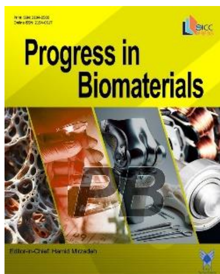

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Performance and Prospects of Bioactive Endodontic Cements: A Comparative Mechanobiological Assessment of Mineral Trioxide Aggregate and Calcium-Enriched Mixture Cement

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Original Research

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Abstract

The success of endodontic therapy critically depends on the effective sealing and biocompatibility of root canal filling materials. This has driven a transition from traditional options towards bioactive alternatives, notably Mineral Trioxide Aggregate (MTA) and Calcium-Enriched Mixture (CEM) Cement, which offer enhanced biological interactions. This study provides a narrative review and performance evaluation of MTA and CEM Cement, with focused analysis of their applications in vital pulp therapy (VPT) and root-end filling (REF). An in-depth examination of their chemical, physical, and biological properties was conducted through a systematic synthesis of extant literature, critically appraising sealing ability, biocompatibility, inflammatory response modulation, antimicrobial efficacy, and long-term clinical success. Both MTA and CEM Cement demonstrate superior biocompatibility, excellent sealing capabilities, and the ability to stimulate hard tissue formation compared to traditional materials. MTA is well-established with a proven track record, though it suffers from a prolonged setting time and potential tooth discoloration. CEM Cement exhibits comparable or superior bioactive properties, including rapid setting, optimal flow, and significant hydroxyapatite generation, leading to promising clinical outcomes in VPT. Evidence confirms that bioactive materials significantly outperform traditional options, validating both MTA and CEM Cement as effective choices, with selection dependent on clinical scenarios and material properties.

Keywords: Mineral Trioxide Aggregate; Calcium-Enriched Mixture Cement; Vital Pulp Therapy; Root-End Filling; Biomaterial Biocompatibility; Bioactive Materials

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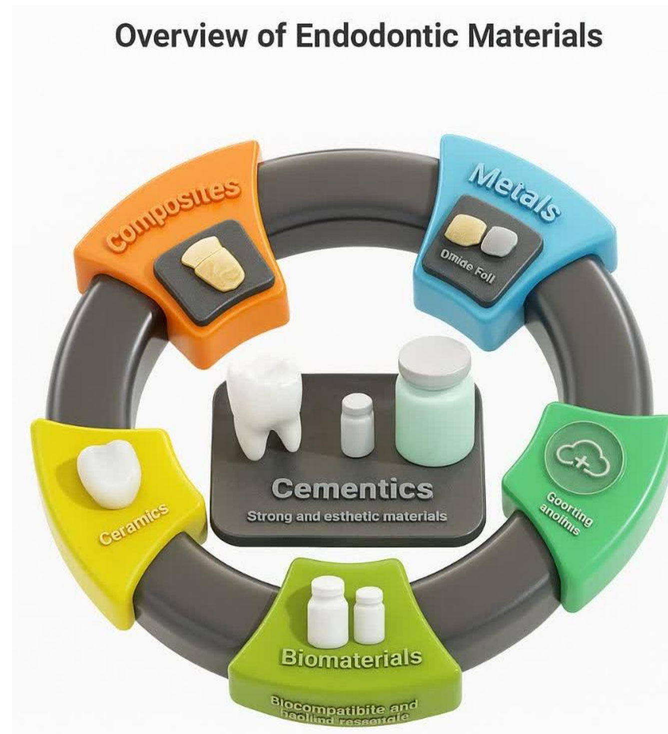

1. Introduction

Dental caries remains a major oral health challenge [1, 2]. Initially, this condition causes mild inflammation in the pulp and the surrounding root tissues, typically accompanied by pain [3]. However, as the disease progresses, it leads to irreversible pulp damage, which is also usually painful, followed by pulp necrosis and peri-apical diseases. In cases where the tooth has an open apex, the condition results in incomplete root development, and even with specialized treatment, the long-term survival of the tooth may be compromised [4-6]. The primary objective in treating permanent teeth with an open apex is to preserve pulp vitality by performing VPT to promote apex genesis [7]. Techniques, direct pulp capping and pulpotomy (partial or full) are employed to encourage natural root development in these teeth. This approach is considered preferable to root canal treatment, as the treated teeth develop stronger tissue, making them more resistant to vertical root fractures [8]. Currently, for dentists, the issue of preserving pulp vitality when treating mature permanent teeth with a closed apex at the time of exposure (whether due to mechanical injury or caries) remains somewhat unclear. This shows the need for solid, evidence-based clinical guidelines [9,10]. Previously, it was recommended that small mechanical exposures (up to about one millimeter) be managed with direct pulp capping. However, in cases of carious exposure indicating irreversible pulp inflammation, root canal treatment was deemed the only viable option [11]. Currently, no definitive guidelines exist on the use of pulpotomy (partial or full) in these scenarios. There is now unanimous agreement on the critical role bacteria play in the development of pulp diseases. In a sterile environment, the pulp has the ability to heal itself; however, in the presence of bacteria, pulp death becomes inevitable. The key to successful VPT lies in the effective control of pathogenic agents [12]. Moreover, with a deeper understanding of dental pulp's defense mechanisms, outdated theories, such as the pulp suffocation (self-strangulation) theory, have been discredited. Recent studies confirm that pulp inflammation begins on the surface and progressively

extends deeper into the tissue [3]. In VPT, it is essential to shield the pulp from its external environment, including the bacteria present in the mouth, by applying appropriate dental materials for protection. Ideal dental pulp covering materials should be able to eliminate bacteria, form a strong barrier against bacterial penetration, be easy to use in clinical practice, and, most importantly, be biocompatible while promoting the formation of a dental bridge beneath the material [13, 14].

The fundamental principles of VPT involve two key phases. The first involves the complete removal of decayed tissue and any bacteria-infected areas. The second focuses on preventing further bacterial contamination. Over the past several decades, calcium hydroxide has been the preferred material in VPT treatments, although other materials have also been utilized [13]. Data indicates that in the United States, over 24 million endodontic procedures are performed annually, with 5.5% involving apical surgery, perforation repair, and related treatments [15]. These procedures are often necessary when inflammation cannot be resolved with standard techniques, often due to the complex anatomy of the canal or inflammation in the apical area. Surgery may also be required to address issues that arise during treatment, root perforations that occur during canal or post-space preparation. In surgical treatments, materials are used to seal the canal contents from peri-radicular tissues and repair root defects. These materials must not only seal dental tissues effectively but also be biocompatible with periodontal tissues. The ideal restorative material for root treatment should adhere to the tooth structure, provide a sufficient seal, be insoluble in tissue fluids, maintain dimensional stability, resist absorption, be radiopaque, and biocompatible [16]. Historically, various materials have been used for root-end filling and perforation repair, including amalgam, zinc oxide-eugenol cements, composite resin, and glass ionomer cements. Unfortunately, none of these materials possess all the ideal properties required for such applications. One material that stands out is MTA, which was introduced in the early 1990s [17]. MTA was introduced in the early 1990s by Dr. Torabinejad and colleagues at Loma Linda University for use in endodontic procedures. Following its introduction, MTA was first discussed in dental literature in 1993, and by 1998, it was approved by the U.S. Food and Drug Administration (FDA) for use in endodontics [18]. Initially, MTA was developed as a root-end filler, but over time, it has been applied in a variety of treatments, including pulp capping, pulpotomy, apex genesis, as an apical barrier in teeth with open apices, and for the repair of root perforations and as a root canal filling material [19].

In recent years, older materials have been replaced by more advanced biocompatible alternatives, including MTA and CEM Cement. CEM Cement, in particular, has demonstrated superior sealing abilities compared to other materials and is widely used in VPT treatments [20]. As a bio-restorative material, CEM promotes the formation of higher-quality reparative dentin. Clinical studies evaluating the use of CEM for various VPT treatments, direct pulp capping and pulpotomy, have shown significant success, positioning CEM as an effective pulp capping material across a range of VPT procedures [21]. MTA, as well, is recognized as a bioactive material that encourages the formation of hard tissue while maintaining biocompatibility, making it highly suitable for dental applications. The aim of this research is to provide a detailed overview of different filling materials used for root-end treatments, along with a comprehensive analysis of the methods, applications, and properties of MTA and CEM Cement [21].

Research into material properties has been a prolific and expansive field of study, driven by the continuous quest to enhance performance, durability, and functionality across engineering and medical disciplines [22-26]. Within this broad domain, the study of biomaterials represents a particularly dynamic and critical subfield, which has garnered significant scholarly interest due to its direct implications for human health and medical device innovation [27-31]. This focus underscores the fundamental role and importance of biomaterials, which are uniquely engineered to interact with biological systems to support, augment, or replace damaged tissues and organs, thereby forming the cornerstone of modern regenerative medicine and advanced clinical therapies [32-36]. Despite the well-documented advantages of contemporary bioactive materials like MTA and CEM Cement over traditional options, a significant research gap persists in the form of a synthesized, critical appraisal that directly contrasts their properties, clinical protocols, and therapeutic efficacy within the broader context of evolving endodontic biomaterials. While numerous studies extol their individual merits, the literature lacks a consolidated framework that systematically evaluates their comparative performance, delineates precise clinical indications, and integrates emerging adjuncts, such as laser technology, into a cohesive treatment paradigm.

This study aims to bridge this gap by providing a comprehensive narrative review and performance evaluation of MTA and CEM Cement, with a focused analysis of their application in VPT and REF procedures. To achieve this, the present work conducts an in-depth examination of the chemical, physical, and biological properties of these materials, alongside a detailed analysis of their clinical methodologies, including

placement techniques, handling characteristics, and management of complications. Key methodologies involve a systematic synthesis of extant literature to critically appraise evidence on sealing ability, biocompatibility, inflammatory response modulation, and long-term clinical success rates. The central question this research seeks to answer is: How do the intrinsic properties and clinical application protocols of MTA and CEM Cement influence their therapeutic outcomes in endodontic therapy, and what is their comparative standing in the hierarchy of contemporary bioactive materials? The primary objective is to establish an evidence-based comparative profile that can guide material selection and optimize clinical practice. The novelty of this study lies in its integrated approach, which not only provides a side-by-side analysis of MTA and CEM Cement but also contextualizes them within the historical evolution of endodontic materials and projects future trends, including the synergistic potential of laser applications. The importance of this work is underscored by its potential to directly influence clinical decision-making, moving beyond empirical choices to strategies grounded in a clear understanding of material science and bioactivity. Ultimately, the findings of this review are intended for application by clinicians and researchers alike, serving as a definitive reference to enhance the predictability and success of endodontic treatments, foster improved patient outcomes, and inform the direction of future biomaterial innovation.

2. Comparative evaluation of root end filling materials: and its Alternatives

Endodontic treatments can sometimes fail due to bacterial leakage or the release of endotoxins, which contribute to the formation of pathological lesions. When retreatment options are ineffective or not feasible, endodontic surgery becomes necessary to save the tooth. Factors such as the complexity of the root canal system, insufficient or incorrect instrumentation, and physical barriers often make surgical intervention essential [37]. A critical aspect of endodontic surgery involves cutting the affected root tip and preparing the root-end cavity. The goals of this procedure are to clean the root canal end and create a space for placing a suitable filling material to achieve an effective seal [38]. The successful application of REF materials plays a vital role in ensuring a positive surgical outcome. A review of the history of endodontics reveals that numerous materials have been used for REF over different periods. Despite the wide variety of available materials, none have yet demonstrated all the ideal properties necessary for perfect REF outcomes [39]. Below is an outline of REF materials suggested by researchers and used by dental professionals. In the category of metals, several materials have been utilized for root-end filling, including gold foil, silver, titanium screws, tin posts, amalgam (with and without bonding agents), and gallium alloy. These less common metallic materials have been used for REF, although each presents its own advantages and challenges. This overview highlights the historical use of various REF materials and evaluates the ongoing search for an ideal substance that meets all clinical requirements. In the category of cements, materials used for root-end fillings include zinc oxide, Kuwait, Zinc Super EBA, IRM (a type of ZOE cement), polycarboxylate, zinc phosphate, and glass ionomer cements [40]. These have been employed due to their effectiveness in endodontic treatments. Among biomaterials, MTA, calcium phosphate cement (CPC), and CEM cement are notable for their biocompatibility and regenerative properties, which make them suitable for use in root-end fillings [41]. REF materials have evolved significantly, broadly categorized into metals, cements, and bioactive alternatives (Figure 1). Traditional materials like amalgam and gutta-percha are increasingly supplemented or replaced by bioactive options such as MTA and CEM Cement, which offer superior biocompatibility and tissue interaction. This categorization evaluates the shift towards materials promoting healing rather than merely providing a seal.
The ideal characteristics for root-end filling materials, based on recommendations and the key features to summarize are illustrates in Table 1. Currently, no single material possesses all these properties perfectly. Although there is no conclusive evidence identifying the best material, a review of available data can help guide the selection of an appropriate material for REF.

2.1. Amalgam

Amalgam has been a prevalent choice for REF material over the past century. Its use as a REF material was first reported by Farrar in 1884. Subsequent studies by Hipple (1912), Faulhaber and Neuman (1897), Rhein (1914), and Garvin (1919) confirmed its effectiveness [42]. Over time, the compatibility and sealing ability of amalgam are expected to improve due to the formation of reaction products. Amalgams with high copper content and no zinc are generally preferred because they exhibit superior properties compared to other types. Some studies suggest that using a bonding agent with amalgam can reduce microleakage in root-end fillings [43]. Although freshly mixed amalgam can be cytotoxic due to unreacted mercury, this toxicity diminishes significantly as the material sets. Additionally, zinc, which is released from amalgam, also has cytotoxic effects. Research comparing amalgam, IRM, and Super

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EBA on human periodontal ligament and osteoblast cells found that amalgam had higher cytotoxicity [44].

Despite the expansion upon these drawbacks, initial marginal leakage, contamination with tin and mercury, sensitivity to moisture, and the need for proper cavity preparation, amalgam remains widely used and is generally well-tolerated by tissues. A depth of at least 3 mm is generally considered clinically adequate. Long-term systemic or local toxicity from using amalgam as a REF has not been reported. Amalgam has been effectively employed as a dental filling material in the intraoral environment for many years. However, with modern techniques that involve vertical root-end preparation and the use of ultrasonic devices, the practical application of amalgam as a REF has become more challenging. The difficulty arises from the complexities associated with maneuvering and placing amalgam in areas with restricted access and visibility, making its clinical use more complicated and limited [45].

2.2. Gutta-Percha

Gutta-percha is valued for its adaptability to cavity irregularities, neutral properties, affordability, and corrosion resistance. Each gutta-percha cone typically consists of approximately 19-22% gutta-percha gum, 75-79% zinc oxide powder, and minor amounts of additives (wax), pigments, antioxidants, and mineral salts [46]. Laboratory tests have detected some toxicity in gutta-percha, which is thought to be related to its zinc oxide content.

Table 1: Ideal properties of root-end filling materials and comparative performance of CEM cement.

Ideal Property	Rationale & Clinical Significance	Performance of CEM Cement
Biocompatibility & Bioactivity	Must be non-toxic, non-carcinogenic, and well-tolerated by periradicular tissues. Should stimulate a favorable biological response, such as hard tissue formation (cementogenesis/osteogenesis).	Demonstrates high biocompatibility, comparable or superior to MTA. Promotes regeneration of a near-physiologic dentin-pulp complex and facilitates cementum formation on its surface, leading to excellent periapical healing.
Superior Sealing Ability	Prevents microleakage of bacteria and endotoxins from the root canal system into the periapical tissues, which is critical for long-term success.	Exhibits excellent sealing, often superior to traditional materials like IRM. Its ability to form a hydroxyapatite interface upon contact with dentinal fluid creates a chemical bond and enhances the marginal seal.
Antimicrobial Efficacy	Should possess inherent antibacterial and antifungal properties to disinfect the root-end cavity and prevent recurrent infection.	Shows potent, broad-spectrum antimicrobial activity against common endodontic pathogens (e.g., *E. faecalis*), considered comparable to calcium hydroxide and superior to MTA in some studies.
Appropriate Physical Handling	Requires optimal consistency, flow, and working time for easy placement in surgically challenging sites. Should have adequate radiopacity for visualization.	Offers favorable handling with greater flowability and optimal film thickness compared to MTA. Its rapid setting time and hydrophilic nature facilitate clinical use, even in a moist environment.
Dimensional Stability & Low Solubility	Must remain insoluble in tissue fluids and maintain its volume over time to ensure a permanent seal and not wash out or degrade.	Demonstrates low solubility and dimensional stability once set, ensuring the integrity of the root-end seal is maintained long-term in the biological environment.

However, subcutaneous implantation studies have demonstrated that gutta-percha is generally well tolerated by tissues [47]. Research by Retief and Abdal (1982) found that heat-sealed gutta-percha provided

better sealing than amalgam, Super EBA, and IRM. Despite this, the introduction of thermoplastic gutta-percha has led to a preference for this newer material over traditional gutta-percha for root-end filling [48]. Thermoplastic gutta-percha offers a superior seal compared to both varnished and unvarnished amalgam. Gutta-percha's porous structure initially absorbs moisture from surrounding tissues, causing it to expand. Over time, it compresses, which can compromise the seal and increase microleakage.

Zinc oxide eugenol (ZOE) and its reinforced variants, IRM and Super EBA, are significant in REF materials, although their use in peri radicular surgeries is less frequently reported. Among these, reinforced ZOE cements are highly regarded [49]. IRM is a type of ZOE cement enhanced with 20% by weight of polymethacrylate added to the powder, while Super EBA is modified with ethoxy benzoic acid to improve its setting time and strength [50]. Super EBA generally exhibits superior physical properties compared to traditional ZOE, including higher compressive and tensile strength, a neutral pH, and reduced solubility. Qynick and Oynick proposed using Super EBA as a root-end filling material in 1978. Although both Super EBA and IRM belong to the same group of materials, they have distinct characteristics. Super EBA adheres well to tooth structure and to itself, allowing for layer-by-layer application if necessary. In contrast, IRM lacks this self-adhesive property and is best used as a single mass within the root-end cavity. Both cements exhibit low to moderate toxicity when freshly mixed, likely due to eugenol compounds, but this toxicity diminishes once the cement sets. Long-term inflammation potential appears minimal. Clinical reports indicate that Super EBA provides a favorable restorative response with minimal chronic inflammation at the root apex. Studies suggest that both Super EBA and IRM offer superior performance compared to amalgam [51]. Specifically, Super EBA has demonstrated negligible leakage in laboratory studies. Both Super EBA and IRM have been extensively studied, showing good results in laboratory leakage studies, animal studies, and retrospective human studies. When well-mixed, Super EBA offers good flow, minimal tissue toxicity, and effective handling properties, though mixing requires more skill compared to other REF materials [52]. A minor drawback is that ZOE cements' radiopacity is similar to gutta-percha, which may hinder differentiation from the surrounding tooth structure. While adding radiopaque materials can enhance radiopacity, it may alter the physical or chemical properties of the cements, so such modifications are generally avoided.

2.3. Gold Foil

The use of gold foil as a root-end filling material was first reported by Schuster in 1913 and Lyons in 1920. Gold foil is noted for its excellent tissue compatibility, smooth surface, and favorable texture properties. It has demonstrated only minimal tissue reactions in clinical settings. Compared to materials (IRM), composite resin, amalgam, and glass ionomer, gold foil exhibits the lowest cellular toxicity [50]. Laboratory studies have also shown that gold foil provides superior apical sealing, with the least microleakage among tested materials. However, its use as a root-end filling material may not be necessary due to the challenges associated with maintaining a moisture-free environment during application and the associated cost of the material [48].

2.4. Polycarboxylate Cement

Introduced by Smith in 1968, polycarboxylate cement is known for its initial acidic pH, with a ratio of 1/7 acid to powder, which contributes to its rapid setting time [53]. Despite its initial acidity, when used in direct pulp capping, it can stimulate pulp tissue. However, polycarboxylate cement has shown variable tissue responses when used inside or beyond the root canal apex. Studies on apical leakage indicate that polycarboxylate cement tends to exhibit a higher leakage rate compared to amalgam or gutta-percha when used as a root-end filling material [54].

2.5. Zinc Phosphate Cement

Introduced by Rhein in 1897 for sealing root canals before apical surgery, zinc phosphate cement has demonstrated weaker flow properties compared to materials, Ketac-Endo and amalgam [50]. Electron microscope studies have revealed a lack of proper adaptation between this cement and the root canal walls, leading to significant leakage. Due to its high leakage rate and suboptimal therapeutic outcomes, zinc phosphate cement is generally not recommended for use as a root-end filling material [55].

2.6. Glass Ionomer Cement

Glass ionomer cement is formed through the reaction between calcium aluminosilicate glass particles and an aqueous solution of polyacrylic acid. This material establishes a chemical bond with the tooth structure and has been shown to have favorable histological compatibility [56]. While freshly mixed glass ionomer cement exhibits cytotoxicity, this decreases significantly once the cement has set. Fluoride ions released from the cement can have varying effects on bone cells, either stimulating or inhibiting cell activity, depending on ion

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concentration and culture conditions [57]. Glass ionomer cements are user-friendly and generally do not cause adverse histological changes in periapical tissues. However, their sealing ability can be compromised if the root end cavity is not kept dry during application. The adhesion of glass ionomer cement to dentin is enhanced by using acid conditioners and varnishes. Light-cured, resin-reinforced glass ionomer cements, as developed by Chong et al. (1991), show reduced microleakage due to their improved moisture resistance and minimal shrinkage during polymerization [58]. Recent developments include new glass ionomer cements with glass-metal powders, which exhibit promising properties for root-end filling. Overall, while glass ionomer cements are difficult to place in areas with limited access, studies suggest they perform comparably to amalgam in clinical settings.

2.7. Composite Resin

Composite resins, particularly when used with dentin bonding agents, represent an adaptation of restorative techniques to endodontic surgery. Despite their potential benefits, composite resins have received limited attention as REF materials due to concerns about cytotoxicity and effects on pulp tissue. However, when applied correctly, their cellular toxicity is significantly minimized [16]. Several studies have demonstrated that composite resins exhibit significantly less apical leakage compared to materials (zinc oxide-eugenol, amalgam, varnished gutta-percha, and Ketac-Silver). This suggests that composite resins may effectively seal the root end without necessitating additional cavity preparation [59]. Clinical comparison has shown that composite resins can offer superior results compared to amalgam (Gluma,), a type of composite resin, achieved complete restoration in 74% of cases, compared to 59% with amalgam. Further studies found that resin and light-cured composites demonstrated better tissue compatibility and reduced periapical inflammatory responses compared to amalgam [60]. Research has also indicated that composite resins can support cement genesis and, in some cases, facilitate the reattachment of periodontal ligament fibers. Although this connection suggests potential for long-term clinical success, it remains to be fully validated. Composite resins, especially when used with dentin bonding materials, allow for more conservative cavity preparations. Some studies suggest that a slightly concave cavity may be preferable to a deeper one, as composite materials effectively seal the root end and block the cavity from further exposure [61].

2.8. Calcium Phosphate Cement

CPC is a type of hydroxyapatite cement formed by the reaction between two calcium phosphate compounds: tetra calcium phosphate and dicalcium phosphate. When mixed with water, CPC undergoes a chemical reaction that results in the formation of a hydroxyapatite mass, which is crystalline in nature [62]. The porosity of the final set material depends on the amount of liquid used during mixing. CPC exhibits radiopacity similar to bone and reacts to moisture, water, and even blood by forming hydroxyapatite, which enhances its compatibility. It is well-tolerated by tissues and does not induce toxic inflammatory responses [63]. With a compressive strength exceeding 60 megapascals, CPC maintains its shape and volume over time. Additionally, CPC implants are gradually reabsorbed and replaced by natural bone, which suggests its potential as a suitable root-end filling material [64]. Despite these promising attributes, CPC has not yet received approval from the FDA for clinical use in root-end filling applications.

2.9. Laser Applications in Endodontics

The application of lasers in endodontics has garnered significant interest in recent years. The use of lasers in dentistry was first proposed in 1971 by Weilchman, and since then, the application of different laser types has been extensively researched [65]. The effects of laser radiation depend on the wavelength and energy intensity, and various lasers have been recommended for different endodontic procedures, with adjustments made to the wavelength, radiation time, frequency, and energy intensity. Among the different types of lasers, the Er (it has been identified as particularly effective for endodontic procedures) [66]. Comparisons with other types of lasers, CO_2 and Ho, have highlighted the superiority of Er, in terms of reduced burn risk on root surfaces, improved restoration outcomes, and reduced post-operative discomfort. However, it is important to note that the use of lasers for endodontic surgeries may require more time than traditional methods. Overall, the potential benefits of lasers in endodontics are numerous, and ongoing research is key to fully realizing their potential in this field [67]. In addition to the potential benefits of lasers in endodontic surgery, they also offer several advantages in other areas of endodontic treatment. Firstly, laser energy can be used to generate heat that facilitates the removal of intracanal pulp tissue, resulting in more thorough and efficient root canal disinfection. Secondly, lasers have also been shown to reduce the risk of post-operative inflammatory reactions and discomfort, leading to improved patient satisfaction and comfort. Furthermore, lasers are precise and non-invasive tools that offer improved visualization of the root canal system, allowing for more accurate and

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efficient treatments [68]. Finally, lasers can also be used to enhance the success of root canal treatments by promoting the regeneration of damaged and lost tissues. When used in conjunction with bone grafting materials, lasers can stimulate the migration and differentiation of osteogenic cells, ultimately enhancing the healing process. Overall, the application of lasers in endodontics offers numerous potential advantages in terms of improved treatment efficacy, patient comfort, and regenerative potential [69]. As research in this field continues to progress, it is likely that lasers will become increasingly integrated into routine endodontic procedures. As lasers become more widely accepted and integrated into endodontic treatments, there are several emerging trends that are worth mentioning. Firstly, the development of new and improved laser technologies is a key focus of current research in this field [37]. Ultrashort pulsed lasers show promise for reducing thermal injury risks while still providing effective tissue removal and disinfection. Secondly, there is a growing interest in the use of lasers for non-invasive treatment of dental caries. Thirdly, there is an increasing focus on personalized treatment using lasers. This involves tailoring the laser parameters to the specific needs of individual patients based on factors (tooth anatomy), disease severity, and patient preferences. Finally, there is growing interest in the potential use of lasers in combination with other modalities, photodynamic therapy and stem cell-based tissue regeneration, to provide even more comprehensive and effective treatments [70]. Therefore, the field of endodontics is rapidly evolving with the integration of laser technology, and these emerging trends suggest that we may see significant advancements in the coming years [71].

3.Mineral Trioxide Aggregate

MTA was first introduced in 1993 by Torabinejad at Loma Linda University in the United States. This material has gained widespread use in dentistry, particularly in endodontic procedures. MTA serves various purposes, including as a pulp-capping agent, root-end filling material, and a restorative solution for perforations [72]. MTA is composed of a blend of dicalcium silicate, tricalcium silicate, tricalcium aluminate, and tetra calcium aluminoferrite. It comes in white and gray varieties, which are similar to Portland cement but with variations in specific components, notably the amount of iron oxide. Both types of MTA contain bismuth oxide, which provides radiopacity [49]. When mixed with water, MTA becomes a colloidal gel that hardens into a solid, firm mass within approximately four hours. The initial pH of the mixture is 2.10, which rises to 5.12 after three hours. The key component of MTA is calcium hydroxide, which forms in the presence of moisture and contributes to its properties. Upon application, MTA's high pH promotes a sequence of tissue responses, including necrosis, dystrophic coagulation, and calcification [7]. MTA (Mineral Trioxide Aggregate) is known for its biologically active properties, including its ability to stimulate interleukin production due to its alkaline pH and calcium ion release. Studies Various materials have been compared to MTA for their ability to provide effective marginal sealing, with studies showing that MTA outperforms materials, Super EBA and composite resins in this regard. According to research conducted by multiple scientists, MTA provides a superior level of marginal sealing compared to other materials, Super EBA and IRM. This suggests that MTA may be a preferable choice for dental procedures where marginal sealing is an important factor [73]. MTA promotes healthier apical tissue formation and induces less inflammation compared to other materials. Its bonding with osteoblasts and subsequent formation of new cementum and periodontal ligament fibers are better than with IRM and amalgam [49]. Initial inflammatory responses to MTA are influenced by its high pH, the heat generated during setting, and cytokines (interleukins 1 and 6). Despite some initial inflammation, laboratory studies have shown MTA to be less toxic than amalgam, Super EBA, and IRM. One challenge with MTA is its sensitivity to blood contamination, which can impact its final setting. However, MTA's compressive strength and solubility are comparable to those of zinc oxide-eugenol cements [74].

Although it requires a longer setting time, clinical studies, including Long-term studies, including those conducted by various researchers, have confirmed that MTA performs well as a root-end filling material, even in teeth with open apices. The successful performance of MTA as a root-end filling material in both short-term and long-term studies suggests that it is an effective material for use in root-end procedures, despite any potential application challenges that may arise during use [75]. MTA is considered an ideal material for filling the root canal system and performing root-end surgeries due to its comprehensive set of desirable properties. It effectively seals the root canal system and integrates well with surrounding tissues. For a material to be ideal for such uses, it must be non-toxic, non-carcinogenic, biocompatible, insoluble in tissue fluids, and dimensionally stable [76]. Initially, MTA was introduced as a root-end filling material because existing materials on the market did not meet the ideal criteria for flooding the root end. Today, MTA is widely used in various endodontic procedures, including pulp capping, pulpotomy, apex genesis, creating an apical barrier in

necrotic teeth with open apices, repairing root perforations, treating root resorption, and managing teeth with middle-third root fractures [77]. MTA offers several advantageous properties, antimicrobial and antifungal effects, resistance to solubility in tissue fluids, biocompatibility, stimulation of hard tissue formation, and a high pH that promotes a favorable environment for healing [78]. However, it also has some drawbacks, including potential tooth discoloration, a lengthy setting time, high cost, lack of solvent resistance, and lower compressive strength compared to other materials. Despite these disadvantages, MTA remains a highly effective material in endodontic treatments due to its significant benefits [21].

3.1. History of MTA

Although the treatment of pulp and periapical diseases has a long history, according to Grossman, the field of endodontics saw significant advancement during its fourth period of progress, from 1926 to 1976. During this time, endodontics evolved rapidly due to the standardization of equipment, the publication of the first reference book, the establishment of the American Association of Endodontists, and the introduction of new tools and techniques [79]. These developments improved treatment methods, patient comfort, and success rates. However, for many years, endodontic surgical treatments, closing perforations and treating teeth with open apices, remained challenging, and there was no consensus on the best material for these procedures, making treatment outcomes less predictable [80]. In the fifth period, spanning the past forty years, extensive research has focused on developing ideal chemical compositions for dental materials to enhance their suitability for endodontic treatments.

In November 1993, Lee Monsef and Mahmoud Torabinejad published an article introducing a new dental material called MTA, developed by Torabinejad, for filling perforations in the furcation area. A follow-up article by Torabinejad, Watson, and Pitt Ford, published in December 1993, evaluated MTA’s suitability as a root-end filler in peri radicular surgeries [81]. This article highlighted MTA’s key advantage: its water-based, hydrophilic nature, which allows it to maintain its properties even when in contact with moisture or blood, unlike other commonly used dental materials at the time. Torabinejad and his colleagues reinforced this claim in an article published in 1984. Over the next three years, from 1995 to 1997, Torabinejad and his team published numerous scientific articles in prestigious journals, further exploring the various characteristics and applications of MTA [82].

3.2. Chemical Properties of MTA

MTA is composed primarily of modified Portland cement combined with bismuth oxide. It also includes smaller amounts of other compounds, calcium oxide (Cao), silicon dioxide (SiO_2), potassium sulfate (K_2SO_4), magnesium oxide (MgO), and sodium sulfate (Na_2SO_4) [83]. MTA's primary components are similar to those of Portland cement, specifically dicalcium silicate, tricalcium silicate, tricalcium aluminate, gypsum, and tetra calcium aluminoferrite. Gypsum and tetra calcium aluminoferrite are crucial in determining the setting time of MTA. MTA contains less gypsum compared to Portland cement, about half as much, which contributes to a longer working time. Additionally, MTA has reduced levels of tricalcium aluminate, further extending its working time compared to traditional Portland cement [21].

MTA is available in two forms: gray and white. The gray variant was the original form introduced. However, due to concerns about potential color changes caused by the gray version, the white form was introduced in 2002 [84]. The white MTA contains significantly less iron oxide, which is the primary factor contributing to the color difference. Specifically, the white MTA has 90.8% less iron oxide compared to the gray version, making it more suitable for aesthetic applications where color appearance is a concern. Originally, gray MTA is composed of dicalcium silicate, tricalcium silicate, and bismuth oxide. White MTA, on the other hand, primarily contains tricalcium silicate and bismuth oxide. When MTA powder is mixed with water, it first forms calcium hydroxide and hydrated calcium silicate [85]. This reaction results in the formation of a porous, crystallized gel. The high alkalinity of MTA after hydration is due to the calcium hydroxide, which contributes to its overall properties. The structure of the hydrated MTA consists of a framework of cubic and needle-shaped crystals. The needle-shaped crystals form thick rings that fill the spaces between the cubic crystals. Surface analysis reveals that the crystals in gray MTA are approximately eight times larger than those in white MTA [86]. Although Portland cement can be considered a similar material, MTA is distinct in several ways. MTA has a smaller average particle size, contains fewer heavy metals and toxins, and has a longer working time compared to Portland cement [87]. Additionally, MTA is generally more cleanable and processable than ordinary Portland cement.

3.3. Physical Characteristics of MTA

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When mixed with sterile water at a ratio of 1:3 (liquid to powder), MTA powder forms a gel (colloidal substance). To ensure proper setting, it is recommended to use a wet cotton pellet to temporarily cover the material, maintaining moisture until the next appointment. The hydration process of MTA is influenced by several factors, including the ratio of powder to liquid, the mixing technique (which can affect air bubble inclusion), the pressure applied during compaction, environmental humidity, and the pH and temperature of the environment [88].The physical properties of MTA are significantly affected by these factors. The hydration reaction, involving tricalcium silicate ($3CaO·SiO2$) and dicalcium silicate ($2CaO·SiO_2$), is crucial for its setting and strength. Notably, dicalcium silicate contributes to the material's strength, making it a key component in determining the final characteristics of the set MTA [89].

3.4. Solubility

MTA is generally very insoluble. However, some long-term studies have indicated an increase in its solubility over time. Notably, white MTA tends to be more soluble than gray MTA [90]. The solubility of MTA can be influenced by the powder-to-liquid ratio; specifically, a higher liquid-to-powder ratio increases both the porosity and solubility of the material. More water in the mixture accelerates the release of calcium from MTA. Additionally, the addition of bismuth oxide, a water-insoluble substance, contributes to the low solubility of MTA. Research on the hydration of MTA has demonstrated that bismuth oxide interacts with the calcium and silicate components in MTA, affecting its solubility [91].

3.5. Setting Time

The average setting time for MTA is approximately 165 ± 5 minutes, which is longer than that of amalgam, Super EBA, and IRM. Gray MTA, in particular, exhibits a significantly longer initial and final setting time compared to White MTA. This extended setting period for MTA, especially White MTA, is attributed to its lower content of sulfur and tricalcium aluminate compared to Portland cement [92].

3.6. Retentive Strength

MTA has been evaluated as an adhesive for prefabricated posts and compared with zinc phosphate and glass ionomer cements. The findings revealed that zinc phosphate and glass ionomer cements offer significantly greater retention than MTA. Consequently, MTA is not deemed suitable as an adhesive material for prefabricated posts [93].

3.7. Setting Expansion

MTA exhibits a slight expansion upon hardening, with gray MTA showing more expansion compared to white MTA. Research comparing the hardening expansion of white and gray MTA in HBSS (Hank's Balanced Salt Solution) and sterile water found that gray MTA expanded significantly more than white MTA in both environments. Specifically, gray MTA showed less expansion in HBSS compared to sterile water, whereas white MTA expanded more in HBSS than in sterile water [94]. The differences in expansion between the two types of MTA may be attributed to the composition of the immersion liquid (Hank's solution) or variations in their chemical compositions [95]. These findings indicate that the environment in which MTA is maintained affects its expansion during hardening.

3.8. Compressive Strength

Initially, MTA's compressive strength is notably lower than that of amalgam, IRM, and Super-EBA, measured after 24 hours. However, after three weeks, the compressive strength of MTA becomes comparable to that of IRM and Super-EBA [18]. The variation in compressive strength is partly due to the slower hydration rate of dicalcium silicate compared to tricalcium silicate. The compressive strength of white MTA is generally lower than that of gray MTA at both 3- and 28-days post-mixing. Conversely, some studies have found white MTA to have higher compressive strength compared to gray MTA. Therefore, the compressive strength of MTA is not significantly influenced by the compaction pressure applied [74]. While keeping MTA in dry conditions can reduce its compressive strength, extended contact with moisture improves its strength.

3.9. Radiopacity Evaluation

The average radiopacity of MTA is 17.7 millimeters of aluminum thickness, with white MTA having a higher radiopacity than gray MTA [92]. Although both types contain equal amounts of bismuth oxide, additional components in white MTA led to its increased radiopacity. The method of applying MTA affects its physical properties, with one of its main challenges being the difficulty in handling [96]. Various devices have been developed to make MTA application easier, including Teflon cylinders, syringe (tools, and specialized pluggers). MTA can be inserted using either

the manual (with plugger) or ultrasonic method. The manual method generally provides better material consistency with fewer bubbles compared to the ultrasonic technique. However, ultrasound can be applied both directly and indirectly (by placing the ultrasonic tip on the plugger). Increasing pressure during compaction helps reduce bubbles and microscopic channels in the MTA mass, but applying excessive pressure does not necessarily enhance its physical properties [97]. Aside from ProRoot MTA, which is the primary formulation, other types of MTA have been introduced, including AMTA (Anglus MTA from Brazil) available in both white and gray, and CPM Egeo, a white MTA produced in Argentina [21].

Other MTA-based materials have also been explored, including MTA Bio, light-cured MTA, and MTA root canal sealers (MTA-obtura (Angelus) or Egeo (CPM) sealer). Gray MTA consists of 75% Portland cement, 5% calcium, and 20% bismuth oxide, while Angelus MTA contains 80% Portland cement and 20% bismuth oxide [98]. Studies show that Angelus MTA has a slightly higher pH and releases more calcium than gray MTA, though the difference is minimal. Both types release the same number of arsenic ions, which are considered low in toxicity. Gray MTA has a more uniform chemical composition, particle size, and shape compared to Angelus MTA, whose particles are more irregular. However, Angelus MTA demonstrates better solubility, losing over 30% of its weight within the first 24 hours, exceeding the standard for Portland cement [74]. Dehydrated calcium sulfate in Angelus MTA reduces its setting time to just 10 minutes. The hardening time for Angelus MTA is 28.14 ± 0.49 minutes, which is shorter than that of both white and gray MTA. The Endo CPM sealer, an Argentine version of MTA sealer, has a composition similar to MTA but contains calcium carbonate, which lowers its pH. Both Endo CPM and Angelus MTA promote mineralization in subcutaneous tissues [89].

Several studies have examined the antibacterial and antifungal properties of MTA. While MTA shows limited antimicrobial activity against certain microorganisms, it has been found to have antibacterial effects on some facultative aerobic bacteria but no significant impact on anaerobes. The antifungal properties of MTA have produced mixed results. Some studies indicate that both gray and white MTA exhibit antifungal activity, while others suggest gray MTA has limited or no antifungal effects [99]. One study found that freshly mixed MTA, or MTA after 24 hours of setting, demonstrated antifungal effects against Candida albicans [100]. These antifungal properties may stem from MTA’s high pH or other substances released into the surrounding environment. Regarding the antibacterial properties of MTA, some studies suggest that gray MTA has stronger antibacterial effects than white MTA, while others report that both types show similar levels of antibacterial activity [99]. Therefore, research has demonstrated that MTA has both antibacterial and antifungal properties. However, reducing the powder-to-liquid ratio can diminish these properties. Adding chlorhexidine to white MTA enhances its antimicrobial effects [101]. When chlorhexidine gel is used, MTA does not harden even after 7 days, but when chlorhexidine is added in liquid form, the material hardens sufficiently after 72 hours.

3.10. MTA placement method on its physical properties

The placement method significantly influences MTA's physical properties. A primary challenge with MTA is its difficult handling. To ease its application, various devices have been developed, including Teflon cylinders, syringe-(tools, Messing guns, and specialized pluggers). MTA can be applied using either the manual method (with a plugger) or an ultrasonic technique. The manual approach generally provides better material consistency with fewer bubbles than the ultrasonic method. Ultrasonics can be employed both directly and indirectly by placing the ultrasonic tip on the plugger. While increasing pressure during compaction reduces bubbles and microscopic channels in the MTA mass, applying more pressure does not necessarily enhance MTA's physical properties.

Effective placement of MTA is crucial for its performance, with techniques varying between manual compaction and ultrasonic activation (Figure 2). Manual placement using pluggers generally yields a denser mix with fewer voids, while ultrasonic methods can aid condensation in challenging access situations. Optimizing compaction pressure is essential to minimize microchannels and ensure a reliable seal, regardless of the technique chosen.

Specialized instruments, such as the Messing Root Canal Gun (Figure 3), enhance precision in MTA delivery and hemostatic control during surgical procedures like perforation repair. This device facilitates controlled placement of MTA and associated absorbable barriers, such as collagen or calcium sulfate, ensuring a dry operative field. Precise material application and effective hemostasis are critical factors influencing the success of bioactive material placement. Moving on from the Messing Root Canal Gun, the importance of ensuring proper hemostasis during the perforation repair process. This involves utilizing hemostatic materials, absorbable or non-absorbable barriers, to control bleeding in the affected area. By achieving hemostasis,

the dentist can better visualize the perforation site, allowing for more accurate placement of restorative materials. It is essential to consider both the type of material used and the techniques employed to ensure proper hemostasis and optimize the outcome of the treatment.)

Figure 1. Classification of root-end filling materials: Comparative visualization categorizing traditional materials (metals, cements) alongside contemporary bioactive alternatives like MTA and CEM Cement, highlighting the evolution towards bioactive solutions

Figure 2. Operative techniques for MTA placement: Schematic comparison of manual compaction using pluggers versus ultrasonic compaction methods for applying MTA during procedures like perforation repair and root-end filling, emphasizing differences in consistency and bubble formation

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Figure 3. Depiction of the Messing Root Canal Gun used for controlled delivery of MTA and absorbable hemostatic barriers (e.g., collagen, calcium sulfate) during endodontic procedures requiring perforation repair or hemostasis

3.10. Other Types of MTA

In addition to ProRoot MTA, the primary formulation, several other MTA products are available on the market. These include AMTA (Anglus MTA from Brazil), available in both white and gray, as well as Egeo (CPM) sealer, which is a white MTA produced in Argentina [21]. Other researched MTA variants include MTA Bio, light-cured MTA, and root canal sealers, MTA-obtura (Angelus) and Egeo (CPM) [18].The composition of gray MTA includes 75% Portland cement, 5% calcium, and 20% bismuth oxide. In contrast, MTA Angelus consists of 80% Portland cement and 20% bismuth oxide [94]. Studies indicate that MTA Angelus has a slightly higher pH and releases more calcium compared to gray MTA, though the difference is not significant. Both types release arsenic ions in similar, minimal amounts, which are considered less harmful to the body. Gray MTA has a more uniform chemical composition, particle size, and shape compared to Angelus MTA, which has more irregular particle sizes compared to ProRoot MTA [74]. Additionally, MTA Angelus has higher solubility than Portland cement, losing more than 30% of its weight within the first 24 hours, which exceeds the standard. Compared to white and gray MTA, Angelus MTA has lower radiopacity [72]. The absence of dihydrate calcium sulfate in MTA Angelus reduces its setting time to 10 minutes. The setting time for Angelus MTA is 49.0 ± 28.14 minutes, which is shorter than that of white and gray MTA. The Endo CPM sealer, an Argentine variant of MTA sealer, has a similar composition to MTA but includes calcium carbonate, which lowers its pH. Both Endo CPM and MTA Angelus promote mineralization in subcutaneous tissues [102].

3.11. Disadvantages of MTA

MTA has several notable disadvantages, with tooth discoloration being a primary concern. To address this issue, the manufacturer developed white MTA; however, in vitro studies have shown that even white MTA can change color after just three days of exposure [103]. This color change occurs within the depth of the canal and is attributed to the presence of iron and magnesium elements. Additionally, MTA contains components similar to those in Portland cement, including arsenic, although the concentration in gray MTA is six times lower than in Portland cement. The presence of iron oxide in MTA also interacts with arsenic, contributing to its stabilization [90]. MTA presents several disadvantages, including its insolubility and limited clinical use, which reduce the amount of

arsenic released from the material. Another major drawback is its long setting time, though white MTA has a shorter setting time compared to gray MTA. Additionally, MTA cannot be dissolved if retreatment is needed, although a solvent called Bio Pure MTA has been introduced that reportedly dissolves white MTA within 5 minutes [104]. Other notable disadvantages include its high cost and challenging handling properties, which researchers are actively working to address.

4. Clinical Considerations in the Use of Root-End Filling Materials

In 1983, alongside the publication of research findings, an application for intellectual property rights for MTA, titled "Tooth Filling Material and Its Method of Use," was submitted to the United States Patent and Trademark Office (USPTO). The patent was granted and published in 1995. A subsequent application, filed in 1988, sought to secure intellectual property rights for a dental cavity filling material made from Portland cement. This application was also accepted and published by the USPTO [105]. In the United States, the production and use of dental materials require approval from the Food and Drug Administration (FDA). In 1998, after receiving FDA approval, MTA was marketed under brands (Taha), Beauply, and Protten MTA. However, the material's gray color led to aesthetic concerns, particularly in visible areas of teeth where appearance is important. In response to aesthetic concerns about the traditional gray color of MTA, a new variant of the material with a more tooth (color) was developed and introduced to the market in 2007 under the name of tooth-colored MTA. The development of this new variation was initially proposed by an innovator in 2000 and was approved by the relevant scientific and industrial research organizations in the country. In 2001, a company in Iran received a license to produce and market this new tooth-colored variant of MTA under the brand name Bose MTA, providing a more visually appealing option for patients while maintaining the material's effective performance [106]. Although MTA has been registered with the United States Patent and Trademark Office (USPTO) under two separate claims and dates, it has not been registered with the World Intellectual Property Organization (WIPO) [107]. As a result, Brazil, Argentina, and Iran have been able to produce and market similar products. Today, various types of MTA are available in the dental materials market, with different pricing options. According to documents published by the USPTO, MTA is primarily composed of Portland cement type one, either in its original or modified form, with a surface area of 5500-4000 cm^2/g. A key characteristic of MTA is its ability to set and harden in a moist environment, allowing it to effectively seal and prevent the re-entry of pathogenic bacteria. The chemical composition of MTA includes approximately 65% calcium oxide (Cao) and 21% silica (SiO_2), which together constitute approximately 86% of the weight of the cement. Other components of the cement include alumina (Al_2O_3), iron oxide (Fe_2O_3), and gypsum ($CaSO_4{\cdot}2H_2O$), accounting for the remaining weight. Understanding the composition of MTA is important for researchers and clinicians in endodontics as it helps to inform their decision-making regarding the use and properties of this material in dental procedures [108].

The final MTA powder primarily consists of four key tricalcium compounds: tricalcium silicate ($3CaO{\cdot}SiO_2$), dicalcium silicate ($2CaO{\cdot}SiO_2$), tricalcium aluminate ($3CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$), and tetra calcium aluminoferrite ($4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$) [102]. Among these, calcium oxide is the most significant component. To achieve radiopacity, bismuth oxide (Bi_2O_3) is included in a ratio of 1:4 relative to the other components. The preparation of MTA requires water, with the recommended water content ranging from 10% to 40% by weight of the cement. The optimal water-to-powder ratio is 25%, corresponding to a powder-to-liquid ratio of 3:1. When mixed with water, MTA powder forms a colloidal suspension that hardens within approximately four hours [50]. Observations indicate that the color and chemical composition of MTA are not constant and vary depending on the type of material. Early samples, introduced by Torabinejad and commercialized in the U.S. (ProRoot MTA) and Brazil (Angelus), were gray in color, while more recent generations produced in the U.S., Brazil, Iran, and Argentina have been reported to be white or milky in color. In 2005, a research team led by Mesgari used SEM and EPMA to investigate the chemical composition of both white and gray MTA.Their study revealed that white MTA had significantly reduced levels of alumina (22% less), magnesium oxide (30% less), and most notably, a reduction of over 1000% in iron oxide, compared to gray MTA.These findings have been widely cited and reconfirmed in subsequent research, indicating that the chemical composition of MTA may be influenced by factors ,the manufacturing process and the intended application [18].

5. Clinical Applications of MTA

5.1. Application of MTA in Teeth with Open Apex

A crucial objective in endodontics is the management of necrotic pulps and vital pulp therapy in immature teeth

with open apices. Endodontic specialists continually explore and develop new methods to preserve the vitality of developing teeth and address issues, pulp exposure from trauma or necrotic conditions in teeth with incomplete roots [109]. Historically, calcium hydroxide was the primary material used for treating damaged teeth, including applications, pulp capping, pulpotomy, apexification, and managing root fractures requiring endodontic treatment. Recent research has shown promising results with MTA (Mineral Trioxide Aggregate) in these applications [90]. In two separate studies, MTA was shown to be successful in preserving and maintaining the health of dental pulp tissue. In one study, Jabari far and Khademi demonstrated the effectiveness of MTA for pulpotomy in primary teeth, with both clinical and radiographic evidence confirming its success. In another study, Khademi and Zare compared the use of MTA with calcium hydroxide in cat teeth and found that MTA was able to preserve healthy pulp tissue, while calcium hydroxide resulted in pulp degeneration. These studies, highlight the effectiveness of MTA in preserving pulp vitality compared to traditional materials [110].

The protocol for MTA pulpotomy in immature teeth emphasizes achieving hemostasis and precise material placement to facilitate apexogenesis as shown in Figure 4. Key steps include controlling bleeding, removing coronal pulp tissue, and applying MTA directly onto the vital radicular pulp stumps. Radiographic follow-up demonstrates successful outcomes, including continued root development and apical closure, contrasting with the inflammatory responses often seen with calcium hydroxide.

Calcium hydroxide offers several benefits, including its antibacterial properties and its ability to stimulate the formation of hard tissue in both pulp and peri radicular areas [13]. Its alkaline pH contributes to its biocompatibility, making it generally well-tolerated by surrounding tissues without causing adverse reactions. However, recent reports indicate that calcium hydroxide may reduce the resistance of dentin, increasing the risk of fractures in treated teeth. This is particularly concerning for children's teeth, which are more prone to fractures, especially in the cervical area, after treatment with calcium hydroxide [111].

MTA is considered a suitable alternative to calcium hydroxide due to several advantages. Its primary benefit is its excellent biocompatibility, making it well-tolerated by pulp and periapical tissues [13]. Similar to calcium hydroxide, MTA stimulates the deposition of hard tissue. However, MTA offers superior protection against bacterial penetration and microleakage compared to other dental materials. This is because MTA has good physical compatibility with adjacent dentin and can penetrate into dentinal tubules [16]. MTA also promotes the stimulation of interleukins that encourage osteoblast activity, which aids in pulp repair and regeneration when used as a pulp cap material [112]. This effectiveness has led to its use in apexification and root fracture repair. Unlike calcium hydroxide, MTA does not negatively affect dentin, making it particularly suitable for treating immature necrotic teeth, teeth requiring apexification, and those with horizontal root fractures. The bioactive properties of MTA result in the formation of a more robust dentin barrier after pulpotomy and pulp capping compared to calcium hydroxide and other materials [113].

5.2. Partial Pulpotomy and Pulp Cap

In cases where crown fractures in children and adolescents lead to pulp exposure and necrosis, the long-term survival of these teeth can be significantly compromised. The ability of pulp cells to manage damage depends on maintaining the homeostasis of the dental organ [114]. Immature teeth that lose vitality are at a higher risk of cervical fractures. Therefore, protecting the pulp is crucial until root development is complete, which is indicated by increased root thickness and apical closure [115]. The Cvek pulpotomy technique is a widely used method for protecting traumatized pulps. This technique historically relied on calcium hydroxide to stimulate the formation of a dent in barrier and to exert antimicrobial effects [19]. While the Cvek method boasts a high success rate, it has a notable drawback: once the dentin barrier is established, the restoration must be updated to fill the void left by the calcium hydroxide that has been washed away [116].

The presence of remaining necrotic material can serve as a reservoir for bacteria, or create a space prone to microleakage between the restoration and the tooth. Unlike calcium hydroxide, MTA effectively addresses these issues by providing a robust barrier against microleakage, offering excellent biocompatibility, and forming a durable dentin barrier [72]. This results in increased clinical success rates and eliminates the need for restoration updates, as MTA does not wash away over time. With the introduction of white MTA, this material is particularly recommended for use in the crown area of teeth due to its aesthetic advantages, as it does not cause discoloration or aesthetic issues [117]. The pulp tissue's reaction to MTA is comparable to that of calcium hydroxide, forming a thin layer of necrotic tissue at the dentin barrier's surface. Initially, an extracellular matrix develops in this upper region, which is eventually replaced by hard tissue, while odontoblast (cells) underneath produces reparative dentin. The technique of using MTA shares similarities with

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pulpotomy using calcium hydroxide, particularly in its application and outcomes [3]. The key distinction lies in managing pulp bleeding. This aspect is less critical when using the MTA method. With calcium hydroxide, it's essential to wait until the bleeding from the pulp ceases entirely. In contrast, with MTA, which requires moisture to set, some bleeding does not hinder the process [118]. When using MTA, if a thickness of at least 2 mm is achieved, it does not need additional protection during the hardening process [119]. If the tooth fracture allows for a temporary dressing, a piece of wet cotton should be placed between the dressing and the MTA. Once the MTA has set, restoration can proceed using bonding materials. It is important to monitor the primary tooth periodically to ensure that the dentin barrier forms and root development continues [117]. Calcium hydroxide, used in immature teeth for apexification, has several drawbacks, including repeated fractures at the cervical region, extended treatment duration, unpredictable outcomes, and delays in final restoration [120].

Torabinejad et al. demonstrated that MTA is an effective material for promoting healing at the apex of the tooth. When MTA is used as an apical plug, it creates a barrier that prevents the root canal filling material from extruding beyond the apex, thus eliminating the need for a separate hard tissue barrier. In this way, MTA serves not only to promote healing at the apex, but also to optimize the placement and effectiveness of root canal filling materials [121]. Since its introduction, MTA has been widely reported as successful in apical barrier procedures. The recommended size for an apical MTA plug is 4 mm. One challenge in managing immature teeth with pulp necrosis is the frequent occurrence of cervical root fractures during or after apexification treatment [122]. Due to the weak and thin dentin walls of developing teeth, it is advisable to strengthen these roots to prevent accidental fractures. The cervical area of a tooth can be reinforced either before or after the waxing treatment by applying bonding resin materials to regions prone to fracture. When using MTA as an apical plug in conjunction with apexification, the canal is typically exposed to calcium hydroxide for less than a month [123]. Histomorphometric analyses provide critical evidence of pulp tissue responses to different capping materials, revealing stark contrasts (see Figure 5). Calcium hydroxide often results in incomplete dentin bridges with tunnel defects and chronic inflammation, while MTA promotes thick, continuous hard tissue formation with reduced inflammation. CEM Cement demonstrates near-physiologic dentin-pulp complex regeneration, organized odontoblast layers, and absent inflammation, highlighting its biocompatibility.

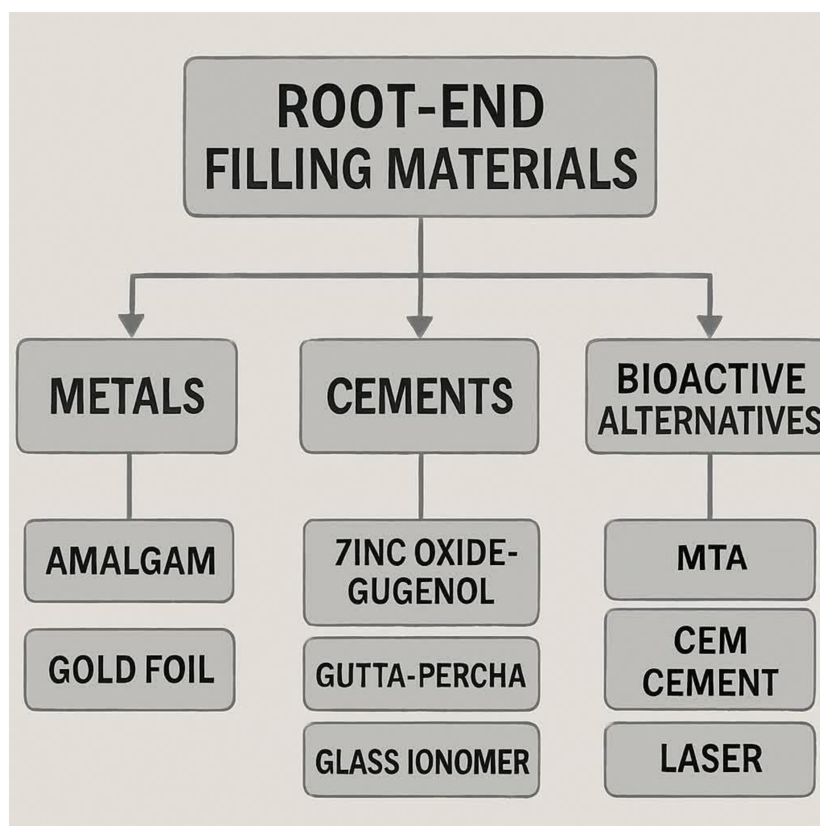

Figure 4. Clinical and radiographic sequence illustrating the technique for MTA pulpotomy, focusing on hemostasis control, MTA application, and long-term outcomes like apexogenesis and periapical healing

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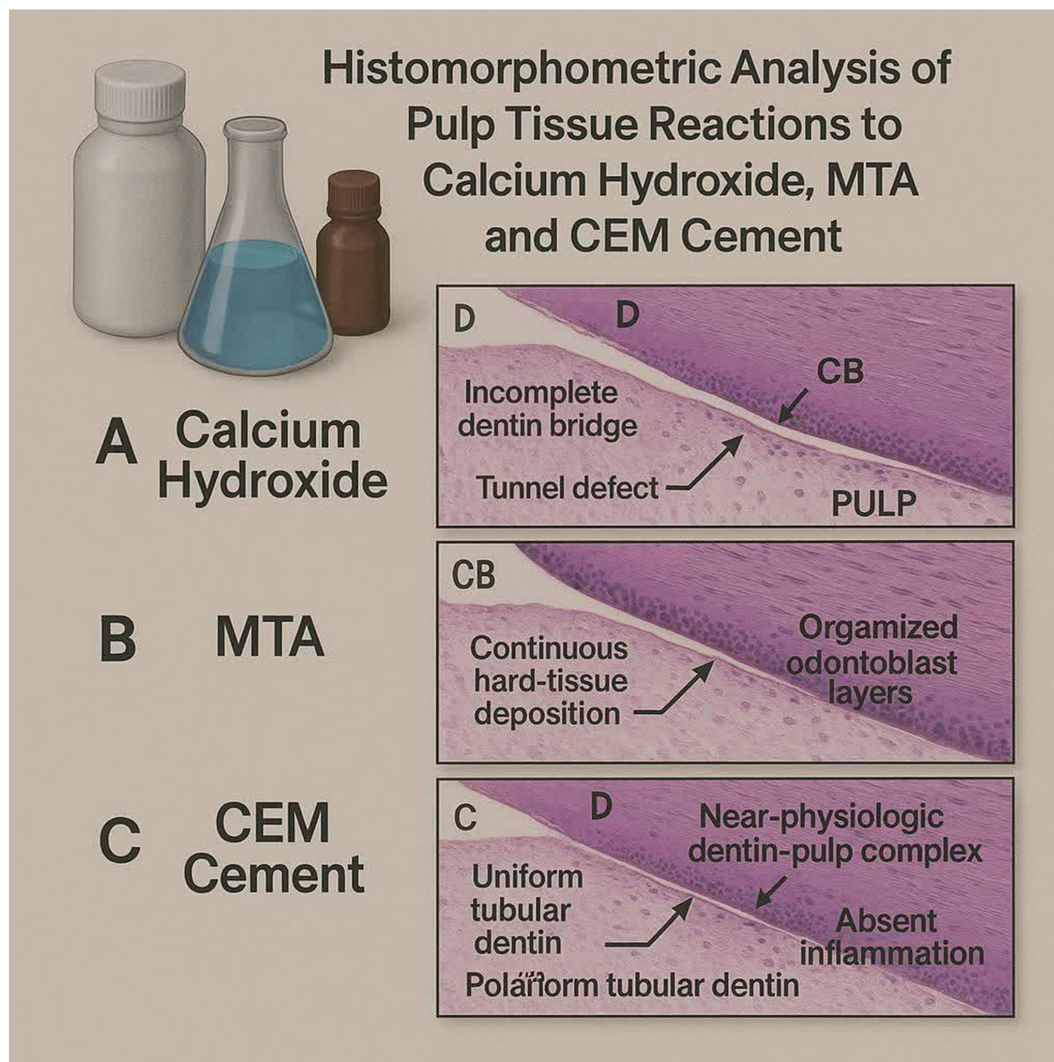

Figure 5. Comparative histological assessment showing pulp responses post-pulpotomy: Calcium Hydroxide (incomplete bridge, inflammation), MTA (continuous hard tissue, minor inflammation), and CEM Cement (uniform tubular dentin, organized odontoblasts, absent inflammation).

5.3. Steps for Apexification Treatment Using MTA

Administer an anesthetic injection to the tooth if needed. Isolate the tooth with a rubber dam and disinfect it using sodium hypochlorite or chlorhexidine [124]. Prepare the access hole to reach the root canal space as usual. Carefully remove necrotic tissue until bleeding is observed, ensuring not to advance beyond the root canal length. Instead of aggressively filing the canal walls, gently scrape the walls and thoroughly rinse with sodium hypochlorite [38]. For effective cleaning, wrap cotton around the endodontic file. Mechanical cleaning of the root canal is limited to avoid further weakening of the tooth by excessive removal of dentin. Therefore, disinfection of the canal should be performed using sodium hypochlorite, followed by treatment with calcium hydroxide. Given that some formulations of calcium hydroxide can increase the brittleness of root canal dentin, exposure to calcium hydroxide should be limited to one to three months, or less [125]. There is good evidence supporting the positive effects of keeping calcium hydroxide in the canal for up to two weeks. After placing the calcium hydroxide, cover it with a cotton pad and apply a temporary restoration. This temporary restoration should remain in place for up to one month to provide adequate protection until the completion of the treatment [126]. In the next session, if needed, the tooth is anesthetized again, isolated with a rubber dam, and the canal is re-entered. Calcium hydroxide is carefully removed from the canal, and the canal is thoroughly washed and dried [11]. Avoid stimulating bleeding from any areas with vital tissue. If bleeding does occur, it can be controlled with a cotton swab dipped in calcium hydroxide powder, and then the canal should be dried again with a paper towel. It is important not to completely dry the canal, as MTA requires moisture to set. Residual calcium hydroxide on the canal walls does not affect the MTA seal [113].

Placing MTA can be challenging, especially for those doing it for the first time. Its consistency is similar to wet sand, making it difficult to handle, but it does not harden immediately, so it can be washed away if necessary. To

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place the MTA, start by accurately determining the apical limit using pluggers with rubber stops marked at the appropriate length [127]. Place a small amount of MTA in the coronal chamber and use pluggers smaller than the canal diameter to carefully push the material towards the apical side where the vital tissue is located. An ultrasonic device can aid in the placement [109]. If all the pulp tissue is necrotic, MTA should be placed at the apical opening of the root canal. Decide beforehand how much of the canal will be filled with MTA. You may choose to use a single apical plug (at least 4 mm of MTA) and fill the remainder of the canal with gutta-percha after the apical plug has set, or fill the entire canal with MTA [124]. In either case, allow the MTA to harden for at least 4-6 hours before completing the treatment. During the hardening period, place a wet cotton ball in the coronal part of the MTA and close the access cavity with a temporary filling material. Once the MTA has set, restore the coronal access cavity with a bonding composite resin. After the apexification treatment with MTA, the tooth should be evaluated through radiography and clinical observation. The desired outcome is an asymptomatic tooth with supporting alveolar tissues that appear radiographically acceptable and free of decay or periapical disease [49].

5.4. Root Fractures

Root fractures often heal with either hard tissue, connective tissue, or a combination of both. In about 25% of cases with root fractures, an infection in the coronal part of the canal can cause lesions along the fracture line, while the apical part typically remains intact. In these cases, treatment is usually required only for the apical portion [79]. When a tooth with a root fracture shows signs of pulp and peri radicular disease, root canal treatment is recommended. Recent retrospective studies of 98 teeth with root fractures have compared various treatments. The best outcomes were observed when treatment focused solely on the coronal part of the root canal [128]. Long-term use of calcium hydroxide in this area helped form a hard tissue barrier at the fracture site, and the canal was subsequently filled at the fracture location.

Considering the potential for long-term use of calcium hydroxide to weaken dentin and the fact that treatment with calcium hydroxide typically spans several months (ranging from 3 to 24 months), utilizing MTA (Mineral Trioxide Aggregate) offers a more efficient treatment duration and avoids dentin weakening [122]. The effectiveness of MTA in treating the roots of teeth with fractures and pulp necrosis can be assessed both radiographically and clinically, with successful outcomes indicated by radiographic evidence of healing and a symptom-free, functional tooth [111]. Currently, there is insufficient data to fully evaluate the clinical outcomes of using MTA for root treatments in teeth with horizontal fractures, though there are several documented successful cases. For a tooth diagnosed with pulp and peri radicular disease, which often presents with lesions around the fractured area, the tooth is anesthetized, isolated with rubber dam, and disinfected with sodium hypochlorite or chlorhexidine [129]. A standard crown access hole is created to reach the root canal system. Necrotic tissue is removed up to the fracture point, and the canal is biomechanically prepared until it is compromised, then flushed with sodium hypochlorite. Depending on the dentist's preference, the canal may be immediately filled with MTA up to the fracture site, or calcium hydroxide may be used as an interim medicament between treatment sessions [19].

Similar to the decision-making process in cases of oxyfication, when dealing with root fractures, one must choose whether to use an MTA "plug" at the level of the fracture or to fill the entire canal with MTA. In either approach, it is advisable to let the MTA set before adding gutta-percha to the coronal portion of the canal and subsequently filling the access cavity. If MTA is placed up to the cervical level, the access cavity can be filled directly on top of the MTA [117]. MTA is also employed as a root end filling material due to its biocompatibility and excellent sealing properties, which make it highly effective compared to other materials. While various materials ,amalgam, Cavit, IRM, Super-EBA, glass ionomer, composite resins, and MTA have been used for root end fillings during apicoectomy, none offer the ideal properties of MTA [130]. A study conducted at Isfahan Dental School investigated the histological response of peri-apical tissue to the use of two different root end filling materials, amalgam and MTA. The results showed that the use of amalgam was associated with a higher incidence of peri-radicular tissue tumors compared to MTA. Additionally, the use of MTA was found to be associated with a high prevalence of cementum formation on the surface of the material [124].

Unlike Super-EBA or IRM, which can be prepared in a loose, mud (consistency) and applied to the root end, MTA cannot be handled in this manner due to its different consistency. MTA requires a drier, sandier mixture because it is prepared by adding more powder to the liquid, making it challenging to mold and apply precisely. To effectively use MTA, the surgical area, including the root end cavity, must be kept completely dry. Care should be taken not to disturb the material before the flap is turned and sutured [131]. MTA can be introduced into the root canal using various methods: a small spoon excavator, a small amalgam carrier, or the

Roydent MAP system, which utilizes small carriers similar to a caulking gun. After placing MTA in the root end cavity and up to the level of the cut dentin, excess moisture should be absorbed with dry cotton, and any surplus material should be removed using cotton. For direct pulp covering or pulpotomy using MTA in decayed teeth, the procedure typically involves two sessions, First, determine whether the pulp is healthy or showing signs of reversible pulpitis. After administering anesthesia, isolate the tooth with a rubber dam [132]. Disinfect the tooth surface with chlorhexidine or sodium hypochlorite, and then remove the underlying enamel with a diamond or carbide bur. Remove the decayed dentin using a carbide bur with a low-speed handpiece or a spoon excavator [133].

You can also apply a decay-detecting dye after drying the decayed dentin with air to help identify all areas of decay. If the dental pulp is exposed during decay removal, control the bleeding by placing a cotton ball soaked in 3-6% sodium hypochlorite for 20-60 seconds [134]. After decay removal, ensure that the pulp area shows some bleeding; absence of bleeding may indicate compromised tissue. If the pulp appears necrotic, a partial or complete pulpotomy or pulpectomy should be performed to reach the viable tissue. Use a diamond bur and a high-speed handpiece for this procedure. Place a cotton ball soaked in 3-6% sodium hypochlorite directly on the exposed pulp for 1-10 minutes to help control bleeding [135]. If homeostasis is not achieved within 10 minutes, the pulp is deemed irreversible, necessitating a more aggressive treatment approach (partial or complete pulpotomy). If homeostasis is achieved, proceed with pulpotomy treatment for the affected tooth. According to the manufacturer's instructions, MTA is mixed with sterile water in a 1:3 ratio until it reaches a clay (consistency). Prepare the MTA using a spoon, plastic instrument, or carrier. Transfer the MTA to the desired area, placing it directly on the exposed pulp. Gently pack the material with a dry cotton to ensure it is at least 1.5 mm thick. If there is any excess material, cover it with a 2 mm thick layer of cotton [136]. After placing the wet cotton, secure the tooth with a temporary restoration. In the follow-up session, typically conducted 5-10 days later, ask the patient about any sensitivity, discomfort while chewing, or pain in the affected tooth before administering anesthesia. Test the vitality of the pulp with a cold test. After local anesthesia and isolating the tooth with a rubber dam, remove the temporary restoration and the cotton. Check if the MTA has properly set, then proceed with a suitable bonding restoration for the final restoration of the tooth [137]. The patient should be examined 6 weeks later to check for any symptoms and perform a cold test. If the results are satisfactory, schedule follow-up visits at 6 and 12 months, and then annually thereafter.

5.5. Pulpotomy of milk teeth

MTA can also be utilized for pulpotomy in primary (milk) teeth. In this method, after removing the pulp down to the canal orifices, MTA mixed with water is placed instead of using cotton soaked in form cresol [138]. A study by Jabari far and Khademi compared the success rates of pulpotomy using form cresol versus MTA in human primary. The results showed that the clinical success rate for MTA was 79.3%, compared to 29.0% for form cresol. These findings suggest that MTA is an effective alternative to form cresol for pulpotomy in primary teeth [139].

5.6. Root canal filling

MTA can be used as a paste filler for root canal sealing. Due to its excellent sealing ability, biocompatibility, and other advantageous properties, MTA is a suitable choice when conventional root canal filling materials are not appropriate [140].

5.7. Secondary Filling

MTA can be used as a crown barrier in root canals for up to 3 months, similar to how glass ionomer is used. MTA is applied to seal the canal effectively [141]. Root canal treatment is complex and can involve various challenges, including errors and complications. The preparation of the access hole and the steps involved in canal formation and cleaning are particularly sensitive and prone to errors, perforation [142]. Perforation occurs when a hole is inadvertently created in the crown or root of the tooth during these procedures. There are also biological perforations that are not due to operator error, those caused by pathological conditions or connections between the canal and periodontal tissues [143]. Root perforation is a significant issue, often reported as the second most common cause of endodontic treatment failure.

5.8. Types of perforations

Root branch or foramen perforation: This refers to a perforation occurring in the foramen area, which generally presents one of the most challenging prognoses during treatment [144]. Perforation: This type of perforation happens when there is an unintended connection between the lateral surface of the root and the periodontal structures. It is often caused by improper alignment of the instruments during post space

preparation or by creating an excessively wide post space [145].

5.9. Perforation repair time

Following a perforation, the primary concerns include gum and periodontal inflammation, infection, and ultimately, tooth loss. An infectious perforation can lead to the development of fibrous connective tissue and abscesses [146]. If the perforation remains exposed to the oral environment, it results in progressive destruction of the periodontal tissue. The critical factor in determining the success of periodontal restoration is the time elapsed between the perforation and its sealing [80]. Research indicates that the best healing outcomes are achieved with immediate restoration.

5.10. Perforation site

The location of a perforation is crucial and significantly impacts the outcome of treatment, in addition to the time between perforation and intervention. The position of the perforation relative to the periodontal area plays a major role in the success of restoration efforts. Perforations that result in bony lesions pose a greater risk to prognosis [147]. Research has shown that the location of the lesion in relation to the marginal gingiva or junctional epithelium is a key factor in healing potential. Perforations near the gingival sulcus often led to inflammation, loss of epithelial attachment, and the formation of a periodontal pocket. Conversely, perforations located further from the sulcus tend to have a healthier periodontium and a more favorable prognosis [148]. Perforations that are well within the bone generally have a higher chance of successful restoration compared to those closer to the bone crest. apical and mid-root perforations not in direct contact with the oral cavity typically have a better prognosis [131].

Perforations can be categorized into three types based on their location, Subgingival, Mid-root and Apical. Subgingival perforations often occur during access cavity preparation and canal location. To prevent these errors, careful attention to the three-dimensional orientation of the tooth is essential. Utilizing three preoperative radiographs, two periapical views and one bitewing can help avoid perforations. Bitewing radiography is particularly effective in revealing the vertical dimensions of the pulp chamber compared to periapical radiography. The use of a surgical microscope and 3D imaging provides the operator with detailed information to assess the tooth in three dimensions [149]. Additionally, before preparing the access cavity, examining the mucosa and probing the root surface can provide valuable clinical information about the root's longitudinal axis [131]. This technique is particularly useful in cases involving veneer access or dental malposition's. Probing the cervical areas to assess the width and circumference of the furcation zone also helps identify the narrowest parts of the tooth structure [150]. Perforations in the middle of the root, particularly in the prepared length, typically occur during post space construction or during the cleaning and shaping of the canal's middle section [38]. To avoid these issues, carefully removing coronal gutta-percha with heat and hand instruments can help guide post drills to stay centered within the canal. This approach minimizes the invasive impact of the tools and reduces the risk of perforation [151]. Additionally, selecting the appropriate post size is crucial; the post should not exceed one-third of the tooth's mesiodistal width and should conform to the canal's anatomy. Apical perforations typically occur during canalization when using large, inflexible files, especially in curved canals or when passing through the apical isthmus. These perforations are often addressed during the canal filling process or through surgical intervention [152].

5.11. Perforation size

Small perforations generally result in less periodontal destruction and epithelial proliferation. In contrast, larger perforations present significant challenges, particularly in achieving a well-condensed seal [153]. The prognosis for larger perforations is more uncertain due to the increased surface area of the sealant in contact with the periodontium, which can allow inflammatory stimuli to persistently affect the surrounding tissues [47]. Additionally, the larger the defect, the more challenging it becomes to achieve a proper marginal seal, which may exacerbate the problem.

5.12. Materials used in perforation repair

The choice of material is crucial for successful perforation repair. An ideal repair material should be antimicrobial, non-toxic, capable of creating a suitable seal, non-absorbable, radiopaque, non-carcinogenic, and promote osteogenesis and cement genesis [154]. It should also be readily available and cost-effective. Furthermore, the material should support the formation of new bone over it and serve as a matrix for the root canal filling material. In 1967, a combination of chloroform-rosin and gutta-percha beads with phosphate cement was introduced for perforation repair. Zinc oxide-eugenol cements were also used, but they often led to chronic inflammatory responses, abscess formation, and breakdown of the alveolar bone [155]. Calcium hydroxide was introduced with the aim of forming hard

tissue and creating a barrier to prevent obturation materials from leaking into the periodontal ligament space. While it helps prevent the growth of granulation tissue into the lesion, it can cause necrosis of adjacent periodontal tissues. In clinical studies, Kuwait Cavit has been evaluated as a material for treating endodontic perforations, showing favorable results in 89% of cases. However, Cavit can produce a mild to moderate inflammatory response when used for repairing furcal perforations. Super EBA, introduced in 1985 for endodontic perforation repair, demonstrated superior adaptation and less spreading compared to amalgam, although its resolution was weaker. Research has shown that Super EBA has a 95% success rate for retrograde treatments over periods ranging from 6 months to 10 years [54]. Glass ionomer cements, introduced in 1990, were found to be comparable to seal glass ionomer and amalgam in effectiveness, with no statistically significant differences. However, glass ionomer cements typically produced an inflammatory response, though this was less severe compared to gutta-percha [156].

5.13. MTA for Perforation Repair

Compared to Super EBA, IRM, and amalgam, MTA (Mineral Trioxide Aggregate) exhibits the lowest toxicity and offers high biological compatibility [87]. It can promote the growth of cement, substances on its surface and typically induces fewer inflammatory responses than other materials. MTA also shows superior marginal adaptation to surrounding dentin compared to amalgam, Super EBA, and IRM. In the presence of blood, MTA is more resistant to leakage than these materials, making it particularly effective in areas exposed to peri radicular fluids. Ongoing research aims to enhance MTA’s properties, including improving its radiopacity, sealing ability, resistance to liquid leakage and bacterial contamination, and reducing technical sensitivity while preserving its biological benefits [47]. Currently, MTA is considered the material of choice for perforation repair.

6. Barriers in Perforation Repair: Material Selection and Clinical Considerations

The use of barriers in perforation repair is a crucial step in ensuring the success of the treatment and preventing potential bacterial contamination. These barriers create a dry environment and provide a scaffold for restorative materials, ultimately leading to better outcomes in the repair process. There are two main types of barriers: absorbable and non-absorbable. Absorbable barriers, collagen membranes and calcium sulfate, are useful for their ability to be resorbed by the body, promoting healing and reducing the need for removal. Absorbable hemostatic agents, collagen membranes and calcium sulfate, have emerged as promising solutions for the management of bleeding in perforated teeth. Research has shown that these materials exhibit excellent tissue compatibility and biocompatibility, leading to improved outcomes in the repair of perforations. These advantages, coupled with their gradual resorption by the body, have made them popular choices for use in clinical settings. On the other hand, non-absorbable barriers are materials that remain in the tooth long-term and do not get absorbed by the body. These materials are effective in maintaining a dry environment and providing a scaffold for restorative materials. Some examples of non-absorbable barriers include MTA and amalgam [157].

6.1. Treatment steps of perforation repair

When a perforation happens and the canal is not yet fully prepared, repairing the perforation is necessary before continuing with endodontic treatment. This repair is important as it manages bleeding, cleans the canal, and makes it easier to fill. The perforated canals should be enlarged and prepared to allow better access to the defect and reduce the need for further instrumentation after the repair [158]. Maintaining the canal's path during the repair is crucial to prevent the restorative materials from obstructing it. To prevent blockage during the repair, a piece of gutta-percha or an endodontic file is placed in the defect. If endodontic treatment fails due to perforation, the material in the root canal aids the dentist in repairing the perforation before performing additional endodontic procedures [159].

6.2. Hemostatic substances in the treatment of perforations

Perforations often result in significant bleeding, so it is crucial for the dentist to be knowledgeable about hemostatic agents to manage the bleeding effectively. Important substances for achieving hemostasis include collagen, calcium hydroxide, calcium sulfate, and freeze-dried bone [160]. Ferric sulfate is another hemostatic material used, but it can leave a clot that may encourage bacterial growth and potentially compromise the outcome [161].

6.3 The use of barriers in perforation repair

In perforation repair, two major challenges are achieving hemostasis and placing restorative materials. Barriers help by creating a dry environment and providing a

scaffold that allows restorative materials to be effectively applied. Barriers are generally categorized into absorbable and non-absorbable types [162]. Absorbable barriers (collagen (Colla Cote)), are used inside the bone rather than within the tooth. They ensure complete hemostasis, have good tissue compatibility, and are absorbed within 10 to 12 days. Collagen membranes are typically used with amalgam, Super EBA, or other non-bonding materials. Calcium sulfate, another absorbable barrier, blocks blood vessels mechanically, is biocompatible, and is absorbed within 2 to 4 weeks, making it a preferred choice for membrane adhesion in various techniques [163]. Non-absorbable barriers include MTA, which offers excellent biocompatibility and can function both as a barrier and a restorative material. MTA is particularly useful in cases where moisture contamination is a risk or where visibility and access are limited. It can serve as the primary radicular filler and be topped with other membranes if needed.

6.4. Treatment of perforations in the coronal third of the canal

First, isolate the affected area. If the perforation is recent and mechanically induced, it will likely be clean and free of infection. In such cases, and if hemostasis is achieved, repair the lesion immediately [164]. However, if the perforation is older and has minor leaks, disinfect the wound before proceeding with the repair. Ultrasonic devices are particularly effective for preparing the perforation site. Once the lesion is properly prepared, use a calcium sulfate buffer with composite resins or a tooth-colored restoration in aesthetically sensitive areas [165]. For less critical areas, amalgam, Super EBA, or MTA can be used for the restoration.

6.5. Treatment of perforations in the middle third or strip perforations

Strip perforations are typically caused by Gates Glidden or Pizorimer drills when preparing a large post space in the wrong direction. These perforations are usually oval-shaped and often have a broad surface. The approach to treating strip perforations is similar to that for coronal third perforations, but with the added challenge of dealing with deeper lesions located farther from the occlusal surface [158]. To manage these deeper defects on the canal's side wall, creating a direct access hole can enhance visibility and facilitate treatment. Most perforations caused by excessive use of instruments are sterile and do not require further intervention. These perforations should be immediately irrigated. If the perforation in the middle third is small, bleeding can be controlled and the working area kept dry, it may be possible to repair it while filling the canal. However, if the perforation is large and the canal cannot be fully dried, the repair should be completed before filling the canal. It is advisable to finish the root canal preparation before repairing the perforation. To prevent canal blockage during repair, a removable space holder can be used inside the canal, positioned more apically than the perforation. MTA is preferred for these cases due to challenging access, limited visibility, and potential difficulties in maintaining a dry environment. Mixed MTA is applied to the perforation site, and endodontic treatment can resume 4 to 6 hours after the MTA has set [166].

6.6. Treatment of Apical Third Perforations

Apical third perforations commonly result from errors during canal formation, often caused by canal blockages and calcification. These perforations are typically addressed through apicoectomy and removal of the apical portion [167]. However, it is advised to first attempt non-surgical root retreatment. The dentist should aim to reopen the blocked canal and insert a pre-bent large file into the canal, guiding it towards the apical area without necessarily reaching the full working length. This file helps preserve the main canal’s path and prevents further blockage during perforation repair. MTA (Mineral Trioxide Aggregate) is then applied, followed by semi-moist cotton placed in the pulp chamber to maintain contact with the MTA, and the tooth is temporarily sealed until the next session. Upon re-entry, the file is removed, and if the MTA has set, the area is rinsed, and root canal preparation is finalized. MTA is preferred for deep perforations, especially when a dry environment cannot be achieved. Regular monitoring of these materials is recommended before placing the permanent restoration. It's important to note that not all perforations can be managed non-surgically, even with advanced techniques and experienced practitioners. Some cases may still require surgical treatment or extraction [129].

7. The Clinical Use and Effectiveness of CEM Cement in Endodontics

CEM cement is a biocompatible material with various endodontic applications. Its unique properties, including antimicrobial and antifungal capabilities, make it an effective choice for sealing root canals, as well as a potential alternative to traditional materials (mineral trioxide aggregate). Additionally, CEM cement has been shown to promote pulp regeneration and improve the healing process, making it a viable option for procedures

(pulpotomy and direct pulp capping). It is also easy to handle and sets quickly, making it an attractive choice for dental practitioners. Despite its promising properties, the long-term clinical effectiveness of CEM cement in endodontics is still being studied. However, early research suggests that it may be a valuable tool in the treatment of dental infections, perforations, and other endodontic procedures [168].

7. Clinical Applications and Procedures of CEM Cement

7.1. Calcium-Enriched Mixed Cement

CEM cement was developed in 2006 by Askari for dental applications. As the name suggests, it is composed of various calcium compounds, including calcium oxide, calcium hydroxide, calcium carbonate, calcium silicate, and calcium phosphate, among other ingredients [169]. While its clinical uses are similar to MTA (Mineral Trioxide Aggregate), its chemical composition differs from both MTA and its base material, Portland cement. CEM cement also has distinct physical properties, better flowability and a more suitable film thickness compared to MTA. Additionally, it sets more quickly [141]. Its flowability is superior to IRM, and although it has demonstrated slightly less microleakage than MTA, the difference is not significant. Cytotoxicity studies of CEM cement have shown results similar to MTA, while its biocompatibility in pulp treatments has proven to be superior to calcium hydroxide and comparable to MTA [72].

Clinical studies using CEM cement for the treatment of irreversible pulpitis have shown very positive outcomes, including the formation of a complete dentin and pulp bridge without underlying inflammation, as confirmed histologically. The antimicrobial properties of CEM cement are considered an advantage, comparable to calcium hydroxide and superior to MTA. CEM cement's ability to produce hydroxyapatite on the surface of REF materials leads to favorable tissue responses [21]. It can generate hydroxyapatite crystals at the interface between the cement and the dentin wall of the root canal, forming a secondary layer that explains its superior resistance to microleakage. Hydroxyapatite, being endogenous to peri radicular tissues, acts as a precursor in the formation of cementum on the surface of CEM cement.

This property ensures that, even when analyzed through electron microscopy, no visible differences exist between CEM cement and the surrounding dentin [170]. A recent clinical trial confirmed histologically that both CEM cement and MTA integrate with root-end dentin, forming a continuous cementum layer, facilitating full regeneration of the periapical complex [171]. With excellent flowability, biocompatibility, and ease of use, even in wet conditions, CEM cement holds significant potential for future applications. However, long-term clinical studies are still required to fully validate its quality. A review of MTA over the past decade reveals that it has been widely used as an effective alternative material, delivering satisfactory clinical outcomes. CEM cement, a newer material introduced to dental science, has demonstrated comparable results to MTA in VPT treatments [21]. When a dentist is performing VPT in cases of exposed pulp, the available data on both MTA and CEM suggest that these materials are ideal choices for achieving successful treatment outcomes.

7.2. Properties of calcium enriched mixed cement

CEM cement, formed by blending a powder with a liquid, is a hydrophilic material that becomes stronger when exposed to moisture or humidity following therapeutic application [89]. It is composed of different calcium-based compounds, including calcium oxide, calcium carbonate, calcium phosphate, calcium silicate, and calcium aluminate, and demonstrates the following properties.

7.2.1. *Antimicrobial and Antifungal Properties*

CEM cement, which contains calcium oxide, exhibits significant antimicrobial activity. Calcium oxide is known for its strong disinfectant properties, particularly within infected dental canals [172]. Comparative studies have shown that CEM cement's antimicrobial effectiveness is on par with calcium hydroxide and surpasses that of both MTA and Portland cement. Specifically, CEM demonstrates effective inhibition against bacteria ,Enterococcus faecalis, Pseudomonas aeruginosa, Staphylococcus aureus, and Escherichia coli. Additionally, when tested for antifungal activity, both MTA and CEM were found to completely eliminate Candida albicans within 24 hours [173].

7.2.2. *Creating a Seal*

Studies have investigated CEM cement's microleakage compared to IRM and three types of MTA (American, Brazilian, and Iranian) as end-of-root filling materials in various environments. The results indicate that the degree of flooding with these materials follows the order: MTA < CEM < IRM, with CEM and MTA causing more flooding than IRM [117]. Additionally, when root canals were filled with CEM combined with single-cone gutta-percha, the apical sealing was comparable to that of the MTA group, while the coronal

sealing was notably superior to that of the MTA group [174].

7.2.3 *Easy Clinical Use*

A study comparing the physical properties of CEM cement with MTA demonstrated that their working times and dimensional changes are similar. However, CEM cement has a shorter setting time, greater flow, and a thinner film thickness compared to MTA. These characteristics are generally regarded as significant benefits for the clinical use of dental materials [90].

7.2.4. *Biocompatibility*

This chapter provides a comprehensive review of the biocompatibility of CEM cement, with a focus on its effects on various cell types, including fibroblasts and human gingival fibroblasts. In this chapter, we will discuss the results of various studies, including those that compared CEM cement's cytotoxicity to traditional materials (IRM and calcium hydroxide). These studies show that CEM cement is superior in terms of biocompatibility, which is a critical factor in its effectiveness for use in direct pulp capping and pulpotomy procedures.

7.2.4.2 *Cytotoxicity*

The cytotoxicity of CEM and MTA was evaluated using the MTT method on L929 fibroblast cells and through electron microscopy on human gingival fibroblast (HGF) cell lines. The findings indicated that CEM and MTA have similar levels of cytotoxicity, which are significantly lower compared to IRM, highlighting their superior biocompatibility [175].

7.2.4.2 *Direct Pulp Coverage*

The microarchitecture of the dentin bridge formed is a key indicator of a material's bioactivity and efficacy (Figure 6). Calcium hydroxide typically induces a thin, often discontinuous bridge with underlying inflammation. MTA stimulates a thicker, more continuous calcified barrier. CEM Cement promotes the formation of a near-physiologic dentin-pulp complex with uniform tubular dentin and well-organized odontoblast layers, signifying superior regenerative potential.

7.2.4.3 *Pulpotomy*

In a study involving pulpotomy treatment on dog premolar teeth, MTA, calcium hydroxide (CH), and CEM were used. The samples were evaluated for inflammation, the quality and thickness of the calcification barrier, pulp vitality, and odontoblast morphology [176]. Long-term radiographic evidence substantiates the efficacy of CEM Cement in vital pulp therapy, demonstrating its ability to promote healing and regeneration (Figure 7). Sequential radiographs document successful outcomes including apexogenesis (root closure), periapical healing of lesions, and the formation of a distinct dentin bridge beneath the material over periods up to 24 months. This evidence supports CEM Cement as a reliable biomaterial for procedures like pulpotomy. A rare case report describes a maxillary central tooth pulpotomy with an open apex exposed due to trauma. After one month, the treatment using CEM material resulted in the successful formation of a dent in bridge and apex genesis [177]. The findings highlight the successful development of a dentin bridge following CEM application and confirm the overall success of apexogenesis. An extensive clinical trial is currently underway to evaluate the treatment of permanent molar teeth with open apices resulting from extensive crown decay and irreversible pulp inflammation [178]. Preliminary results from the apex genesis treatment of these teeth indicate promising outcomes, highlighting the potential of using CEM in pulpotomy procedures for these cases. In a study involving a case series of twelve adult permanent molars with irreversible pulp inflammation, pulpotomy was performed using CEM [179].

This approach yielded fully successful results for the first time after approximately 16 months of treatment with this technique and new material. The study demonstrated that using CEM cement in human third molar teeth allowed for the development of a calcified barrier beneath the cement, effectively enclosing the CEM within the internal environment of the tooth and achieving tissue regeneration [180]. Unlike past concerns with calcium hydroxide—where there was a risk of long-term calcification of the pulp space—no such issue was observed with CEM even after approximately 2 years of follow-up. This treatment approach represents a novel, cost-effective alternative to traditional root canal therapy for managing irreversible pulp inflammation, offering a simpler and successful method for preserving vital pulp [21]. Long-term studies are still needed to further evaluate this treatment's effectiveness. With these findings, many teeth can benefit from this new treatment method. However, it is important to note that this approach is not suitable for teeth that need their root canal space to accommodate a pin or post for the final crown restoration.

7.2.4.4. *Hydroxyapatite Generation*

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In addition to its other properties, CEM cement can generate hydroxyapatite crystals on its surface when placed in a normal saline environment. The structure of these hydroxyapatite crystals closely resembles that of standard hydroxyapatite crystals, a property not exhibited by MTA [181]. This suggests that CEM contains the necessary chemical factors for hydroxyapatite formation, unlike MTA. Furthermore, in an environment similar to interstitial fluid (PBS), CEM produces a greater quantity of hydroxyapatite, enhancing its suitability as a filling material for the root canal by improving its flow characteristics [171].

7.3. Clinical Application

When clinical and radiographic examinations reveal deep decay or trauma that makes pulp exposure inevitable or visible, it is crucial to confirm that the dental pulp is vital before beginning treatment [182]. This confirmation can be achieved through direct observation or vital tests. During treatment, the clinician should also verify pulp vitality by observing bleeding after administering local anesthesia [183]. If the pulp is confirmed to be vital, the presence or absence of an apical lesion on radiographs does not affect the clinical decision. However, in cases of acute apical periodontitis, it is advisable to proceed with caution and consider the treatment as provisional, with clinical decisions based on short-term follow-up results [129]. In cases of decay, infected enamel and dentin should be removed using a high-speed bur with ample water irrigation. When working near the dental pulp, it is advisable to use a tungsten carbide bur or a coarse steel bur at low speed, again with significant water irrigation. It is crucial to isolate the treated tooth from the moment of pulp exposure to prevent recontamination. The primary goal of these procedures is to eliminate pathogenic agents from the tooth cavity while avoiding any further contamination [184].

Before exposing the pulp and entering the pulp chamber, the clinician must ensure that all decay has been thoroughly removed and that the cavity is properly shaped for its final restoration. In pulpotomy procedures, the pulp is partially or entirely removed from the coronal cavity using a high-speed bur with thorough irrigation. The remaining pulp should resemble a clean surgical wound. Next, establish sufficient hemostasis by placing a wet sterile cotton pellet on the area for about 5 minutes. While some researchers suggest rinsing the wound with sodium hypochlorite, this is not recommended due to the lack of evidence supporting its superiority over normal saline and the potential risk of damage to the remaining pulp tissue from this caustic agent [185].

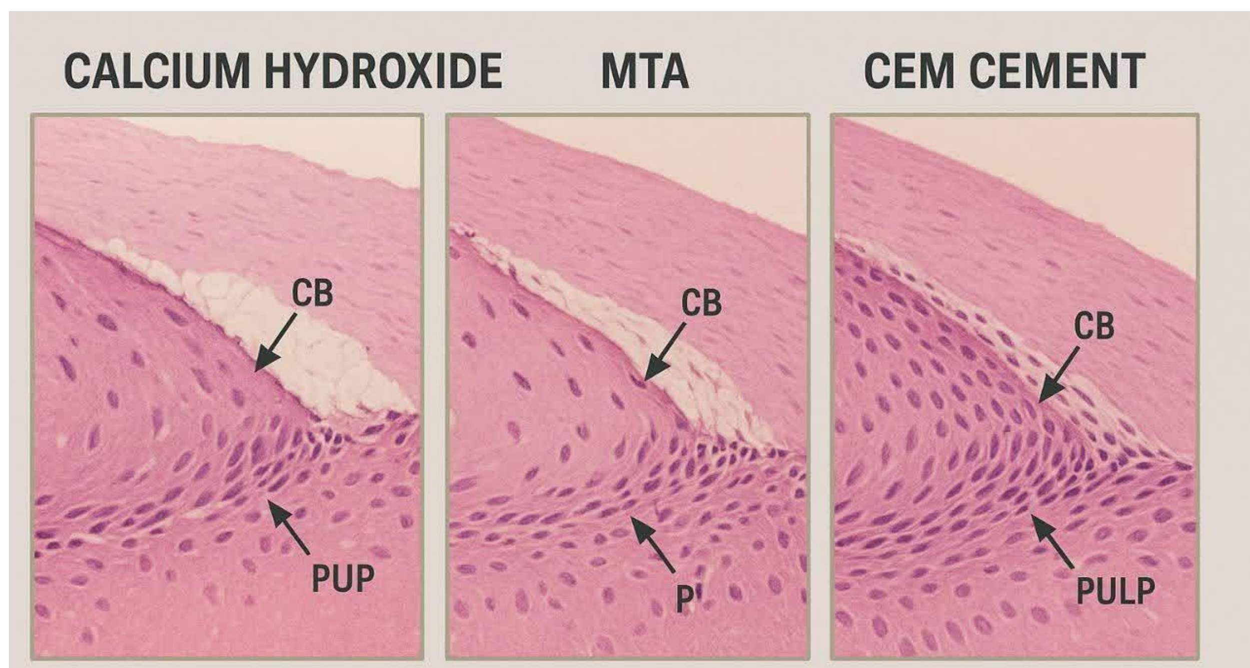

Figure 6. Comparative histological evaluation demonstrating the quality and structure of the hard tissue barrier formed beneath Calcium Hydroxide, MTA, and CEM Cement, showcasing differences in bridge integrity and pulp tissue health

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Table 2: comparative summary of MTA and CEM cement: properties and clinical outcomes based on recent evidence [49, 72, 77, 90, 99, 112, 120, 170, 174, 181, 185, 186, 188-194]

Property / Outcome	Mineral Trioxide Aggregate (MTA)	Calcium-Enriched Mixture (CEM) Cement
Key Composition	Tricalcium silicate, dicalcium silicate, bismuth oxide, calcium aluminate.	Various calcium compounds including calcium oxide, calcium silicate, calcium phosphate, calcium carbonate.
Setting Time	Long setting time (~165 ± 5 minutes); can be a clinical drawback.	Shorter setting time compared to MTA, facilitating faster clinical procedures.
Bioactivity & Hard Tissue Formation	Excellent. Forms calcium hydroxide upon hydration, creating a high-pH environment that stimulates hydroxyapatite formation and a thick, continuous dentin bridge.	Excellent, with superior hydroxyapatite-forming ability in physiological-like environments. Promotes a uniform, tubular dentin bridge with well-organized odontoblast layers.
Biocompatibility & Pulp Response	High biocompatibility; induces less inflammation than traditional materials. Promotes cementogenesis and periodontal ligament regeneration.	High biocompatibility, comparable or superior to MTA in some studies. Noted for absent or minimal inflammation and regeneration of a near-physiologic dentin-pulp complex.
Antimicrobial Efficacy	Demonstrates antibacterial and antifungal properties, largely attributed to its high pH. Efficacy can be variable against some anaerobic species.	Potent and broad-spectrum antimicrobial activity, considered comparable to calcium hydroxide and superior to MTA against certain pathogens like Enterococcus faecalis.
Sealing Ability	Superior marginal sealing and resistance to microleakage compared to amalgam, IRM, and Super-EBA.	Exhibits superior sealing ability compared to many materials; forms a hydroxyapatite interface with dentin, leading to comparable or slightly better sealing than MTA in some studies.
Clinical Success in Vital Pulp Therapy (VPT)	High long-term success rates for pulpotomy and direct pulp capping, validated in numerous studies.	High and promising success rates; shown to be an effective alternative to MTA with successful apexogenesis and periapical healing in immature teeth.
Tooth Discoloration	A significant drawback, particularly with gray MTA; white MTA reduces but does not eliminate the risk.	Less potential for tooth discoloration compared to MTA, making it more favorable for aesthetically critical areas.
Handling Properties	Challenging handling due to sandy consistency; difficult to manipulate in restricted access areas.	Favorable handling with better flowability and optimal film thickness, making it easier to use clinically.

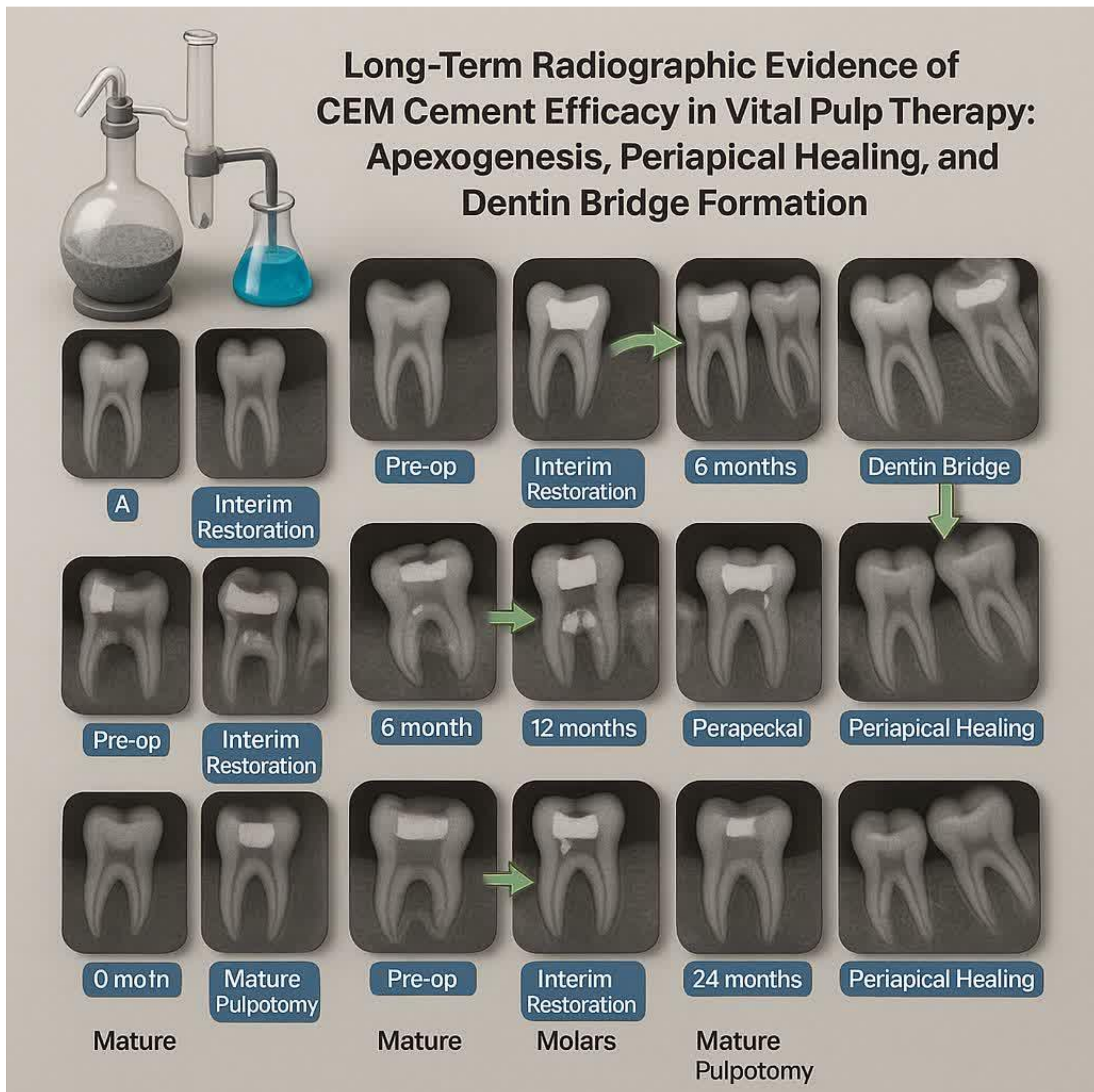

Figure 7. Schematic of sequential radiographs documenting vital pulp therapy outcomes with CEM Cement, including apexogenesis, periapical healing, and dentin bridge formation over a 24-month period

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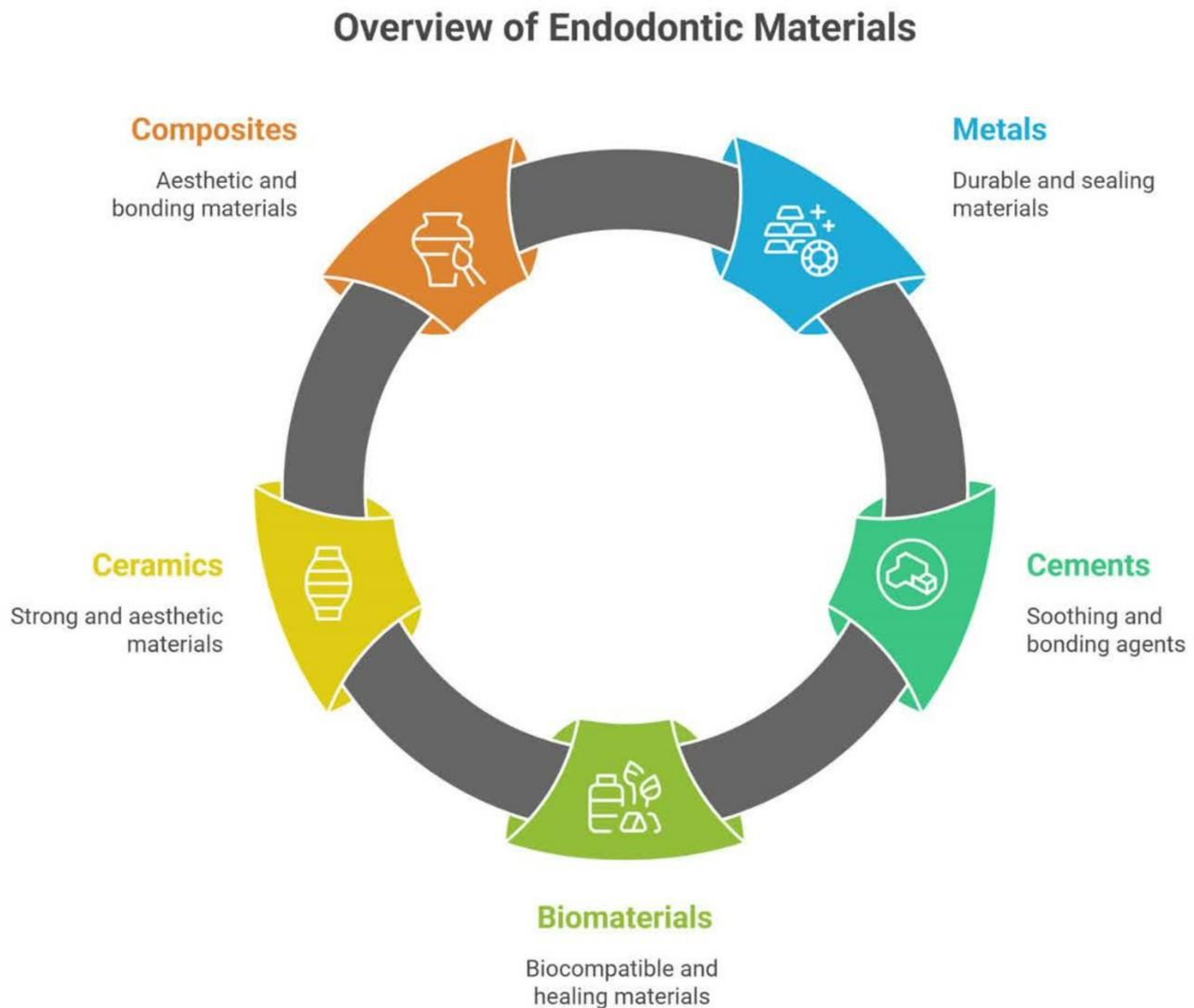

Figure 8. Classification highlighting biomaterials as a distinct group focused on biocompatibility and healing, positioning bioactive alternatives like MTA and CEM Cement alongside traditional restorative and sealing materials

Once hemostasis is achieved, apply a layer of pulp covering material, CEM cement, with the appropriate consistency (about a 3:1 powder-to-liquid ratio) [186]. Use a piece of dry sterile cotton to gently place the material on the remaining pulp tissue, ensuring good contact with the pulp and the cavity walls. Verify that the pulp is covered with an adequate thickness of material and that a complete physical barrier is formed. Confirm that there is no blood leakage [182]. The final step involves restoring the cavity to ensure the best coronal seal. This can be achieved with light-cure resin or by reconstructing the crown using amalgam or a stainless-steel crown. During this process, use suitable instruments, a pear-shaped condenser correctly to avoid applying excessive pressure, which could lead to breakage or deformation of the pulp covering material [187].

Biomaterials represent a distinct and advanced category within endodontic materials, characterized by their biocompatibility and ability to promote healing (Figure 8). Unlike traditional composites, metals, or cements focused on restoration or sealing, bioactive biomaterials like MTA and CEM Cement are specifically engineered to interact favorably with biological tissues, stimulating hard tissue formation and regeneration, which is paramount for procedures like VPT and perforation repair.

The comprehensive analysis of MTA (Section 3) and CEM Cement presented herein evaluates their status as premier bioactive materials in modern endodontics. To synthesize the key evidence and facilitate a direct comparison of their characteristics and clinical performance based on recent literature, a summary is provided in Table 2 [49, 72, 77, 90, 99, 112, 120, 170, 174, 181, 185, 186, 188-194].

8. Conclusion

Evidence supports the use of various materials in dental treatments, although some require further evaluation to fully understand their effects and long-term clinical applications. MTA is a versatile material with

applications including pulp capping, vital pulp therapy, root-end filling, treatment of teeth with open apices, as a retrograde filling material, perforation repair, pulpotomy in primary teeth, and management of coronal fractures and root canal fillings. MTA, a hydrophilic cement with distinctive chemical properties, is known for its biocompatibility. It was first introduced as an endodontic filling material in 1998. The initial gray version was later replaced by a milky-colored variant to address aesthetic concerns.

MTA is derived from Type I Portland cement. The chemical composition of gray and white MTA (Mineral Trioxide Aggregate) is very similar to that of the corresponding Portland cements, with the main difference being the inclusion of bismuth oxide in MTA, which acts as a radiopaque marker. White MTA differs from gray MTA primarily in its reduced content of alumina, magnesium oxide, and notably, iron oxide. Additionally, white MTA features smaller particles and crystals with a more uniform particle size distribution. The hydration reaction of MTA produces calcium hydroxide, which contributes to its biocompatibility by generating a hydroxide-rich environment near living tissue. Calcium released from MTA reacts with phosphate ions in the surrounding environment to form hydroxyapatite. However, MTA has some drawbacks, including potential tooth discoloration, a long setting time, and the absence of a suitable solvent for retreatment. On the other hand, CEM cement represents a new generation of regenerative endodontic materials with the ability to form hydroxyapatite, making it well-suited for filling and flooding applications. It demonstrates excellent tissue compatibility and clinical results confirm its efficacy in promoting complete regeneration of peri radicular tissues. CEM cement is appropriate for various types of vital pulp treatments, with numerous studies validating its effectiveness. The choice of root-end filling material is influenced by multiple factors, and while there is no single material universally preferred in all cases, CEM cement and MTA both show promising results. It is crucial to base dental practices on evidence and the findings from various laboratory and clinical studies. To further validate the effectiveness of these materials, randomized controlled trials are necessary, as they provide highly reliable results. Currently, both MTA and CEM cement have demonstrated successful histological outcomes, including cement genesis, and are recommended for clinical use.

Competing Interests Statement

The authors have declared that no competing interests exist.

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Authors Contribution
All authors have contributed equally to prepare the paper.

Availability of data and materials
The datasets supporting the conclusions of this study are included within the article.

Conflict of interests
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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