

Original Article

Tooth Discoloration Following Regenerative Endodontic Treatment Using Biodentine versus MTA: A Randomized Controlled Trial

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ABSTRACT

The present randomized investigation sought to compare the magnitude of color alteration following regenerative therapy employing Biodentine against mineral trioxide aggregate (MTA), each serving as a coronal plug material in fully developed anterior teeth diagnosed with pulp necrosis and apical periodontitis. 36 individuals presenting with mature single-canaled teeth affected by necrotic pulp and apical periodontitis took part in the study. Participants were randomly assigned to two arms, each comprising 18 subjects (n = 18). An identical initial therapeutic intervention was administered to both arms. After 2 weeks, a regenerative approach using the blood clot technique was performed; either Biodentine or MTA served as the coronal plug, with material type randomly assigned to each tooth. The shade of each tooth was subsequently captured using a shade guide and a digital image, both of which served as the baseline record. The principal outcome measure was tooth discoloration, determined by tracking shade shifts at follow-up time points of 6, 9, 12, and 18 months relative to baseline. A digital photograph was obtained at every scheduled follow-up appointment. Among those receiving Biodentine, 2 individuals were lost to follow-up, and postoperative discoloration was absent in 0% (0 of 16) of the remaining patients. In the MTA arm, 3 individuals were lost to follow-up, and minor postoperative discoloration was noted in 13.3% (2 of 15) of patients. The comparison between arms did not reach statistical significance (P = 0.226), with a risk ratio (95% confidence interval) equal to 0.19 (0.01, 3.63). Regenerative treatment using the blood clot method, with either MTA or Biodentine as the coronal plug material, demonstrated comparable stability of tooth shade and appears suitable for adoption in anterior teeth, where esthetic outcomes are a clinical priority.

Keywords: Biodentine, Mature teeth, Mineral trioxide aggregate, Regenerative endodontic procedure, Tooth discoloration

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Introduction

Regenerative endodontic procedures (REPs) stand as a biologically oriented departure from conventional endodontic care [1]. Their fundamental purpose is to replace or repair damaged dental structures while fostering the regeneration of the pulp–dentin complex, often through the incorporation of biological elements, such as blood clots [2, 3].

Motivated by encouraging data from REPs conducted on young, immature necrotic teeth, fresh proposals have emerged advocating the application of these procedures to mature, necrotic permanent teeth burdened by pulp necrosis and apical periodontitis [4]. Some recent clinical reports on this treatment approach have been published [5-8], collectively highlighting the superior biological profile of REPs and their potential as an advantageous alternative to conventional root canal treatment (RCT) [9, 10].

Tooth discoloration constitutes a documented adverse sequela—a meaningful esthetic drawback that may manifest after regenerative endodontic intervention. This complication is particularly relevant for anterior teeth, given that favorable esthetic results are patient-driven endpoints with a direct bearing on everyday quality of life [11]. The problem has been traced to the specific agents used during REP [12], with the primary culprit being mineral trioxide aggregate (MTA), a material commonly used as a coronal barrier and known to induce chromatic alterations in dental hard tissues [13].

MTA itself is a biocompatible compound well regarded for supporting tissue healing without eliciting periapical inflammatory responses. It simultaneously establishes a durable seal against the passage of microorganisms [14]. Nonetheless, discoloration persists as its main clinical liability [13]; accordingly, Biodentine has been advanced as a suitable replacement, as it mimics the mechanical behavior of native human dentin and circumvents the drawbacks associated with white MTA [15]. At present, however, no work has been undertaken to verify its performance in safeguarding the original tooth shade when incorporated into REPs performed on mature permanent teeth.

Although a handful of clinical trials [5-8] have demonstrated the therapeutic success of REPs in teeth with completed root development, none have examined the likelihood of discoloration associated with these regenerative approaches. In light of this gap, the present prospective, randomized, controlled clinical investigation sets out to scrutinize the comparative performance of Biodentine versus MTA, each deployed as a barrier within the pulp space, regarding their influence on the chromatic stability of anterior teeth following regenerative management of mature single canals affected by pulp necrosis and apical periodontitis.

Materials and Methods

The present randomized clinical trial was drafted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The work was executed in full adherence to the Declaration of Helsinki. Both the protocol for this prospective, two-arm, parallel-group, double-blind, randomized clinical trial and the accompanying informed consent document received ethical clearance from the Research Ethics Committee of the Faculty of Dentistry. The trial protocol was formally registered on www.clinicaltrials.gov (Identifier No.: NCT04018456). Recruitment of the entire study

sample was carried out single-handedly by a single operator from the endodontics department's outpatient clinic, Faculty of Dentistry. All aspects of the procedures were clarified upfront to patients deemed suitable and willing to join the trial—this included the possible benefits, known hazards, and the intended schedule of follow-up visits. Once these details had been conveyed, participants were asked to endorse a printed informed consent form and were provided a duplicate for their records.

Sample size calculation

Estimation of the required sample size was performed using G-Power, a freely distributed software from the University of Trier, Germany (www.gpower.hhu.de). A minimum of 16 patients per arm was determined to be a suitable sample, yielding a combined sample of 32 patients (across 2 arms) capable of detecting a minimal clinically relevant difference in tooth discoloration between the two study arms. Statistical power was fixed at 80%, with the α error probability established at 0.05. The figure was then inflated to anticipate incomplete datasets: the initial 32 patients were scaled up to 36 to offset an expected dropout rate of 10%. The size of the effect targeted for detection was approximated based on the proportion of the variable under study, as drawn from previously published scientific work [6].

Eligibility criteria

Every individual enrolled in the study was between 10 and 35 years of age, had generally favorable health, and had anterior teeth with a single root canal and a fully formed root (closed apex), exhibiting necrotic pulp and apical periodontitis. Excluded from participation were patients with developmental tooth defects (such as dens invaginatus or palatogingival grooves), who had undergone previous root canal treatment, who would ultimately require a post-and-core definitive restoration, or who had generalized chronic periodontitis.

Patient examination

Both past medical and dental histories were compiled for all participants. A detailed clinical and radiographic evaluation of the target tooth was conducted to corroborate the working diagnosis of necrotic pulp with apical periodontitis. Enrolled patients had to demonstrate the following: a complete lack of responsiveness to cold and electric pulp testing when measured against the contralateral tooth, or an adjacent tooth, should the contralateral one be missing. Radiographic inspection identified teeth with a

periapical radiolucent area measuring greater than 3 mm. The clinical assessment further comprised periodontal probing depths, tenderness elicited by percussion and palpation across the apical territory of the implicated teeth, and the identification of any sinus tract.

Randomization and blinding

Every participant had an equal probability of being assigned to one specific treatment arm by random allocation [16]. All subjects enrolled in the study were randomly assigned to either the intervention arm (Biodentine) or the control arm (MTA) using a computer-generated random sequence (www.random.org) prepared by the principal investigator. Eighteen subjects constituted each arm, maintaining an allocation ratio of 1:1. Assignment to arms followed a randomized sequence printed on sealed opaque envelopes numbered sequentially from 1 to 36. At the second treatment session, every participant selected one envelope. The study design ensured participant and outcome assessor blinding. The assessor who rated changes in tooth shade based on digital photographs remained entirely uninformed about which arm each participant belonged to (experimental versus control).

Regenerative procedures

All clinical interventions were performed by a single highly experienced investigator [5-7].

First appointment

Local infiltration anesthesia was achieved by administering 1.7 ml of 4% articaine hydrochloride with epinephrine at a dilution of 1:200,000 (Septodont, Saint-Maur-des-Fosses Cedex, France). The tooth was then isolated using a rubber dam, and an endodontic access cavity was opened. Working length was gauged with an apex locator (Root ZX, J. Morita) and later verified by means of an intraoral parallel periapical radiograph (Digora, Digital ScaNeo imaging plate size 2) to ensure the measurement remained 0.5–1 mm short of the radiographic apex. Canal instrumentation was accomplished with stainless steel hand K files (Mani, Japan) carried to the master apical file under abundant, low-pressure irrigation using 20 ml of 1.5% NaOCl dispensed through a closed-ended, single-side-vented needle. The canal space was then thoroughly dried using paper points. Calcium hydroxide (Metapaste, Metabiomed, Korea) was introduced, and the access opening was sealed using a temporary restorative material (Nucavfil PSP Dental Co. Ltd., Belvedere, Kent, UK). In instances of postoperative discomfort,

the participant received advice to self-administer an analgesic consisting of 400 mg of Ibuprofen (Brufen 400 mg tablets, Abbott Pharmaceuticals, Egypt). The patient was then discharged for 2 weeks, during which the clinical response to the initial therapeutic phase was evaluated. If any signs or symptoms indicative of an unresolved infection persisted, provision existed to extend the antimicrobial treatment period or switch to alternative antimicrobial agents.

Second appointment

The patient received anesthesia using 3% mepivacaine without a vasoconstrictor (Scandonest, Septodont, France). A rubber dam was applied to isolate the tooth, and the previously placed calcium hydroxide was flushed out through gentle irrigation with 20 ml of 1.5% NaOCl. The canal was subsequently rinsed with saline, followed by a final irrigation with 20 ml of 17% EDTA, after which it was dried with paper points. Hemorrhage was provoked inside the canals by overinstrumenting and rotating a precurved K-file sized #25 or #30 at a point 2–3 mm beyond the radiographic apex. The blood was left undisturbed in the canal for several minutes to allow clot formation. Following this, participants were randomly assigned to either the intervention arm, in which Biodentine cement (BD, Septodont, Saint Maur des Fosses, France) was applied, or the control arm, in which MTA cement (Angelus Indústria de Produtos Odontológicos S/A, Brazil) was applied. A collagen sponge (Gelatin hemostatic collagen sponge, Hong Kong Medi CO Limited) was positioned in the canal, atop the blood clot, to serve as a barrier controlling the apical extent of the bioactive material. Should induction of bleeding prove unsuccessful, that particular case was withdrawn from the study.

Thereafter, the powder and liquid components of either Biodentine or MTA were blended according to the respective manufacturer's recommendations. A layer 3 mm in thickness was meticulously delivered over the collagen sponge, staying below the cemento-enamel junction, and was gently adapted against the dentinal walls using a moistened cotton pellet. A radiograph was obtained to verify the position and quality of the cervical plug material.

Once the initial setting of the MTA or Biodentine had been completed—a process generally requiring about 15 minutes per the manufacturer's guidance—a composite restoration was performed during the same appointment to seal the access cavity. A shade of composite that closely approximated the natural tooth color was chosen using a shade guide produced by the same manufacturer as the composite material (Tetric N,

Ivoclar Vivadent). The restorative sequence commenced with the application of a single-bond universal adhesive (3M Oral Care ESPE, Germany) over the dentin, thereby avoiding the need to acid-etch dentin in the vicinity of MTA and Biodentine. A layer of flowable composite was then placed to cover these materials. For the enamel, etching was performed once the MTA or Biodentine was fully covered, after which a universal adhesive bond and composite restoration (Tetric N, Ivoclar Vivadent) were finalized. The tooth shade was then documented using a Shade Guide (Tetric N, Ivoclar Vivadent) and a digital photograph, which served as the baseline record for comparison at subsequent follow-up visits. Every photograph was captured under identical clinical conditions and camera settings to ensure precision and uniformity when tracking any color shift. The patient was made aware of the importance of attending long-term follow-up assessments, which were scheduled accordingly.

Postoperative examination

All participants were summoned back at 6, 9, 12, and 18 months, at which time a principal examiner clinically evaluated the treated teeth. Photographs for color assessment in each case were obtained following the same protocol as the baseline images and were reassessed by a second examiner. The calibration outcomes from the two examiners were compared, and whenever disagreement arose, reevaluation was conducted until consensus was reached.

Discoloration of teeth

The primary endpoint of this investigation was to evaluate tooth discoloration. The evaluation protocol consisted of visually inspecting the shade of color at each visit, which was logged for subsequent comparison. The shade and photograph obtained at every visit were compared with the baseline photograph captured immediately after composite

placement at the conclusion of the second appointment. This comparison determined whether the tooth was discolored [17]. Treatment success hinged on the absence of discoloration and any color shift. Conversely, any deviation in shade or discoloration was classified as a failure.

Statistical analysis

Data normality was examined using the Shapiro–Wilk test. Continuous data were expressed as mean \pm standard deviation, median, minimum, maximum, and 95% confidence interval, and comparisons were performed using the Mann–Whitney U-test. Categorical data were presented as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test when more than 20% of the expected cell counts were less than 5. The threshold for statistical significance in the primary test was set at $P < 0.05$. All statistical computations were performed using SPSS software (IBM Corp., released 2017; IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, USA).

Results and Discussion

For this trial, 80 patients were initially recruited from the endodontic department's outpatient clinic. A total of 36 patients satisfied the inclusion criteria and were formally enrolled in the study, with 18 individuals ($n = 18$) allocated to each arm. Two participants in the intervention arm (Biodentine) and three in the control arm (MTA) dropped out due to an inability to attend their scheduled follow-up visits; thus, the final analysis comprised 31 patients. The CONSORT flowchart illustrates the movement of participants throughout the trial (**Figure 1**). No statistically significant differences emerged between the arms in baseline characteristics—namely, age, tooth type distribution, and preoperative discoloration ($P > 0.05$) (**Table 1**).

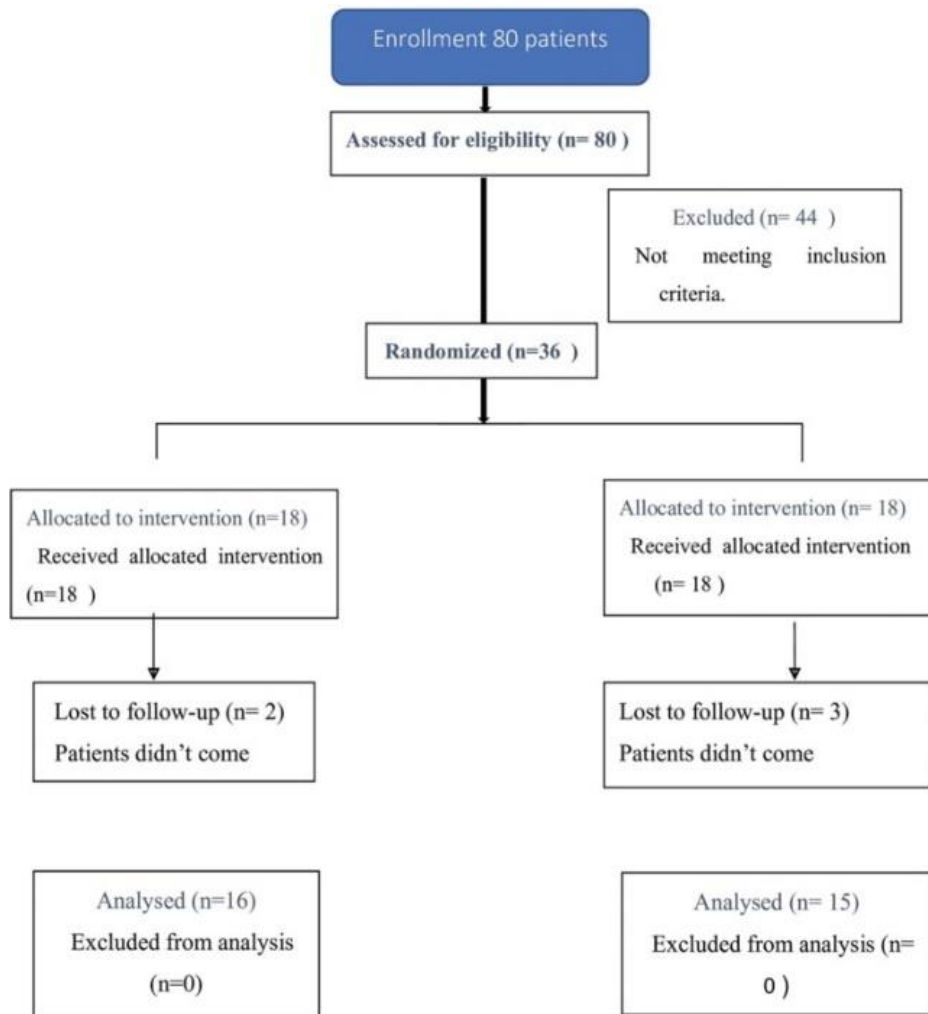


Figure 1. Consolidated Standards of Reporting Trials flow diagram of the study

Table 1. Baseline characteristics of the included study participants within the Biodentine and mineral trioxide aggregate groups

Parameter	P-value	MTA (n = 18)	Biodentine (n = 18)
Age (years)			
Mean ± SD	0.465	22.5 ± 12.1	25.6 ± 13.7
Median (range)		18 (10–35)	21.5 (10–35)
Tooth category, n (%)			
Maxillary central incisors	0.625	10 (55.6)	13 (72.2)
Maxillary lateral incisors		5 (27.8)	4 (22.2)
Mandibular central incisors		3 (16.7)	1 (5.6)
Preoperative discoloration, n (%)			
Present	1.0	4 (22.2)	4 (22.2)
Absent		14 (77.8)	14 (77.8)

None (0%) of the 16 patients within the Biodentine arm exhibited postoperative tooth discoloration. By contrast, in the MTA arm, 2 (13.3%) of 15 patients displayed postoperative tooth discoloration at the 6-month follow-up; however, no further progression was noted during the ensuing follow-up intervals (9, 12, and 18 months) (**Figures 2 and 3**). The difference between the two arms did not reach statistical significance ($P =$

0.226), with a risk ratio (95% confidence interval) = 0.19 (0.01, 3.63). Among patients with tooth discoloration, only a subtle alteration was observed, and individuals expressed satisfaction with their tooth shade, rendering any supplementary intervention unnecessary.

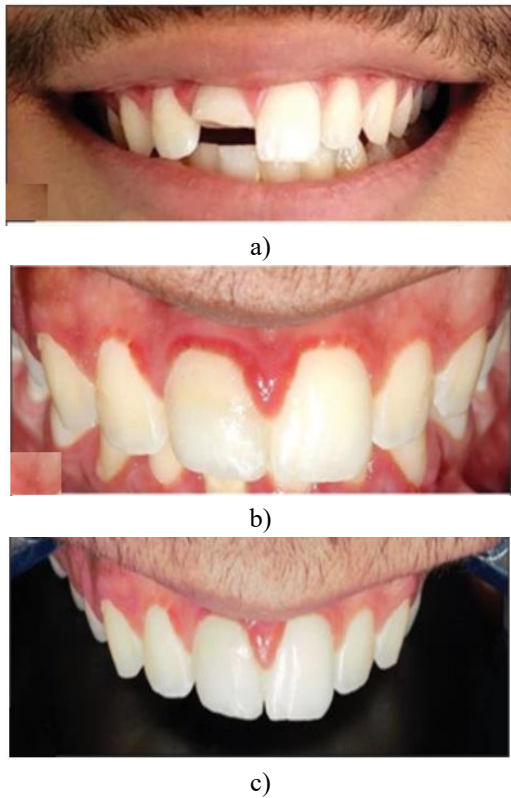


Figure 2. Representative case for a non-discolored upper right central incisor in the mineral trioxide aggregate group, (a) preoperative image, (b) immediate postoperative image, (c) image after 18-month follow-up

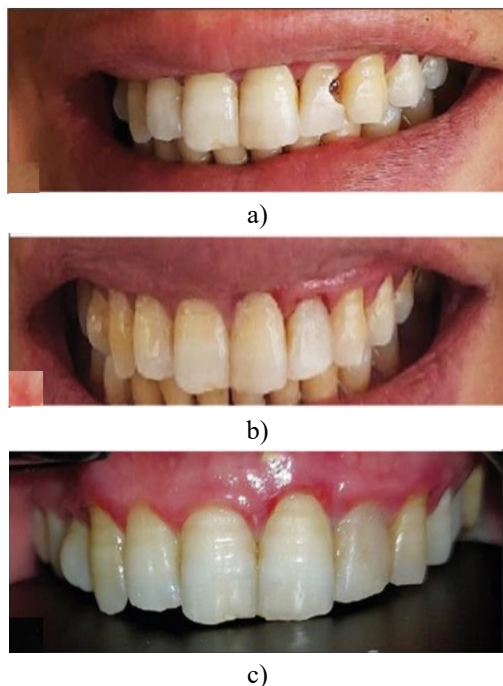


Figure 3. Representative case for a discolored upper left lateral incisor in the mineral trioxide aggregate group: (a) preoperative image, (b) immediate postoperative image, and (c) image after 18-month follow-up

18-month follow-up showing slight grayish discoloration.

All patients across both arms exhibited favorable coronal restorations.

Root canal treatment (RCT) is widely adopted as a conventional modality for addressing pulpal disease, whether or not it is accompanied by apical pathosis. The core of this therapy involves sealing the root canal space with filling materials [18]. A considerable shortcoming of RCT is that treated teeth lose their natural defensive capabilities and proprioceptive feedback, rendering them more prone to external forces, fractures, and reinfections [18]. A growing body of literature has documented that REPs can produce favorable results by resolving clinical signs and symptoms, demonstrating complete periapical tissue healing, and reestablishing pulp tissue vitality [10]. Beyond this, REP may restore homeostasis and innate defense mechanisms, potentially supporting long-term tooth survival [9].

Initially, REPs were recommended for revascularizing the dental pulp in immature permanent teeth to promote further root development, thicken dentinal walls, and achieve apical closure [19]. Emerging data indicate that REPs may constitute a viable treatment alternative for mature teeth with pulp necrosis and apical periodontitis, with a higher likelihood of yielding a positive response to electric pulp testing after REPs [1, 18]. Still, REPs are not without their drawbacks, one of which is tooth discoloration. This complication can profoundly impact patients when anterior teeth are involved, given the special esthetic considerations in this zone. The discoloration problem is commonly associated with commonly used materials like MTA. Yet, the existing body of work has shown discoloration only when MTA is placed over exposed pulp and positioned within an access cavity. No investigation has examined tooth discoloration arising when MTA is employed in REP and located in the cervical third of the root, well beneath the cemento-enamel junction [13, 14]. It is this gap that the present study addresses by evaluating the efficacy of Biodentine compared with MTA in relation to tooth discoloration after REPs performed on mature teeth with necrotic pulp and apical periodontitis.

This work was designed as a randomized clinical trial, enrolling 36 individuals with necrotic pulp and apical periodontitis confined to single-canal adult teeth—specifically maxillary and mandibular incisors. The aim was to standardize the REP protocol for anterior mature teeth [5-7] because discoloration is a significant esthetic concern, particularly in the anterior region. It

may have a detrimental effect on the quality of life of adolescents, children, and their families. Desirable esthetics and a satisfactory appearance are outcomes centered on the patient.

Disinfection of the canal system is critical to the success of REP, especially where apical periodontitis is present [10]. To achieve sufficient disinfection while preserving stem cell viability and dentine-derived growth factors (GFs), a lower NaOCl concentration (1.5%) was used [20]. As the terminal irrigant, 17% EDTA was applied to promote the liberation of GFs that foster stem cell migration, angiogenesis, proliferation, and differentiation [20, 21]. The NaOCl-EDTA sequence promotes the formation of additional connective tissue within the pulp canal, thereby enhancing regenerative capacity [21]. Mechanical preparation remains necessary to debride infected dentin, disrupt biofilm, and create a space for irrigant delivery [5-7].

For successful regeneration to occur, maximizing bacterial clearance via intra-canal disinfection is indispensable. Intracanal medicaments, chiefly calcium hydroxide (CaOH₂) and triple antibiotic paste (TAP), are routinely used in REP, and the AAE (2013) [3] endorses the application of one of these. TAP, a blend of minocycline, metronidazole, and ciprofloxacin, was formerly popular in regenerative protocols. Unfortunately, tooth discoloration has been tied to the minocycline component and the inherent difficulty of completely flushing TAP from the root canal [12, 22]. Published data indicate that both medicaments exhibit comparable efficacy in mature teeth [9]; nevertheless, CaOH₂ is preferred over other options because it does not produce chromatic alteration and releases GFs from dentin, which, in turn, promotes the proliferation of stem cells originating from the apical papilla [18]. In line with this, the present study elected to use CaOH₂ rather than the discoloration-inducing TAP, thereby removing a potential confounding factor that might otherwise skew the findings.

A blood clot was used as a scaffold to support the regeneration of dental pulp-like tissue by mesenchymal stem cells (MSCs). The process involves provoking bleeding within a thoroughly disinfected root canal, which brings MSCs into the canal environment. As the blood clot organizes, it forms a three-dimensional matrix rich in GFs that entraps MSCs and sets the stage for new tissue formation [23, 24]. The actual presence and widespread distribution of MSCs within the root canal systems of mature permanent teeth have been substantiated by investigators employing the induced bleeding technique [25]. They documented an influx of

MSCs into the root canal system [25]. A blood clot remains the most commonly used method in regenerative procedures owing to its simplicity and ease of execution [26]. Although other scaffolds—such as platelet-rich fibrin and platelet-rich plasma—have been described, none have been demonstrated to surpass a blood clot in effectiveness [27]. As such, the induced bleeding technique remains the benchmark regenerative procedure [26].

In the present trial, MTA and Biodentine were chosen as coronal barrier materials, reflecting their status as the most widely adopted biomaterials for coronal sealing [26]. MTA is the more extensively used of the two, owing to its biocompatibility, sealing properties, and marginal adaptation [13]. It demonstrates low neurotoxicity and cytotoxicity, is both fungicidal and bactericidal, and triggers the release of signaling molecules that promote the formation of new tissue [28]. Its alkaline pH and calcium hydroxide release confer robust antimicrobial activity. It also facilitates the angiogenic cascade by modulating vascular endothelial GF a single day following placement [29]. Biodentine, on the other hand, displays characteristics akin to those of MTA. It stimulates the formation of hard tissue bridges, is biocompatible with pulp fibroblasts [15], and can upregulate anti-inflammatory cytokines while simultaneously downregulating pro-inflammatory mediators [30].

In all cases, an adhesive-bonded composite restoration was delivered as the definitive solution, in accordance with the AAE 2013 guidelines [3]. Adopting this restorative approach not only ensures an aesthetically pleasing outcome but also eliminates the risk of coronal microleakage. This point is essential, as microleakage could act as a confounding variable, distorting results and negatively affecting regenerative outcomes.

Discoloration of teeth was designated as the primary endpoint given its patient-centered nature and its direct influence on quality of life [11]. Merely 13% of teeth within the MTA arm displayed discoloration, whereas no instances of discoloration were detected within the Biodentine arm.

These findings diverge from those reported in two prior investigations, namely Arslan *et al.* [6] and Vallés *et al.* [31], both of which reported a higher frequency of tooth discoloration than the present study. Such discrepancy might stem from the differing constituents of the white MTA products employed—(Cerkamed MTA; Wojciech, Nisko, Poland) in the work of Arslan *et al.* [6] and (ProRoot MTA, Dentsply) in that of Vallés *et al.* [31]. These particular white MTA formulations incorporate bismuth oxide as the radiopacifying agent, a compound widely regarded as

the principal culprit behind discoloration [32, 33]. This stands in contrast to the white MTA (Angelus, Brazil) used in the present trial, for which the manufacturer asserts that calcium tungstate is the radiopacifier rather than bismuth oxide. <https://conteudo.angelus.ind.br/mta-angelus-angelusdental>.

A range of radiopacifying agents has been scrutinized for their potential to induce color alteration. The evaluated agents encompassed MTA Angelus containing bismuth oxide, an MTA-type material formulated with calcium tungstate, and one containing zirconium oxide [34]. The investigators observed that dental discoloration became clearly apparent when MTA Angelus incorporating bismuth oxide was placed in direct contact with dentine. Conversely, cement formulations lacking bismuth oxide did not provoke dental discoloration. Accordingly, the adoption of calcium tungstate or zirconium oxide as suitable replacements for bismuth oxide in MTA has been advocated [34]. In the current study, the MTA Angelus product had been modified to feature calcium tungstate in place of bismuth oxide.

Biodentine is inherently tooth-colored, and its formulation replaces bismuth oxide with zirconium oxide. It does not induce tooth discoloration, even when situated above the cemento-enamel junction [31]. Moreover, MTA Angelus is free of aluminoferrite and contains only minimal amounts of iron, aluminum, and magnesium oxides [14]; this may point to one plausible mechanism underlying white MTA discoloration—namely, oxidation of the iron content associated with the calcium aluminoferrite phase of the powder [35]. In truth, the precise pathway through which MTA causes discoloration remains incompletely understood [13]. Nonetheless, additional factors beyond MTA composition may play a role [34], including blood contamination [35] and the interaction between bismuth oxide and sodium hypochlorite residues that may persist on dentinal surfaces [36].

In the present investigation, individuals whose teeth exhibited discoloration manifested only a subtle shade change, and those affected expressed satisfaction with their tooth color; consequently, no further intervention was undertaken. By contrast, a variety of strategies have been proposed to counteract MTA-related discoloration, including internal bleaching [37, 38].

The authors further explored additional key outcomes of REPs, specifically the resolution of periapical lesions and the reestablishment of pulp sensibility within the treated teeth. Their results yielded noteworthy findings regarding the capacity of REPs to resolve periapical pathosis and restore sensibility in

mature teeth afflicted by pulp necrosis and apical periodontitis [39].

Conclusion

Within the constraints of the present study, the evidence indicates that regenerative treatment using the blood clot technique, with either MTA or Biodentine as coronal plug material, can achieve equivalent color stability without an appreciable risk of tooth discoloration. This observation is particularly relevant for anterior teeth, where esthetic considerations are paramount, as both materials can provide meaningful guidance to dental practitioners and investigators engaged in dental regenerative therapies.

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Ethics Statement: None

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