation.

Due to the small sample size, Fishers' exact test was used to examine univariate associations between MTA position (outcome variable) and the categorical variables of the study. For continuous variables, the assumptions of normality and homoscedasticity were firstly examined through Kolmogorov-Smirnov/Shapiro-Wilk and Levene's test respectively. Since these assumptions were not fulfilled for any of the continuous variables, Kruskal-Wallis tests were used to examine their univariate associations with MTA position.

Since the study's outcome variable (MTA position) presented a small number of cases in its two of its three categories, it was dichotomised and binary logistic regression testing was used to examine the effects of study predictors. For the same reason, the predictor indicating the reason for MTA plug was also dichotomised. Essential assumptions of logistic regression were tested as follows:

- Linearity: The Box-Tidwell test was performed by including all interactions between continuous variables and their log transformations in the binary logistic regression model. If the interaction term was significant, then the original predictor was not linearly related to the logit of the dependent variable (i.e. the linearity assumption was violated).
- Absence of multicollinearity: The tolerance and VIF test were obtained through running linear regression model (note: although the depended variables were dichotomous, the interested is only on determining collinearity between covariates, as such linear regression was performed). A tolerance of 0.1 was considered as the threshold indicating more significant correlation between a specific covariate and the rest of covariates. Due to the small sample size of this study, a VIF exceeding 2.5 was considered as indicating a problematic amount of collinearity (Johnston et al 2018).

Analysis was performed using descriptive statistics in SPSS Version 25.0 (Armonk, NY: IBM Corp) and critical p-value was set at 0.05 for all tests.

Results

Sample characteristics

Apexification with an artificial barrier has been performed in 58 roots of 52 patients in the Postgraduate Clinic of Endodontics during the last 20 years. Three of them were excluded from the present study due to iatrogenic procedural errors that prevented the original canal anatomy to be addressed. Two more were excluded as the material used as an artificial barrier was not MTA. Biodentine was used as the apical barrier in one of them and TotalFill BC putty was used for the other. Finally, data regarding N=53 dental roots from 47 different individuals were analysed. As shown in **Table 5**, the majority of study participants were male (n=29 or 54.7%), with median (IQR) age of 41 (30) years. The majority of teeth were anterior (n=32 or 60.4%) and were located at the maxilla (n=38 or 71.7%). Incomplete root formation was the reason for MTA plug for about half of roots (n=27 or 50.9%), followed by apical external root resorption (n=18 or 34%) and overenlargement of the apical foramen (n=4 or 7,5%). The rest were teeth that had previously undergone surgical endodontic retreatment (n=4 or 7,5%). Only 5 roots out of the 53 reviewed presented with divergent canal walls. The median (IQR) of apical diameter was 79.9 (28.5), while retreatment was the type of treatment for the majority of roots (n=39 or 73.6%). MTA position was ideal for most roots (n=33 or 62.3%). Periapical lesion was present in n=32 (or 60.4%) of roots, with median (IQR) dimension of periapical lesion equal to 7.5 (5.9) mm.

Univariate associations with MTA position

Univariate tests were used to examine associations between MTA position and the rest of the study variables. As shown in Table 6, no variable was statistically significantly associated with MTA position (p-values>0.05), apart from the dimension of the periapical lesion which was nearly significant (p-value=0.057).

Table 5. Descriptive characteristics of a sample of N=53 dental roots.

Variable (N=53)	**n**	**%**
Gender		
Male	29	54.7
Female	24	45.3
Age (years), median [IQR (min, max)]	41	30 (10, 74)
Type of tooth		
Anterior	32	60.4
Posterior	21	39.6
Tooth position		
Maxilla	38	71.7
Mandible	15	28.3
Reason for MTA plug		
Incomplete root formation	27	50.9
External resorption	18	34.0
Previous surgical retreatment	4	7.5
Overenlargement of apical foramen	4	7.5
Apical diameter, median [IQR (min, max)]	79.4	28.5 (29.4, 128.5)
MTA position		
Ideal	33	62.3
Overfill	14	26.4
Underfill	6	11.3

Type of treatment		
Treatment	14	26.4
Retreatment	39	73.6
Presence of periapical lesion		
Yes	32	60.4
No	21	39.6
Dimension of periapical lesion (mm), median [IQR (min, max)]	7.5	5.9 (2.5, 19)

*<u>Abbreviations</u>: **IQR**: interquartile range, **mm**: millimetres*

Figure 2. Examples of different MTA apical barrier positions. (a) Ideal. (b) Overfill. (c) Underfill (distal canal).

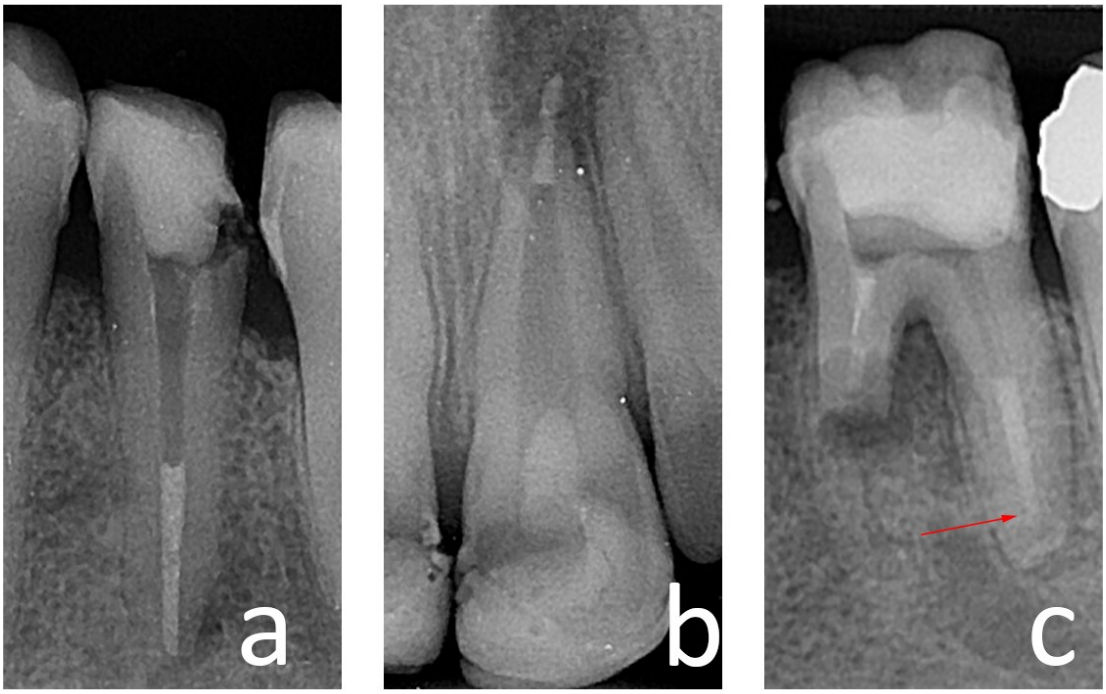


Table 6. Univariate associations between MTA position and the independent variables in a sample of N=53 dental roots.

Independent variable	Statistic	p-value
Gender	5.129	0.075
Age	1.216	0.544
Type of tooth	0.485	0.841
Tooth position	4.716	0.093
Reason for MTA plug	4.361	0.606
Apical diameter	0,109	0.947
Type of treatment	0.513	0.904
Presence of periapical lesion	0.485	0.841
Dimension of periapical lesion	5.730	0.057

Fishers' exact and Kruskal-Wallis tests for categorical and continuous variables respectively.

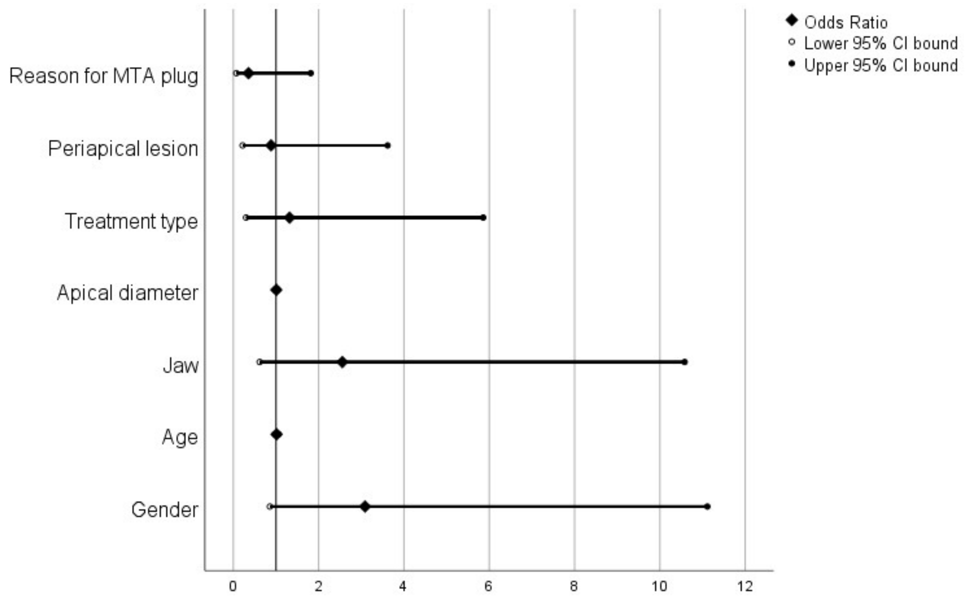
Effects of study variables on dichotomised MTA position

Binary logistic was performed to explore the effect of independent study variables on MTA position (dichotomized dependent variable). In terms of logistic regression assumptions, linearity was met, since all interactions of the Box-Tidwell test were non-significant. Absence of multicollinearity was violated for tooth type (VIF=3.02>2.5), thus, this variable was excluded from the model.

Univariate binary logistic regression models indicated that none of the variables was statistically significantly associated with the dichotomized MTA position (all p-values>0.05).

The binary logistic regression model including all variables was not a statistically significant improvement of the null model (omnibus test p-value=0.257>0.05) and this was also the case when performing forward and backward model selection processes. The model explained 21.9% of the variation in MTA position (Nagelkerke's R^2=0.219), exhibited good fit to the data (Hosmer and Lemeshow test p-value=0.750>0.05) and correctly classified 70.6% of cases (52.6% in over/under fill and 81.3% of cases in the ideal in MTA position category). Model results are presented in **Figure 3**. None of the study variables was statistically significantly associated with the dichotomized MTA position (all p-values>0.05).

Figure 3. Binary logistic regression forest plot over MTA position (dichotomised) in a sample of 53 dental roots.



*<u>Abbreviations</u>: **CI**: confidence interval*

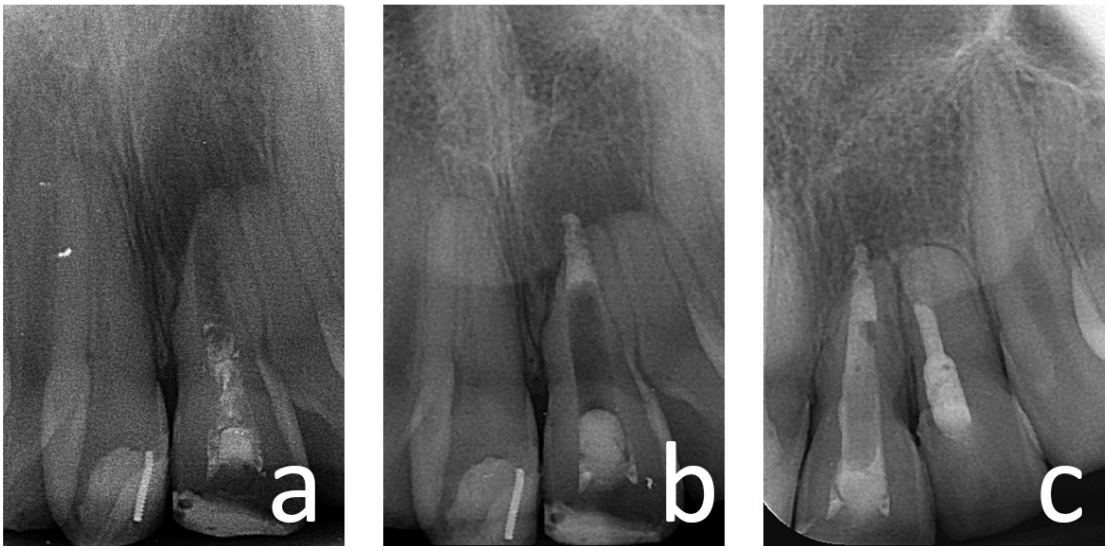
Radiographic outcome

Thirty four roots were treated with an MTA apical barrier apexification technique since October 2016. Follow up radiograpghs were found for 23 of these roots. The 23 roots corresponded to 21 teeth in 18 patients. The follow up period ranged from 5 to 36 months, with a mean value of 14 months. The PAI scores awarded for the preoperative and follow up radiograph are shown in **Table 7**.

Table 7. PAI scores awarded for preoperative and follow-up radiographs.

PAI	**1**	**2**	**3**	**4**	**5**
Preoperative	0	3	6	5	9
Follow Up	7	8	5	1	2

Figure 4. A successful case treated with apexification with MTA apical barrier. (a) Pre-operative radiograph (PAI=5). (b) Post-operative radiograph. Extrusion of the material in the periapical tissues is observed. (c) Follow-up radiograph after18 months (PAI=2).



The absolute success rate of the teeth treated with MTA apexification was 65,2%. Of the cases that were not considered healed, one was deemed an absolute failure with an increase of the PAI score (**Figure 5**) and two others did not show any improvement of their PAI score on the 7-month follow up (**Figure 6**). The rest exhibited an improved PAI score that would classify them as healing cases. As a result, the relative success rate of the roots treated with MTA apexification was 87%.

Figure 5. Failed case treated with apexification with MTA apical barrier. (a) Pre-operative radiograph (PAI=2). (b) Post-operative radiograph. (c) Follow-up radiograph after 32 months (PAI=3).

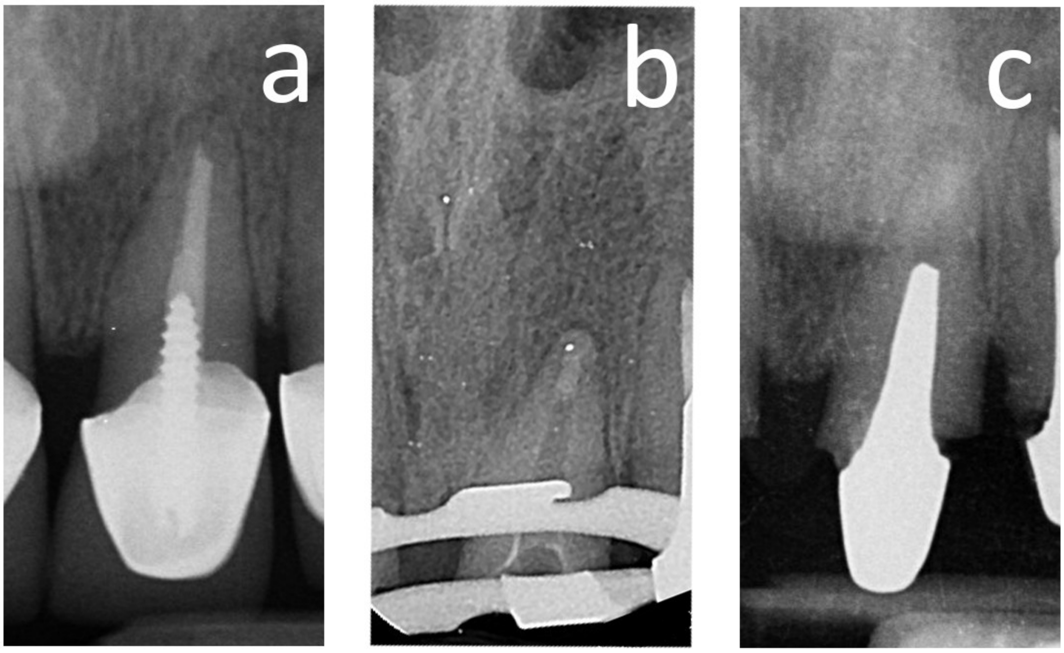


Figure 6. Failed case treated with apexification with MTA apical barrier.
(a) Pre-operative radiograph (PAI=5). (b) Post-operative radiograph. (c) Follow-up radiograph after 7 months (PAI=5).

Discussion

The aim of the present study was to identify the pre-operative factors that could potentially lead to a non-ideal placement of MTA when applying the apical plug technique to treat teeth with necrotic pulp and open apices. In 2013, Mente et al have identified MTA extrusion as a borderline prognostic factor that could affect the outcome of the MTA apical plug technique. However, recent studies showed that MTA extrusion may lead only to late healing and does not directly affect the outcome (Demiriz & Hazar Bodrumlu 2017, Roy et al 2021). It should be noted that these studies have a small sample size and that the only failures reported were observed in the extrusion groups.

Apart from the demographic data, the other factors that were examined in the present study for possible association to the placement of the MTA were the apical diameter of the tooth, the presence and size of the periapical lesion, the aetiology of the open apex and the type of treatment.

The measurements of the apical diameter and the maximum diameter of the apical lesion were performed on the pre-operative periapical radiographs with the use of Adobe Photoshop software, based on the methodology that Ahmed et al (2021) used to measure root length and apical diameter changes following pulpotomy in mandibular first permanent molars. In the past, Boley Gauge (Kleier & Barr 1991) and milimetrical rulers (Dominguez Reyes et al 2005) have been used to measure the apical diameter on pre-operative radiographs, but these methods are not very accurate, especially in foramina that are smaller than 1mm.

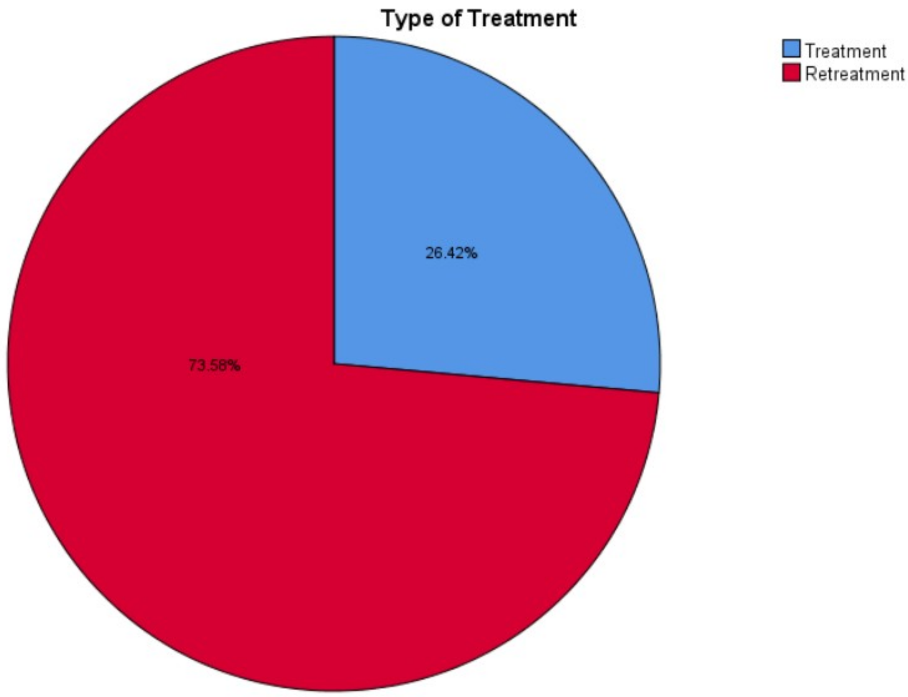
The results of the present study suggest that there was no statistically significant association between the ideal placement of the MTA during apexification and the variables reviewed. The only factor with a nearly statistically significant association was the size of the periapical lesion.

An important reason for the absence of statistically significant results is the small size of the sample. Management of teeth with necrotic pulp and wide apices is not a common procedure in Endodontics. Furthermore, a significant number of this type of teeth, especially in younger patients, may be treated in the Postgraduate Clinic of Pediatric Dentistry. It should also be taken into account that the teeth treated with apexification with an artificial barrier but without the use of MTA as the apical plug material were removed from the sample.

An interesting finding was the range of the initial apical diameter of the teeth that were ultimately treated with MTA apical plug. The mean apical diameter of the cases reviewed in the present study was 79,4. There is no agreement in the literature regarding the minimum apical diameter that constitutes a tooth eligible for the apexification with MTA apical barrier technique. Mente et al (2013) reported that they used the MTA apical barrier technique to treat teeth with an apical diameter of at least 40. Sarris et al (2008) reported a minimum apical diameter of 60, while Ree & Schwartz (2017) stated that the indication for this treatment modality is an apical foramen gauged to size 70 or larger. Other authors applied the MTA plug on teeth with an apical foramen larger than 80 (Kandemir Demirci et al 2020). In the present study, out of the 53 roots examined, only 2 presented measurements of an apical diameter larger than size 120 and only 9 foramina were measured to be larger than 100. A possible explanation for this is that teeth with wider, “blunder-buss” type foramina were treated with the application of REPs rather than apexification techniques.

The option of REPs for the management of non-vital teeth with open apices could affect the results regarding the age and the type of treatment. Thirty-eight out of 47 patients in the present study were adults and 73,6% of the roots were previously treated (**Figure 7**). This finding could be the result of younger patients seeking treatment in the Postgraduate Clinic of Pediatric Dentistry or that in young patients without previous endodontic intervention REPs are considered to be a better option for the management of this type of teeth.

Figure 7. Type of treatment among the cases reviewed.



Interestingly, Nosrat et al (2021) reported that there is potential for successfully applying REPs after previously failed treatments (either REP or conventional endodontic treatment). Nevertheless, there are no clinical studies with higher quality of evidence that would support the management of previously treated teeth with regenerative techniques.

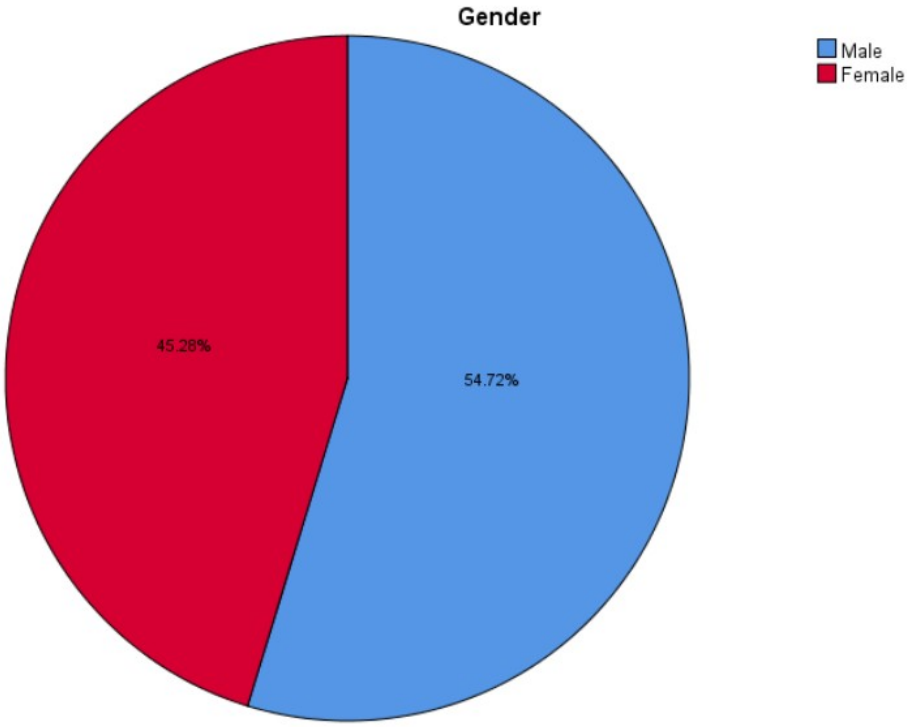
The stage of the root development could potentially play some part in the extrusion of the material in the apexification with MTA apical plug technique. Sarris et al (2008) reported that in teeth with wide open apices and at the stages 1-3 of root development, extrusion of MTA was easier to occur and the marginal adaptation on the dentinal walls and the sealing ability of the material could be adversely affected. Moore et al (2011) stated that the placement of MTA is frequently ideal with more mature teeth (stage 4-5 of root development) and reported a significant association between ideal placement and non-divergent apices. In the present study, only 5 roots presented with divergent apices and in 3 of them non-ideal placement of the

MTA plug was observed (**Figure 8)**. Due to the small sample, compared to the non-divergent group, no statistical analysis of the results was performed.

Figure 8. Pre-operative (a) and post-operative (b) radiographs of a tooth exhibiting divergent canal walls on the distal canal. Significant unintentional extrusion of MTA is observed.

The distribution of the cases by sex did not show any significant tendency towards males or females (54,7% vs 45,3% - **Figure 9**). This finding may not be consistent with the presumption that males are more predisposed to develop teeth with necrotic pulp and open apices due to the higher incident of traumatic injuries (Glendor 2008, Andersson 2013), but it is in agreement with the findings of other similar studies (Witherspoon et al 2008, Mente et al 2013, Ree & Schwartz 2017). Only Simon et al (2007) reported a higher percentage (66,7%) of male patients who received MTA apexification treatment. It should be noted that the teeth reviewed in the present study are only those that were treated with MTA apexification and not the total number of teeth with necrotic pulp and open apices that were treated in the Postgraduate Clinic of Endodontics.

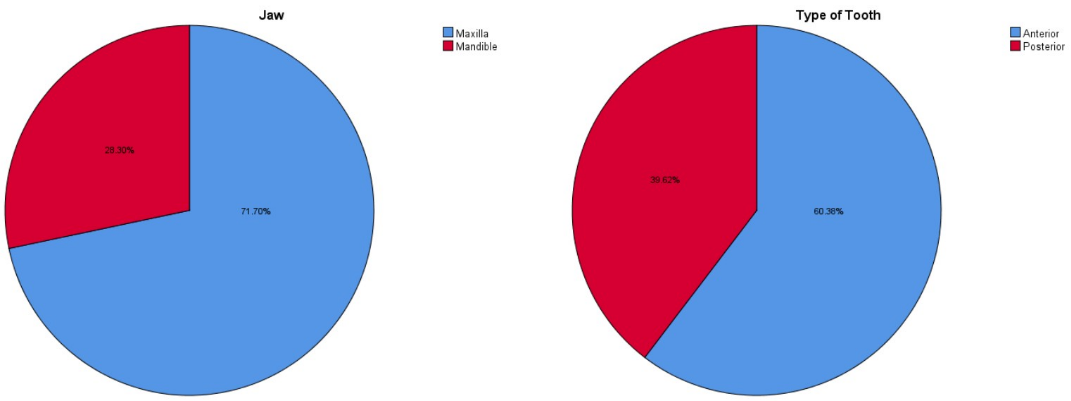
Figure 9. Gender distribution among the patients of the present study.



Regarding the position and the type of the teeth, the majority was found in the maxilla (71,7%) and 60,4% were located in the anterior area of the maxilla or the mandible (**Figure 10**). These results are to be expected, as anterior teeth and especially maxillary anterior teeth are more prone to traumatic injuries (Lam 2016).

The absolute radiographic success rate of the 23 roots reviewed in the present study was 65,2% which is in agreement with previous studies (Simon et al 2007, Witherspoon et al 2008, Jeeruphan et al 2012, Kandemir Demirci et al 2020). A significant 21,8% showed an improved PAI score at the follow-up radiograph and those cases were classified as “healing”. One possible explanation of the high percentage of “healing” cases is the short follow-up period of the MTA apexification cases completed after the induction of the Digital Patient Records. After pulling together the “healed” and “healing” cases, the relative radiographic success was 87%, which is comparable to the previous studies, as shown in Table 2.

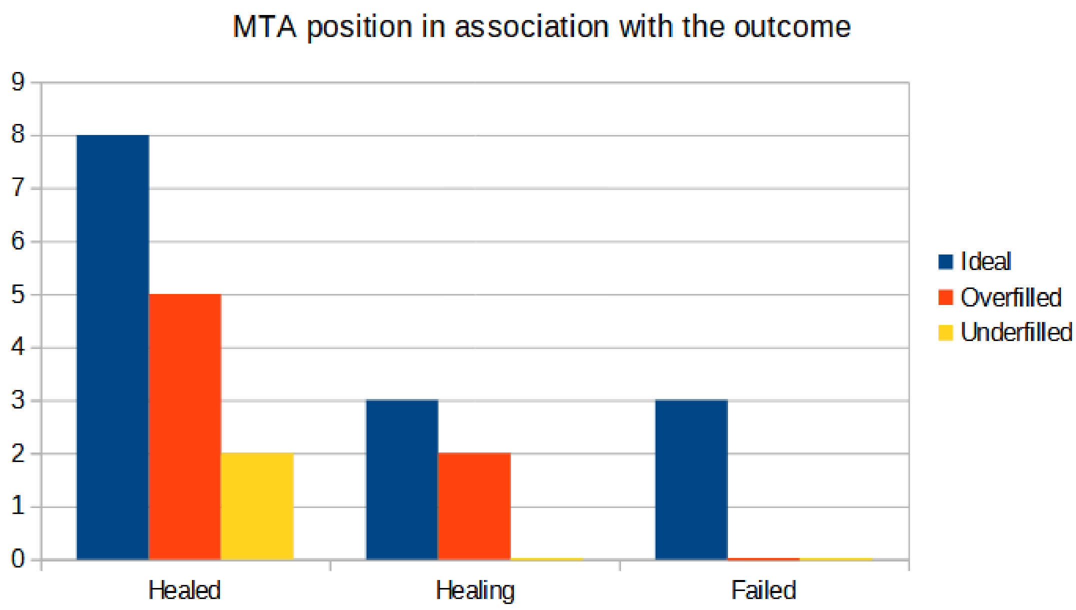
Figure 10. Distribution of roots based on position and type of tooth.



In 8 of the roots that were “healed” the MTA was ideally placed at the apex, 2 were underfilled and in 5 the material was extruded in the periapical tissues. This finding seems to be consistent with the studies that support that the extruded MTA does not impair the healing of periapical tissues, as shown in **Table 3**. Due to the small sample of the roots reviewed, no statistical analysis was performed on the factors that could affect the outcome of the MTA plug technique (**Figure 11**).

One of the main limitations of the present study is that the use of an apical matrix has not been recorded. Collagen sponge has been used as an artificial barrier in order to prevent extrusion of the material in the periapical tissues in very wide or “blunder-buss” type apical foramina (Ree & Schwartz 2017). The use of an apical barrier to condense the MTA against and its adaptation to the dentinal walls would minimize the risk of a possible extrusion but could prevent the material from being placed ideally and possible lead to an underfilled canal.

Figure 11. Distribution of MTA position in relation to the outcome of the cases reviewed.



In very large lesions the amount of the matrix material needed to provide a solid base for MTA to be placed ideally is often underestimated by the clinician, which can result in extrusion of the MTA despite the use of a matrix. This fact can possibly explain the nearly significant association between MTA extrusion and the size of the periapical lesion, even though the use of the matrix was not taken into consideration in the present study.

Another limitation is the use of periapical radiographs for the measurements of the apical diameter and maximum apical lesion size. Conventional radiographs are a projection of a three-dimensional object onto a two-dimensional image. That would indicate that the diameters which were possible to measure for the radiometric analysis were only in the mesio-distal and not the bucco-lingual dimension.

In addition, slight differences in horizontal or vertical angulation of the x-ray tubehead could result in image distortion and subsequently to different measurements of the afore-mentioned dimensions. From the x-rays that were reviewed for the purposes of the present study, no noticeable distortions of the radiographical images were observed. The use of a paralleling radiographic technique for the vast majority of the x-rays taken in the Postgraduate Clinic of Endodontics could be the main reason for this.

To overcome the inherent limitations of conventional dental radiography, a pre-operative CBCT could be used as the basis for the radiometric analysis. In a study performed on human cadavers, two methods for determining the initial apical diameter, first file to bind and CBCT, were compared to micro-CT. The authors concluded that CBCT imaging showed good accuracy and reliability in measuring the diameter of the apical canal and that the data collected can be used to plan the following canal enlargement (Campello et al 2019). Another study that compared the accuracy of CBCT and µCT for volumetric measurement of artificial bone lesions ex-vivo reported that both modules were very accurate compared to physical measurements (Ahlowalia et al 2013). Nevertheless, the CBCT dose radiation can be equivalent to 3-6 digital panoramic radiographs (Signorelli et al 2016). Considering the young age of many of the patients who seek treatment for non-vital teeth with open apices, CBCT should not be indicated for the sole reason of apical gauging or volumetric analysis of the periapical lesion.

Conclusions

The data of the present study do not provide indications of associations between MTA position and the rest of the study predictors. These results should be interpreted with much caution since the sample size is small and the study may lack statistical power to produce reliable estimates. Further research in sufficiently larger samples sizes is required.

Summary

Introduction: Apexification with MTA apical barrier is a widespread technique that is used to manage immature permanent teeth with necrotic pulp and open apices. Due to the difficult handling properties of MTA, unintentional extrusion of the material into the periapical tissues has been described in the literature. Despite the fact that there is no agreement in the effect of the extruded MTA in the outcome of the treatment, a delayed healing has been observed.

Aim: To identify the preoperative factors that could possibly affect the ideal placement of MTA apical plug in apexification technique. Secondly, to determine the outcome of this procedure in teeth treated by postgraduate students in the Postgraduate Clinic of Endodontics.

Materials & Methods: A search was conducted in the archives of the Postgraduate Clinic of Endodontics to identify the cases that were treated with the technique of MTA apical plug from January 2000 to December 2021. Cases without good quality pre-operative and post-operative radiographs and cases with altered anatomy that has not been possible to be addressed were excluded from the sample. Analogue radiographs (x-ray films) were digitized and radiometric analysis was performed on the digital radiographs with the use of an appropriate software (Adobe Photoshop 2020, Adobe, San Jose, CA).

The data that were collected from patients' files and the pre-operative and post-operative radiographs were the following: (i) age, (ii) sex, (iii) tooth position, (iv) the type of treatment, (v) the reason why the MTA plug technique was selected, (vi) the presence of a periapical lesion and its size, (vii) the size of the apical foramen based on the preoperative radiograph and (viii) the position of the MTA apical plug.

For the cases treated after the October 2016 and a follow-up radiograph was available in the Digital Records, the radiographic outcome was recorded, using the Periapical Index (PAI) to evaluate the state of the periapical tissues.

Results: The results of the present study were the following:

I. No statistically significant correlation between the ideal placement of the MTA apical plug and the pre-operative factors reviewed could be recorded. The only factor with a nearly statistically significant association was the size of the periapical lesion.

II. Regarding the radiographic outcome, the absolute success rate of the cases reviewed was 65,2% and the relative success rate was 87%.

Conclusions: The data of the present study do not provide indications of associations between MTA position and the rest of study predictors. There results should be interpreted with much caution since the sample size is small and the study may lack statistical power to produce reliable estimates.

Greek Summary

Εισαγωγή: Η δημιουργία τεχνητής ακρορριζικής απόφραξης με την χρήση MTA αποτελεί μια διαδεδομένη τεχνική για την αντιμετώπιση μονίμων δοντιών με νεκρό πολφό και αδιάπλαστο ακρορρίζιο. Η δυσκολία στον χειρισμό του MTA μπορεί να οδηγήσει σε έξοδο του υλικού στους περιακρορριζικούς ιστούς. Αν και δεν υπάρχει συμφωνία στην βιβλιογραφία σχετικά με την επίδραση της εξόδου του υλικού στην επιτυχία της θεραπείας, αναφέρεται ότι μπορεί να επιμηκύνει τον χρόνο επούλωσης.

Σκοπός: Η ταυτοποίηση των προεπεμβατικών παραγόντων που πιθανόν να επηρεάζουν τον έλεγχο του μήκους κατά την τοποθέτηση του βύσματος MTA σε δόντια με νεκρό πολφό και ανοικτό ακρορρίζιο. Δευτερευόντως, η αξιολόγηση της επιτυχίας της συγκεκριμένης τεχνικής στα περιστατικά που αντιμετωπίστηκαν από τους μεταπτυχιακούς φοιτητές Ενδοδοντίας.

Υλικό και Μέθοδος: Πραγματοποιήθηκε αναζήτηση στα αρχεία της Μεταπτυχιακής Κλινικής Ενδοδοντίας για τα περιστατικά που αντιμετωπίστηκαν με την τεχνική της τεχνητής απόφραξης με βύσμα MTA από τον Ιανουάριο του 2000 έως και τον Δεκέμβριο του 2021. Τα περιστατικά χωρίς καλής ποιότητας αρχική και τελική ακτινογραφία και αυτά στα οποία υπήρχε ιατρογενής αλλοίωση της μορφολογίας του ριζικού σωλήνα που δεν κατέστη δυνατό να αντιμετωπιστεί επιτυχώς εξαιρέθηκαν από την μελέτη. Οι αναλογικές ακτινογραφίες (σε φιλμ) ψηφιοποιήθηκαν και στη συνέχεια πραγματοποιήθηκαν μετρήσεις με την χρήση κατάλληλου λογισμικού (Adobe Photoshop 2020, Adobe, San Jose, CA).

Τα δεδομένα που συλλέχθησαν από τους φακέλους ασθενών και τις αρχικές και τελικές ακτινογραφίες είναι τα εξής: (i) η ηλικία, (ii) το φύλο, (iii) η θέση του δοντιού στον φραγμό, (iv) το είδος της θεραπείας, (v) ο λόγος που επιλέχθηκε η τεχνική του βύσματος MTA, (vi) η παρουσία και το μέγεθος της περιακρορριζικής αλλοίωσης,

(vii) το μέγεθος του ακρορριζικού τρήματος με βάση την αρχική ακτινογραφία και (viii) η θέση του βύσματος MTA.

Επιπρόσθετα, η ακτινογραφική επιτυχία της θεραπείας αξιολογήθηκε στα περιστατικά που αντιμετωπίστηκαν μετά τον Οκτώβριο του 2016, εφόσον υπήρχε διαθέσιμη ακτινογραφία επανεξέτασης στον Ηλεκτρονικό Φάκελο Ασθενούς. Χρησιμοποιήθηκε ο δείκτης PAI (Periapical Index) για να αξιολογηθεί η κατάσταση των περιακρορριζικών ιστών.

Αποτελέσματα: Τα αποτελέσματα της παρούσας εργασίας ήταν τα ακόλουθα:

I. Δεν διαπιστώθηκε στατιστικά σημαντική συσχέτιση μεταξύ της θέσης του βύσματος MTA και των προεπεμβατικών παραγόντων που εξετάστηκαν. Ο μονός παράγοντας που προσέγγιζε στατιστικά σημαντική συσχέτιση ήταν το μέγεθος της περιακρορρίζικης αλλοίωσης.

II. Όσο αφορά στην ακτινογραφική αξιολόγηση της επιτυχίας της ενδοδοντικής θεραπείας, απόλυτη επιτυχία διαπιστώθηκε στο 65,2% των περιστατικών, ενώ σχετική επιτυχία στο 87%.

Συμπεράσματα: Τα δεδομένα της παρούσας μελέτης δεν παρέχουν ενδείξεις συσχέτισης μεταξύ της θέσης του βύσματος MTA και των παραγόντων που μελετήθηκαν. Τα αποτελέσματα αυτά θα πρέπει να αξιολογηθούν με προσοχή καθώς το μέγεθος του δείγματος είναι μικρό και πιθανόν να μην μπορεί να ανιχνεύσει στατιστικά σημαντικές διαφορές.

APPENDIX

Complete data collected from the cases treated with MTA apexification

No	Age	Tooth	Type of Tooth	Jaw	Reason for MTA plug	Apical Diameter	MTA Position	Type of Treatment	Periapical Lesion
1	16	11	Anterior	Maxilla	Incomplete root formation	99,5	Ideal	Retreatment	4x7,5mm
2	29	22	Anterior	Maxilla	Incomplete root formation	49,3	Overfill	Retreatment	11x8,5mm
3	28	11	Anterior	Maxilla	External apical resorption	49,6	Ideal	Treatment	5x7,5mm
4	54	35	Posterior	Mandible	External apical resorption	41,4	Ideal	Treatment	7x12mm
5	14	37 (D)	Posterior	Mandible	Incomplete root formation	103,9	Underfill	Treatment	-
6	30	21	Anterior	Maxilla	Undergone surgical retreatment	111,2	Ideal	Retreatment	-
7	10	42	Anterior	Mandible	Incomplete root formation	80,3	Underfill	Retreatment	3,5x2,5mm
8	42	23	Anterior	Maxilla	External apical resorption	80,9	Underfill	Retreatment	2,5x1mm
9	20	11	Anterior	Maxilla	Undergone surgical retreatment	94	Ideal	Retreatment	9,5x7mm
10	39	21	Anterior	Maxilla	Incomplete root formation	128,5	Underfill	Retreatment	-
11	65	46 (D)	Posterior	Mandible	External apical resorption	81,6	Overfill	Retreatment	3.5x7mm
12	65	47 (D)	Posterior	Mandible	External apical resorption	83,5	Ideal	Retreatment	-
13	66	22	Anterior	Maxilla	Undergone surgical retreatment	76,8	Ideal	Retreatment	5x4.5mm
14	66	23	Anterior	Maxilla	Undergone surgical retreatment	104,1	Ideal	Retreatment	7x8mm

15	40	21	Anterior	Maxilla	Incomplete root formation	90	Ideal	Treatment	2,5x1,5mm
16	31	11	Anterior	Maxilla	Overenlargement of the apical foramen	88,9	Ideal	Retreatment	-
17	27	45	Posterior	Mandible	Incomplete root formation	72,6	Ideal	Retreatment	3x1mm
18	61	12	Anterior	Maxilla	External apical resorption	62,9	Overfill	Retreatment	3,5x2,5mm
19	43	11	Anterior	Maxilla	Incomplete root formation	127	Ideal	Treatment	11,5x10,5mm
20	10	46 (D)	Posterior	Mandible	Incomplete root formation	66	Overfill	Retreatment	3,5x4mm
21	64	37 (D)	Posterior	Mandible	Incomplete root formation	79,4	Ideal	Retreatment	-
22	55	21	Anterior	Maxilla	External apical resorption	77,4	Ideal	Retreatment	-
23	51	36	Posterior	Mandible	External apical resorption	29,4/35,4	M ideal, D underfill	Treatment	3x2mm
24	11	.11	Anterior	Maxilla	Incomplete root formation	79,9	Overfill	Retreatment	-
25	11	21	Anterior	Maxilla	Incomplete root formation	91,3	Overfill	Treatment	9x7mm
26	54	24 (B)	Posterior	Maxilla	External apical resorption	39,2	Overfil	Retreatment	-
27	68	45	Posterior	Mandible	Incomplete root formation	52,8	Underfill	Retreatment	-
28	72	15	Posterior	Maxilla	External apical resorption	65	Ideal	Retreatment	-
29	74	24 (P)	Posterior	Maxilla	External apical resorption	68,2	Ideal	Retreatment	-
30	58	21	Anterior	Maxilla	Incomplete root formation	93,4	Overfill	Treatment	-
31	60	15	Posterior	Maxilla	External apical resorption	57,5	Ideal	Retreatment	-
32	42	35	Posterior	Mandible	Incomplete root formation	63,3	Ideal	Retreatment	-

33	13	21	Anterior	Maxilla	Incomplete root formation	83,4	Overfill	Retreatment	7x9,5mm
34	43	25	Posterior	Maxilla	Incomplete root formation	76,4	Ideal	Retreatment	-
35	44	24 (B)	Posterior	Maxilla	Overenlargement of the apical foramen	74,2	Ideal	Retreatment	-
36	59	37 (D)	Posterior	Mandible	Overenlargement of the apical foramen	60	Ideal	Retreatment	-
37	25	21	Anterior	Maxilla	Incomplete root formation	69,8	Ideal	Treatment	-
38	13	11	Anterior	Maxilla	Incomplete root formation	85,4	Ideal	Treatment	5x8mm
39	35	11	Anterior	Maxilla	Incomplete root formation	90,2	Overfill	Retreatment	-
40	41	21	Anterior	Maxilla	Incomplete root formation	116,8	Ideal	Retreatment	5x9mm
41	17	24	Posterior	Maxilla	Incomplete root formation	65,6	Ideal	Retreatment	3x1mm
42	40	21	Anterior	Maxilla	Incomplete root formation	117,3	Ideal	Retreatment	4x4mm
43	40	12	Anterior	Maxilla	Incomplete root formation	93,3	Overfill	Treatment	7x8mm
44	31	11	Anterior	Maxilla	External apical resorption	64,7	Ideal	Treatment	8x11mm
45	31	12	Anterior	Maxilla	External apical resorption	54,2	Ideal	Retreatment	same
46	50	11	Anterior	Maxilla	Overenlargement of the apical foramen	80,9	Ideal	Retreatment	7,5x9,5mm
47	41	12	Anterior	Maxilla	External apical resorption	75	Ideal	Retreatment	4,5x7mm
48	27	11	Anterior	Maxilla	Incomplete root formation	113,6	Ideal	Retreatment	8x9mm
49	21	21	Anterior	Maxilla	Incomplete root formation	101,4	Overfill	Retreatment	-

50	20	21	Anterior	Maxilla	Incomplete root formation	62,9	Ideal	Treatment	19x14,5mm
51	43	37	Posterior	Mandible	External apical resorption	85/69,5	Overfill	Retreatment	4x2,9mm

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