

Distribution Information

AAE members may reprint this position statement for distribution to patients or referring dentists.

About This Document

The following statement was prepared by the AAE Special Committee on Vital Pulp Therapy.

©2021

The guidance in this statement is not intended to substitute for a clinician's independent judgment in light of the conditions and needs of a specific patient.

AAE Position Statement on Vital Pulp Therapy

Introduction

The American Association of Endodontists is dedicated to excellence in the art and science of endodontics and to the highest standards of patient care. The basis for endodontic treatment utilizes the best available evidence from scientific and clinical studies in concert with the accumulated clinical knowledge and judgment of the practitioner.

Vital pulp therapy (VPT) techniques are means of preserving the vitality and function of the dental pulp after injury resulting from trauma, caries, or restorative procedures. VPT procedures have traditionally included indirect or direct pulp capping, and partial or complete pulpotomy.¹

For years, the focus of VPT was on the preservation of the radicular pulp in immature adult teeth, so as to assure completion of root formation (apexogenesis). Today, the focus of VPT is broader; practitioners may have treatment options to consider other than pulpectomy or root canal therapy (RCT) in mature teeth, including teeth previously thought to have irreversibly inflamed pulps.

This position statement addresses diagnostic considerations, caries management, pulp management, placement of biomaterials, and restoration. The intent of the authors is to consider vital pulp therapy from the perspective of the practice of specialty endodontics. However, this statement may be of use to any practitioner in assessing whether they have the appropriate expertise and armamentarium to perform VPT procedures in appropriately selected cases.

Diagnostic Considerations for VPT

A basic tenet for clinical dentistry is that treatment is recommended and performed after the formulation of a sound diagnosis. This has been considered of particular relevance when vital pulp therapy was to be considered.

The current AAE diagnostic terminology assigns a vital pulp to one of three categories: "normal," "reversible pulpitis" or "irreversible pulpitis" (which could be symptomatic or asymptomatic).²

Traditionally the designation of a pulpal diagnosis is based upon the clinician's consideration of a patient's pain history, and appropriate clinical testing to assess the status of the pulp including the application of cold stimulus and electric pulp testing. These tests would be best termed pulp sensibility tests, as definitive tests of pulp vitality, such as measures of pulp oxygen tension, are not currently available for clinical use.³

The primary provoked response to pulp sensibility testing, indicating more severe pulpal inflammation is described as an exaggerated and "lingering" response to cold stimulus, with the underlying pathomechanisms of c-fiber sensitization and inflammation-induced hypersensitivity.^{4,5}

In addition to such pulp sensibility testing, percussion tests may infer pulpal conditions from the presence of symptomatic apical periodontitis; with the presence of percussion pain, i.e., mechanical allodynia, the pulp is considered to be in an irreversibly inflamed state.⁶

Diagnostic quality intraoral radiographs of the suspected teeth are recommended to evaluate accurately the extent of root formation and other concomitant hard tissue changes.⁷

Historically, there has been a widespread belief that, even in aggregate, clinical test results are not well correlated with histologic descriptions of the pulpal status.^{8,9} The viewpoint that VPT is an option only for cases where testing results were consistent with "reversible pulpitis" has recently been challenged.^{10,11,12} Based on clinical, biological and theoretical considerations, the irreversibility of the pulpal disease has come into question. Histologic evidence of the progression of pulpitis suggests that there is no discrete boundary that would render a pulp beyond repair.¹¹ Rather, pulpitis may be interpreted as a temporally and spatially graded disease, with some suggesting the following terms for gradation: "initial", "mild", "moderate" and "severe pulpitis."^{10,12}

Research is underway to understand the role of inflammatory mediators that better indicate pulpal status.^{13,14} For example, point of care analysis could use dentinal fluid¹⁵ (without pulp exposure) or pulp blood¹⁶ (with pulp exposure) to determine markers associated with tissue degradation, such as matrix metalloproteinase-9.

In the absence of clinically available molecular biologic tests, direct observation of the pulp (use of a surgical microscope is recommended) can give relevant information for determining the suitability of the case for VPT. First, a misdiagnosed necrotic pulp can be accurately identified. Secondly, direct observation of pulp tissue during and after achieving hemostasis offers additional diagnostic information about the condition of the pulpal tissue.¹⁷ Utilizing direct visualization of the pulp, it appears that even symptomatic pulps may be candidates for VPT.¹⁸

Caries Management

Complete caries removal is essential to eliminate infected tissues and visualize pulp tissue conditions under magnification when pulpal exposures occur.^{19,20} Residual caries compromises necessary observations of pulpal inflammation levels and areas of potential necrosis. Accordingly, predictable management of vital pulp tissue should not be performed without complete removal of both demineralized enamel and infected dentin. Hard or firm dentin and dentin below white spot enamel lesions is infected by bacteria in both active and arrested lesions. Specifically, histobacteriological studies have consistently shown the presence of chronic inflammatory cell infiltrates and subclinical pulp inflammation where carious tissues are retained, thus potentially compromising pulp vitality.^{21,22} Additionally, adhesion of bonding resins to sound dentin has shown higher micro-tensile bond strengths compared to caries-affected dentin.^{23,24}

The use of caries detectors or laser fluorescence during caries removal can be helpful adjuncts to assist the clinician in removing diseased tissues, particularly when close to the pulp cavity.^{25,26,27} Therefore, the clinician can focus on complete removal of demineralized infected dentin, rather than avoiding pulp exposure, to improve the chances of pulpal repair.²⁸ Detectors can create an objective standard for all clinicians during caries removal without reliance exclusively on clinical philosophy or subjective judgement.²⁹

Use of Sodium Hypochlorite

Sodium hypochlorite is an antimicrobial solution that provides hemostasis, disinfection of the dentinpulp interface, biofilm removal, chemical removal of the blood clot and fibrin, and clearance of dentinal chips along with damaged cells at the mechanical exposure site.³⁰

Examination of pulp tissues after exposure with magnification is a critical step in pulp assessment. Hemorrhage must be controlled to allow clinical assessment of inflammatory levels and identify potential necrotic tissues that require removal before application of an appropriate biomaterial. Hemostasis for the pulp tissue is typically achieved by bathing the resected pulp tissue in sodium hypochlorite for 5 to 10 minutes, although recommended durations may vary, either via direct passive irrigation or on a sodium hypochloritesoaked cotton pellet.^{31,32,33,34,35,36,37,38,39,40,41,42,43,44,45} Although several hemostatic options are available, sodium hypochlorite can be used safely in direct contact with pulp tissue at various concentrations, from dilute solutions to full bottle strength, without compromising pulp integrity.^{30,46,47,48} Sodium hypochlorite has not been shown to adversely alter pulp cell recruitment, cytodifferentiation, and hard tissue deposition.⁴⁹ Sodium hypochlorite also eliminates composite staining, addressing an aesthetic concern.

Use of Contemporary Materials in VPT

Calcium silicate cements (CSC) have gained momentum for use in vital pulp therapy (VPT) procedures.^{50,51} CSCs are a class of materials that include tricalcium silicates, dicalcium silicates, hydraulic calcium silicate cements, and "bioceramics." Clinical outcomes have demonstrated consistent success with these materials and mineral trioxide aggregate (MTA) is one of many tricalcium silicates that is widely used and the most extensively studied. When MTA and other CSCs are used for VPT procedures in permanent teeth with symptomatic or asymptomatic irreversible pulpitis, success rates range from 85-100% at 1-2 years.^{26,35,38,42,45,52,53,54} However, it is noteworthy that calcium hydroxide, glass ionomer cements (GICs) and resinbased materials trail in clinical outcomes and demonstrate a lower range of success varying from 43%-92%.42,55,56

Immunomodulatory effects of the new generation of biomaterials provide an added and much needed benefit to their biocompatible, osteogenic and bioactive properties.^{13,57,58,59,60,61,62,63,64,65,66,67} The formation of mineralized barriers using CSCs show improved quality over calcium hydroxide-based materials.^{50,68,69,70}



Silicate materials also possess favorable physicochemical characteristics that include high alkalinity, intratubular mineralization, inhibition of biofilm formation, reduction of robust proinflammatory mediators and post-operative pain during dental pulp procedures.^{57,58,63,70,71} The newer generations of CSCs do demonstrate improved setting times^{72,73,74} including modified compositions that reduce tooth discoloration.^{61,71,72,73,75} The choice of a biomaterial must therefore be made on existing evidence with considerations for patient centered outcomes, reliable mineralized tissue formation and continued pulp vitality.

Immediate Placement of Permanent Restorative Material

Restoration of the teeth is a critical step in endodontic procedures. Immediate restoration should be a part of the restorative treatment plan for a tooth receiving VPT.

Teeth undergoing VPT using CSCs as the primary sealing material and restored immediately with a long-term restoration have a high success rate.^{19,41,76,77,78,79,80,81,82} Although studies have shown some success with delayed final restoration in the short to medium term^{35,83}, long-term assessments have demonstrated that a minimal time span⁸⁴ between placement of a foundational restoration^{44,85} after vital pulp treatment is a strong predictor for successful outcomes.^{32,33,34,36,42,43,51,52,86,87,88,89,90,91,92,93,94}

Indicated advantages of immediate restoration include benefits in the prevention of microleakage, protection of the biomaterial layer, reduction of post-operative sensitivity and thermal conductivity, and establishment of a foundation for cuspal coverage restoration should it be required. No negative impacts of restoring the teeth immediately have been indicated. An appropriate waiting period is recommended prior to additional tooth preparation for definitive (cuspal coverage) restoration. A practitioner, using professional judgment and clinical expertise, should consider absence of signs and symptoms and susceptibility of the tooth to fracture to assess whether the tooth is ready for a definitive restoration after completion of VPT.

Summary

The primary goal of VPT procedures is the creation of optimal conditions for pulp tissue repair and preservation. The amount of pulp tissue removed or retained is dependent on tissue viability assessments based on access for visualization to evaluate hemorrhage control and clinical tissue appearance.⁸⁶

A pretreatment diagnosis of irreversible pulpitis is not necessarily an indication for pulpectomy, as more conservative treatment could be considered.^{35,43,44,95,96}

Procedural decisions for the amount of pulp tissue retention or removal should be based on operator assessments, clinical judgement, overall treatment plan, and the patient's general oral and systemic health status. Authors would encourage additional clinical trials to assess long-term outcomes of vital pulp therapy and the development of chairside techniques utilizing biomarkers to assess pulpal viability. A review of the endodontic diagnostic terminology used to classify the severity of pulpal disease is also warranted.

References

- 1. American Association of Endodontists. *Glossary* of Endodontic Terms. Tenth Edition. 2020.
- 2. Levin L, Law AS, Holland GR, et al. Identify and define all diagnostic terms for pulpal health and disease states. *J Endod.* 2009;35:1645-1657.
- 3. Chen E, Abbott PV. Dental pulp testing: a review. *Int J Dent.* 2009;v2009.
- 4. Hargreaves K, Swift JQ. Mechanisms and management of pain due to inflammation. *Northwest Dent.* 1991;70:47-49.
- Diogenes A, Henry MA. Pain pathways and mechanisms of the pulpdentin complex. In: Hargreaves KM, Goodis HE, Tay FR, eds. Seltzer's and Bender's dental pulp. 2nd ed. Hannover Park, II: Quintessence Publ.; 2012.
- 6. Owatz CB, Khan AA, Schindler WG, et al. The incidence of mechanical allodynia in patients with irreversible pulpitis. *J Endod.* 2007;33:552-556.
- 7. McDonald RE, Avery DR, Dean JA. Treatment of deep caries, vital pulp exposure, and pulpless teeth. In: Dean JA, Avery DR, McDonald RE, eds. *McDonald and Avery's dentistry of the child and adolescent. 9th ed.* St. Louis, MO: Mosby/ Elsevier; 2011.
- 8. Baume LJ. Diagnosis of diseases of the pulp. *Oral Surg Oral Med, Oral Pathol.* 1970;29:102-116.
- 9. Dummer PMH, Hicks R, Huws. Clinical signs and symptoms in pulp disease. *Int Endod J.* 1980;13:27-35.
- 10. Rechenberg D-K, Zehnder M. Call for a review of diagnostic nomenclature and terminology used in endodontics. *Int Endod J.* 2020; in press.
- 11. Ricucci D, Siqueira JF Jr, Li Y, Tay FR. Vital pulp therapy: histopathology and histobacteriologybased guidelines to treat teeth with deep caries and pulp exposure. *J Dent.* 2019;86:41-52.

- Wolters WJ, Duncan HF, Tomson PL, et al. Minimally invasive endodontics: a new diagnostic system for assessing pulpitis and subsequent treatment needs. *Int Endod J.* 2017;50:825-829.
- 13. Rechenberg D-K, Galicia JC, Peters OA. Biological markers for pulpal inflammation: a systematic review. *PLOS One.* 2016;29.
- Zanini M, Meyer E, Simon S. Pulp inflammation diagnosis from clinical to inflammatory mediators: a systematic review. *J Endod.* 2017;43:1033-1051.
- Zehnder M, Wegehaupt F, Attin T. A first study on the usefulness of matrix metalloproteinase 9 from dentinal fluid to indicate pulp inflammation. *J Endod.* 2011;37:17-20.
- 16. Mente J, Petrovic J, Gehrig H, et al. A prospective clinical pilot study on the level of matrix metalloproteinase-9 in dental pulpal blood as a marker for the state of inflammation in the pulp tissue. *J Endod.* 2016;42:190-197.
- 17. Bogen G, Dammaschke T, Chandler N. Vital pulp therapy. In: Berman L, Hargreaves KM, eds. *Pathways of the pulp. 12th ed.* St. Louis, MO: Elsevier; 2021.
- 18. Lin LM et al. Vital pulp therapy of mature permanent teeth with irreversible pulpitis from the perspective of pulp biology. *Aust Endod J.* 2020;46:154-165.
- 19. Asgary S, Hassanizadeh R, Torabzadeh H, Eghbal MJ. Treatment outcomes of 4 vital pulp therapies in mature molars. *J Endod.* 2018;44:529-535.
- 20. Matsuo T, Nakanishi T, Shimizu H et al. A clinical study of direct pulp capping applied to carious-exposed pulps. *J Endod.* 1996;22:551.

- Ricucci D, Siqueira JF Jr, Rôças IN, Lipski M, Shiban A, Tay FR. Pulp and dentine responses to selective caries excavation: a histological and histobacteriological human study. *J Dent.* 2020 Sep;100:103430. doi: 10.1016/j. jdent.2020.103430. Epub 2020 Jul 13. PMID: 32673638.
- Ricucci D, Siqueira JF Jr. Bacteriologic status of non-cavitated proximal enamel caries lesions. a histologic and histobacteriologic study. *J Dent.* 2020 Sep;100:103422. doi: 10.1016/j. jdent.2020.103422. Epub 2020 Jun 29. PMID: 32615236.
- 23. Nakajima M, Sano H, Burrow MF, Tagami J, Yoshiyama M, Ebisu S, Ciucchi B, Russell CM, Pashley DH. Tensile bond strength and SEM evaluation of caries-affected dentin using dentin adhesives. *J Dent Res.* 1995;74:1679-1688.
- 24. Yoshiyama M, Tay FR, Torii Y, Nishitani Y, Doi J, Itou K, Ciucchi B, Pashley DH. Resin adhesion to carious dentin. *Am J Dent.* 2003;16:47-52.
- 25. Hosoya Y, Taguchi T, Tay FR. Evaluation of a new caries detecting dye for primary and permanent carious dentin. *J Dent.* 2007;35:137-143.
- 26. Neves Ade A, Coutinho E, De Munck J, Van Meerbeek B. Caries-removal effectiveness and minimal-invasiveness potential of caries-excavation techniques: a micro-CT investigation. *J Dent.* 2011;39:154-62.
- 27. Sadasiva K, Kumar KS, Rayar S, Shamini S, Unnikrishnan M, Kandaswamy D. Evaluation of the efficacy of visual, tactile method, caries 26 detector dye, and laser fluorescence in removal of dental caries and confirmation by culture and polymerase chain reaction: an *in vivo* study. J Pharm Bioallied Sci. 2019;11(Suppl 2):S146-S150.
- 28. Langeland K. Management of the inflamed pulp associated with deep carious lesion. *J Endod.* 1981;7:169.

- 29. T Fusayama. Two layers of carious dentin: diagnosis and treatment. *Oper Dent.* 1979; 4:63-70
- 30. Hafez AA, Cox CF, Tarim B et al. An *in vivo* evaluation of hemorrhage control using sodium hypochlorite and direct capping with a one- or two-component adhesive system in exposed nonhuman primate pulps. *Quintessence Int.* 2002;33:261-272.
- 31. Cho S-Y et al. Prognostic factors for clinical outcomes according to time after direct pulp capping. *J Endod.* 2013;39(3):327-331.
- 32. Jang Y et al. A randomized controlled study of the use of proroot mineral trioxide aggregate and endocem as direct pulp capping materials: 3-month versus 1-year outcomes. *J Endod.* 2015;41(8):1201-1206.
- 33. Kang CM et al. A randomized controlled trial of various MTA materials for partial pulpotomy in permanent teeth. *J Dent.* 2017;60:8-13.
- 34. Kundzina R et al. Capping carious exposures in adults: a randomized controlled trial investigating mineral trioxide aggregate versus calcium hydroxide. *Int Endod J.* 2017;50(10):924-932.
- Linsuwanont P, Wimonsutthikul K, Pothimoke U, Santiwong B. Treatment outcomes of mineral trioxide aggregate pulpotomy in vital permanent teeth with carious pulp exposure: the retrospective study. *J Endod.* 2017;43(2):225-230.
- 36. Linu S et al. Treatment outcome following direct pulp capping using bioceramic materials in mature permanent teeth with carious exposure: a pilot retrospective study. *J Endod.* 2017;43(10):1635-1639.
- 37. Parinyaprom N et al. Outcomes of direct pulp capping by using either proroot mineral trioxide aggregate or Biodentine[™] in permanent teeth with carious pulp exposure in 6- to 18-year-old patients: a randomized controlled trial. *J Endod.* 2018;44(3):341-348.

- 38. Qudeimat MA, Alyahya A, Hasan AA. Mineral trioxide aggregate pulpotomy for permanent molars with clinical signs indicative of irreversible pulpitis: a preliminary study. *Int Endod J.* 2017;50(2):126-134.
- 39. Suhag K et al. Success of direct pulp capping using mineral trioxide aggregate and calcium hydroxide in mature permanent molars with pulps exposed during carious tissue removal: 1-year follow-up. *J Endod.* 2019;45(7):840-847.
- 40. Taha NA, Abdelkhader SZ. Outcome of full pulpotomy using Biodentine[™] in adult patients with symptoms indicative of irreversible pulpitis. *Int Endod J.* 2018;51(8):819-828.
- 41. Taha NA, Abdulkhader SZ. Full pulpotomy with Biodentine[™] in symptomatic young permanent teeth with carious exposure. *J Endod.* 2018;44(6):932-937.
- 42. Taha NA, Khazali MA. Partial pulpotomy in mature permanent teeth with clinical signs indicative of irreversible pulpitis: a randomized clinical trial. *J Endod.* 2017;43(9):1417-1421.
- 43. Taha NA, Ahmad MB, Ghanim A. Assessment of mineral trioxide aggregate pulpotomy in mature permanent teeth with carious exposures. *Int Endod J.* 2017;50(2):117-125.
- 44. Tan SY, Yu VSH, Lim KC, Tan BCK, Neo CLJ, Shen L, Messer HH. Long-term pulpal and restorative outcomes of pulpotomy in mature permanent teeth. *J Endod.* 2020;46:383-390.
- 45. Uesrichai N, Nirunsittirat A, Chuveera P, Srisuwan T, Sastraruji T, Chompu-Inwai P. Partial pulpotomy with two bioactive cements in permanent teeth of 6- to 18-year-old patients with signs and symptoms indicative of irreversible pulpitis: a noninferiority randomized controlled trial. *Int Endod J.* 2019;52(6):749-759.

- 46. Demir T, Cehreli ZC. Clinical and radiographic evaluation of adhesive pulp capping in primary molars following hemostasis with 1.25% sodium hypochlorite: 2-year results. *Am J Dent.* 2007;20:182-188.
- 47. Tang HM, Nordbö H, Bakland LK. Pulpal response to prolonged dentinal exposure to sodium hypochlorite. *Int Endod J.* 2000;33:505-508.
- 48. Witherspoon DE. Vital pulp therapy with new materials: new directions and treatment perspectives—permanent teeth. *J Endod.* 2008;34:S25-28.
- 49. Bogen G, Kim JS, Bakland LK. Direct pulp capping with mineral trioxide aggregate: an observational study. *J Am Dent Assoc.* 2008;139:305-315.
- 50. Bakland LK, Andreasen JO. Will mineral trioxide aggregate replace calcium hydroxide in treating pulpal and periodontal healing complications subsequent to dental trauma? a review. *Dental Traumatology: Official Publication of International Association for Dental Traumatology.* 2012;28(1):25-32.
- 51. Parirokh M, Torabinejad M, Dummer PMH. Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview – part I: vital pulp therapy. *Int Endod J.* 2018;51(2):177-205.
- 52. Asgary S, Eghbal MJ, Bagheban AA. Longterm outcomes of pulpotomy in permanent teeth with irreversible pulpitis: A multicenter randomized controlled trial. *Am J Dent.* 2017;30(3):151-155.
- 53. Caliskan MK. Pulpotomy of carious vital teeth with periapical involvement. *Int Endod J.* 1995;28(3):172-176.
- 54. Caliskan MK. Success of pulpotomy in the management of hyperplastic pulpitis. *Int Endod J.* 1993;26(2):142-148.

- 55. Bergenholtz G. Evidence for bacterial causation of adverse pulpal responses in resin-based dental restorations. *Critical Reviews in Oral Biology and Medicine: an Official Publication of the American Association of Oral Biologists.* 2000;11(4):467-480.
- 56. de Souza Costa CA, do Nascimento AB, Teixeira HM. Response of human pulps following acid conditioning and application of a bonding agent in deep cavities. *Dental Materials: Official Publication of the Academy of Dental Materials.* 2002;18(7):543-551.
- 57. Asgary S, Shahabi S, Jafarzadeh T, Amini S, Kheirieh S. The properties of a new endodontic material. *J Endod*. 2008;34(8):990-993.
- 58. Byers MR, Narhi MV. Dental injury models: experimental tools for understanding neuroinflammatory interactions and polymodal nociceptor functions. *Crit Rev Oral Biol Med.* 1999;10(1):4-39.
- 59. Ding S-J, Kao C-T, Chen C-L, Shie M-Y, Huang T-H. Evaluation of human osteosarcoma cell line genotoxicity effects of mineral trixoide aggregate and calcium silicate cements. *J Endod.* 2010;36(7):1158-1162.
- 60. Faraco IM Jr, Holland R. Response of the pulp of dogs to capping with mineral trioxide aggregate or a calcium hydroxide cement. *Dent Traumatol.* 2001;17(4):163-166.
- 61. Kohli MR, Yamaguchi M, Setzer FC, Karabucak B. Spectrophotometric analysis of coronal tooth discoloration induced by various bioceramic cements and other endodontic materials. *J Endod.* 2015;41(11):1862-1866.
- 62. Luo Z, Li D, Kohli MR, Yu Q, Kim S, He W-X. Effect of Biodentine[™] on the proliferation, migration and adhesion of human dental pulp stem cells. *J Dent.* 2014;42(4):490-497.
- 63. Moinzadeh AT, Aznar Portoles C, Schembri Wismayer P, Camilleri J. Bioactivity potential of EndoSequence BC RRM putty. *J Endod.* 2016;42(4):615-621.

- 64. Opačić-Galić V, Petrović V, Živković S, Jokanović V, Nikolić B, Knežević-Vukčević J, et al. New nanostructural biomaterials based on active silicate systems and hydroxyapatite: characterization and genotoxicity in human peripheral blood lymphocytes. *Int Endod J.* 2013;46(6):506-516.
- 65. Paranjpe A, Smoot T, Zhang H, Johnson JD. Direct contact with mineral trioxide aggregate activates and differentiates human dental pulp cells. *J Endod.* 2011;37(12):1691-1695.
- 66. Rao A, Rao A, Shenoy R. Mineral trioxide aggregate–a review. *The Journal of Clinical Pediatric Dentistry.* 2009;34(1):1-7.
- 67. Wongwatanasanti N, Jantarat J, Sritanaudomchai H, Hargreaves KM. Effect of bioceramic materials on proliferation and odontoblast differentiation of human stem cells from the apical papilla. *J Endod.* 2018;44(8):1270-1275.
- 68. Alsalleeh F, Chung N, Stephenson L. Antifungal activity of endosequence root repair material and mineral trioxide aggregate. *J Endod.* 2014;40(11):1815-1819.
- 69. Huang TH, Yang CC, Ding SJ, Yeng M, Kao CT, Chou MY. Inflammatory cytokines reaction elicited by root-end filling materials. *J Biomed Mater Res B Appl Biomater*. 2005;73(1):123-128.
- 70. Yoo JS, Chang SW, Oh SR, Perinpanayagam H, Lim SM, Yoo YJ, Oh YR, Woo SB, Han SH, Zhu Q, Kum KY. Bacterial entombment by intratubular mineralization following orthograde mineral trioxide aggregate obturation: a scanning electron microscopy study. *Int J Oral Sci.* 2014 Dec;6(4):227-232.
- 71. Steffen R, van Waes H. Understanding mineral trioxide aggregate/Portland-cement: a review of literature and background factors. *Eur Arch Paediatr Dent.* 2009;10(2):93-97.

- 72. Camilleri J, Cutajar A, Mallia B. Hydration characteristics of zirconium oxide replaced Portland cement for use as a root-end filling material. *Dental Materials.* 2011;27(8):845-854.
- 73. Siboni F, Taddei P, Prati C, Gandolfi MG. Properties of NeoMTA Plus and MTA Plus cements for endodontics. *Int Endod J.* 2017;50(S2):e83-e94.
- 74. Torabinejad M, Parirokh M, Dummer PMH. Mineral trioxide aggregate and other bioactive endodontic cements: an updated overview– part II: other clinical applications and complications. *Int Endod J.* 2018;51(3):284-317.
- 75. Aly MM, Taha SEE, El Sayed MA, Youssef R, Omar HM. Clinical and radiographic evaluation of Biodentine[™] and mineral trioxide aggregate in revascularization of non-vital immature permanent anterior teeth (randomized clinical study). *Int J Paediatr Dent.* 2019;29(4):464-473.
- 76. Barrieshi-Nusair KM, Qudeimat MA. A prospective clinical study of mineral trioxide aggregate for partial pulpotomy in cariously exposed permanent teeth. *J Endod.* 2006;32(8):731-735.
- 77. Brizuela C et al. Direct pulp capping with calcium hydroxide, mineral trioxide aggregate, and Biodentine[™] in permanent young teeth with caries: a randomized clinical trial. J Endod. 2017;43(11):1776-1780.
- 78. Chailertvanitkul P et al. Randomized control trial comparing calcium hydroxide and mineral trioxide aggregate for partial pulpotomies in cariously exposed pulps of permanent molars. *Int Endod J.* 2014;47(9):835-842.
- 79. Harms CS, Schafer E, Dammaschke T. Clinical evaluation of direct pulp capping using a calcium silicate cement-treatment outcomes over an average period of 2.3 years. *Clinical Oral Investigations.* 2019;23(9):3491-3499.

- 80. Hilton TJ et al. Comparison of CaOH with MTA for direct pulp capping: a PBRN randomized clinical trial. *J Dent Res.* 2013;92(7 Suppl):16S-22S.
- 81. Mente J et al. Mineral trioxide aggregate or calcium hydroxide direct pulp capping: an analysis of the clinical treatment outcome. *J Endod.* 2010;36(5):806-813.
- Qudeimat MA, Barrieshi-Nusair KM, Owais AI. Calcium hydroxide vs mineral trioxide aggregates for partial pulpotomy of permanent molars with deep caries. *European Archives* of Paediatric Dentistry: Official Journal of the European Academy of Paediatric Dentistry. 2007;8(2):99-104.
- Marques MS, Wesselink PR, Shemesh H. Outcome of direct pulp capping with mineral trioxide aggregate: a prospective study. J Endod. 2015;41(7):1026-1031.
- 84. Mente J et al. Treatment outcome of mineral trioxide aggregate or calcium hydroxide direct pulp capping: long-term results. *J Endod.* 2014;40(11):1746-1751.
- 85. Demarco FF et al. Influence of the restoration quality on the success of pulpotomy treatment: a preliminary retrospective study. *J Appl Oral Sci.* 2005;13(1):72-77.
- 86. Alqaderi HE, Al-Mutawa SA, Qudeimat MA, MTA pulpotomy as an alternative to root canal treatment in children's permanent teeth in a dental public health setting. *J Dent.* 2014;42(11):1390-1395.
- 87. Asgary S, Eghbal MJ. Treatment outcomes of pulpotomy in permanent molars with irreversible pulpitis using biomaterials: a multi-center randomized controlled trial. *Acta Odontol Scand.* 2013;71(1):130-136.
- Asgary S et al. Five-year results of vital pulp therapy in permanent molars with irreversible pulpitis: a non-inferiority multicenter randomized clinical trial. *Clin Oral Investig.* 2014.



- 89. Asgary S et al. One-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter, randomized, non-inferiority clinical trial. *Clin Oral Investig.* 2013;17(2):431-439.
- 90. Asgary S, Eghbal MJ, Ghoddusi J. Two-year results of vital pulp therapy in permanent molars with irreversible pulpitis: an ongoing multicenter randomized clinical trial. *Clin Oral Investig.* 2014;18(2):635-641.
- 91. Caliskan MK, P. Guneri P. Prognostic factors in direct pulp capping with mineral trioxide aggregate or calcium hydroxide: 2- to 6-year follow-up. *Clinical Oral Investigations.* 2017; 21(1):357-367.
- 92. El-Meligy OAS, Avery DR. Comparison of mineral trioxide aggregate and calcium hydroxide as pulpotomy agents in young permanent teeth (apexogenesis). *Pediatric Dentistry.* 2006;28(5):399-404.
- 93. Galani M et al. Comparative evaluation of postoperative pain and success rate after pulpotomy and root canal treatment in cariously exposed mature permanent molars: a randomized controlled trial. *J Endod.* 2017; 43(12):1953-1962.
- 94. Nosrat A, Seifi A, Asgary S. Pulpotomy in caries-exposed immature permanent molars using calcium-enriched mixture cement or mineral trioxide aggregate: a randomized clinical trial. *Int J Paediatr Dent.* 2013;23(1):56-63.
- 95. Ricucci D, Loghin S, Siqueira JF Jr. Correlation between clinical and histologic pulp diagnoses. *J Endod.* 2014;40:1932-1939.
- Krastl G, Galler K, Dammaschke T, Schäfer E. Is pulpotomy a valid treatment option for irreversible pulpitis? *Dtsch Zahnärztl Z Int.* 2021;3:80-87.