# Comparing the Success of Biodentine™ vs. Ferric Sulfate

# in Primary Molar Pulpotomies

BY

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THESIS

Submitted as partial fulfillment of the requirements
for the degree of Master of Science in Oral Sciences
in the Graduate College of the
University of Illinois at Chicago, 2018

Chicago, Illinois

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## DEDICATION

This thesis is dedicated to my family ….

To my father Richard who passed away just before I graduated from dental school and didn't have the opportunity to see everything that he taught me pay off. It is because of the work ethic that you instilled in me from such a young age that I have been able to achieve such great success in my life. To my mother Kathleen who is always there to pick me up when I fall. Your relentless positivity and belief in me has helped me get through some of the toughest times from trying to get into dental school all the way through completing my pediatric residency. To my sister Mary Rose who is the ultimate role model and someone I try to emulate. You are always putting others before you, myself included, and I will never be able to repay you for your selflessness while I have been in school.

Without your love and support over the years I would not be where I am today. It is because of your sacrifices that I have been able to continue my education and accomplish all of my goals. With a family like you every day is Christmas!

Thank you and I love you!

## ACKNOWLEDGEMENTS

- Dr. da Fonseca and the department of Pediatric Dentistry for allowing me to conduct this study in the graduate clinic.
- The Pediatric Dental Residents of the Class of 2018 for helping perform treatment for the study.
- Dr. Kratunova for all her guidance, encouragement, and dedication.
- Dr. Brar for continuing the study and completing data collection for the remainder of the 24 month follow-up period.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| AAPD | American Academy of Pediatric Dentistry |
| ADA | American Dental Association |
| BD | Biodentine™ |
| COD | College of Dentistry |
| CODC | Clinical Outcome Data Collection |
| EHR | Electronic Health Record |
| FS | Ferric Sulfate |
| IDC | Initial Data Capture |
| MTA | Mineral Trioxide Aggregate |
| PCO | Pulp Canal Obliteration |
| PI | Principal Investigator |
| PIL | Patient Information Leaflet |
| PG | Post-graduate |
| RODC | Radiographic Outcome Data Collection |
| SPR | Study Participation Request |
| STS | Study Title Sheet |
| UIC | University of Illinois at Chicago |
| ZOE | Zinc Oxide Eugenol |

## SUMMARY

Pulp treatment in primary teeth is a core discipline of clinical pediatric dentistry. According to the American Academy of Pediatric Dentistry (AAPD), the key objective of pulp therapy is to maintain the health and integrity of primary teeth and their supporting structures, as well pulp vitality, where achievable.

Pulpotomy in primary teeth is a clinical procedure characterized by amputation of the coronal pulp, obtaining successful hemostasis and treating the remaining vital radicular pulp with an active medicament, followed by restoring the tooth with consideration to achieving optimal coronal seal.

Many pulpotomy medicaments have been used over the years with various success. For decades, Formocresol (FC) had been considered the gold standard agent, however recent concerns with its potential carcinogenicity have driven it out of favor. Instead, Ferric Sulfate (FS) has become the material of choice due to its proven record of similar clinical success to FC. Lately, new bioceramic materials (such as Mineral Trioxide Aggregate and Biodentine™) are increasingly popular in pediatric endodontics as these allow for regeneration of the remaining radicular pulp tissue. Recent studies have demonstrated superior clinical outcomes of the bioactive agents when compared to other materials.

While the search for the most effective, biocompatible and price efficient primary molar pulpotomy material is continuous, clinical trials of high quality design are required to support evidence-based guidelines. To the best of our knowledge, Biodentine™ (BD) has not been compared directly only to FS. Hence, the current study is unique by design and addresses this gap in the literature.

This is a parallel design randomized controlled clinical trial that aimed to compare the clinical and radiographic performance of BD and FS (used as control) as pulpotomy medicaments in primary molars over a period of two years with a recall every six months.

Participants for this study were recruited from the pool of patients attending the Post-graduate (PG) clinic at the Pediatric Dentistry Department of the College of Dentistry (COD), University of Illinois at Chicago (UIC). Inclusion and exclusion criteria were specified separately for the patients and for the teeth requiring treatment. Informed consents from the parents/ guardians and assents from the pediatric participants (7 years of age and older) were obtained. In total, 60 subjects were recruited. A random digit table was used for participant allocation into two groups (BD and FS). Each subject received one pulpotomy procedure as part of the study. Ten trained operators, all with experience in pediatric dentistry, performed the interventions (pulpotomy procedures) by following a standard step-by-step guide, designed for the study purposes and based on the manufacturers' instructions. After six months, one designated examiner, specialist pediatric dentist, performed the clinical assessment of the teeth treated with BD and FS pulpotomies according to standardized criteria. This study is in progress and will continue with 6 monthly evaluation over a period of 2 years, in total. Every 12 months, a radiographic assessment is also intended according to specified standards.

A prospective power calculation was conducted, based on reported clinical success rates from previous studies. It estimated that 18 teeth in total (9 in each group) would achieve a power of 0.92.

The data was coded and captured on evaluation forms specifically designed for the purposes of the study. The data gathered through all study forms was transferred into Microsoft® Excel 2016 and the statistical analysis was carried out with IBM SPSS Statistics.

# I. INTRODUCTION

## I.1 Background

### I.1.1 Pulpotomy in Primary Teeth

Pulp therapy is a fundamental aspect of pediatric dental clinical practice. Following appropriate diagnosis of the pulp status, indicated endodontic interventions are categorized either as vital or non-vital pulp therapy. Vital pulp therapy is typically recommended for teeth diagnosed with reversible pulpitis. It is an umbrella term encompassing indirect pulp cap, direct pulp cap, and pulpotomy. Non-vital pulp therapy is indicated for irreversibly inflamed or necrotic pulps and it is the intervention of pulpectomy. According to the AAPD the key objective of vital pulp therapy is to sustain the health and integrity of the teeth and their supporting structures, and where possible to maintain the vitality of the pulp. Pulpotomy in primary teeth is defined as the procedure where "the coronal pulp tissue is amputated, and the remaining vital radicular pulp tissue surface is treated with a long-term clinically successful medicament".[1] The concept and the actual technique of the procedure have not changed since its inception, however the choice of active medicaments applied over the remaining vital radicular pulp tissue has largely evolved over the years.

Generally, the procedure consists of multiple treatment steps. Pulpotomy can be planned in advance after a clinical diagnosis of reversible pulpitis, or it can be decided intraoperatively when a pulp exposure is encountered during caries excavation. All of the carious tooth structure must be removed along with the roof of the pulp chamber. If no bleeding is observed, this is a sign that the pulp tissue has undergone necrosis and vital pulp therapy is no longer a treatment option, instead a pulpectomy or extraction should be considered.[2] When bleeding is observed, the coronal pulp tissue is removed and amputated at the level of the root canal orifices. Hemostasis is achieved at the level of

the canal orifices using a moist cotton pellet and pressure. Usually, successful hemorrhage control is achieved within 4-5 min, indicating normal and healthy radicular pulp, otherwise, the radicular pulp tissue is considered hyperemic and infected.[2,3] This would also disqualify the tooth from being a candidate for pulpotomy treatment as it is considered an evidence that the infection has gone beyond the level of the coronal pulp tissue, in which case a pulpectomy should be performed. If hemostasis is achieved readily, the selected pulpotomy medicament is placed over the remaining radicular pulp tissue as indicated and the pulp chamber is filled with appropriate lining material. Preferably, any tooth that undergoes pulpotomy treatment should be subsequently restored with a full coronal coverage restoration to obtain ideal coronal seal. In pediatric dentistry, most commonly used are stainless steel crowns (SSC), zirconia pediatric crowns or pre-veneered crowns.[1-3]

### I.1.2 Pulpotomy medicaments for primary teeth

Various pulpotomy agens have been proposed and utilized over the years, some with only experimental value, while others were established as standards. The ideal properties of a pulpotomy material include bactericidal, biocompatible, ability to promote healing to the remining vital radicular pulp and to be indifferent to the process of physiological resorption of the root of the tooth.[4] The currently available therapeutic agents can be assigned into three main groups with regard to their immediate effect on the radicular pulp.[4]

For decades in the past, FC has been considered the gold standard pulpotomy medicament. It is used as 20% (1:5 dilution) Buckley's FC solution and applied directly to radicular pulp on a cotton pellet for approximately five minutes. It contains formaldehyde, cresol, glycerin and water. It achieves superficial tissue fixation and has bactericidal properties. The reported success rates in the literature ranges from 55% to 97%.[5,6] In 2004

the International Agency for Research on Cancer classified formaldehyde as carcinogenic in humans. Although, the evidence of potential mutagenic and cytotoxic hazards associated with its dental use is controversial, FC is gradually driven out of favour.[5,6]

**Table 1. Classification of Pulpotomy Agents**

| Preservation in a healthy state | Devitalisation | Tissue Regeneration |
|---|---|---|
| • Ferric Sulphate<br>• Bioactive cements: Mineral Trioxide Aggregate (MTA), Biodentine™(BD)<br>• Lasers<br>• Electrocoagulation<br>• Calcium Hydroxide<br>• Sodium Hypochlorite | • Formocresol<br>• Glutaraldehyde | • Bone Morphogenic Proteins<br>• Collagen |

Sodium Hypochlorite (NaOCl), (3-6%) is a hemostatic and bactericidal agent, inexpensive and readily available. As a pulpotomy agent is placed on a cotton pellet over the radicular pulp for 30 seconds followed by a water rinse. The pulp chamber is then filled with Zinc Oxide Eugenol (ZOE) cement and the tooth is restored with SSC. The reported range of success in the literature is 74-100%.[7] Disadvantages to its use, include documented risks of external/internal root resorption and radicular bone loss have been associated with its use.[7]

Calcium Hydroxide has also been advocated as a pulpotomy medicament, however it has been shown to have consistently lower success rates in comparison to FS and FC. The use of lasers in primary tooth pulpotomies, although expensive, is promising with further research needed for definitive results.[2.3]

Newly introduced bioceramic materials (such as MTA and Biodentine™) are developed to promote regeneration of the remaining pulp tissue. Recent studies have demonstrated superior clinical outcomes (96%-100%) of MTA pulpotomies compared to

most other pulpotomy medicament choices.[8] While the search for the most effective, biocompatible and price efficient primary molar pulpotomy material is continuous, clinical trials of high quality design are required to support the evidence-based guidelines.

### I.1.3 Biodentine™

BD is a tricalcium silicate (Ca3SiO5)-based inorganic nonmetallic restorative cement introduced to the dental market as a 'bioactive dentine substitute'.[9,10] Allegedly, this material has superior physical and biological properties such as user-friendly material handling, faster setting time, increased compressive strength, increased density, decreased porosity and induction of reparative dentine synthesis when compared to other bioceramic cements.[9] It is possible to mix BD in the capsule that it is packaged in, using a titrator that allows for more uniform mixing and more consistent viscosity to the material. The consistency to which the BD is mixed to form a stiff enough putty that allows the material to be placed accurately and without sticking to the instrument of application. When BD is placed over vital pulp tissue it produces a superficial layer of necrosis. This necrotic tissue in turn stimulates an inflammatory/healing response that results in odontoblasts laying down tertiary/reparative dentin. The hard tissue barrier forms relatively fast (within weeks), with only few vascular inclusions and provides a tight seal on contact with the dentinal walls. Even though ultimately it is this dentin bridge which seals off the vital pulp tissue, the BD forms a strong bond with the remaining dentin preventing any contamination while the reparative dentine is forming.[9,10]

### I.1.4 Ferric Sulfate

FS (Fe2[SO4]3) as a 15.5% solution (Astringedent™, Ultradent Products) has been used commonly as a coagulative and hemostatic retraction agent for crown and bridge

impressions and is slightly acidic.[11] The mechanism of action of FS is still not fully understood, but it has been established that the reaction of blood with both the ferric and sulfate ions leads to agglutination of the blood proteins. The formed products act as plugs and occlude the capillary orifices. Therefore, unlike conventional clotting agents, FS affects hemostasis through a chemical reaction with blood.[11,12] FS was proposed and subsequently widely used as a pulpotomy agent based on its mechanism of controlling hemorrhage. It is also believed that its ability to induce a physiological blood clot minimizes the chances for inflammation and internal resorption in the remaining radicular pulpal tissue as the metal-protein complex stops propagation of irritation-inducing components.[13]

## II. Review of the Literature

A review of the current literature in English language, evaluating the success of pulpotomies completed with BD and/or with FS as definitive agents and done on primary molars was performed. As per the defined inclusion criteria, the studies had to evaluate pulpotomies completed in primary molars, compare either BD or FS, have follow-up of at least 12 months, and teeth restored with SSC. Studies, that were excluded were not written in English, pulpotomies were completed on teeth other than primary molars, materials other than FS or BD were used as pulpotomy agents, the follow-up was less than 12 months, and the pulpotomised teeth were not restored with SSC.

The search of Google Scholar, NCBI and PubMed data bases with the MeSH terms “Biodentine”, “Pulpotomy”, “Ferric Sulfate” “Primary”, “Molar”,” Pulp”, “Pediatric” used in various combinations identified 6 clinical trials assessing BD and 13 involving FS.

Of the studies that were included, the reported success rates for BD ranged from 95% to 100% for clinical performance and 80% to 95% for its radiographic outcomes (Table 2). In five of the six articles, BD was compared to MTA and no statistically significant differences were noted between the success of these two agents.

Togaru *et al.,* (2016) reported that both MTA and BD have success rates of 95.5% at 1-year follow-up.[13] Rajasekharan *et al.,* (2016) also found the clinical success for BD to be as high as 95.24% and the radiographic success to be 94.4%, which was not significantly different from MTA (100% and 90.9% respectively).[14]

This study provided the longest follow-up time of 18 months, which is six months longer than any of the other reported trials.[14] Kusum *et al.,* (2016) documented 100% clinical success rate for both BD and MTA, however they described lower rates of radiographic outcomes (80% and 92% respectively but not statistically significant in difference).[15] Cuadros Fernandez *et al.,* (2016) also confirmed that both MTA (92% clinical/ 97% radiographic success) and BD (97% clinical/ 95% radiographic success) are highly

efficacious pulpotomy agents.[16] El Megily *et al.,* (2016) was the only clinical trial that compared BD to FC and reported in 6 months 100% clinical success for both medicaments.[17]

Pulp canal obliteration (PCO) is a normal healing response of vital pulps and results in thickening of the radicular walls and in significant decrease of the pulp canal space. Most studies described that teeth treated with BD as a pulpotomy agent exhibited radiographic signs of PCO. For example, El Megily *et al.,* (2016), reported that 17.9% of the BD pulpotomies resulted in PCO in contrast to 12.5% of those in the FC group.[17] Rajasekharan *et al.,* (2016) had a similar observation and reported higher frequency of PCO in the BD pulpotomies versus those with MTA.[14]

**Table 2. Summary of studies of BD as primary molar *pulpotomy* agent**

| Study | Aim | Materials & Outcomes |
|---|---|---|
| Togaru et al., 2016 | Clinical and Radiographic Evaluation of Success of Two Commercially Available Pulpotomy Agents in Primary Teeth, BD and MTA: An In Vivo Study | 90 teeth included, 95.5% success rate, no significant difference BD and MTA, only 1 year follow-up, doesn't say restoration type |
| El Meligy et al., 2016 | Comparison Between BD and FC for Pulpotomy of Primary Teeth: A Randomized Clinical Trial | 112 teeth (56 FC, 56 BD), all restored w/ SSC, only had 3mo and 6mo follow-up, 100% success for both groups at both times, slightly higher pulp canal obliteration w/ BD (17.9% compared to 12.5%) |
| Rajasekharan et al., 2016 | Efficacy of Three Different Pulpotomy Agents in Primary Molars - A Randomized Control Trial | 82 teeth total, follow-up at 6/12/18months, 69 teeth included at 18 months (15.85% loss to f/u), No significant difference between the 3 groups, BD had 95.24% success clinically and 94.4% radiographically, BD had significantly more pulp canal obliteration than MTA |
| Kusum et al., 2016 | Clinical and Radiographic Evaluation of MTA, BD and Propolis as Pulpotomy Medicaments in Primary Teeth | 75 teeth total, follow-up 3/6/9months, both BD and MTA had 100% clinical success rates but radiographically BD was 80% and MTA was 92% (no significant difference) |
| Cuadros-Fernandez et al., 2016 | Short-term Treatment Outcome of Pulpotomies in Primary Molars Using MTA and BD: A Randomized Clinical Trial | 84 teeth, follow-up at 6/12months, restored w/ ZOE and SSC, MTA success was clinical-92% and radio-97% and BD success was clinical 97% and radio-95% |
| Niranjani et al., 2016 | Clinical Evaluation of Success of Primary Teeth Pulpotomy Using MTA, Laser and BD - An In Vivo Study | 60 teeth, follow-up at 3mo/6mo, no significant difference between the three groups |

Since, BD is a newly introduced primary tooth pulpotomy agent most publications evaluating it are very recent (in the past 1 to 2 years) and have a relatively short follow up period (6 to 18 months). Longer review of the outcomes is needed to see how BD performs over the lifetime of primary molars. The study with the longest recall of 18 months reported a participant dropout rate of 15.85%, while the trials of shorter duration (6 and 12 months) did not lose any subjects.

Pulpotomies in primary molars completed with FS were evaluated in 13 research trials (Table 3).

**Table 3**. **Summary of studies of FS as primary molar pulpotomy agent**

| **Study** | **Aim** | **Success Rate** |
|---|---|---|
| **Havale *et al.,* 2013** | Clinical and Radiographic Evaluation of Pulpotomies in Primary Molars with FC, Glutaraldehyde and FS | 30 in primary molars in each group (90 total), 1-year follow-up at 3 months intervals, clinical and radiographic success rates were glutaraldehyde (100%/83.3%), FS (96.7%/63.3%), FC (86.7%/56.7%) |
| **Fernandez *et al.,* 2013** | Clinical and Radiographic Outcomes of the Use of Four Dressing Materials in Pulpotomized Primary Molars: A Randomized Clinical Trial with 2-year Follow-up | 2-year follow-up at 6-month intervals; compared FC, MTA, FS, Sodium Hypochlorite; no statistical difference in success |
| **Odabas *et al.,* 2012** | Clinical and Radiographic Success Rates of MTA and FS Pulpotomies Performed by Dental Students | 1 year follow up at 3 months intervals; compared FS and MTA; Clinical and radiographic success, FS (84.7%/78.2%), MTA (94.7%/92.1%); most common cause of radiographic failure for both was internal resporption; no statistical significant difference |

| | | |
|---|---|---|
| **Huth *et al.,* 2012** | Long-term Effectiveness of Four Pulpotomy Techniques: 3-year Randomized Controlled trial | 3 year-follow up at 6 month intervals; 200 primary molars; 4 groups & success rates are: FS (97%); FC (92%), Laser (89%), Calcium Hydroxide (75%), no statistically significant difference between the 4 groups found; |
| **Erdem *et al.,* 2011** | Success Rates of MTA, FS, and FC Pulpotomies: A 24-month Study | 2 year-follow up at 6-month intervals; MTA, FS, FC, ZOE were compared; success rates, MTA (96%), FS (88%), FC (88%), ZOE (68%); ZOE was significantly worse than MTA; no significant difference between the other three; |
| **Doyle *et al.,* 2010** | MTA Produces Superior Outcomes in Vital Primary Molar Pulpotomy | Conducted by combining medicaments, results are not well aligned with what we are studying |
| **Sonmez *et al.,* 2008** | A Comparison of Four Pulpotomy Techniques in Primary Molars: A Long-term Follow-up | 56 teeth; 2 year-follow up at 6-month intervals; success rates of FC (76.9%), FS (73.3%), Calcium Hydroxide (46.1%), MTA (66.6%); |
| **Vargas *et al.,* 2006** | Preliminary Evaluation of Sodium Hypochlorite and FS for Pulpotomies in Primary Molars. | 5% NaOCl vs FS; 1 year-follow up at 6-monthly recall; NaOCl clinical success 100%, radiographic success at 12 months was 79% (showed internal resorption); FS clinical success 85% and radiographic success at 62%; |

| | | |
|---|---|---|
| **Huth *et al.,* 2005** | Effectiveness of 4 Pulpotomy Medicaments in Primary Molars | 2 year-follow up at 6-monthly recall: clinical success was FC (96%,) laser (93%), Calcium Hydroxide (87%), FS 100%; only Calcium Hydroxide was significantly worse |
| **Chien *et al.* 2001** | How Does Zinc Oxide-Eugenol Compare to Ferric Sulphate as a Pulpotomy Material? | Both 100% success at 3 months. |
| **Fei *et al.,* 2001** | A Clinical Study of Ferric Sulfate as Pulpotomy Agent in Primary Teeth | FS vs FC with 1 year-follow up at 3-monthly recall; FS had 96.6% success and FC had 77.8% success |
| **Ibricevic & al-Jame Q, 2000** | Ferric Sulfate as Pulpotomy Agent in Primary Teeth: Twenty Month Clinical Follow-up | FS vs FC; with 20 month-follow up at 3-monthly recall; 100% clinical success for both groups; radiographic success for both groups was 97.2% with 2.8% showing internal resorption |
| **Fuks *et al.,* 1997** | FS vs Dilute FC in Pulpotomized Primary Molars: Long-term Follow Up | FS vs FC: with 34 month-follow up at 6-monthly recall; FS success was 92.7%, FC was 83.8%; Rate of internal resorption was 7.2% for FS and 5.4% for FC; |

The reported success rates ranged from 62% to 100% through various follow-up times (from 3 months to 3 years). Havale *et al.,* (2013) compared three pulpotomy agents

including FS, Glutaraldehyde and FC with a one-year follow-up.[18] They concluded that FS had success rate of 96.7%, clinically and 63.3%, radiographically.[18] It had a very similar performance to the other two medicaments. FC had a clinical success rate of 86% and a radiographic one of 56.7%, while glutaraldehyde had a 100% clinical and 83.3% radiographic success.[18] Fernandez *et al.,* (2013) compared FS to FC, MTA, and Sodium Hypochlorite and reported no significant difference in between the groups after two years.[19] Odabas *et al.,* (2012) compared FS to MTA with one-year follow-up. FS showed 84.7% tooth survival and radiographic success of 78.2%. However, MTA outperformed it with 94.7% clinical and 92.1% radiographic success.[20] The most common cause of radiographic failure in both groups was internal resorption and the differences were not statistically significant.[20] Huth *et al.,* (2012) compared four different pulpotomy medicaments with a follow-up up at 6-month intervals for three years in total. The success rates for the four groups were, 97% for FS, 92% for FC, 89% for Laser, and 75% for Calcium Hydroxide respectively and there was no statistically significant difference between the groups.[21] Sonmez *et al.,* (2008) also compared four different medicaments, including FC, FS, MTA, and Calcium Hydroxide. At the two-year follow-up, this study showed a success rate for MTA of only 66.6%, which is particularly low, compared to most other studies that worked with this material. FC showed the highest success at 76.9% followed by FS at 73.3% and Calcium Hydroxide at 46.1%.[22] Vargas *et al.,* (2006) was the only study that compared the clinical and radiographic success of FS to Sodium Hypochlorite. At 12 months, FS demonstrated 85% clinical and 62% radiographic success compared to 100% clinical success and 79% radiographic success of the Sodium Hypochlorite. [23]

FS has been established as an inexpensive, user friendly, biocompatible and efficient pulpotomy agent based on a number of studies with a good quality design. It is the most commonly used pulpotomy medicament in the contemporary pediatric dental

practice. However, its outcomes can vary to as low as 73% for the clinical and 62% for the radiographical success.[23-33] BD was shown to result in more predictable pulpotomies in primary molars with success rates consistently higher than 94%.[34-38] Being a relatively new material on the market, BD has had a lot less research support and the available studies are of a shorter follow up.

In the literature to date, BD has never been compared directly to the current standard pulpotomy agent FS and such study is highly needed for appropriate clinical practice recommendations. The current randomized controlled clinical trial comparing the two pulpotomy agents, FS and BD is unique by design and is addressing the identified gap in the literature.

## III. Aim and Objectives of the Study

This is a parallel design randomized controlled clinical trial that aims to compare the clinical and radiographic performance of BD and FS (control) as pulpotomy agents in primary molars over a period of two (2) years with a recall every six (6) months.

The study's objectives include:

- To evaluate a number of clinical variables related to the success of primary molar pulpotomy procedures completed with BD and FS;
- To evaluate a number of radiographic variables related to the success of primary molar pulpotomy procedures completed with BD and FS;
- To compare BD and FS as pulpotomy agents in primary molars;
- To make clinical practice recommendations for the use of pulpotomy agents in primary molars.

## IV. Hypotheses of the Study

The Null Hypotheses of the study are:

- There is no statistical difference in the clinical success of primary molars treated with pulpotomy procedure using either BD or FS as a pulpotomy agent.
- There is no statistical difference in the radiographic success of primary molars treated with pulpotomy procedure using either BD or FS as a pulpotomy agent.

The PICOT question is

- Will healthy pediatric patients (3 to 9 years of age) receiving pulpotomy treatment for primary molars (Population; P) using BD (Intervention; I) in comparison with pulpotomy using FS (Control; C) show increased clinical and radiographic success based on a set of specified criteria (Outcome; O) when followed up for 24 months (Time; T)?

## V. Materials and Methods

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of the UIC (Appendix A).

### V.1 Study Site

This research trial was performed at the graduate clinic of the Pediatric Dentistry Department, College of Dentistry, UIC.

Only treatment appointment, conducted under general anesthesia was held at the University of Illinois at Chicago Hospital. All other study visits were carried out at the Pediatric Dentistry Department, College of Dentistry, UIC.

### V.2 Study Subjects

Study participants were selected from the pool of patients attending the PG clinic of the Pediatric Dentistry Department at the COD, UIC. Inclusion and exclusion criteria were specified separately for the selected patients and for the teeth indicated for treatment. The study was intended only for healthy subjects as history of significant medical findings may have altered treatment decisions. For example, patients with congenital cardiac disease, who are at risk of residual infection may require additional therapeutic interventions that could potentially deviate the study process. Furthermore, the age group of the participants was chosen with consideration to the average normal lifespan of deciduous molars. The teeth indicated for pulpotomy were selected based on preliminary clinical diagnosis of reversible pulpitis or intraoperative carious pulp exposure.

All inclusion and exclusion criteria, per tooth and per patient, are summarized in Table 4.

**Table 4: Summary of Inclusion and Exclusion Criteria**

| | Inclusion Criteria | Exclusion Criteria |
|---|---|---|
| **Patient** | • Medically Fit (ASA* I or II)<br>• Age range: 3 to 9 years of age<br>• Obtained informed consent<br>• English speakers | • Medically Compromised (ASA*III to VI)<br>• Younger than 3 or older than 9 years of age<br>• Informed consent not obtained<br>• Non-English speakers |
| **Tooth** | • Type tooth: primary molar<br>• Tooth with deep caries extending into the inner third of dentin<br>• Tooth with symptoms of provoked pain of short duration<br>• Tooth with symptoms of pain relieved upon removal of stimulus<br>• Tooth with adjacent healthy soft tissue (no sinus tract)<br>• Tooth with no radiographic evidence of furcation/apical pathology<br>• Tooth with no radiographic signs of physiological root resorption | • Tooth other than mandibular primary molar<br>• Tooth requiring extraction due to:<br>  • Non-restorable crown defect<br>  • Root resorption due to ectopic first permanent molar<br>  • Orthodontic therapy<br>• Tooth with symptoms of:<br>  • Spontaneous unprovoked pain<br>  • Pain at night time<br>  • Constant pain with need for analgesics<br>  • Sinus tract |

| | | |
|---|---|---|
| | | • Excessive mobility (not associated with trauma or exfoliation)<br>• Tooth with radiographic evidence of furcation/apical pathology<br>• Tooth with radiographically detectable physiological root resorption |

*American Society of Anesthesiologists (ASA)

Male and female patients, 3 to 9 years of age, were enrolled in this study as they typically have fully formed primary dentition or early mixed dentition with available primary molars. The study investigated pulpotomy procedure in primary molars. Children younger than 3 years of age were excluded from the study, as they may not yet have a fully formed primary dentition. Children older than 9 years of age typically have primary molars close to exfoliation and would not benefit from the proposed pulp therapy methods. Patients with significant medical history were excluded from study enrollment as the priority of their medical condition may limit their availability for participation. All relevant study forms were available in English. Parents/ guardians who were non-English speakers were excluded from enrollment, as they had a significant disadvantage in understanding the purpose and the participation process of the study.

V.3 Enrolment Process

Study participants were selected from the pool of patients attending the graduate clinic at the Pediatric Dentistry Department of the COD at UIC. The principal investigator

(PI) reviewed the daily schedule of the PG Pediatric Dental Clinic on the electronic health-record (EHR) system at UIC and accessed the past notes of the booked patients to search for potential study participants according to the specified inclusion criteria. The PI identified prospective subjects by tracking existing active dental treatment plans and new dental treatment plans that met tooth and patient eligibility requirements. Thus, a list of potential participants with their EHR patient numbers was generated. Each of these patients and their parent/guardians were approached by the PI at the time when they attend the PG clinic for their scheduled dental treatment appointment. The PI provided a brief verbal description of the study, a Patient Information Leaflet (PIL, Appendix B), and a Study Participation Request form (SPR, Appendix F). This was done in a respectful manner to the patient and his/her parent/guardian's privacy. The conversations were held in a dental cubicle or operatory where no other staff members or members of the public would recognize that they were a potential study enrolment process. The PIL, aided with pictorial material, offered detailed information on the two pulpotomy agents used in the study and a clear explanation of all advantages and disadvantages of the proposed treatment materials. It also provided a description of the study participation process and associated risks and benefits. The SPR form required the parent/guardian to provide contact details including the prospective participant's name and phone number. This form was given directly to the PI. The PI used the collected information from the SPR forms to contact and schedule appointment with the prospective participants. Once a potential study participant was identified, the PI performed a brief dental exam to establish whether the patient truly fulfilled the inclusion criteria of the clinical trial. Sufficient time for consideration before enrollment was provided for as long as the patient or his/her parent/guardian required to make an informed decision. No coercion was used. However, the parents/guardians were expected to make a decision within a reasonable period of time in order to avoid delay in their child's dental care. Patients and parents/guardians,

who were interested in research participation, were asked to complete and sign the consent (parental permission, Appendix D) and the assent form (for children 7 years of age and older, Appendix E) of the study. For those participants that required advanced behavior management options, the treatment was performed with the adjunct of inhalational sedation (nitrous oxide), oral conscious sedation or general anesthesia. Furthermore they had to sign "Authorization To Use And Disclose (Release) Health Information For a Research Study" form (Appendix C) in order for the EHR to be accessible to the research personnel during the study process. Each participant received an individual study number. A master list of the participants' study numbers with the respective patients' EHR numbers was generated for the study purposes. This was necessary to avoid multiple patient enrollments and provided ability to gain access to the participant's EHR at each of the recall visits. The master list will be permanently destroyed along with all other study documentation 5 years after the research trial is completed. Patients who did not meet the study's inclusion criteria or for whom an informed parental permission (consent) and assent (where applicable) could not be obtained were not enrolled in the study and were advised to continue their dental care as previously planned. With regard to reimbursement from dental insurance companies, the American Dental Association (ADA) has established a set of standardized coding for dental procedures. The primary molar pulpotomy, regardless of the used pulpotomy agent, is an itemized procedure and is fully covered by most dental insurances. The reimbursement for dental treatment was not altered by this study since the dental treatment plan remained unchanged. The subjects did or did not receive any financial incentives and the cost of the dental treatment plan was the same regardless of study participation.

## V.4 Operators

Ten designated and trained operators (pediatric dentistry residents and one

specialist pediatric dentist) completed the pulpotomy procedures in this research trial. They all underwent a training processes specific for the purposes of this study. It consisted of reviewing the pulpotomy procedures from the literature, studying the step-by-step guide designed for this trial, learning the manufacturers' instructions for the use of BD and FS as pulpotomy agents, practicing on typodont teeth and completing a workshop on BD led by a Septodont® representative.

## V.5 Procedure and Armamentarium

### V.5.1 Biodentine™

Biodentine™ was developed by Septodont® as a new class of dental material that could conciliate high mechanical properties with excellent biocompatibility as well as a bioactive behavior (Table 5).

**Table 5: Biodentine™ by Septodont®**

| Brand | Manufacturer | Company Logo |
|---|---|---|
| Biodentine™ | *Septodont P.O. Box 68*<br>*Cambridge, Ontario*<br>*Canada N1R 5S9* | septodont |

Its chemical composition is based on the $Ca_3SiO_5$ (Table 6). BD is a dentin substitute indicated for use in the crown for temporary enamel restorations, permanent dentin restorations, deep or large carious lesions, deep cervical or radicular lesions, pulp capping or pulpotomy. The material can also can be used in the root for root and furcation perforations, internal and external resorptions, apexification and retrograde surgical filling.

**Table 6. Biodentine™ chemical content**

| |
|---|
| *Powder* |
| *Tri-calcium Silicate (C3S) Main core material* |
| *Di-calcium Silicate (C2S) Second core material* |
| *Calcium Carbonate and Oxide Filler* |
| *Iron Oxide Shade* |
| *Zirconium Oxide Radiopacifier* |
| *Liquid* |
| *Calcium chloride Accelerator* |
| *Hydrosoluble polymer Water reducing agent* |

The BD comes in capsules containing tricalcium silicate powder and capsules with aqueous calcium chloride solution and excipients (Figure 1).

The mixing instructions according to the product manufacturer and accurately followed in this study are described in Figure 2.

**Fig. 1: Biodentine™ kit: powder in capsules and liquid in capsules**

**Figure 2. Step by step Biodentine™ mixing instructions**

1.Take a capsule and gently tap it on a hard surface to loosen the powder.
2.Open a capsule and place it on the white capsule holder.
3.Detach a single-dose container of liquid and gently tap on the sealed cap to force all the liquid down the container.
4.Twist cap to open. Be careful that no drop of liquid falls out of the single dose container.
5.Pour 5 drops from the single-dose container into the capsule.
6.Close the capsule. Place the capsule on a mixing device, such as Technomix, Tac 400 (Lineatac), Silamat, Cap-Mix, Rotomix, Ultramat etc., at a speed of 4000 – 4200 rotations/min.
7.Mix for 30 seconds.
8.Open the capsule and check the material's consistency. If a thicker consistency is preferred, wait for 30 sec to 1 min before checking again. Do not exceed the working time.
9.Collect Biodentine with the instrument supplied in the box. Depending on the desired application, you may handle Biodentine with an amalgam carrier, a spatula or a Root Canal Messing Gun. Rapidly rinse and clean the instruments to remove any residual material.

V.5.2 Ferric Sulfate

Astringedent® (Viscostat®) is the brand name by the manufacturer Ultradent (Table 6, Figure 2). It is an aqueous, 15.5% ferric sulfate solution with a pH of ~1.0. Astringedent® is known as the "classic" hemostatic agent and has ability to achieve profound hemostasis in seconds.

***Table 7:*** Astringedent®

| Brand | Manufacturer | Company Logo |
|---|---|---|
| Astringedent® (Viscostat®) 15.5% Ferric Sulfate | Ultradent Products, Inc. 505 W. 10200 S. South Jordan, UT 84095 | ULTRADENT PRODUCTS, INC. |

***Fig. 3:*** Astringedent®


V.5.3 Regulatory Compliance

Both BD and FS fully comply with the U.S. and international regulations for product safety and are FDA approved.

V.6 Tooth Allocation

Each participant received a pulpotomy procedure on a single primary molar as part of the study. The subjects were assigned to either the BD Group or the FS Group using a Random Digit Table based on the order that they were enrolled in the study. From a table of random numbers, a list of 30 odd and 30 even numbers in a random sequence was generated. In the order of study enrolment, each subject who received an odd number from the generated list was assigned to the BD Group. Those participants who received even numbers were assigned to the FS Group. Sealed envelopes were used to conceal the randomization. The allocation of the participants into the two groups was performed at each subject recruitment by opening an envelope that was pre-made and sealed by the PI.

V.7 Pulpotomy Procedure

All primary molars included in the study had the pulpotomy procedure completed in a uniform manner, by following a step-by-step guide of a recommended standard

intervention and the manufacturers' instructions for the application of each of the two pulpotomy agents (Table 7).

### V.8 Initial Data Capture

After completing the pulpotomy procedures the operators were required to fill out an Initial Data Capture (IDC) Form (Figure 3, Appendix _), designed to record the information about the specific tooth diagnosis requiring the pulpotomy, the medicament used and any other comments related to the operative treatment.

### V.9 Examiner

One designated and blinded examiner, a specialist pediatric dentist, assessed the study teeth with completed pulpotomies at 6 months. The evaluation was completed according standardized criteria, defined for the purposes of this study.

Since all endodontically treated teeth included in this trial were restored with SSC, the examiner was blinded for the type of pulpotomy material. The same examiner is designated to complete the future planned 6 monthly clinical and 12 monthly radiographic assessments.

Radiographically, the BD and the ZOE cement (used as a liner over the FS treated teeth), have a significantly different degree of opacity and the examiner will not be blinded for the radiographic evaluation. The examiner is required to complete a clinical outcome data collection form and a radiographic outcome data collection, both specifically created for the purposes of this study.

**Table 8. Step-by-step study guide for the pulpotomy procedures**

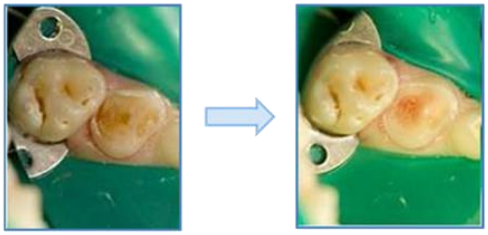
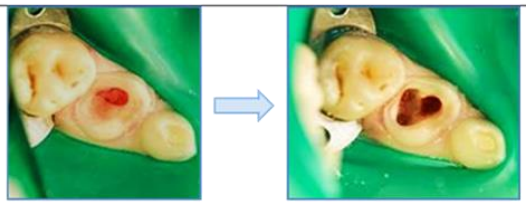
| | |
|---|---|
| • Local anesthesia<br>• Rubber dam isolation<br>• Removal of caries |  |
| • Removal of the roof of the pulp chamber with a non-end cutting bur<br>• The coronal pulpal tissue is removed with sharp sterile excavator or large round bur in a slow hand piece |  |
| Medicament for direct application to radicular pulp stumps to include:<br>• FS Group: 15.5% Ferric Sulfate solution burnished on pulp stumps with microbrush: 15sec to achieve hemostasis, followed by thorough rinsing and drying<br>• BD Group: IBD paste is mixed with sterile water to a sandy consistency, which is gently packed over radicular pulp with proprietary carrier |  |
| • Application of a lining, zinc oxide eugenol cement for the FS Group<br>• Filling up the pulp chamber and the tooth cavity with the BD material |  |

**Figure 4.** Initial Data Capture Form

**Initial Data Capture Form**

| | |
|---|---|
| Date | |
| Participant's number | |

| Tooth Number / Category | #A | #B | #I | #J | #K | #L | #S | #T |
|---|---|---|---|---|---|---|---|---|
| **Indication for pulpotomy**<br>1. Caries<br>2. Developmental / genetic defect<br>3. Tooth surface loss (erosion/ attrition)<br>5. Other (describe) | | | | | | | | |
| **Gingival Health**<br>0= healthy<br>1= mild inflammation<br>2= moderate inflammation<br>3= severe inflammation | | | | | | | | |
| **Plaque Index**<br>0= no plaque<br>1=film at gingival margin<br>2=moderate accumulation<br>3= abundance of plaque | | | | | | | | |
| **Pulpotomy Agent used**<br>1= BD<br>2= FS | | | | | | | | |
| **Definitive restoration**<br>Amalgam<br>Resin composite<br>GIC/ RMGIC<br>SSC<br>Esthetic crown<br>Other / describe | | | | | | | | |
| **Other Comments regarding this treatment:** | | | | | | | | |

V.10 Outcome Data Collection

The collection of study outcome data was designed to reflect on uniform,

standardized criteria for clinical and radiographic evaluation of the success of pulpotomized teeth. These criteria are based on diagnostic decision pathways, commonly accepted in pediatric dentistry in determining presence/absence of residual infection and/or pulp disease progression. The set of criteria, both for the clinical and the radiographic success, were adapted from the criteria used in another study with similar design from the research group of Rajasekharan *et al.,* (2016).[10] Each criterion is described in such manner as to reflect on a number of potential sequelae from the pulpotomy intervention. Furthermore, each criterion is assigned a numerical score. The numerical values of the diagnostic descriptions allow for data coding and ease of statistical analysis. The outcome data criteria specified and standardized for the purposes of this study are summarized in Table 8 and Table 9. The two sets of evaluation criteria were included in two forms for data collection, namely Clinical Outcome Data Collection Form and Radiographic Outcome Data Collection Form (Figure 5 & 6; Appendix H & I). Both forms are especially created for this research trial.

V.11 Criteria for Clinical Success

Determinants for clinical success were specifically identified for the study purposes to include:

1) Restoration (including restorative material under the SSC) is in-tact and sound.
2) No mobility beyond physiologic mobility.
3) Absence of soft tissue pathology.

Failure to meet any of these criteria was considered as a clinical failure for the purposes of this study.

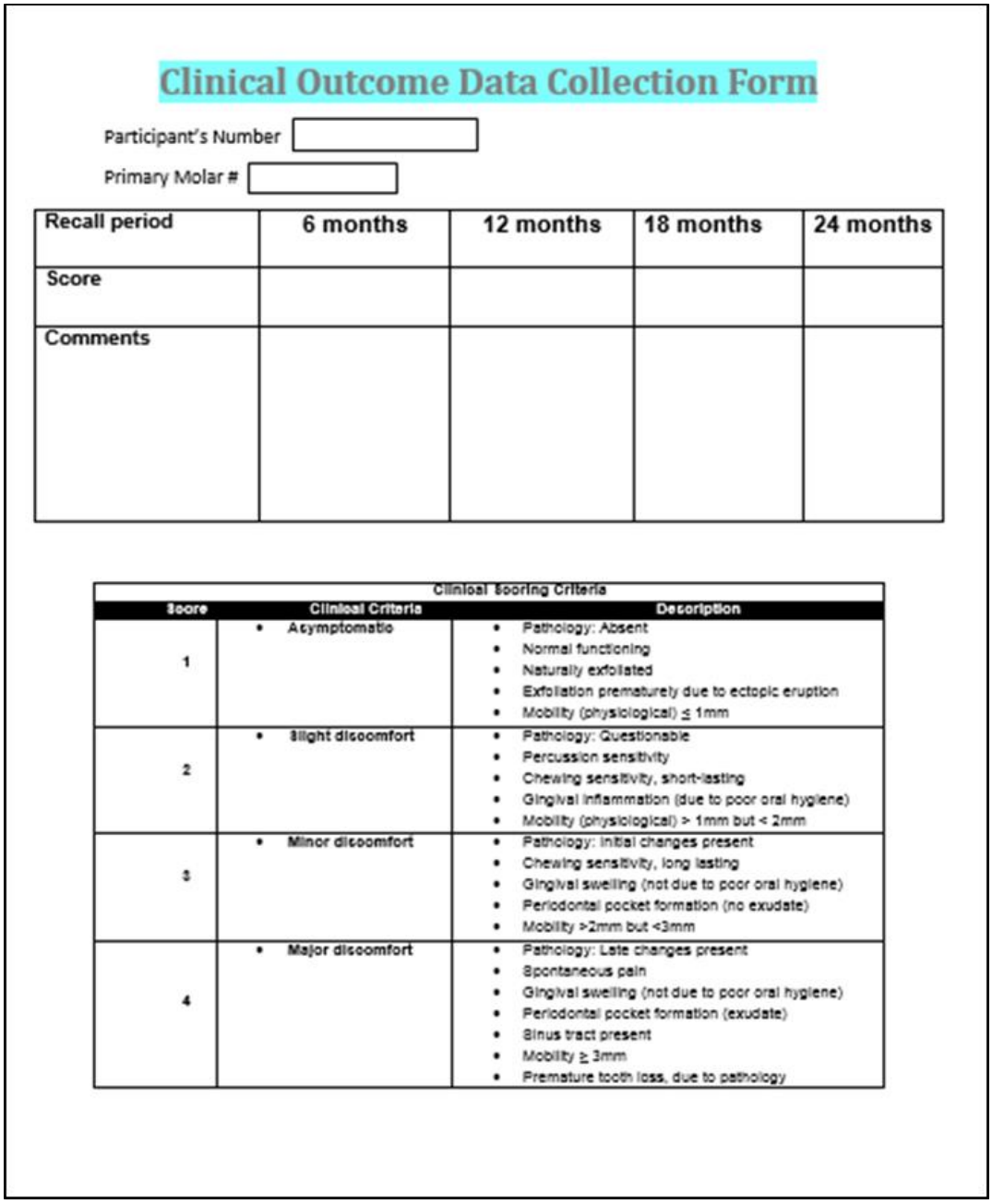
**Table 9.** Criteria for clinical success (adapted from Rajasekharan *et al.,* 2016[10])

| Clinical Scoring Criteria | | |
|---|---|---|
| **Score** | **Clinical Criteria** | **Description** |
| 1 | • Asymptomatic | • Pathology: Absent<br>• Normal functioning<br>• Naturally exfoliated<br>• Exfoliation prematurely due to ectopic eruption<br>• Mobility (physiological) ≤ 1mm |
| 2 | • Slight discomfort | • Pathology: Questionable<br>• Percussion sensitivity<br>• Chewing sensitivity, short-lasting<br>• Gingival inflammation (due to poor oral hygiene)<br>• Mobility (physiological) > 1mm but < 2mm |
| 3 | • Minor discomfort | • Pathology: Initial changes present<br>• Chewing sensitivity, long lasting<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (no exudate)<br>• Mobility >2mm but <3mm |
| 4 | • Major discomfort | • Pathology: Late changes present<br>• Spontaneous pain<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (exudate)<br>• Sinus tract present<br>• Mobility ≥ 3mm<br>• Premature tooth loss, due to pathology |

**Table 10.** Criteria for radiographic success (adapted from Rajasekharan *et al.*, 2016[10])

| Radiographic Scoring Criteria | | |
|---|---|---|
| **Score** | **Radiographic Criteria** | **Description** |
| 1 | • No changes present | • Internal root canal form tapering from chamber to the apex<br>• PDL/periapical regions: normal width and trabeculation |
| 2 | • Pathological changes of questionable clinical significance | • External changes are not allowed (widened periodontal ligament (PDL))<br>• Abnormal inter-radicular trabeculation or variation on radiodensity<br>• Internal resorption acceptable (nonperforated)<br>• Calcific metamorphosis is acceptable and defined as: uniformly thin root canal; shape (nontapering); variation in radiodensity from canal to canal (one cloudier than the other)<br>• Dentine bridge formation (one or more canals) |
| 3 | • Pathological changes present | • External changes are present, but not large<br>• Mildly widened PDL<br>• Minor inter-radicular radiolucency with trabeculation still present<br>• Minor external root resorption<br>• Internal resorption changes are acceptable, but not if external change is also present (perforated form) |
| 4 | • Pathological changes present requiring an immediate extraction of the tooth | • Frank osseous radiolucency present, endangering permanent successor |

**Figure 5.** Clinical Outcome Data Collection Form



## Clinical Outcome Data Collection Form

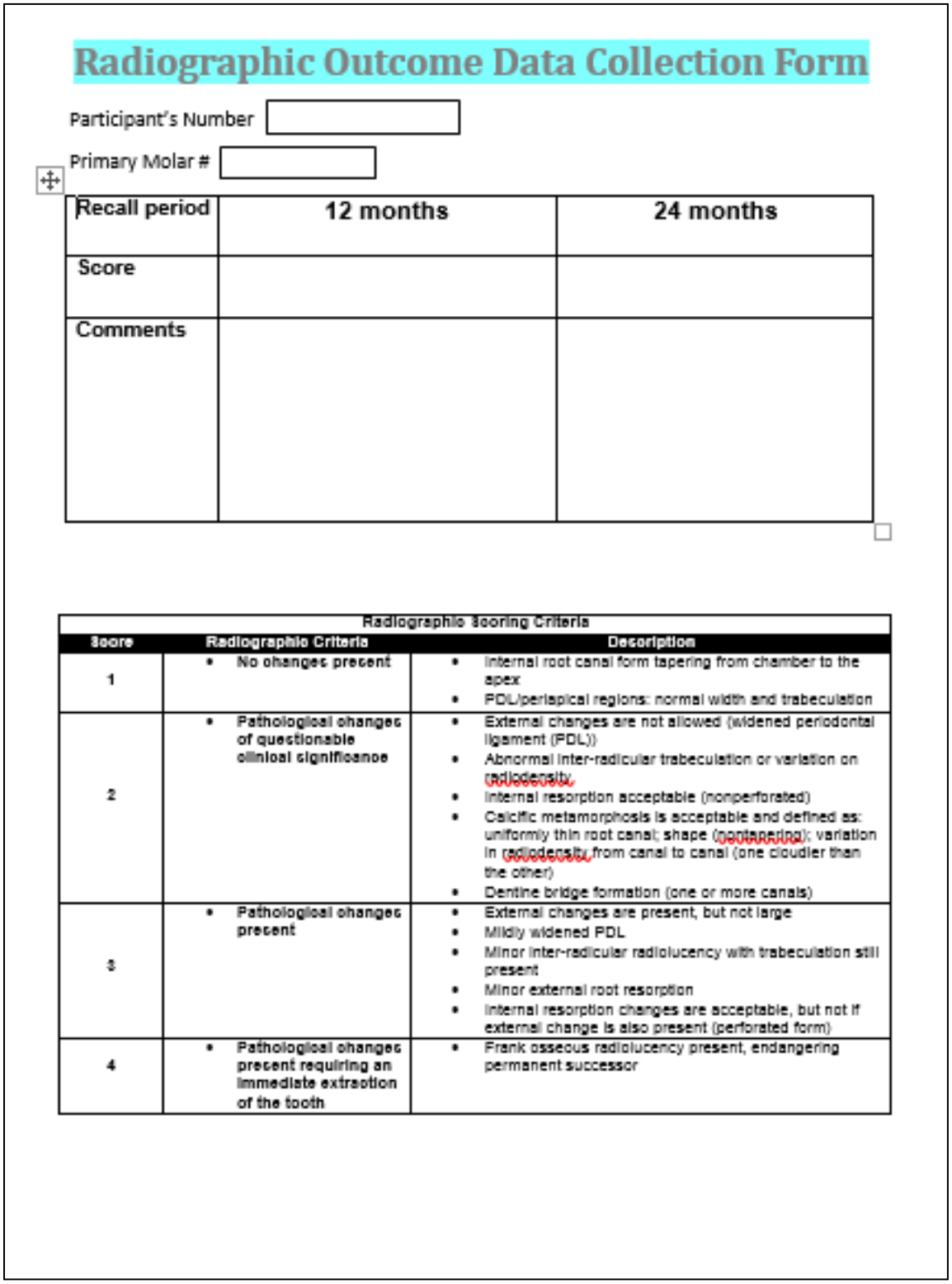
Participant's Number

Primary Molar #

| Recall period | 6 months | 12 months | 18 months | 24 months |
|---|---|---|---|---|
| Score | | | | |
| Comments | | | | |

| Clinical Scoring Criteria | | |
|---|---|---|
| **Score** | **Clinical Criteria** | **Description** |
| 1 | • Asymptomatic | • Pathology: Absent<br>• Normal functioning<br>• Naturally exfoliated<br>• Exfoliation prematurely due to ectopic eruption<br>• Mobility (physiological) ≤ 1mm |
| 2 | • Slight discomfort | • Pathology: Questionable<br>• Percussion sensitivity<br>• Chewing sensitivity, short-lasting<br>• Gingival inflammation (due to poor oral hygiene)<br>• Mobility (physiological) > 1mm but < 2mm |
| 3 | • Minor discomfort | • Pathology: Initial changes present<br>• Chewing sensitivity, long lasting<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (no exudate)<br>• Mobility >2mm but <3mm |
| 4 | • Major discomfort | • Pathology: Late changes present<br>• Spontaneous pain<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (exudate)<br>• Sinus tract present<br>• Mobility ≥ 3mm<br>• Premature tooth loss, due to pathology |

**Figure 6.** Radiographic Outcome Data Collection Form



# Radiographic Outcome Data Collection Form

Participant's Number

Primary Molar #

| Recall period | 12 months | 24 months |
|---|---|---|
| Score | | |
| Comments | | |

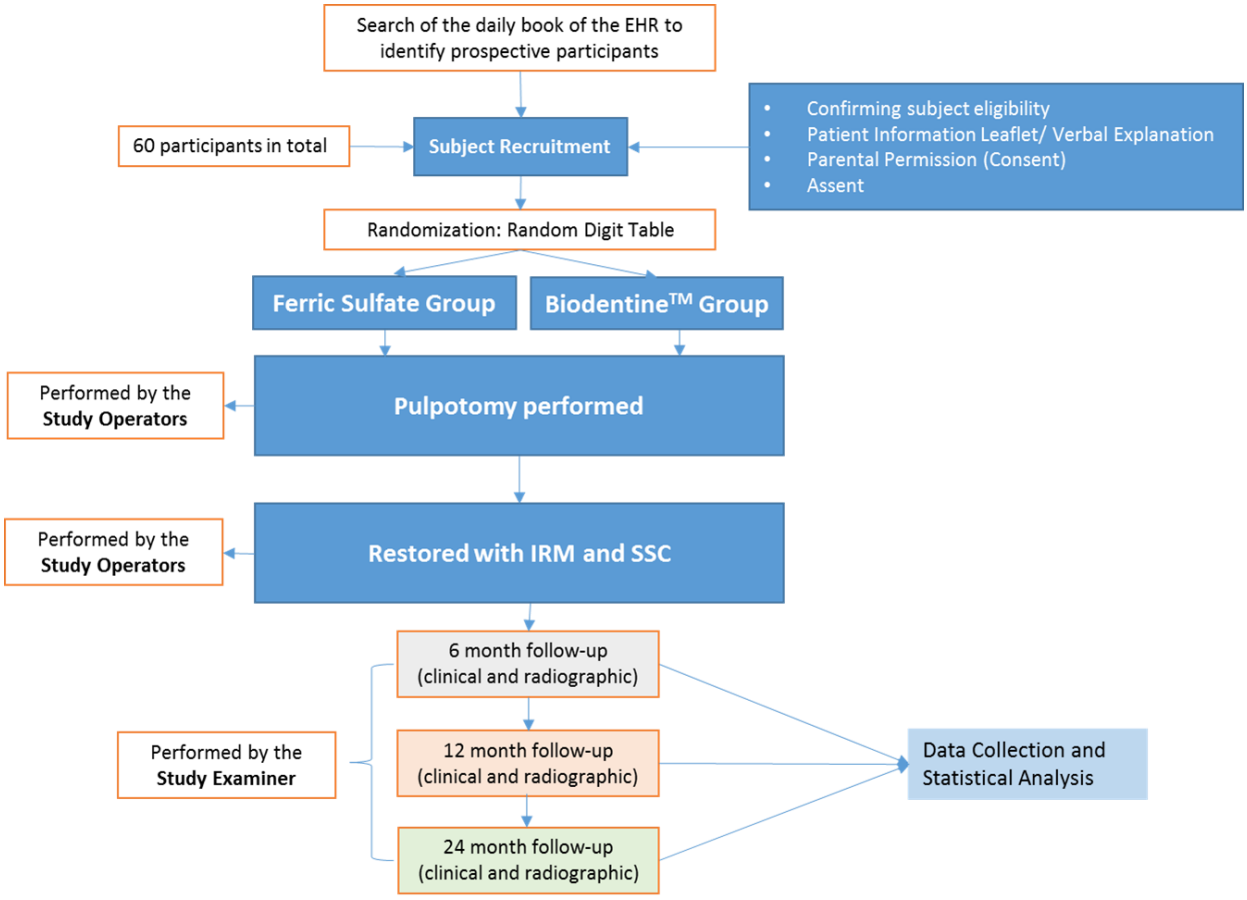
**Radiographic Scoring Criteria**

| Score | Radiographic Criteria | Description |
|---|---|---|
| 1 | • No changes present | • Internal root canal form tapering from chamber to the apex<br>• PDL/periapical regions: normal width and trabeculation |
| 2 | • Pathological changes of questionable clinical significance | • External changes are not allowed (widened periodontal ligament (PDL))<br>• Abnormal inter-radicular trabeculation or variation on radiodensity<br>• Internal resorption acceptable (nonperforated)<br>• Calcific metamorphosis is acceptable and defined as: uniformly thin root canal; shape (contouring); variation in radiodensity from canal to canal (one cloudier than the other)<br>• Dentine bridge formation (one or more canals) |
| 3 | • Pathological changes present | • External changes are present, but not large<br>• Mildly widened PDL<br>• Minor inter-radicular radiolucency with trabeculation still present<br>• Minor external root resorption<br>• Internal resorption changes are acceptable, but not if external change is also present (perforated form) |
| 4 | • Pathological changes present requiring an immediate extraction of the tooth | • Frank osseous radiolucency present, endangering permanent successor |

V.12 Flow Chart of the Study Process

The study design is illustrated in the Flow Chart presented in Figure 7.

**Figure 7.** Flow Chart of the Study Process




V.13 Statistical Analysis

Data gathered through all study forms were transferred into Microsoft Excel Spreadsheet (*Microsoft Inc., Redmond, WA, USA*). The data file was stored on a password-protected computer. The Excel data file was then transferred to the IBM SPSS statistical software program for statistical analysis. All data were assigned a numerical value in order to complete statistical analysis.

The clinical success rates of 78% for FS and 94% for BD reported in the literature were used, in order to determine the number of subjects for the study that can demonstrate

the same difference between the two pulpotomy agents. A prospective power analysis was carried out using these numeric results for the Two-Sample T-Test allowing unequal variance. According to the power calculation, a sample size of 18 (9 in each group) would be needed to achieve 92% power to reject the null hypothesis of equal means.

The data analysis consisted of univariate descriptive statistics to describe demographic information. Nonparametric statistics (Chi-square) was used to analyze the success of the two medicaments at their six month follow-up clinical evaluation. A p-value of $<0.05$ was used to determine statistical significance for the Chi-square test.

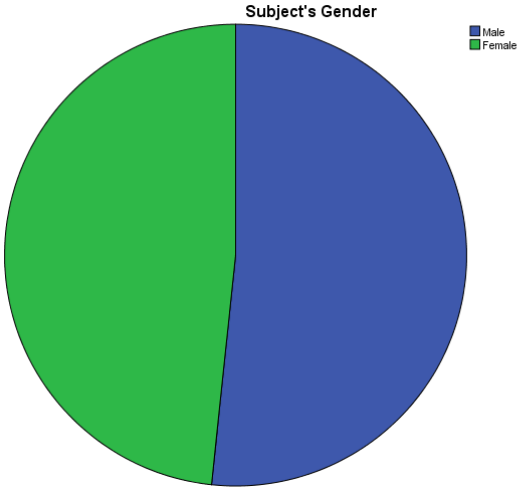
## VI. Results

### VI.1 Descriptive Data Analysis of the Initial Sample

A total of 60 participants were recruited over a period of 6 months (from June 1st 2017 to December 10th 2017).

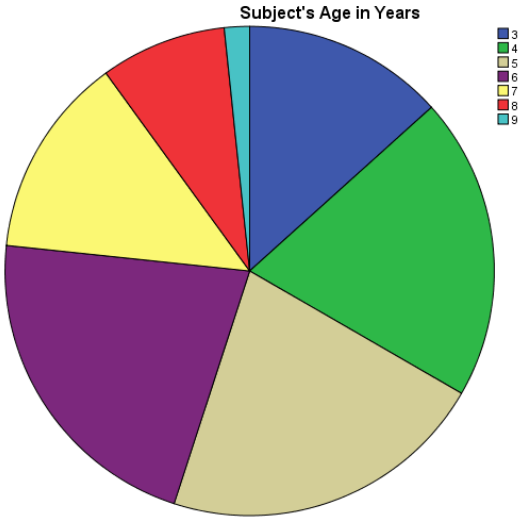
There was a slight male prevalence of 51.7% (N=31), while the females were 48.3% of the initial sample (N=29).

**Figure 8. Gender Distribution of the Initial Sample**



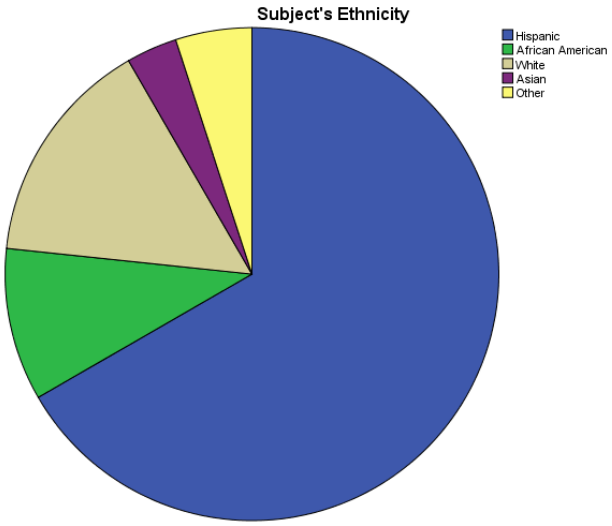

With respect to the age distribution of the 60 subjects included in the study eight (13.3%) were three years old, 12 (20%) were four years old, 13 (21.7%) were five years old, 13 (21.7%) were six years old, eight (13.3%) were seven years old, five (8.3%) were eight years old, and one (1.7%) was nine years old. Thirty eight (63.4%) of the 60 pulpotomies were performed on subjects between the ages of four and six years old. The average age of the sample was 5.3 years of age and the median age was 6 years.

**Figure 9. Age Distribution of the Initial Sample**




The ethnic distribution of the sample included 40 (66.7%) Hispanic, nine (15%) White, six (10%) African American, two (3.3%) Asian, and three (5%) of other ethnicities.

**Figure 10. Ethnic Distribution of the Initial Sample**

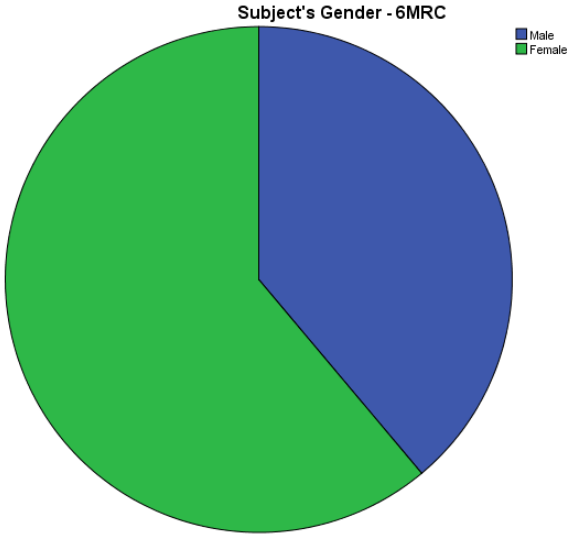



All 60 participants were medically healthy, without any reported conditions and classified into ASA I category.

VI.2 Descriptive Data Analysis of the Return Sample at 6 months

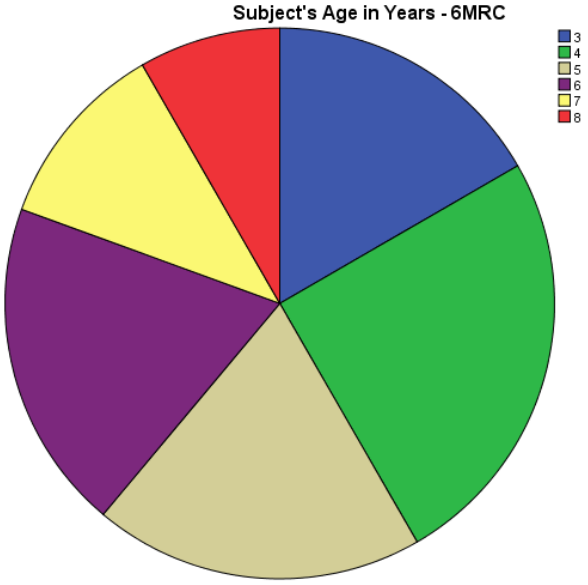
At 6 months, 36 subjects returned for clinical evaluation of the intervention. There was distinct female prevalence with 22 (61.1%), while only 14 (38.9%) males returned.

**Figure 11. Gender Distribution of the Return Sample at 6 months**



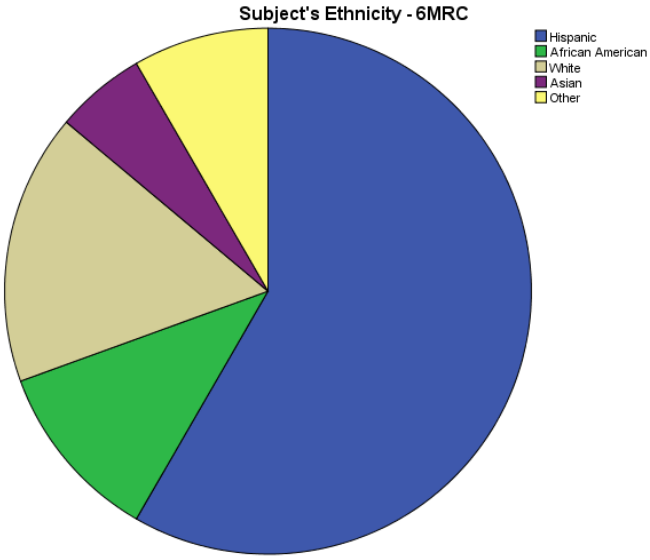

The return sample also consisted of six (16.7%) 3 year-olds, nine (25%) 4 years-olds, seven (19.4%) 5 year-olds, seven (19.4%) 6 year-olds, four (11.1%) patients were seven years of age, while only three (8.3%) were eight years old; twenty three (63.8%) of the 36 pulpotomies that returned for six month follow-up were performed on subjects between the ages of four and six years old. The average age of the return sample was 4.8 years and the median was 5 years.

**Figure 12. Age Distribution of the Return Sample at 6 months**




With respect to the ethnic distribution, out of the 36 subjects that returned for their six month follow-up 21 (58.3%) were Hispanic, six (16.7%) were White, four (11.1%) were African American, two (5.6%) were Asian, and three (8.3%) were of other ethnicities.

**Figure 13. Ethnic Distribution of the Return Sample at 6 months**

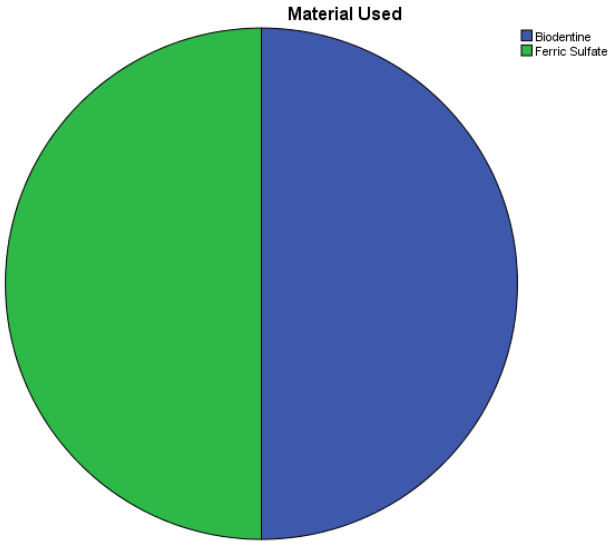


All return participants were fit and healthy medically and categorized as ASA I patients.

VI.3 Descriptive Data Analysis of the Initial Sample of Pulpotomized Teeth

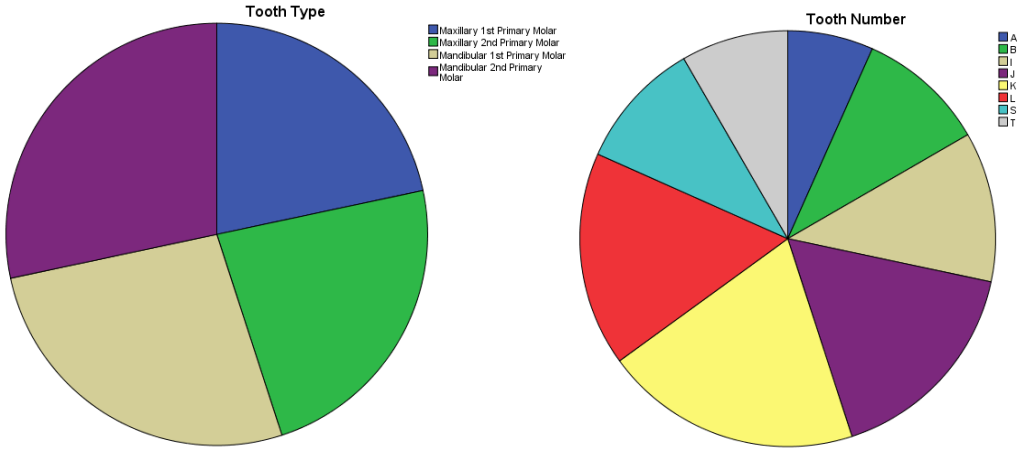
There was intended equal distribution between the type of material used for each group with 30 (50%) pulpotomies completed using BD and 30 (50%) completed using FS.

**Figure 14. Material Type Distribution of the Initial Sample of Pulpotomized Teeth**



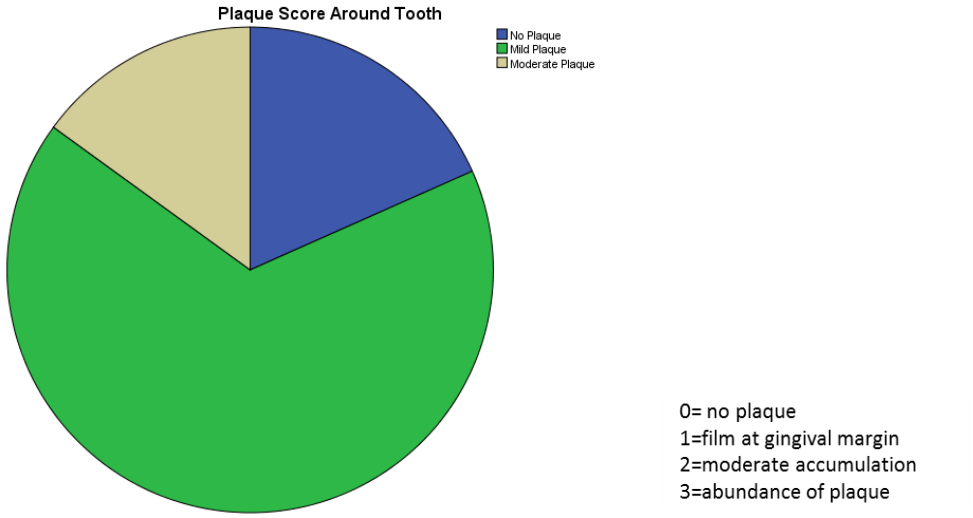

Of the 60 pulpotomies that were completed 13 (21.7%) were maxillary first primary molars. Six (10%) were maxillary right first primary molars and seven (11.7%) were maxillary left first primary molars. Fourteen (23.3%) where maxillary second primary molars, four (6.7%) where maxillary right second primary molars and ten (16.7%) where maxillary left second primary molars. Sixteen (26.7%) were mandibular first primary molars, 6 (10%) were mandibular right first primary molars and ten (16.7%) were mandibular left first primary molars, while 17 (28.3) were mandibular second primary molars. Five (8.3%) where mandibular right second primary molars and 12 (20%) were mandibular left second primary molars.

**Figure 15. Tooth Type & Number Distribution of the Initial Sample of Pulpotomized Teeth**



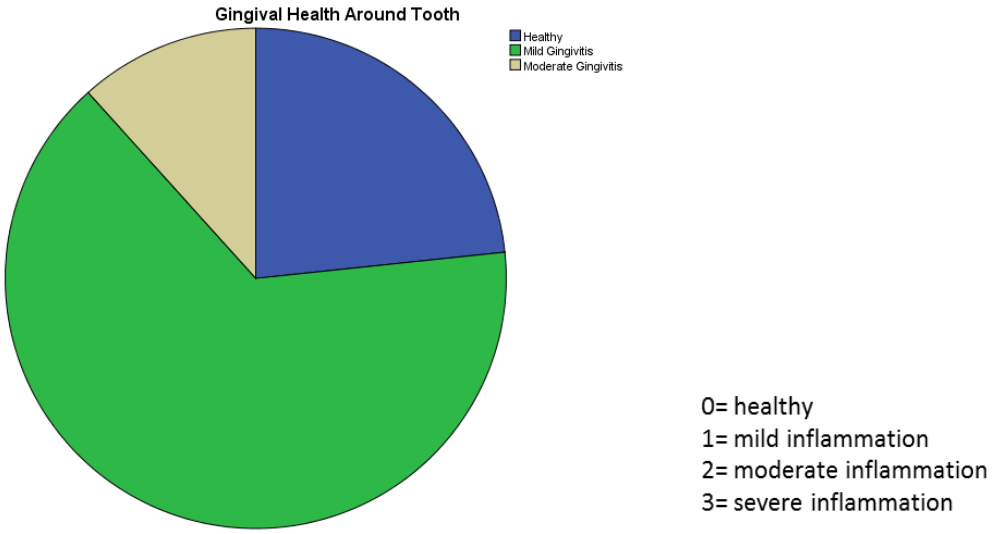

All 60 teeth (100%) that received pulpotomy treatment were restored with SSC and had an initial diagnosis of reversible pulpitis with large carious lesions extending into pulp. The amount of plaque present at the time the pulpotomy was performed was recorded for all 60 subjects. Eleven (18.3%) had no plaque present (score=0), 40 (66.7%) had a mild amount of plaque present (score=1). Nine (15%) had a moderate amount of plaque present (score=2), and no one had a score of 3.

**Figure 16. Plaque Score Distribution of the Initial Sample of Pulpotomized Teeth**



The gingival health of the teeth at the time of pulpotomy treatment was recorded for all 60 subjects. Fourteen (23.3%) had healthy gingiva, score of 0; 39 (65%) had mild gingivitis or score of 1. Seven (11.7%) had moderate gingivitis (score of 2) and none scored 3 e.g. severe inflammation of the marginal gingiva.

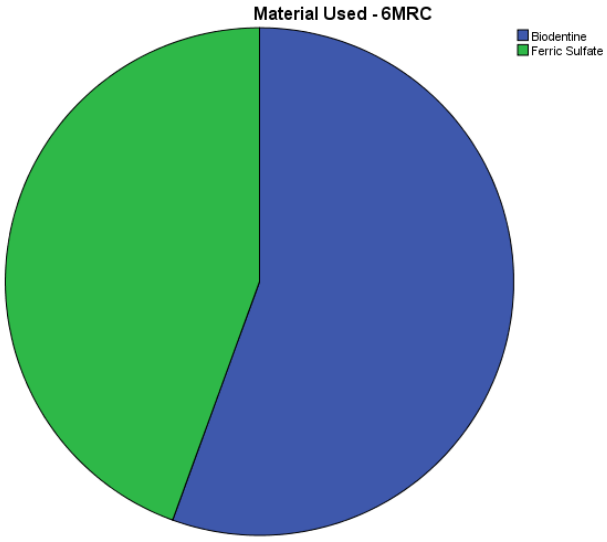
**Figure 17. Gingival Score Distribution of the Initial Sample of Pulpotomized Teeth**




VI.4 Descriptive Data Analysis of the Return Sample of Pulpotomized Teeth

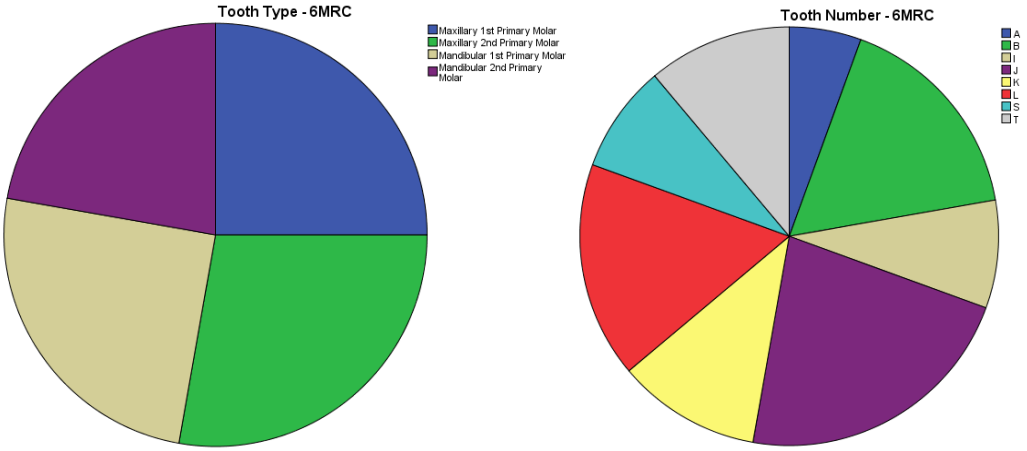
Of the 36 subjects who returned for their six month follow-up 20 (55.6%) had pulpotomies completed using BD and 16 (44.4%) had pulpotomies completed using FS.

**Figure 18. Material Type Distribution of the Return Sample of Pulpotomized Teeth**




Of the 36 pulpotomies that returned for six month follow-up nine (25%) were maxillary first primary molars. Six (16.7%) were maxillary right first primary molars and three (8.3%) were maxillary left first primary molars. Ten (27.8%) were maxillary second primary molars. Two (5.6%) were maxillary right second primary molars and eight (22.2%) were maxillary left second primary molars. Nine (25%) were mandibular first primary molars. Three (8.3%) were mandibular right first primary molars and six (16.7%) were mandibular left first primary molars. Eight (22.2%) were mandibular second primary molars. Four (11.1%) were mandibular right second primary molars and four (11.1%) were mandibular left second primary molars.

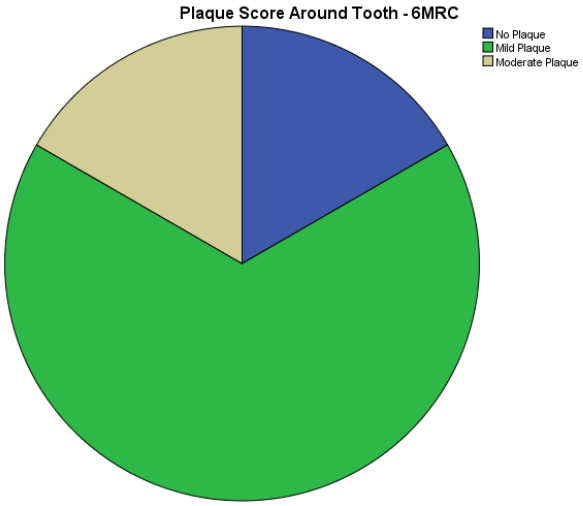
**Figure 19. Tooth Type & Number Distribution of the Return Sample of Pulpotomized Teeth**




All patients that return had intact SSC in place (100%) and all were treated with pulpotomy due to a large carious lesion extending to the pulp with the diagnosis of reversible pulpitis.

Of the 36 subjects who returned for their six month follow-up six (16.7%) had no plaque present at this evaluation point, 24 (66.7%) had a mild amount of plaque present and six (16.7%) had a moderate amount of plaque.

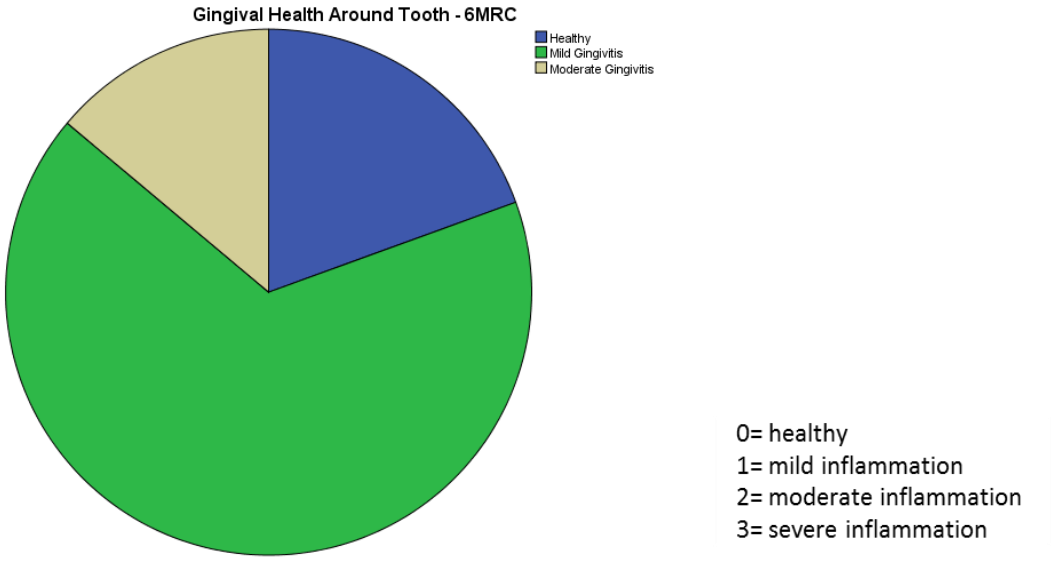
**Figure 20. Plaque Score Distribution of the Return Sample of Pulpotomized Teeth**




0= no plaque
1=film at gingival margin
2=moderate accumulation
3=abundance of plaque

Of the 36 subjects that returned for their six month follow-up seven (19.4%) had healthy gingiva at evaluation (score of 0), 24 (66.7%) had mild gingivitis (score 1) and 5 (13.9%) had moderate gingivitis (score of 2).

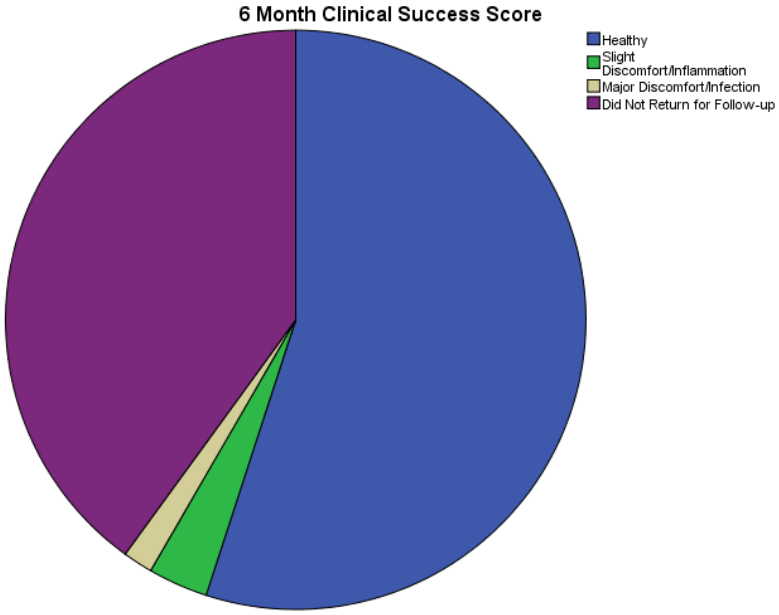
**Figure 21. Gingival Score Distribution of the Return Sample of Pulpotomized Teeth**




VI.5 Clinical Success Data Analysis of the Return Sample of Pulpotomized Teeth

Of the total sample of 60 subjects that participated in the study, the majority, or 36 (60%) returned for their six month follow-up, while 24 (40%) did not return. Upon clinical examination of the 36 subjects that returned for their six month follow-up, 33 (91.7%) were healthy, two (5.5%) were experiencing slight discomfort or had slight inflammation around the tooth that received treatment, and one (2.8%) patient had major discomfort and infection associated with the tooth that had received treatment. Since this tooth required subsequent extraction, it was considered a major failure according to the clinical outcome categorization. Hence, of the 36 pulpotomies that returned for six month follow-up 35 (97.2%) were considered to be successful and one (2.8%) was considered to be a failure.

**Figure 22. Overall Clinical Success Score Distribution of the Return Sample of Pulpotomized Teeth**



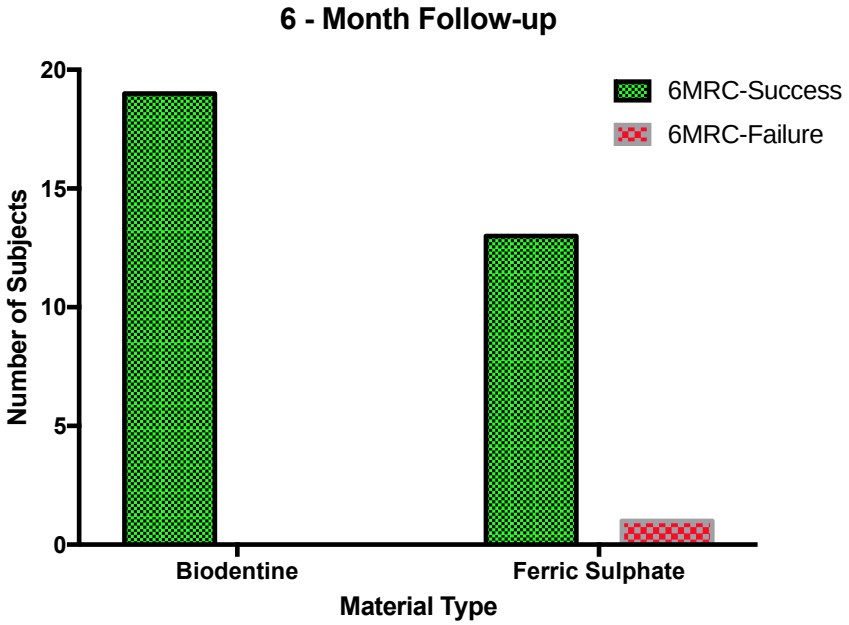

VI.6 Clinical Success Data Analysis of the Biodentine™ Group

Eighteen (90%) of the 20 pulpotomies completed using BD that returned for six month follow-up were healthy and two (10%) had slight discomfort or mild inflammation around the tooth that received treatment. However, according to the set of clinical outcome categories, all of the pulpotomies are considered successful and the BD group showed 100% clinical success in 6 months.

VI.7 Clinical Success Data Analysis of the Ferric Sulfate Group

Fifteen (93.7%) of the 16 pulpotomies completed using FS that returned for six month follow-up were healthy and one (6.3%) experienced major discomfort and infection associated with the tooth that received treatment and this tooth required extraction. Therefore, at six month follow-up the FS group exhibited 93.7% success and 6.3% failure.

**Figure 23. Difference Between Groups at Six Month Follow-up**




VI.8 Clinical Success Data Analysis of Difference Between Two Groups

At six month clinical follow-up, the FS group exhibited 93.7% success and 6.3% failure, while the BD group showed 100% success. Statistical analysis was run using Chi-square and it was determined that there was no statistically significant difference between the two groups ($x^2 = 0.2368$; $p < 0.05$).

## VII. Discussion

Out of the 36 subjects that returned for follow-up only one tooth was diagnosed with clinical failure due to the presence of a draining sinus tract adjacent to the tooth. Such clinical finding is directly associated with the status of the pulp and is a tell sign of ongoing and advanced infection. A radiographic examination, indicated for treatment decision making, had confirmed the spread of infection into the periradicular structures. The failed tooth was a mandibular first primary molar and the child's age at the time of failure was 5 years old. Hence, it can be discussed that the physiological resorption can not have played any contributing role to the failure of the treatment. It can be assumed, that if the pre-operative diagnosis and the intra-operative determination of the pulpal status were correct and that of reversible pulpitis, the properties of the pulpotomy agent have a large part to play in the ultimate outcome. It can also be argued, that such early failure of the therapy indicates greater disadvantage of the FS. However, in pediatric patients clinical symptoms and history do not correlate well with the actual status of the pulp. Furthermore, FS, being a hemostatic agent, may have obscured adequate intra-operative determination of the pulpal inflammation and may have prevented detection of hyperaemic pulp requiring non-vital therapy. In the failed case, it was established that participant had a lack of homecare with brushing and flossing from the parents. Not only was there a considerable amount of plaque on the patient's teeth at the recall visit but there were also new carious lesions on other teeth. The patient's parents were not very forthcoming with information about the patient's diet but it can be assumed that there were no significant improvements in the patient's diet since the previous examination. This further indicates the possibility that the initial diagnosis of the tooth was incorrect and the tooth was never a good candidate for vital pulp therapy. This highlights one of the major downsides to using FS as a pulpotomy medicament. If the radicular pulp tissue never truly achieved hemostasis prior to placement of the FS, the FS would have still formed a blood clot and achieved hemostasis

even if the remaining radicular pulp tissue was hyperemic. This would mean that infected tissue was left inside the tooth and it was never properly cleaned out. Hence, it is imperative to achieve hemostasis of the radicular pulp prior to placement of FS so that any remaining inflamed tissue is not able to be masked by the clotting abilities of the FS.

Almost every subject included in the study had mild to moderate gingivitis with visible plaque on their teeth. Their poor oral hygiene is likely a major reason for their high caries rate and the need for extensive restorative treatment. Even though hygiene instructions were provided to the patients and parents, poor oral hygiene was still persistent at the six month follow-up visit. Home care instructions were reviewed with patients and parents as well as visual demonstrations provided in an attempt to improve oral hygiene.

Every patient included in the study met the criteria for being considered high caries risk. This also means that they are at an increased risk for future caries and recurrent caries on previously restored teeth. Unless drastic changes in home care and diet were made since treatment was completed it can be assumed that all of the pulpotomies that were completed are not being maintained under ideal conditions. Any restorative treatment that is not well maintained will have a shorter life expectancy than if it were taken care of properly. Thus it is important to educate patients and their parents about the importance of good diet and home care and the role that it plays on the long term success of dental treatment.

An additional criteria that should have been considered for inclusion in the study was likelihood to follow through with regular recalls. Patients who received treatment in urgent care were less likely to return to the clinic once they were no longer experiencing any discomfort. This was true for both new patients and patients of record. Patients who received treatment under general anesthesia were also less likely to return for recall appointments after all of their restorative treatment had been completed. It is unclear whether this is due to the parent's low oral health literacy or a genuine lack of care for their

children's oral health. A third reason for which patients did not return was distance traveled to get to the clinic. Patients who drove multiple hours to come to the clinic were less likely to return after the completion of restorative treatment.

One of the most convenient features of BD that is not discussed very often is its ease of mixing. After adding a few drops of liquid to the capsule it can be mixed using a triturator to repeatedly achieve the desired consistency and not have to worry about the ratio of powder to liquid each time. The firm consistency to which the BD is able to be mixed allows for much easier application to the desired area, especially when compared to other bioceramic materials that are available. However, due to the hydrophilic nature of the material, once it is placed it begins to absorb water from the dentinal tubules and the previously firm material starts to become less viscous. This is both a positive and negative attribute of BD. This decrease in viscosity after placement does allow the material to flow better and give an even covering of the floor of the pulp chamber. But by losing some of is firmness that also means that the material can be displaced much easier. Recent studies showed that after three minutes of setting the material did not show any displacement when other restorative materials were placed over the BD.[10-12] When the crowns were placed over the BD in this study no disruption to the BD was observed. Unfortunately, though the BD did not hold up as well against the force of the water from the high speed hand piece. The reason that this was discovered was because many teeth had to finish being prepped after completion of the pulpotomy procedure was completed. As stated before, BD is a hydrophilic material so it was important that no moisture was present during its placement or the material would lose its viscosity and become very challenging to place and control. This meant no bleeding from the gingiva could be present during the time of BD placement and therefore interproximal reduction was often times completed after the placement of the BD. If not enough time was given for the BD to set prior to using the high speed hand piece the water from the high speed hand piece

would wash the BD out of the pulp chamber. If a cotton pellet was able to be placed over the BD, so as to protect it from wash out, the interproximal reductions were able to be completed while the BD was setting instead of waiting the three minutes for it to set before working again.

This issue with the washing out of the BD during use of the high speed hand piece also ties in with the issue of the manufactures instructions of needing to fill the entire pulp chamber with BD. This is a significant waste of material. A 2mm layer of BD over the pulpal floor provides a more than adequate seal of the vital radicular pulp tissue. This means that the remainder of the chamber could be filled with a different restorative material, covering and protecting the BD. Another study, conducted at UIC, which results await publication, had showed *in vitro* that both IRM and RMGI would be adequate restorative materials to place over the BD. Not only would this reduce the cost of the procedure but this would also protect the BD from washout and the high speed hand piece could be used right away.

The biggest challenge that BD presents to pediatric dentists is its packaging. As previously mentioned, a significantly less about of BD could be used and the remainder of the pulp chamber restored by another material with benefits other than reduction in cost. Not only does filling the whole pulp chamber with BD waste materials but triturating a whole capsule for a primary molar pulpotomy leaves the pediatric dentist discarding a large portion of the material that was never used. Even when completing multiple pulpotomies at the same time and completely filling the chambers with BD, four pulpotomies were able to be completed with ample material for left over. In the operating room where multiple quadrants of teeth are able to be isolated at one time and many pulpotomies can be completed at the same time, being able to triturate one capsule of material for all of them is very beneficial. But in a clinic setting where restorative treatment is typically completed but the quadrant there is an excessive amount of material in one

capsule. The amount of material required for the pulpotomies would decrease even further if the pediatric dentist was choosing not to restore the whole chamber with BD and covering it with a second material.

Over the course of the first 10 months of the study some opportunistic radiographs of teeth treated with BD became available. This may have been due the pulpotomy having been competed during an urgent care visit and then seen on a subsequent radiograph during the patient's initial comprehensive exam or due to variations in timing of treatment and the need for updated radiographs during recall appointments. The BD was significantly less radiopaque compared to the IRM that was used to fill the chambers of the teeth treated with FS and the opacity of the BD matched that of the surrounding dentin. Due to the radiographs being taken so soon after placement of the BD there were no calcific changes or dentinal bridge formation observed. No pulp canal obliteration or internal resorption was observed in any of the radiographs. In one radiograph the BD appeared to travel past the orifice and into the canal. No pathological signs or symptoms were present at the time but the tooth should be monitored to see if the presence of BD in the roots effects the physiologic resorption of the roots and natural exfoliation of the tooth.

The strength of this study is comparable to the current literature on other materials that are used for primary molar pulpotomies. All operators participating in the study were educated on the proper technique prior to beginning the study and those performing follow-up data collection were calibrated for uniformity. Patients were randomly assigned to each material so that there was no bias in which patients received treatment with which material. The patients will be followed-up for a period of 24 months at six month intervals obtaining clinical and radiographic data. For these reasons this study will be regarded as having high quality of evidence and be an excellent resource for clinicians to help guide them in their decision making of which medicament to use when performing primary molar pulpotomies.

Prior to beginning the study all providers that would be participating in the study were trained on the proper technique for performing a pulpotomy. This was done in lecture given by the lead investigator of the study. All providers participating in the study were also educated on how to properly use both pulpotomy medicaments that were being used in the study. This was done both by a lecture and a hands on workshop lead by a manufacturer's representative.

Based off of the initial power calculation it was determined that a minimum of nine subjects were needed for each of the two groups. Knowing that patients would inevitably be lost to follow-up a sample size of 60 subjects was determined to be adequate (30 for the BD and 30 for the FS group). At the six month follow-up only 55% of patients returned to the clinic for their recall appointment. Fortunately, at least 14 subjects from each group returned which exceeded the original power calculation. However it is highly likely that even more patients will be lost to follow-up over the two year period of the study and a sample size of 60 patients may be inadequate. After completing the first round of recall appointments it was clear that patient selection for inclusion in the study should have been given more consideration. Patients who had a pulpotomy completed in urgent care should not have been included in the study as they were less likely to return to the clinic once they were no longer experiencing any discomfort. Patients who did not show up for recall appointments between their initial exam and treatment under general anesthesia. The parents of these patients did not value oral health and as a result were less likely to return to the clinic after the completion of restorative treatment. Patients who had to travel a long distance to get to the clinic were less likely to return for recall appointments after completion of restorative treatment. 60 total patients may have been and adequate sample size but the decision to include a patient in the study should have been thought about more carefully and factors other than the dentistry been considered.

## VIII. Study Conclusions

The following conclusions can be made based on the results of this study:

- The clinical performance of BD and FS (control) as pulpotomy agents in primary molars was similar at 6 months evaluation with 100% success rate for BD and 93.7% for FS.
- Both pulpotomy agents can be recommended at short term.
- The Null Hypotheses was not rejected by the results obtained at this stage of the study process.
- Larger sample size and a longer evaluation period, including radiographic assessment are needed for definitive results.

## IX. Cited Literature


1. AAPD Guideline on Pulp Therapy for Primary and Immature Permanent Teeth. Pediatr Dent. 2016 Oct;38(6):280-288.
2. Rodd HD, Waterhouse PJ, Fuks AB, Fayle SA, Moffat MA; British Society of Paediatric Dentistry. Pulp therapy for primary molars. Int J Paediatr Dent. 2006 Sep;16 Suppl 1:15-23.

   Carrotte P. Endodontic treatment for children. Br Dent J. 2005 Jan 8;198(1):9-15.
3. Fuks AB, Papagiannoulis L. Pulpotomy in primary teeth: review of the literature according to standardized criteria. Eur Arch Paediatr Dent. 2006 Jun;7(2):64-71; discussion 72. Review.
4. Srinivasan V, Patchett CL, Waterhouse PJ. Is there life after Buckley's Formocresol? Part I -- a narrative review of alternative interventions and materials. Int J Paediatr Dent. 2006 Mar;16(2):117-27. Review.
5. Patchett CL, Srinivasan V, Waterhouse PJ. Is there life after Buckley's formocresol? Part II - Development of a protocol for the management of extensive caries in the primary molar. Int J Paediatr Dent. 2006 May;16(3):199-206.
6. Casas MJ, Kenny DJ, Johnston DH, Judd PL. Long-term outcomes of primary molar ferric sulfate pulpotomy and root canal therapy. Pediatr Dent. 2004 Jan-Feb;26(1):44-8.
7. Vostatek SF, Kanellis MJ, Weber-Gasparoni K, Gregorsok RL. Sodium hypochlorite pulpotomies in primary teeth: a retrospective assessment. Pediatr Dent. 2011 Jul-Aug;33(4):327-32.
8. Peng L, Ye L, Tan H, Zhou X. Better outcomes in pulpotomies on primary molars with MTA. Evidence-Based Dentistry 2007;8:11-12.

9. Zanini M, Sautier JM, Berdal A, Simon S (2012) Biodentine induces immortalized murine pulp cell differentiation into odontoblast-like cells and stimulates biomineralization. Journal of Endodontics 38, 1220–6.
10. Rajasekharan S, Martens LC, Cauwels RG, Verbeeck RM 2014) Biodentine material characteristics and clinical applications: a review of the literature. European Archives of Paediatric Dentistry 15, 147–58.
11. Lemon RR, Steele PJ, Jeansonne BG: Ferric sulfate hemostasis: effect on osseous wound healing. J Endodontics 19:170-173, 1993.
12. Schroeder U: Effect of an extra—pulpal blood clot on healing following experimental pulpotomy and capping with calcium hydroxide. Odont Revy 24:257-268, 1973.
13. Togaru H, Muppa R, Srinivas N, Naveen K, Reddy VK, Rebecca VC. Clinical and Radiographic Evaluation of Success of Two commercially Available Pulpotomy Agents in Primary Teeth: An in vivo Study. J Contemp Dent Pract. 2016 Jul 1;17(7):557-63.
14. Rajasekharan S, Martens LC, Vandenbulcke J, Jacquet W, Bottenberg P, Cauwels RG. Efficacy of three different pulpotomy agents in primary molars: a randomized control trial. Int Endod J. 2016 Mar;50(3):215-228.
15. Kusum B, Rakesh K, Richa K. Clinical and radiographical evaluation of mineral trioxide aggregate, biodentine and propolis as pulpotomy medicaments in primary teeth. Restor Dent Endod. 2015 Nov;40(4):276-85.
16. Cuadros-Fernández C, Lorente Rodríguez AI, Sáez-Martínez S, García-Binimelis J, About I, Mercadé M. Short-term treatment outcome of pulpotomies in primary molars using mineral trioxide aggregate and Biodentine: a randomized clinical trial. Clin Oral Investig. 2016 Sep;20(7):1639-45.

17. El Meligy OA, Allazzam S, Alamoudi NM. Comparison between biodentine and formocresol for pulpotomy of primary teeth: A randomized clinical trial. Quintessence Int. 2016;47(7):571-80
18. Havale R, Anegundi RT, Indushekar K, Sudha P. Clinical and radiographic evaluation of pulpotomies in primary molars with formocresol, glutaraldehyde and ferric sulphate. Oral Health Dent Manag. 2013 Mar;12(1):24-31.
19. Fernández CC, Martínez SS, Jimeno FG, Lorente Rodríguez AI, Mercadé M. Clinical and radiographic outcomes of the use of four dressing materials in pulpotomized primary molars: a randomized clinical trial with 2-year follow-up. Int J Paediatr Dent. 2013 Nov;23(6):400-7.
20. Odabaş ME, Alaçam A, Sillelioğlu H, Deveci C. Clinical and radiographic success rates of mineral trioxide aggregate and ferric sulphate pulpotomies performed by dental students. Eur J Paediatr Dent. 2012 Jun;13(2):118-22.
21. Huth KC, Hajek-Al-Khatar N, Wolf P, Ilie N, Hickel R, Paschos E. Long-term effectiveness of four pulpotomy techniques: 3-year randomised controlled trial. Clin Oral Investig. 2012 Aug;16(4):1243-50.
22. Sonmez D, Sari S, Cetinbaş T. A Comparison of four pulpotomy techniques in primary molars: a long-term follow-up. J Endod. 2008 Aug;34(8):950-5.
23. Vargas KG, Packham B, Lowman D. Preliminary evaluation of sodium hypochlorite for pulpotomies in primary molars. Pediatr Dent. 2006 Nov-Dec;28(6):511-7.
24. Casas MJ, Layug MA, Kenny DJ, Johnston DH, Judd PL. Two-year outcomes of primary molar ferric sulfate pulpotomy and root canal therapy. Pediatr Dent. 2003 Mar-Apr;25(2):97-102.
25. Chien MM, Setzer S, Cleaton-Jones P. How does zinc oxide-eugenol compare to ferric sulphate as a pulpotomy material? SADJ. 2001 Mar;56(3):130-5.

26. Erdem AP, Guven Y, Balli B, Ilhan B, Sepet E, Ulukapi I, Aktoren O. Success rates of mineral trioxide aggregate, ferric sulfate, and formocresol pulpotomies: a 24-month study. Pediatr Dent. 2011 Mar-Apr;33(2):165-70.
27. Fei AL, Udin RD, Johnson R. A clinical study of ferric sulfate as a pulpotomy agent in primary teeth. Pediatr Dent. 1991 Nov-Dec;13(6):327-32.
28. Fischer DE: Tissue management: A new solution to an old problem. General Dentistry 178-182, May-June 1987.
29. Fuks AB, Holan G, Davis JM, Eidelman E. Ferric sulfate versus dilute formocresol in pulpotomized primary molars: long-term follow up. Pediatr Dent. 1997 Jul-Aug;19(5):327-30.
30. Fuks AB, Holan G, Davis JM, Eidelman E. Ferric sulfate versus dilute formocresol in pulpotomized primary molars: long-term follow up. Pediatr Dent. 1997 Jul-Aug;19(5):327-30.
31. Holan G, Fuks AB, Ketlz N. Success rate of formocresol pulpotomy in primary molars restored with stainless steel crown vs amalga. Pediatr Dent. 2002 May-Jun;24(3):212-6.
32. Loh A, O'Hoy P, Tran X, Charles R, Hughes A, Kubo K, Messer LB. Evidence-based assessment: evaluation of the formocresol versus ferric sulfate primary molar pulpotomy. Pediatr Dent. 2004 Sep-Oct;26(5):401-9.
33. Ibricevic H, al-Jame Q. Ferric sulfate as pulpotomy agent in primary teeth: twenty month clinical follow-up. J Clin Pediatr Dent. 2000 Summer;24(4):269-72.
34. Doyle TL, Casas MJ, Kenny DJ, Judd PL. Mineral trioxide aggregate produces superior outcomes in vital primary molar pulpotomy. Pediatr Dent. 2010 Jan-Feb;32(1):41-7.

35. Fuks AB, Papagiannoulis L. Pulpotomy in primary teeth: review of the literature according to standardized criteria. Eur Arch Paediatr Dent. 2006 Jun;7(2):64-71; discussion 72. Review.
36. Huth KC, Paschos E, Hajek-Al-Khatar N, Hollweck R, Crispin A, Hickel R, Folwaczny M. Effectiveness of 4 pulpotomy techniques—randomized controlled trial. J Dent Res. 2005 Dec;84(12):1144-8
37. Markovic D, Zivojinovic V, Vucetic M. Evaluation of three pulpotomy medicaments in primary teeth. Eur J Paediatr Dent. 2005 Sep;6(3):133-8
38. Niranjani K, Prasad MG, Vasa AA, Divya G, Thakur MS, Saujanya K. Clinical Evaluation of Success of Primary Teeth Pulpotomy Using Mineral Trioxide Aggregate(®), Laser and Biodentine(TM)- an In Vivo Study. J Clin Diagn Res. 2015 Apr;9(4):ZC35-7.

## APPENDIX A

UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

**Approval Notice**
**Initial Review (Response to Modifications)**

May 15, 2017

Myles Clancy, D.M.D.
Pediatric Dentistry
801 S. Paulina Street
Room 267, M/C 850
Chicago, IL 60612-7211

**RE: Protocol # 2017-0192**
**"Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies"**

Dear Dr. Clancy:

Your Initial Review (Response to Modifications) was reviewed and approved by the Expedited review process on May 9, 2017. You may now begin your research.

Please note the following information about your approved research protocol:

**According to OPRS records, Shahad Al Shamali has not satisfied either initial human subject protections or HIPAA research training requirements and is not approved to participate in this research study. To participate in the project, this individual will need to be added through an amendment. Information regarding UIC HSP educational requirements and options available to satisfy this requirement can be found: http://research.uic.edu/compliance/irb/education-training. Also, a Hotmail address was listed for Shahad Al Shamali which is not permissible for University business. Please be reminded that a UIC email address is required.**

**Protocol Approval Period:** May 9, 2017 - May 9, 2018
**Approved Subject Enrollment #:** 60 Total
**Additional Determinations for Research Involving Minors:** The Board determined that this research satisfies 45CFR46.405, research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects. Therefore, in accordance with 45CFR46.408, the IRB determined that only one parent's/legal guardian's permission/signature is needed. Wards of the State may not be enrolled unless the IRB grants specific approval and assures inclusion of additional protections in the research required under 45CFR46.409. If you wish to enroll Wards of the State contact OPRS and refer to the tip sheet.

Phone: 312-996-1711 http://www.uic.edu/depts/ovcr/oprs/ FAX: 312-413-2929

**Performance Sites:** UIC
**Sponsor:** None
**Research Protocol(s):**

a) Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version 3, 5/02/2017

**Investigational Device:** Astringedent (15.5% Ferric Sulfate solution)
Biodentine ™
**Device Risk Determination:** Non-significant - Exempt

**Recruitment Material(s):**

a) Patient Information Leaflet: Randomized Clinical Trial Comparing the Success of Two Primary Molar Pulpotomy Materials, Version 2, 04/05/2017

**Informed Consent(s):**

a) Waiver of informed consent granted [45 CFR 46.116(d)] for the identification of potential subjects in the recruitment phase of the research

**Assent(s):**

a) Assent (7 to 9 years): Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version 2, 04/05/2017

**Parental Permission(s):**

a) Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version 3, 5/02/2017

**HIPAA Authorization(s):**

a) Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version: 1, Date: February, 14th 2017
b) Review Preparatory to Research acknowledged [45 CFR 164.512(i)(1)(ii)]

**Please note the Review History of this submission:**

| Receipt Date | Submission Type | Review Process | Review Date | Review Action |
|---|---|---|---|---|
| 02/15/2017 | Initial Review | Convened | 02/28/2017 | Modifications Required |
| 04/07/2017 | Response To Modifications | Convened | 04/25/2017 | Modifications Required |
| 05/02/2017 | Response To Modifications | Expedited | 05/09/2017 | Approved |

Please remember to:

→ Use your **research protocol number** (2017-0192) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with all requirements in the guidance document,
"UIC Investigator Responsibilities, Protection of Human Research Subjects"
*(http://tigger.uic.edu/depts/ovcr/research/protocolreview/irb/policies/0924.pdf)*

**Please note that the UIC IRB has the prerogative and authority to ask further questions, seek additional information, require further modifications, or monitor the conduct of your research and the consent process.**

**Please be aware that if the scope of work in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.**

We wish you the best as you conduct your research. If you have any questions or need further help, please contact OPRS at (312) 996-1711 or me at (312) 355-1404. Please send any correspondence about this protocol to OPRS at 203 AOB, M/C 672.

Sincerely,

Sheilah R. Graham, MPH
IRB Coordinator, IRB # 3
Office for the Protection of Research Subjects

Enclosure(s):

1. **Assent Document(s):**
   a) Assent (7 to 9 years): Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version 2, 04/05/2017
2. **Parental Permission(s):**
   a) Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version 3, 5/02/2017
3. **HIPAA Authorization(s):**
   a) Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies, Version: 1, Date: February, 14th 2017
4. **Recruiting Material(s):**
   a) Patient Information Leaflet: Randomized Clinical Trial Comparing the Success of Two Primary Molar Pulpotomy Materials, Version 2, 04/05/2017

cc: Marcio Da. Fonseca, Pediatric Dentistry, M/C 850
Evelina Kratunova, Faculty Sponsor, Pediatric Dentistry, M/C 850

**APPENDIX B**

APPROVAL
STARTS 5/09/2017 — EXPIRES 5/09/2018
UIC UNIVERSITY OF ILLINOIS AT CHICAGO INSTITUTIONAL REVIEW BOARD

## Patient Information Leaflet

Research Project

### Randomized Clinical Trial Comparing the Success of Two Primary Molar Pulpotomy Materials

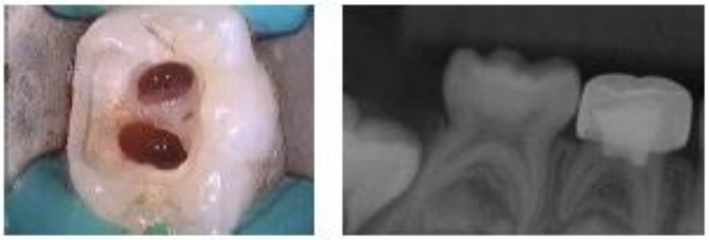
### Introduction:

Your child needs dental treatment on his/her baby back tooth (molar) which has deep decay (caries). When the decay gets very close to the nerve (pulp), the baby tooth can get an infection and become painful. In order to fix the baby tooth, a procedure called "pulpotomy" or baby root canal therapy, has to be done. This means that after removing all the decay from the tooth, the dentist also has to cut off the top part of the pulp. (Fig.1).

**Figure 1. Tooth decay and Pulpotomy**


A special medication (pulpotomy medicament) has to be placed in the tooth then to keep the remaining nerve alive. To restore the tooth to its full shape and size, the dentist will cover the baby molar with a metal cap (crown) made from stainless steel. This will make the tooth stronger and will prevent it from crumbling down (Fig. 2).

**Figure 2: Pulpotomy (Left); Radiograph of a tooth that had a pulpotomy done and and has been covered with stainless steel crown (Right);**



# Patient Information Leaflet

In this research project, we are testing two different pulpotomy medicaments. One of these is Ferric Sulfate, which we currently use for our pulpotomy treatments. Ferric Sulfate causes clotting (coagulation) of the blood of the remaining pulp. The other material is Biodentine™. It is a newer medicament, which has been used for both adult and baby teeth. It works by creating a hard barrier over the remaining nerve and protecting it from any infection. There are many study projects done in the past that have shown both medicaments (Ferric Sulfate and Biodentine™) to be safe and useful. With this project we want to see how well each material works on baby teeth and also to compare the two between each other.

**Figure 3: Ferric Sulfate (Left), Biodentine™ (Right)**


**What does this involve?**

We will recruit participants who are children between 3 to 9 years of age, who are medically fit and healthy and need pulpotomy (baby root canal therapy) on primary molars (baby back tooth). Each participant will get his/hers baby back tooth treated with one of the two pulpotomy agents, BiodentineTM or Ferric Sulfate. Which medicament a patient will receive will be determined by assignment of treatment group by chance, similar to tossing a coin. After the pulpotomy is completed, the participant will be called back to the clinic every 6 months. At that visit the tooth will be checked for a number of important items including the tooth stability (mobility), health of the surrounding gum, pain or discomfort on tapping, presence of any abscess or infection. At the recall every year the tooth will also be x-rayed to check for any changes in the roots or in the bone holding it in the mouth. These signs will help the researchers determine the success of the pulpotomy procedures and ultimately of the pulpotomy medicaments.

**Where will this treatment take place?**

This research will be done at the Pediatric Dentistry Department, College of Dentistry, UIC (801 S Paulina St, Chicago, IL 60612) and the associated University of Illinois at Chicago Hospital (1740 W Taylor St Chicago, IL 60612).

# Patient Information Leaflet

**How long will this take?**

As part of the study, your child will make five visits to the clinic. At the first one, which typically lasts about an hour, your child will receive the pulpotomy therapy. The other four will be spread 6 months apart and will coincide with the standard regular recall that your child is required to get at their dental home (as per the American Academy of Pediatric Dentistry). The recall visits will last approximately 30 minutes. The total period of study participation will be 2 years.

**What are the potential risks and discomforts?**

There are common short and long term risks associated with any baby back tooth pulp (nerve) therapy. Short-term issues include pain or discomfort from the treatment. Long-term complications may include root shrinkage, infection and tooth abscess. These are risks apparent with any baby root canal therapy and regardless of the pulpotomy agent used. Should any of these occur; a prompt and appropriate follow up treatment will be provided for your child. If one of the pulpotomy agents is a lot worse than the other, participants in that group will have poorer outcomes than those in the other group. There is a risk of loss of confidentiality. There is a risk of eye infection with Ferric Sulfate. There are no other known risks associated with the use of Ferric Sulfate and Biodentine™ as pulpotomy agents.

**Are there benefits to taking part in the research?**

There may be no direct benefits to your child by participating in the study. It is hoped that knowledge gained from this research may benefit others that will require treatment with pulpotomy agents in the future.

**Do I have to take part?**

No, you do not have to be a part of this study. If you decide that you do not want your child included in the study, we will still carry out treatment of your child's back tooth. It will not affect your right to treatment.

**Can I withdraw my child from the study?**

Yes, you can decide to withdraw from the study at any point even if you have been involved at the start.

**Confidentiality:**
Your child's identity will remain confidential. His/her name will not be published and will not be disclosed to anyone outside the study group.

**Confidentiality of Information:**
Your child will be identified on all records/data by a participant's number. Access to your child's records and data from this study will be limited to the dentists in the

research group. Any computerised information will be stored on password-protected computers with restricted access. The study data will be kept for 5 years after the study is completed in a locked cabinet but will not be used for any future unrelated studies without your permission.

**Access to Data:**
The data collected regarding your child will be available for you to see at any point during the study by asking a team member.

**Permission:**
Study permission is granted by the UIC Institutional Review Board.

**Use of the data:**

The results from this study will be published in a suitable dental journal or can be presented in a lecture format so others can benefit from the information.

**Who is the Principal Investigator of this study?**

Dr. Myles Clancy
Resident in Pediatric dentistry
UIC College of Dentistry
Department of Pediatric Dentistry
801 South Paulina Street, Chicago, Illinois 60612

**Decision to participate:**
If you make a decision to participate in our study you can inform the Principal Investigator Dr. Myles Clancy by completing and submitting the attached Study Participation Request Form. You can submit the form using one of the following options:

- Place the form **in the box with the study title** provided in the Pediatric Dental Clinic.
- Post to the address:
  **Dr. Myles Clancy**
  **UIC College of Dentistry**
  **Department of Pediatric Dentistry**
  **801 South Paulina Street, Chicago, Illinois 60612**
- Email to: mclanc4@uic.edu

**APPENDIX C**

HIPAA Authorization Template V2.9, 03/13/07

APPROVED

DATE: 5/09/2017

UIC UNIVERSITY OF ILLINOIS AT CHICAGO INSTITUTIONAL REVIEW BOARD

**University of Illinois at Chicago**
**Authorization To Use And Disclose (Release) Health Information For a Research Study**

## Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies

State and Federal laws, including the Health Insurance Portability and Accountability Act (HIPAA), require researchers to protect your child's health information. This form describes how researchers, with your authorization (permission), may use and release (disclose or share) your child's protected health information in this research study. **Please read this form carefully.**

Your child has been asked to take part in a research study. The study has already been described to you in a separate consent form. By signing this form you are permitting Dr. Myles Clancy, Pediatric Dentistry Department, COD, UIC and his research team to create, get, use, store, and share protected health information that identifies your child for the purposes of this research study.

**Description of protected health information that may be used and released (disclosed or shared)**
The health information includes all information created and/or collected during the research as described in the 'Parental Permission for Participation in Research' entitled Research Information and Parental Permission for Participation in Biomedical Research.
Protected health information may include results of tests, procedures or surveys that are part of the research. Health information in your child's dental record may be used and released if it is needed for the research; for example, past medical conditions or medications or information related to illness or hospitalizations that occur during your participation in the research.

The dental health information includes name, phone numbers, email addresses, date of birth and dental record number.

**Research use of your protected health information:**
During the conduct of the research, the researchers may use or share your health information:

- With each other and with other researchers involved with the study;
- With law enforcement or other agencies, when required by law;

- With representatives of government agencies: Food and Drug Administration, review boards including the University of Illinois at Chicago Institutional Review Board and other persons who watch over the conduct of research;

**Protection of your health information**
The researchers agree to protect your child's health information and will only share this information as described in this Authorization and the Parental Permission for Participation in Biomedical Research Form.

When your child's health information is given to people outside of the research study, those agencies that receive that health information may not be required by federal privacy laws (such as the Privacy Rule) to protect it. They may also share your information with others without your permission, if permitted by laws that they have to follow.

**Expiration of Authorization**
This Authorization expires at the end of the study but can be cancelled sooner if you decide to withdraw your permission.

**Withdrawal or removal from the study**
You may change your mind and cancel this Authorization at any time. To cancel this Authorization, you must write to:

**Myles Clancy, D.M.D.**
**Pediatric Dentistry Department, COD, UIC**
**801 S. Paulina Street,**
**Room 267 (MC850)**
**Chicago, IL 60612-7211**
**Phone 312 996-7532**
**Fax: 312 413-8006**
**Email: mclanc4@uic.edu**

If you cancel this Authorization, your child may no longer be allowed to take part in the research study. Even if you cancel this Authorization, the researchers may still use and disclose health information they have already obtained to maintain the integrity and reliability of the research and to report any adverse (bad) effects that may have happened to your child.

**Contact information for questions about my rights under HIPAA**
If you have questions or concerns regarding your privacy rights under HIPAA, you should contact the University of Illinois at Chicago Privacy Officer at Ph: (312) 996-2271.

If you have not already received a copy of the Notice of Privacy Practices, you should ask for one. You will be given a copy of this Authorization after it has been signed to keep for your records.

**Right to Refuse to Sign this Authorization**
You do not have to sign this Authorization. However, because your child's dental health information is required for research participation, if you decide not to sign this Authorization form, it will only mean your child cannot take part in this research. Not signing this form will not

affect your child's non-research related treatment, payment or enrollment in any health plans or your child's eligibility for other medical benefits.

**Signature of Subject**

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions, and my questions have been answered to my satisfaction. I authorize the use and disclosure of my child's protected health information for this research.

_____
Printed name of Subject

_____ _____
Signature of Parent /Guardian or of Subject — Date (must be same as Subject's)

_____
Printed name of Parent / Guardian

Describe relationship to subject (Check one below)
☐ Parent
☐ Legal guardian
☐ Other; specify _____

_____

_____

**APPENDIX D**


**University of Illinois at Chicago**

**Research Information and Parental Permission for Participation in Biomedical Research**

## Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ vs. Ferric Sulfate in Primary Molar Pulpotomies

Your child is being asked to participate in a research study. Researchers are required to provide a Parental Permission form such as this one to tell you about the research, to explain that taking part is voluntary, to describe the risks and benefits of participation, and to help you to make an informed decision. You should feel free to ask the researchers any questions you may have.

**Principal Investigator Name and Title**: Dr. Myles Clancy, DMD
**Department and Institution**: Pediatric Dentistry Department, University of Illinois at Chicago
**Address and Contact Information**:
801 S. Paulina Street,
Room 267 (MC850)
Chicago, IL 60612-7211
Phone 312 996-7532
Fax: 312 413-8006
Email: mclanc4@uic.edu
**Emergency Contact Name and Information**:
Dr. Evelina Kratunova, BDS, MDS, DChDent
Phone 312 996-1984
Fax: 312 413-1638
Email: evekrat@uic.edu

**Conflict of Interest:** Your child's health care provider may be an investigator on this research protocol, and as an investigator, is interested in both your child's clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your child's care from a clinician who is not associated with this project. Your child is not obligated to participate in any research project offered by his/hers clinician. Your child's participation in this research study is voluntary and he/she does not have to participate. The decision to not participate will not affect your child's clinical care now or in the future.

**Why is my child being asked?**

- A pulpotomy is a type of baby root canal treatment, which is a standard procedure done in pediatric dentistry and is used to treat teeth with large cavities extending to the pulp (nerve) of the tooth. The procedure involves removing all of the decay from the tooth as well as the top part of the nerve of the tooth. A medicament (pulpotomy agent) is then placed over the remaining nerves of the roots of the tooth and then the tooth restored with a filling or a crown (cap).
- Dentists can use different medicaments to do pulpotomy. The current standard pulpotomy agent is called 'Ferric Sulfate'. However, in the recent years another material is getting popular as well. Its trade name is Biodentine™.
- Your child requires pulpotomy on his/her baby (primary) back teeth (molars). It is important to hold on to the baby back teeth in order to have space for the adult teeth to grow/erupt so this pulpotomy treatment needs be completed.
- We are asking your permission for your child to be a participant in a research study that investigates the effectiveness of the two types pulpotomy agents (Biodentine™ and Ferric Sulfate) for primary molars.
- We recruit participants who are children between 3 to 9 years of age, who are medically fit and healthy and need pulpotomy (baby root canal therapy) on primary molars.
- Participation in this study does not affect your child's dental treatment needs. Your child will receive the same dental treatment as planned by his/hers dentist regardless of taking part or not in the research.
- Your child's participation in this research is voluntary. Your decision whether or not your child should participate will not affect your child's current or future dealings with the University of Illinois at Chicago. **If you decide to let your child participate, your child will be free to withdraw at any time without affecting that relationship.**
- Approximately 60 subjects will be involved in this research at UIC.
- All subjects would qualify for the treatments outside of the research.

**What is the purpose of this research?**

- The study is being done to test how the two types of pulpotomy agents (medicaments), Biodentine™ and Ferric Sulfate, work in baby back teeth treated with pulpotomy procedure over a period of time (2 years).
- A pulpotomy is considered successful if the treated tooth remains well and without any problems until it naturally falls out.
- Both of these materials are safe and approved for use by the U. S. Food and Drug Administration (FDA). In addition, there are studies, which show that both pulpotomy agents work well and are successful in keeping the teeth healthy and without any pain, discomfort or infection. However, this study is one of a kind as it will compare the two medicaments directly to each other.

**What procedures are involved?**

- This research will be done at the Pediatric Dentistry Department, College of Dentistry, UIC (801 S Paulina St, Chicago, IL 60612) and the associated University of Illinois at Chicago Hospital (1740 W Taylor St Chicago, IL 60612).
- We recruit participants who are children between 3 to 9 years of age, who are medically fit and healthy and need pulpotomy (baby root canal therapy) on primary molars.
- Each participant will get his/hers back baby tooth treated with one of the two pulpotomy agents, Biodentine™ or Ferric Sulfate. Which medicament a patient will receive will be determined by chance, similar to tossing a coin.
- After the pulpotomy is completed, the participant will be called back to the clinic every 6 months. At that visit the tooth will be checked for a number of important items including the tooth stability (mobility), health of the surrounding gum, pain or discomfort on tapping, presence of any abscess or infection.
- At the recall every year the tooth will also be x-rayed to check for any changes in the roots or in the bone holding it in the mouth.
- These signs will help the researchers determine the success of the pulpotomy procedures and ultimately of the pulpotomy agents.
- As part of the study, your child will make five visits to the clinic. At the first one, which typically lasts about an hour, your child will receive the pulpotomy therapy. The other four will be spread 6 months apart and will coincide with the standard regular recall that your child is required to get at their dental home (as per the American Academy of Pediatric Dentistry). The recall visits will last approximately 30 minutes.
- The total period of study participation will be 2 years.

**What are the potential risks and discomforts?**

- There are common short and long term risks associated any baby back tooth pulp (nerve) therapy. Short-term issues include pain or discomfort from the treatment. Long-term complications may include root shrinkage, infection and tooth abscess.
- These are risks apparent with any nerve therapy on a baby back tooth and regardless of the pulpotomy agent used. Should any of these occur; a prompt and appropriate follow up treatment will be provided for your child.
- If one of the pulpotomy agents is a lot worse than the other, participants in that group will have poorer outcomes than those in the other group.
- There is a risk of loss of confidentiality.
- There is a risk of eye infection with Ferric Sulfate.
- There are no other known risks associated with the use of Ferric Sulfate and Biodentine™ as pulpotomy agents.

**Will I be told about new information that may affect my decision to participate?**

- During the course of the study, you and your child will be informed of any significant new research findings (either good or bad), such as changes in the risks or benefits resulting from participation in the research or new alternatives to participation, that might

cause you to change your mind about continuing in the study. If new information is provided to you and your child, your parental permission to continue participating in this study may be re-obtained.

**Are there benefits to taking part in the research?**

- There may be no direct benefits to your child by participating in the study.
- It is hoped that knowledge gained from this research may benefit others that will require treatment with pulpotomy agents in the future.

**What other options are there?**

- If you decide that you do not want your child included in the study, he/she will receive the dental care as originally planned.
- The receipt of dental care as planned can include Biodentine™ or Ferric Sulfate restorative per choice of the dentist.

**What about privacy and confidentiality?**

- The people who will know that your child is a research participant are only the members of the research team. No information about your child, or provided by you, during the research, will be disclosed to others without your written permission, except if necessary to protect your child's rights or welfare or if required by law.
- Study information which identifies your child and the parental permission form signed by you can be looked at and/or copied for examining the research by the U.S. Food and Drug Administration (FDA)
- A possible risk of the research is that your child's participation in this study or information about your child and his/her dental health might become known to individuals outside the research. However, every effort will be made by the research team to prevent this from happening.
- Participants will be identified by a study number, which is allocated to them at the time of study enrolment. All study data will be coded using only the participants' study numbers and not including any other personal identifiers. The key to the code (personal information matching participants 'study numbers) along with all participants' personal information and records will be kept confidential at all times. Only the research team will have access to the study documentation. Hard copy files, parental permission forms, assent forms and data collection sheets will be stored in a locked cabinet in the room 269-D at the Pediatric Dentistry Department of the College of Dentistry, UIC. All computerized records, including the key to the data coding, will be protected in an encrypted folder on a password protected UIC computer.
- When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity.
- All research records will be kept for 5 years after study completion and then will be destroyed. The discarding of all electronic and paper documentation will follow strictly the policy of the Pediatric Dentistry Department, College of Dentistry, UIC for confidential information disposal.

- If you and/or your child disclose actual or suspected abuse, neglect, or exploitation of a child, or disabled or elderly adult, the researcher or any member of the study staff must, and will, report this to Child Protective Services (i.e. Department of Family and Human Services), Adult Protective Services, and/or the nearest law enforcement agency.

**What if I am injured as a result of my participation?**

- If you get ill or injured from being in the study, UIC will help you get medical treatment. You should let the study doctor know right away that you are ill or injured. If you believe you have become ill or injured from this study, you should contact Dr. Myles Clancy at telephone number (617) 419-0405.

- You should let any health care provider who treats you know that you are in a research study. If you do seek medical treatment, please take a copy of this document with you because it may help the doctors where you seek treatment to treat you. It will also provide the doctors where you seek treatment with information they may need if they want to contact the research doctors.

- You or your health insurance plan will be billed. No money has been set aside to pay the costs of this treatment. Health insurance plans may or may not cover costs of research-related injury or illness. You should check with your insurance company before deciding to participate in this research study. The study staff will assist you in obtaining pre-authorization from your insurance company. Costs not covered by insurance could be substantial.

- UIC has not set aside any money to pay you or to pay for your treatment if you get ill or injured from being in the study. There are no plans for the University to provide other forms of compensation (such as lost wages or pain and suffering) to you for research related illnesses or injuries. The only exception to this policy is if it is proven that your injury or illness is directly caused by the negligence of an UIC employee.

  By signing this form, you are not giving up any legal rights to seek compensation of injury

**What are the costs for participating in this research?**

- There will be no additional cost associated with the research project to the patients who enroll as participants in this study.
- As a standard of care to all patients whose dental home is the post-graduate pediatric dentistry department clinic, UIC, the following pattern of patient encounter is recommended:
  - An initial oral exam and development of treatment plan;
  - Visits to complete all dental treatment including dental filling, pulpotomy procedures, etc.;

- Periodic oral exam (recall) every 6 months after the dental treatment is completed to make sure that all teeth stay healthy.

- A pulpotomy procedure, regardless of the material used, is billed at the post-graduate pediatric dentistry department clinic, UIC to the price of $139.00. The cost for each periodic oral exam (recall) visit is $28.00 and the cost for an x-ray is $19.00.
- We will contact your insurance company to confirm coverage for the above listed procedures. It is anticipated that your child will be fully covered.
- If your insurance company does not provide coverage for these procedures or if your child does not have a dental insurance, the patient or the patient's family will be responsible to cover the cost that will include the pulpotomy procedure ($139.00), 4 recall visits (4 x $28= $111.00) and 2 x-rays of the tooth (2 x $19=$38.00) or a total of $289.00 payable over a period of 2 years. This cost is part of the standard of care to any patient who is a regular attender and his/her dental home is the post-graduate pediatric dentistry department clinic, UIC.
- If you decide to enroll your child in the study, there will be no added cost to the standard of care fees.
- The Pediatric Dentistry Department, College of Dentistry, UIC is supporting this study. The company Septodont, the manufacturer of Biodentine™, will provide all of the material required for the study to the researchers free of charge.

**Will I be reimbursed for any of my expenses or paid for my participation in this research?**

- Your child will not be offered any payment for being in this study.

**Can I withdraw or be removed from the study?**

- If you decide to enroll your child in this study, you are free to withdraw your parental permission and discontinue your child's participation at any time without affecting your child's future care at UIC. However, you should understand that if you choose to withdraw your parental permission after the procedures have been performed the results from the research procedures will be irreversible and cannot be undone.
  Your child has the right to leave the study at any time without a penalty. For your child's safety, however, you should consider the investigator's advice about how to leave the study.

**Who should I contact if I have questions?**

Contact the researchers:

- *Dr. Myles Clancy*
  *Phone: 312 996 7532*
  *Email: mclanc4@uic.edu*
- *Dr. Evelina Kratunova*
  *Phone 312 996-1984*
  *Email: evekrat@uic.edu*

- If you have any questions about this study or your child's part in it,

- If you feel your child has had a research-related injury (or a bad reaction to the study treatment), and/or
- If you have questions, concerns or complaints about the research:
  - *Dr. Marcio da Fonseca*
    *Pediatric Dentistry Department Head*
    *Email: marcio@uic.edu*
  - *Dr. David Avenetti*
    *Post-Graduate Program Director*
    *Email: avenetti@uic.edu*

**What are my child's rights as a research subject?**

- If you have questions about your child's rights as a research subject or concerns, complaints, or to offer input you may call the Office for the Protection of Research Subjects (OPRS) at 312-996-1711 or 1-866-789-6215 (toll-free) or e-mail OPRS at uicirb@uic.edu.

**Remember**:

- Your child's participation in this research is voluntary. Your decision whether or not to permit your child to participate will not affect your child's current or future relations with the University. If you decide to permit your child's participation, your child is free to withdraw at any time without affecting that relationship.

**Signature of Subject**:

I have read (or someone has read to me) the above information. I have been given an opportunity to ask questions and my questions have been answered to my satisfaction. I agree to my child to participate in this research. I will be given a copy of this signed and dated form.

_____ _____
Signature Date

_____
Printed Name

_____ _____
Signature of Person Obtaining Consent Date (must be same as subject's)

_____
Printed Name of Person Obtaining Consent

**APPENDIX E**

University of Illinois at Chicago


## ASSENT TO PARTICIPATE IN RESEARCH
**For children 7 to 9 years of age**

**Title:** Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies

1. My name is Dr. Myles Clancy.

2. We are asking you to take part in a research study because we are trying to learn more about two materials that dentists usually use when they do baby nerve (pulp) therapy when they fix teeth with large holes.

3. If you agree to be in this study you will get your baby tooth fixed with one of those two materials. Here is what will happen:
   - The dentist will first clean all the decay from your tooth.
   - Then he/she will take out the nerve (pulp) that is unwell and will place the material (that we are studying) in the deepest part of the hole of the tooth.
   - After that the dentist will put a filling or a crown on the baby tooth.
   - Then you will visit us in the clinic again (every 6 months) to check how is the tooth doing and to see if you have any problems with it. At two of these visits we will also take a special picture (x-ray) of your tooth. This will show us how is the tooth holding in your mouth.

4. There are some unwanted things (risks) that can also happen. For example your tooth may start hurting again or may get a buble (swelling) beside it. Then we may have to do some more work here in the clinic to fix it or even we might have to take it out if its too unwell. However, we will make our best to take a good care of you and your tooth.

5. There are some good things that can also happen if you take part in the study. We will be checking your teeth regularly and if the material that we used to fix your tooth is better than some of the others, your tooth will stay healthy and well for very long time.

6. Please talk this over with your parents before you decide whether or not to participate. We will also ask your parents to give their permission for you to take part in this study. But even if your parents say "yes" you can still decide not to do this.

7. If you don't want to be in this study, you don't have to participate. Remember, being in this study is up to you and no one will be upset if you don't want to participate or even if you change your mind later and want to stop.

8. You can ask any questions that you have about the study. If you have a question later that you didn't think of now, you can call me at (312) 996-7532 or ask me next time.

9. Signing your name at the bottom means that you agree to be in this study. Your dentist will continue to treat you whether or not you participate in this study. You and your parents will be given a copy of this form after you have signed it.

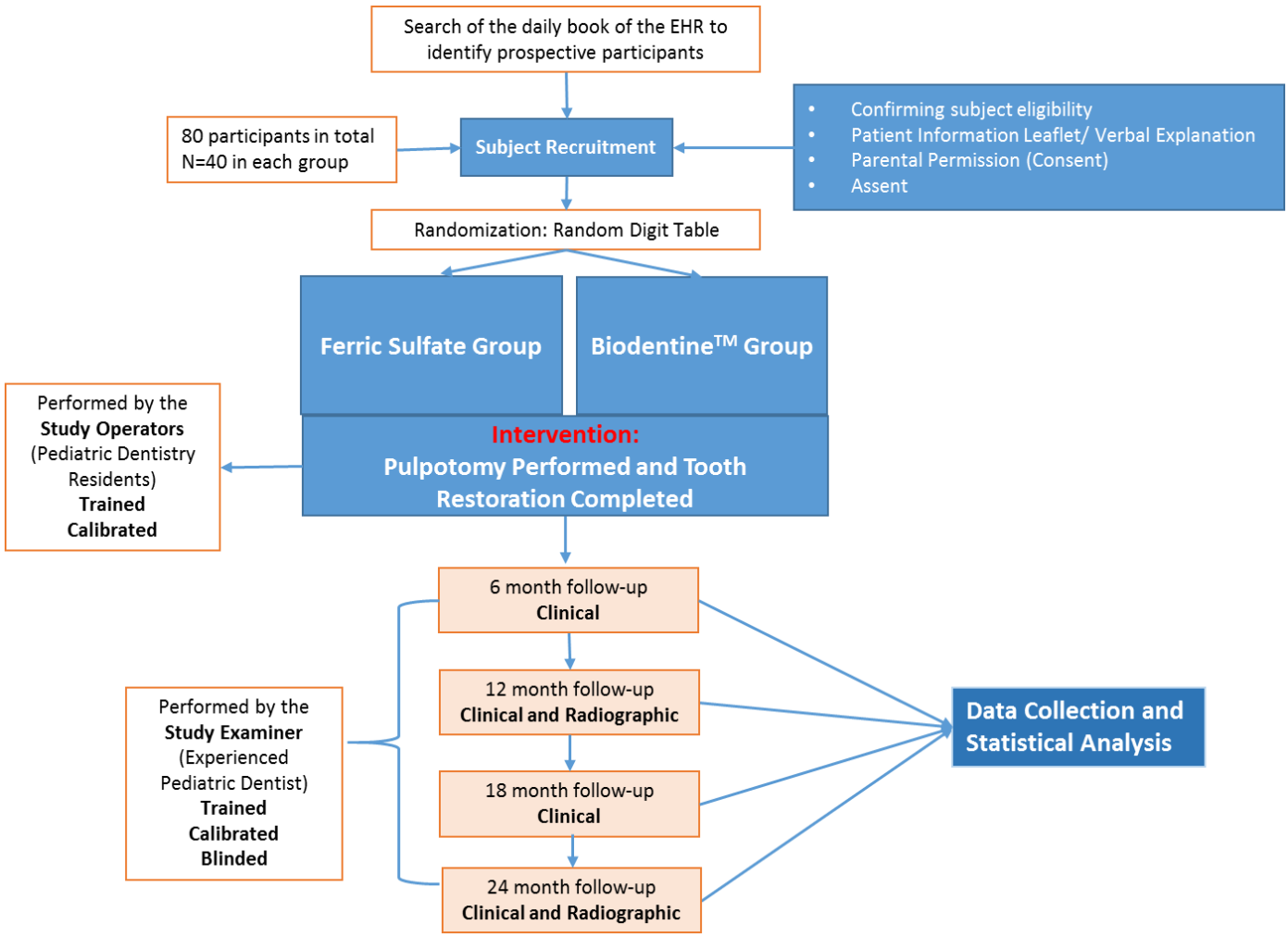
_____ _____

Name of Subject Date

_____ _____ _____

Signature Age Grade in School

## APPENDIX F


Search of the daily book of the EHR to identify prospective participants
80 participants in total N=40 in each group
Subject Recruitment
Confirming subject eligibility
Patient Information Leaflet/ Verbal Explanation
Parental Permission (Consent)
Assent
Randomization: Random Digit Table
Ferric Sulfate Group
Biodentine™ Group
Performed by the Study Operators (Pediatric Dentistry Residents) Trained Calibrated
Intervention: Pulpotomy Performed and Tooth Restoration Completed
6 month follow-up Clinical
12 month follow-up Clinical and Radiographic
18 month follow-up Clinical
24 month follow-up Clinical and Radiographic
Performed by the Study Examiner (Experienced Pediatric Dentist) Trained Calibrated Blinded
Data Collection and Statistical Analysis

**APPENDIX G**

## Initial Data Capture Form

| | |
|---|---|
| Date | |
| Participant's number | |

| Tooth Number<br>Category | #A | #B | #I | #J | #K | #L | #S | #T |
|---|---|---|---|---|---|---|---|---|
| **Indication for pulpotomy**<br>1. Caries<br>2. Developmental / genetic defect<br>3. Tooth surface loss (erosion/ attrition)<br>5. Other (describe) | | | | | | | | |
| **Gingival Health**<br>0= healthy<br>1= mild inflammation<br>2= moderate inflammation<br>3= severe inflammation | | | | | | | | |
| **Plaque Index**<br>0= no plaque<br>1=film at gingival margin<br>2=moderate accumulation<br>3= abundance of plaque | | | | | | | | |
| **Pulpotomy Agent used**<br>1= BD<br>2= FS | | | | | | | | |
| **Definitive restoration**<br>Amalgam<br>Resin composite<br>GIC/ RMGIC<br>SSC<br>Esthetic crown<br>Other / describe | | | | | | | | |
| **Other Comments regarding this treatment:** | | | | | | | | |

**APPENDIX H**

# Clinical Outcome Data Collection Form

Participant's Number

Primary Molar #

| Recall period | 6 months | 12 months | 18 months | 24 months |
|---|---|---|---|---|
| Score | | | | |
| Comments | | | | |

| Clinical Scoring Criteria | | |
|---|---|---|
| **Score** | **Clinical Criteria** | **Description** |
| 1 | • Asymptomatic | • Pathology: Absent<br>• Normal functioning<br>• Naturally exfoliated<br>• Exfoliation prematurely due to ectopic eruption<br>• Mobility (physiological) ≤ 1mm |
| 2 | • Slight discomfort | • Pathology: Questionable<br>• Percussion sensitivity<br>• Chewing sensitivity, short-lasting<br>• Gingival inflammation (due to poor oral hygiene)<br>• Mobility (physiological) > 1mm but < 2mm |
| 3 | • Minor discomfort | • Pathology: Initial changes present<br>• Chewing sensitivity, long lasting<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (no exudate)<br>• Mobility >2mm but <3mm |
| 4 | • Major discomfort | • Pathology: Late changes present<br>• Spontaneous pain<br>• Gingival swelling (not due to poor oral hygiene)<br>• Periodontal pocket formation (exudate)<br>• Sinus tract present<br>• Mobility ≥ 3mm<br>• Premature tooth loss, due to pathology |

**APPENDIX I**

# Radiographic Outcome Data Collection Form

Participant's Number

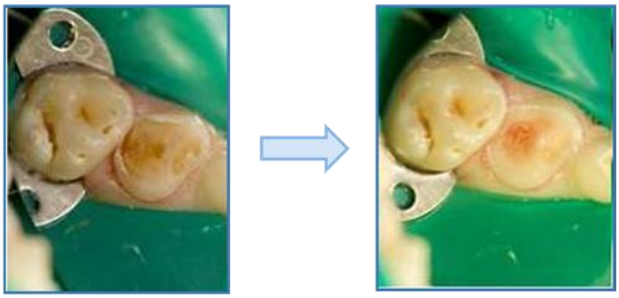
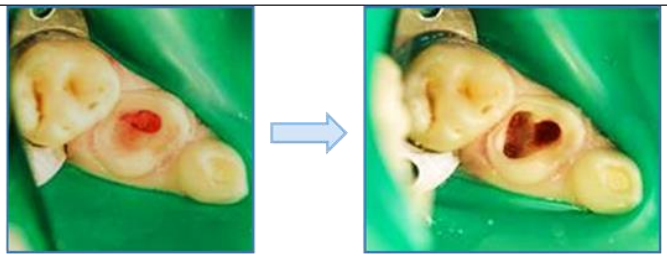
Primary Molar #

| Recall period | 12 months | 24 months |
|---|---|---|
| Score | | |
| Comments | | |

**Radiographic Scoring Criteria**

| Score | Radiographic Criteria | Description |
|---|---|---|
| 1 | • No changes present | • Internal root canal form tapering from chamber to the apex<br>• PDL/periapical regions: normal width and trabeculation |
| 2 | • Pathological changes of questionable clinical significance | • External changes are not allowed (widened periodontal ligament (PDL))<br>• Abnormal inter-radicular trabeculation or variation on radiodensity<br>• Internal resorption acceptable (nonperforated)<br>• Calcific metamorphosis is acceptable and defined as: uniformly thin root canal; shape (tapering); variation in radiodensity from canal to canal (one cloudier than the other)<br>• Dentine bridge formation (one or more canals) |
| 3 | • Pathological changes present | • External changes are present, but not large<br>• Mildly widened PDL<br>• Minor inter-radicular radiolucency with trabeculation still present<br>• Minor external root resorption<br>• Internal resorption changes are acceptable, but not if external change is also present (perforated form) |
| 4 | • Pathological changes present requiring an immediate extraction of the tooth | • Frank osseous radiolucency present, endangering permanent successor |

**APPENDIX J**

| | |
|---|---|
| • Local anesthesia<br>• Rubber dam isolation<br>• Removal of caries |  |
| • Removal of the roof of the pulp chamber with a non-end cutting bur<br>• The coronal pulpal tissue is removed with sharp sterile excavator or large round bur in a slow hand piece |  |
| Medicament for direct application to radicular pulp stumps to include:<br>• FS Group: 15.5% Ferric Sulfate solution burnished on pulp stumps with microbrush: 15sec to achieve hemostasis, followed by thorough rinsing and drying<br>• BD Group: MTA paste is mixed with sterile water to a sandy consistency, which is gently packed over radicular pulp with proprietary carrier |  |
| • Application of a lining, zinc oxide eugenol cement for the FS Group<br>• Filling up the pulp chamber and the tooth cavity with the BD material |  |

**Curriculum Vita**

**Myles Richard Clancy, D.M.D.**

**Education:**

2016 – Present University of Illinois at Chicago – College of Dentistry

*Masters in Oral Sciences*

Pediatric Dentistry Residency

Projected Completion: June 2018

20012 – 2016 Tufts University School of Dental Medicine

*Doctor of Dental* Medicine

Honors: Graduated summa cum laude

2005 – 2009 Saint Anselm College

*Bachelor of Arts*

Major: Biology

Honors: Graduated cum laude

**Board Examinations:**

NBDE Part I – Pass

NDBE Part II – Pass

**Licensure:**

CDCA Licensure Exam – Pass

Illinois State Dental License

Illinois State Controlled Substance License

**Work Experiences:**

2017 – 2018 Little Teeth Big Smiles, Children's Dentistry

*Associate Dentist*

Forest Park, IL

2017 – 2018 Elmhurst Dentistry for Kids

*Associate Dentist*

Elmhurst, IL

2012 – 2014 Dream Smile Dental

*Dental Assistant (part time)*

Canton, MA

2010 – 2012 The Center For Pediatric Dental Care and Orthodontics

*Dental Assistant*

Brookline, MA

2009 – 2010 Lux Dental

*Dental Assistant*

Quincy, MA

**Presentations:**

| | |
|---|---|
| 2018 | Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies.<br>*Presented at the AAPD Annual Session, Honolulu, HI*<br>*Presented at the UIC Clinic and Research Day, Chicago, IL* |
| 2017 | Biodentine™, A Superior Alternative to Ferric Sulfate in Primary Molar Pulpotomy Procedure<br>*Presented at the UIC Clinic and Research Day, Chicago IL* |
| 2016 | Some Fluoride Thing<br>*Presented at Tufts University School of Dental Medicine Clinic and Research Day, Boston, MA* |

**Research:**

| | |
|---|---|
| 20016 - 2018 | Randomized Controlled Trial Comparing the Clinical and Radiographic Success of Biodentine™ Vs. Ferric Sulfate in Primary Molar Pulpotomies.<br>Mentor: Evelina Kratunova, MDS, MFD, D.Ch.Dent., FFD<br>University of Illinois at Chicago Department of Pediatric Dentistry Chicago, IL |

| | |
|---|---|
| 2015 – 2016 | Fluoride Thing<br>Mentor: Gerard Kugel, DMD, MS, PhD<br>Tufts University School of Dental Medicine<br>Boston, MA |

**Honors and Awards:**

| | |
|---|---|
| 2016 | Tufts University Alpha Omega Academic Achievement award for the highest graduating GPA |
| 2016 | Tufts University Clinical Excellence in Pediatric Dentistry award |
| 2016 | Inducted into Omicron Kappa Upsilon (OKU) National Dental Honor Society |
| 2015 | Omicron Kappa Upsilon (OKU) award for the highest clinical sciences GPA |
| 2013-2016 | Tufts University Merit Scholarship |

**Affiliations:**

| | |
|---|---|
| 2017 – Present | International Association for Dental Traumatology (IADT) |
| 2016 – Present | Illinois Society for Pediatric Dentists (ISPD) |
| 2016 – Present | Chicago Dental Society (CDS) |
| 2015 – Present | American Academy of Pediatric Dentistry (AAPD) |
| 2012 – Present | American Dental Association (ADA) |