THE INFLUENCE OF INTRAOPERATIVE FACTORS ON CLINICAL OUTCOME OF VITAL PULP THERAPY

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A thesis submitted to the faculty at the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Science in the School of Dentistry (Endodontics).

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ABSTRACT

Tam Minh Trinh: The Influence Of Intraoperative Factors On Clinical Outcome Of Vital Pulp Therapy
(Under the direction of Asma Khan)

Endodontics is the specialty of dentistry aimed at preserving the natural tooth through the diagnosis, prevention, and/or treatment of pathology associated with the dental pulp and peri-apical tissues. While the pulp is an immunocompetent tissue that has the ability to heal, the prognosis of vital pulp therapy continues to be debated. The inability to accurately assess the degree of inflammation of cariously exposed pulps leads to aggressive and expensive treatment. This project seeks to identify the intraoperative factors that may affect outcome of Vital Pulp Therapy (VPT) on mature teeth with cariously exposed pulps.

Our specific aims are to identify intraoperative factors influencing outcome of VPT on fully developed permanent teeth and determine the best practice protocol of VPT. A prospective observational study of VPT on mature teeth with exposed pulp will be conducted in the DDS clinic at the School of Dentistry. Standardized questionnaire and protocols will be used to create a database for evaluating influencing intraoperative factors affecting outcomes of VPT on fully developed permanent teeth. The evaluated intraoperative factors were not statistically significant on the outcome of treatment. This prospective observational study showed that with thorough case selection and appropriate protocol, VPT is a predictable treatment option to pulp exposures on asymptomatic teeth with matured apices.

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Section 1.1 Introduction

Endodontics is the specialty of dentistry aimed at preserving the natural tooth through the diagnosis, prevention, and treatment of pathology associated with the dental pulp and peri-apical tissues (1). Endodontic treatments consist of vital pulp therapy {VPT [direct pulp capping (DPC); partial pulpotomy (Cvek pulpotomy); or complete pulpotomy]}, non-vital pulp therapy [non-surgical root canal therapy (NSRCT) and retreatment (Re-Tx)], and periapical microsurgery. To perform the suitable endodontic treatment, the dental practitioner must first diagnose the pulpal and periapical status of the teeth in question. Accurate diagnosis leads to biologically based treatment regimens to prevent or treat apical periodontitis, which ultimately preserves the natural dentition.

Teeth have been regarded as vestigial sensors that have gradually adapted to synthesize mineralized matrix and eventually neurosensory organs for mastication (2). The natural tooth is composed of a series of mineralized tissues comprised of enamel, dentin, and cementum that surround a non-mineralized tissue, the dental pulp. The dental pulp is a specialized connective tissue located in the central part of the tooth. The pulp proper is the central mass of the pulp that consist of loose connective tissue, blood vessels, and nerves (3). Within the dental pulp, there are many components such as odontoblast, pulp fibroblast, macrophage, dendritic cell, lymphocyte, mast cell, ground substance, and pulp interstitium. The most specialized cell of the dental pulp is odontoblast. Odontoblast are responsible for dentinogenesis at tooth development and during aging (4). The pulp and dentin function as a

unit and are considered the “dentin-pulp complex”, and the odontoblasts are a vital part of this system. The odontoblasts are located in the periphery of the dental pulp tissue, with extension into the inner part of dentin. Dentin is produced by odontoblast and the dental pulp is protected by the dentin and enamel. Teeth are faced with myriad of injuries that threaten the vitality of the pulp. The dental pulp, similar to other connective tissues, has the capacity to mount proper inflammatory/immune responses against injury and microbial infections and to recover from them (5-7).

The healing potential of the dental pulp is well established. Healing includes the processes of resolution, regeneration, and repair. One of the main functions of the inflammatory process is to heal injured tissue. Healing may occur as a result of either resolution or repair. Resolution can only occur if regeneration is possible. The more highly specialized the tissue, the less is the capacity for regeneration (8). Similar to all other connective tissues, repair of tissue injury begins with ingestion of debris by macrophages, followed by proliferations of fibroblasts, capillary buds, and the formation of collagen (4, 8, 9). Being a highly specialized connective tissue, the dental pulp has a disadvantage of insufficient collateral circulation (9), which reduced its healing capacity as seen with matured apices of permanent teeth compared to immature apices teeth (3, 10-14).

The dynamic relationship of the pulp-dentin complex suggests an integral function of the pulp, which includes the formation and the nutrition of the dentin and the innervation and defense of the tooth. Odontoblasts represent an important element in the dentin-pulp complex. Residing in the periphery of the pulp tissue, odontoblasts have processes that extend into the dentin. The interdependence of the “pulp-dentin complex” suggests that impacts on dentin may affect the pulpal components and disturbances in the dental pulp will

affect the quantity and quality of the dentin production. Mutually linked, injuries to either will affect both components (2, 3).

Direct exposures to the oral cavity are a threat to the dental pulp tissue as the lack of epithelia and the slow rate of odontoblast's dentin bridge formation cannot quickly hinder the ingress of noxious microbes (6, 7). Dentin formation is imperative to the defense of the pulp. Depending on when it was formed, dentin can be classified as primary, secondary, or tertiary. Primary dentin is the regular tubular dentin formed before eruption. Secondary dentin is the regular circumferential dentin formed after tooth eruption, whose tubules remain continuous with that of primary dentin. Tertiary dentin or reparative dentin is the irregular dentin that is formed in response to abnormal stimuli or injury, such as caries, trauma, restorative procedures, and excessive tooth wear (4). Chronic pulpal inflammation caused by deep caries produces reparative dentin (9). Pulpal injuries such as dental caries are localized, destructive, and result in progressive infection of the tooth structure. If left untreated, dental caries will progress into the pulp resulting in pain caused by pulpal inflammation, necrosis, periapical abscess, and life threatening infection. The progressing carious lesion elicits an inflammatory response characterized by reparative dentin formation or pulpal pain if the inflammation progress further into the pulp (4, 9, 15). Inflammation is a complex protective response aimed at eliminating noxious stimuli produced by pathogens and reestablishing pulpal homeostasis (7-9). After removing the noxious stimuli and partially inflamed pulp, the remaining healthy tissue can be conserved to produce a hard tissue barrier that seals and protects the pulp from future microbial ingress.

Section 1.2 Etiology

Traumatic injuries can affect the pulp to various degrees. Mild injuries often result in brief loss of sensation, but do not adversely affect the vascularity. The dental pulp is a dynamic tissue that responds to external injuries in varying ways (16). Such injuries are categorized as acute or chronic. Acute injuries to the dental pulp are traumatic injuries resulting in damages of many dental and perapical structures. Traumatic injuries are life-long injuries and require understanding of healing patterns of the dental pulp for proper management. In many cases, dental trauma results in endodontic treatments for permanent teeth that are caries-free.

Widely regarded as the most prevalent chronic disease in both children and adults, dental caries is a transmissible bacterial disease process caused by acids from cariogenic bacterial metabolism demineralizing tooth structure (17, 18). Dental caries is an etiological factor that can lead to pulpal and periapical pathologies. It is well recognized that the pulp has the capacity to trigger an inflammatory response that is both cellular and humoral (9). In the progressing front of the carious lesion, bacterial enzymes, toxins, and metabolites are released that stimulate nearby pulpal tissue (7, 9). Three basic reactions tend to protect the pulp against caries: (a) inflammatory and immune reactions, (b) a decrease in dentin permeability, and (c) tertiary dentin formation (4). These protective functions are significantly reduced when the remaining dentin thickness is minimal (19). If left unhindered, bacterial invasion into the pulp will activate various complement pathways, which can produce a protective or injury response to the pulp (7). Tissue conservation and preventative management of caries progression are treatment of dental caries for such patients (17, 18).

Section 1.3 Treatments of Permanent Teeth with Pulpal Pathologies

Endodontic pathologies involve either the pulp and/or periapical structures of the tooth. Suitable endodontic treatment depends on the accurate diagnosis of the pulp and periapical status. According to the American Association of Endodontists' (AAE) definition, asymptomatic irreversible pulpitis is a clinical diagnosis based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing and that root canal treatment is indicated (20). These teeth are not associated with clinical symptoms and usually respond normally to thermal testing. However, these teeth have trauma or deep caries that would likely result in exposure following caries excavation. This diagnostic category, along with lack of diagnostic tests that accurately differentiate between normal and diseased pulps, has led to a treatment conundrum. While most dentists are aware that the pulps may have the ability to recover, they also know that the pulps may become necrotic leading to periapical disease. As such, pulpectomy and non-surgical root canal therapy are the conventional treatments of asymptomatic permanent teeth with carious pulp exposure. (20-22).

In the past two decades, there have been tremendous advances in our clinical "tools" (ie, materials, instruments, and medications) and understanding of trauma and tissue engineering fields that can be applied to regeneration of a functional pulp-dentin complex. Development of new materials has led to resurgence in treatment alternatives with asymptomatic permanent teeth with carious pulp exposures (5-7, 23). VPT have been traditionally used on immature permanent teeth with aims of preserving the vitality and function of the remaining pulp tissue to provide maturation of the roots and apices (24). Such applications of VPT are widely seen in permanent mature apices teeth with predictable success (12, 25, 26).

Section 1.4 High Value Care and Public Health Dentistry

Increasing costs of health care are a cause of concern to patients, governments, and the health profession around the world (27). VPT may provide a treatment alternative to root canal therapy. When completed under the prescribed protocol, VPT may be completed in one appointment at greatly reduced cost. VPT, then, is an example of a High Value Care (HVC) procedure. HVC refers to the method that assesses the benefits, harms, and costs of interventions and thus predicts care that adds the greatest value to the patient (28). When evaluating HVC with respect to VPT, we are able to offer patients a lower cost procedure that maintains the vital, immunocompetent pulp and greater resistant to masticatory function by preserving greater tooth structure, than is usually seen in the NSRCT procedure.

VPT has a substantial impact on health care cost and delivery from the public health perspective. Many patients avoid dental care due to access to trained specialists and financial burden (29, 30). The cost of VPT compared with NSRCT is significantly less expensive for patients. A recent study reported direct pulp capping (DPC) to be more cost-effective than conventional root canal therapy (RCT). Teeth treated by DPC were retained for long periods of time at significantly reduced lifetime costs compared with teeth treated by RCT (31).

VPT is one of the few procedures in dentistry that has reduced the cost of technology and delivery of services to prevent oral disease (apical periodontitis). VPT treatment maintains a short learning curve for the practitioner, a relatively low cost armamentarium, and can be provided in a single appointment in comparison to traditional NSRCT. This may provide an alternative treatment to patients with limited access to care and financial challenges. Therefore, VPT treatment avoid tooth loss and the need to restore the edentulous

spaces at a much higher cost (27, 30). With greater avenue for practitioners to provide preventative treatments to address

Section 1.5 Biological Based Treatments

The biological objective of VPT is preserving the vitality of the pulp to allow continue development of the root and defense from bacterial insult. The clinical aim of VPT is promoting protective hard tissue barrier formation after injury. By debriding the area of bacteria and noxious stimuli, the pulp is provided a chance to heal (5, 6). Tissue repair is preceded by inflammation (8). The process starts when odontoblast-like cells recruited from the cell-rich zone and subodontoblastic layer migrate to the site of injury for repair (32).

Partial pulpotomy, full pulpotomy or pulp amputation are procedures defined as "the removal of the coronal portion of the vital pulp as a means of preserving the vitality of the remaining radicular portion" (33). In this situation, the apical portion of the pulp is assumed to be healthy and the coronal pulp is inflamed (15). Hemorrhage control has been a surrogate indicator for removal of sufficient inflamed tissue and etiological factors (34). After complete amputation of the coronal pulp, a pulp capping material is place over the pulp floor and the remaining exposed tissue in the canal orifices. Partial pulpotomy has shown reliable success using calcium hydroxide. The success of VPT is highly dependent on case selection, removal of inflamed tissue, and providing an aseptic environment for the pulp to heal.

Section 1.6 Pulp Capping Materials

A variety of pulp dressing materials have been investigated and used over the last century to address the biological and clinical aims of preserving the vital pulp. The list of

pulp dressing materials range include calcium hydroxide (CH) products, calcium phosphate, zinc oxide, growths factors, and tricalcium silicate products, including mineral trioxide aggregate (MTA) (10, 12, 15, 23, 35, 36). Calcium hydroxide's antibacterial and dentinogenic effects made it the universal standard for vital pulp therapy (VPT) since its inception in 1920s by Hermman (29, 37). However, CH's degradation over time, tunnel defects in dentinal bridges induced by CH, and poor sealing properties have created interest in alternative pulp capping materials. Despite CH's universal use, long-term outcome studies on VPT with CH have been inconsistent (10, 36, 38). Retrospective studies evaluated outcome of VPT with CH reported success of 87% at 5 years recall and other with 10-year recall with significantly lower success at 13% (36, 38). The differences in success rates of these reported studies may result from confounding variables of retrospective study design.

The sealing ability of pulp capping material and restoration are fundamental in preventing ingress of bacteria and providing suitable environment for healing of the injured pulp. Tricalcium silicate has been used as a bone cement and has shown adequate biocompatibility and bioactivity (39). Tricalcium silicate is bioactive and hydrates into calcium silicate hydrate (C-S-H) and calcium hydroxide (Portlandite) that reacts in the presence of physiological fluids producing hydroxyapatite mostly at the surface of the tricalcium silicate paste (40). The first tricalcium silicate approved by the Federal Drug Administration (FDA) in the USA and is commercially available is Mineral Trioxide Aggregate (MTA) (41). Like many tricalcium silicate products currently on the market, MTA induces a high pH in the surrounding area and have better sealing ability than CH (42). MTA's introduction in the early 1990s and is the first tricalcium silicate available for use in dentistry allowed for improved treatment. With its superior sealing ability and stability for

restoration, MTA showed a significantly higher success rate, less pulpal inflammatory response, and more predictable hard dentin bridge formation than CH (35).

The success of VPT is highly predictable with the proper diagnosis and case selection (15, 22). While proper diagnosis and case selection are vital to biological based treatment selection, the outcome of success for VPT also predicates on many intraoperative variables. The gap in knowledge is not whether VPT is successful, but which intraoperative factors impact the outcome of VPT treatment. There is insufficient knowledge on the clinical factors that influence the outcome of VPT. Identification of these additional intraoperative factors may assist the practitioner in achieving success with VPT. This study will contribute to identifying the potential intraoperative factors that influence VPT outcome.

MANUSCRIPT

Section 1.1 Introduction:

Endodontics is the specialty of dentistry aimed at preserving the natural tooth through the diagnosis, prevention, and treatment of pathology associated with the dental pulp and peri-apical tissues (1). Endodontic treatments consist of vital pulp therapy {VPT [direct pulp capping (DPC); partial pulpotomy (Cvek pulpotomy); or complete pulpotomy]}, non-vital pulp therapy [non-surgical root canal therapy (NSRCT) and retreatment (Re-Tx)], and periapical microsurgery. Accurate diagnosis leads to suitable treatments, thus preventing or treating apical periodontitis, which ultimately preserves the natural dentition.

Teeth encounter many injuries that threaten the vitality of the pulp (16). The dental pulp, like other connective tissues, has the capacity to mount proper inflammatory/immune responses against injuries and microbial infections. The dental pulp's capacity to heal and recover from such injuries are widely established (5, 7). Direct exposures to the oral cavity are a threat to the dental pulp tissue because the lack of epithelia and the slow rate of odontoblast's dentin bridge formation cannot quickly hinder the ingress of noxious microbes (7, 23). Treatments of asymptomatic pulpal exposures of matured permanent teeth have included NSRCT and VPT (22). VPT is a viable treatment option for matured permanent teeth with pulp exposure (11). VPT provides high value care as it is less expensive and is completed in a single appointment. Lack of utilization of VPT for asymptomatic matured permanent teeth with pulp exposure is due to prior studies reporting poor predictability of

outcome and wide range of success rates (10). Understanding intraoperative factors that influence the outcome of VPT will provide better case selection and guidelines for treatment of asymptomatic matured permanent teeth with pulp exposure.

The objective of this prospective observational study is to identify potential influencing intraoperative factors, such as isolation type, isolation prior to exposure, tooth type, exposure size, hemorrhage control, exposure site, and restoration type on the outcome of VPT in patients with asymptomatic matured permanent teeth with pulp exposure.

Section 1.2 Materials and Methods

This study was approved by the Office of Human Research Ethics Committee at our institution (#15-2275). Healthy men and women (aged 15 and older) with vital pulp exposures of permanent teeth with matured apices were recruited for the study. Exclusion criteria were a) American Society of Anesthesiologist Classification ≥ II b) traumatic pulp exposure c) history of spontaneous pain in the tooth being treated or d) lack of hemorrhage control. Written informed consent was obtained for all study subjects.

Operators were trained using a standardized protocol to perform the treatment procedures. The standardized protocol was as followed: once an exposure was identified, the tooth was first isolated using a rubber dam or an Isovac™ (Innerlite, Inc, Santa Barbara, CA). Caries removal was completed and verified with caries indicator (Sable™ Seek® and Seek®, Ultradent Products, Inc, South Jordan, UT). Pulpal hemorrhage was controlled with a sterile cotton pellet moistened with 4.125% sodium hypochlorite applied to the exposure site for 60 seconds. Hemostasis was evaluated and if pulpal hemorrhage was not controlled, the clinician used a sterile round diamond bur and prepped 1 mm circumferentially into the

exposure site to remove the inflamed pulp tissue. The preparation site was irrigated and the sodium hypochlorite moistened cotton pellet was applied for 60 seconds again. This was repeated up to 3 cycles to control the hemorrhage; if hemostasis was not achieved after 3 cycles, the tooth was excluded from the study.

Once hemostasis was obtained, a periodontal probe was used to measure the largest diameter of the exposure site. MTA Angelus (Angelus, Londrina, PR, Brazil) was prepared following the manufacturer's instruction and used to seal the exposure site entirely, followed by a layer of Vitrebond (3M Vitrebond, St.Paul, Minn.). An amalgam or resin based restoration was placed immediately and a periapical radiograph was exposed.

All study subjects were then evaluated at four time points. The first three time points were 24-hours, 1 week, and 3 months post-operatively via phone to collect data on post-operative symptoms using a standardized questionnaire. At 6 months after the procedure, the study subjects were asked to return for clinical and radiographic exams. The clinical exams were standardized and were all performed by calibrated operators (BY, TT, MS). The exam included palpation, percussion, mobility, probing depths, cold sensibility testing [Endo Ice (Endo-Ice, Coltene, Altstätten, Switzerland), and electric pulp testing (EPT)]. A periapical radiograph was also exposed. Success of treatment is defined as a functional tooth with absence of clinical and radiographic pathology.

Section 1.3 Statistical Analysis

Sample size analysis was based on prior studies on vital pulp therapy (11, 13). The main outcome variable for this study was success or failure. Data was analyzed using the "R" function "glm" for generalized linear model with family (success/failure) as "binomial".

We also examined the data for association between selected peri-operative predictors and post- treatment pain. For size of the exposure, the data was log transformed and linear regression was fit with the predictor and outcome variable. All the statistical analysis was performed in R statistical software (version 3.2.3, www.cran.r-project.org).

Section 1.4 Results

Over several hundred study subjects were recruited from October 2015 to March 2017. Seventy-three study subjects enrolled in the study. The cohort comprised of 49 females and 24 males. The age distribution ranged from 15 to 80 years old. The median age was 46 years old while the average age is 46.7 years old. The spread of different tooth type are 34 molar, 19 pre-molar, and 20 anterior.

The study evaluated six intraoperative factors. Isolation before exposure was about even with 45% of no isolation vs 55% with isolation. The choice for type of isolation was predominately rubber dam isolation with [76% of Rubber Dam vs 24% Others (Isovac or cotton roll isolation)]. Hemorrhage control was assessed using the number of attempts at partial pulpotomy, which had 78% of teeth had immediate hemostasis without partial pulptomy, 21% of teeth needed one attempt of partial pulptomy to achieve pulpal hemostasis, and 1% of teeth needed two attempts of partial pulptomy to achieve pulpal hemostasis. The locations of exposure sites were 14 buccal/lingual, 16 occlucal, and 40 interproximal.
Of the 73 total subjects, 51 of study subjects were able to return for a 6 months evaluation. The recall rate at 6 months was 69.9% of recall at 6 months. At 6-month evaluation, the success for VPT treatment is 80.4%.

Using the generalized linear model with predictors – pain at 24 hours, pain at 1 week and pain at 3 months, tooth type and patient' age, we found that pain at 3 months is significantly associated with failure of treatment ($p=0.028$). We also noted marginal significance between patients' age and failure of treatment ($p=0.059$). There is a higher failure rates in older patients. On analyzing our data for an association between exposure size and post-treatment pain, a marginal significance ($p=0.0596$) was noted between exposure size and pain at 24 hours. However, there is no association between exposure size and pain at 1 week, 3 months, or outcome of treatments.

Statistical analysis did not find any differences for the evaluated intraoperative factors on outcome of VPT treatment. Intraoperative factors, such as isolation type, isolation prior to exposure, tooth type, exposure size, hemorrhage control, exposure site, and restoration type did not have a significant difference on the influence of outcome on VPT treatment in patients with asymptomatic matured permanent teeth with pulp exposure.

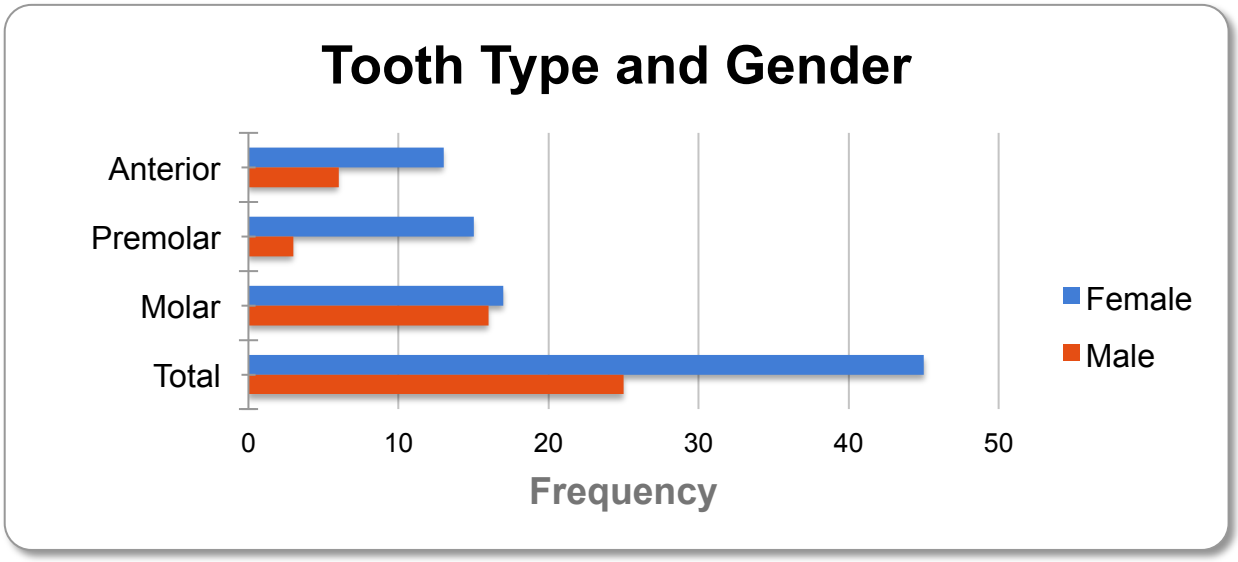

Figure 1: Tooth Type and Gender Distribution of Study Subjects.

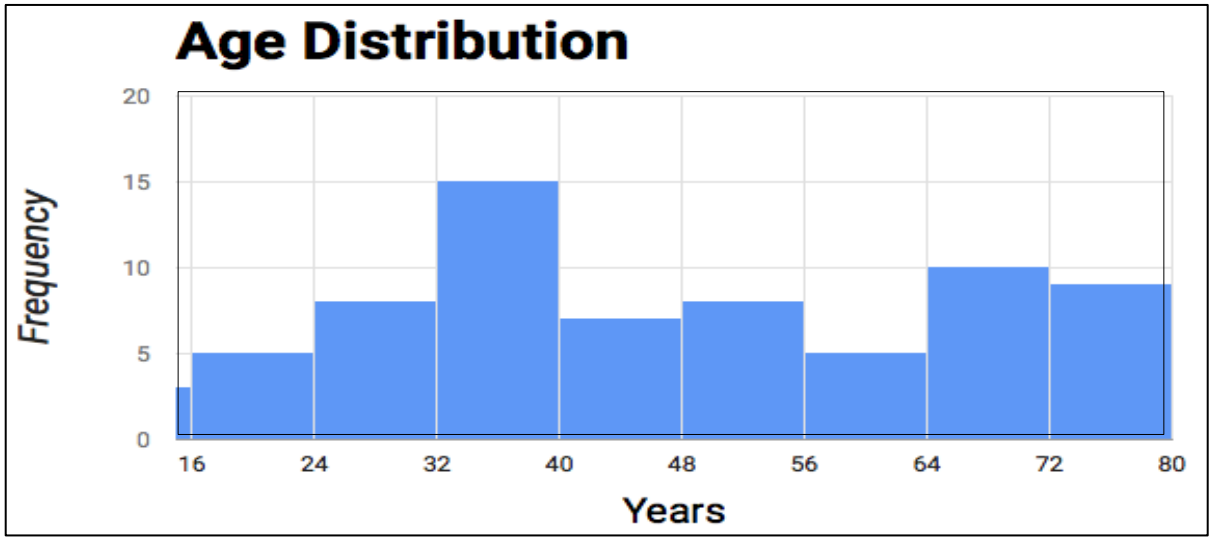

Figure 2: Age Distribution of Study Subjects ranging from 16 to 80 years old

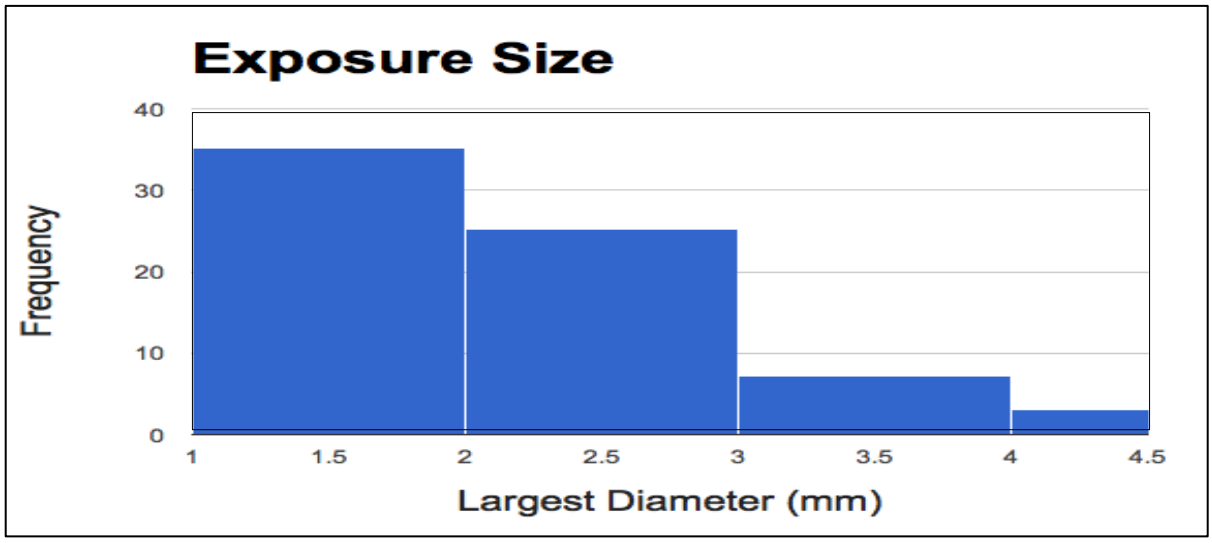

Figure 3: Distribution of exposure size. Measured in largest diameter of the exposure size and ranged from 1mm to 4.5mm.

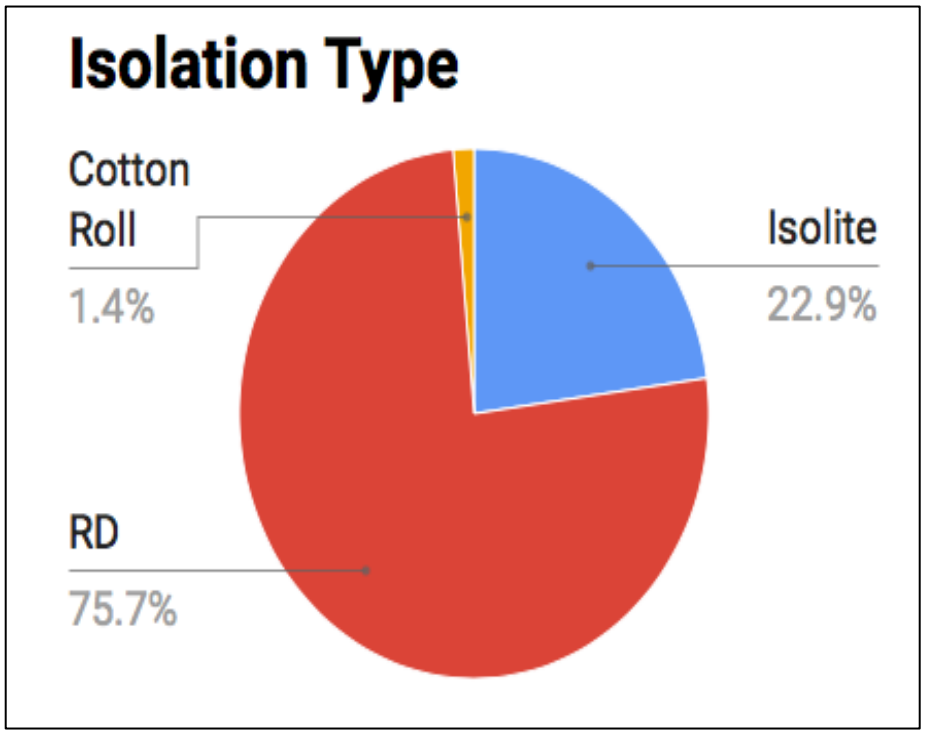

Figure 4: Distribution of isolation type. Isolation includes rubber dam, isovac, and cotton roll.

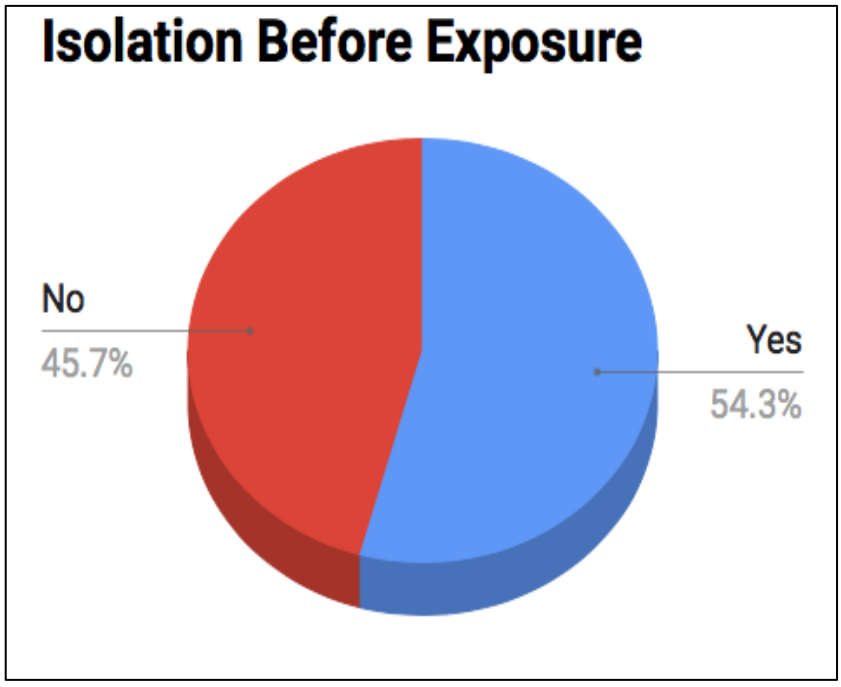

Figure 5: Distribution of the use of isolation before exposure or not.

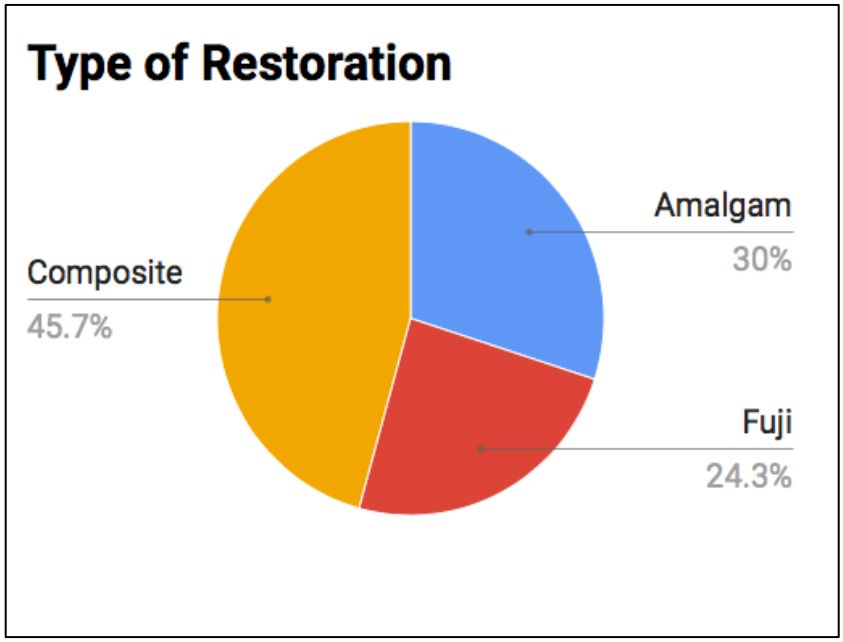

Figure 6: Type of restorative materials used for immediate placement of restoration.

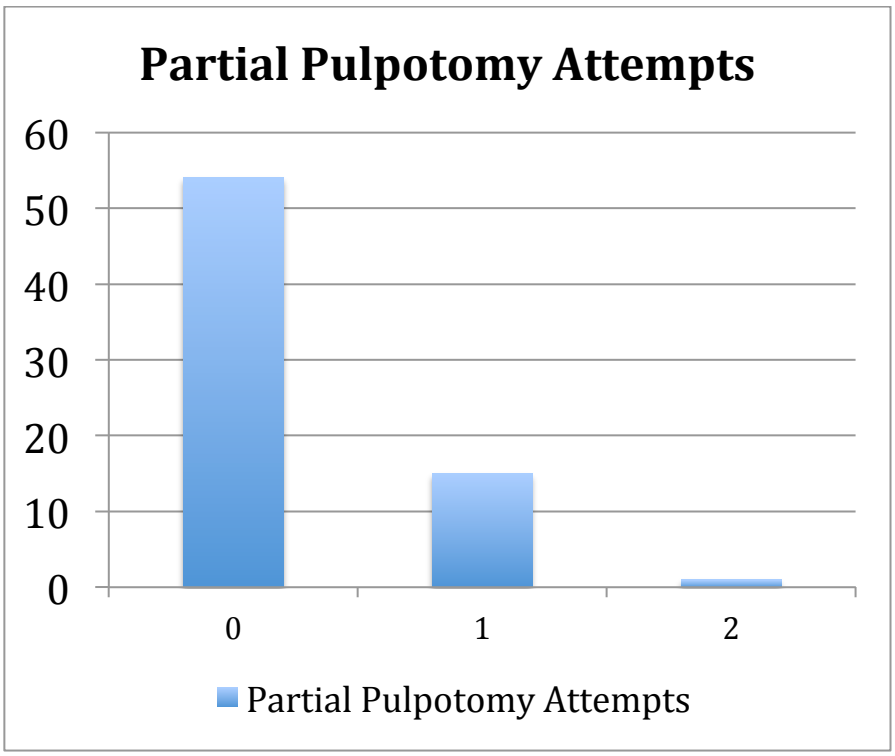

Figure 7: Dental Pulp hemorrhage control using the number of attempts at partial pulpotomy as a surrogate indicator.

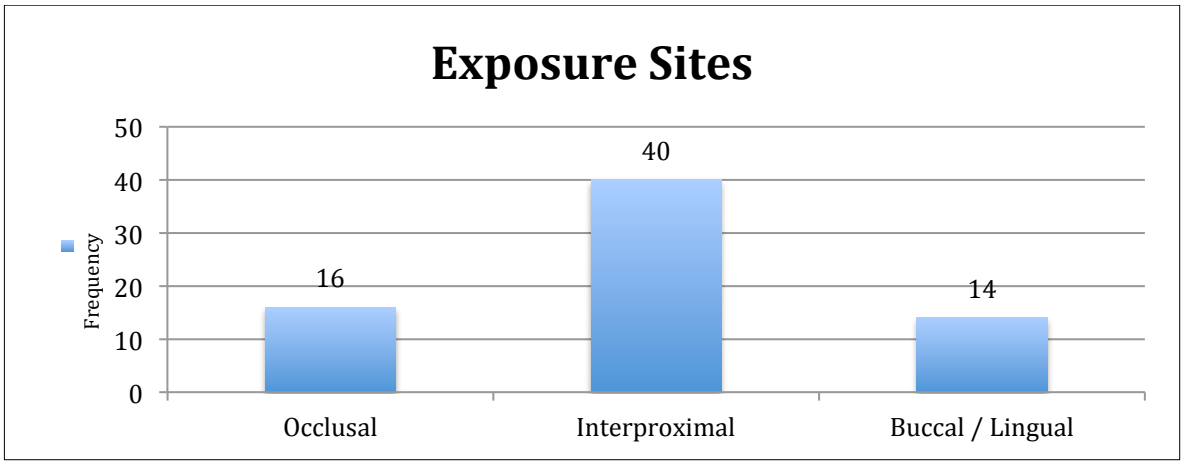

Figure 8: Location of the exposure sites.

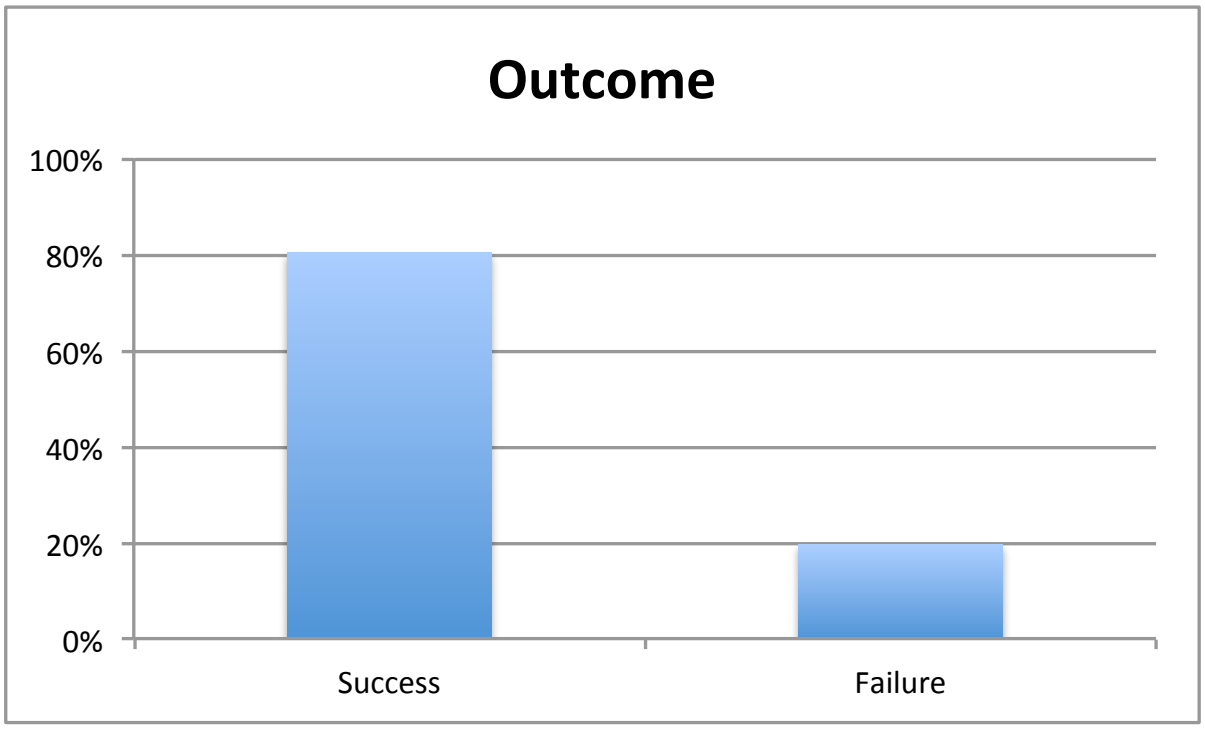

Figure 9: Outcome of VPT Treatment at 6 months.

DISCUSSION

Prior studies used wide-ranging criteria to evaluate success of VPT treatment outcome. Most studies used radiographic evaluation (12, 13, 34). These evaluations lack assessments of pulp vitality; instead the measure of success was an absence of periapical radiolucency. In these retrospective studies, the treatment protocols, time of restoration, and operators were not calibrated. Inconsistencies in treatment protocols resulted in varying VPT success rates (11, 13, 36, 38). In contrast, a limited number of prospective studies had examined the outcomes of VPT (11, 43). The long-term success of VPT outcome in these studies can be credited to standardized protocol and new biocompatible material. The outcomes of VPT treatment were widely evaluated and have established results. Although, limited studies have prospectively examined the influence of intraoperative factors on outcome.

Previous studies suggested intraoperative factors (hemostasis, age, and exposure size) impacted outcome of VPT treatment (13, 34, 36). Our study evaluated intraoperative factors, such as isolation type, isolation prior to exposure, tooth type, exposure size, hemorrhage control, exposure location, and restoration materials. In our study, standardized protocol and calibrated operators made this the first prospective study to evaluate intraoperative factors that influences VPT outcome. We defined success as a functional tooth with the absence of clinical and radiographic pathology. This was determined by conducting an in person

examination at six months follow-up. This examination included an evaluation of periapical radiograph and clinical testings (percussion, palpation, probing depths, endo ice, and EPT).

Some studies suggested that an operator's skill influence the treatment outcome of VPT (11, 36, 38, 44, 45). Many prior studies have a single-operator, who is a highly skilled specialist or clinician, performing the VPT treatment (10-13, 26, 34, 38). Our study had third and fourth year dental students performing VPT treatment with direct supervision of endodontic residents. As dental students, these providers have minimal skill sets compared to experienced general practitioners and dental specialists. The outcome of treatment in our study showed similar success with previous studies (10). Experience of operator appears to not influence the outcome of VPT treatment when proper protocol and guidelines are followed. However, the success of VPT treatment may have higher results with experience clinicians than dental students as more data are collected. Limited data may account for the lack of significant difference in success between experienced clinicians and dental students.

A deviation of our study compared to prior studies is the placement of restoration. In previous studies (11, 25), the operators used 2-visits protocol for placement and evaluation of MTA over the exposure sites. This methodology can have potential micro-leakage from temporary restorations during intra-appointments. Two-visits MTA placement will have unnecessary removal of tooth structure and possible disruption of MTA seal when temporary restorations are removed at subsequent appointment. Immediate placement of final restoration has been reported to have significantly higher success rate (within 1 or 2 days versus a longer time period) (36). In our study, final restorations were placed immediately after VPT. Timely placement of permanent restorations controlled variability such as early

leakage and provided immediate radiographic evaluation of MTA placement. This protocol allowed a favorable environment for the pulp to heal.

Prior understanding of pulpal disease is largely established on histology studies (46-48). Based on these concepts, dental pulps exposed during caries excavation have varying degree of inflammation, which cannot be accurately assessed from clinical examination. Bacterial ingress into pulp tissue will result in necrosis (34, 46). As results of these studies, the most common treatment for carious pulp exposures was complete extirpation of the pulp tissue and conventional endodontic treatment (9, 46). VPT was performed only when exposure is small (<1mm^2 exposure size) (34). However, recent studies reported success for VPT treatment with large carious exposures (>1mm) (11, 12). Our study showed success for VPT treatment regardless of the exposure size.

The innate healing potential of the dental pulp is well recognized. In a recent histological study correlating clinical pulp diagnosis and histologic pulp diagnoses, Ricucci et al 2014 characterized histologically irreversible pulpitis from caries at one coronal pulp horn while the other pulp horn of the same tooth showed completely normal pulp tissue (49). The localized inflammation of the injured pulp horn showed that despite having direct interaction with bacteria, there are potential for healing if the irritants are removed. Such findings along with other studies show no differences between young and old pulp in the regenerative capacity from injuries (50).

The resolution of inflammation leads to healing (8). In a carious pulp exposure, the underlying pulp tissue is inflamed to a varying or unknown extent. The success of VPT depends on the removal of etiology and providing suitable environment for healing (5, 6, 15). Currently there are no chair-side tests to assess the extent of inflammation of the pulp. The

degree of bleeding had been used as an indicator of inflammation (13). In an attempt to control bleeding and remove appropriate etiology, our study used the number of times performing partial pulpotomy as a surrogate indicator. Contrast to some studies suggesting aggressively removing the coronal pulp tissue when carious exposure occur to ensure all irritants and inflamed pulp tissue are removed (14, 51). Excessive removal of healthy pulp tissue is not indicated. Our study found no significant impact on the number of attempts of partial pulpotomy and treatment outcome. Our results are in agreement with other studies; a severely inflamed pulp will heal when the etiology is removed (14, 34, 51). Perhaps in the future, a chair-side test can provide immediate assessment of vitality of the pulp tissue via degree of inflammation.

This study examines partial pulptomy as a treatment factor that can influence outcome. Partial pulptomy is defined as the removal of portion of the vital coronal pulp as a means of preserving the remaining pulp tissue. While pulpotomy is a more intrusive procedure defined as the complete removal of the coronal portion of the vital pulp leaving the remaining tissue in the canal orifices is defined as the removal of portion of the vital coronal pulp as a means of preserving the remaining pulp tissue (15). Both treatments aim at removing irritants that are obstructing the healing process of the remaining pulp tissue. Both treatments were traditionally reserved for immature permanent teeth with exposed vital pulps (52).

The reservation of VPT for immature teeth was based on two fundamental understandings of the pulp tissue. In immature teeth, there are more stem cells and more blood supply in the pulp tissue compared to mature teeth (4). Increased blood supply is important in wound healing and repair. Adequate blood supply is vital to transport immune

cells into the area of pulpal injury and to remove harmful mediators. Sufficient blood flow also provides fibroblasts with nutrients to synthesize collagen. Healing would be impaired with a limited blood supply. Unlike most connective tissues, the pulp is limited in collateral circulation (4, 53, 54). Certain changes in the pulp appeared to be related to the aging process. The decrease in the number of nerves, blood supply, cellularity, and pulpal neuropeptides suggested regenerative capacity becomes poor with aging (2, 53, 54). The decline in cellularity and increase in the number and thickness of collagen fibers alters the composition of the pulp interstitium (4). Hyaluronidases and chondroitin sulfatases are lysosomal and bacterial degrading enzymes that attack components of the pulp interstitium (55, 56). During infection and inflammation, the physical properties of the pulp tissue may be altered due to production of degrading enzymes. In addition to the deleterious effect, these enzymes also pave the way for the damaging effects of bacterial toxins, compounding the degree of damage (57). Yet, evidence supports that aging result in an increased resistance of pulp tissue to the action of proteolytic enzymes, hyaluronidase, and sialidase (58). However, these evaluations cannot translate to the aging pulp's ability to cope with injuries. Studies showed no differences between young and old pulp in the regenerative capacity (50). Our findings revealed patient-factor, such as age, did not affect the outcomes of VPT. These results are in agreement with previous reported studies (34, 36, 38).

Our results suggested that despite varying intraoperative factors, VPT is highly predictable (11, 13, 59). Closer evaluation of the failures of VPT treatment revealed that two teeth had cracks extending into the roots and another had cuspal fracture. Such failures is not reflective of VPT treatment, but of restorative or functional failures. In contrast, NSRCT may have prevented the expansion of the longitudinal fractures. Traditionally NSRCT is the initial

treatment of a three-part management for an endodontically involved tooth. The immediate placement of the core build up and crown may prevent the propagation of the crack into the roots. However, the assumption is that the crack did not extend into the roots prior to VPT treatment. The mode of failures shed light on the misleading failure rates of VPT treatment. Evaluation of the mode of failures in future studies may provide better insight for VPT treatment guidelines and influencing factors not thoroughly evaluated.

Future studies are needed with different tricalcium silicate. Newer generations of tricalcium silicate have proposed improved handling, quicker setting time, and less staining of teeth. Evaluation of these factors can improve treatment protocols and provide better options for patients. In addition, studies with larger number of study subjects are indicated. Greater number of study subjects will improve the statistical power for evaluating the impact of intraoperative factors. This may provide better understanding into different factors that previously are not significant or have not been evaluated. Along with increased in number of study subjects, a longer recall follow up is necessary. Research had suggested a majority of failures would occur in the first 100 days post-treatment (13). Longer recall time allow for evaluation of late failure as Barthel et al (36) showed significant decreased in success from 5 years to 10 year recall. Having longer evaluation will allow more perioperative factors to be assessed for influence of outcome.

Within the limits of the study, the evaluated intraoperative factors did not have a statistical significant impact on the outcome of treatment; the result is in agreement with recent studies supporting the application of VPT for permanent teeth with carious pulp exposure (25, 26, 44). As we hypothesized, the result followed the biological support of elimination of irritants and creation of healing environment will produce predictable outcome

for VPT treatment. Association between exposure size and post-operative pain provided better understanding in post-operative pain management of VPT treatment. This prospective observational study showed that with thorough case selection and appropriate protocol, VPT is a viable treatment option to pulp exposures on asymptomatic teeth with matured apices.

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