Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors: A Randomized Controlled Trial

By

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A thesis submitted in conformity with the requirements for the degree Master of Science
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**Purpose:** To compare clinical and radiographic outcomes and survival of mineral trioxide aggregate/ferric sulfate (MTA/FS) pulpotomy and root canal therapy (RCT) in carious vital primary maxillary incisors.

**Methods:** Asymptomatic carious vital primary incisors with pulp exposure in healthy children aged 18 to 46 months were allocated randomly to receive MTA/FS pulpotomy or RCT. Clinical and radiographic post-treatment assessments occurred at 6-month intervals for up to 40 months. Two disinterested raters classified each incisor into one of the following radiographic outcomes: N=incisor without pathologic change; \( P_o \)=pathologic change present, follow-up recommended; \( P_x \)=pathologic change present, extract.

**Results:** Eighteen-month outcomes demonstrated no statistical difference in clinical or radiographic outcomes for MTA/FS pulpotomy and RCT incisors \( (P>.05) \). Survival analysis demonstrated no statistically significant difference in survival for MTA/FS pulpotomy and RCT incisors \( (P>.05) \) over a 6 to 40 month follow-up interval.

**Conclusions:** MTA/FS pulpotomy is an effective treatment for carious vital primary incisors.
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**Abbreviations**

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<th>Description</th>
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<tr>
<td>AAPD</td>
<td>American Academy of Pediatric Dentistry</td>
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<tr>
<td>Ca(OH)(_2)</td>
<td>calcium hydroxide</td>
</tr>
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<td>DPC</td>
<td>direct pulp capping</td>
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<td>ECC</td>
<td>early childhood caries</td>
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<td>EPT</td>
<td>electric pulp test</td>
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<td>FBS</td>
<td>fetal bovine serum</td>
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<td>FC</td>
<td>formocresol</td>
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<td>FS</td>
<td>ferric sulfate</td>
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<td>IPT</td>
<td>indirect pulp therapy</td>
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<tr>
<td>IRM</td>
<td>Interim Restorative Material</td>
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<tr>
<td>MTA</td>
<td>mineral trioxide aggregate</td>
</tr>
<tr>
<td>NaOCL</td>
<td>sodium hypochlorite</td>
</tr>
<tr>
<td>PC</td>
<td>Portland cement</td>
</tr>
<tr>
<td>PBS</td>
<td>phosphate buffered saline</td>
</tr>
<tr>
<td>PCO</td>
<td>pulp canal obliteration</td>
</tr>
<tr>
<td>PDL</td>
<td>periodontal ligament</td>
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<tr>
<td>ppm</td>
<td>parts per million</td>
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<tr>
<td>QOL</td>
<td>quality of life</td>
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<td>RCT</td>
<td>root canal therapy</td>
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<td>ZOE</td>
<td>zinc oxide eugenol</td>
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Chapter 1 - Literature review

1. Introduction

Dental caries is an infectious, transmissible, chronic disease that can lead to the pathological destruction of dental hard and soft tissue. Dental caries can cause inflammation and necrosis of the dental pulp. Pulpitis, left untreated, can lead to a disruption in the normal growth and development of a child, pain, cellulitis, abscess and systemic infection.\(^1,2\) Treatment for inflamed pulps includes pulp therapy or extraction. The premature loss of primary maxillary incisors can adversely affect a child’s occlusion, psychosocial development, articulation accuracy and facial esthetics.\(^3\)\(^-\)\(^8\) Pulp therapy allows for the preservation of primary teeth with inflamed pulps in a quiescent state. Currently, there is a paucity of dental literature with regards to pulp therapy in primary incisors.

2. The pulp-dentin complex

Dentin and pulp are histologically distinct but are often considered a single functional entity termed the pulp-dentin complex due to their similar embryological origin and integrated function. The pulp produces dentin and provides nutrients and innervation to the dentin while the dentin provides protection for the pulp.\(^9\)

2.1. Anatomy and histology of the primary dental pulp

The primary dental pulp is a specialized soft tissue of mesenchymal origin that forms during the sixth week in utero.\(^9\) Pulp tissue is primarily composed of connective tissue
fibers, fibroblasts, odontoblasts, ground substance, interstitial fluid, Schwann/nerve cells, endothelial cells, red blood cells, white blood cells and stem cells. The pulp occupies the central portion of a tooth and is encased within mineralized dentin.

The morphology of the pulp tends to conform to the general anatomical shape of the tooth. The root canal system includes the pulp chamber, which contains the coronal pulp, and the root canal, which contains the radicular pulp. The pulp tissue terminates at the apical foramen where the majority of nerves and vessels enter and leave the tooth. In a developing tooth, the apical foramina are initially large but reduce in diameter as the tooth matures through secondary dentinogenesis. Accessory and lateral canals, as well as their foramina, may exist along the root surface providing a limited collateral source of innervation and fluid exchange.

Maxillary primary incisors tend to have a single canal. The pulp chamber tends to be oval and compressed labio-lingually when viewed in cross-section. Maxillary primary incisors have a slight S-shape when viewed proximally with the cervical portion tending to curve lingually while the apical half curves labially. Accessory and lateral canals are rare. The labial surface of the maxillary central primary incisors may display a longitudinal groove but root bifurcation is rare.

Histologically, 4 distinct zones characterize the dental pulp. The zones are the odontoblast layer, cell-free zone, cell-rich zone and pulp core. The first zone is the odontoblast layer located at the periphery of the pulp chamber. This layer is comprised
of a single layer of odontoblasts and their processes that extend into the dentin. Odontoblasts are responsible for the synthesis and secretion of the predentin extracellular matrix and dentin mineralization. Odontoblasts are present as a single layer of cells that appear 3 to 5 cells thick due to variations in height and cell crowding that result in staggering of the odontoblasts. Dentin, capillary networks, terminal axons of unmyelinated nerve fibers, collagen fibrils, proteoglycans, dendritic cells and fibronectins comprise the substance among odontoblasts and their processes.

Odontoblasts are post-mitotic terminally differentiated cells that cannot proliferate to replace irreversibly injured odontoblasts. Stem cells are capable of differentiating into odontoblast-like cells when primary odontoblasts are irreversibly injured in the dental pulp. Stem cells comprise between 2 to 9 percent of cells in the dental pulp in primary teeth. Odontoblast-like cells have a similar function and morphology to odontoblasts, however the mechanisms by which odontoblast-like cells form or differentiate are different from odontoblasts.

The second zone is the cell-free zone, or also termed the cell-free zone of Weil, located adjacent to the odontoblasts and predominantly in the coronal pulp. This zone is comprised of a rich network of unmyelinated nerve fibers (Raschkow's plexus), blood capillaries and fibroblast processes. This zone is responsible for providing nutrients to the odontoblast and sensory innervation to the dentin.

The third zone is the cell-rich zone where cellular density is highest among the 4 zones.
This layer is comprised of fibroblasts, stem cells, macrophages, lymphocytes, capillaries and nerve fibers.

The pulp core is the fourth zone and characterized by the major vessels and neural fibers of the pulp. This zone is also comprised of fibroblasts, stem cells, macrophages and collagen fibers. The zone characteristically shows an overall increase in cellular density towards the root apex. This layer is histologically similar to the cell-rich zone but is differentiated by a lower density of fibroblasts.  

2.2. Neurovascular component of the primary dental pulp

The neurovasculature regulates the interstitial environment, sensory conduction, inflammatory responses and dentinogenesis within the pulp. The pulp vasculature maintains homeostasis of pulp tissue through the transportation of nutrients, hormones and gases and the removal of metabolic waste products.

The dental pulp vasculature is a microcirculatory system as it lacks true arteries and veins with its largest vessels being arterioles and venules. The majority of blood vessels enter and leave the pulp through the apical foramen. A smaller number of blood vessels enter and exit through accessory foramina. As arterioles enter the apical foramen and extend coronally, their lumen increases in size and the frequency of lateral branching increases. These lateral branches further divide to form an extensive capillary network in the coronal portion of the pulp. Arteriovenous anastomoses occur throughout the pulp tissue. Arteriovenous shunts permit blood to flow directly from the arterial to the venous
side of circulation bypassing the capillary network. The vascular system is composed of extensive venules that traverse apically and exit through the apical foramen.9

The lymphatic system is a network of vessels that aid in local tissue homeostasis through nutrient and fluid distribution and the recirculation of interstitial fluid into the bloodstream. Lymph vessels in the pulp are found predominantly in the pulp horns and to a lesser extent, throughout the root.16,17 Unlike the vascular components of the pulp where capillaries are not able to absorb high molecular proteins, the lymphatic system is able to remove high molecular weight solutes from pulp tissue thereby reducing interstitial osmotic pressure.

Nerve fibers within the pulp-dentin complex are responsible for sensory conduction and neurogenic modulation of microcirculation, inflammatory reactions and implicated in dentinogenesis.18,19 Sensory nerve fibers within the pulp have their cell bodies situated in the trigeminal ganglion and sympathetic fiber bodies are located in the cervical sympathetic ganglia. The majority of nerve fibers enter the teeth through the apical foramen as a component of the neurovascular bundle. As the neurovascular bundle extends coronally, nerve fibers branch with increased frequency with the majority of nerve endings terminating in the cell-free zone to form the subodontoblastic plexus of Raschkow. A small number of nerve endings extend further into the dentinal tubules.

Six types of sensory neurons are present in the human dental pulp: A-beta, A-delta-fast, A-delta-slow, nociceptive C, glial derived neurotrophic factor regulated C and polymodal
nociceptive C fibers. Approximately 80 percent of sensory axons are unmyelinated. The exact function of each individual type of nerve fiber is unclear but A-fibers and C-fibers have functional overlap as both can induce a nociceptive response. The majority of these sensory neurons, when stimulated, provoke a nociceptive response. However, some demonstrate an efferent function through the release of neuropeptides and increase of blood flow within the dental pulp.\textsuperscript{20-22}

Sympathetic fibers of the pulp are less numerous than sensory fibers. They are located deeper within the pulp and follow a similar distribution pattern to the vasculature of the pulp.\textsuperscript{23} Activation of sympathetic nerve fibers tends to lead to the vasoconstriction of adjacent blood vessels and a reduction in pulpal blood flow.\textsuperscript{24-25} Some sympathetic neurons, however, release neuropeptides that stimulate vasodilation and increase blood flow.\textsuperscript{26}

### 2.3. Dentin

Dentin is porous mineralized tissue made up of collagen and apatite crystals. In utero, epithelial cells in the inner and outer dental epithelium proliferate from the cervical loop of the enamel organ to form Hertwig’s epithelial root sheath. The epithelial sheath grows apically until it encloses the pulp.\textsuperscript{9} Immature teeth have larger apical foramina and thinner dentin walls than mature teeth. As teeth mature and dentin is produced, root canals narrow and the apical foramina decrease in diameter. Maxillary primary incisors complete root formation and constriction of the apex at 18 to 24 months of age or approximately 1 year after eruption into the oral cavity.\textsuperscript{27}
Odontoblasts secrete an organic matrix that forms primary, secondary and tertiary dentin. Primary and secondary dentin, the majority of tooth hard structure, consists of organized dentin tubules and odontoblastic processes (Figures 2 and 3). Primary dentin is formed until root development is complete. Secondary dentin is circumpulpal dentin that develops after root formation is complete. Tertiary dentin forms in response to noxious stimuli such as caries, attrition, trauma, masticatory forces and restorative procedures. Tertiary dentin is produced by odontoblasts and odontoblasts-like cells and can be reactionary or reparative. Reactionary dentin is secreted by preexisting odontoblasts and tends to be well organized and tubular. Reparative dentin is secreted by stem cells that mature to become odontoblast-like cells. Stem cells from the pulp must be recruited and induced to differentiate into odontoblast-like cells prior to the secretion of a dentin matrix. Reparative dentin can show a broad spectrum of appearances ranging from regular and tubular to dysplastic and atubular.\textsuperscript{18}

Dentin contains fluid-filled tubules that facilitate the hydrodynamic stimulation of nerve fibers in dentin and pulp tissue. Dentinal tubules are continuous with the pulp and allow for fluid exchange between dentin and pulp tissue.\textsuperscript{28} An increase in dentinal tubule fluid flow stimulates an increase in fluid and protein flow out of the pulp into dentin.\textsuperscript{29} The outward fluid flow is postulated to have a protective flushing action that reduces the diffusion of noxious substances into the pulp. Dentinal tubules may undergo sclerosis in response to various stimuli including caries, attrition, abrasion and erosion. Dentin sclerosis occurs when the dentinal tubules become partially or completely filled with hydroxyapatite and whitlockite crystals.\textsuperscript{18} Dentin sclerosis reduces the permeability of
dentin by obstructing tubules and thereby reducing irritation to the pulp.\textsuperscript{30}

2.4. Neurovascular differences between primary and permanent pulps

In general, the anatomy and histology of primary and permanent dental pulps are similar. Primary and permanent tooth pulp horns show significantly greater neural density than all other regions of the coronal pulp.\textsuperscript{31} The innervation of blood vessels and distribution of neurons along blood vessels are also similar in both dentitions.\textsuperscript{32} However, permanent teeth have a greater density of neurons in all regions of the pulp than primary teeth.\textsuperscript{31,33,34} Despite the difference in neural density between primary and permanent teeth, no clinical differences in sensory or somatic responses have been demonstrated between primary and permanent teeth.

The number and distribution of blood vessels in the pulp horn and subodontoblastic regions of primary and permanent molar pulps are similar.\textsuperscript{35} However, primary molars demonstrate a greater number of vessels in the mid-coronal region of the pulp than permanent molars. The difference in vascularity is speculated to reflect increase functional demands of the physiological resorption process or wider apical foramina that facilitate more blood vessels to enter the pulp of primary compared to permanent teeth.\textsuperscript{35}

The leukocyte density in the pulp horn and mid-coronal regions of the pulp is greater in primary than permanent teeth.\textsuperscript{36} The greater number of leukocytes in the primary than permanent tooth pulps is speculated to be related to the physiological resorption process in primary teeth or a greater immune response in primary teeth than permanent teeth.
secondary to more porous enamel and dentin that is less resistant to antigenic substances.\textsuperscript{36}

### 2.5. Pain perception in primary and permanent teeth

Clinicians report anecdotally that primary teeth are less sensitive to noxious stimulation than permanent teeth, however there is currently no high quality evidence to support this assertion.\textsuperscript{33,37} Though primary teeth contain fewer neurons and myelinated neural fibers than permanent teeth, the overall anatomy and distribution of neural tissue within primary and permanent pulps are similar.\textsuperscript{31-33,35,36} Pulp sensibility testing demonstrates primary and permanent teeth respond similarly to noxious stimuli.\textsuperscript{38,39} Although neural density is greater in permanent teeth than primary teeth, investigators have not been able to differentiate between specific nerve populations in the pulp. The greater neural density in permanent than primary teeth may not correlate with an increase in sensory neural fibers that are responsive to noxious stimuli.\textsuperscript{31}

An immature autonomic system in infants and children is speculated to be the cause of nociceptive responses reported less frequently in the primary dentition than permanent dentition. However, there is evidence that nocioceptive receptors, though still immature, are functional in the fetus.\textsuperscript{40} Reflex movements often characterize noxious responses. Examples of reflex movements include withdrawal reflexes, increases in heart rate and facial movements. Muted reflex responses to noxious stimuli in infants might be related to immature sympathetic responses in children and not their ability to perceive pain.\textsuperscript{41,42}
Children may report less pain in decayed teeth due to their cognitive development. For a child to designate the intensity of a pain experience, the child must be able to rank the severity of their pain. Approximately 40 percent of 5- and 6-year-old children experienced difficulty using pain scales because they are not able to rank their pain. Children who acquire caries at an early age may have limited experience being free of dental pain and therefore may not be able to easily differentiate between painful and pain-free states.

2.6. Summary

The pulp and dentin are considered a single functional entity due to their integrated function and similar embryological origin. Dentin is a mineralized tissue that surrounds the pulp and protects the pulp from injury. Dentinal tubules are continuous with the pulp and allow for fluid exchange between dentin and pulp tissue. The majority of neural fibers and blood vessels enter and exit the pulp through the apical foramen. A smaller number of blood vessels enter and exit through accessory foramina.

The pulp-dentin complex is comprised of an extensive neural, vascular and lymphatic system that is involved in tissue homeostasis through the transportation of nutrients, hormones and gases and through the removal of metabolic waste products. Primary pulps demonstrate fewer nerve fibers and greater vascular density than permanent pulps. Minor differences exist between the dental pulps of primary and permanent teeth but overall the function and structure of permanent and primary pulps are similar.
3. Physiologic root resorption and exfoliation of primary maxillary incisors

Physiological root resorption is a normal process that leads to the exfoliation of primary teeth. There is a paucity of literature regarding the initiation of physiological root resorption of primary maxillary incisors however, there is evidence documenting the development and eruption of permanent maxillary incisors. Physiological root resorption typically starts at approximately 5 to 7 years of age but can begin as early as 4 years of age in primary maxillary incisors based on extrapolated data from permanent tooth development. Primary maxillary incisors exfoliate and are replaced by permanent maxillary incisors between the ages of 7 and 9 years of age. Normal tooth exfoliation may be disrupted by periapical/periradicular pathosis and pulp therapy.

4. Dental caries

Dental caries is an infectious, transmissible, chronic disease that can lead to the pathological destruction of dental hard and soft tissue. Caries has a multifactorial etiology that involves a carbohydrate substrate, susceptible tooth surface as well as acidogenic (acid-producing) and aciduric (acid-tolerating) bacteria.

Dental plaque is a biofilm that forms on tooth surfaces where microorganisms and dietary carbohydrates concentrate. Dental plaque associated with sound tooth structure consists predominantly of non-acidogenic and non-aciduric bacteria from which acid production is minimal. Acidogenic bacteria in dental plaque produce acids as a by-product of carbohydrate metabolism. Under prolonged acidic conditions, aciduric bacteria become dominant through selective adaptation. Acid production subsequently leads to a decrease
in environmental pH. The critical pH threshold at which dissolution of enamel commences is pH 5.5. A persistently low environmental pH promotes demineralization of tooth surfaces that can progress to the destruction of hard and soft tooth structure.

Dental caries is the most common chronic bacterial infectious disease in children. Dental caries is 5 times more common than asthma and 7 times more common than hay fever in children. Caries risk considerations unique to infants and young children include timing of cariogenic bacteria acquisition, ad libitum infant/early childhood feeding practices and establishment of childhood feeding preferences. Inappropriate dietary practices (e.g. non-nutritive feedings) and lack of oral hygiene put the primary dentition at risk for decay soon after eruption. The maxillary incisors are at particular risk due to prolonged exposure to fermentable carbohydrates during suckling primarily during sleep. Mandibular incisors are not equally affected as maxillary incisors as the tongue covers mandibular incisors during suckling protecting them somewhat from carbohydrate exposure.

4.1. Effect of dental caries on the pulp-dentin complex

Caries is the most common cause of pulpal inflammation. Cariogenic bacteria can induce pulpal inflammation through direct contact or contact of their byproducts with the pulp-dentin complex. The immune system is often unable to access and eliminate pathogenic microorganisms affecting enamel, dentin and cementum because of the avascular nature of these tissues. Unlike infections in other parts of the body, caries often requires local intervention, as systemic therapies are not effective treatment against caries.
The pulp is a microcirculatory system encased in dentin that resists volume changes within the pulp. These properties of the pulp-dentin complex gave rise to the pulp self-strangulation theory. The theory suggests that with the limited volume exchange and the rigid encased environment of the pulp, edema secondary to inflammation decreases blood flow which then causes an increase in interstitial pressure to the point that exceeds pulp vascular pressure. Subsequently, vascular collapse and pressure necrosis of the pulp may occur through cessation of blood flow. However, there is weak evidence to support the theory of pulp strangulation as increases in pulpal interstitial pressure from inflammation have been demonstrated to not result in vascular collapse and necrosis. Increases in pulp interstitial pressure at the site of inflammation are caused by increases in blood vessel permeability and plasma exudation as well as vasodilation of blood vessels. However, the pulp opposes increases in interstitial pressure by increasing lymphatic drainage, capillary filtration, blood flow, dentinal fluid movement and angiogenesis. As long as physiological feedback mechanisms that counteract increases in interstitial pressure remain functional, the pulp has the ability to restrict pulp inflammation to the site of injury.

The natural course of pulpitis is not well understood. The inflammatory response is a complex series of events under the influence of multiple regulatory systems including the paracrine, autocrine and endocrine systems. A transient inflammatory response is useful in clearing foreign antigens and producing an environment conducive to regeneration and healing. However, severely damaged pulp tissue may not be capable of healing and may progress to necrosis. With the accumulation of areas of local tissue necrosis, eventual
complete necrosis of the pulp may occur.

4.2. Pulp inflammatory/immune response to dental caries

Inflammation is a complex mechanism initiated in response to harmful stimuli and can be classified as either acute or chronic.急性炎症是宿主对有害刺激的即时反应，并以血管扩张、血管通透性增加和白细胞招募为特征。慢性和进展性炎性反应

Acute inflammation is the immediate response of a host to harmful stimuli and characterized by vasodilation, increased vascular permeability and recruitment of leukocytes.慢性和进展性炎性反应

Leukocytes remove pathogens via the vascular and lymphatic systems.慢性和进展性炎性反应

The duration of acute inflammation can last minutes to days.慢性和进展性炎性反应

Outcomes of acute inflammation include tissue healing with or without fibrosis or progression to chronic inflammation. Acute inflammation progresses to chronic inflammation in cases of persistent injury or infection, prolonged exposure to toxic agents or autoimmune diseases.

Chronic inflammation is a low-grade inflammatory response that aims to remove or contain harmful stimuli while mediating the destruction of inflamed and necrotic tissue in order to promote new tissue growth. Chronic inflammation can last for days to years.慢性和进展性炎性反应

The transition from acute to chronic is gradual and marked by a change in cellular components, tissue destruction and repair of injured tissue. Chronic inflammation is characterized by the accumulation of lymphocytes, plasma cells and macrophages, angiogenesis and lymphangiogenesis. Angiogenesis and lymphangiogenesis enhance transport of fluid, proteins and immune cells to meet increased demands for fluid movement.慢性和进展性炎性反应

Dentin sclerosis and production of tertiary dentin are unique features seen only in chronic inflammation of the pulp-dentin complex.慢性和进展性炎性反应

Dentin sclerosis reduces the
permeability of the pulp-dentin complex and tertiary dentin forms an additional barrier against bacteria and their toxins.\(^{59}\)

### 4.3. Pulp histological changes in response to dental caries

In general, pulpal inflammation increases as carious lesions increase in size or progresses towards the pulp.\(^{36,60-63}\) The presence, absence and quality of tertiary dentin varies among carious lesions and correlates with the nature of the caries progression.\(^{62,64}\) In slowly progressing lesions, tertiary dentin is more often reactionary. In rapidly progressing lesions, reparative dentinogenesis is more often reported as the death of primary odontoblasts is more likely to occur than in slowly progressing carious lesions.\(^{65}\)

In teeth with rapidly progressing dentin lesions, tertiary dentin tends to be atubular or less tubular and less calcified than teeth with slowly progressing dentin lesions.

Caries is a dynamic process and may alternate between periods of rapid and slow progression. Carious lesions can also present with multiple caries progression rates within a single lesion.\(^{64}\) As a consequence, pulp histopathology may be representative of a blend of multiple caries progression rates.

### 4.4. Dentin sclerosis and formation of tertiary dentin in response to dental caries

The formation of tertiary and sclerotic dentin in carious teeth is proposed to be a protective mechanism against the ingress of pathogenic bacteria and their byproducts. Dentin tubules are a path by which bacteria and their toxins may gain access to the pulp. Sclerotic dentin reduces the permeability of the dentin to bacteria. Bacteria progresses
through dentinal tubules more slowly in vital than necrotic dentin.\textsuperscript{66} The difference in the rates of bacterial ingress between vital and necrotic dentin is speculated to be due to the fluid flow from the pulp toward the dentin-enamel junction and immunoglobulins present in vital dentin. Formation of tertiary dentin and dentin sclerosis indicates that the dental pulp is vital and has the potential for pulpal regeneration and repair.

Tertiary dentin is speculated to act as a barrier between the pulp and pathogenic bacteria and their byproducts. An association between tertiary dentin formation and resolution of pulpal inflammation has been demonstrated.\textsuperscript{55} In rats, caries-induced pulpitis was reported to subside after tertiary dentin formation occurred at the pulp-dentin interface.\textsuperscript{55} However, pulpal inflammation was again reported once caries progress into tertiary dentin. The effectiveness of tertiary dentin as a barrier against pathogenic bacteria may be dependent on the structure of tertiary dentin, which can be variable. Tertiary dentin tends to be more irregular, less mineralized, have more cellular inclusions and contains fewer dentinal tubules than primary and secondary dentin. Mild injuries tend to form tertiary dentin that is more regular and mineralized resembling primary and secondary dentin while more severe injuries are associated with more irregular and less mineralized dentin. The dentinal tubules between secondary and tertiary dentin are often discontinuous.

Tertiary dentin can form at the site of pulp exposure where a pulp-capping medicament has been placed over the pulp exposure and the tooth is sealed with a liner and/or restoration. Tertiary dentin that forms at the site of pulp exposure is often termed a
Many dentin bridges contain remnants of pulp tissue, operative debris and structural defects that present where the pulp is in contact with the pulp-capping medicament. Though formation of a dentin bridge is postulated to be protective against bacterial invasion, it is unclear if a dentin bridge provides an effective barrier against bacteria and bacterial toxins.

4.5. Pulp histology in symptomatic and asymptomatic carious teeth

Pain is a subjective sensation involving multiple physiological processes including sensory, emotional, conceptual and behavioral aspects. Pain history in children with grossly carious primary teeth is not correlated with the degree of pulpal inflammation or density of vasculature or neural density within the pulp.

4.6. Summary

Dental caries is an infectious chronic disease and the most common cause of pulpal inflammation. The pulp-dentin complex is capable of undergoing dynamic tissue changes in response to caries including increases in fluid circulation and permeability, infiltration of leukocytes, angiogenesis, dentin sclerosis and tertiary dentin formation in order to maintain tissue homoeostasis. The rate of caries progression is often reflected by the quality of tertiary dentin and degree of dentin sclerosis. Slowly progressing lesions tend to have tertiary dentin resembling normal tubular dentin while rapidly progressing lesions are associated with atubular dentin or the absence of tertiary dentin. As caries progresses, the severity of inflammation within the pulp increases and pulp necrosis and infection can be the consequence. Pain history in primary teeth is not correlated with the
degree of pulpal inflammation or density of innervation within the pulp.

5. Rationale for preservation of the primary dentition

A healthy primary dentition can be important for normal growth and development. The premature loss of primary maxillary incisors can adversely affect a child’s occlusion, psychosocial development, articulation accuracy and facial esthetics.1-8,69

Primary teeth aid in the mastication of food with variations in tooth shape that reflect different functional roles. Incisors are chisel or wedged shaped teeth that are used in parcelling food. Canines are used to tear and rip food and primary molars are used to grind and chew food.

5.1. Effect of dental treatment of primary teeth on normal growth and development

Oral health can be an integral part of overall general health.1,5,69 Children with early childhood caries (ECC) are more likely to suffer from malnutrition and failure to thrive than children who are caries-free.1,69 Fourteen percent of children with ECC weighed less than 80 percent of their ideal weight, satisfying a criterion for the designation of failure to thrive.1 Twenty-five percent of children with severe ECC exhibited evidence of malnutrition by anthropometry.69 Blood tests were more effective than anthropometry for detection of nutritional deficiency. Blood tests results demonstrated evidence of inadequate iron intake with low serum ferritin in 80 percent, iron depletion in 24 percent, iron deficiency in 6 percent and iron deficiency anemia in 11 percent of children with ECC. Chronic iron deficiency is associated with impaired physical growth, brain
development and behavioral development and decreased activity level.

There is low-level evidence to support that children with ECC exhibited normal growth and development after dental rehabilitation.¹ Children with ECC who underwent comprehensive dental treatment under general anesthesia exhibited significant catch up growth post-dental treatment.¹ After approximately 1.5 years after dental rehabilitation, the weight of children with ECC who underwent dental rehabilitation was not different from caries-free children.

5.2. Effect of dental treatment of primary teeth on quality of life

Children with ECC have a lower quality of life (QOL) than children who are caries-free.⁵ Parents of children affected by ECC perceive their children to have greater pain, poorer oral function and more psychological issues related to their oral health compared to children free of caries.⁵ However, after dental rehabilitation, children with ECC demonstrate significantly improved QOL 4-weeks post-dental rehabilitation.

Parents, regardless of socioeconomic status, all agree grossly carious teeth and carious teeth with visible sinus tracts are unhealthy and unattractive.⁶ Children without caries show more teeth when smiling and evaluate their own smiles more positively than children with ECC. Parents also evaluate the smiles of caries-free children more positively than children with ECC.⁷⁰ Dental features are reported to be the fourth most common cause for teasing between the ages of 9 and 13 after height, weight and hair.³
5.3. Effect of premature loss of primary teeth on speech

Conflicting low-level evidence exists to whether children with premature loss of their primary maxillary incisors demonstrate more articulation errors than children with intact dentitions.\textsuperscript{4,71} However, no children with premature loss of their primary maxillary incisors demonstrate speech articulation errors that persist into adolescence and adulthood.\textsuperscript{4}

5.4. Summary

Untreated dental caries in the primary dentition is associated with malnutrition and failure to thrive. Caries-free children or children who have undergone dental rehabilitation demonstrate higher QOL than children with ECC. Parents of children affected by ECC perceive their children to have greater pain, poorer oral function and more psychological issues related to their oral health compared to children free of caries. Though children with premature loss of primary incisors may demonstrate more speech articulation errors than children with intact dentitions, speech articulation errors do not persist into adolescence and adulthood.

6. Diagnosis of pulp status

The status of the pulp determines the treatment choice in pulp therapy. Vital pulp therapy is reserved for teeth with pulps that maintain their reparative and healing potential. Non-vital pulp therapy is utilized in teeth with pulps that have lost their reparative and healing potential. Non-vital pulp therapy is indicated in necrotic pulps or vital pulps injured beyond repair. Vital pulps injured beyond repair will eventually progress to necrosis if
left untreated.

Various terminology and classification systems to describe pulpal status have been developed by clinicians over the years. In 2008, the American Association of Endodontists convened a consensus conference on diagnostic terminology in an attempt to standardize the terminology used for the classification of pulp status. Pulp status is categorized into four classifications: normal pulp, reversible pulpitis, irreversible pulpitis and necrotic pulp. Reversible pulpitis is where the pulp is inflamed but the pulp maintains its reparative and healing potential. Irreversible pulpitis is where the pulp is inflamed and the pulp does not have reparative or healing potential. Necrotic pulps can function as a substrate for bacterial growth and lead to localized or systemic infections.

A limitation of this classification system is that the diagnosis of pulp status is subjective and may not be representative of the actual histological state of the pulp. Objective assessment of pulp status would require the removal and histological examination of affected tissue, which is not practical in a clinical setting. Thus, the accurate clinical diagnosis of pulp status may not correspond with the exact histologic condition of the pulp. To cope with this diagnostic dilemma, clinicians and investigators differentiate between pulp status categories on an empirical basis using clinical and radiographic signs correlated with histological signs of pulpal inflammation and infection.

An association between the degree of pulpal inflammation and outcome of vital pulp therapy has been demonstrated in primary molars. The degree of inflammation in the
pulp was measured using an inflammatory mediator (prostaglandin E2) prior to vital pulp therapy. Higher prostaglandin E2 counts correlated positively with unacceptable outcomes of vital pulp therapy.

Clinicians rely on clinical and radiographic interpretation using accepted signs and symptoms that indicate the severity of pulpal inflammation. However, the degree of pulp inflammation that delineates reversible pulpitis from irreversible pulpitis is currently unknown. Clinicians consider inflammation of radicular pulp tissue as irreversible pulpitis despite no evidence to support that this is an accurate measure of the pulps healing capacity. Pulps free of radicular pulpal inflammation contain healthy pulp tissue with the capacity to heal and candidates for vital pulp therapy.

Clinicians assess multiple clinical signs and symptoms and radiographic signs to determine pulp status. Clinical signs and symptoms that clinicians often use to assess pulp status include pain, tooth percussion sensitivity, tooth mobility and/or presence of swelling, sinus tract/fistulae. Radiographic diagnostic signs clinicians tend to use when determining pulp status include presence of widened periodontal ligament (PDL), periapical or furcation radiolucency, external or internal root resorption and/or pulp canal obliteration (PCO).

6.1. Diagnosis of pulp status: accuracy of clinical and radiographic findings
Clinicians are able to correctly predict which primary teeth do not have radicular pulpal inflammation and are candidates for vital pulp therapy based on clinical and radiographic
findings in the majority of cases (81 to 92 percent). A small proportion of primary teeth (8 to 19 percent) considered candidates for vital pulp therapy present with undiagnosed radicular pulp inflammation that may affect treatment outcomes. Clinicians are also able to predict primary teeth that were not candidates for vital pulp therapy based on clinical and radiographic findings in 82 percent of cases.

Koch and Nyborg correlated clinical and radiographic findings with histological pulpal inflammation in 48 carious primary molars. Of the 26 primary molars judged to be candidates for vital pulp therapy based on clinical and radiographic findings, 92 percent of molars demonstrated inflammation confined to the coronal pulp. Of the 22 molars for which vital pulp therapy was contradicted, 82 percent demonstrated inflammation of the radicular pulp. In a similar study, Schroder demonstrated that of 37 primary molars considered candidates for vital pulp therapy based on clinical and radiographic findings, 81 percent demonstrated inflammation confined to the coronal pulp while 19 percent of teeth demonstrated radicular pulp inflammation. Kassa et al. demonstrated, in the absence of clinical or radiographic evidence of irreversible pulpitis or pulp necrosis, only 1 of 78 carious primary molars presented with histological widespread inflammatory changes extending into the radicular pulp.

6.2. Diagnosis of pulp status: dental history

Clinicians routinely use pain history as an indicator of pulp status. Clinicians tend to consider symptoms of severe, persistent, nocturnal or spontaneous pain as indicators of irreversible pulpitis or pulp necrosis while symptoms of mild to moderate or intermittent
pain as indicators of reversible pulpitis. Despite the routine use of pain history in primary teeth as an indicator of pulpal inflammation, there is conflicting and no strong evidence to associate pain history with pulpal inflammation.

In grossly carious primary molars, pain histories from children and their guardians were not reliable predictors of pulpal inflammation.\textsuperscript{31} Grossly carious primary molars with a positive pain history were not associated with differences in pulp innervation, vasculature or leukocyte cell infiltration when compared to grossly carious molars with a negative pain history.

In another investigation, children with a history of persistent pain had significantly more radicular pulp inflammation than children with a dental history of intermittent pain.\textsuperscript{60} Children that presented with persistent pain in carious molars upon histological examination demonstrated radicular pulp inflammation in 64 percent (16 of 25) of molars while children that presented with intermittent molar pain demonstrated radicular inflammation in only 17 percent (4 of 23) of molars.\textsuperscript{60}

Despite existing evidence that pain history does not always demonstrate good correlation to the histopathological condition of the pulp, clinicians still routinely use pain history to aid in determining pulp status. This discrepancy may be related to the complex nature of pain and diagnosis of pulp status and not that an association does not exist.
6.3. Diagnosis of pulp status: clinical findings

Some clinical findings have been correlated to histological pulpal inflammation in carious primary molars. Molars that presented with clinical signs and/or symptoms of pain, sinus tract/fistula, swelling, pathological tooth mobility and/or pulp exposure were assessed histologically.\(^\text{76}\) Of 53 molars assessed, 92 percent demonstrated inflammation or necrosis of the coronal pulp and 76 percent of molars demonstrated inflammation or necrosis of the radicular pulp.

Clinicians routinely consider the presence of swelling, fistulae/sinus tracts, tenderness to tooth percussion and/or pathological tooth mobility as contraindications of vital pulp therapy. Swellings, fistulae or sinus tracts associated with carious primary teeth demonstrate a strong correlation to pulp necrosis and periapical pathoses.\(^\text{77}\) Investigators often consider tenderness to tooth percussion or tooth mobility contraindications of vital pulp therapy despite any strong evidence that these measures are strongly correlated with pulpal inflammation or infection.\(^\text{60,78}\) A strong correlation between the histopathological condition and tenderness to tooth percussion or tooth mobility has not been demonstrated may be because of the multiple pathological processes that can cause tenderness to tooth percussion or tooth mobility. Causes of these clinical findings can include pulpitis, infection, trauma, periodontal disease or normal physiological processes.

Carious pulp exposures in primary molars are associated with pulpal inflammation.\(^\text{78}\) Eighty-four percent of 44 primary molars with carious pulp exposures had inflammation that was confined to the coronal pulp, while 16 percent of molars demonstrated
inflammation of the radicular pulp. Of 35 molars without clinical pulp exposure, 94 percent demonstrated inflammation confined to the coronal pulp. Carious pulp exposure in primary incisors, unlike primary molars, demonstrated more variability in the degree of pulpal inflammation. Of 24 incisors with pulp exposures, histological examination revealed normal pulps in one-third, reversible pulpitis in one-third and irreversible pulpitis/necrosis in one-third of incisors. Of 29 incisors without clinical pulp exposure, 69 percent demonstrated normal pulps, 10 percent demonstrated reversible pulpitis and 21 percent demonstrated irreversible pulpitis/necrosis. The difference in the degree of pulpal inflammation between pulps with and without exposure were statistically significant. Carious pulp exposures are strongly correlated with pulp inflammation, however not the extent of pulpal inflammation. A better indicator of the extent of pulpal inflammation might be to compare the extent or size of the carious pulp exposure to pulpal inflammation and not simply the presence or absence of a pulp exposure. Primary incisors with carious pulp exposure appear to demonstrate a greater variability in histopathological conditions than molars with carious pulp exposures. The histological variability of incisors may be a perceived rather than an actual difference as the investigation did not take into consideration size of the pulp exposures. In addition, the investigation did not account for the lack of anatomical distinction between the coronal and radicular pulp tissue of incisors.

Large carious lesions (>1mm in diameter) are associated with greater pulp inflammation when compared to small carious lesions (<1mm) in diameter. Radicular pulpal inflammation was present in 74 percent (17 of 23) of molars with large sized carious
lesions and only 12 percent (3 of 25) of molars with small sized carious lesions. Primary molars with proximal caries demonstrate greater extent and severity of pulpal inflammation than primary molars with caries confined to the occlusal surface when caries depth are equal to, or greater than, 50 percent of the total dentin thickness. Primary molars with proximal caries and clinically visible marginal ridge breakdown are associated with significantly more extensive coronal pulp inflammation than carious lesions without marginal ridge breakdown. Of molars with caries affecting less than two-thirds of the marginal ridge width, 90 percent of molars demonstrated coronal pulp inflammation while 100 percent of molars with caries affecting greater than two-thirds of the marginal ridge width demonstrated coronal pulp inflammation.

Direct evaluation of pulp tissue can aid in determining a clinical diagnosis of pulp status. Dark (deep red or purple) colored or excessive bleeding from an exposed or amputated pulp is associated with extensive pulpal inflammation in the primary dentition. Primary molars that presented with dark red or purple bleeding demonstrated significantly more pulpal inflammation than molars that presented with light red colored bleeding. Primary molars that presented with dark red or purple bleeding demonstrated radicular inflammation in 71 percent (15 of 21) of molars while molars that presented with light red bleeding upon coronal pulp amputation demonstrated radicular inflammation in 16 percent (4 of 25) of molars. In the same study, molars that were judged to have excessive hemorrhage upon coronal pulp amputation demonstrated significantly more pulpal inflammation than molars that presented with minimal hemorrhage upon coronal pulp amputation. Of 13 molars that presented with excessive
hemorrhage, radicular inflammation was demonstrated in 77 percent of molars. Of 19 molars that presented with minimal hemorrhage, 11 percent demonstrated radicular inflammation. Dark (deep red or purple) colored or excessive bleeding from an exposed or amputated pulp demonstrates a strong correlation with pulpal inflammation.

Prolonged bleeding time following coronal pulp amputation has been considered a sign of radicular pulp inflammation that contraindicates vital pulp therapy. Waterhouse et al. assessed treatment outcomes of vital pulpotomy measured against mean bleeding time following coronal pulp amputation. Bleeding times associated with acceptable clinical and radiographic outcomes compared to bleeding times of those teeth with unacceptable outcomes demonstrated no statistical significant difference. Mean bleeding time in molars with acceptable post-operative clinical and/or radiographic outcomes (n=64) was 6.4 minutes compared with 6.9 minutes for teeth with unacceptable treatment outcomes (n=15). Pulp bleeding time is an unreliable predictor of pulp therapy outcome.

6.4. Diagnosis of pulp status: radiographic findings

Common radiographic signs cited as contraindications to vital pulp therapy in primary teeth include furcation or periapical radiolucencies, external root resorption, internal root resorption or widened PDL as these signs are associated with pulpal inflammation and/or pulp necrosis. Teeth with any of these radiographic features are not appropriate candidates for vital pulp therapy.

Radiographic images of primary teeth that demonstrate furcation and periapical
Radiolucencies are associated with necrotic pulps where an abscess, a granuloma or a cyst has developed secondary to an odontogenic infection. Furcation radiolucencies occur predominantly in primary molars rather than permanent molars because of the porous pulp floor and the presence of numerous accessory canals in the floor of the pulp chamber. Apical radiolucencies are predominantly observed in permanent teeth and primary incisors and canines. External root resorption on radiographic imaging is indicative of pulp necrosis or extensive pulpal inflammation that has spread to adjacent periapical tissues. The appearance of internal root resorption on radiographs is most commonly associated with pulpal inflammation in vital pulps. Though some internal resorption has been shown to arrest or reverse, internal root resorption may represent widespread inflammation that may affect treatment outcomes.

A widened PDL on radiographic exam may be representative of an inflamed or infected PDL secondary to an inflamed or necrotic pulp. In irreversible pulpitis, inflammation of the pulp may involve the entire length of the root(s) and extend into the PDL. Widened PDL on radiographic exam has been demonstrated to be associated with pulpal inflammation. Carious primary molars that presented with the radiographic appearance of a widened PDL demonstrated radicular inflammatory cell infiltration in 86 percent of molars while molars that presented with a radiographic appearance of a normal PDL only demonstrated radicular inflammation in 33 percent of molars.

PCO or calcific metamorphosis on radiographic images results from the formation of tertiary dentin in the root canal produced by the chronic stimulation of odontoblasts and
odontoblasts-like cells. The severity of PCO depends on the degree and duration of the stimulus. PCO can be a physiological process that does not necessitate treatment in the absence of signs or symptoms of infection.82-86

6.5 Diagnosis of pulp status: non-standard tests

Non-standard diagnostic tests in primary teeth include response to sensibility tests, laser Doppler flowmetry, pulse oximetry and selective anesthesia. Pulp sensibility tests assess pulp vitality through stimulation of pulpal sensory neurons and assessment of patient response. Sensibility tests include: heat test, cold test, electric pulp test (EPT) and cavity test. Thermal (hot and cold) and EPT are the most common tests used to assess pulp vitality. These tests are affordable, easy to use and reliable in permanent teeth.39 Abnormal responses include prolonged sensations, immediate severe pain or absence of a response. Petersson et al. compared the hot test, cold test and EPT efficacy for identifying viable nerve tissue in permanent teeth. Hori et al. in a similar study compared the hot test, cold test and EPT efficacy in identifying the presence of vital nerve tissue in primary teeth. Pulpal status was determined by direct inspection of the pulp after access cavity preparation to assess the presence or absence of bleeding. The results of Petersson et al. and Hori et al. are summarized in Table 1.38,39 Sensitivity and specificity results of hot test, cold test and EPT appear similar when identifying vital pulps in the primary and permanent dentition.

There is limited evidence to support the standard use and cost versus benefit of sensibility testing in the primary dentition. Clinicians have historically relied heavily on dental
history, clinical findings and radiographic findings for diagnosis of pulp status in primary teeth without standard use of sensibility testing. One reason is clinicians are already able to predict pulp status, based on clinical and radiographic findings, with relative accuracy (88 percent). The added benefit of sensibility testing may be minimal with the reported sensitivities and specificities reported in Hori et al. The limited use of sensibility testing in the primary dentition is also anecdotally attributed to unreliable responses, additional time requirements, uncooperative behavior in children and/or concern that the tests may provoke apprehension, fear and behavior management concerns. A limitation of sensibility testing is it reflects the presence of conducting nociceptive fibers and not the overall qualitative health of the pulp. Functioning pulpal sensory neural tissue is only one aspect of pulpal health and does not take into account the health of the vasculature and immune components of the pulp. Sensibility testing in primary teeth may be of value when clinical and radiographic assessment is inconclusive.

Pulp vitality can be assessed with the cavity test using mechanical stimulation through cavity preparation. Limitations of this test are loss of tooth structure and, like other sensibility tests, the test does not assess overall pulpal health, only the presence of viable nerve tissue. Laser Doppler flowmetry and pulse oximetry have been used to detect pulpal blood flow. Both tests are not commonly used in clinical practice. Laser Doppler flowmetry is showing promising results in regards to accurate and reliable assessments of pulp status. Pulse oximetry, in contrast, is to date an unreliable test in the assessment of pulp status.
6.6. Diagnosis of pulp status: concerns

Contraindications to vital pulp therapy include history of spontaneous or lingering provoked pain, swelling, fistula/sinus tract, tenderness to percussion and pathological mobility. Radiographic findings repeatedly considered contraindications to vital pulp therapy include periapical or furcation radiolucency, widened PDL space, internal root resorption or external root resorption. These classic signs and symptoms that contraindicate vital pulp therapy may have to be reevaluated in the near future.

New research has demonstrated superior outcomes of calcium enriched-mixture pulpotomy when compared to RCT in permanent teeth with irreversible pulpitis at 2-years post-treatment. Though the results of this study have not been reproduced, the results of the investigation raise the concern that may be the current diagnostic criteria used demarcating reversible and irreversible pulpitis should be reevaluated. Measures such as vascularity or pluripotent potential of stem cells might be better diagnostic indicators of the reparative potential of pulp tissue and should be investigated in the future.

6.7. Summary

The choice of vital pulp therapy technique and outcome of treatment is dependent on the accurate diagnosis of pulp status. Primary teeth presenting with reversible pulpitis or inflammation confined to the coronal pulp are considered candidates for vital pulp therapy. Primary teeth presenting with irreversible pulpitis, pulp necrosis or radicular pulp inflammation are not candidates for vital pulp therapy as widespread inflammation
may negatively affect pulp therapy outcomes.

Clinicians are able to predict which primary teeth are candidates for vital pulp therapy with relative accuracy using a combination of clinical signs and symptoms and radiographic signs. However, there is not always a good correlation between individual clinical signs and symptoms and radiographic signs and the histopathological condition of the pulp.

Clinical findings that may aid in diagnosis of pulp status include location of the carious lesion, presence of pulp exposure, presence of swelling, presence of fistula/sinus tract, tenderness to tooth percussion, tooth mobility, abnormal responses to sensibility tests, degree of pulpal bleeding and color of exposed pulp tissue. Presence of swelling, fistula/sinus tract, excessive hemorrhage upon carious pulp exposure and/or dark red or purple bleeding upon coronal pulp amputation are strongly correlated with radicular pulp inflammation or necrosis. Bleeding time is routinely used in the diagnosis of pulp status, however evidence demonstrates bleeding time is an unreliable indicator of pulpal therapy outcome.

Radiographic signs that contraindicate vital pulp therapy in primary teeth include the presence of furcation or periapical radiolucencies, external root resorption, internal root resorption or widened PDL. PCO can be a pathophysiological process that does not necessitate treatment in the absence of signs or symptoms of infection.
7. Vital pulp therapy

Primary teeth with the diagnosis of reversible pulpitis are candidates for vital pulp therapy. Vital pulp therapy is contraindicated in primary teeth with irreversible pulpitis or necrotic pulps. Outcomes of pulp therapy are influenced by diagnosis, clinical technique, choice of pulp medicament, restoration marginal seal and host immune reaction. Treatment options of vital pulps with reversible pulpitis in primary teeth include: indirect pulp therapy (IPT), direct pulp capping (DPC), pulpotomy, RCT and extraction.

7.1. Indirect pulp therapy

Indirect pulp therapy is a procedure in which carious dentin surrounding the pulp is left in place to avoid an anticipated pulp exposure in reversibly inflamed teeth. In IPT, the carious dentin at the periphery of a carious lesion is removed, a medicated liner is placed over the residual carious dentin and the tooth is restored. Placement of a liner and sealing with a restoration stops the progression of the caries process within the carious lesion. Indirect pulp therapy also relies on the repair and healing potential of a vital pulp to remove existing cariogenic bacteria and stimulate new hard tissue formation adjacent to the carious lesions. Variations in the IPT technique include extent of caries removal, quantity and quality of remaining carious dentin, single versus multiple appointment(s), complete versus partial caries removal and choice of restorative material and liner.

There is currently no consensus with regards to the proportion of caries that should be removed and quality of dentin that should remain for IPT. There is evidence that the
restoration marginal seal is a greater factor in IPT outcomes than the debridement of
caries. In IPT, the substrate or source of nutrition for cariogenic bacteria is eliminated
through sealing of carious dentin. Thus, the number of cariogenic bacteria decrease and a
shift towards a less cariogenic flora occurs.\textsuperscript{93-95} The decrease in cariogenic bacteria and
flora shift eventually leads to the arrest of the caries process.\textsuperscript{96-98} Type of lining material
does not affect IPT outcomes as high rates of acceptable outcomes in IPT have been
demonstrated regardless of liner type used.\textsuperscript{99,100}

Indirect pulp therapy can be performed as a one-step (ultraconservative) approach where
a permanent restoration is placed immediately after IPT or as a two-step (step-wise)
approach where an intermediate restoration is placed after IPT and the tooth is reentered
at a later date for placement of a definitive restoration. Currently, there is no consensus
on the preferred technique. Both one- and two-step procedures have shown favorable
clinical outcomes in retrospective trials.\textsuperscript{99,101-104}

Pulpotomy is the most commonly taught pulp therapy technique for asymptomatic vital
primary molars followed by IPT.\textsuperscript{105} Prospective and retrospective studies have reported
IPT acceptable outcome rates between 73 and 95 percent.\textsuperscript{101-103,106-110} Indirect pulp
therapy is demonstrating promising results in regards to pulp therapy outcomes, however
a limited body of literature exist to support IPT compared to pulpotomy and only 1 weak
low-level study has directly compared IPT and pulpotomy in primary teeth.\textsuperscript{102} The
retrospective study assessed 133 primary molars treated with IPT or formocresol (FC)
pulpotomy. Of 55 IPT treated molars, 93 percent of molars demonstrated acceptable
outcomes over a 5-year period. Of 78 FC pulpotomy treated molars, 74 percent demonstrated acceptable outcomes over a 5-year period. The study demonstrated IPT had superior outcomes to FC pulpotomy however the level of evidence was weak. The study did not standardize restorations and the time frame in which treatment was performed between the 2 groups. A proportion of FC pulpotomy treated molars were restored with Interim Restorative Material (IRM) where the acceptable outcome rate was 39 percent. As well, all pulpotomies were performed between 1970 and 1990 while all IPT treatments occurred after 1990 by predominantly a single practitioner. Based on this investigation, there is inadequate evidence to indicate IPT is superior or even equivalent to FC pulpotomy.

The majority of clinicians prefer pulpotomy to IPT. Reasons why clinicians may prefer pulpotomy to IPT are familiarity, there is a greater body of literature investigating pulpotomy and more clinicians were trained in pulpotomy than IPT. Many clinicians argue that the pulp may be diseased beneath carious lesions where healing and repair of the pulp may not be possible. Evidence suggests deep caries, in particular proximal lesions, may present with extensive inflammation and pulpotomy would ensure the removal of inflamed pulp tissue leaving only vital and uninflamed radicular tissue with the potential for healing and repair.

7.2. Direct pulp capping

Direct pulp capping is the placement of a medicated base in direct contact with carious, traumatic or mechanically exposed pulp tissue. Direct pulp capping in primary teeth has
demonstrated poor outcomes. The most common sequelae of unacceptable treatment outcomes of DPC are abscess and internal root resorption. Calcium hydroxide (Ca(OH)$_2$) is the most common DPC medicament used. A randomized controlled trial reported clinical and radiographic acceptable outcome rates of Ca(OH)$_2$ DPC treated molars were 62 and 53 percent at 24 months post-treatment.

7.3. Pulpotomy

Pulpotomy is the amputation of coronal pulp tissue often followed by the placement of a medicament on the remaining vital radicular pulp tissue. The pulpotomy is the most widely used and taught vital primary pulp therapy technique by pediatric dentists in North America. The pulpotomy is the accepted standard of care for carious exposures of primary molars with reversible pulpitis. However, there is currently no accepted standard of care for primary incisors with reversible pulpitis.

Pulpotomy techniques are categorized broadly into 3 groups: devitalization, preservation and regeneration. Devitalization techniques include FC, gluteraldehyde, electrosurgery and laser pulpotomy. Preservation techniques include ferric sulphate (FS), sodium hypochlorite (NaOCL) and ZOE pulpotomy. Regenerative techniques include Ca(OH)$_2$ and MTA pulpotomy. Regardless of the pulpotomy technique, the radicular pulp should remain asymptomatic without signs or symptoms of pain or infection.

7.4. Formocresol pulpotomy

The FC pulpotomy is the most common technique taught in dental schools and used by
pediatric dentists in North America. The most common formulation of FC is 35 percent cresol, 19 percent formaldehyde and 15 percent glycerin in an aqueous solution. The active ingredients in FC are formaldehyde and cresol. Formaldehyde is a tissue fixative and prevents tissue autolysis through the formation of stable molecular crosslinkings resistant to breakdown. Cresol is antimicrobial, cytotoxic and able to emulsify with formaldehyde. The glycerin in FC acts as a vehicle for the formaldehyde and cresol as well as an emulsifying agent preventing the polymerization of the formaldehyde.

7.4.1. Formocresol pulpotomy technique

The most common FC pulpotomy technique used is coronal pulp amputation followed by hemostasis with pressure using moist cotton and then application of FC on a cotton pellet. The application of FC on the remaining pulp tissue ranges from 1 to 5 minutes. Variations in FC application that ranged between 1 and 5 minutes did not affect clinical or radiographic outcomes. Longer applications of FC were associated with poorer clinical and radiographic outcomes and complete loss of pulp tissue vitality with formation of fibrous granulation tissue. Variations in the FC pulpotomy technique include modifications to the concentration of FC, number of appointments involved in treatment, application time of FC, type of base used and pressure hemostasis with or without the use of a FC dampened cotton pellet.

Full strength FC is the most commonly used form of FC used by pediatric dentists for pulpotomy. The second most commonly used form of FC used by pediatric dentists is a
1:5 dilution of full strength FC. Full strength FC and 1:5 dilution of FC have demonstrated similar clinical, radiographic and histological outcomes.\textsuperscript{134}

7.4.2. Effect of formocresol on pulp histology

Full-strength FC applied to vital pulp tissue for 5 minutes produces 3 distinct histological zones within the pulp. The 3 zones that develop are the zone of fixation (eosinophilic/acidophilic zone), the pale staining zone (an area of poor cellular definition and marked by a reduction in cells and fibers) and the zone of inflammation.\textsuperscript{123,126,127} In general, pulp tissue in contact with FC is devitalized through fixation. The fixative effect diminishes apically as pulp tissue in the apical third is often normal and retains its vitality.\textsuperscript{135}

The most common histopathological finding of FC pulpotomy treated primary molars is chronic inflammation.\textsuperscript{136} However, histological findings in FC pulpotomy treated molars range from normal pulp tissue to complete necrosis of the pulp. The pulp status of 22 primary molars were assessed histologically 3 to 5 years after FC pulpotomy.\textsuperscript{136} All teeth that underwent histological assessment were deemed to have acceptable clinical and radiographic outcomes at the time of extraction. The study demonstrated a wide variation in pulp histology that ranged from normal pulp tissue to complete pulp necrosis. Of the 22 molars assessed, 10 molars presented with chronic inflammation, 7 with normal pulp tissue, 4 with partial necrosis and 1 with complete necrosis. Overall, 95 percent of primary molars treated with FC pulpotomy in this investigation remained vital though chronic inflammation was a common finding.\textsuperscript{128} Despite the range of histological
findings, the majority of FC pulpotomy treated teeth are not associated with pain or infection.

7.4.3. Formocresol pulpotomy outcomes: clinical trials, systematic reviews, and meta-analyses

The clinical outcomes for FC pulpotomy reported have ranged from 87 to 100 percent and the radiographic outcomes have ranged from 56 to 100 percent over follow-up periods from 6 to 74 months (Appendix 1A). FC pulpotomy demonstrates superior clinical and radiographic outcomes compared to Ca(OH)$_2$ and equivalent clinical and radiographic outcomes to FS, laser and electrosurgery.$^{137,138}$ MTA demonstrates superior radiographic outcomes when compared to FC.$^{84,139-145}$ The most common reported pathological radiographic finding of FC pulpotomy was internal root resorption.

7.4.4. Formocresol concerns

Concerns regarding the safety of FC include the allergenic, irritant, mutagenic and carcinogenic potential of formaldehyde. Adverse effects are primarily in the respiratory and digestive tract system through inhalation and ingestion.$^{146}$

Formaldehyde is an irritant and exposure to high concentrations of formaldehyde can cause burning sensations in the eyes, nose and throat. Long-term exposure to moderate formaldehyde concentrations is linked to adverse respiratory symptoms.$^{147}$ Chronic low levels of formaldehyde exposure were associated with irritation of the eyes and mucous membranes and permanent respiratory impairment including signs and symptoms of
chronic obstructive lung disease in both occupational and residential environments.\textsuperscript{148-150} No immune responses or allergic reactions against formaldehyde have been reported.\textsuperscript{151-153}

Formaldehyde is listed as a known human carcinogen by the International Agency for Research on Cancer, Health Canada and The Agency for Toxic Substances and Disease Registry in the United States Department of Health and Human Services. Formaldehyde is listed as a known carcinogen based on sufficient evidence of carcinogenicity from studies in humans and animals and data on biological mechanisms of carcinogenesis.\textsuperscript{154-156} Formaldehyde can react covalently with amino and sulfhydryl groups in DNA and form unstable DNA-protein crosslinks.\textsuperscript{157} The most common types of DNA damage include sister chromatid exchanges, micronuclei and chromosomal aberrations and deletions.\textsuperscript{158,159}

Concerns have been expressed regarding the safety and use of FC in dentistry as systemic spread of formaldehyde after pulpotomy has been reported.\textsuperscript{160} However, evidence indicates FC pulpotomy procedures poses a minimal risk of cancer to children.\textsuperscript{161,162} The plasma concentration of FC was analyzed in 30 children undergoing 85 primary tooth pulpotomies.\textsuperscript{163} Preoperative and post-operative blood samples were taken at 5, 15, 30, 60, 90 and 120 minutes. Formaldehyde was undetectable above baseline physiologic concentration. In another study, lymphocytes were assessed for chromosomal aberrations in 20 children treated with FC pulpotomy.\textsuperscript{161} Two venous blood samples were collected from each child, the first prior to FC pulpotomy (experimental group) and the second 24
hours after pulpotomy (treated group). There was no statistically significant difference between the experimental and treated groups with regards to chromosomal aberrations. However, the results demonstrated FC pulpotomy induced severe chromosomal aberrations in 1 patient. This was concerning to the authors as no cause was found.

Concerns have been expressed regarding the occupational exposure of dental professions to formaldehyde in pediatric dentistry. Exposure of formaldehyde to dental professionals with the regular use of FC pulpotomies has not been investigated. The Canadian Labour Code acceptable occupational exposure limits for formaldehyde are an average of 0.3 parts per million (ppm) over an 8-hour period and 1 ppm over a 15-minute period. The National Institute for Occupational Safety and Health in the United States has stated that formaldehyde may cause acute inhalation toxicity at concentrations of 20 ppm and higher. Discerning the occupational exposure to formaldehyde for dental professionals is difficult and has not been assessed. Exposure to formaldehyde depends on dose and type of FC used, distance from FC and length of exposure. Ambient levels of formaldehyde were measured using an infrared spectrophotometer from FC within a dental clinic. Measurements were taken over a 5-minute period at a distance of 46 cm, to replicate the typical exposure distances for dental professionals, and 3 cm, to assess close contact with FC. The formaldehyde ppm of a saturated no. 3 cotton pellet with Buckley’s FC was 0.4 ppm at 46 cm and 7.56 at 3 cm. The formaldehyde concentration of saturated no. 3 cotton with 1:5 dilution of Buckley’s was 0.14 at 46 cm and 1.52 cm. At the typical exposure distance for dental professionals, dental professionals exposure to formaldehyde are likely within the Canadian Labour Code acceptable occupational exposure limits for formaldehyde. However, without the judicious use of formaldehyde,
dental professionals may be at risk of overexposure to formaldehyde.

7.4.5. Formocresol pulpotomy summary

Formocresol is the most utilized pulpotomy agent in pediatric dentistry in North America, however concerns regarding the mutagenic, carcinogenic and irritant properties of FC have been reported. European clinicians have shifted away from the use of FC in preference for alternative medicaments due to these concerns. Formocresol is an effective pulpotomy agent with reported acceptable clinical outcomes ranging from 87 and 100 percent and acceptable radiographic outcomes ranging from 56 and 100 percent at 6 to 74 months follow-up.

The International Agency for Research on Cancer has recommended the substitution of formaldehyde containing materials for safer alternatives due to the potential mutagenic and carcinogenic properties of formaldehyde in FC. As a result, alternative pulpotomy medicaments to FC are being investigated. No significant differences in clinical and radiographic outcomes were noted between FC when compared to FS, NaOCl, laser and electrosurgery. Formocresol demonstrated superior clinical and radiographic outcomes to Ca(OH)$_2$ and inferior radiographic outcomes when compared to MTA pulpotomy.

7.5. Glutaraldehyde pulpotomy

Glutaraldehyde is an organic compound used to disinfect medical and dental equipment, as it is an effective anti-microbial. Glutaraldehyde is a superior fixative, provides a more stable protein bond, is less penetrating and is faster acting when compared to FC.
Organic impurities in glutaraldehyde vary and their presence can result in unpredictable fixative properties. Buffering of glutaraldehyde improves tissue fixation when compared to unbuffered solutions of glutaraldehyde, however buffered preparations over time become unstable.

Weak evidence has reported glutaraldehyde pulpotomy acceptable clinical outcome rates between 82 and 98 percent and acceptable radiographic outcome rates between 76 and 79 percent 12 to 36 months post-treatment. No strong evidence exists to indicate glutaraldehyde pulpotomy efficacy or equivalency to FC pulpotomy. Glutaraldehyde has not become widely investigated or accepted as a vital pulpotomy medicament because buffered preparations have a limited and unpredictable shelf-life.

7.6. Zinc oxide eugenol pulpotomy

Zinc oxide eugenol is used as a pulpotomy base, root canal filling and intermediate restorative material in the primary dentition. Zinc oxide eugenol is available non-reinforced or reinforced with polymethyl methacrylate. Zinc oxide is a filler with high tensile and compressive strength and eugenol has anodyne and antibacterial properties. The effectiveness of ZOE as base pulpotomy material is attributed to its marginal seal and release of eugenol. The marginal seal of ZOE is comparable to other polycarboxylate and non-eugenol temporary restorative materials. In cases of restoration failure, the eugenol in ZOE may aid in slowing the progression of caries due to its antibacterial properties. Zinc oxide eugenol is not stable in the presence of water and after setting ZOE may release eugenol and minimal amounts of zinc through
hydrolysis. Hydrolysis of the bonds between molecules of eugenol and zinc hydroxide yield free eugenol and insoluble zinc hydroxide.\textsuperscript{179}

Classically, ZOE has been used as a base material for pulpotomies. However, a few studies have assessed ZOE as a pulpotomy base without the use of any other pulpotomy medicament. Clinical and radiographic outcomes of ZOE pulpotomy were demonstrated to be inferior to FC and MTA pulpotomy.\textsuperscript{128,182-184} Severe chronic pulpal inflammation, internal root resorption and abscess are the most common reported cause of unacceptable outcomes in ZOE pulpotomy. Abscess, inflammation and internal root resorption associated with ZOE pulpotomy are speculated to be caused by the release of free eugenol or presence of impurities in ZOE.\textsuperscript{85,97} Eugenol in direct contact with pulp tissue is cytotoxic.\textsuperscript{181} Cellular respiration is depressed in human dental pulp cells and mouse fibroblasts when in contact with eugenol.\textsuperscript{178} Impurities in eugenol are residual compounds from the separation of eugenol from oil of cloves and/or degradation products from aging eugenol.\textsuperscript{185,186} ZOE pulpotomy is not recommended for the treatment of carious primary teeth with reversible pulpitis.

7.7. Ferric sulfate pulpotomy

Ferric sulfate is a hemostatic agent prepared by oxidizing ferrous sulfate with nitric acid in the presence of sulfuric acid. It is used to obtain hemostasis in endodontic surgery, control gingival hemorrhage and as a pulpotomy medicament. Ferric sulfate has a pH of 1. When FS comes into contact with blood, a dark brown or greenish brown coagulum forms.\textsuperscript{187} The precipitation and agglutination of ferric ions and blood proteins
mechanically occludes and seals cut blood vessels aiding in hemostasis. Commercial FS preparations include an aqueous 15.5 percent FS solution (Astringedent™), an aqueous 21 percent FS solution (Stasis™) and a 20 percent FS gel (ViscoStat™).

7.7.1. Effect of ferric sulfate on soft tissues

Prolonged contact of FS with vital soft tissues produced persistent inflammation and a foreign body reaction. The effect of FS on osseous healing was assessed by applying FS to osseous defects in rabbit mandibles. Defects were either filled with a 15.5 percent FS solution until hemostasis was achieved and closed (experimental group) or closed after physiologic clot formation (control group). Histological examination conducted 18 and 46 days after treatment of the defects demonstrated no inflammation in the control group while the FS group demonstrated a foreign body reaction, delayed healing, acute inflammation and abscess formation. However, the investigators did not rinse away excess FS solution, remove the FS coagulum or standardize the volume of FS used. Studies using a similar methodology, except for FS being rinsed away after a 5-minute application in osseous defects, demonstrated no significant differences between healing in the experimental and control groups. Thus, excess FS may delay healing in soft tissue and should be removed after application to soft tissue.

7.7.2. Ferric sulfate pulpotomy outcomes: clinical trials, systematic reviews, and meta-analyses

Reported acceptable clinical outcome rates for FS pulpotomy ranged from 78 to 100 percent at 24 months. Reported acceptable radiographic outcomes for FS pulpotomy in
primary molars ranged from 61 to 100 percent with follow-up times ranging from 6 to 36 months (Appendix 1B). Ferric sulfate pulpotomy demonstrated superior outcomes to Ca(OH)$_2$ and laser pulpotomy and inferior outcomes to MTA pulpotomy, MTA/FS pulpotomy and vital RCT.$^{144,82,83,191,192}$ Ferric sulfate and FC pulpotomy have shown equivalent outcomes.$^{84,137,138,193}$ Survival probability determined from survival analysis ranged from 0.62 to 0.90 at 3 years for FS pulpotomy-treated primary teeth.$^{191,85}$

7.7.3. Ferric sulfate pulpotomy techniques

Two FS pulpotomy procedures have been described in literature. In one technique, 15.5 percent FS aqueous solution is burnished on the radicular pulp stumps after coronal pulp amputation.$^{82}$ After approximately 15 seconds, the FS is rinsed away. If hemostasis is not achieved after the initial application of FS, the tooth is considered to have radicular pulp inflammation and non-vital pulp therapy or extraction is indicated. If hemostasis is achieved, a fortified ZOE mixture is used to seal the pulp chamber. The other FS technique reported in literature is similar to the first technique described except hemostasis is obtained using a cotton pellet with pressure prior to FS application.$^{194}$ The benefit of the first technique described over the second is clinical efficiency.

There have been no reports of preference or direct comparison between the two techniques by clinicians to date. Studies that used the FS technique that did not achieve hemostasis prior to FS application demonstrated radiographic outcomes between 59 to 74 percent with a follow-up ranging from 24 to 36 months and internal root resorption rate between 17 and 55 percent.$^{82,83,191,192}$ Studies that used the FS technique that did achieve
hemostasis prior to FS application demonstrated radiographic outcomes ranging from 73 to 100 percent with a follow-up of 12 to 36 months and an internal root resorption rate ranging from 1 to 11 percent. FS pulpotomies in which hemostasis was achieved prior to FS application, appear to show more acceptable outcomes and less reports of internal root resorption than FS pulpotomies where hemostasis was not achieved prior to FS application. Whether this is a perceived or actual difference in outcomes between the techniques is undetermined and requires further investigation.

7.7.4. Ferric sulfate pulpotomy and internal root resorption

Internal root resorption has been reported as the most common pathological finding in FS pulpotomy outcome studies. The reported prevalence of internal root resorption of FS pulpotomy has ranged from 5 to 55 percent (Appendix 1B). Reported internal root resorption in primary teeth treated with FC pulpotomy has ranged from 4 to 17 percent.

Three hypotheses for internal root resorption reported in FS pulpotomies have been advanced. One hypothesis is that application of FS may prevent the accurate diagnosis of the inflammatory state of the radicular pulp. As FS can cause the immediate hemostasis of the cut radicular pulp stumps, the characteristics (e.g. color and extent) of the bleeding might not be accurately assessed. However the ability to clinically assess pulpal bleeding characteristics in FS pulpotomy is similar to other pulpotomy techniques such as FC pulpotomy. The only characteristic that can not be assessed in a similar manner is bleeding time which is an unreliable measure of pulp therapy outcome. A second
A hypothesis as to the cause of internal root resorption in FS pulpotomy treated teeth is ZOE in direct contact with the radicular pulp causes inflammation that results in internal root resorption. The direct contact of ZOE with radicular pulp can cause a chronic inflammation that is postulated to lead to internal root resorption. Vital pulp tissue in direct contact with ZOE and eugenol has been associated with moderate to severe inflammatory responses. A third hypothesis for the increased rate of internal root resorption in FS pulpotomies is ferric ions and ferric-blood coagulum results in inflammation and causes internal root resorption.

Perforation of the root from internal root resorption can induce an inflammatory response in the PDL and the surrounding bone and produce an unacceptable outcome. Some instances of internal root resorption in FS pulpotomy were shown to be self-limiting or remain asymptomatic and did not interfere with normal exfoliation. A prospective clinical trial reported areas of internal resorption in FS pulpotomy treated primary molars that remained unchanged over 34 months via radiographic follow-up. However, a randomized controlled study demonstrated molars exhibiting internal root resorption on post-treatment radiographic examination were significantly more likely to have an unacceptable radiographic outcome ($P<.0001; OR:9.90$). Though internal root resorption has the potential to arrest and not interfere with exfoliation, there is good evidence to demonstrate internal root resorption is associated with unacceptable pulp therapy outcomes.
7.8. Sodium hypochlorite pulpotomy

Sodium hypochlorite is used as an endodontic irrigant in RCT. NaOCl aids in removing coagulum, controlling hemorrhage, removing dentin chips and formation of dentin bridged. A randomized controlled trial compared the clinical and radiographic outcomes of 3 percent NaOCl and a 1:5 dilution of Buckley’s FC in primary molars of healthy children. Both groups demonstrated 100 percent acceptable clinical outcomes at 12-months. Radiographic outcomes at 12-months demonstrated 80 percent (12 of 15) of NaOCl and 90 percent (9 of 10) of FC pulpotomy treated molars had acceptable outcomes. No significant differences in clinical or radiographic outcomes were demonstrated between NaOCL and FC at 12-months. Another randomized controlled trial compared the clinical and radiographic outcomes of NaOCL, FC, FS and MTA pulpotomy. No statistically significant differences in radiographic outcomes were found among all the groups at 24 months of follow-up. However, both studies suffered from large sample wastage over the follow-up period. Sodium hypochlorite pulpotomy should not be considered an alternative to FC or FS pulpotomy.

7.9. Calcium hydroxide pulpotomy

Calcium hydroxide is a crystalline, highly alkaline and soluble basic salt. Though frequently used in the permanent dentition, use of Ca(OH)₂ in the primary dentition has been controversial. Calcium hydroxide pulpotomy has frequently been associated with the development of abscesses, chronic pulpal inflammation and internal root resorption.
The clinical and radiographic outcomes of Ca(OH)$_2$, FS and Er:YAG laser pulpotomy were compared to FC pulpotomy over a 3-year follow-up period.\textsuperscript{137} Calcium hydroxide pulpotomy was 3 times more likely to have an unacceptable outcome than FC pulpotomy ($P=.07$; Wald chi square test). Formocresol and Ca(OH)$_2$ pulpotomy were compared in a similar study.\textsuperscript{138} Clinically acceptable outcomes after 24-months were reported in 96 percent of FC and 87 percent of Ca(OH)$_2$ pulpotomy treated molars. Radiographically acceptable outcomes after 24-months were 87 percent in the FC group and 53 percent in the Ca(OH)$_2$ group. Calcium hydroxide demonstrated inferior combined clinical and radiographic outcome rates when compared to FC pulpotomy treated molars ($P<.05$, Wald chi-square). A meta-analysis comparing MTA and Ca(OH)$_2$ concluded MTA demonstrated superior clinical and radiographic outcomes to Ca(OH)$_2$.\textsuperscript{144} A statistically significant difference was found between MTA and Ca(OH)$_2$ outcomes with a relative risk of 0.19 at 12-months and 0.38 at 24-months post-treatment.

The preponderance of evidence has demonstrated Ca(OH)$_2$ pulpotomy outcomes are inferior to FC and MTA.\textsuperscript{137,138,201-203} Calcium hydroxide is not recommended for use as a pulpotomy medicament in vital primary teeth.

\textbf{7.10. Vital root canal therapy in primary teeth}

Vital RCT is the removal of coronal and radicular pulp tissue followed by obturation of the root canal system.\textsuperscript{204} Unlike in the permanent dentition, shaping of the canals is not performed. Common irrigation solutions include sterile water, NaOCl, hydrogen peroxide or saline.\textsuperscript{205-212}
The ideal root canal filling material would be antimicrobial, easy to manipulate, easily removed if necessary, resorbable at the same rate as the primary tooth root, biologically safe, cost effective, radiopaque, adhesive to root canal walls, non-shrinking, non-soluble and nontoxic to periapical tissues and undisturbing to the development and eruption of succedaneous teeth. A variety of materials are used as obturation agents in primary teeth. Among the most common are: ZOE, ZOE with FC, Ca(OH)$_2$, Kri paste, Endolase and Vitapex. Zinc oxide eugenol is the most common obturation material used in RCT for primary teeth.

### 7.10.1. Vital primary root canal therapy outcomes: clinical trials, systematic reviews, and meta-analyses

Evidence has reported acceptable clinical outcomes of vital RCT ranging between 96 to 100 and acceptable radiographic outcomes ranging between and 59 to 91 percent at 6- to 24-months follow-up (Appendix 1C). Vital RCT was reported to have comparable outcomes to FC and FS pulpotomy. Though evidence has demonstrated equivalent outcomes for vital RCT and FC pulpotomy in primary teeth, the technique has not been widely accepted for the treatment of primary molars as it is more technically challenging than pulpotomy and may require additional time to complete.

An association between RCT outcomes and degree of root fill in primary teeth has been demonstrated. Primary teeth with canals that are overfilled have poorer outcomes than teeth with canals filled to the apex or underfilled. The outcomes of RCT primary teeth with canals underfilled, filled to the radiographic apex and
overfilled were compared. Acceptable outcome rates were reported in 87 percent (32 of 37) of underfilled canals, 89 percent (16 of 18) of canals filled to the radiographic apex and 58 percent (15 of 26) if overfilled canals. Overfilled canals demonstrated significantly poorer outcomes than primary teeth that were underfilled or filled to the radiographic apex ($P=.011$). The sample included both vital and non-vital primary teeth. Another study showed incisors with gross overfill of the pulp canal with ZOE demonstrated statistically significant more unfavorable outcomes than slightly overfilled, underfilled and filled to the radiographic apex in primary incisors ($P<.001$).\textsuperscript{222} Obturation material extrusion beyond the apex should be avoided.

A variety of obturation techniques have been developed for primary teeth. Methods of obturation include: pressure syringes, premixed syringes, lentulo spirals and endodontic pluggers. Previous in vitro and in vivo studies of obturation methods in primary teeth showed that the lentulo spiral performed equivalent to or better than other techniques.\textsuperscript{210,213,220,223-226}

### 7.10.2. Ectopic eruption of succedaneous teeth following primary root canal therapy

Retrospective studies have demonstrated an association between ZOE RCT and the delayed exfoliation of the treated primary teeth, retention of obturation material prior and after the exfoliation of primary teeth and ectopic eruption of succedaneous teeth\textsuperscript{205-207,214,217} Retained ZOE particles have been observed in gingiva and alveolar bone, however infections associated with retained ZOE have not been reported.\textsuperscript{205,207,214} Zinc oxide eugenol obturation paste was retained in the gingiva in 73 percent (11 of 15) of
subjects after exfoliation of RCT treated primary incisors.\textsuperscript{207}

Incomplete resorption of ZOE is implicated in the deflection of erupting succedaneous teeth. The reported prevalence of anterior crossbite in the early mixed dentition is 8 percent. However, the reported incidence of succedaneous teeth erupting into anterior crossbite following primary incisor ZOE RCT is 20 percent.\textsuperscript{214,227} Thirty percent (24 of 81) of primary teeth treated with RCT are reported to require extraction because of delayed exfoliation and over-retention. Retained ZOE may be related to non-resorbing reinforcing agents in ZOE, such as silica.

There is limited evidence in the area of delayed exfoliation of primary teeth, retention of obturation material prior and after the exfoliation of primary teeth and ectopic eruption of succedaneous teeth. The studies are retrospective in nature with a small sample size. Based on available evidence, RCT therapy may be associated with retention of ZOE filling materials after the exfoliation of treated primary teeth and ectopic eruption of succedaneous teeth.

\textbf{7.11. Mineral trioxide aggregate pulpotomy}

Mineral trioxide aggregate is a hydraulic silicate cement introduced by Torabinejad in 1993 and patented in 1995 as a root-end filling material.\textsuperscript{228} Since its introduction, MTA has been used for pulp capping, pulpotomy, apical barrier formation in teeth with open apices, repair of root perforations and root canal fillings.\textsuperscript{229} Reported uses of MTA in the primary dentition have included use as a DPC, IPT and pulpotomy medicament.
The composition of MTA powder varies among commercial products available, however MTA powder is essentially a refined Portland cement (PC) with the addition of bismuth oxide, a radiopacifier. The principal constituents in MTA are tricalcium silicate and dicalcium silicate. Mineral trioxide aggregate powder may also contain varying smaller amounts of tricalcium aluminate, tricalcium oxide, silicate oxide, gypsum and bismuth oxide with the proportion of constituents varying among commercial products.\textsuperscript{229} Mineral trioxide aggregate is commercially available in several forms. Commercially available MTA products, at the time of writing, are listed in Table 2.

Clinkers are irregular lumps produced by sintering various minerals during the cement kiln stage. Mineral trioxide aggregate powder is formed from clinkers made of various raw minerals including lime, silica, aluminum oxide and ferric oxide. The constituents and their proportions may vary based on raw materials and clinker process used to form the MTA powder. Though chemical compositions and setting times may vary between types of MTA, the majority of physical and chemical properties between the various forms are not significantly different.\textsuperscript{229} MTA Bio is an MTA-based material that is fully synthesized in laboratory. According to the manufacturer, the goal of this new formulation is to avoid the presence of arsenic, which is detected in other MTA-based materials and PC.

\subsection{Mineral trioxide aggregate chemical properties}

The addition of water to MTA powder results in a colloidal gel that solidifies to a hard structure within 14 minutes to 2 hours and 40 minutes depending on the type of MTA.\textsuperscript{229}
A unique advantage of MTA compared to other traditional materials such as composite or glass ionomer is that the setting of MTA is not adversely affected by the presence of water. However, the presence of blood or serum during setting of MTA can alter the physical and chemical properties of MTA. The surface of MTA, when set in water, shows a crystalline structure while the surface of MTA set in fetal bovine serum (FBS), saliva or fresh blood demonstrates the absence of a crystalline structure.\textsuperscript{230,231} Proteins in saliva and/or blood may prevent the complete hydration and setting of MTA. In vitro, blood and serum interfered with the setting of MTA, whether this finding is clinically significant is undetermined at this time. When preparing and using MTA, blood and saliva contamination should be minimized as contamination could compromise the chemical and physical properties of MTA.

Mineral trioxide aggregate when placed adjacent to dentin forms hydroxyapatite. When MTA powder is mixed with water, calcium and Ca(OH)\textsubscript{2} are formed. Hydroxyapatite forms from Ca(OH)\textsubscript{2} and calcium released from MTA and phosphate and hydroxyl ions from body fluids.\textsuperscript{232-234} The morphology of the hydroxyapatite at the dentin-MTA interfaces will vary depending on the pH and calcium/phosphate ratio.\textsuperscript{235}

MTA powder exposed to moisture can compromise the chemical set of MTA when mixed at a later time. Therefore, once a sachet of MTA powder is opened, the unused powder can be used up to 4 weeks later, provided it is stored in a water and airtight container.\textsuperscript{236}
7.11.2. Mineral trioxide aggregate physical properties

Physicals properties of MTA investigated have included solubility, particle size, pH, seal and expansion.\textsuperscript{229} The majority of evidence reports low or no solubility for MTA.\textsuperscript{228,237-239} Higher water-to-powder ratios increases MTA solubility and porosity. Excess condensation pressure and/or dry storage conditions decrease the compressive strength of MTA.\textsuperscript{240-242} Greater condensation pressure results in fewer voids and microchannels reducing water uptake that hinders MTA setting.\textsuperscript{242} Dry storage conditions delay the complete set of MTA.\textsuperscript{240}

Set MTA particle sizes range from 1 to 10 µm\textsuperscript{243} whereas MTA powder particles prior to mixing with water range from 1 to 30 µm.\textsuperscript{244} Some MTA particles are as small or smaller than the diameter of dentinal tubules (\textasciitilde1.5 µm). The size of MTA particles may aid in the sealing ability of MTA.\textsuperscript{245} This hypothesis may not be clinically relevant as dentinal tubules after root canal preparation are not open unless the smear layer is removed. Mineral trioxide aggregate is alkaline and the pH of MTA rises from 10.5 to 12.5 approximately 3 hours after mixing.\textsuperscript{246} This pH rise is due to the formation of Ca(OH)\textsubscript{2} during the hydration process. The pH of MTA declines overtime but has been demonstrated to maintain an alkaline pH value throughout a 78 day observation period.\textsuperscript{247}

Dye leakage, bacterial leakage and fluid infiltration studies have shown that MTA has a better seal and less microleakage when compared to traditional materials such as amalgam, GI cement and ZOE.\textsuperscript{248} The sealing ability of MTA is speculated to be attributed to the formation of hydroxyapatite precipitates at the MTA-dentin interface.
leading to a chemical bond between MTA and dentin. These hydroxyapatite precipitates at the MTA-dentin interfacial space extend into the dentinal tubules and form tag-like structures. These tag-like structures are speculated to be the result of calcium ions released from MTA that diffused through dentinal tubules and react with phosphate ions in the tissue fluid eventually yielding hydroxyapatite. MTA also undergoes slight expansion upon setting, which may contribute to its sealing ability.

7.11.3. Mineral trioxide aggregate antimicrobial properties

Mineral trioxide aggregate may be considered to have an indirect antimicrobial effect because of its sealing properties and resultant limited microleakage. However, MTA may have limited benefit as a direct antimicrobial despite its alkaline pH. Mineral trioxide aggregate demonstrates no antimicrobial activity against anaerobes, which predominate the majority of flora found in root canals, but did have some effect on some facultative bacteria.

7.11.4. Effect of mineral trioxide aggregate on soft tissues

Subcutaneous tissue response to MTA is characterized by mild to moderate inflammation that resolves within 30 days. In a rat study, investigators assessed the histological response of subcutaneous tissue to MTA, Ergeo CPM, another form of commercially available MTA, and a control group where only a polyethylene tube was implanted. Mild chronic inflammation was observed in the MTA and CPM groups after 7 and 14 days. At day 30, no difference was found between all groups as all groups presented with a similar mature fibro-collagen tissue and minimal inflammation.
7.11.5. Mineral trioxide aggregate hard tissue formation properties

Mineral trioxide aggregate induces and conduces dentin, bone and cementum formation. It is associated with the up-regulation of various types of cytokines and biologic markers associated with proliferation and differentiation of progenitor cells, odontoblastic activity, matrix formation and mineralization. MTA releases Ca(OH)$_2$ and calcium that stimulates the proliferation of human dental pulp cells and is speculated to trigger the differentiation of odontoblast-like cells in the dental pulp, resulting in production of mineralized tissue. Calcium and Ca(OH)$_2$ also interact with phosphate-containing fluids to form apatite precipitates.

The ability of MTA to induce reparative dentinogenesis or dentin bridge formation has been demonstrated in animal and human studies in which DPC or pulpotomy was performed on mechanically or cariously exposed pulps. As a pulp capping agent, MTA demonstrated greater dentin bridge formation and less porous dentin bridges when compared to Ca(OH)$_2$ in histological studies. Results may be explained by the superior seal, lower solubility, ability to stimulate more signaling molecules and greater release of calcium ions of MTA when compared to Ca(OH)$_2$.

The association between MTA and dentinogenesis may be predominantly related to the release of calcium by MTA. MTA releases significantly more calcium ions than Ca(OH)$_2$. When a similar amount of calcium (0.3 mmol/L) released by MTA was added to dental pulp cells, in the absence of MTA, cellular proliferation activity was similar to that observed with MTA. The study concluded that the continuous release of
calcium ions from MTA was associated with proliferation of human dental pulp cells.\textsuperscript{263}

\subsection*{7.11.6. Mineral trioxide aggregate properties to adjacent restorative materials}

An in vitro study demonstrated that partially set MTA continues to set to completion when GI cement is placed over MTA.\textsuperscript{279,280} The setting of MTA and GI cement are unaffected by the presence of the one another and the GI cement demonstrates no signs of dehydration.\textsuperscript{279} Composite resin restorations do not affect the setting of MTA when placed adjacent.\textsuperscript{280} However, compressive strength of MTA is significantly decreased when MTA is etched with 37 percent phosphoric acid within 4 hours of mixing versus 96 hours after mixing.\textsuperscript{281} When placing acid-etch composites adjacent to MTA within 96 hours of mixing, acid etching of MTA should be minimized as etching could compromise the chemical and physical properties of MTA. An intermediate layer of GI cement can be placed to prevent contact between the MTA and acid-etch.

\subsection*{7.11.7. Mineral trioxide aggregate concerns}

The carcinogenic and mutagenic potential of MTA was assessed in multiple studies.\textsuperscript{248} MTA is a non-carcinogenic and non-mutagenic material.\textsuperscript{248} The Ames mutagenicity test demonstrated that MTA is not mutagenic.

The cytotoxicity of MTA was assessed by measuring various cellular parameters (e.g. proliferation and viability) of different cells in direct or indirect contact with MTA. The cytotoxicity of set MTA, when compared to other common restorative materials, is less than amalgam, Super EBA and IRM. Cells in contact with set MTA showed higher
viability and proliferative activity than amalgam, Super EBA and IRM.\textsuperscript{282} However, MTA in a freshly mixed state demonstrates a higher cytotoxicity than amalgam, Super EBA and IRM.\textsuperscript{283}

The presence of heavy metal contaminants in MTA is a concern. These heavy metals include chromium, lead and, in particular, arsenic. Arsenic is a natural component of the earth’s crust and is widely distributed throughout the environment including in the air, water and land. Humans are exposed to elevated levels of inorganic arsenic through drinking contaminated water, using contaminated water in food preparation and irrigation of food crops, industrial processes, eating contaminated food and smoking tobacco. Fish, shellfish, meat, poultry, dairy products and cereals can also be dietary sources of arsenic, although exposure from these foods is generally much lower than exposure through contaminated groundwater.\textsuperscript{284}

The International Agency for Research on Cancer (IARC) has classified arsenic and arsenic compounds as carcinogenic to humans.\textsuperscript{285} A review of the latest scientific evidence conducted in 2010 by the Joint Food and Agriculture Organization of the United Nations (FAO) and World Health Organization Expert Committee on Food Additives (JECFA) determined the lower limit/benchmark dose for a 0.5 percent increased incidence of lung cancer (BMDL0.5) from epidemiological data was 3.0 $\mu$g/kg body weight per day (2 to 7 $\mu$g/kg body weight per day based on the range of estimated total dietary exposure). The current recommended limit of arsenic in drinking-water is 10 $\mu$g/litre.\textsuperscript{286}
The amount of arsenic ion released in ProRoot MTA and Angelus MTA were compared and both materials release similar amounts of arsenic at values that were not harmful to the human body and well below the tolerable arsenic levels found in drinking water.\textsuperscript{287} Mineral trioxide aggregate has been approved by the U.S. Food and Drug Administration (FDA) since 1998.\textsuperscript{288}

The clinical use of ProRoot MTA is safe in terms of its heavy metal contents.\textsuperscript{289,290} One gram of ProRoot MTA and Tooth-colored ProRoot MTA contains minimal amounts of arsenic, approximately 0.003 µg and 0.002 µg. MTA is a hardened bound material with low solubility therefore minimal heavy metal ions are released from the cement.

### 7.11.8. Mineral trioxide aggregate discoloration

According to the manufacturer and various clinical reports, a gray color change of ProRoot MTA is to be expected.\textsuperscript{291} Discolored MTA may cause teeth to change in color or show through restorations and effect esthetics. Manufacturer’s instructions recommend that MTA materials should not be used in visible areas (e.g. above crestal bone level). Case reports have described coronal tooth discoloration associated with Tooth-colored ProRoot MTA\textsuperscript{292,293} although a single case report demonstrated discoloration was reversible with removal of MTA and bleaching.\textsuperscript{294} The cause and mechanism of MTA discoloration is currently unknown. Speculations to the cause of discoloration of Tooth-colored ProRoot MTA include the presence of iron, contamination of MTA with blood and formation of black metallic bismuth under light irradiation.
The presence of iron in ProRoot MTA is speculated to cause the gray discoloration of MTA. Due to the concern of discoloration of ProRoot MTA, Tooth-colored ProRoot MTA was introduced where the iron content was substantially less than ProRoot MTA.\textsuperscript{291,295} However, Tooth-colored ProRoot MTA also demonstrates gray discoloration in both in vivo and in vitro studies.\textsuperscript{296-298}

MTA discoloration could also be attributed to the interaction between red blood cells and setting MTA. The mechanism of MTA discoloration is hypothesized to be similar to the discoloration of traumatized teeth where the hemolysis of erythrocytes and the accumulation of hemoglobin and hematin molecules get embedded in dentin tubules. The slow setting process of MTA may permit the absorption and subsequent hemolysis of erythrocytes from the adjacent pulp tissue thus resulting in MTA discoloration. However, MTA discoloration occurs in the absence of blood.\textsuperscript{298,299} The presence of red blood cells exacerbates the discoloration of MTA.\textsuperscript{300} An in vitro study demonstrated the presence of blood within the root canal adjacent to setting MTA exacerbated the discoloration of MTA when compared to the setting MTA in the absence of blood ($P=.03$). The mechanism by which blood exacerbates MTA discoloration is currently unknown.

Watts et al., while assessing the effects of pH and mixing agents on setting of MTA in vitro, found that all MTA specimens (regardless of mixing agent, pH, or time) turned gray after 3 days (Figure 4).\textsuperscript{298} Portions of MTA exposed to phosphate buffered saline (PBS) remained light in color. All MTA specimens that discolored were placed into PBS
solution and MTA specimens displayed fading of the discoloration throughout the 28-day trial on the exterior portion of the MTA specimens. The internal portions of the specimens upon fracture remained dark. The study indicated that discoloration decreased when MTA was exposed to anaerobic PBS environment.

Valles et al. conducted a pilot study in which Tooth-colored ProRoot MTA was sealed in test tubes and half were saturated with pure oxygen while the other half was saturated with pure nitrogen to simulate an oxygen-free environment. The surface color of the oxygen-saturated samples changed from white to gray after exposure to curing light irradiation, however, the color of the nitrogen-saturated samples remained stable.

Valles et al. evaluated the color stability of MTA after irradiation with 3 different curing lights and with a fluorescent lamp in an oxygen-free environment. Thirty samples of MTA were divided into 4 experimental groups (Optilux curing light, Bluephase curing light, Demi curing light and fluorescent lamp) and 1 negative control group where the sample was exposed to no light. The samples in the curing light groups were immersed in glycerine to facilitate an oxygen-free environment. All the groups eventually demonstrated discoloration except for the negative control group at all time intervals ($P>$0.05) (Figure 5). No differences were observed between the fluorescent lamp and the negative control group at day 1. However, after 5 days, the fluorescent lamp group also displayed darkening of the sample surface similar to the other 3 experimental groups.

MTA contains 20 percent bismuth oxide and is added to MTA to enable its differentiation
from adjacent structures on radiographs. The investigators speculated discoloration of MTA is secondarily caused by the formation of metallic bismuth under light irradiation. Bismuth oxide undergoes a thermal dissociation under high temperature resulting in metallic black bismuth and oxygen. The reduced black crystals of bismuth could be responsible for the darkening of MTA. The presence of these black crystals were identified on X-ray diffraction in discolored MTA. Bismuth oxide can be excited by heat or light and turn bismuth oxide dark in an oxygen-free environment. However, bismuth oxide remains stable when heated or irradiated in the presence of oxygen. Oxygen is speculated to inhibit the formation of metallic bismuth however the exact mechanism is unknown. One explanation may be the partial pressure of oxygen at high temperature prevents formation of metallic bismuth. Another possible explanation is oxygen absorbs the energy from light instead of the bismuth oxide or the bismuth oxide once excited reacts with oxygen instead of remaining in its reduced black state. Either way, oxygen appears to act as a quencher that quickly deactivates the excited state of bismuth oxide, preventing a light-induced discoloration of MTA.

In a follow-up study, the authors assessed the influence of light irradiation and oxygen on the color stability of Tooth-colored ProRoot MTA, MTA Angelus White, white PC, PC with the addition of bismuth oxide and Biodentine. Biodentine is a calcium silicate-based material with similar properties to MTA composed mainly of tricalcium silicate, calcium carbonate, zirconium oxide and calcium chloride. Each material was exposed to various light conditions and an oxygen and oxygen-free environment. A spectrophotometer was used to determine the color of each specimen at 0 seconds, 120
seconds and 5 days. All materials with bismuth oxide (Tooth-colored ProRoot MTA, MTA Angelus White and PC with the addition of bismuth oxide) demonstrated dark discoloration after light irradiation in an oxygen-free environment when compared to Biodentine and PC \((P<.05, \text{ANOVA})\). Groups exposed to no light or to an atmospheric oxygen environment demonstrated color stability. PC and Biodentine maintained color stability in all conditions over time and showed no significant differences in color when compared to one another \((P>.05)\). This study demonstrated in an oxygen-free environment, irradiation with a light cure or fluorescent lamp and the presence of bismuth oxide altered calcium silicate based materials leading to color changes.

The mechanism of MTA discoloration is still not fully understood, but recent evidence suggests tooth discoloration is associated with metallic black bismuth oxide formed from the reaction of bismuth oxide with light in a non-oxygenated environment. Discoloration of MTA may not be a concern in the future as manufactures are distributing MTA where zirconium oxide has replaced bismuth oxide as a radiopacifier. Also, alternative materials are being manufactured and distributed (e.g. BioDentine and PC) that have similar properties to MTA and are color-stable.

**7.11.9. Mineral trioxide aggregate pulpotomy techniques**

Two MTA pulpotomy techniques have been described in literature. The technique most reported on is coronal pulp amputation, followed by pressure with a cotton pellet to obtain hemostasis and finally placement of MTA over the radicular pulp stumps. The cotton pellet is placed with pressure between 1 and 5 minutes until hemostasis is
achieved.

To improve clinical and time efficiency, Doyle et al., described an alternative technique in which FS was applied for 10 to 15 seconds after coronal pulp amputation to achieve hemostasis prior to the placement of MTA. The application of FS allows for hemostasis to be achieved within 10 to 15 seconds and was adapted from FS pulpotomy techniques previously described in the literature. Ferric sulfate application prior to MTA placement did not alter clinical or radiographic outcomes for MTA primary molar pulpotomies ($P > .05$).

7.11.10. Mineral trioxide aggregate pulpotomy outcomes: clinical trials, systematic reviews and meta-analyses

The clinical acceptable outcomes for MTA pulpotomy reported have ranged from 97 to 100 and radiographic acceptable outcomes for MTA pulpotomy have ranged from 67 to 100 percent over follow-up periods between 6- to 74-months (Appendix 1D). MTA pulpotomy demonstrates superior radiographic outcomes when compared to FC, FS, Ca(OH)$_2$, laser and ZOE pulpotomy. The most common radiographic finding associated with the MTA pulpotomy was PCO.

Lin et al., in a systematic review and meta-analysis, compared clinical and radiographic outcomes of different pulpotomy medicaments in primary molars. Thirty-seven studies were included in the systematic review and 22 in the meta-analysis. The study concluded MTA pulpotomy demonstrated superior radiographic outcomes to FC and FS
pulpotomy at 18 to 24 months. MTA pulpotomy also demonstrated clinical and radiographic outcomes superior to Ca(OH)$_2$ and laser pulpotomy. Shirvani et al. compared MTA and FC pulpotomy in a systematic review and meta-analysis. The results demonstrated MTA outcomes were superior to FC outcomes in primary molar pulpotomy. The relative risks of an unacceptable outcomes in FC pulpotomy was 2.7 times at 12 months and 2.4 times at 24 months when compared to MTA pulpotomy. Anthonappa et al. in a systematic review evaluated the current evidence to support the long-term effectiveness of MTA as a pulpotomy medicament in primary molars. The study concluded that there was no evidence that MTA pulpotomy was superior to FC pulpotomy due to low-quality evidence. A weakness of the study was the use of a ‘modified standard assessment criteria’ scale developed from Curzon & Toumba. This scale has not been subjected to validity and reliability testing and was initially devised to assess restorations in primary teeth. Without the use of an appropriate quality scale, the results and conclusion of the study may be biased and not representative of the existing evidence.

7.11.11. Mineral trioxide aggregate and portland cement

Mineral trioxide aggregate is a refined form of PC. The most common use of PC is the production of concrete. Portland cement and MTA have similar major constituents. Clinical and radiographic outcomes of MTA and PC pulpotomy in primary teeth were demonstrated to be similar in a single weak randomized control trial with a small sample. Despite the similarities between PC and MTA, PC has not been used routinely in humans. Concerns include its heavy metal contents, lack of a radio-opacifier,
comparatively larger setting expansion, relatively high solubility increasing the release of heavy metals in some forms and lack of Health Canada and US federal approval for clinical use.\textsuperscript{254,287,311-313} Portland cement is manufactured worldwide and controlling the quality, composition and biocompatibility of various forms of PC would be a significant challenge.\textsuperscript{314}

7.11.12. Summary of mineral trioxide aggregate review

MTA pulpotomy has demonstrated superior radiographic outcomes compared to the FC, FS, laser, Ca(OH)\textsubscript{2} and ZOE pulpotomy. MTA has low solubility, good seal and induces hard tissue formation. Drawbacks of MTA include its discoloration of treated teeth and short-term storage capacity once exposed to moisture.

8. Outcome assessment of vital pulp therapy in primary teeth

Multiple opinions regarding criteria for acceptable and unacceptable vital pulp therapy outcomes have been reported and debated in literature. Clinicians agree that clinical signs or symptoms of persistent or spontaneous pain, soft tissue swelling, fistula/sinus tract, tenderness to percussion or pathological tooth mobility are considered an unacceptable outcome of vital pulp therapy. There is also consensus among authors that radiographic signs of furcation or periapical radiolucencies or external root resorption are unfavorable outcomes of vital pulp. However, clinicians have disputed whether or not widened PDL, mobility, PCO and internal root resorption should be considered unacceptable outcomes of vital pulp therapy.
Outcome assessment based on widened PDL or mobility has not been reliable. A widened PDL on radiographic exam may be representative of inflammation or infection associated with irreversible pulpitis and necrotic pulps. However, trauma may also cause inflammation and widening of the PDL. Also, accurate assessment of a widened PDL on a radiograph may not be reliable as it is dependent on subjective assessment by a clinician, radiographic technique and patient cooperation. A randomized controlled trial demonstrated widened PDL was not associated with unacceptable outcomes in molars treated with vital pulp therapy ($P=.99; \text{OR}:1.01$). Mobility in primary teeth can be representative of a dental abscess or pathological root resorption, however assessment of mobility in primary teeth by clinicians can be subjective even with the use of scales. As well, mobility can be associated with a number of causes such as trauma, infection, pathological root resorption and physiological root resorption.

Investigators have disputed whether or not the presence of internal root resorption is an unacceptable treatment outcome. Some authors have considered internal root resorption an unacceptable outcome of pulp therapy only if the internal root resorption is progressive and/or perforation of the root canal system occurs.$^{131,198,315,316}$ A randomized controlled trial demonstrated molars exhibiting internal root resorption on post-treatment radiographic examination were significantly more likely to have an unfavorable radiographic outcome ($P<.0001; \text{OR}:9.90$).$^{83}$ Though internal root resorption has been associated with unacceptable outcomes, internal root resorption has not been designated an unacceptable outcome or failure in multiple studies.$^{82,83,85,191,192,203,316-318}$ Clinicians often monitor internal root resorption in the absence of signs and/or symptoms of
infection as primary teeth with internal root resorption may remain quiescent until their exfoliation.

PCO results from odontoblastic activity and deposition of hard tissue along the wall of the root canal within a vital pulp. A randomized controlled trial demonstrated molars with evidence of PCO on post-treatment radiographs were significantly less likely to have an unacceptable radiographic outcome ($P=.0008$; OR: 0.08). Many investigators agree that PCO results from odontoblastic activity within a vital pulp and is an acceptable outcome of vital pulp therapy.

Clinicians do not regard all radiographic pathological changes occurring after vital pulp therapy as an indication for immediate extraction or non-vital pulp therapy as long as the pulp treated tooth remains asymptomatic without extension of pathoses to supporting structures. Offered a clinical scenario involving an 8-year-old healthy child presenting with an asymptomatic primary molar 3 years post-vital pulp therapy with radiographic evidence of pathologic root resorption, over 60 percent of predoctoral pediatric dentistry program directors and pediatric dentists surveyed opted to observe the molar rather than extract or provide primary RCT.

Multiple radiographic outcome evaluations protocols have been developed and modified by various investigators to distinguish between minor pathological changes that allow for observation versus major pathological changes necessitating extraction or non-vital pulp therapy. These radiographic evaluation methods were
developed to simulate day-to-day clinical decision-making as clinicians are often prepared to accept a limited degree of radiographic pathosis as long as the tooth remains asymptomatic.

Doyle et al. published a modification of the rating scale used previously by Casas et al., Yacobi et al. and Payne et al. in which 2 disinterested raters classified pulp treated primary teeth into 1 of 3 outcomes based on radiographic evaluation: N=incisor without pathologic change; P₀=pathologic change present, follow-up recommended; and Pₓ=pathologic change present, extract. Primary teeth rated N or P₀ are considered acceptable outcomes of vital pulp therapy. Teeth rated as Pₓ are considered unacceptable outcomes. The original scale published in Casas et al., Yacobi et al. and Payne et al. included a fourth outcome category H which represented treated teeth with radiographic changes associated with normal physiologic molar resorption. This category was integrated into the N category in Doyle et al.

Howley et al. published a modification of the radiographic rating scale used by Zurn and Seale and adapted from Flaitz et al. Two calibrated standardized examiners not otherwise involved in the study performed the radiographic outcome assessment. Radiographic outcomes of vital pulp therapy were evaluated and were classified into 1 of 3 outcomes: S=success; Q=questionable, observe; and F=failure, extract. Criteria for S outcome in pulpotomy treated primary incisors are tapering internal root canal, normal trabeculation in periapical region and no external pathological changes. Contained internal resorption and calcific metamorphosis are considered acceptable. Criteria for S
outcome in vital treated primary incisors are tapering internal root canal, normal trabeculation in the periapical region and no external pathological changes. Resorption of the root canal medicament is considered an acceptable outcome. Criteria for Q outcome are the presence of questionable periapical radiolucency with trabeculation still present and/or questionable external root resorption. Criteria for F outcome are perforating internal resorption, frank radiolucency and/or pathological external root resorption. Primary teeth rated S are considered acceptable outcomes vital pulp therapy including pulpotomy and RCT. Teeth rated as Q and F are considered unacceptable outcomes. The study categorized Q as an unacceptable outcome because the majority of teeth rated as Q progressed to F during the study period.

The rating scales in Doyle et al. and Howley et al. appear similar as both rate pulp treated teeth into categorical outcomes. However, the rating scale in Howley et al. defines the pathological radiographic changes that corresponded to each outcome and provides specific criteria used to score each primary tooth treated. These scoring systems attempted to quantify and categorize radiographic changes. The raters who performed the radiographic evaluation in Doyle et al. were not given specific radiographic criteria for each outcome classification but instead were asked to use their clinical judgment.

8.1. Concerns regarding outcome assessment in pulp therapy

Concerns have arisen regarding the standardization, validity and reliability of outcome assessment in pulp therapy studies. The efficacy of pulp therapy outcomes has been measured in various ways. Though clinical and radiographic assessment is the most
reported method used to evaluate pulp therapy outcomes, other reported methods have included histological assessment and survival analysis. In addition to different evaluation methods used across various pulp therapy outcome studies, these studies have also assessed outcomes at different times and there has been no consensus regarding the definition of outcomes.\textsuperscript{320} An example would be the lack of consensus in criteria defining acceptable and unacceptable treatment outcomes. Despite many similarities, most investigators have used their own criteria.

In an attempt to standardize outcome assessment in pulp therapy outcome studies, Sma’il-Faugeron et al. developed a standardized core set of clinical and radiographic component outcomes that could be used to define acceptable and unacceptable outcomes for all randomized controlled trials assessing pulp therapy outcomes in primary teeth.\textsuperscript{320} The investigators performed a systematic review of all outcomes used in randomized controlled trials comparing pulp therapy treatments for primary molars. Using a 3-round Delphi process, the investigators had expert authors and dentists refine all outcomes previously reported in the systematic review to what they considered the most relevant component outcomes. The process identified the following 5 component outcomes that the investigators suggested should be used to assess acceptable and unacceptable outcomes of a pulp treatment. The 5 components were soft-tissue pathosis, pain, pathologic mobility, pathologic radiolucency and pathologic root resorption. This standardized system would aid in assessing the effectiveness of pulp treatments in primary teeth across various studies and resolving one of the largest criticisms of pulp therapy literature. However, it might be an oversimplified outcome rating system that
might not take into account all factors clinicians consider when evaluating outcomes. This standardized outcome assessment might not be a realistic representation of day-to-day clinical scenarios.

A limitation of these rating scales is that no study has assessed the validity of these radiographic rating systems. These rating systems have relied heavily on the association between radiographic signs of pathosis and the histopathological state of infection or inflammation of the pulp. However, these scales have demonstrated reliability among evaluators or raters. Reliability has been assessed using inter- and intra-rater reliability. Kappa scores for inter- and intra-rater reliability have ranged from fair to excellent/very good based on Cohen’s and Fleiss’ kappa score and the Landis and Koch interpretation (Table 3).

8.2. Survival analysis

Survival analysis is a statistical technique that deals with the analysis of time duration from an intervention until an event occurs, such as death in biological organisms or failure in mechanical systems. Survival analysis is a statistic used by insurance companies to estimate life expectancy. It has been adopted for clinical trials out of the concern that clinical and radiographic outcome rating systems are not standardized. Survival of pulp treated primary teeth can be defined as the probability that the teeth of interest, at a given time, will still exist after treatment. Essentially, it is a prognostic statistic and predicts the likelihood of the survival of a tooth at various time points in the future. Using the Kaplan-Meier approach to survival analysis, the exact time of a non-
survival event is used to calculate survival probability and can be used to predict survival until the next event or follow-up interval. Survival curves can be generated for various treatment groups and predicted survival in each treatment group can be compared using the Mantel-Cox Log-Rank Test (log-rank test). The Cox proportional hazards model can generate the hazard or probability of an event at a specific time, given survival of the tooth up to this time and allows adjustment for any number of covariates, whether they are discrete or continuous.322

Criteria for survival and non-survival have varied in the literature. In general, treated teeth that develop clinical or radiographic pathosis are considered to have an unacceptable treatment outcome. Subjects that drop out or are lost to follow-up are no longer available for observation and can provide no additional data. These teeth are considered to be at risk of a non-survival event and considered censored. Censored observation occurs when the information about the survival time of a treated tooth is unknown.321

Some investigators have defined non-survival of treated teeth as teeth with unacceptable clinical or radiographic outcomes, exfoliated and extracted during the follow-up interval.82,83,191,192 Other investigators defined survival as unacceptable clinical and radiographic outcome of a treated tooth.85,323

9. Pulp therapy in primary incisors

Currently, there is no consensus with regard to a standard of care for the treatment of
carius vital primary incisors with reversible pulpitis. Thirty-eight percent of a randomly selected sample of AAPD members preferred pulpotomy, 33 percent preferred RCT and 23 percent preferred indirect pulp therapy for treatment of reversibly inflamed primary incisor pulps.\textsuperscript{219} Survey respondents were asked to provide the rationale for selection of their preferred primary incisor pulp technique. Of the 33 percent of survey respondents who preferred RCT, 56 percent reported that it was the technique taught in the specialty program from which they had graduated and 33 percent reported their belief that incisor pulpotomy had poor outcomes.

The vital molar pulpotomy is the technique used by most pediatric dentists, the most common technique taught in pediatric dentistry residency programs and the accepted standard of care for carious exposures of asymptomatic vital primary molars in North America.\textsuperscript{90,119} The AAPD guideline on pulp therapy states a pulpotomy is indicated when caries removal results in pulp exposure, however this guideline does not differentiate between posterior and anterior primary teeth.\textsuperscript{90} Although the vital pulp therapy outcomes reported in primary molars cannot be extrapolated to primary incisors, the anatomy and histology of the pulp in incisors and molars are similar and one would expect similar outcomes between the two forms of teeth. Little evidence exists to substantiate that pulpotomy of vital primary incisors have poor outcomes.

Flatiz et al. and Coll et al. were some of the first papers to compare primary incisor pulp techniques in the 1980s.\textsuperscript{207,319} Flaitz et al. in a retrospective study compared FC pulpotomy and ZOE RCT outcomes.\textsuperscript{319} A total of 144 primary incisors, 57 FC
pulpotomy and 87 RCT incisors, were evaluated. The sample included vital and non-vital incisors as well as incisors treated for caries and trauma. Radiographic evaluation demonstrated 69 percent of FC pulpotomy and 84 percent of RCT treated incisors were considered acceptable outcomes. Major weaknesses of the study were the treatment groups included vital and non-vital incisors and pulpotomy was used to treat non-vital incisors. Coll et al. in a retrospective study assessed the clinical and radiographic outcomes of FC pulpotomy, IPT and RCT of carious and traumatized primary incisors. Forty-five subjects from a private practice were included in the study. Indications for pulpotomy treatment were primary incisors with carious or traumatic pulp exposure presenting with reversible pulpitis. Indications for IPT were similar to that of pulpotomy except no carious or traumatic pulp exposure was present. Indications for RCT were based on clinical and radiographic signs of irreversible pulpitis or pulpal necrosis. Total overall outcome combined clinical and radiographic outcomes. Total acceptable outcomes reported were 86 percent (24 of 28) for FC pulpotomy, 92 percent (24 of 26) for IPT and 78 percent (21 of 27) for RCT treated incisors with a mean follow-up between 42 to 46 months post-treatment. Weaknesses of the study included different inclusion criteria for each treatment group, a small sample and no comparative statistics between treatment groups were reported.

Payne et al. in a clinical trial evaluated the clinical and radiographic outcomes of ZOE RCT in vital primary teeth 24 months post-treatment. The sample consisted of healthy children with primary incisors and/or molars presenting with reversible pulpitis. At 24 months post-treatment, acceptable radiographic outcomes were observed in 83 percent
(124 of 150) of RCT treated incisors. Yacobi et al., in a similar study to Payne et al., also evaluated outcomes of RCT of carious primary incisors and molar with reversible pulpitis.\textsuperscript{221} The sample consisted of 106 subjects and acceptable radiographic outcomes were 76 percent of RCT treated teeth 12 months post-treatment. At 24 months post-treatment, 59 percent of RCT treated teeth were considered acceptable radiographically. Primosch et al. in a retrospective study also evaluated the clinical and radiographic outcomes of RCT with the addition of a 4-minute application of FC prior to obturation.\textsuperscript{222} Acceptable radiographic outcome of RCT was 81 percent (65 of 80) of treated incisors after a mean duration of 18 months.

Casas et al. in a randomized controlled trial compared FS pulpotomy and RCT in cariously exposed vital primary incisors with reversible pulpitis.\textsuperscript{192} Subjects were assessed for clinically and radiographically 12- and 24-months post-treatment. Acceptable clinical outcomes were observed in 78 percent (32 of 41) of FS pulpotomy and 100 percent (36 of 36) of RCT treated incisors 24 months post-treatment. Acceptable radiographic outcomes were observed in 42 percent (5 of 12) of FS pulpotomy and 73 percent (8 of 11) of RCT treated incisors. FS pulpotomy and RCT demonstrated no significant difference in clinical and radiographic outcomes ($P<.05$). RCT treated incisors demonstrated significantly higher survival rates than FS pulpotomy treated incisors 24 months post-treatment ($P=.04$, log-rank test). One weakness of this study was the large sample wastage. The final sample size was only 23 incisors with a dropout rate of over 50 percent.
Aminabadi et al. in a randomized controlled trial assessed the clinical and radiographic outcomes of FC pulpotomy and RCT in primary incisors. Teeth were reassessed 12 and 24 months post-operatively. Criteria for acceptable and unacceptable clinical and radiographic outcomes were not clearly defined. At 24 months post-treatment, 87 percent (40 of 47) of FC pulpotomy and 96 percent (44 of 45) of RCT treated incisors demonstrated acceptable clinical outcomes. Clinical outcomes did not differ between FC pulpotomy and RCT ($P > .05$). Acceptable radiographic outcomes were shown in 76 percent (35 of 47) of FC pulpotomy and 91 percent (42 of 45) of RCT treated incisors. RCT had significantly more acceptable radiographic outcomes than FC pulpotomy ($P < .05$). Major weaknesses of this study included that the methodology did not define the parameters for an acceptable clinical and radiographic outcome. The study also used a very low concentration of FC (1.5 percent) for FC pulpotomy treatment.

Howley et al. in a split mouth randomized controlled trial compared FC pulpotomy and Vitapex RCT outcomes in carious vital primary incisors with reversible pulpitis. Twenty-nine subjects with 50 matched pairs of incisors were enrolled from a private pediatric dental office. Subjects were recalled at approximately 6-month intervals with a follow-up time ranging from 5 to 23 months (mean=13.0+/-5.6 months). At 15 to 23 months post-treatment, 89 percent (29 of 33) of FC pulpotomy and 73 percent (20 of 27) of Vitapex RCT treated incisors had acceptable radiographic outcomes. FC pulpotomy and RCT demonstrated equivalent clinical and radiographic outcomes ($P > .05$).

Three randomized controlled trials on pulp therapy in primary incisors have been
published to date. Casas et al. demonstrated RCT incisor survival was significantly higher than FS pulpotomy incisor survival, however the study suffered from large sample wastage. Two prospective studies have demonstrated conflicting results when comparing FC pulpotomy and RCT in vital primary incisors. Howley et al. demonstrated equivalent radiographic outcomes when comparing FC pulpotomy and RCT, however, Aminabadi et al. demonstrated radiographic outcomes of FC pulpotomy were inferior to RCT. These conflicting results may be due to different methodologies. Aminabadi et al. used a 1.5 percent dilution of FC and a self-cure resin with questionable marginal seal where as Howley used full-strength Buckley’s FC and SSC. Overall, evidence produced in Howley et al. is representative of a higher quality randomized controlled trial based on Jadad scoring and Consort guidelines than Aminabadi et al.

Reported clinical outcomes of pulpotomy treated incisors ranged from 78 to 100 and radiographic outcomes of pulpotomy treated incisors ranged from 59 to 89 percent over follow-up periods from 12 to 24 months (Appendix 1E). Reported clinical outcomes of RCT treated incisors ranged from 96 to 100 and radiographic outcomes of RCT treated incisors ranged from 73 to 91 percent over follow-up periods between 12 to 65 months (Appendix 1E). The most common radiographic finding noted in pulpotomy treated incisors was calcific metamorphosis. Based on available evidence, FC pulpotomy and RCT are effective treatment options for carious vital primary incisors.

Despite a reported anecdotal belief that pulpotomy of vital primary incisors have poor outcomes there is little evidence-based literature to support this. There is currently no
strong evidence to support the use of RCT over pulpotomy in carious primary incisors with reversible pulpitis. Potential benefits of pulpotomy versus RCT include the pulpotomy is a simpler time efficient technique and more cost effective to the patient. The Ontario Dental Association Dental Fee Guide of 2013 reports the mean cost of a primary incisor RCT was twice the cost of a pulpotomy. The reported risk of ectopic eruption of succedaneous teeth and the retention of RCT obturation materials in the periodontium risk with primary RCT may not be an issue in pulpotomy treated incisors.\textsuperscript{207,214}

10. Restoration of primary incisors

Currently, there is a dearth of evidence regarding the restoration of primary teeth that have undergone pulp therapy, however the restoration of permanent teeth that have undergone pulp therapy has been assessed. Coronal restorations were demonstrated to have a significantly greater impact on periapical health than the quality of the RCT in the permanent dentition.\textsuperscript{325,326} RCT treated teeth that had amalgam or composite restorations were 6 times more likely to be lost than crowned permanent teeth.\textsuperscript{327} A retrospective study evaluated the outcome of 220 endodontically treated permanent teeth without crown coverage.\textsuperscript{328} Overall acceptable outcome rates of RCT treated permanent teeth were 96 percent at 1-year, 88 percent at 2-years and 36 percent at 5-years. The results of these studies all substantiate a strong association between coronal restoration and the survival of RCT teeth in the permanent dentition.\textsuperscript{327} There is little evidence that has assessed the effect of restoration type and pulp therapy longevity in the primary dentition.
Treatment options for restoring primary incisors with pulp therapy have included: GI restorations, resin bonded composite restorations, resin bonded composite strip crowns, SSC, porcelain veneered SSC, resin faced SSC, polycarbonate crowns, polyester crown, porcelain crowns and zirconium crowns. The longevity of these restorations in a clinical setting has not been extensively researched. No prospective studies regarding the restoration of primary incisors has been published, as the majority of studies were retrospective studies. Of 90 papers concerning the restoration of primary anterior teeth with pre-formed crowns or crown forms, none of the papers were considered strong clinical evidence based on the Curzon & Toumba scale. Reported failure rates of strip crowns ranged between 0 to 50 percent and pre-veneered metal crowns were 32 to 39 percent in this literature review.

Composite strip crowns are a common choice for the restoration of primary incisors. Strip crowns are esthetically pleasing and easily repaired if subsequently chipped or fractured. However, strip crowns are technique-sensitive as moisture contamination may compromise esthetics and/or longevity. Adequate tooth structure must be available to ensure sufficient surface area for bonding and retention. When additional retention is required in primary incisors due to loss of adequate tooth structure, use of the composite resin short-post technique (Figure 6) may be considered. A case series assessed the retention rate of the composite resin short-post technique in RCT primary incisors for one year. The study followed 92 teeth and observed no loss of retention in any of the incisors. Four of the 92 teeth were reported to have recurrent decay, 3 crowns were reported to have incisal fractures and 4 crowns displayed severe attrition.
The longevity of resin bonded composite strip crowns placed in primary maxillary incisors was assessed retrospectively.\textsuperscript{331} Two hundred children, aged 22 to 48 months, who had resin strip crowns placed with a follow-up of 24 months were included in the study. Strip crowns were considered to be acceptable if the surface appeared smooth, without chipping or caries, the color remained good or acceptable and radiographically, the margins were properly adapted, without overhangs, and there was no evidence of pulpal or periapical pathosis. Eighty percent of the restorations were judged to have acceptable outcomes. The number of carious surfaces of the tooth at baseline influenced the treatment outcome. Central and lateral incisors with 4 carious surfaces had a higher strip crown failure rate than strip crowns on 1 or 2 surfaces (P<.001).

The photographic and radiographic outcomes of composite resin strip crowns on non-pulp treated maxillary primary incisors were assessed in a retrospective study.\textsuperscript{332} One hundred forty-five restorations, placed in 52 children, were evaluated after a minimum of 18 months (mean=31 months). The retention rate was 83 percent in strip crowns followed-up between 18 and 24 months and 78 percent in those followed-up for over 36 months. Ninety-two percent of the teeth demonstrated healthy pulps and 6 percent demonstrated pulpal changes that did not require immediate treatment. Two percent of teeth showed radiographic evidence of pulpal pathology requiring non-vital pulp therapy or extraction. Ninety-nine percent of the strip crowns demonstrated either no gingival inflammation (43 percent) or mild marginal gingivitis (56 percent).

Parental satisfaction was evaluated and compared with clinical outcomes of bonded resin
composite strip crowns in maxillary primary incisors.\textsuperscript{333} Two pediatric dentists independently rated clinical outcomes based color photographs of primary maxillary incisors treated with strip crowns. Parental satisfaction regarding the esthetics of the crowns was evaluated through a questionnaire. One hundred and twelve restorations, placed for an average of 18 months (range=6-25 months) were evaluated. Overall parental satisfaction with the treatment was excellent, however, parental satisfaction with regard to color was the lowest. No significant differences were found between dentist and parent evaluations of color, size, and overall appearance \((P=.19)\). Parents rated their overall satisfaction as being positive regardless of their poor ratings of color, size, or overall appearance. However, a significant relationship was found between shorter survival and decreasing overall parental satisfaction \((P=.046)\). Parental satisfaction with bonded resin composite strip crowns for the treatment of primary incisors with large or multi-surface caries was excellent however parents’ dissatisfaction was most often related to color and survival of the restorations.

Esthetics has been a concern of clinicians in pulp treated primary incisors.\textsuperscript{334} In a retrospective study, clinical and radiographic outcomes of maxillary incisors restored with composite resin strips crowns were assessed. Incisors that had pulp treatment were judged to have far more significant color match discrepancies than those without pulp treatment.\textsuperscript{334} MTA, ZOE, Endoflas and iodoform are obturation materials reported to have the potential to discolor coronal structure in primary teeth.

No prospective trials have been done to assess restorations with pulp therapy in primary
incisors. Available evidence reports restoration longevity of resin strip crowns is 50 to 100 percent over a 2 to 3 year follow-up. The resin bonded strip crown is a treatment modality that appears esthetically pleasing for parents and, for clinicians, provides a functionally satisfactory means of restoring decayed primary incisors in young children. Esthetic outcomes of teeth that discolored secondary to pulp therapy were a concern reported by authors when placing strip crowns. Coronal restoration seal may affect outcomes of pulp therapy. With restoration longevity for resin strip crowns ranging from 50 to 100 percent over a 2 to 3 year follow-up period, longevity of restoration may be a confounding factor in the assessment of pulp therapy.

11. Summary of literature review

Dental caries is the most common chronic disease in children. Maxillary primary incisors are one of the most commonly affected teeth in ECC. Caries that extends to the pulps of primary maxillary incisors is common. The premature loss of primary maxillary incisors can adversely affect a child’s occlusion, articulation accuracy, esthetics and psychosocial development. Treatment of these teeth often requires pulp therapy or extraction.

Successful pulp treatment for cariously exposed vital primary incisors avoids premature tooth loss and maintains incisors in a quiescent state. The choice of pulp therapy and outcome of treatment is dependent on the pulp status of the tooth. Reversibly inflamed pulps are candidates for vital pulp therapy. Treatment options of vital pulps with reversible pulpitis in primary teeth include IPT, pulpotomy, RCT and extraction. Currently, there is a paucity of dental literature with regards to vital pulp therapy in
primary incisors.

Pulp therapy in primary molars has been extensively investigated. The pulpotomy is the accepted standard of care for carious exposures of vital primary molars with reversible pulpitis. It is the most widely used and taught vital primary pulp therapy technique in North America. Variations in the pulpotomy technique include use of FC, FS, NaOCl, ZOE, electrosurgery, lasers, Ca(OH)$_2$, GA and MTA. Superior radiographic outcomes of MTA pulpotomy have been demonstrated when compared to FS, FC and Ca(OH)$_2$ in primary molars.

Only 3 randomized controlled trials have been published to date regarding vital pulp therapy in primary incisors.$^{192,219,324}$ Based on the current state of evidence, clinicians have no guidance with regards to the treatment of vital primary incisors with reversible pulpitis. No study has been published to date that has assessed the outcomes of MTA pulpotomies in primary incisors. MTA vital primary incisor pulpotomy could offer a clinically efficient and cost-effective therapy for vital primary incisors with extensive caries compared to other therapies such as RCT and FC pulpotomy. Furthermore, using FS to induce hemostasis after coronal pulp amputation prior to placement of MTA would improve the clinical efficiency of the pulpotomy procedure.
1.12. References


46. Marsh PD, Martin MV, Lewis MAO. *Oral Microbiology.* Elsevier Science Health Science Division; 2009.


272. Menezes R, Bramante CM, Letra A, Carvalho VG, Garcia RB. Histologic evaluation of pulpotomies in dog using two types of mineral trioxide


1.13. Tables & Figures

Table 1. Sensitivity and specificity of sensibility test in the primary (Hori et al. 2011) and permanent dentition (Petersson et al. 1999)

<table>
<thead>
<tr>
<th></th>
<th>Cold Test</th>
<th>Hot Test</th>
<th>Electric Pulp Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Permanent Dentition</td>
<td>0.83</td>
<td>0.93</td>
<td>0.86</td>
</tr>
<tr>
<td>Primary Dentition</td>
<td>0.73</td>
<td>0.75</td>
<td>0.87</td>
</tr>
</tbody>
</table>
Table 2. Commercially available forms of mineral trioxide aggregate (MTA)\textsuperscript{312}

<table>
<thead>
<tr>
<th>Materials</th>
<th>Distributor</th>
<th>Production Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>ProRoot MTA</td>
<td>Dentsply Tulsa Dental</td>
<td>Tulsa, Oklahoma, USA</td>
</tr>
<tr>
<td>Tooth-Colored MTA</td>
<td>Dentsply Tulsa Dental</td>
<td>Tulsa, Oklahoma, USA</td>
</tr>
<tr>
<td>Gray MTA Angelus</td>
<td>Angelus Indústria de Produtos Odontológicos Ltda.</td>
<td>Londrina, PR, Brazil</td>
</tr>
<tr>
<td>White MTA Angelus</td>
<td>Angelus Indústria de Produtos Odontológicos Ltda.</td>
<td>Londrina, PR, Brazil</td>
</tr>
<tr>
<td>Angelus MTA-Obtura</td>
<td>Angelus Indústria de Produtos Odontológicos Ltda.</td>
<td>Londrina, PR, Brazil</td>
</tr>
<tr>
<td>Egeo CPM in white</td>
<td>Egeo S.R.L.</td>
<td>Buenos Aires, Argentina</td>
</tr>
<tr>
<td>Egeo CPM sealer</td>
<td>Egeo S.R.L.</td>
<td>Buenos Aires, Argentina</td>
</tr>
<tr>
<td>MTA Bio</td>
<td>Angelus Indústria de Produtos Odontológicos Ltda.</td>
<td>Londrina, PR, Brazil</td>
</tr>
<tr>
<td>Study</td>
<td>Kappa Score Method</td>
<td>Interpretation Method</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Mettlach et al. 2013</td>
<td>Cohen’s</td>
<td>N/A</td>
</tr>
<tr>
<td>Howley et al. 2012</td>
<td>Cohen’s</td>
<td>1</td>
</tr>
<tr>
<td>Doyle et al. 2010</td>
<td>Cohen’s</td>
<td>0.68</td>
</tr>
<tr>
<td>Zurn and Seale 2008</td>
<td>Cohen’s</td>
<td>N/A</td>
</tr>
<tr>
<td>Casas et al. 2004b</td>
<td>Fleiss’</td>
<td>0.71</td>
</tr>
<tr>
<td>Casas et al. 2004a</td>
<td>Fleiss’</td>
<td>0.61</td>
</tr>
<tr>
<td>Casas et al. 2003</td>
<td>Fleiss’</td>
<td>0.71</td>
</tr>
<tr>
<td>Payne et al. 1993</td>
<td>Fleiss’</td>
<td>0.84</td>
</tr>
<tr>
<td>Yacobi et al. 1991</td>
<td>Fleiss’</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Figure 1. Schematic representation of dentin, predentin, odontoblasts layer, cell-free zone and cell-rich zone within the pulp. Adapted from Nanci 2008.
Figure 2. Schematic diagram of the various types of dentin and their distribution within a tooth. Attrition (blue arrow), abrasion (toothbrush) and cavitation secondary to caries are shown to stimulate tertiary dentin. Adapted from Nanci 2008.
Figure 3. Histological section of dentin. The black arrows depict a region where dentinal tubules change orientation delineating the junction between primary and secondary dentin. Adapted from Nanci 2008.
Figure 4. (A) Discolouration of Tooth-coloured MTA noted after 3 days. Note whiter end (top) was open to PBS solution. (B) Tooth-coloured MTA sample after 3 day-set in mold followed by 1 week of air exposure.
Figure 5. Spectrophotometric images of samples of Tooth-colored ProRoot MTA irradiated with various light sources taken at different time points.
Figure 6. Composite resin short-post technique.

Adapted from Judd et al. 1990.
### 1.14. Appendix

#### 1.14.1. Summary of published vital pulp therapy investigations

Appendix 1A. Summary of published formocresol pulpotomy clinical controlled trials, meta-analysis and systematic reviews. Formocresol, FC; mineral trioxide aggregate, MTA; calcium hydroxide, Ca(OH)₂; ferric sulphate, FS; root canal therapy, RCT; sodium hypochlorite, (NaOCl); ≥, not significantly different than; >, significantly higher acceptable outcome rates than; <, significantly lower outcomes rates than.

<table>
<thead>
<tr>
<th>Investigators</th>
<th>*Level of Evidence</th>
<th>Follow-up (months)</th>
<th>Statistical Analysis</th>
<th>FC Acceptable Outcomes (%)</th>
<th>Statistical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin et al. 2014²⁴⁶</td>
<td>la</td>
<td>18-24</td>
<td>Odds ratio</td>
<td>Meta-analysis and systematic review</td>
<td>FC &lt; MTA (P&lt;.05) for radiographic outcome FC &gt; Ca(OH)₂ (P&lt;.05) for clinical outcome FC &gt; Ca(OH)₂ (P&lt;.05) for radiographic outcome FC &gt; laser (P&lt;.05) for clinical outcome FC &gt; laser (P&lt;.05) for radiographic outcome</td>
</tr>
<tr>
<td>Shirvani et al. 2014²⁵⁵</td>
<td>la</td>
<td>6-24</td>
<td>Relative risk</td>
<td>Meta-analysis</td>
<td>FC 3.85 at 6 months, 2.70 at 12 months and 2.44 at 24 months the relative risk for an unacceptable outcome compared to MTA</td>
</tr>
<tr>
<td>Mettlach et al. 2013³³³</td>
<td>Ib</td>
<td>6-42</td>
<td>Percent acceptable outcomes</td>
<td>Clinical = 99 Radiographic = 79 Survival clinical = .95 Survival radiographic = .47</td>
<td>MTA &gt; FC (P&lt;.001) for radiographic outcome MTA &gt; FC (P&lt;.001) for radiographic survival</td>
</tr>
<tr>
<td>Ruby et al. 2013³⁰⁰</td>
<td>Ib</td>
<td>12</td>
<td>Percent acceptable outcome</td>
<td>Clinical = 100 Radiographic = 90</td>
<td>FC = NaOCl (P&lt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Howley et al. 2012²²⁹</td>
<td>Ib</td>
<td>15-23</td>
<td>Percent acceptable outcome</td>
<td>Clinical = 100 Radiographic = 89</td>
<td>FC = RCT (P&lt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Sushynski et al. 2012²⁻⁹</td>
<td>Ib</td>
<td>24</td>
<td>Percent acceptable outcome</td>
<td>Clinical = 98 Radiographic = 85</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcome</td>
</tr>
<tr>
<td>Huth et al. 2012³⁶⁷</td>
<td>Ib</td>
<td>36</td>
<td>Percent acceptable outcome</td>
<td>Total (clinical and radiographic) = 72</td>
<td>FC = Er:YAG = Ca(OH)₂ = FS (P&gt;0.05) for total (clinical and radiographic) outcome</td>
</tr>
<tr>
<td>Fernandez et al. 2012³⁻⁵</td>
<td>Ib</td>
<td>24</td>
<td>Percent acceptable outcome</td>
<td>Radiographic = 95</td>
<td>FC = FS = MTA = NaOCl (P&lt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Godhi et al. 2011³⁵⁵</td>
<td>Iib</td>
<td>12</td>
<td>Percent acceptable outcome</td>
<td>Radiographic = 88</td>
<td>FC = MTA (P&gt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Erdem et al. 2011³⁶²</td>
<td>Ib</td>
<td>24</td>
<td>Percent acceptable outcome</td>
<td>Total (clinical and radiographic) = 96</td>
<td>FC = MTA = FS (P&gt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Ansari and Ranjipour 2010³⁰⁶</td>
<td>Ib</td>
<td>24</td>
<td>Percent acceptable outcome</td>
<td>Radiographic = 90</td>
<td>FC = MTA (P&gt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Simancas-Pallares et al.2010³⁷⁷</td>
<td>la</td>
<td>6 to &lt; 74</td>
<td>Systematic review</td>
<td>MTA &gt; FC for clinical and radiographic outcomes</td>
<td></td>
</tr>
<tr>
<td>Zealand et al. 2010³⁰⁰</td>
<td>Ib</td>
<td>6</td>
<td>Percent acceptable outcome</td>
<td>Clinical = 97 Radiographic = 86</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcome</td>
</tr>
<tr>
<td>Subramanian et al.2009³⁵⁵</td>
<td>Ib</td>
<td>24</td>
<td>Percent acceptable</td>
<td>Clinical = 100 Radiographic = 85</td>
<td>FC = MTA (P&lt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Study</td>
<td>Level</td>
<td>Duration</td>
<td>Study Design</td>
<td>Outcome</td>
<td>Clinical Outcomes</td>
</tr>
<tr>
<td>-------------------------------</td>
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<td>-------------------</td>
</tr>
</tbody>
</table>
| Aminabadi et al. 2008<sup>34</sup> | lb    | 24       | Percent acceptable outcome | Clinical = 87  
Radiographic = 76 | RCT > FC (P<.05) for radiographic outcomes |
| Bahrololoom et al. 2008<sup>39</sup> | lb    | 9        | Percent acceptable outcome | Clinical = 100  
Radiographic = 97 | FC = ES (P>.05) for clinical and radiographic outcomes |
| Ng and Messer 2008<sup>40</sup> | la    | 4-91     | Percent acceptable outcome | Meta-analysis | MTA > FC (P<.05) for clinical and radiographic outcomes |
| Noorollahian 2008<sup>41</sup> | lb    | 24       | Percent acceptable outcome | Clinical = 100  
Radiographic = 100 | MTA = FC (P>.05) for clinical and radiographic outcomes |
| Sonmez et al. 2008<sup>36</sup> | lb    | 24       | Percent acceptable outcome | Radiographic = 77 | FC = FS = Ca(OH)<sub>2</sub> = MTA (P>.05) for clinical and radiographic outcomes |
| Zurn and Seale 2008<sup>55</sup> | lb    | 13-24    | Percent acceptable outcome | Clinical = 97  
Radiographic = 97 | FC > Ca(OH)<sub>2</sub> (P>.05) for clinical and radiographic outcomes |
| Aeinehchi et al. 2007<sup>45</sup> | lb    | 6        | Percent acceptable outcome | Clinical = 100  
Radiographic = 89 | MTA > FC (P<.05) for radiographic outcomes |
| Peng et al. 2007<sup>42</sup> | Ila   | > 6      | Percent acceptable outcome | Meta-analysis | FC = FS (P>.05) for clinical and radiographic outcomes |
| Peng et al. 2006<sup>42</sup> | Ila   | 1-74     | Percent acceptable outcome | Meta-analysis | MTA > FC (P<.05) for radiographic outcomes |
| Holan et al. 2005<sup>36</sup> | lb    | 4 to 74  
(mean=38) | Percent acceptable outcome | Radiographic = 83 | FC = MTA (P>.05) for radiographic outcomes |
| Huth et al. 2005<sup>38</sup> | lb    | 24       | Percent acceptable outcome | Total (clinical and radiographic) = 85  
FC > Ca(OH)<sub>2</sub> (P=.001) for total (clinical and radiographic) outcome  
FC = Er:YAG = FS (P>.05) for total (clinical and radiographic) outcome |
| Saltzman et al. 2005<sup>52</sup> | lb    | 3-15     | Percent acceptable outcome | Clinical = 100  
Radiographic = 88  
FC = Laser+MTA (P>.05) for clinical and radiographic outcomes |
| Agamy et al. 2004<sup>54</sup> | lb    | 12       | Percent acceptable outcome | Clinical = 90  
Radiographic = 90  
FC = MTA (P>.05) for clinical and radiographic outcomes |
| Loh et al. 2004<sup>53</sup> | la    |         | Meta-analysis | FS = FC (P>.10) for clinical and radiographic outcomes |
| Ibricevic and Al-Jame 2003<sup>55</sup> | lb    | 42-48    | Percent acceptable outcome | Radiographic = 94 | FC = FS (P>.05) for clinical and radiographic outcomes |
| Dean et al. 2002<sup>55</sup> | lb    | 5-12     | Percent acceptable outcome | Clinical = 99  
Radiographic = 87  
FC = ES (P>.05) for clinical and radiographic outcomes |
| Ibricevic and Al-Jame 2000<sup>56</sup> | lb    | 20       | Percent acceptable outcome | Clinical = 100  
Radiographic = 97  
FC = FS (P>.05) for clinical and radiographic outcomes |
| Fuks et al. 1997<sup>51</sup> | llb   | 6 to 34  
(mean=20) | Percent acceptable outcome | Radiographic = 84 | FC = FS (P>.05) for clinical and radiographic outcomes |

Appendix 1B. Summary of published ferric sulphate pulpotomy clinical controlled trials, meta-analysis and systematic reviews. Formocresol, FC; mineral trioxide aggregate, MTA; calcium hydroxide, Ca(OH)_2; ferric sulphate, FS; root canal therapy, RCT; sodium hypochlorite, NaOCl.

<table>
<thead>
<tr>
<th>Investigators</th>
<th>*Level of Evidence</th>
<th>Follow-up (months)</th>
<th>FS Acceptable Outcomes (%)</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Lin et al. 2014               | Ia                 | 18-24              | Meta-analysis and systematic review | FS > Ca(OH)_2 (P<.05) for clinical outcome  
FS > Ca(OH)_2 (P<.05) for radiographic outcome  
FS > laser (P<.05) for clinical outcome  
FS > laser (P<.05) for radiographic outcome  
FS < MTA (P<.05) for radiographic outcome |
| Huth et al. 2012              | Ib                 | 36                 | Total (clinical and radiographic) = 76 | FS = Er:YAG = Ca(OH)_2 = FC (P>.05) for total (clinical and radiographic) outcome |
| Fernandez et al. 2012         | Ib                 | 24                 | Radiographic = 100 | FS = FC = MTA = NaOCl (P>.05) for clinical and radiographic outcomes |
| Erdem et al. 2011             | Ib                 | 24                 | Total (clinical and radiographic) = 88 | FS = MTA = FC (P>.05) for clinical and radiographic outcomes |
| Doyle et al. 57              | Ib                 | 6-38 months        | Radiographic = 74 | MTA > FS (P<.05) for radiographic outcomes  
MTA & MTA/FS > eugenol-free FS (P<.05) for radiographic outcomes  
FS = MTA/FS & eugenol-free FS (P>.05) for radiographic outcomes  
MTA = MTA/FS = FS (P>.05) for survival  
MTA > eugenol-free FS (P<.05) for survival |
| Sonmez et al. 2008             | Ib                 | 24                 | Radiographic = 73 | FS = FC = Ca(OH)_2 = MTA (P>.05) for clinical and radiographic outcomes |
| Peng et al. 2007              | Ia                 | ≥ 6 months         | Meta-analysis | FS = FC (P>.05) for clinical and radiographic outcomes |
| Huth et al. 2005              | Ib                 | 24                 | Total (clinical and radiographic) = 85 | FS = Er:YAG = FC (P>.05) for total (clinical and radiographic) outcome |
| Casas et al. 2004             | Ib                 | 36 months          | Radiographic = 67 | RCT > FS (P>.05) for radiographic outcomes  
RCT > FS (P>.05) for survival |
| Casas et al. 2004             | Ib                 | 24 months          | Clinical = 78  
Radiographic = 59 | FS = RCT (P>.05) for radiographic outcomes  
RCT > FS (P>.05) for survival |
| Casas et al. 2003             | Ib                 | 24 months          | Radiographic = 61 | FS = RCT (P>.05) for radiographic outcomes  
RCT > FS (P>.05) for survival |
| Loh et al. 2004               | Ia                 |                   | Meta-analysis | FS = FC (P>.10) for clinical and radiographic outcomes |
| Ibricevic and Al-Jame 2003    | Ib                 | 42-48              | Radiographic = 92 | FS = FC (P>.05) for clinical and radiographic outcomes |
| Ibricevic and Al-Jame 2000    | Ib                 | 20                 | Clinical = 100  
Radiographic = 97 | FS = FC (P>.05) for clinical and radiographic outcomes |
| Fuks et al. 1997             | IIB                | 6 to 34            | Radiographic = 93 | FS = FC (P>.05) for clinical and radiographic outcomes |

Appendix 1C. Summary of published vital root canal therapy clinical controlled trials and retrospective studies. Formocresol, FC; mineral trioxide aggregate, MTA; calcium hydroxide, Ca(OH)$_2$; ferric sulphate, FS; root canal therapy, RCT; sodium hypochlorite, (NaOCl).

<table>
<thead>
<tr>
<th>Investigators</th>
<th>*Level of Evidence</th>
<th>Follow-up (months)</th>
<th>RCT Acceptable Outcomes (%)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Howley et al. 2012</td>
<td>Ib</td>
<td>15-23</td>
<td>Clinical = 100 Radiographic = 73</td>
<td>RCT = FC (P&gt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Aminabadi et al. 2008</td>
<td>Ib</td>
<td>24</td>
<td>Clinical = 96 Radiographic = 91</td>
<td>RCT &gt; FC (P&lt;0.05) for radiographic outcomes</td>
</tr>
<tr>
<td>Casas et al. 2004</td>
<td>Ib</td>
<td>36 months</td>
<td>Radiographic = 86</td>
<td>RCT &gt; FS (P&lt;0.05) for radiographic outcomes</td>
</tr>
<tr>
<td>Casas et al. 2004</td>
<td>Ib</td>
<td>24 months</td>
<td>Clinical = 100 Radiographic = 81</td>
<td>RCT &gt; FS (P&lt;0.05) for survival</td>
</tr>
<tr>
<td>Casas et al. 2003</td>
<td>Ib</td>
<td>24 months</td>
<td>Radiographic = 91</td>
<td>RCT &gt; FS (P&lt;0.05) for survival</td>
</tr>
<tr>
<td>Payne et al.</td>
<td>IIb</td>
<td>24 months</td>
<td>Total (clinical and radiographic) = 83</td>
<td></td>
</tr>
<tr>
<td>Yacobi et al.</td>
<td>IIb</td>
<td>12 to 24 months</td>
<td>Radiographic = 76 at 12 months Radiographic = 59 at 24 months</td>
<td></td>
</tr>
</tbody>
</table>

Appendix 1D. Summary of published mineral trioxide aggregate clinical controlled trials and retrospective studies. Formocresol, FC; mineral trioxide aggregate, MTA; calcium hydroxide, Ca(OH)₂; ferric sulphate, FS; root canal therapy, RCT; sodium hypochlorite, (NaOCl); Portland cement, (PC).

<table>
<thead>
<tr>
<th>Investigators</th>
<th>*Level of Evidence</th>
<th>Follow-up (months)</th>
<th>MTA Acceptable Outcomes (%)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin et al. 2014</td>
<td>la</td>
<td>18-24</td>
<td>Meta-analysis and systematic review</td>
<td>FC 1.52 x more likely to fail than MTA for radiographic outcome (P&lt;.05) Ca(OH)₂ 2.13 x more likely to fail than FC for clinical outcome (P&lt;.05) Ca(OH)₂ 4.55 x more likely to fail than MTA for radiographic outcome (P&lt;.05) Laser 3.76 x more likely to fail than FC for clinical outcome (P&lt;.05) Laser 3.88 x more likely to fail than FC for radiographic outcome (P&lt;.05)</td>
</tr>
<tr>
<td>Shirvani et al. 2014</td>
<td>la</td>
<td>6-24</td>
<td>Meta-analysis</td>
<td>MTA relative risk of failure 0.26 compared to FC at 6 months MTA relative risk of failure 0.37 compared to FC at 12 months MTA relative risk of failure 0.41 compared to FC at 24 months</td>
</tr>
<tr>
<td>Metlach et al. 2013</td>
<td>lb</td>
<td>6-42</td>
<td>Clinical = 99 Radiographic = 95 Survival clinical = .98 Survival radiographic = .90</td>
<td>MTA &gt; FC (P&lt;.001) for radiographic outcome MTA &gt; FC (P&lt;.001) for radiographic survival FC 5.1 x more likely to fail than MTA (P&lt;.05)</td>
</tr>
<tr>
<td>Anthonappa et al. 2017</td>
<td>la</td>
<td>6 to 74 months</td>
<td>Systematic review</td>
<td>MTA = FC for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Sushynski et al. 2012</td>
<td>lb</td>
<td>24</td>
<td>Clinical = 100 Radiographic = 97</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcome</td>
</tr>
<tr>
<td>Fernandez et al. 2012</td>
<td>lb</td>
<td>24</td>
<td>Radiographic = 93</td>
<td>MTA = FC = FS = NaOCl (P&gt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Godhi et al. 2011</td>
<td>lbb</td>
<td>12</td>
<td>Radiographic = 96</td>
<td>MTA = FC (P&gt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Erdem et al. 2011</td>
<td>lb</td>
<td>24</td>
<td>Total (clinical and radiographic) = 88</td>
<td>MTA = FC = FS (P&gt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Ansari and Ranijour 2010</td>
<td>lb</td>
<td>24</td>
<td>Radiographic = 95</td>
<td>MTA = FC (P&gt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Doyle et al. 2013</td>
<td>lb</td>
<td>6-38 months</td>
<td>Radiographic = 96 for MTA and 87 for MTA/FS</td>
<td>MTA &gt; FS (P&lt;.05) for radiographic outcomes MTA &amp; MTA/FS &gt; eugenol-free FS (P&lt;.05) for radiographic outcomes MTA/FS = FS (P&lt;.05) for radiographic outcomes MTA = MTA/FS = FS (P&lt;.05) for survival MTA &gt; eugenol-free FS (P&lt;.05) for survival</td>
</tr>
<tr>
<td>Simancas-Pallares et al. 2010</td>
<td>la</td>
<td>6 to &lt; 74 months</td>
<td>Systematic review</td>
<td>MTA &gt; FC for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Zealand et al. 2010</td>
<td>lb</td>
<td>6</td>
<td>Clinical = 100 Radiographic = 95</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcome</td>
</tr>
<tr>
<td>Subramanian et al. 2009</td>
<td>lb</td>
<td>24</td>
<td>Clinical = 100 Radiographic = 95</td>
<td>FC = MTA (P&lt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Ng and Messer 2008</td>
<td>lb</td>
<td>4-91</td>
<td>Meta-analysis</td>
<td>MTA &gt; FC (P&lt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Noorollahian 2008</td>
<td>lb</td>
<td>24</td>
<td>Clinical = 100 Radiographic = 94</td>
<td>MTA = FC (P&gt;0.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Sonmez et al. 2008</td>
<td>lb</td>
<td>24</td>
<td>Radiographic = 67</td>
<td>FC = FS = Ca(OH)₂ = MTA (P&gt;.05) for clinical and radiographic outcomes</td>
</tr>
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<td>Aeinchi et al. 2007</td>
<td>lb</td>
<td>6</td>
<td>Clinical = 100 Radiographic = 100</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcomes</td>
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<tr>
<td>Peng et al. 2006</td>
<td>IIa</td>
<td>1-74</td>
<td>Meta-analysis</td>
<td>MTA &gt; FC (P&lt;.05) for radiographic outcomes</td>
</tr>
<tr>
<td>Holan et al. 2005</td>
<td>lb</td>
<td>4 to 74 (mean=38)</td>
<td>Radiographic = 97</td>
<td>FC = MTA (P&gt;0.05) for radiographic outcomes</td>
</tr>
</tbody>
</table>
| Agamy et al. 2004<sup>a</sup> | 1b | 12 | Clinical = 100 for gray MTA and 80 for white MTA
Radiographic = 100 for gray MTA and 80 for white MTA | Gray MTA = white MTA = FC (P>.05) for clinical and radiographic outcomes |
---|---|---|---|---|

Appendix 1E. Summary of published pulp therapy of primary incisor investigations. Formocresol, FC; mineral trioxide aggregate, MTA; calcium hydroxide, Ca(OH)$_2$; ferric sulphate, FS; root canal therapy, RCT; NaOCl, sodium hypochlorite; ZOE, zinc oxide eugenol.

<table>
<thead>
<tr>
<th>Investigators</th>
<th>*Level of Evidence</th>
<th>Follow-up (months)</th>
<th>Acceptable Outcomes (%)</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Howley et al. 2012$^{19}$</td>
<td>Ib</td>
<td>15-23</td>
<td>Clinical FC pulpotomy = 100 RCT = 100 Radiographic FC pulpotomy = 89 RCT = 73</td>
<td>RCT = FC pulpotomy ($P$&gt;.05) for clinical and radiographic outcomes</td>
</tr>
<tr>
<td>Aminabadi et al. 2008$^{24}$</td>
<td>Ib</td>
<td>24</td>
<td>Clinical FC pulpotomy = 87 RCT = 96 Radiographic FC pulpotomy = 76 RCT = 91</td>
<td>RCT &gt; FC pulpotomy ($P$&lt;.05) for radiographic outcomes</td>
</tr>
<tr>
<td>Primosch et al. $^{22}$ Retrospective study</td>
<td>III (mean=34)</td>
<td>16-53</td>
<td>Radiographic RCT = 81</td>
<td></td>
</tr>
<tr>
<td>Casas et al. 2004$^{12}$</td>
<td>Ib</td>
<td>36</td>
<td>Clinical FS pulpotomy = 78 RCT = 100 Radiographic FS pulpotomy = 59 RCT = 81</td>
<td>RCT &gt; FS pulpotomy ($P$=.05) for radiographic outcomes RCT &gt; FS pulpotomy ($P$&lt;.05) for survival</td>
</tr>
<tr>
<td>Payne et al. $^{137}$</td>
<td>IIb</td>
<td>24</td>
<td>Total (clinical and radiographic) RCT = 83</td>
<td></td>
</tr>
<tr>
<td>Yacobi et al. $^{221}$</td>
<td>IIb</td>
<td>12 to 24</td>
<td>Radiographic RCT = 76 at 12 months RCT = 59 at 24 months</td>
<td></td>
</tr>
<tr>
<td>Flaitz et al. $^{259}$ Retrospective study</td>
<td>III (mean=37)</td>
<td>12-65</td>
<td>Radiographic FC pulpotomy = 72 RCT = 86</td>
<td></td>
</tr>
<tr>
<td>Coll et al. $^{207}$ Retrospective study</td>
<td>III Mean Pulpotomy = 44 IPT = 42 RCT = 46</td>
<td>Total (clinical and radiographic) FC pulpotomy = 86 IPT = 92 RCT = 78</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Chapter 2. Manuscript

Mineral Trioxide Aggregate/Ferric Sulfate Pulpotomy for Vital Primary Incisors:
A Randomized Controlled Trial

2.1. Abstract

Purpose: To compare clinical and radiographic outcomes and survival of mineral trioxide aggregate/ferric sulfate (MTA/FS) pulpotomy and root canal therapy (RCT) in carious vital primary maxillary incisors.

Methods: Asymptomatic carious vital primary incisors with pulp exposure in healthy children aged 18 to 46 months were allocated randomly to receive MTA/FS pulpotomy or RCT. FS was used to induce hemostasis after coronal pulp amputation prior to the placement of MTA in MTA/FS pulpotomy treated incisors. Clinical and radiographic post-treatment assessments occurred at 6-month intervals for up to 40 months. Two disinterested raters classified each incisor into one of the following radiographic outcomes: N=incisor without pathologic change; P_o=pathologic change present, follow-up recommended; P_x=pathologic change present, extract.

Results: Eighteen-month outcomes demonstrated no statistical difference in clinical outcomes for MTA/FS pulpotomy and RCT incisors (P=.52). No statistical difference in radiographic outcomes for MTA/FS pulpotomy and RCT for P_x outcomes was demonstrated (P=.63). Survival analysis demonstrated no statistically significant difference in survival for MTA/FS pulpotomy and RCT incisors (P=.22) over a 6 to 40 month follow-up interval.

Conclusions: MTA/FS pulpotomy is an effective treatment for carious vital primary incisors.
2.2. Objectives

1. To compare clinical and radiographic outcomes of MTA/FS pulpotomy and RCT in carious vital primary maxillary incisors.

2. To compare the survival of vital primary incisors treated with MTA/FS pulpotomy and RCT.

3. To investigate the association between radiographic findings and MTA/FS pulpotomy and RCT outcomes.
2.3. Introduction

Dental caries is the most common chronic disease in children.\textsuperscript{1} Primary maxillary incisors are teeth commonly affected by caries in young children. Caries often extends to the pulps of primary maxillary incisors necessitating either pulp therapy with restoration or extraction. The premature loss of primary maxillary incisors can adversely affect a child’s dental occlusion, ability to properly size food boluses for swallowing, speech articulation, facial esthetics and psychosocial development.\textsuperscript{2-10} Pulp treatment of cariously exposed vital primary incisors may prevent premature tooth loss as well as eliminate pain. Currently, there is a paucity of outcome investigations with regards to pulp therapy in primary incisors.

Pulpotomy is the amputation of inflamed coronal pulp tissue often followed by the placement of a medicament on the remaining vital radicular pulp tissue. The pulpotomy is the vital primary molar pulp technique used by most pediatric dentists, the most common vital primary molar pulp technique taught in pediatric dentistry specialty programs and the accepted standard of care for carious exposures of vital primary molars in North America.\textsuperscript{11-12} There is currently no consensus with regard to standard of care for treatment of vital primary incisors. Thirty-eight percent of a randomly selected sample of American Academy of Pediatric Dentistry (AAPD) members preferred pulpotomy for the treatment of vital primary incisors, 33 percent preferred root canal therapy (RCT) and 23 percent preferred indirect pulp therapy.\textsuperscript{13} Of the 33 percent of survey respondents that reported they preferred RCT, 56 percent reported that they preferred RCT as it was the preferred technique taught in their specialty program and 33 percent reported their belief
that incisor pulpotomy had poor outcomes. Little evidence exists to substantiate the perception that vital primary incisor pulpotomy has poor outcomes.

A variety of techniques have been investigated for the treatment of primary vital molars. Recently, superior outcomes for mineral trioxide aggregate (MTA) primary molar pulpotomy have been reported when compared to other common pulpotomy medicaments including formocresol (FC) and ferric sulfate (FS). ¹⁴⁻¹⁹

No outcome investigation assessing MTA pulpotomy in primary incisors has been published. MTA pulpotomy could offer a clinically efficient or cost effective therapy for vital primary incisor pulps compared to commonly used alternative therapies such as the 5-minute FC pulpotomy or RCT technique. Using FS to induce hemostasis after coronal pulp amputation prior to placement of MTA could further improve the clinical efficiency of the pulpotomy procedure. ¹⁹

2.4. Methods

Approval to perform the investigation was obtained from the Research Ethics Board of The Hospital for Sick Children, Toronto, Canada (No. 1000019443). The investigation was registered with ClinicalTrials.gov Protocol and Registration System (ID NCT02019563). The procedures, possible risks, discomforts and possible benefits were explained to the parents of the patients involved at least 24 hours prior to being offered participation into the study. Informed consent was obtained by the pediatric dentist providing oral rehabilitation.
Healthy children, 18 to 42 months of age, with one or more carious asymptomatic primary maxillary incisors where removal of dental caries was likely to produce vital pulp exposure were invited to participate in the investigation. Eligible incisors had no signs or symptoms of inflammation extending beyond the coronal pulp and were restorable. Exclusion criteria included history of spontaneous pain or lingering provoked pain, swelling, fistula or sinus tract, tenderness to percussion and pathological mobility. Incisors with preoperative radiographic evidence of periapical or periradicular radiolucency, a widened periodontal ligament (PDL) space, physiological resorption, incomplete root formation, internal or external root resorption, pulp canal obliteration (PCO) or pulp calcifications were also excluded.

Sample size was determined using a sample size calculation program (PS Power and Sample Size Calculation Program, Version 3.0.43). Sample size was calculated using outcomes from Casas et al. comparing FS and vital primary RCT outcomes.\textsuperscript{20} Sample size calculation produced a required sample size of 61 incisors per group to detect a significant difference (80% power, two-sided 5% significance level).

Five pediatric dentists (PLJ, MJC, EJB, RDF, IYS) completed all pulp therapy. Each subject was randomly allocated to one of two treatment groups using a computer generated simple random numbers sequence. Each subject received the same pulp therapy on all eligible incisors. The pediatric dentist, nurse or assistant would assign subjects to the appropriate treatment group at the time of dental surgery. The randomization sequence was concealed until treatment was initiated. One investigator
(TDN) generated the randomization sequence and performed random quality assurance checks to ensure compliance with the randomization protocol. All other contributors to the study were blinded to generation and implementation of the treatment assignment.

All treatment was provided under general anesthesia with rubber dam isolation. Following caries removal and pulp exposure, the pulp chamber was accessed using a sterile no. 56 bur in a water-cooled high-speed handpiece. The access was refined using a sterile no. 4 or 6 round bur in a slow-speed handpiece. The remaining pulp was treated using either one of the two of the following pulp therapy techniques:

**MTA/FS pulpotomy.** The coronal pulp was amputated to a depth of approximately 2 millimeters below the free gingival margin with a no. 56 high-speed bur or slow speed no. 4 or 6 round bur. Ferric sulfate 15.5 percent solution (Astringedent®, Ultradent Products Inc, Salt Lake City, UT, USA) was applied using a syringe (Dento-Infusor®, Ultradent Products Inc, Salt Lake City, UT, USA) to the radicular pulp surface for 10 to 15 seconds. The pulp chamber was then flushed with sterile water from an air-water syringe. If hemostasis was not achieved the incisor was eliminated from the study. If hemostasis was achieved, MTA (Tooth-colored ProRoot®, Dentsply, Tulsa Dental, Tulsa, OK, USA) was applied to the amputated pulp surface to a thickness of not less than 1 mm using an amalgam carrier. MTA was prepared according to the manufacturer’s instructions. Excess MTA was removed and the pulp chamber was sealed with a layer of light cured glass ionomer (Vitrebond™ Plus, 3M Dental Products, St. Paul, MN, USA). A retentive undercut was prepared within the canal using a no. 4 slow speed round bur.
This allowed for a more retentive resin core when the incisors were restored with an acid etch resin (Spectrum\textsuperscript{®} TPH\textsuperscript{®}, Dentsply/Caulk, Milford, DE, USA).

**RCT.** Pulp tissue was removed en bloc using 2 or more endodontic files (Hedstrom\textsuperscript{®}, Dentsply, Tulsa Dental, Tulsa, OK, USA). If the pulp was not fully removed in its entirety in the initial attempt, this step was repeated until all pulp tissue was extirpated. The canal was then irrigated with sterile water, lightly air dried using an air-water syringe and obturated with non-reinforced ZOE (Zinc Oxide Powder and Eugenol USP, Keystone Industries, Myerstown, PA, USA) using a spiral paste filler (Lentulo\textsuperscript{®} Spiral Filler, Dentsply, Tulsa Dental, Tulsa, OK, USA). Excess ZOE was removed and a retentive undercut was prepared within the canal using a no. 4 slow speed round bur. The pulp chamber was sealed with a thin layer of light cured glass ionomer (Vitrebond\textsuperscript{TM} Plus, 3M Dental Products, St. Paul, MN, USA) and restored with acid etch resin (Spectrum\textsuperscript{®} TPH\textsuperscript{®}, Dentsply/Caulk, Milford, DE, USA).

Incisors were assessed clinically and radiographically at 6-month intervals up to 40 months post-treatment. All follow-up data was recorded on preprinted data collection sheets, entered into a computer database (FileMaker Pro 11, FileMaker Inc, Santa Clara, MN, USA) and exported into a spreadsheet (Microsoft Excel\textsuperscript{TM} 2011, Microsoft Canada Inc, Missisauga, ON, Canada). A single investigator (TDN), who did not complete any pulp therapy or participate in radiographic evaluation, performed all the clinical assessments. At each follow-up assessment, subjects and their parents/guardians were asked to report any history of pain and/or swelling related to the pulp treated incisors.
Clinical findings assessed included presence or absence of the treated incisor, presence of restoration and if present whether the restoration was intact or not, localized gingival erythema, swelling, fistula/sinus tract, pathological tooth mobility, tenderness to percussion and tenderness to palpation. Clinical findings considered unacceptable outcomes included spontaneous pain, tenderness to percussion, fistula/sinus tract, soft tissue swelling and/or pathological tooth mobility associated with the pulp treated incisor.

Radiographic outcomes were categorized using the rating scale published in Doyle et al. Two disinterested experienced pediatric dentists (DRF, SSC) classified each treated incisor into one of three outcomes based on radiographic evaluation: N=incisor without pathologic change; Po=pathologic change present, follow-up recommended; and Px=pathologic change present, extract. Incisors rated N or Po were considered an acceptable radiographic outcome while incisors rated as Px were considered unacceptable. Raters were not given specific radiographic criteria for each outcome classification but were asked to use their clinical judgment. Raters were blinded to any patient identifying information, date of the recall and date of treatment. Evaluators assessed radiographs that were randomized by patient and date of recall.

Radiographs were taken of all treated incisors with a maxillary no. 2 occlusal phosphor storage plate (ScanX™, Air Techniques Inc, Melville, NY, USA) at each assessment. All radiographs were available in digital format and were projected onto a 21.5 inch widescreen LCD Picture Archiving and Communication System (PACS) diagnostic monitor (ZR22w Monitor, HP, Palo Alto, CA, USA) at a resolution of 1920 x 1080 @ 60
Radiographic findings assessed included presence or absence of periapical radiolucency, pathological external root resorption, widened PDL space, physiological root resorption, internal root resorption, PCO, dentin bridge and whether the restoration was intact or not.

Univariate logistic regression was used to compare outcomes of incisors treated by MTA/FS pulpotomy and RCT. Clinical and radiographic outcomes of each intervention were calculated considering previous and unacceptable outcomes at the time of recall. A binary logistic generalized estimating equation model was used to analyze predictor variables such as age, gender, tooth and treatment provider between the two treatment groups ($\alpha$-level=0.05) given as an odds ratio with 95% confidence interval (OR±95% CI). Univariate logistic regression was used to assess the association between pathological radiographic findings and radiographic outcomes. Chi-square tests were applied to assess the effect of radiographic findings on radiographic outcomes. Chi-square tests and $t$-tests were used to compare differences in demographics. All tests were interpreted at a 0.05 level of significance. The inter-rater and intra-rater reliability were calculated and interpreted using Cohen's unweighted kappa statistic. Subjects and incisors were followed up at 6-month intervals up to 40 months.

Kaplan-Meier survival curves were generated for the MTA/FS pulpotomy and RCT treatment groups. The log-rank test was used to statistically compare survival of incisors. One treated incisor was randomly selected from each subject for survival analysis to preserve independence of observations. Incisors from all recalled subjects, regardless of
follow-up time, were included in the survival analysis. All data was entered into a Microsoft Excel\textsuperscript{TM} spreadsheet and analyzed using SAS\textsuperscript{®} (SAS\textsuperscript{®}, SAS Institute Inc., Cary, NC, USA).

2.5. Results

Subjects were recruited at The Hospital for Sick Children between September 2010 and September 2012. Inclusion into the study was offered to 115 eligible subjects (54 males; 61 females). Twenty subjects (10 males; 10 females) declined participation and 25 subjects (11 males; 14 females) were declined participation into the study by the surgeon. Reasons subjects were declined participation by the surgeon included no pulp exposure upon caries removal or the pulp was necrotic. A single incisor was declined participation because hemostasis was not achieved after 10 to 15 second application of FS. A total of 171 maxillary primary incisors in 70 subjects were enrolled in the study (Figure 1). The average age of subjects at the time of treatment was 31 months with a standard deviation of 6 months and subjects ages ranged between 18 and 46 months. The MTA/FS group consisted of 100 incisors in 41 subjects (19 males; 22 females) and the RCT group consisted of 71 primary incisors in 29 subjects (14 males; 15 females). No difference in gender distribution ($P=.90$, chi-square test) or age at the time of treatment ($P=.27$, sample t-test) was shown between the MTA/FS pulpotomy and RCT groups. When the logistic regression analyses were corrected for age, gender, tooth and treatment provider, the effect of age, gender, tooth and treatment provider were not significant ($P>.05$, chi-square test).
At 12-month follow-up, 65 of 70 (93 percent) of subjects and 157 of 171 (92 percent) of incisors returned for follow-up. Subjects lost included 3 subjects that could not be contacted and 2 subjects that declined an offer for a recall appointment. Incisors lost included 12 to follow-up or drop out and 2 to trauma. At 18-month follow-up, 57 of 70 (81 percent) of subjects and 132 of 171 (77 percent) of incisors returned for follow-up. Subjects lost included 7 subjects that could not be contacted and 6 subjects that declined an offer for a recall appointment. Incisors lost included 30 to follow-up or drop-out, 7 to trauma and 2 to exfoliation (Figure 1).

No difference between MTA/FS pulpotomy and RCT clinical outcomes were demonstrated at 12-month ($P=.51$, chi-square test) and 18-month ($P=.52$, chi-square test) follow-up. Acceptable clinical outcomes were demonstrated in 98 percent (88 of 90) of MTA/FS pulpotomy and 100 percent (67 of 67) of RCT incisors at 12-month and 96 percent (68 of 71) of MTA/FS pulpotomy and 99 percent (60 of 61) of RCT incisors at 18-month follow-up. Of the 4 incisors considered to have an unacceptable clinical outcome, 2 incisors were associated with a fistula/sinus tract, 1 incisor was associated with a history of spontaneous pain and tenderness to percussion and 1 incisor was associated with soft tissue swelling, pathological tooth mobility and tenderness to percussion.

Radiographic outcomes were not statistically different between MTA/FS pulpotomy and RCT incisors for $P_x$ outcomes at 12-month ($P=.21$, chi-square test) and 18-month ($P=.63$, chi-square test) follow-up (Table 1 and 2). Acceptable radiographic outcomes of incisors
rated N or P o comprised 97 percent (87 of 90) of MTA/FS pulpotomy and 91 percent (61 of 67) of RCT incisors at 12-month follow-up and 92 percent (65 of 71) of MTA/FS pulpotomy and 89 percent (54 of 61) of RCT incisors at 18-month follow-up.

Incisors demonstrating any pathological change or rated P o or P x comprised 8 percent (7 of 90) of MTA/FS pulpotomy and 22 percent (15 of 67) of RCT incisors at 12-month follow-up and 10 percent (7 of 71) of MTA/FS pulpotomy and 21 percent (13 of 61) of RCT incisors at 18-month follow-up. RCT incisors were statistically significantly more likely to demonstrate any pathologic radiographic change (P o or P x) than MTA/FS pulpotomy incisors at 12 months post-treatment (P=.04, chi-square test) . A similar tendency was not demonstrated at 18-months post-treatment (P=.01, chi-square test).

Incisors exhibiting a periapical radiolucency (P<.0001; chi-square test), external root resorption (P<.0001; chi-square test), widened PDL space (P<.0001; chi-square test) or internal root resorption (P=.009; chi-square test) on post-treatment radiographic examination were significantly more likely to have a P x outcome.

Intra-rater agreement was perfect for incisors with outcome P x (K=1.0, Cohen’s kappa). Inter-rater agreement was almost perfect for incisors with outcome P x (K=0.84; Cohen’s kappa).

Outcome data from treated incisors of 66 of 70 (94 percent) of subjects who returned for recall during the 6 to 40 month follow-up period contributed to the survival analysis. To
ensure statistical independence of the observations, each subject contributed only one incisor to the survival analysis by random draw. Thirty-eight observations for MTA/FS pulpotomy and 28 observations for RCT incisors were available for survival analysis. Incisors extracted due to unacceptable clinical outcomes or rated as $P_x$ were considered to not meet the criteria for survival. Incisors were censored if lost to follow-up, exfoliated, lost to trauma or had a non-occurrence of a failure before the trial end. Kaplan-Meier survival curves for treated molars in each group are shown in Figure 3. The survival rate was 0.94 for MTA/FS pulpotomy and 0.92 for RCT at 12-month follow-up and 0.87 for MTA/FS pulpotomy and 0.88 for RCT at 18-month follow-up. Survival analysis demonstrated no significant difference in survival for MTA/FS pulpotomy and RCT incisors ($P=.27$, log-rank test) over a 6 to 40 month follow-up interval.

2.6. Discussion

Twelve- and 18-month clinical and radiographic outcomes and survival analysis demonstrated no statistically significant difference between MTA/FS pulpotomy and RCT treated asymptomatic vital primary incisors with carious pulp exposure. However, RCT treated incisors demonstrated on radiographic examination, significantly more pathological changes ($P_o$ or $P_x$) than MTA/FS pulpotomy treated incisors at 12 months post-treatment. This difference was not demonstrated at 18-months post-treatment.

Only 3 other randomized controlled trials have compared pulpotomy and RCT outcomes in vital primary incisors. Howley et al. compared the clinical and radiographic outcomes of FC pulpotomy and RCT up to 23 months post-treatment. Clinical and radiographic
outcomes of FC pulpotomy and RCT were not statistically different ($P>0.05$). Aminabadi et al. also compared the clinical and radiographic outcomes of FC pulpotomy and RCT.\textsuperscript{21} Radiographic outcomes were significantly more favorable for RCT than FC pulpotomy 2-years post-treatment ($P<.05$). Casas et al. compared FS pulpotomy and RCT outcomes in asymptomatic vital primary incisors.\textsuperscript{20} The study found no significant difference in clinical or radiographic outcomes of FS pulptomy and RCT. However, RCT incisors demonstrated a significantly higher survival rate than FS pulpotomy incisors 2-years post-treatment ($P=.04$). Methodology and small sample size issues limit the interpretatively of the outcomes from Aminabadi et al. and Casas et al.

Esthetics is a reported concern of clinicians and parents in pulp treated primary incisors.\textsuperscript{22} MTA, ZOE, Endoflas and iodoform are obturation materials reported to have the potential to discolor coronal tooth structure in primary teeth. Tooth-colored ProRoot MTA has demonstrated gray discoloration in both in vivo and in vitro studies.\textsuperscript{23-25} The mechanism of MTA discoloration is still not fully understood, but recent evidence suggests tooth discoloration is associated with metallic black bismuth oxide formed from the reaction of bismuth oxide with light in a non-oxygenated environment.\textsuperscript{26-28} Prominent gray discoloration of MTA can cause teeth to change in color or show through restorations and effect esthetics. Discoloration of MTA may not be a concern in the future as manufactures are distributing MTA where zirconium oxide has replaced bismuth oxide as the radiopacifier. Also, alternative materials are being manufactured and distributed (e.g. BioDentine and Portland cement) that are purported to have similar properties to MTA and are color-stable.\textsuperscript{27}
There is a perception among some pediatric dentists “that pulpotomies do not work in primary incisors.” The AAPD guideline on pulp therapy states a pulpotomy is indicated when caries removal results in vital pulp exposure in primary teeth. MTA/FS pulpotomy is an acceptable pulp therapy technique for asymptomatic vital primary incisors with carious pulp exposure. The advantage of MTA/FS pulpotomy when compared to RCT technique in primary incisors is clinical efficiency.

2.7. Conclusion

MTA/FS pulpotomy is an effective treatment for carious vital primary incisors with pulp exposure.

2.8. Acknowledgements

The investigators would like to thank Drs. Sonia Chung and David Farkouh for rating radiographs and Drs. Randi Fratkin and Ihab Suwwan for providing clinical care to a portion of the study subjects. We would also like to thank Derek Stephens for statistical support throughout the investigation.
2.9. References


2.10. Figures & Tables

Figure 1. Flowchart demonstrating the number of incisors and subjects recruited, treated and recalled at 12- and 18-month follow-up.
Table 1 and 2. Radiographic outcomes of MTA pulpotomy and RCT treated incisors at 12- and 18-month follow-up.

### 12-Month Radiographic Outcomes

<table>
<thead>
<tr>
<th></th>
<th>MTA/FS ( n = 90 )</th>
<th>RCT ( n = 67 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>83 (92%)</td>
<td>52 (78%)</td>
</tr>
<tr>
<td><strong>Po</strong></td>
<td>4 (5%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td><strong>Px</strong></td>
<td>3 (3%)</td>
<td>6 (9%)</td>
</tr>
</tbody>
</table>

N=normal incisor without pathologic change; Po=pathologic change present, follow-up recommended; Px=pathologic change present, extract. 
\( n \)=number of incisors in each treatment group. 
There was no statistically significant difference between MTA pulpotomy and RCT incisors for Px outcomes \( P=.21 \).

### 18-Month Radiographic Outcomes

<table>
<thead>
<tr>
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<th>MTA/FS ( n = 71 )</th>
<th>RCT ( n = 61 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>64 (90%)</td>
<td>48 (79%)</td>
</tr>
<tr>
<td><strong>Po</strong></td>
<td>1 (1%)</td>
<td>6 (10%)</td>
</tr>
<tr>
<td><strong>Px</strong></td>
<td>6 (9%)</td>
<td>7 (11%)</td>
</tr>
</tbody>
</table>

N=normal incisor without pathologic change; Po=pathologic change present, follow-up recommended; Px=pathologic change present, extract. 
\( n \)=number of incisors in each treatment group. 
There was no statistically significant difference between MTA pulpotomy and RCT incisors for Px outcomes \( P=.64 \).
Figure 2a and 2b. Example of incisors treated with MTA/FS pulpotomy (top) and RCT (bottom).
Figure 3. Kaplan-Meier Curves for MTA/FS pulpotomy and RCT treated primary incisors in subjects returning 6 to 40 months post-treatment. Censored subjects are indicated with a “+”.
2.11. Appendix

2.11.1. Protocol

A prospective outcome investigation of mineral trioxide aggregate pulpotomy in primary maxillary incisors

Principal investigator: Dr Peter L Judd

Co-investigators: Dr Michael J Casas, Dr. Edward J Barrett

Statement of the problem

The primary maxillary incisors are important in masticatory function, occlusal development, articulation and self-esteem\(^1\). Cariously exposed vital pulps of primary incisors require pulp treatment to avoid infection, pain and premature tooth loss. Unfortunately, there is a paucity of investigations of maxillary incisor pulp treatment.

The formocresol pulpotomy is the most popular vital primary molar pulp technique in North America and the UK.\(^2,3\) However, concerns about the safety of the active component of formocresol, 19% formalin, persist.\(^4\) Concerns include immune sensitization, mutagenicity and carcinogenicity.\(^5,6\) Interactions between formaldehyde and rat DNA have produced experimental tumours. As a consequence, formaldehyde represents a substantial human carcinogenic risk.\(^7\) The International Agency for Research
on Cancer (IARC) of the World Health Organization classified formaldehyde as a known human carcinogen.\(^8\)

The root canal/zinc oxide and eugenol (RCT/ZOE) technique has been shown to have the best outcomes and significantly higher survival rates than other vital pulp techniques for treatment of carious exposed, inflamed pulps of the primary incisors.\(^1,9\) Consequently, it is the clinical standard for vital pulp therapy for primary incisors at The Hospital for Sick Children. However, RCT/ZOE has not been accepted into the mainstream of the dental profession because it is a technically demanding procedure, expensive to provide and requires a longer treatment time than pulpotomy procedures.

Mineral trioxide aggregate (MTA) is dental cement that consists of discrete crystals (87% calcium, 3% silica, 10% oxygen) and amorphous structure (33% calcium, 49% phosphate, 2% carbon, 3% chloride, 6% silica). It has a pH of 12.5 and sets to solid consistency in under three hours with a compressive strength of 40 MPa at 24 hours.\(^10\) MTA is biocompatible and is associated with dental hard tissue formation in contact with the dental pulp.\(^10\)\(^-\)\(^12\) MTA pulpotomy produced superior clinical and radiographic outcomes in primary molars.\(^1,12\)\(^,13\) If MTA primary molar pulpotomy outcomes were replicated in primary incisor pulpotomies, a simpler, less time intensive cost-effective therapy for vital primary incisor pulps would be available for children with primary incisor caries. Furthermore, using ferric sulfate (FS) to induce haemostasis after coronal pulp amputation prior placement of MTA would improve the clinical efficiency of the
procedure. FS application prior to MTA placement did not significantly alter outcomes for MTA primary molar pulpotomies.\textsuperscript{13}

**Objective of this investigation**

The objective of this investigation is to compare statistically the clinical and radiographic outcomes of MTA pulpotomies and RCT/ZOE in primary maxillary incisors. This investigation will compare one and two year outcomes of conventional RCT/ZOE (control) with the MTA pulpotomy. The experimental group will have MTA applied to amputated pulp stump after hemostasis is achieved using FS. The control group will have the pulp tissue removed completely and the empty canal filled with ZOE.

**Materials and Methods**

Typical children with one or more carious primary maxillary incisors where removal of dental caries will likely to produce a vital pulp exposure will be eligible for the protocol. The incisors included in the study will exhibit no radiographic evidence of physiological or pathological root resorption or periapical radiolucencies. Children with maxillary incisors that present with an associated swelling will not be included in the study. This investigation will be submitted to and approved by the Research Ethics Board at The Hospital for Sick Children prior to commencement. A consent form will be completed and signed for each subject prior to treatment. Dentists will offer inclusion to eligible subjects and their parents in person at the time of initial consultation and treatment planning for oral rehabilitation for early childhood caries. Only dentists will offer
inclusion in this trial. Specialist dentists who complete or supervise treatment for eligible children will acquire consent.

The pulp technique used will be determined by random selection and will be consistent for each child (each child will receive the same pulp treatment on all eligible incisors). The inclusion criteria for pulp treatment are the same for all eligible incisors: asymptomatic exposure of vital pulp by caries, no clinical or radiographic evidence of pulp degeneration (such as internal/external root resorption and/or periapical bone destruction or swelling) and possibility of proper restoration of the tooth.

The pulp treatment techniques will be carried out as follows:

1. ZOE/RCT (control)
   A. After complete removal of all caries, open pulp chamber
   B. Pulp tissue removed in its entirety with two or more Haedstrom endodontic files
   C. Canal irrigated with water followed by light air dry
   D. Canal filled with non-reinforced ZOE using spiral paste filler
   E. Excess ZOE removed from coronal chamber and retentive core prepared using #4 slow speed round bur
   F. Apply thin layer of light-cured glass ionomer dentin liner
   G. Tooth restored with acid etch resin restoration

2. MTA/FS pulpotomy
   A. After complete removal of all caries, open pulp chamber
B. Remove coronal pulp to a depth of 2mm below free gingival margin with high speed bur

C. Apply 15.5% solution of FS (Astringedent®) using Dento-Infusor® syringe to amputated pulp surface for 10-15 seconds

D. Flush Astringedent® from pulp chamber with water.
   (i) If bleeding does not stop after a 15 second application of Astringedent®, then proceed to a primary ZOE/RCT or extraction.
   
   *This tooth is no longer eligible for this study.*

E. Apply MTA paste to cover over the exposed amputated pulp surface and a margin of not less that 1mm beyond the pulp dentin interface

F. Apply thin layer of light-cured glass ionomer dentin liner

G. Restore with acid etch resin

One hundred sixty subjects will be enrolled in the investigation. Subject will reside in the GTA at time of inclusion to increase the likelihood of return for reassessment. Subjects will be English-speaking to allow for ease of follow-up assessment. Subjects will be reassessed at 6, 12 and 24 months after treatment for routine clinical and radiographic follow-up. Sample wastage (subjects lost to follow-up) in a two year prospective longitudinal pulp outcome study has been demonstrated to be approximately 50 per cent at this institution. Numbers of subjects and individuals excluded from the investigation (did not meet inclusion criteria, refused to participate, lost to follow-up) will be recorded.
Data analysis

The data unit for survival analyses will be a single primary maxillary incisor from each child to preserve the independence of the observations. For subjects with multiple treated incisors, one incisor will be selected for inclusion by random draw. Treated incisors will be compared to each other for survival and presence of a number of clearly defined radiographic and clinical signs. Surviving teeth will be categorized and tabulated according to clinical and radiographic signs. Radiographic analysis of treated teeth will be subjected to blinded assessment by independent expert raters. Their assessments will be subjected to measures of inter-rater and intra-rater reliability. Outcome measures will be statistically compared. The generalized estimating equation will be employed due to the lack of independence of the observations for statistical comparisons of clinical and radiographic outcomes.

References


2.11.2. Research consent form

Title of Research Project:
A prospective outcome investigation of mineral trioxide aggregate pulpotomy in primary maxillary incisors

Investigator(s):
Dr. Peter L Judd, Dentist-in-Chief 416-813-6008
Dr. Michael J. Casas, Director of Clinics 416-813-6018
Dr. Ed Barrett, Staff Pediatric Dentist 416-813-8220

Purpose of the Research:
This research investigation looks at the effectiveness of an alternative to our standard root canal technique for upper front teeth. Each technique is designed to eliminate the widespread use of formaldehyde (a known hazardous chemical) products in children. We demonstrated previously the effectiveness of this alternative root canal technique in children’s back (molars) teeth. This alternative technique uses a material that promotes nerve healing, is technically less demanding and requires less treatment time than our standard root canal technique. A root canal procedure will only be performed if it is required and the tooth is restorable. If the tooth is not restorable or it is infected the tooth will require extraction.

Description of the Research:
Approximately 160 children will participate in the study; eighty case subjects and eighty control subjects. The child’s health record will be viewed for research purposes. Your dentist will decide on the need for root canal treatment based upon the amount of decay in your child’s front teeth. This will be decided after your child is asleep.

1. If your child’s tooth decay is mild, root canal treatment will not be needed and your child will not be suitable for this trial.
2. If tooth decay is too severe, extraction will be needed and your child will not be suitable for this study.
3. If the decay is moderate, root canal treatment is needed because decay has reached the nerve.

Two methods of root canal treatment are being compared in this study:
1. mineral trioxide aggregate (MTA) root canal treatment
2. zinc oxide and eugenol root canal treatment (a standard SickKids technique)

The dentist will randomly (like a toss of a coin) select from the two choices for the treatment that your child will receive. All front teeth treated in this study will be examined at follow-up visits and x-rayed at the 6, 12 and 24 month anniversaries of your child’s treatment date or until they are ready to fall out naturally. This is the routine schedule that we following for all root canal treated teeth.
Potential Harms:
We know of no harm that taking part in this study could cause your child. However, no root canal technique is successful in all cases and occasionally a tooth may need to be extracted. Although MTA has been shown to be an effective technique in the molar teeth, it is possible that it will not be as effective as the standard of care.

Potential Discomforts or Inconvenience:
There are no anticipated discomforts associated with either technique that is not within the normal experience of root canal therapy in children. Although most children do not experience any discomfort, minor pain medication (e.g. Tempra) may be required within the first day or two following treatment.

Potential Benefits:
We anticipate that this alternate root canal technique will be as effective as the standard method based on our recently completed study using this technique on children’s molars. This study demonstrated superior results to the standard root canal technique when used in back teeth. Furthermore, this technique takes less time which means reduced treatment time in the dental chair or time spent under a general anesthetic. If this technique produces similar results in treating the front teeth, then this may become the new standard of care.

To individual subjects:
You (your child) will not benefit directly from participating in this study other than the possibility of a better successful outcome than the standard root canal technique.

Results of the research study will be available should you be interested.

To society:
Dentists are more likely to use this alternative technique which is technically less demanding, less expensive and requires less treatment time (important in treating young children) and helps to eliminate the widespread use of formaldehyde (a known hazardous chemical) products in children.

Alternatives to participation:
As discussed at your child’s consultation appointment, alternative treatments at Sick Kids are zinc oxide-eugenol root canal treatment (one of the treatments in this study) or ferric sulfate root canal treatment or extraction, which is acceptable therapy for teeth with decay that reaches the nerve.

Confidentiality:
We will respect your privacy. No information about who you are (your child is) will be given to anyone or be published without your permission, unless the law requires us to do this. For example, the law requires us to give information about you (your child) if a child has been abused, if you (your child) has an illness that could spread to others, if you or someone else talks about suicide (killing themselves), or if the court orders us to give them the study papers.

Sick Kids Clinical Research Monitors may see your child’s health record to check on the study.
By signing this consent form, you agree to let these people look at your child’s records. We will put a copy of this research consent form in your child’s patient health records. We will give you a copy for your files.

The data produced from this study will be stored in a secure, locked location. Only members of the research team (and maybe those individuals described above) will have access to the data. This could include external research team members. Following completion of the research study, the data will be kept as long as required and then destroyed as required by Sick Kids policy. Published study results will not reveal your identity.

**Reimbursement:**
We will reimburse you $10.00 for each recall visit to defray your costs of transportation to the hospital and in recognition of your time and effort.

**Participation:**
If you choose to let your child participate in this study, you can take your child out of the study at any time. The care your child gets at Sick Kids will not be affected in any way by whether you take part in this study.

New information that we get while we are doing this study may affect your decision to take part in this study. If this happens, we will tell you about this new information. And we will ask you again if you still want to be in the study.

In some situations, the study doctor may decide to stop the study. This could happen even if the treatment given in the study is helping your child. If this happens, the study doctor will talk to you about what will happen next.

If your child becomes ill or are harmed because of study participation, we will treat your child for free. Your signing this consent form does not interfere with your legal rights in any way. The study staff, any people who gave money for the study, or the hospital are still responsible, legally and professionally, for what they do.

**Conflict of Interest:**
Dr. Peter Judd and the other research team members, have no conflict of interest to declare.

**Sponsorship:**
Dr. Peter Judd and the Department of Dentistry at the Hospital for Sick Children are the sponsor and funder of this research study.
Research Ethics Board

Consent:
By signing this form, I agree that:
1) You have explained this study to me. You have answered all my questions.
2) You have explained the possible harms and benefits (if any) of this study.
3) I know what I could do instead of having my child take part in this study. I understand that I have the right to refuse to let my child take part in the study. I also have the right to take my child out of the study at any time. My decision about my child taking part in the study will not affect my child’s health care at Sick Kids.
4) I am free now, and in the future, to ask questions about the study.
5) I have been told that my child’s medical records will be kept private except as described to me.
6) I understand that no information about my child will be given to anyone or be published without first asking my permission.
7) I have read and understood pages 1 to 4 of this consent form. I agree, or consent, that my child___________________ may take part in this study.
8) If I have any questions I can call Dr. Peter Judd at 416-813-6008.

____________________  ____________________________
Printed Name of Parent/Legal Guardian  Parent/Legal Guardian’s signature & date

____________________  ____________________________
Printed Name of person who explained consent  Signature & date

____________________  ____________________________
Printed Witness’ name (if the parent/legal guardian does not read English)  Witness’ signature & date

If you have any questions about this study, please call __________________ at__________________

If you have questions about your rights as a subject in a study or injuries during a study, please call the Research Ethics Manager at 416-813-5718.
2.11.3. Procedural data collection form

DATA CAPTURE FORM

For SickKids dental staff use only

Circle teeth treated and code the pulp technique used (bold) as defined:

**MTA/FS:** MTA pulpotomy with FS

**ZOE/RCT:** Zinc oxide and eugenol root canal treatment

<table>
<thead>
<tr>
<th>52</th>
<th>51</th>
<th>61</th>
<th>62</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Submit this form to Dr. Peter Judd upon completion of treatment
### 2.11.4. Clinical data collection form

#### CLINICAL EVALUATION DATA FORM

<table>
<thead>
<tr>
<th>Tooth #</th>
<th>52</th>
<th>51</th>
<th>61</th>
<th>62</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Is the tooth present?</strong>&lt;br&gt; <em>If no, explain (i.e. exfoliated, lost to trauma or extracted)</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is the restoration intact?</strong>&lt;br&gt; <em>If no, explain (i.e. recurrent caries, missing or mobile restoration)</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is there erythema, swelling or a fistula?</strong>&lt;br&gt; <em>If yes, which one and explain.</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is there pathological tooth mobility?</strong>&lt;br&gt; <em>If yes, explain.</em></td>
<td>None</td>
<td>M1</td>
<td>M2</td>
<td>M3</td>
</tr>
<tr>
<td><strong>Is there percussion sensitivity?</strong>&lt;br&gt; <em>If yes or can’t tell, explain.</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is there palpation sensitivity?</strong>&lt;br&gt; <em>If yes or can’t tell, explain.</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is there a history of pain?</strong>&lt;br&gt; <em>If yes or can’t tell, explain.</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is there a history of swelling?</strong>&lt;br&gt; <em>If yes or can’t tell, explain.</em></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.11.5. Radiographic data collection form

<table>
<thead>
<tr>
<th>Tooth #: 52 51 61 62</th>
<th>Tooth #: 52 51 61 62</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating: N P₀ Pₓ Pₓ</td>
<td>Rating: N P₀ Pₓ Pₓ</td>
</tr>
<tr>
<td>Periapical radiolucency:</td>
<td>present absent</td>
</tr>
<tr>
<td>Pathological external root resorption:</td>
<td>present absent</td>
</tr>
<tr>
<td>Widened PDL:</td>
<td>present absent</td>
</tr>
<tr>
<td>Physiological root resorption:</td>
<td>present absent</td>
</tr>
<tr>
<td>Internal root resorption:</td>
<td>present absent</td>
</tr>
<tr>
<td>Pulp canal obliteration:</td>
<td>present absent</td>
</tr>
<tr>
<td>Dentin bridge:</td>
<td>present partial absent</td>
</tr>
<tr>
<td>Restoration Intact:</td>
<td>intact not-intact</td>
</tr>
</tbody>
</table>
2.11.6. Ethics approval

PROTOCOL REFERENCE # 29065

June 6, 2013

Dr. Peter Judd    Dr. Trang Nguyen
FACULTY OF DENTISTRY  FACULTY OF DENTISTRY

Dear Dr. Judd and Dr. Trang Nguyen,

Re: Administrative Approval of your research protocol entitled, “A prospective outcome investigation of mineral trioxide aggregate pulpotomy in primary maxillary incisors”

We are writing to advise you that the Office of Research Ethics (ORE) has granted administrative approval to the above-named research protocol. The level of approval is based on the following role(s) of the University of Toronto (University), as you have identified with your submission and administered under the terms and conditions of the affiliation agreement between the University and the associated TAHSN hospital:

- Graduate Student research - hospital-based only
- Storage or analysis of De-identified Personal Information (data)

This approval does not substitute for ethics approval, which has been obtained from your hospital Research Ethics Board (REB). Please note that you do not need to submit Annual Renewals, Study Completion Reports or Amendments to the ORE unless the involvement of the University changes so that ethics review is required. Please contact the ORE to determine whether a particular change to the University's involvement requires ethics review.

Best wishes for the successful completion of your research.

Yours sincerely,

Daniel Gyewu
REB Manager

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