



Annex Table

	Clinical context	Follow-up	Materials or REP procedure	Assessment	Results
	Porcine model				
Jang et al. 2020 (34)	REP Healthy immature premolar teeth	1-3 months	MTA Extrinsic synthetic gelatin-based matrix (Floreal, Baxter, CA, USA) Extrinsic synthetic fibrin-based matrix (Greenplast-Q, Green-Cross, Seoul, Korea)	2D Radiography Histology	<u>Histological & radiographic examination</u> 1) pulp-like tissues and deposition of newly formed tertiary dentin with apex maturation 2) No intraradicular mineralized tissue deposition microvasculature and odontoblastic layers aligned on the root dentin 3) Infiltration of inflammatory cells and the resorptive lesions with the presence of inflammatory cells were observed in the root canal system
Guo et al. 2021 (33)	Bioengineered incisor tooth implantation	6 months	natural DTM combined with autologous stem cell aggregates	Histology Immunohistochemistry SEM	<u>Histological observation</u> 1) Bioengineered implanted teeth regenerated pulp tissue - Odontoblastic layer - Blood vessels on coronary third 2) Periodontal tissue regeneration + cementum cells, Sharpey's periodontal fibers and blood vessels on apical third

Dog model					
Siddiqui et al. 2021 (35)	REP infected mature incisors & canine	7,14, 28 days	SLan angiogenic target peptide. Vs SLed dentinogenic control peptide	Histology Immunohistochemistry	<u>Histological observation</u>
					1) Sled failed revascularization 2) SLan Successful revitalization - Poor disorganized tissue and soft tissue in the canal - Presence of vessels - Nerve bundle - Odontoblast-like layer on intracanal dentin - Calcification or disorganized hard tissue - Significant cellular infiltration

Kim et al. 2021 (36)	REP Healthy mature premolar teeth	12 weeks	Collagen membrane vs amniotic membrane + calcium silicate-based cement	Histology	<p><u>Histological observation</u></p> <p><u>Collagen membrane</u></p> <ol style="list-style-type: none"> 1) Mesial root showing regenerated fibrous tissue and mineralized tissue 2) Island of regenerated mineralized tissue partly attached to the native dentin 3) Sharpey's fiber-like fibrous tissue attachment to the regenerated mineralized tissue and the lining of cells that are not odontoblast-like. 4) Newly regenerated mineralized tissue onto the native dentin. 5) Root apex showing apical closure with apical ramifications and no periapical inflammation. <p><u>ACM</u></p> <ol style="list-style-type: none"> 1) Odontoblast-like cells were identified in 75% of the roots 2) Fibrous connective tissue with perfused blood vessels 3) Mesial root showing regenerated fibrous connective tissue without periapical inflammation. 4) Root apex showing apical closure with apical ramifications and no periapical inflammation.
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Abbas et al. 2020 (37)	REP Infected immature premolar teeth	1 week, 1 month, 3 months	Chitosan loaded - demineralized bone matrix - dexamethazone corticosteroid vs control healthy teeth + MTA	Histology	<p><u>Histological observation</u></p> <p><u>Early time</u></p> <p>1) Presence of regenerated tissues in the apical and middle thirds of the roots resembling a periodontal ligament tissue 2) inflammatory cell infiltration and dilated blood vessels decreasing</p> <p><u>1 month</u></p> <p>1) Mild to moderate periapical inflammation. complete</p> <p><u>3 months</u></p> <p>1) Absence of inflammatory cell infiltration</p> <p>2) Formation of mineralised hard and periodontal ligament-like tissues</p> <p>3) Prominent hypercementoid proliferation with a fibrous scaffold in PDL</p> <p>4) Maturation of the tissues in the periapical space which showed almost a complete maturation in PDL, alveolar bone with multiple accentuated reversal lines and osteons. 5) Osteoblastic rimming on the outer peripheries of bone</p>
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Khazaei et al. 2020 (38)	REP Healthy immature premolar teeth	3 months	(Buccal fat) vs (BC + Buccal fat) + MTA	Histology Immunohistochemistry and PCR	<u>Histological observation</u>
					<u>Buccal fat</u> - 50% acute & chronic inflammation - No complete calcified bridge - No necrosis 75% - DSPP, COL1A1, ALP are expressed <u>BC + Buccal Fat</u> - Chronic inflammation - Complete calcified bridge: osteodentine - No Necrosis - DSPP, COL1A1, ALP, DMP1 are expressed
Zaky et al. 2020 (39)	REP Infected immature premolar teeth	3 months	Collagen sponge vs PRF vs MTA	Histology Immunohistochemistry 2D Radiographic	<u>Histological observation</u>
					1) Highly cellular through the length of the root canal with rich vascularity. 2) Inflammatory cells—manifested as an inflammatory plug: filled the apical foramen and bone and root resorption + no signs of regeneration or cellular 3) Non-inflamed roots also showed some intracanal mineralization with bone/cementum-like lamellar structures

Mounir et al. 2019 (40)	REP Infected immature premolar teeth	1, 3, 6 months	Recombinant amelogenin protein RAP vs MTA	Histology Immunohistochemistry	<u>Histological observation</u> 1) Stem cells present: MSCs and SCAPs; 2) Regenerated tissues surrounding the root apices showed immune reactivity to Sox2, peripherin, CGRP and GFAP 3) Immunohistological evidence of the regeneration of peripherin neuronal intermediate filaments // GRP-reactive central nerves
El-Tayeb et al. 2019 (41)	REP Infected immature premolar teeth	2 weeks; 1 & 2 months	Propolis vs MTA	Radiographic Histopathology Histology	<u>Radiographic observation</u> 1) Increase in root length and dentin thickness 2) Decrease in apical diameter <u>Histologic observation</u> <u>Propolis</u> 1) Formation of cementum like tissue on the inner aspect of the root dentin 2) Pulp like tissue with areas of osteoid <u>MTA</u> 1) Formation of new layer of dentin like tissue 2) Fibrous connective tissue with islands of cementum like tissue inside the root canal space

Huang et al. 2019 (42) REP
 Infected immature incisor teeth
 3 & 6 months
 (Autologous pulp transplantation + BC) vs (BC) + MTA

**Radiographic
 Histology
 Immunohistochemistry**

Radiographic analysis

- 1) Decreased apical diameter
- 2) Increase in root wall thickness
- 3) Apical closure
- 4) Periapical healing
- 5) New hard tissue deposition

Histological and immunohistochemical

Autologous pulp transplantation

- 1) Canal walls had newly formed dentin-like tissue with dentinal tubules,
- 2) a lot of DSP+
- 3) Presence blood vessels
- 4) Presence fibrous tissue

Control group

- 1) Deposition of cementum-like tissue
- 2) Few DSP+
- 3) Presence blood vessels
- 4) Presence fibrous tissue

El Halaby et al. 2020 (43)	REP Infected immature premolar teeth	1, 2, 3 months	(Blood clot) vs (17% EDTA + blood clot) vs (PRF) vs (17% EDTA + PRF) + MTA	2D Radiography Histology	<p><u>Histological & radiographic examination</u></p> <p><u>All groups</u></p> <p>1) Increase in root length and thickness with signs of apical closure</p> <p><u>BC</u></p> <ul style="list-style-type: none"> - Vital tissue infiltration along the apical two-thirds of the pulp - Fibrous tissues and calcified structures inside the pulp space - Partial hard tissue formation - Signs of apical closure and mild inflammation <p><u>17% EDTA + blood clot</u></p> <ul style="list-style-type: none"> - Vital tissue infiltration along the pulp space, - Fibrous tissue formation inside the pulp space - Signs of complete hard tissue formation - Apical closure and mild inflammatory cell infiltration <p><u>PRF</u></p> <ul style="list-style-type: none"> - Vital tissue infiltration along the pulp space - Odontoblast-like cells with increased vascularity inside the pulp - Complete hard tissue formation - Signs of apical closure and no signs of inflammation <p><u>17% EDTA + PRF</u></p> <ul style="list-style-type: none"> - Vital tissue infiltration along the pulp space - Odontoblast-like cells undergoing differentiation with increased vascularity inside the pulp space - Complete hard tissue formation, signs of apical closure and no signs of inflammation
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El Kalla et al. 2019 (44)	<p>REP</p> <p>Infected immature teeth + healthy im- mature premolar teeth</p>	6 months	PRF +Portland cement vs Calcium Hydroxide	Histology	<p><u>Histological observation</u></p> <p>Infected teeth</p> <p>PRF</p> <ul style="list-style-type: none"> - Apical closure - Hard tissue on internal walls - Newly formed blood vessels <p>Calcium hydroxide: same but lower percentages.</p> <p>Non-infected teeth</p> <p>PRF</p> <ul style="list-style-type: none"> - Pulp closure - Hard tissue on internal walls - New pulp tissue formation <p>Calcium hydroxide: same but lower percentages.</p> <p>root canal space</p>
Alqahtani et al. 2018 (45)	<p>REP</p> <p>Infected immature molar + premolar teeth</p>	2 months	Decellularized Swine Dental Pulp ECM vs BC	<p>Histology</p> <p>Immunohisto- chemistry</p> <p>Radiographic</p>	<p><u>Histological & radiographic observation</u></p> <p><u>All groups</u></p> <ul style="list-style-type: none"> - Intracanal mineralization <p><u>DP-ECM</u></p> <ul style="list-style-type: none"> - DSP+ and CD31+ - pulp native microenvironment to recruit vascular cells

Yoo et al. 2021 (46)	REP Infected immature premolar teeth	3 months	BC + ProRoot MTA	Histology Micro-CT	<u>Radiographic examination</u> - Radiographic repair of periapical radiolucency - Continued root development - Apical closure <u>Canal microenvironments histologically</u> - Devoid of bacteria contained - New mineralized - Pulp-like tissues
Zarei et al. 2017 (47)	REP Infected immature premolar teeth closed and open apices	3 months	BC + Propolis vs BC + MTA vs BC + parafilm	Immunohisto- chemistry	<u>Histological observation</u> For MTA and Propolis - VEGF and factor VIII higher at 1 month than 3 months Expression of VEGF and factor VIII - Higher for Propolis than MTA group - Higher in open apices in propolis group than closed - Higher in closed apices in MTA group than open

Londero et al. 2015 (48)	REP Infected immature premolar teeth	7 months	(BC) vs (BC + Gelfoam) + MTA	Histology	<p><u>Histological observation</u></p> <p>BC</p> <ul style="list-style-type: none"> - Mineralized tissue covering dentinal wall = cementum - Increase in root length - Ingrowth of the external cementum into the root canal space <p>BC + Gelfoam</p> <ul style="list-style-type: none"> - Mineralized tissue covering root canal space = bone like tissue - Vascularized tissue - Matrix with osteocytelike embedded cells - Osteoblastlike cells on the surface - Vital tissue formed in the root canal space = periodontal ligament - Inflammatory cells: cervical third of the root canal next to MTA plug
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Stam-bolsky et al. 2016 (49)	REP Infected immature premolar teeth	6 months	<p>Group A1: disinfection with sodium hypochlorite (SH) and blood clot (BC) as scaffold;</p> <p>Group A2: disinfection with SH and PRP as scaffold;</p> <p>Group B1: disinfection with SH and (mTAP) dressing for 15 days, and BC blood clot as scaffold;</p> <p>Group B2: disinfection with SH and mTAP dressing, and PRP as scaffold.</p>	2D Radiography Histology	<p><u>Histological & radiographic examination</u></p> <p><u>Experimental groups</u></p> <ul style="list-style-type: none"> - Different grades of arrested dentin development - Gain of thickness of the apical third - Bone-like or cementum-like tissues <p>1) Vital tissue within canal spaces: in all group</p> <ul style="list-style-type: none"> - More vital tissue in B2 group <p>2) Hard-tissue deposition on radicular dentin walls: in all group</p> <ul style="list-style-type: none"> - B2 group maximal percentage <p>Apical closure</p> <ul style="list-style-type: none"> - B2 group maximal percentage
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Wang et al. 2010 (50)	REP Infected immature premolar teeth	3 months	(BC) vs (BC + collagen type I) + MTA	Histology	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - 43.9% of experimental teeth having hard tissue - 29.3% having vital tissues in the canal spaces <p><u>BC</u></p> <ul style="list-style-type: none"> - Root thickness and length increased <p><u>BC + Collagen I</u></p> <ul style="list-style-type: none"> - Arrested dentin development - Gain of thickness of the root = ingrowth of cementum-like - No odontoblast layer - Entire bridge = cementum -like - Tissues resembling cementum, PDL and bone
Zhang et al. 2014 (51)	REP Infected immature premolar teeth	3 months	PRP vs MTA	2D radiography Histology	<p><u>Histological & radiographic examination</u></p> <ul style="list-style-type: none"> - Apex closed PRP > BC - Thickening of the canal wall with ingrowth of cellular cementum-like tissues PRP > BC - Cementocyte-like cells were present in the newly formed tissues PRP > BC - Pulp-like tissue formation in the canal space PRP > BC

Palma et al. 2017 (52)	REP Infected immature premolar teeth	3 months	(BC) vs (HA:CS) vs (P:CS) + MTA	Histologic Observation Histomorpho- metric analysis	<p><u>Histological observation</u></p> <p><u>BC</u></p> <ul style="list-style-type: none"> - Resolution periapical lesion - Root thickness and length - Apical closure - Bridge of cementum and dentin next to MTA - Highly vascularized connective tissue - Newly formed tissue intracanal = cementum - Some specimen present odontoblastic layer - Intracanal bone and alveolar bone in periapical area <p><u>HA:CS scaffold</u></p> <ul style="list-style-type: none"> - Resolution of periapical lesions (less than BC) - Root thickness and length (same as BC) - Apical closure (better than BC) - Bridge of cellular cementum - Highly vascularized connective tissue moderate inflammation - Several areas of trabecular bone tissue <p><u>P:CS Scaffold</u></p> <ul style="list-style-type: none"> - Resolution of periapical lesions (less than BC and better HA:CS) - Root thickness and length (better as BC and HA:CS) - Apical closure (better than BC and HA:CS) - Intracanal cementum next to dentin & apical third root - Vascularized tissue without inflammation - Bone tissues or osteoid like in small areas
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Saoud et al. 2015 (53)	REP Infected immature incisor teeth	3 months	BC + MTA	Histology	<p><u>Histological observation</u></p> <p><u>Mineralized tissue</u></p> <ul style="list-style-type: none"> - Mineralized tissue next to MTA: Bone-like and cementum= repairing tissue. -Hard tissue barrier was formed more apically - Cells resembling elongated fibroblasts or mesenchymal cells with collagen fiber - A concentration of inflammatory cells and scattered mineralized tissue nodules in the loose connective tissue <p><u>Soft tissue</u></p> <ul style="list-style-type: none"> - Loose connective tissue rich in blood vessels - Without the presence of polarized columnar or flattened odontoblast-like cells - No definite nerve fibers
Zhu et al. 2014 (54)	REP Infected immature premolar teeth	3 months	(BC) vs (PRP) vs (Autologous DPSCs) vs (autologous DPSCs + PRP) + MTA	Immunohistochemistry Histology	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Vital tissue BC > PRP, DPSCs + PRP > PRP - Periostine + BC > DPSCs + PRP > PRP, DPSCs <p>2 types of mineralized tissue into canal space: cellular island and inner surface dentin walls.</p> <ul style="list-style-type: none"> - Nestin + None of them - TRAP + BC > DPSCs + PRP, PRP, DPSCs - DSP+ Into the tubules but no cells - BSP and OCN Expression in Alveolar Bone and Root Canal Space

Moradi et al. 2016 (55)	REP Infected immature premolar teeth	3 months	(BC + PRP) vs (BC) + MTA	Immunohisto- chemistry Histology	<p><u>Histological observation</u></p> <p><u>Vital tissue</u></p> <ul style="list-style-type: none"> - More without new vital tissue in both group than vital tissue - More vital tissue MTA group than PRP group <p><u>Factor VIII expression</u></p> <ul style="list-style-type: none"> - More expression on both group after 1 month than 3 month - 1month: MTA group > PRP group - 3 months: MTA group < PRP group <p><u>VEGF expression</u></p> <ul style="list-style-type: none"> - More expression on both group after 1 month than 3 month - 1month : MTA group < PRP group - 3 months : MTA group < PRP group
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Fahmy et al. 2017 (56)	REP Infected mature premolar teeth	1 month	<p>(1) Double-antibiotic-paste/Blood clot,</p> <p>(2) Ciprofloxacin/collagen,</p> <p>(3) Double-antibiotic-paste/Collagen,</p> <p>(4) Modified Tri-antibiotic-paste /collagen,</p> <p>(5) Ciprofloxacin/Gel-foam,</p> <p>(6) Double-antibiotic-paste/Gelfoam,</p> <p>(7) Modified Triantibiotic- paste/Gelfoam.</p>	Histology Immunohisto-chemistry	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Different protocol are plausible for REP of mature canals with new intra-canal tissue - Elarged apices to 0,6 mm for better REP procedure - Neo-formed tissue better with collagen and Ciprofloxin or Dianti-biotic - Vascularity same as neo-formed tissue - Hard tissue: Cementum like with collagen and Ciprofloxin or Di-antibiotic or no mineralized tissue - Inflammation: every group has more mild inflammation except tri-antibiotic past / Gelfaom
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Khademi et al. 2014 (32)	REP Infected immature teeth vs Healthy immature premo- lar teeth	3 and 6 months	BC + MTA in inflamed vs vital pulp	2D Radiography Histology	<p><u>Radiographic observation</u></p> <ul style="list-style-type: none"> - At 3 months : Better apical closure on vital pulp than inflamed pulp - At 3 months : Better Thickness canal walls on vital pulp than inflamed pulp - At 6 months : Better apical closure for inflamed pulp - At 6 month : Same results on Thickness canal walls for inflamed pulp - At 6 months : Better healing periapical lesion for inflamed pulp <p><u>Histologic observation</u></p> <ul style="list-style-type: none"> - Inflammation in periapical tissue : mild for all groups - Nature of coronally proliferated tissue : Granulation for all groups - New hard tissue is distinct for most of the specimen of each group or Limited on dentinal walls.
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Thibodeau et al. 2007 (57)	REP Infected immature premolar teeth	3 months	(BC) vs (collagen type I) vs (BC + Collagen type I) + MTA	2D Radiography Histology	<p><u>Radiographic evaluation</u></p> <p>Thickening of Root Canal Walls</p> <ul style="list-style-type: none"> - Collagen + BC > BC > Collagen <p>Apical Closure</p> <ul style="list-style-type: none"> - BC > Collagen > Collagen + BC <p>Healing of Periapical Radiolucency's</p> <ul style="list-style-type: none"> - BC > Collagen + BC > Collagen <p><u>Histological observation</u></p> <p>Hard-Tissue Deposition on Radicular Dentin Walls</p> <ul style="list-style-type: none"> - Collagen + BC > BC > collagen <p>Histological apical closure</p> <ul style="list-style-type: none"> - Collagen + BC = BC > Collagen <p>Histological Vital Tissue Within Canal Spaces</p> <ul style="list-style-type: none"> - Collagen + BC = BC > Collagen
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Rodríguez-Benítez et al. 2015 (58)	REP Infected immature premolar teeth	6 months	Gp 1: NaOCl/Blood Clot Gp 2: NaOCl/PRP Gp 3: NaOCl/TAP/Blood Clot Gp 4: NaOCl/TAP/PRP	2D Radiography	<u>Radiographic examination</u> Radiographic Healing of periapical radiolucency Gp 4 > Gp 3 > Gp2 > Gp1 Increase in Root Thickness Gp 4 > Gp 3 > Gp2 = Gp1 Radiographic Apical Closure Gp 4 > Gp 3 > Gp2 = Gp1
Zhou et al. 2017 (59)	REP Infected immature premolar teeth	3 months	(BC) vs (BC + PRF) + MTA	2D Radiography Histology	<u>Radiographic observation</u> - Periapical healing for all groups - Increasing root length and thickness are almost the same for both groups - Better resistance fracture for BC + PRF > BC alone. <u>Histologic observation</u> - Newly formed mineralized tissue with Cementocyte-like cells at the apex and along the internal canal wall for both groups - Bone like structure in canal space almost for all specimen for both groups

El Ashry et al. 2016 (66)	REP Infected immature premolar teeth	1,5 to 3 months	(BC) vs (BC + collagen) vs (BC + EDTA) vs (BC + EDTA + collagen) vs (BC + MTAD) vs (BC + MTAD + collagen) + MTA	2D Radiography Histology	<p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - All experimental groups increase in root length and thickness - All experimental groups decrease in apical diameter among <p><u>Histological observation</u></p> <ul style="list-style-type: none"> - More bone resorption for blood clot + collagen, blood clot + EDTA + collagen, blood clot + MTAD + collagen - New pulp space tissue : resembled the periodontal connective tissue with various inflammatory cells and angiogenesis - New hard tissue in the canal space : cementoid like tissue with different shape and Thickness
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Da Silva et al. 2010 (61)	REP Infected immature premolar teeth	4 weeks	Group 1: apical negative pressure irrigation vs Group 2: conventional irrigation plus Tri-antibiotic intracanal dressing + BC + MTA	Histology	<p><u>Histological observation</u></p> <p><u>Group 1</u></p> <ul style="list-style-type: none"> - Dense, well-structured ingrowth connective tissue - Young fibroblasts - Rich blood vessels - Mineralized tissue along canal walls <p><i>Periapical region :</i></p> <ul style="list-style-type: none"> - intense revascularization - advanced repair process - absence of inflammatory cells <p><u>Group 2</u></p> <ul style="list-style-type: none"> - Connective tissue ingrowth into the root canal - Less exuberant vessels and nerve bundles than group 1 - connective tissue ingrowth reached the middle and apical canal third - Mild inflammation - Beginning of the formation of mineralized tissue along the root canal walls <p><i>Periapical region :</i></p> <ul style="list-style-type: none"> - intense revascularization - advanced repair process - few of inflammatory cells (macrophages, plasmocytes)
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Pagliarin et al. 2016 (62)	REP Infected immature premolar teeth	7 months	(Triple antibiotics) vs (propolis) + MTA	Histology	<p><u>Histological observation</u></p> <p>New mineralized tissue formation on dentinal walls and in root canal space</p> <ul style="list-style-type: none"> - Cementum-like mineralization for both groups <p>Presence of vital tissue in root canal space</p> <ul style="list-style-type: none"> - Periodontal-like for both groups <p>Apical extension of root</p> <ul style="list-style-type: none"> - Present for both groups <p>Inflammatory reaction</p> <ul style="list-style-type: none"> - Moderate > severe > mild = absent for propolis - Severe > Mild > absent
Zhu et al. 2012 (63)	REP Infected immature premolar teeth	3 months	1) Blood clot vs 2) autologous DPSC vs 3) PRP vs 4) BC +DPSCs +PRP + MTA	Histology	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Vital Tissues in the Canal Space - Vital full-length BC > PRP > Mixture > DPSCs - Vital half-length DPSCs = PRP = mixture - Necrotic DPSCs > PRP > Mixture - Close to MTA = Osteoid hard tissue - Cementum-like tissue and periodontal ligament-like tissue along the dentinal wall - Rare specimen with bone-like tissue

Sheep model					
Altai et al. 2017 (64)	REP Infected immature incisor teeth	6 months	BC + MTA	Micro-CT Histology	<u>Radiographic examination</u>
					<u>Histological observation</u>
					- Increasing in root length
					- Increasing root wall thickness
					- Decreasing root diameters
					Root maturation and thickening of the walls
					- Hard tissue deposition in all experimental teeth.
					- Hard tissues in the apical portion of the root were more developed than in the coronal portion
Ferret model					

Alexander et al. 2020 (22)	REP Healthy immature canine teeth	3 months	(SynOss Putty) vs (BC)+ MTA	3D Radiography Histology	<p><u>Histologic observation</u></p> <p><u>BC</u></p> <ul style="list-style-type: none"> - Root canal thin - Apices were closed - No odontoblast layer <p>root canal space filled bone-like tissue</p> <p><u>Synoss Putty</u></p> <ul style="list-style-type: none"> - Root canal thin - Apices were closed - No odontoblast layer - No signs of new tissue formation - Intracanal and periapical inflammation <p><u>Radiologic observation</u></p> <p>Apical Diameter: No significant difference between groups</p>
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Tora- binejad et al. 2018 (23)	REP with residual incisors dental pulp tissue	3 months	<ul style="list-style-type: none"> - complete pulp extirpation - pulp amputation to 1–2 mm short of the radiographic apex - pulp amputation 2–4 mm from the radiographic apex BC + MTA 	3D Radiography Histology	<p><u>Histological & radiographic examination</u></p> <p><u>Complete pulp extirpation teeth</u></p> <ul style="list-style-type: none"> - Presence of bone inside the root canal <p><u>Pulp amputation 1–4 mm</u></p> <ul style="list-style-type: none"> - Presence hard tissue bridges <p><u>All groups present</u></p> <ul style="list-style-type: none"> - Apical closure - Normal tissue - Absence of intracanal/ periapical inflammation - Wall thickening increased
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Verma et al. 2017 (26)	REP Infected immature canine teeth	3 months	(BC) vs (DPSCs + hy- drogel scaffold) + MTA	2D Radiography Histology Bacteriology	<p><u>Radiographic Examination</u></p> <ul style="list-style-type: none"> - Increase in root wall thickness - Increase canal width - Decrease in canal diameter - Increase in root length - Presence/absence of radiographic lesion <p>--> No significant difference between two groups</p>
					<p><u>Histologic observation</u></p> <p>BC group : 2 distinct histologic patterns of tissue organization</p> <ul style="list-style-type: none"> - Loosely organized connective tissue - Newly deposited mineralized tissue - Some specimen osteodentin mixed with loose connective tissue (both groups) - Specimen without radiographic growth had inside de canal space bony island <p>No radiographic growth = residual bacteria : significant</p>

Tora-binejad et al. 2015(24)	REP Infected immature canine teeth	3 months	(BC + Gelfoam) vs (PRP) + MTA	Histology	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Bone or cementum mixed with connective tissues on apical third for some PRP & BS + Gelfoam - Resolution of a periapical lesion + hard tissue ingrowth for all groups - Connective tissue contained vessels and fibroblasts. - Coronal to the ingrowth of hard tissue and connective tissue, granulation tissue and inflammatory cells - Thickening of the root walls: bone-like and cementum-like tissue - PRP group showed a more prominent ingrowth of hard tissue in the apex than BC/Gelfoam group.
Tora-binejad et al. 2014 (25)	REP Infected immature canine teeth	3 months	(BC) vs (BC + PRP) + MTA	Histology	<p><u>Histologic observation</u></p> <ul style="list-style-type: none"> - Ingrowth of bonelike tissue from the apical region extending to the coronal third of the root for almost all specimen of both group - Bonelike tissue mixed with connective tissue + blood vessels and fibroblasts - Most of the specimen of both group showed inflammatory cells: macrophages and lymphocytes - No significant difference between groups.

Mice Model					
Yadlapati et al. 2017 (21)	Ectopic	1,5 months	VEGF-loaded fiber + root fragment + MTA	Histology	<u>Histologic evaluation</u> Implanted VEGF - New vessel formation - Mild inflammation: macrophages presence around the implanted fibers - Decrease of inflammation - Increase of new blood vessels
Li et al. 2016 (20)	Ectopic	2 months	Root tooth + (DPSC) vs (VEGF-loaded HG-MS) vs (VEGF-loaded HG-MS + DPSC) + MTA	Histology Immunohistochemistry	<u>Histologic observation</u> - Soft tissue formation in the roots: VEGF-loaded HG-MS - Pulp-like tissue: DPSCs group DPSCs differentiated into odontoblast-like cells and aligned with the existing tubular root dentin. - regenerate tissue fulfilled whole root and reach coronal third: VEGF-loaded HG-MS/DPSC group <u>vWF and CD31</u> VEGF-loaded HG-MS/DPSC group > VEGF-loaded HG-MS <u>Nestin and DSP</u> DPSC and VEGF-loaded HG-MS/DPSC groups > VEGF-loaded HG-MS <u>Human mitochondrial</u> - Pulp-like and odontoblast-like cells were marked strongly
Rat Model					

Edanami et al. 2020 (31)	REP Immature molar teeth	1 month	BC + MTA on residual healthy pulp	Histology Immunohisto- chemistry	<p><u>Histologic observation</u></p> <p>Teeth with 0.81–0.91 mm of remnant pulp healed</p> <ul style="list-style-type: none"> - Pulp like tissue : dentin and osteodentin <p>Teeth with 0.60–0.63 mm of remnant pulp healed</p> <ul style="list-style-type: none"> - Pulp like tissue : dentin and osteodentin <p>Teeth with 0.13–0.43 mm of remnant pulp healed</p> <ul style="list-style-type: none"> - (PDL)-like tissue, dentin and osteodentin, and cementum-like <p>Teeth with disorganization of pulp and apical tissues at 0.150.38 mm beyond the root apex healed</p> <ul style="list-style-type: none"> - PDL-like, cementum-like, dentin associated mineralized tissue and intra-canal bone.
Wen et al. 2020 (16)	Ectopic	3 months	Tooth slice + rBMSC (collagen scaffold) + iRoot BP rBMSC (collagen scaffold) The collagen	Histology Immunohisto- chemistry	<p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Analysis on neovascularization : new blood vessels were greater in BP1/3 than in M1/3 and D1/3 - DSP : immunoreactivity in all pulp-like tissues (rBMSC gp) - PGP9,5 : labeling in soft tissue intense in the nerve-like cells - CD31 suggested angiogenesis in the new pulp tissues (rBMSC+ iRoot BP significant) - rBMSC : pulp like tissue filled the tooth slice + regeneration of blood vessels - Collagen : fibrous tissue inside and outside the tooth

Chen et al. 2021 (30)	REP Mature Healthy Molar teeth	1 month	L-sEVs N-sEVs BMSCs BMSCs + L-sEVs BMSCs + N-sEVs	Histology Immunohisto- chemistry	<u>Histologic observation</u> - N-sEVs and L-sEVs modulate BMSC proliferation, migration, angiogenesis, and differentiation. - Both enhanced the structure of the regenerated tissue closer to that of a normal dental pulp in vivo. - L-sEVs had a more significant effect than N-sEVs. - L-sEVs more blood vessels, loose connectives tissue than N-sEVs - Collagen fibers arranged along the dentin wall - More TGF- β expressed L-sEVs than N-sEVs
Na- beshima et al. 2018 (29)	REP Mature Healthy Molar teeth	2 months	Group I : BC vs Group II : BC + 5 μL of VEGF + light-curing glass-ion- omer cement	Histology Immunohisto- chemistry	<u>Histologic observation</u> - Formation of loosen connective tissue without presence of odontoblasts in all specimens - Necrotic tissue surrounded by collagen fibers in all, although necrotic spots were more evident in group 1 than in group 2 - Formation of highly cellular and well-developed tissue with presence of fibroblasts and functional vessels filled with blood cells - Newly formed tissue in most of specimens from both groups and thirds

Gomes-Filho et al. 2012 (19)	Ectopic	7, 15 days and 1, 2, 3 months after implantation	In polyethylene tubes: TAP (antibiotic mixture) vs CHP calcium hydroxide powder with saline	Histology	<u>Histologic observation</u> <ul style="list-style-type: none">- Day 7 and 15, moderate chronic inflammatory cell infiltration by lymphocytes and macrophages was found in a fibrous capsule for TAP ,CHP, control- Intensity of inflammation reduced on days 30, 60, and 90- Thin fibrous capsule developed near the tubes for TAP, CHP & control- Dystrophic mineralization was only observed with calcium hydroxide.- Day 7 and 15, thin fibrous capsule formation and moderate cell inflammatory infiltration by lymphocytes and macrophages was observed with macrogol/propylene glycol- Mild inflammatory cell infiltration and a reduction in the thickness of the fibrous capsule was evident from day 30
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Moreira et al. 2017 (28)	REP Mature Healthy Molar teeth	1 month	Blood clot + PBM (photobiomodulation)	Histology Immunohisto- chemistry	<p><u>Histologic observation</u></p> <p><u>Group control:</u></p> <p>No tissue formation</p> <p><u>Group PBM:</u></p> <ul style="list-style-type: none"> - Root canal filled with immature connective tissue fewer and thinner collagen fibers than the originally preserved dental pulp - Blood vessels exhibiting SMA-positive cells in their walls - S-100-positive cells underneath the odontoblast-like cell layer - STRO-1-positive cells in perivascular niches
Ruang- sawasdi et al. 2014 (18)	Ectopic	3 months	human teeth roots + fi- brin gel	Histology Immunohisto- chemistry	<p><u>Histologic observation</u></p> <p><u>Fibrin gel :</u></p> <ul style="list-style-type: none"> - Improve tissue formation - 43% of total root filled by new tissue - Development small blood vessels - New tissue looks like normal pulp with cell-rich zone, cell-free zone, and odontoblast layer - Odontoblast-like cells found close to the dentinal wall - BSP+ areas were in the cells integrated to the dentinal wall - DSP+ areas in predentin in roots filled with fibrin gel, while they were absent in the formerly empty root canals.

Scarparo et al. 2011 (27)	REP Infected immature teeth vs vital pulp	3,6,9 weeks	triple antibiotic paste+ silver amalgam	Radiographic Histology	<p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Better increasing of root length with polyATB after 3- and 6-weeks post-treatment and significantly different from control. - Better decreasing root canal width with polyATB after 3- and 6-weeks post-treatment and significantly different from control. - Better decreasing Periapical lesion with polyATB after 3- and 6-weeks post-treatment than control. <p><u>Histological observation</u></p> <ul style="list-style-type: none"> - Induction of necrosis arrested root formation - Variable inflammatory response to treatment - Half of the roots showed formation of a cementum-like tissue on its apical portion - External new formed cementum
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Rabbit model					
El-Backly et al. 2008 (17)	Ectopic	12 days	rDPSCs+spoly(lactic-co-glycolic acid) polymers scaffolds	Histology	<u>Histological observation</u>
					<u>Group I:</u> - No sign of a fibrous tissue capsule - Lot of newly forming blood vessels and budding capillaries - Increased cellularity in the form of numerous stellate-shaped or fibroblast-like cells. <u>Group II:</u> - Capsule seems to contain fibrous tissue - Columnar cells arranged in tubular-like structures parallel tubules like a dentine-like appearance

Table S2: Animal models for Ectopic and Rep techniques.

Author/ Years	Clinical context	Follow-up	Materials or REP pro- cedure	Assessment	Results
Human model	REP Periapical infec- tion with com- pletely formed roots	6,12,18 months	SealBio vs Obturation	clinical signs PAI	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - PAI score diminution - Presence or absence of clinical signs and symptoms - Healed—combined radiographic and clinical normalcy Healing—reducing radiolucency with clinical normalcy Diseased—if the radiolucency persisted without change with or without clinical normalcy. <p>Both groups showed equally favorable outcomes at the end of 18 months without any statistically significant differences.</p>
					<p><u>Success</u></p> <p>TAP + irrigation = sterile roots</p> <ul style="list-style-type: none"> - Maintenance of a sterilized canal system with the help of a coronal seal - Use of negative pressure irrigation system. - Placement of triple antibiotic paste in the canals which reduces the bacterial load tremendously by penetrating the dentinal tubules

Aly et al. 2019 (85)	<p>REP</p> <p>Necrotic immature permanent anterior incisor teeth</p>	3, 6, 9, and 12 months.	BC + MTA vs BC + Biodentine	<p>Clinical tests</p> <p>2D Radiography</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Complete regression of signs and symptoms: pain, swelling, and sinus or fistula 100% with Biodentine and 95% MTA. - Discoloration: Biodentine 8% / MTA 59% <p><u>Radiological analysis</u></p> <ul style="list-style-type: none"> - Root length increasing but no significant Biodentine 5,64% and MTA 5,02%. <p><u>Fail:</u></p> <ul style="list-style-type: none"> - Presence of pain on biting and pain on percussion at 12-month follow-up - Might be due to the increased bacterial growth in the dentinal tubules
Brizuela et al. 2020 (115)	<p>REP</p> <p>Periapical lesion Mature permanent incisor, premolar and canine teeth</p>	6-12 months	UC-MSCs + Collagen membrane + Biodentine vs gutta percha (ENDO)	<p>Clinical tests</p> <p>3D Radiography</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Thermal and Electrical Tests REP > ENDO <p><u>Radiographic analysis</u></p> <p>Dimensions of the Apical Lesions: diminution in both group but better with ENDO technique</p>

Arslan et al. 2019 (86)	REP Necrotic Mature Teeth incisors with Periapical lesion	12 months	BC + MTA vs endo- dontic treatment	Clinical tests Radiographic analysis 2D with image J with scoring (measure the change of lesion size between pre- and postoperative radiographs)	<p>Clinical tests</p> <ul style="list-style-type: none"> - Absence of clinical signs and symptoms <p>Success treatment: 92, 3% favorable, which 15% respond positively to electrical vitality, test.</p> <p>Radiographic examination</p> <p>80% radiographic outcomes favorable.</p> <ul style="list-style-type: none"> - No statistical significant difference between groups terms of the pre-operative radiographic lesion score - Absence and reduction of the radiolucency were observed in 85% of CRCT-treated teeth compared with 92.4% of REP-treated teeth - Reduction of the periapical lesion 25% CRCT-treated / 46.2% REP - The number of discolored teeth REP group 38.5 <p>Fail</p> <ul style="list-style-type: none"> - remnants of microbial irritants and necrotic pulp tissues. None of the teeth with failure had pain, percussion, or palpation pain: 6/46
Ragab et al. 2019 (87)	REP Necrotic Immature Permanent incisors	6 months to 12 months follow up	With PRF vs PRF + MTA	2D Radiography	<p>Radiographic examination</p> <ul style="list-style-type: none"> - Root length increase through the follow up period with PRF 8,8% to 12,3% or without 7,7% to 14,8%.- Apical barriers were observed in 5 cases in-group (A) and 7 cases in-group (B). Observation calcific barrier: No PRF > PRF - Decrease in the perimeter of the periapical radiolucency. Both groups decrease perimeter - No statistically significant differences between the 2 groups.

El-Kateb et al. 2020 (114)	REP Mature necrotic incisors teeth with periapical lesions	1, 3, 6, 9, and 12 months	Protaper Next files X3 test vs X5 control BC + Biodentine	MRI: regenerate pulp-like tissue Radiographic evaluation: assess periapical healing. Clinical tests	<p>Clinical tests</p> <ul style="list-style-type: none"> - No pain, no sensitivity to percussion, or swelling 100% - Cold test response positive for 77,8% Biodentine group and 88,9% for control. - EPT: 66,7% Biodentine group and 88,9% control group. - 83% of all the cases treated responded positively to cold after 12 months, whereas 77% of all cases responded positively to the EPT. <p>MRI</p> <ul style="list-style-type: none"> - The significant decrease in the SI to reach the normal contralateral teeth - More organized tissue in the canal, dentin deposition and mineralization <p>2D radiographic examination</p> <ul style="list-style-type: none"> - Complete healing of the periapical lesion on both groups
Sallam et al. 2020 (6)	REP Necrotic imma- ture permanent premolar, molar, and incisors teeth	3,6,9 months	Contaminated teeth: PRF vs Calcium Hy- droxide Non contaminated PRF vs Calcium Hydroxide	Radiographic examination and measurement	<p>Clinical Success 100%</p> <ul style="list-style-type: none"> - No pain either spontaneous or on biting recorded as present or absent by asking the patient. - No tenderness to pressure or percussion - No tenderness to palpation of adjacent soft tissues. - No sinus tract or swelling in adjacent soft tissues. <p>Radiographic examination</p> <ul style="list-style-type: none"> - Significant difference in all intervals regarding root length in PRF subgroups and calcium hydroxide. - Increase in root length and thickness, - Decreased diameter of apical foramen

Rizk et al. 2020 (126)	<p>REP</p> <ul style="list-style-type: none"> - permanent necrotic maxillary central incisors with incomplete root - with or without periapical lesions - pulp involvement due to caries or trauma 	3, 6, 9 and 12 months	PRF + MTA vs PRP + MTA	<p>Clinical tests</p> <p>Radiographic analysis and measurement</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - resolution of pain, swelling, mobility and sinus/fistula = 100% success - Discoloration: PRF > PRP - All REP: 0% no respond to pulp sensibility tests (thermal (cold/heat), and electric pulp tester) <p><u>Radiographic analysis</u></p> <ul style="list-style-type: none"> - Increase root length PRP > PRF - Increase root width PRP < PRF - Increase in bone density PRP > PRF - Decrease in apical diameter PRP > PRF <p>But no statistical significant differences</p> <p>No sign of calcification/obliteration.</p>
Jiang et al. 2017 (88)	<p>REP</p> <p>Non-vital Immature premolar teeth</p>	3, 6, 9 and 12 months	Bio-gide collagen on blood clot + MTA	<p>Clinical tests</p> <p>Radiographic evaluation by measurement</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Complete resolution of signs and symptoms. - EPT, n (%) Control 18%/ test 33% <p><u>Radiographic analysis</u></p> <ul style="list-style-type: none"> - Increase in root length, n (%) Control 100% / Test 100% - Increase in dentin wall thickness in the apical third of the root, n (%) Control 91% / test 86% - Increase in dentin wall thickness in the middle third of the root, n (%) Control 55% / 100% test - Narrowing of apical foramen width, n (%) 91% control/ 100% test - Discoloration, n (%) 64% control / 71% test Calcification, n (%) 55% control /48% test

ElSh-eshtawy et al. 2020 (7)	<p>REP</p> <p>Immature Permanent anterior incisors teeth with necrotic pulps</p>	3, 6, 9 and 12 months	(BC+ PRP) vs (BC) + MTA	<p>Clinical tests</p> <p>Radiographic evaluation by measurement</p>	<p><u>Clinical tests</u></p> <p>- thermal and electric pulp testing: No response</p> <p><u>Radiographic examination</u></p> <p>- Root length: BC > PRP</p> <p>- Dentine wall thickness BC < PRP</p> <p>- Apical foramen width BC > PRP</p> <p>- Radiographic root area BC > PRP</p> <p>3/31 fail cases because of reinfection</p>
Rizk et al. 2019 (89)	<p>REP</p> <p>Necrotic Immature Permanent incisors teeth</p>	3, 6, 9, and 12 months	(PRP) vs (BC) + MTA	<p>Clinical tests</p> <p>Radiographic evaluation by measurement with image J</p>	<p><u>Clinical tests</u></p> <p>- resolution of pain, swelling, mobility, and sinus/fistula = 100% success</p> <p>- 100% no response to pulp test</p> <p><u>Radiographic outcome</u></p> <p>- Root length PRP > BC</p> <p>- Root thickness PRP > BC</p> <p>- Increase in bone density PRP > BC</p> <p>- Decrease in apical diameter PRP > BC</p> <p>No difference significant</p>

de-Jesus- Soares et al. 2020 (128)	REP Necrotic imma- ture incisor teeth	21 days	Different treatments interappointment medication Root canal samples were taken before treatment (S1), after 6% NaOCl irrigation (S2), and after interap- pointment medication (S3).	Radiographic evaluation Bacteria Quantification by qPCR	<u>Clinical tests</u> - Spontaneous pain 0% - Pulp sensibility (cold test) 0% - Pulp sensibility (electric test) 27% (2 cases TAP group/ 1 case CHP) - Pain on percussion 0% - Pain on palpation 0% - Sinus tract 0% - Abscess 0% <u>Radiographic examination</u> - Periapical lesion 0% - Root canal thickness 73% (TAP 60%/ CHP 83%) - Root length increase 82% (TAP 60%/ CHP 100%) better CHP > TAP - Root resorption 0% - Apical closure (TAP 80%/ CHP 100%) 3 cases failed before the 1st review appointment and 1 recurrent trauma.
Ramachan- dran et al. 2020 (65)	REP Immature permanent incisors teeth with necrotic pulps and apical periodontitis	6 & 12 months	(BC) vs (BC + PRP) + MTA	2D Radiography	<u>Clinical tests</u> - None of them responded to vitality testing on the follow-up visits. - None of the cases had increased periapical radiolucency <u>Radiographic examination</u> - BC group: RRA increased 3% to 9,8% at 12 months - PRP group: RRA increased 4,5% to 9,6% at 12 months 4 years after 2 patients creation calcification barrier

Botero et al. 2017 (90)	<p>REP</p> <p>Pulp necrosis on an immature permanent premolar and molar tooth or patients with at least 1 open apex of 1 mm or more in diameter</p>	3,12,24 months	(BC + Collacote piece + MTA) vs Calcium Hydroxide	Clinical tests 2D Radiographic	<p><u>No results on clinical or radiographic success.</u></p> <p>Collacote piece + MTA group: success rate of 71% 100% success for delayed group / CaOH₂</p>
Shivashankar et al. 2017 (91)	<p>REP</p> <p>Necrotic immature permanent teeth & trauma and/or caries</p>	3rd, 6th, 9th and 12th months	(PRF) vs (PRP) vs (BC) + MTA	<p>Clinical examination</p> <p>Radiographic evaluation by measurement with image J</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Absence of pain, inflammation or swelling - 2 failed with PAI= 4 even asymptomatic - PAI score 1 or 2 <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Complete healing majority of patient - Root Lengthening and Lateral Wall Thickness better PRF > PRP > BC - Presence of a normal periodontal ligament space <p>Vitality responses 15% PRF, 13,3% BC, 15,8%.</p> <p>PAI score 3,4,5 = failure: 10/118</p>

Bezgin et al. 2015 (69)	REP Necrotic single-rooted immature incisor and premolar teeth	3 months and 18 months	(BC) vs (PRP + BC) + MTA	Clinical examination Radiographic evaluation by measurement with image J	<u>Clinical tests</u> - Asymptomatic - Positive response to vitality testing (50% PRP / 20% BC) <u>Radiographic examination</u> - Complete apical closure - Increase in RRA - BC group exhibited a mean increase of 12.6% - 9.86% in the PRP group Difference between groups was statistically insignificant - No discoloration in relation to the triple antibiotic paste/ - Crown discoloration caused by MTA (60%) Successful outcomes PRP: 50% /// 20% BC
Nagy et al. 2014 (70)	REP Immature permanent incisor teeth with necrotic pulps	3, 6, 12, 24, months	MTA (apexification) vs (BC + MTA) vs (BC + hydrogel with FGF+ MTA)	Clinical examination Radiographic evaluation by measurement with image J	<u>Clinical & radiographic success</u> MTA, REG, and FGF groups were 100%, 90%, and 80% <u>Radiographic examination</u> 1) Increase in Root Length: YES for all groups - No significant difference between the REG and FGF - FGF > REG. 2) Increase in Root Thickness: YES - No significant difference between the REG and FGF - FGF < REG. 3) Decrease in Apical Diameter. YES - MTA group was significantly different from the REG and FGF 4) Periapical Bone Density - Significant improvement in bone density all groups. - No significant difference was found between all groups through the whole follow-up period 3/29 fail because symptomatic

Alagl et al. 2017 (71)	REP Non-vital immature permanent premolar and incisor teeth	5-12 months	(BC) vs (PRP +BC)+ MTA	Clinical test 2D radiography 3D radiography	<u>Clinical tests</u> - Resolution of signs and symptoms all patients - Sensitivity tests: 80% PRP / 40% BC <u>Radiographic examination</u> - Decreased lesion size both groups - Increased bone density both groups - Increased Root length both groups PRP > BC - Complete apical closure: PRP > BC Mean difference in the root length was found to be statistically significant
Nagata et al. 2014 (129)	REP Immature incisor teeth diagnosed with pulp necrosis caused by hard tissue dental trauma and/or some severe luxation	9-19 months	Intracanal medica- ment: TAP vs calcium hydroxide and 2% CHX gel	Microbiological and PCR Clinical tests Radiographic Examination	<u>Microbiological analysis</u> - Progressive disinfection help to destroy every bacteria - Bacterial reduction: irrigation solutions. <u>Clinical tests</u> - Complete reduction of spontaneous pain, pain on percussion, pain on palpation, fistula, and abscess - No pulp response <u>Radiographic examination</u> - No info
Narang et al. 2015 (122)	REP Necrotic imma- ture permanent teeth with or without associ- ated apical perio- dontitis	6-18 months	MTA apexification vs (BC) vs (PRF clot) vs (PRP + collagen) + resin-modified glass ionomer cement	Clinical tests 2D Radiography	<u>Clinical tests</u> - Asymptomatic with no tenderness on either percussion or palpa- tion. - Swelling and sinus had resolved completely. <u>Radiographic analysis</u> - Periapical healing PRF 98% > PRP 80% > BC 60% > MTA 58% - Apical closure: 66.67% BC, 40% PRF, and 60% PRP showed good ap- ical closure. - Root lengthening 99% PRF > 60% PRP & BC - Dentinal wall thickening: 60% of the cases in Group PRF; good

results were obtained in 50% of cases in Group BC and 20% of cases in Group PRP

Nakashima et al. 2017 (123)	REP Mature incisor/molar permanent teeth	1, 2, 4, 12, 24,28,32 weeks	MDPSCs were trans- planted with granulo- cyte colony-stimulat- ing factor (G-CSF) in atelocollagen into pulpectomized teeth.	Clinical Tests Radiographic Examination MRI radiography	<u>Clinical tests</u> Negative on - Cold/hot pain - Percussion pain - Tenderness Positive - Electric pulp test <u>Radiographic examination</u> - 24/28 weeks : obliteration of the enlarged apical portion following pulpectomy in three cases (patients 1, 3, and 5)
Ibrahim et al. 2021 (116)	REP necrotic upper central incisor ma- ture, pulp necro- sis associated with apical periodontitis.	3, 6, 9 and 12 months	iPRF + Biodentine	Clinical tests 3D radiography	<u>Clinical tests</u> - no pain, swelling or fistula formation <u>Radiographic examination</u> - Periapical lesion decrease iPRF > control

Cerqueira-Neto et al. 2021 (132)	<p>REP</p> <p>Traumatized</p> <p>Immature necrotic maxillary incisor</p> <p>Permanent Teeth with pulp necrosis and periapical lesion</p>	24 months	<p>Single visit: BC + scaffold</p> <p>2 visits : BC + scaffold + coltosol</p>	<p>Clinical tests</p> <p>2D Radiography</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - No failure clinical - Pulp sensibility: 9% vs 33,3% <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Interappointment 82% vs Single visit 100% - Root development evaluation: 45,5% vs 66,7% - Decrease of apical diameter ID < SV - Increase of root width ID < SV - Increase in root length ID < SV
El Ashiry et al. 2016 (60)	<p>REP</p> <p>immature permanent teeth with necrotic dental pulps.</p>	<p>2 weeks,</p> <p>6, 12, and</p> <p>24 months</p>	BC + MTA	<p>Clinical tests</p> <p>2D Radiography</p>	<p><u>Clinical criteria</u></p> <ul style="list-style-type: none"> - Patient were asymptomatic - No pulp sensibility thermal and percussion - No swelling <p><u>Radiographic analysis</u></p> <ul style="list-style-type: none"> - Increased root length increased - Root canal wall thickness. - Resolution of periapical lesion

Nosrat et al. 2019 (121)	<p>REP</p> <p>Immature healthy premolar maxillary and mandibular</p>	2.5–7.5 months	<p>Blood clot + SynOss Putty or SynOss only</p>	<p>Teeth extraction</p> <p>2D Radiography</p> <p>Histology</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Normal mobility, probing depths - No signs or symptoms of endodontic disease - Negatively to sensibility tests except for 1 patient.(Synoss putty + BC) <p><u>Radiographic analysis</u></p> <ul style="list-style-type: none"> - All extracted teeth had immature apices - Comparison of the MTA level between these teeth showed well-controlled placement in all SynOss Putty cases versus poor control <p><u>Histological observation</u></p> <ul style="list-style-type: none"> - New tissue formation - No resorption, inflammation in the newly formed intracanal tissues - Normal connective tissue with fibroblasts, and blood vessels. - Newly formed mineralized tissue <p>2 types of newly formed mineralized tissue</p> <ol style="list-style-type: none"> 1) Cementum-like tissue near the scaffold and dentinal wall 2) Bonelike islands in the root canal space and deposition of a mineralized cementum-like tissue on the dentinal walls.
Lovelace et al. 2011 (136)	<p>REP</p> <p>immature permanent incisors & premolar maxillary or mandibular single-rooted immature tooth with open apices</p>	1 month	<p>Collect an intracanal blood sample after BC.</p>	<p>Biochemical tests</p> <p>PCR to identify stem cells in the canal</p>	<p><u>PCR finding</u></p> <ul style="list-style-type: none"> - Indicated the significant accumulation of transcripts for the stem cell markers CD73 and CD105 compared to systemic blood. - No change in expression of the differentiation markers ALK-P, DSPP, ZBTB16, and CD14

Meschi et al. 2021 (124)	REP Immature Permanent incisors and premolar teeth with necrotic pulp	3, 6, 12, 24, and 36 months	BC + Collaplug + Portland cement vs BC + LPRF + Portland cement	2D/ 3D Radiography	<u>Radiographic analysis</u> <ul style="list-style-type: none"> - All control teeth healed - Root length/ apical area/ root thickness for both groups - Healing periapical lesion: Control > LPRF - Decreased PAI: Control > LPRF
Yoshpe et al. 2021 (8)	REP immature incisor teeth Pulp necrosis + Apical Periodontitis	24 months 30 months	PRF + MTA	2D Radiography Clinical tests	<u>Clinical tests</u> <ul style="list-style-type: none"> - No sensitivity to percussion or palpation <u>Radiographic examination</u> <ul style="list-style-type: none"> - No radiolucency, - Apices of both roots were closed with a thicker dentin wall. - Resolution of the periapical lesion - Apical closure
Jiang et al. 2020 (93)	REP Immature premolar and incisors teeth after trauma	3,7,11 months 3, 29,44;60 months	Collagen matrix + BC + MTA	Clinical tests Radiographic (CBCT) examinations	<u>Clinical tests</u> <ul style="list-style-type: none"> - Electrical pulp testing: 50% - Subjective symptoms: 100% asymptomatic <u>Radiographic examination</u> <ul style="list-style-type: none"> - Healing of the apical lesion: 100% - Detached apical root tip: 100% - Thickening of the root canal wall (main root): 100% - Significantly continued development (main root): 100% - Thickening of the root canal wall (detached root tip): 100% - Significantly continued development (detached root tip): 100%
Sabeti et al. 2021 (94)	REP Immature incisors teeth after trauma	18 months	BC + MTA	Clinical tests Radiographic (CBCT) examinations	<u>Clinical tests</u> <ul style="list-style-type: none"> - Sensibility testing / electric pulp testing: positive - Asymptomatic

					<u>Radiographic examination</u>
					- No symptoms
					<u>Clinical tests</u>
					- asymptomatic and tested negatively on thermal testing with percussion and palpation responses
Yoshpe et al. 2020 (117)	REP Four cases (5 teeth) of posttraumatic immature incisors teeth diagnosed with necrotic pulp and apical Periodontitis or chronic apical abscess	36 months	PRF + Resorbable Collagen Plug + Biodentine	Clinical tests 2D Radiography	<u>Radiographic examination</u> - Calcified bridge 3 mm coronal to the apex - Resorption appeared to be arrested - Normal periodontal ligament surrounded the mesial and apical aspects of the root - Intact periodontal ligament surrounding the root - Resorption had been arrested - Calcified substance filled the root canal; in the middle third of the root canal, a calcified bridge had developed
Cymerman et al. 2020 (120)	REP 1 immature tooth with apical periodontitis 3 mature teeth with chronic apical abscess/ acute apical abscess/ asymptomatic apical	20-72 months	BC + SynOss Putty	Clinical tests Radiographic examinations CBCT	<u>Clinical tests</u> - No pain on percussion/palpation/biting. - The probing depths and mobility of all teeth were within normal limits (ie, ≤3-mm probing depths and ≤1-mm mobility) <u>Radiographic examination</u> - The apical diameters ranged from 1–3.7 mm - All teeth showed complete osseous healing of the periapical lesions - The root canal spaces showed partial to complete mineralization - Varying degrees of apical closure were detected in recall radiographs and CBCT images

periodontitis

Gaviño et al. 2017 (95)	REP Three mature incisors teeth with apical periodontitis	1, 2, 6, 12, 24, 36, and 50 months	BC + PRP + MTA	Clinical tests Radiographic examination	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Asymptomatic and exhibited negative percussion, palpation, and thermal tests <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Complete bone healing around the root apex and invagination of the bone inside the canal forming irregular calcified structures; a slight increase of root length - Presence of cortical plates and the resolution of the periapical lesion - Repair of the periodontal ligament around the apex - Presence of a calcified structure just below the MTA barrier and irregular calcified tissue over the entire internal root walls in the apical third of the canal - Resolution of the periapical lesion
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Terauchi et al 2021 (96)	REP Three cases mature molars teeth with apical periodontitis	1 week, 3 months, 24 months	BC + MTA	Clinical tests	Clinical tests - Asymptomatic and responded to cold, heat, and electric pulp tests
				Radiographic examination	Radiographic examination - Combined Root Canal Therapies in Multirrooted Teeth with Pulpal Disease - Asymptomatic - Improvement of the periradicular alveolar bone and evidence of palatal canal apical narrowing and remineralization with re-establishment of the cortical plate - Presented with minimal (1+) mobility and all periodontal probings were within normal limits - Absence of periapical lesions - Restitution of supporting bone and absence of periapical lesions
Nazzal et al. 2018 (130)	REP Traumatized immature teeth with necrotic pulp	24 months	Using Bi-antibiotic past for disinfection Then finish with glass ionomer	Clinical tests	Clinical tests - Cold test : 100% negative - EPT : 45% positive
				2D Radiography	Radiographic examination root length / root length: - 1 = 1/4 root length - 2 = 1/2 root length 1% - 3 = 2/3 root length 73% - 4 = complete root length with open apex 26% - Root width Increased 55% / No change 45% - Root length increased 64%/ No change 36% - Apical foramen width Decreased 82% / Increased 18% - Discoloration 3 cases failed : lost to follow up/ trauma/ calcific barrier probably due to long-term use of calcium hydroxide

Jung et al. 2008 (97)	REP 9 immature premolar teeth with pulpal necrosis and apical periodontitis	12- 60 months	BC + MTA	2D Radiography	<u>Radiographic examination</u> - Continued development of the apex - Thickening of the dentinal walls were obvious - Dentinal walls displayed continued thickening with closure of the apex - Complete resolution of the radiolucency with continued apical closure
McTigue et al. 2013 [67]	REP 32 immature incisors & premolar teeth with pulpal necrosis and apical periodontitis	12- 48 months	BC + MTA	Clinical tests 2D Radiography	<u>Radiographic examination</u> - Apical healing: 97% - Closure of the root apex : 75% - Root walls thickened : 72% - Root length increased : 66% - Ideal placement level for MTA was approximately 3 mm apical to the CEJ - Calcific bridge formation 9 teeth failed to achieve at least 2 of the 3 root maturation parameters: apical closure; root wall thickening; and root lengthening.
Li et al. 2017 (99)	REP Immature Permanent premolar Necrotic Evaginated Teeth with or without apical periodontitis	24 months	BC + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - All asymptomatic - 25% responsiveness to the pulp sensibility <u>Radiographic examination</u> - 90% No periapical lesion - RRA increased - Apical diameter decreased - Root length Increased

Saoud et al. 2014 (100)	REP Immature permanent incisor teeth with necrotic dental pulp.	12 months	BC + MTA	Clinical tests 2D Radiography	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - No signs of tenderness to percussion or palpation, a swelling or sinus tract, or spontaneous pain: 100% - None of the teeth regained responsiveness to pulpal sensibility tests (cold, heat, and electrical) during the one year follow up period. 100% <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Complete resolution of periapical lesion - Complete radiographic apical - Apical diameter increased - Length of the root increased - Width of root wall increased - Hard-tissue bridge formation that occurred within the canal and not apex
Dabbagh et al. 2012 (101)	REP Immature permanent incisor teeth with necrotic dental pulp.	24 months	BC + MTA	Clinical tests 2D Radiography	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Cold test - Periodontal probing <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Increased root formation <p><u>Problems</u></p> <ul style="list-style-type: none"> - Discoloration of the crown; - Failure to produce bleeding - Collapse of the mineral trioxide aggregate (MTA) material into the canal

Dudeja et al. 2015 (102)	REP Immature, non-vital permanent incisors teeth	6 months to 36 months	BC + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - Asymptomatic <u>Radiographic examination</u> - Increase in root length as well as increase in the thickness of lateral dentinal wall - IOPA showed further increase in root length and thickness of lateral dentinal walls and complete resolution of periradicular radiolucency - Increasing resolution of periradicular radiolucency and almost closure of open apices
Ulusoy et al. 2017 (103)	REP Necrotic primary molars	18 months	BC + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - Asymptomatic - No discoloration <u>Radiographic examination</u> - Complete resolution of periapical and inter-radicular radiolucency - Evidence of re-established periodontal space along the roots
Cehreli et al. 2011 (104)	REP Immature necrotic permanent first incisor and molar molars	10 months	BC + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - Positive to cold test <u>Radiographic examination</u> - Increase in the root dimensions - Increase in the root wall thickness and root length - Complete or advanced apical closure.

Mehrvarzfar et al. 2017 (119)	REP Necrotic teeth immature	6 months	BC +calcium-enriched mixture (CEM) cement	Clinical tests 2D Radiography	<u>Clinical tests</u>
					<ul style="list-style-type: none"> - Asymptomatic - Not responsive to cold test - Positively to EPT test <u>Radiographic examination</u> <ul style="list-style-type: none"> - Healing of periradicular radiolucency - Thin layer of dentinal bridge formed on CEM plug - Thickening of the lateral dentinal walls - Elongation of the root, - Apical closure with formation of the apical barrier tooth was not responsive to cold test - Positively to EPT test at maximum output power - Second case same as the first but not responsive to EPT and cold tests.
Sachdeva et al. 2015 (105)	REP Immature incisor pulp necrosis	3, 6, 12, 24 and 36 months	BC + PRP clot + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u>
					<ul style="list-style-type: none"> - Not responsive to cold tests - Delayed positive on EPT <u>Radiographic examination</u> <ul style="list-style-type: none"> - Resolution of the periapical lesion - Increased thickening of the root walls, - Increased root development - Continued apical closure of the root apex
Shiehzhadeh et al. 2014 (112)	REP Traumatic injury Pulp necrosis on immature incisor and molar teeth	3, 6, 12, 24, months	BC + DPSCs + (PLGA- PEG) + MTA or GIC	2D Radiography	<u>Radiographic evaluation</u>
					<ul style="list-style-type: none"> - Asymptomatic - No signs of the sinus tract - Indication of continued development of the apex of the tooth around the obturating materials

- Remained functional with continued bone healing and bone completely healed

Lin et al. 2014 (106)	REP Traumatic injury on immature teeth which was avulsed and replanted	24 months	BC + MTA	Histologic and histobacteriologi c observation	<p><u>Histology observation</u></p> <ul style="list-style-type: none"> - Extensive dentin resorption altering the radicular contour - Some areas: calcified tissue resembling cementum covering the resorbed dentin - Fragments of periodontal ligament with no inflammatory cells could be seen attached to this tissue - Root canal was apparently empty, with remnants of an amorphous material (likely MTA) - Apical canal was filled with necrotic debris <p><u>Histobacteriology observation</u></p> <ul style="list-style-type: none"> - Bacterial aggregates on the root canal walls - Bacterial staining revealed that the necrotic mass filling the foramen was a thick bacterial biofilm exhibiting different bacterial concentrations - Bacterial cells were predominant over the extracellular matrix in the foraminal area, where the biofilm extended beyond the root canal limits, faced with a concentration of polymorphonuclear leukocytes <p>Failure can be = inadequate root canal disinfection without mechanical debridement</p>
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Becerra et al. 2014 (107)	REP Immature permanent premolar with chronic apical abscess	12 months, 18 months, 24 months	BC + MTA	Radiographic observation HE (tooth extraction)	<p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Periapical radiolucency decreased. - Asymptomatic <p><u>Histologic observation</u></p> <ul style="list-style-type: none"> - Fibrous connective tissue characterized mainly by fibroblasts and collagen fibers - Nonmineralized, with the exception of an island of dystrophic calcification apically, close to the foramen - Apical third of the canal: cementum-like tissue - Tubule-like structures of mineralized tissue or odontoblast-like cells could be observed in the canal. - Mild to moderate concentrations of chronic inflammatory cells: in the apical connective tissue - No odontoblast-like cells (rather only fibroblasts) could be seen layering the newly formed cementum
Chen et al. 2013 (108)	REP Necrotic immature permanent premolar tooth	1,3,6,9, 12 months	BC + MTA	Clinical tests 2D Radiography	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - asymptomatic <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Resolution of periapical radiolucency - Increased thickening and lengthening of the root showed continual development of the root - Presence of isolated island in the canal and become like a bridge

Chang et al. 2013 (109)	REP 3 immature incisor teeth with periapical lesion	36 months	BC + MTA	Clinical tests CBCT examination	<u>Clinical tests</u> - absence of clinical signs and symptoms with adequate function. <u>Radiographic examination</u> - significant reduction of periapical radiolucent lesion was noted and the overfilled MTA was completely surrounded by bony (or bone-like) tissues - Osseous repair and a continuous lamina dura-like structure could be observed along with the extruded MTA. - Complete healing of the periapical lesion with the extruded MTA intermingled with regenerated bone with a periodontal ligament-like space between them
Lenzi et al. 2012 (110)	REP 2 immature teeth with crown fracture	21 months	BC + MTA	Clinical tests 3D Radiography	<u>Clinical tests</u> - Asymptomatic <u>Radiographic examination</u> - Distinct thickening of the dentinal walls and closure of the apex of the root + patient remained asymptomatic (1st tooth) - No evidence of revitalization could be seen - Apical radiolucency had resolved completely - Distinct radiopaque barrier was seen at the apical opening, suggesting the formation of a hard-tissue barrier. (2nd tooth failed)
Shin et al. 2009 (111)	REP Immature teeth with necrotic pulp	2 - 19 months	BC + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - Asymptomatic - No tenderness to percussion or palpation - Ice test and electric pulp test were negative. <u>Radiographic examination</u> - Evidence of complete periradicular bone healing and root maturation - Complete resolution of condensing osteitis

Bakhtian et al. 2017 (118)	REP 4 immature incisors teeth with necrotic pulps	9 - 18 months	BC + PRF scaffold + Biodentine	Clinical tests 2D Radiography	<u>Clinical tests</u> - Asymptomatic
					<u>Radiographic examination</u> - periapical lesion healed - Apical closure - Root thickening for all cases
Plascencia et al. 2016 (113)	REP Crown fracture on immature incisor tooth	20 months	BC + MTA	Clinical tests 2D Radiography Tomographic signs	<u>Clinical tests</u> - No signs and symptoms of endodontic re-infection upon
					<u>Radiographic examination</u> - No signs and symptoms of endodontic re-infection upon
Shimizu et al. 2013 (127)	REP Immature incisor tooth with traumatic injury (Pulpal necrosis / chronic apical abscess)	12 months / 26-months crown fracture: tooth extraction for histology	BC + light-cured composite restoration (Amelogen Plus)	2D Radiography Histology of the crown fracture	<u>Radiographic examination</u> - More significant increases in root width - Increase in the radiographic area of the root
					<u>Histology observation</u> - Most apical portion of the canal was filled with newly formed mineralized tissue - Uninflamed vital connective tissue was noted enclosed in the mineralized tissue - Newly formed mineralized tissue appeared to resemble cementum-like tissue with incremental lines and osteocyte-like lacunae - Necrotic tissue was also present between the canal dentin and the mineralized tissue - The apical canal appears obliterated by calcified tissue - No pulp-like tissue characterized by the presence of polarized odontoblast-like cells aligning the dentin-like tissue was observed. - Immunohistochemical staining was only positive for BSP

Meschi et al. 2016 (136)	REP	11 months	BC + MTA	2D Radiography Histology Immunohistochemistry	<u>Histology observation</u>
	Infected Immature permanent molar tooth				<u>HE</u> <ul style="list-style-type: none"> - Calcified bridge with cell inclusions next to MTA - Connective pulp-like tissue with blood vessels and most apically - Internal resorption of the root dentin and osteodentin apposition (atubular tertiary dentine with cells entrapped) - External root surface resorption and cementum apposition appear underneath the periodontal ligament <u>IHC</u> <ul style="list-style-type: none"> - CD34+ with the blood vessels - Stromal cells in the PLT reacted positive to the OC staining <u>Radiographic examination</u> <ul style="list-style-type: none"> - Increase root length and in root width
Chen et al. 2012 (92)	REP	6 to 26 months	BC + MTA	2D Radiography	<u>Radiographic examination</u>
	Immature permanent incisor teeth with infected necrotic pulp and apical periodontitis /Abscess				<ul style="list-style-type: none"> - Increased thickening of the canal walls and continued root maturation - No significant continuation of root development with the root apex - Continued root development with the apical foramen remaining open - Severe calcification (obliteration) of the canal space - Hard tissue barrier formed in the canal between the coronal MTA plug and the root apex.

Meschi et al. 2018 (72)	REP Infected immature permanent incisors teeth	3, 6, 12, 24, and 36 months	BC + biodegradable bovine collagen plug + MTA	Clinical tests / PAI 2D/3D Radiography	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - Teeth were asymptomatic - Negatively on carbon dioxide snow and electrical pulp testing. - Discoloration by MTA <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Periapical lesion healed - PAI between 1 and 2 <p><u>REP healing</u></p> <ul style="list-style-type: none"> - Increased thickening of the root canal walls and continued root maturation - No significant continuation of root development with the root apex becoming blunt and closed - Severe calcification (obliteration) of the root canal space <p><u>3D analysis by measuring</u></p> <ul style="list-style-type: none"> - Increases root hard tissue volume - Increases root length - Increases root area - Decreases Periapical lesion area - Presented bone ingrowth inside the root canal, calcification or no uniform root development <p>fail PAI > 3-5</p>
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				<u>Clinical test</u>	
				- Sensibility test : negative	
				- percussion test : negative	
				- electric test : negative	
				<u>Radiographic examination</u>	
				<u>CBCT</u>	
				- Ankylosed	
				- presence periapical lesion (2nd case)	
				- Periapical lesion healed (3rd case)	
				<u>Histology observation</u>	
				<u>TCM+ IHC</u>	
				- Presence of vessels	
				- Presence of mineralized tissues next to MPC and some mineralized island tissue.	
				- Presence of conjunctive repaired tissue	
				<u>Micro-CT</u>	
				- presence of calcified bridge MPC	
				Failure due to trauma case 1, No mineralization in the apex case 2, Bacteria invasion case 3.	
				<u>Radiographic examination</u>	
				- Increases Apical closure	
				- Increases root length growth	
				- Increases thickening of the root walls	
				- Decreases apical rarefaction	
				<u>Photographs observation</u>	
				- discolored teeth or not 3 of 47 failed due to ankyloses	

REP
Meschi et al. 2019 (125)
 Infected immature permanent incisors teeth caused by trauma
 3 and 5,5 months
 6 and 7 months
 20 & 22 months
 BC + biodegradable bovine collagen plug + Portland cement

Radio 2D/3D +
Micro CT
Histology
Immunohistochemistry

REP
Elfrink et al. 2021 (73)
 Incisors immature traumatized teeth
 6-78 months
 BC + MTA

Photographs
2D Radiography

Pereira et al. 2020 (74)	REP Traumatized immature incisors teeth	9 to 36 months	BC + collagen fiber + MTA	Clinical tests 2D Radiography	<u>Clinical tests</u> - 93,75% successful clinical outcomes: asymptomatic <u>Radiographic examination</u> - Increase in root length - Increase in root width - Decrease in apical diameter Failure: retraumatized tooth 1/16
Chrepa et al. 2020 (75)	REP Immature permanent incisors, premolar and molar teeth with pulp necrosis	12 – 96 months	BC + collaplug MTA vs BC + collaplug + Biodentine	Clinical tests 2D/3D Radiography	<u>Clinical tests</u> - 43/51 (84,3%) successful outcomes - Reestablishment of pulp sensibility: 54% - Tooth discoloration: 62% (because of MTA) <u>Radiographic examination</u> - 91.4% demonstrated an increase in median RRA 5 cases showed a median gain in length - Dentin wall thickness increased - Increase in RRA was 20% (9.6%–27.3%) 8 fails - use of Ca(OH) ₂ and a lower concentration of 1.5% NaOCl were associated with a higher risk of failure - long-standing biofilm structure formed as a result of caries and its insufficient disinfection
Sutam et al. 2018 (133)	REP Immature teeth with necrotic pulp	/	/	Clinical tests 2D Radiography	<u>Quantitative radiographic measurement methods</u> - Bose et al's Method: The Percentage Change of the Root Length and Root Width - Alobaid et al's Method (the Percentage Change of the Root Length and Root Width) - Flake et al's Method (RRA Measurement) - In any case of measurement, the % change root length, width and

radiographic root area increased.

- 18.7% failed, as they had to be extracted due to serious root resorption. 3/14 teeth and 1 missed recall

Mittman et al. 2020 (76)	REP Traumatized Immature Permanent incisors	22 months	BC + collagen sponge + MTA	Clinical tests 2D Radiography	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - periapical radiolency: improved - alveolar bone loss: 56.3% developed root resorptions - Ankylosis: 31.3% displayed signs of ankylosis - Super/Infraposition - Sensitivity - Percussion - Discoloration: 92.9% <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Increased root thickness: no significant - Pulp space : no significant - Dentin wall widths and apical foramen: no significant - Significant difference could only be found in the decrease of apical foramina <p>81.3% of the teeth survived revascularization and regained sensitivity 18.7% failed, as they had to be extracted due to serious root resorption.</p>
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Zizka et al. 2021 (98)	<p>REP</p> <p>Immature permanent teeth with a diagnosis of pulp necrosis with or without periapical radiolucency</p>	<p>3, 6, 9, 12, 18 and 24 months</p>	<p>BC + MTA</p> <p>AAEP protocol vs Modified protocol</p>	<p>Clinical tests</p> <p>2D radiography</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - signs or symptoms of apical periodontitis - discoloration - PAI <p>Radiographic</p> <ul style="list-style-type: none"> - root length change - root width change - root area change <p>- most of the cases failed in the first year and mostly in the AAEP (American Association of Endodontists) group where calcium hydroxide and lower concentrations of calcium hydroxide were used</p> <p>- Higher concentration of hypochlorite no adverse effects in the mean of radiographic root length or width, but the change in radiographic root area was noticeable when a low concentration of sodium hypochlorite was used</p>
Bose et al. 2009 (131)	<p>REP</p> <p>Immature Teeth with Necrotic Root 40 control cases (20 apexification cases and 20 nonsurgical root canal treatments</p>	<p>0-36 months</p>	<p>TAP vs CaOH₂ vs formocresol</p>	<p>2D analysis with image J</p>	<p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - root wall thickness: TAP >> Ca(OH)₂ or formocresol groups - root canal length : Ca(OH)₂ > TAP > Formocresol - Ca(OH)₂ was radiographically restricted to the coronal half of the root canal system, it produced better results than when it was placed beyond the coronal half. - Radiographic evidence of hard tissue deposition was noticed

Linsuwano et al. 2017 (76)	REP Immature permanent teeth with a diagnosis of pulp necrosis with or without periapical radiolucency	12-61 months	BC + MTA	2D/3D Radiography	<u>Clinical tests</u> - asymptomatic <u>Radiographic examination</u> - Root length increased - Root width increased - No visible signs of apposition of mineralized tissue - Newly produced mineralized tissue is thickening with slight apposition on root canal wall in apical third. - Mineralization of detached apical papilla 76% were considered as successful 4 failed cases were diagnosed as chronic apical abscess with the presence of sinus tract 1 tooth was associated with a defective restoration
Estefan et al. 2016 (78)	REP Immature necrotic permanent maxillary incisors into 2 groups (9- 13 years // 14-18 years)	12 months	BC + MTA	2D radiography	<u>Radiographic examination</u> - An increase in root length: Young > older age groups - An increase in root thickness - A decrease in apical diameter: Failure in 2 of the 35 recalled cases Younger patients are better candidates for REP Diameter: predictability factor 0.5mm successful but e better with diameters > 1mm.
Peng et al. 2017 (79)	REP Diagnosis of pulp necrosis on premolar teeth	48 months	BC+ MTA or GIC	Clinical tests 2D radiography	<u>Clinical tests</u> - Success rate MTA > GIC - discoloration 19 cases for MTA and 4 GIC - Obliteration observed MTA<GIC <u>Radiographic examination</u> - Slight increase in root length for MTA and GIC

- Dentin thickness a little more important for MTA than GIC but not significant.

Chan et al. 2017 (83)	<p>REP</p> <p>Immature necrotic permanent molar, premolar and incisors teeth</p>	<p>1, 2, 3, 6, 12, 18, 24, and 30 months</p>	<p>BC + Collaplug + MTA</p>	<p>Clinical tests</p> <p>2D radiography</p>	<p><u>Clinical tests</u></p> <ul style="list-style-type: none"> - 92,8% cases successful - No positive response <p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Absence of radiographic pathosis 100% - Significant increases in the average root length - Root thickness area - 30.8% of the cases showing complete apical closure
Jeeruphan et al. 2012 (81)	<p>22 calcium hydroxide apexification cases, 19 MTA apexification cases, and 20 revascularization cases</p>	<p>21-30 months</p>	<p>BC + Collaplug + MTA</p>	<p>Clinical tests</p> <p>2D radiography</p>	<p><u>Radiographic examination</u></p> <ul style="list-style-type: none"> - Root width was significantly greater REP > Apexification - Increase of root length was significantly greater REP > Apexification - Survival rate of the REP and MTA apexification were greater than apexification calcium hydroxide - Complete healing similar between all groups
Bukhari et al. 2016 (82)	<p>REP</p> <p>Necrotic immature premolar and</p>	<p>7-72 months</p>	<p>BC + Bioceramic Putty vs BC + MTA</p>	<p>Clinical tests</p> <p>2D/3D radiography</p>	<p><u>Clinical and radiographic analysis</u></p> <ul style="list-style-type: none"> - (75%) healed completely - 3 cases (10.7%) failed during the observation period

	molar teeth with or no periapical periodontitis				- 3 cases failed 10% incomplete healing. No specific info
Chen et al. 2016 [80]	Immature incisors teeth (21 apexification and 17 REP)	3 to 12 months	MTA apexification vs REP with MTA + BC	Clinical tests 2D radiography	<u>PAI scoring for REP vs Apexification</u> - Complication for apexification lead to fracture 14% - 17% present obliteration for REP procedure - More cases healed with REP, more cases are diseased with apexification.
Song et al. 2017 (84)	REP Necrotic premolar teeth immature permanent and chronical abscess vs apexification	24.9 months	BC + MTA	Clinical tests 2D/3D radiography	<u>Clinical and radiographic examinations</u> - resolution of apical periodontitis - root development - intracanal calcification 73% resolution of apical periodontitis Calcification intracanal: 62% with 28% classified as calcific barrier (severe calcification) 72% present canal obliteration
Shah et al. 2012 (137)	REP Mature permanent teeth with pulp and Periapical infection	6 – 24 months	SealBio	2D/3D radiography	<u>Radiographic examination</u> - decreased lesion size - increased HU cementum - increased HU bone - CBCT - PAI (increased density of bone and cementum)