Articaine versus lidocaine for a primary intraseptal injection.

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By

Tera Elaine Pandrangi, D.M.D.

Graduate Program in Dentistry

The Ohio State University

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Master’s Examination Committee

Dr. John M. Nusstein, D.D.S., M.S., Advisor

Dr. Melissa Drum, D.D.S., M.S.

Dr. Sara Fowler, D.M.D., M.S.

Dr. Al Reader, D.D.S., M.S.

Dr. F. Michael Beck, D.D.S., M.A.
Abstract

Intraseptal anesthesia has been described as a technique to anesthetize individual teeth. However, limited research has been done to evaluate its efficacy. The purpose of this study was to compare the anesthetic efficacy of primary intraseptal injection of articaine and lidocaine, administered with a computer-controlled local anesthetic delivery (CCLAD) system, in asymptomatic mandibular first molars.

Using a crossover design, 100 subjects randomly received intraseptal injections of 1.4 mL of 4% articaine and 2% lidocaine, both with 1:100,000 epinephrine, at two separate appointments. Injections were given in the interdental papillae, mesial (0.7 mL) and distal (0.7 mL) to the first molar. An electric pulp tester was used to test for pulpal anesthesia. Pain of injection, post-operative pain, and heart rate were also evaluated. Data were statistically analyzed.

Anesthetic success rate for the mandibular first molar was 35% for articaine and 28% for lidocaine solutions, with no statistically significant difference (p > 0.05). No significant differences were found between articaine and lidocaine for pain of injection. All injection pain ratings were in the “mild” pain category, except for mesial needle insertion pain, which was in the “moderate” pain category. There were no significant differences between articaine and lidocaine for changes in heart rate. Postoperative pain decreased each day with no significant differences between solutions.
The anesthetic efficacy of articaine was not significantly better than lidocaine for primary intraseptal anesthesia of the mandibular first molar. Primary intraseptal injection does not achieve sufficient success rates of pulpal anesthesia to support its use.
Dedication

To Tyler: Thank you for your love and patience throughout this process. I am so grateful that Ohio State Endo brought me back to Columbus so I could meet you. You bring laughter and joy to my life and I am very fortunate to have you by my side.

To my parents: Thank you for all of your support throughout my entire education. I wouldn’t be where I am today without your love and devotion to my success. You have been exceptional examples to me, both professionally and personally.
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VITA

January 14, 1986 ........................................... Born – Westlake, Ohio

2008 .............................................................. B.S. Biology
.............................................................. The Ohio State University,
.............................................................. Columbus, Ohio

2013 .............................................................. Doctor of Dental Medicine
.............................................................. Midwestern University
.............................................................. Glendale, Arizona

2015 .............................................................. Master of Science and
.............................................................. Specialization in Endodontics,
.............................................................. Post-Doctoral Certificate,
.............................................................. The Ohio State University,
.............................................................. Columbus, Ohio

FIELDS OF STUDY

Major Fields: Dentistry

Specialization: Endodontics
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Chapter 1

Introduction

Intraseptal anesthesia is the deposition of the anesthetic solution directly into the interdental septum – allowing placement of solution through the porous crestal alveolar bone and hence into the medullary bone surrounding the tooth. The possible benefit may be unwanted soft tissue anesthesia of the lip which occurs with the inferior alveolar nerve block.

Intraseptal anesthesia has been evaluated previously (1-6). Success rates have varied from 76% to 90% depending on how success was measured (extractions, restorative procedures, and experimental monitoring with an electric pulp tester). Heart rate increase has been reported in some studies (1, 4, 5) but not in others (6). Postoperative pain was reported in 71% of the treated sites (5).

Articaine was approved for use in the United States in April 2000 (7). The formulation is known as Septocaine (Septodont, Inc., New Castle, DE) and is available as a 4% solution with 1:100,000 or 1:200,000 epinephrine. Articaine is classified as an amide, but contains a thiophene ring instead of a benzene ring like other amide local anesthetics (7). A second molecular difference between articaine and other amide local anesthetics is the extra ester linkage incorporated into the articaine molecule (7), which results in hydrolysis of articaine by plasma esterases. Isen (8) states that 90% to
95% of articaine is metabolized in the blood while only 5% to 10% is broken down in the liver. The plasma half-life has been reported to be as low as 20 minutes (9, 10).

Only one study has used articaine with epinephrine for primary intraseptal anesthesia in mandibular first premolars (6). The highest dose in the study by Biocanin et al (6) was only 0.8 mL – divided in equal doses (0.4 mL) between the mesial and distal aspects of the premolar. Further studies are indicated to determine if articaine is superior to lidocaine using a larger volume of local anesthetic.

Traditionally, intraseptal injections have been administered with a conventional syringe (1-5). The CCLAD (CompuDent, Wand, Milestone Scientific, Deerfield, IL) local anesthesia system was developed to deliver a controlled amount of anesthetic solution at a precise and continuous flow rate (11). The CCLAD has been advocated for infiltration injections, nerve block injections, intraseptal, and intraligamentary injections (11). Additionally, the CCLAD is potentially capable of delivering 1.4 mL of anesthetic solution compared to only 0.8 mL total with previous intraseptal injections (6). Therefore, there is a possibility of delivering more anesthetic solution intraosseously.

No study has compared the efficacy of articaine and lidocaine for intraseptal anesthesia when used as a primary technique in asymptomatic, mandibular posterior teeth. Therefore, the purpose of this prospective, randomized, double-blind study was to compare the anesthetic efficacy of the intraseptal injection of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine, administered with a computer-controlled local anesthetic delivery system, in mandibular posterior teeth. Pain of injection, heart rate increase and post-injection pain was also be studied.
Lidocaine Hydrochloride

Nils Lofgren originally formulated lidocaine in 1943. He started in the 1930s by working with dimethylamino acetotoluidide, an isomer of gramine. This compound was given to him and Holger Erdtman by Hans von Euler-Chelpin, who isolated gramine and was studying its relation to genetic and enzyme mapping in barley. Erdtman and Lofgren were tasked with synthesizing the isomer of gramine in von Euler-Chelpin’s laboratory. Erdtman placed it on his tongue and realized it had anesthetic qualities. Erdtman and Lofgren continued to work with dimethylamino acetotoluidide, creating several different compounds, but none of them were able to compete with procaine, the commonly used local anesthetic at the time. Lofgren continued the work and found that with the addition of a methyl group to one of the compounds they had previously prepared, he had formulated a compound called LL30. He gave it to his assistant Bengt Lundqvist, who discovered that LL30 was an active anesthetic and had a longer duration of action than procaine. From 1944 to 1947, Torsten Gordh and his wife conducted the first clinical evaluations of lidocaine. They found that the numbness with procaine lasted about 17 minutes, whereas with lidocaine it lasted about 70 minutes (12). Lidocaine HCl was approved by the FDA in 1948 (13).

The chemical structure of lidocaine hydrochloride is 2-diethylamino-2, 6-acetoxyxilidide hydrochloride, classifying it as an amide local anesthetic. It is converted to the active metabolites N-ethylglycine and 2, 6-xylidide, which is further transformed to the inactive metabolite 4-hydroxy-2, 6-xylidide. Metabolism occurs in the liver and is mostly mediated by the enzyme CYP1A2. Excretion of lidocaine occurs via the kidneys.
and approximately 90% is excreted as metabolites, primarily 4-hydroxy-2, 6-dimethylaniline. Since lidocaine powder is not soluble in water, it is first dissolved in hydrochloric acid which creates lidocaine hydrochloride, a salt that is water-soluble. The pH of a plain solution of lidocaine is 6.5, but when vasoconstrictor is added the pH is lowered to 5.0-5.5. The lowered pH keeps the vasoconstrictor in a more stable form so that it will not deteriorate as quickly. Lidocaine’s half-life is approximately 90 minutes (13-15).

Only 2% solutions of lidocaine are available in dental cartridges, each containing 1.7 mL of solution. Epinephrine concentrations include 1:50,000, 1:100,000, or 1:200,000. Outside the United States, 1:80,000 epinephrine concentrations are available. Epinephrine is added to the dental cartridge to produce vasoconstriction of the local blood vessels, which increases the efficacy of the lidocaine by reducing the rate of its absorption into the surrounding tissues. A 1.7 mL cartridge of 2% lidocaine with 1:100,000 epinephrine consists of 20 mg/mL of lidocaine, 0.018 mg/mL epinephrine as the bitartrate, 6.5 mg/mL sodium chloride, 1.2 mg/mL potassium metabisulfite as the preservative for the vasoconstrictor, and 0.25 mg/mL edetate disodium. A 1-2 mm nitrogen bubble can be found in the cartridge, which is inserted as the cartridge is sealed to prevent oxygen from entering and oxidizing the vasoconstrictor (13, 15).

Lidocaine is a pregnancy category B drug, which means that studies have been performed on animals without adverse effects to the fetus, but no studies have been done on pregnant women (15). The maximum single dose of lidocaine is 7.0 mg/kg. Doses above the recommended maximum could potentially cause convulsions, coma, respiratory arrest, and cardiovascular depression. Although patients may claim they are
allergic to local anesthetics, they have usually just had an increase in heart rate due to the epinephrine or an episode of syncope due to the injection itself. Reports of true allergic reactions to local anesthetics do rarely occur; however, IgE-mediated hypersensitivity reactions have never been confirmed (16).

**Articaine Hydrochloride**

The local anesthetic known as articaine was originally prepared by Rusching and colleagues in 1969 and was called carticaine at the time. Its clinical use began in 1976 in Germany. It was introduced in Canada in 1984 when its name was changed to articaine. Subsequently, its use in the United Kingdom began in 1998, the United States in 2000, and Australia in 2005 (17, 18).

The chemical structure of articaine hydrochloride is 4-methyl-3(2-[propylamino]propionamido)-2-thiophenecarboxylic acid, methyl ester hydrochloride. It is classified as an amide local anesthetic; however, it is the only amide with a thiophene ring containing an ester side chain. Articaine’s metabolism takes place by plasma carboxyesterase and also by microsomal enzyme P450 in the liver (19). It is excreted through the kidneys and approximately 89% is excreted as metabolites, primarily articainic acid which is physiologically inactive. Articaine’s properties differ from those of other amide local anesthetics, including its higher plasma protein binding and increased liposolubility (17). The pH of articaine with vasoconstrictor is 4.4-5.4. Articaine’s half-life is approximately 27 minutes (13).
Articaine is available in dental cartridges as 4% solutions with 1:100,000 or 1:200,000 epinephrine. A 1.7-mL cartridge of 4% articaine with 1:100,000 epinephrine contains 40 mg/mL articaine, 0.018 mg/ml epinephrine tartrate, 1.60 mg/mL sodium chloride, and 0.50 mg/mL sodium metabisulfate as the preservative for the epinephrine. A nitrogen bubble can also be found in articaine cartridges (19).

Articaine is a pregnancy category C drug, which means that animal studies have shown adverse effects on the fetus, but no studies have been done on pregnant women. Fetal deaths and skeletal abnormalities were seen in rabbits when given four times the maximum recommended dose, which is 7.0 mg/kg (19). Due to articaine’s rapid transformation into an inactive metabolite, it is considered one of the safer local anesthetics available since there is a lower risk for systemic toxicity and overdose, even with a 4% solution. However, as with all local anesthetics, it has the potential to be unsafe if doses above those recommended are used. Some potential adverse effects include dizziness, disorientation, tremors, convulsions, hypotension, cardiac depression, and respiratory arrest (18).

**Computer-Controlled Local Anesthetic Delivery (CCLAD) System – “The Wand®”**

Milestone Scientific introduced The Wand® in 1997. It was the first generation of their Computer-Controlled Local Anesthetic Delivery (CCLAD) system. It is composed of a disposable handpiece and a delivery unit. The plastic handpiece, or “Wand,” is held with a pen grasp and accepts a Luer Lok needle. Tubing is attached to the handpiece on one end and a hollow cylindrical unit on the other end which accepts a standard dental
anesthetic cartridge. The cartridge is placed inside the cylinder and then attached to the base delivery unit. A micropressor inside the delivery unit controls a piston which pushes a plunger up into the dental cartridge to express the anesthetic solution. The solution then passes through the tubing attached to the handpiece and through the needle. A foot pedal is also attached to the base unit. By pressing lightly on the foot pedal, the injection rate of 0.005 mL/s is activated. At this rate, a 1.7 mL cartridge is delivered in 5 minutes and 40 seconds. A faster rate of 0.03 mL/s is activated by applying heavier pressure on the foot pedal. At this rate, a 1.7 mL cartridge is delivered in approximately 1 minute. The activated rate is monitored with audible chimes and visible indicator lights from the base unit. The unit also has the ability to aspirate. When that feature is on, aspiration is controlled by the foot pedal and also monitored with the audible chimes (20).

Milestone Scientific claims that their product The Wand® allows for a more accurate needle insertion via the bidirectional rotation technique which avoids needle deflection in the soft tissues. When using this technique, the operator’s fingers are closer to the needle tip than with a traditional dental syringe and there is no thumb loop on the “Wand.” The “Wand” needle is rotated back-and-forth upon insertion in soft tissue so that, in theory, it will reach its target without deflection, as is seen with traditional syringes (20). Kennedy and coauthors compared the use of the CCLAD with the bidirectional rotation technique and a traditional dental syringe for the inferior alveolar nerve block and found no difference in success rates between the two (21).

Because of the slow and controlled rate of injection, the Wand® has been thought to provide a less painful injection than a conventional dental syringe. Numerous investigators have found a significant reduction in pain of injection when using The
Wand® in comparison to a traditional dental syringe (22-27). Kudo and coauthors and Krochak and coauthors have reported that when patients receive less painful dental injections, they will have less fear and anxiety regarding future injections at subsequent appointments (28, 29).

**Failure of Inferior Alveolar Nerve Block**

Achieving successful pulpal anesthesia of the mandibular teeth on a consistent basis is very challenging. The inferior alveolar nerve block is the injection most commonly used for mandibular anesthesia, with soft tissue numbness success rates of 80-85% (30). Success in this case is achievement of lip numbness, not necessarily pulpal anesthesia. These success rates are much lower than those of maxillary nerve blocks or infiltrations, which are generally 95% or higher (13). The lower success rates for the inferior alveolar nerve block (IANB) could be attributed to the inability to easily locate the inferior alveolar nerve and potential individual anatomical variations, which could further hinder placement of the anesthetic near the nerve. In order to anesthetize the inferior alveolar nerve, the anesthetic solution must be deposited within 1 mm of the nerve itself. The depth of soft-tissue penetration necessary and the variation in height of the mandibular foramen make it difficult to achieve this accurately in every case (13). However, even accurate placement of the needle may not result in a higher success rate of the inferior alveolar nerve block. Hannan and coauthors used a medical ultrasound’s doppler feature for direct visualization and placement of the needle next to the
neurovascular bundle. This allowed for confirmation of an accurate injection, but it did not increase the rate of pulpal anesthesia from a conventional inferior alveolar nerve block (31). Simon and coauthors used a peripheral nerve stimulator to administer the inferior alveolar nerve block and provide confirmation of accuracy of the placement of the needle. In comparison to the conventional inferior alveolar nerve block, adding the use of the peripheral nerve stimulator did not increase the success rate of pulpal anesthesia (32).

Profound lip numbness indicates that the inferior alveolar nerve was affected by the local anesthetic; however, it does not indicate that pulpal anesthesia has been achieved. Vreeland and coauthors studied the inferior alveolar nerve block with varying concentrations of lidocaine and epinephrine and tested the mandibular teeth with an electric pulp tester. Although all subjects reported profound lip numbness, not all had pulpal anesthesia. Therefore, pulp anesthesia is not guaranteed if lip numbness occurs with an accurate inferior alveolar nerve block (33). Successful pulpal anesthesia with the inferior alveolar nerve block, alone, ranges from only 10% in the central incisor to about 51% in the first molar (34). There are several theories for why the failure rate of the inferior alveolar nerve block is so high.

One theory is that the mylohyoid nerve provides accessory innervation to the mandibular teeth, which leads to failure of the IANB since the mylohyoid nerve is not anesthetized with the traditional IANB. This theory was studied by Clark and coauthors, who compared the IANB by itself to the combination of the IANB and the mylohyoid nerve block. They used a peripheral nerve stimulator to confirm the location of the mylohyoid nerve through visible movement of the floor of the mouth. This group
reported that the addition of the mylohyoid nerve block did not significantly increase pulpal anesthesia success with the inferior alveolar nerve block (35).

Deflection of the needle upon insertion and placement has been thought to cause failure of the IANB. The bidirectional rotation technique (described earlier), using the CompuDent® CCLAD system, was developed by Hochman and Friedman (36). The conventional IANB was compared with the bidirectional technique using the CCLAD by Kennedy and coauthors. They found there was no significant difference in pulpal anesthesia success rates (21).

Orientation of the needle bevel was studied by Steinkruger and coauthors (37). The IANB was administered with the bevel of the needle oriented toward the mandibular ramus and away from the mandibular ramus. It was concluded that there was no significant difference in pulpal anesthesia between the two groups. Therefore, the orientation of the needle bevel does not improve the success of the IANB (37).

The central core theory may also provide an explanation for the high failure rate of the inferior alveolar nerve block in asymptomatic patients. The theory states that nerves on the outside of the bundle supply posterior teeth, while those on the inside supply anterior teeth. Even if the anesthetic solution is placed in the correct location, it may not reach all the nerves in the bundle to provide adequate pulpal anesthesia of all mandibular teeth on that side (38, 39).

Other anesthetic solutions, solution volumes, and concentrations have been studied in the attempt of improving success rates of the IANB. Increasing the volume of lidocaine injected to 3.6 mL, or two dental cartridges, did not increase the success rate of pulpal anesthesia (40). Similarly, increasing the concentration of epinephrine to 1:50,000
for the IANB also showed no difference versus 1:100,000 epinephrine for pulpal anesthesia (41). Wali and coauthors combined both of these ideas and used 3.6 mL of 2% lidocaine with 1:50,000 epinephrine for the IANB, but did not find an increase in the success rate of pulpal anesthesia when compared to one cartridge of 2% lidocaine with 1:100,000 epinephrine (42). The addition of hyaluronidase (43) or meperidine (44) to lidocaine solutions also did not increase pulpal anesthesia for the IANB. Carbonated local anesthetics have been shown to be more effective due to their ability to become trapped in the nerve, causing the associated carbon dioxide to depress nerve activity (45). These concepts were applied in an attempt to increase success rates of pulpal anesthesia with the IANB, but Chaney and coauthors found no difference between lidocaine hydrocarbonate and lidocaine hydrochloride (45). Diphenhydramine with epinephrine proved to be less effective than lidocaine with epinephrine for pulpal anesthesia with the IANB (46).

Although articaine is generally thought to provide a more profound anesthetic effect (47), when 4% articaine with 1:100,000 epinephrine was compared to 2% lidocaine with 1:100,000 epinephrine for the inferior alveolar nerve block, Mikesell and coauthors found no significant difference (48). Mannitol (a sugar-alcohol) has the ability to disrupt the nerve perineurium and allow the local anesthetic to reach the central portion of the nerve (49). When added to lidocaine, mannitol increased the success of pulpal anesthesia with the IANB by 15-20%. Mannitol/lidocaine combinations are not currently available, but may be utilized in combination with lidocaine in the future (34).
Supplemental Anesthesia

Because the failure rate of the IANB is so high, many supplemental techniques have been developed for increasing success of mandibular pulpal anesthesia. Some of these techniques include the periodontal ligament (PDL) injection, the intraosseous (IO) injection, mandibular infiltration injections, and the intraseptal (IS) injection.

One technique used for supplemental anesthesia following an IANB is the periodontal ligament (PDL), or intraligamentary, injection. A 27-gauge short needle is recommended to be used for this injection technique (13), and is inserted along the mesial or distal side of the tooth to the depth of the gingival sulcus, parallel to the long axis of the tooth. The needle may be placed on the buccal or lingual side of the tooth, or both, and on the mesial and/or distal aspects. As the solution is deposited, it is important that the operator feel resistance and the solution should not flow back out of the sulcus (13). The pressure of the PDL injection pushes the anesthetic solution into the marrow spaces around the tooth by forcing it through the cribriform plate, making it a type of intraosseous injection (50, 51).

Devices other than conventional syringes may be used to give the injection, including the Ligma-Ject, Henke-Ject, and Soft-Ject from Henke Sass Wolf, and the CompuDent CCLAD system (the Wand®) and the STA Single Tooth Anesthesia system from Milestone Scientific. The STA system is the current version of the Wand®. The advantage of using the STA unit is that it provides the operator indicators of the amount of back-pressure encountered during the injection (34). Although back-pressure is needed
for success, the mechanism of action of the intraligamentary injection is not pressure anesthesia (50, 51).

Success rates of pulpal anesthesia with the PDL injection have been reported ranging from 18-100% (34). Childers and coauthors administered a supplemental intraligamentary injection using 2% lidocaine with 1:100,000 epinephrine following an IANB. With the supplemental intraligamentary injection, pulpal anesthesia was increased for 23 minutes (52).

The intraosseous (IO) injection is an additional technique used after the IANB for supplemental anesthesia. There are several different systems which can be used, but all involve perforation of the cortical bone and deposition of the local anesthetic into the cancellous bone. The site of the IO injection is generally 2 mm apical to the gingival margin centered with the interdental papilla in attached gingiva. The cortical plate is perforated with a beveled wire perforator in a slow-speed handpiece and the anesthetic solution is then directly deposited into the cancellous bone (13). Dunbar and coauthors studied the efficacy of a supplemental intraosseous injection of 2% lidocaine with 1:100,000 epinephrine following an IANB. Subjects who received just the IANB had a 42% success rate and those who received the IANB and the supplemental intraosseous injection had a 90% success rate (53).

Mandibular infiltrations have been studied with different types and amounts of anesthetic. Foster and coauthors found that adding a buccal infiltration of 2% lidocaine with 1:100,000 epinephrine to an IANB did not significantly increase pulpal anesthesia in the mandibular first molar (54). Haase and coauthors found that the addition of 4%
articaine with 1:100,000 epinephrine to the IANB resulted in a higher success rate of 88%, versus the addition of 2% lidocaine with 1:100,000 epinephrine at only 71% (55).

**Supplemental Injection Techniques Used as Primary Injections**

These supplemental injection techniques are useful in increasing the success of pulpal anesthesia following an inferior alveolar nerve block. Research on the success of a primary injection may indicate whether the injection would be valuable as a supplemental technique for obtaining mandibular pulpal anesthesia. This was shown with the PDL, IO and buccal infiltration injection techniques.

Schleder and coauthors (56) performed a primary intraligamentary injection using 2% lidocaine with 1:100,000 epinephrine and found a 79% success rate for the mandibular first molar and 63% for the mandibular first premolar. Berlin and coauthors (57) used the CompuDent® CCLAD to administer a primary intraligamentary injection and compared 1.4 mL of 4% articaine with 1:100,000 epinephrine to 1.4 mL of 2% lidocaine with 1:100,000 epinephrine in the mandibular first molar. Pulpal anesthesia was 86% for articaine and 74% for lidocaine, with no significant difference between the two anesthetics (57). The duration of pulpal anesthesia was approximately 20 minutes longer than other studies (56, 58) using the high-pressure syringe. This could be because more solution can be deposited using the CCLAD unit.

Coggins and coauthors administered 1.8 mL of 2% lidocaine with 1:100,000 epinephrine, via primary intraosseous injection and found a 75% success rate in the
mandibular first molar (59). Similarly, Replogle and coauthors found a 74% success rate (60). Gallatin and coauthors used both the Stabident and X-Tip systems with 1.8 mL of 2% lidocaine with 1:100,000 epinephrine and found 93% success in the mandibular first molar (61).

Meechan and coauthors found that a primary mandibular buccal infiltration of 1.8 mL of 2% lidocaine with 1:100,000 epinephrine resulted in only a 32% success rate (62). Kanaa and coauthors found that 1.8 mL of 4% articaine with 1:100,000 epinephrine had a significantly higher success rate of pulpal anesthesia than 1.8 mL of 2% lidocaine with 1:100,000 epinephrine as a primary buccal infiltration of the mandibular first molar (63).

An additional technique potentially useful for supplemental mandibular anesthesia is the intraseptal injection, which may be simpler to administer than the PDL or IO injections. Although the intraseptal injection could be useful for supplemental anesthesia, it has only been studied as a primary injection technique (1, 3, 5, 6, 64, 65).

**Intraseptal (IS) Anesthesia**

The IS injection utilizes a 27-gauge short needle which is inserted in the center of the interdental papilla, approximately 2 mm below the tip of the papillary triangle, centered between the adjacent teeth (13). Saadoun and Malamed recommend the needle be inserted at a 40°-45° angle to the long axis of the tooth in the frontal plane and at a right angle to the soft tissue in the sagittal plane, with the direction of the needle bevel toward the root apex (64). The rationale for this injection technique is attributed to the
bony anatomy surrounding the roots of the teeth. The medullary canals of the cancellous bone terminate into very small perforations in the alveolar bone within the interdental septum. This is where the local anesthetic gains access to the cancellous bone spaces. The injection is given with back pressure, similar to the PDL injection. As the injection is administered and back pressure is encountered, the indication of a good injection is no leakage of anesthetic solution from the sulcus and gingival blanching of the papilla (64).

Kim and coauthors (1) conducted a study in dogs using crystalline blue dye to show that anesthetic solution reaches the periapical region of the teeth after administration of the intraseptal injection. The inferior alveolar nerve bundle and area surrounding the apex of the tooth were stained, similar to what occurs with the IO and PDL injections. They also monitored pulpal blood flow following administration of mandibular block and intraseptal injections of 2% lidocaine with 1:100,000 epinephrine. Pulpal blood flow was measured using injection of radioisotope-labeled microspheres via a cardiac catheter to the left ventricle before and after administration of the local anesthetic. Five minutes after the IS injection, pulpal blood flow was reduced to 9.6% in mandibular molars with the IS injection, in comparison to 47.2% with the mandibular block injection (1).

Clinical applications of the IS injection include root planing, minor gingival surgical procedures, removal of fractured cusps retained by periodontal attachment, placement of gingival retraction cord, matrix bands, or wedges, and bone sounding for determination of biologic width (14). Woodmansey suggested repeating the injection on the opposite side of the papilla and again on both the buccal and lingual sides of the papilla on the other side of the tooth being anesthetized for a total of 4 injections (3).
Marin reported an onset of anesthesia of 20-30 seconds following the IS injection. Duration was as long as 45 minutes. Anesthesia of alveolar bone, periodontal ligament, cementum, and pulp lasted for 30-60 minutes. Marin discussed the advantage of the ability to anesthetize teeth in multiple quadrants during the same appointment and being able to avoid waiting for onset of anesthesia (65). For endodontic procedures, Marin recommended 2% lidocaine with 1:50,000 epinephrine for a primary intraseptal injection, as reduction in pulpal blood flow is not of concern and which allows for “painless pulp extirpation.” Marin further stated, “supplemental intrapulpal injections, used when necessary, ensure complete comfort” (65). Patients returned for follow-up examinations and had no adverse reactions (65).

Saadoun and Malamed performed a study involving periodontal surgery with the use of primary IS anesthesia (64). They completed 100 periodontal surgeries on 54 patients with moderate-to-advanced periodontal disease. The types of procedures performed included open flap curettage (with or without osseous surgery), apically positioned flap with osseous recontouring, graft, and root amputation. All surgeries included buccal and palatal flap curettage. All procedures were performed using intraseptal anesthesia with 2% lidocaine with 1:50,000 epinephrine, with or without the use of oral sedation. Patients were asked about pain that occurred during the injection and 73% reported a “near” painless needle insertion, but all (100%) felt the sensation of pressure during solution deposition. Most patients did not like the amount of time it took and the number of injections necessary (12 per sextant and 18 per quadrant). The time between injection and beginning the procedure was 1 minute, on average. The authors recommended allowing 5-15 seconds for onset of anesthesia and stated that onset was
generally immediate. The extent of anesthesia was measured to be 21-25 mm around the injection site, included all keratinized gingiva, and extended beyond the mucogingival junction. Cortical and alveolar bone anesthesia was adequate for the procedures for every patient. Pulpal anesthesia lasted 30-60 minutes, as determined by root planing without discomfort to the patient. Sensitivity with the ultrasonic scaler occurred toward the end of the procedure, indicating that pulpal anesthesia had worn off. When patients were asked whether they would prefer the IANB or the IS injections, most preferred IS anesthesia. The authors initially used 2% lidocaine with 1:100,000 epinephrine, but stopped due to excessive bleeding and patient discomfort. Switching to 2% lidocaine with 1:50,000 epinephrine decreased bleeding and prolonged the duration of anesthesia. Saaoud and Malamed also noted the frequent occurrence of leakage of the anesthetic solution during the injection, causing a bad taste in the patient’s mouth (64).

Brkovic and coauthors studied primary IS and PDL anesthesia for extraction of maxillary teeth (5). Included in the study were 35 healthy patients requiring extraction of both maxillary lateral incisors. Each patient had 2 appointments within 2 weeks, one for each extraction. Intraseptal anesthesia was used for the first appointment and periodontal ligament anesthesia for the second. For the intraseptal injections, 0.2 mL was given at 4 different sites per tooth: mesiobuccal, distobuccal, mesiolingual, and distolingual, for a total of 0.8 mL of solution. The same amount of anesthetic was used for the periodontal ligament injections at the 4 different sites. Pinprick testing was performed on the buccal and lingual surfaces every 15 seconds to determine onset of anesthesia. Blood pressure and heart rate were measured before and after administration of anesthesia. Because of severe pain during tooth extraction, 4 teeth from the intraseptal group and 3 teeth from
the periodontal ligament group were excluded and additional infiltration was required to complete the procedure. Therefore, the intraseptal injections resulted in an 88.6% success for extractions and 91.4% for the periodontal ligament injections. However, 24% of the patients in the intraseptal group reported feeling pain and 19% felt pain in the periodontal ligament group. The width of the anesthetic field was significantly greater for the intraseptal group. Postoperative pain was reported by the patients to be 70.9% in the intraseptal group and 81.3% in the periodontal ligament group. Heart rate increased at 10, 15, and 30 minutes after administration of anesthesia in both groups compared to basal values (5).

Biocanin and coauthors studied IS and PDL anesthesia of articaine using the CCLAD device (6). Healthy volunteers (180) were randomly assigned to different volumes of 4% articaine with 1:100,000 epinephrine. The 3 groups were 0.4 mL (16 mg of articaine and 4 µg of epinephrine), 0.6 mL (24 mg of articaine and 6 µg of epinephrine), or 0.8 mL (32 mg of articaine and 8 µg of epinephrine). Each participant received one of the three amounts of anesthetic via the IS or PDL injection, making a total of 6 groups comprised of 30 participants each. This was not a repeated-measures study – patients were not controlled. The CCLAD was used to administer half the anesthetic on the mesial aspect of the mandibular first premolar and the other half on the distal aspect of the same tooth (6). The same injection techniques for the IS and PDL injections were applied as previously described by Brkovic and coauthors (5). The only difference in injection technique was the use of the CCLAD for injection and 30-gauge needles in this study, as opposed to 27-gauge needles on a pressure syringe. Success was defined as achieving 2 or more consecutive 80 readings, with no response from the
participant, using an electric pulp tester. For the intraseptal injections, 0.4 mL resulted in 73.0% success, whereas 0.6 mL and 0.8 mL resulted in 90% success. Duration of pulpal and soft tissue anesthesia was measured in those who achieved successful pulpal anesthesia. On average, 0.4 mL caused 9.4 minutes of pulpal anesthesia and 40.6 minutes of soft tissue anesthesia, 0.6 mL resulted in 14.7 minutes of pulpal anesthesia and 54.4 minutes of soft tissue anesthesia, and 0.8 mL achieved 24.2 minutes of pulpal anesthesia and 70.0 minutes of soft tissue anesthesia. Cardiovascular measures were also recorded for those who achieved pulpal anesthesia. In all 6 groups, there were no significant differences in systolic and diastolic blood pressure, mean arterial pressure, and heart rate as measured prior to injection, during injection, and after injection. Biting sensitivity postoperatively was only reported in those who received the PDL injections. After receiving the intraseptal injections, 3 reported a hematoma in the region of the papilla (1 given 0.6 mL and 2 given 0.8 mL). The results of the study showed no significant dose-dependent relationship between the groups given the intraseptal injections. However, there was a significant relationship between dose and duration of pulpal and soft tissue anesthesia. According to Biocanin and coauthors, clinically acceptable pulpal anesthesia was achieved in 0.4-0.8 mL doses of 4% articaine with 1:100,000 epinephrine given via the IS injection technique (6).
Purpose

No study has compared the efficacy of articaine and lidocaine for intraseptal anesthesia when used as a primary technique in asymptomatic, mandibular posterior teeth. Therefore, the purpose of this prospective, randomized, double-blind study was to compare the anesthetic efficacy of the intraseptal injection of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine, administered with a computer-controlled local anesthetic delivery system, in mandibular posterior teeth. Pain of injection, heart rate, and post-injection pain were also studied.
Chapter 2

Materials and Methods

One hundred adult subjects participated in this study. All were in good health as determined by a health history and oral questioning. Inclusion criteria included: 18 years and older; in good health (ASA classification I or II); informed consent granted. Exclusion criteria consisted of: allergy to local anesthetics; history of significant medical problem (ASA classification III or greater); recently taken CNS depressants (including alcohol or any analgesic medications); pregnancy; lactating; or inability to give informed consent. The Ohio State University Human Subjects Review Committee approved the study, IRB # 2013H0425. Written informed consent (Appendix E), HIPAA authorization (Appendix F), and medical history (Appendix D) were obtained from each subject.

Before the experiment, each subject was randomly assigned a six-digit number from a random number table (random.org). Subjects randomly received intraseptal injections of articaine and lidocaine solutions at two separate appointments spaced at least one week apart, in a crossover design. The anesthetic to be given at each appointment and which side to use at both appointments was randomly distributed (random.org). The cartridges of anesthetic solutions administered were blinded by completely removing the labels. The stoppers in all cartridges were gray. The expiration
dates on the cartridges were checked before the labels were removed. Each cartridge was placed into a coin envelope and labeled with the patient’s six-digit study number and either visit #1 or visit #2 which corresponded with the anesthetic to be given at each visit, as was previously randomly selected.

The 100 subjects received intraseptal injections of 1.4 mL of 4% articaine (56 mg) with 1:100,000 epinephrine (14 µg) (Septocaine, Septodont Inc., New Castle, DE) at one appointment and 1.4 mL of 2% lidocaine (28 mg) with 1:100,000 epinephrine (14 µg) (Xylocaine, Dentsply Pharmaceutical, York, PA) at the other appointment using the Computer-Controlled Local Anesthesia Delivery (CCLAD) system (CompuDent®, Milestone Scientific, Deerfield, IL). With the crossover design, there were 200 sets of intraseptal injections administered and each subject served as his or her own control. The same side randomly chosen for the first injection was used again for the second injection. One operator gave all injections.

The test teeth were the mandibular first and second molars, and second premolar. The contra-lateral mandibular canine was used as the unanesthetized control to ensure that the electric pulp tester (EPT) was operating properly and that the subject was responding appropriately during the experiment. Clinical examinations indicated that all test teeth were free of caries, large restorations, and periodontal disease, and that none had a history of trauma or sensitivity.

At the beginning of the first appointment and before any injections were given, the experimental teeth and control canine were tested three times by means of a Kerr electric pulp tester (Analytic Technology Corp., Redmond, WA) to record baseline vitality. All test teeth in the experiment were vital, as confirmed with the EPT. After
isolation with cotton rolls and drying with gauze, toothpaste (Colgate Total, Colgate-Palmolive Company) was applied to the EPT probe tip, which was placed midway between the gingival margin and the occlusal edge of the tooth being tested. The current rate was set on the pulp tester at 25 seconds to increase from no output (0) to the maximum output (80). Each subject was grounded by holding the metal EPT lip clip between their thumb and a forefinger. The numeric read-out at initial sensation was recorded. Trained personnel who were blinded to the anesthetic solutions performed all pre-injection and post-injection tests.

At the beginning of each appointment, each subject was connected to a pulse oximeter (Criticare Systems, Inc., Waukesha, WI) by means of a sensor placed over the nail bed of an index finger free of any nail polish or artificial nails. Heart rate was monitored for five time periods. Period 1- baseline heart rate readings were recorded at one-minute intervals during the 8-minute pre-injection resting period (8 readings) while the subject was sitting upright. Period 2- heart rate readings were recorded following needle insertion at fifteen-second intervals during anesthetic solution deposition on the mesial aspect of the mandibular first molar (10 readings). Period 3- heart rate readings were recorded following needle insertion at fifteen-second intervals during anesthetic solution deposition on the distal aspect of the first molar (10 readings). Period 4- heart rate readings were recorded at fifteen-second intervals for two minutes immediately after both injections were completed (8 readings). Period 5- heart rate readings were recorded at two-minute intervals for 28 minutes following completion of the intraseptal injections and Period 4 readings (14 readings).
Each intraseptal injection was administered using a Computer-Controlled Local Anesthetic Delivery system, or CCLAD, (Milestone Scientific, Deerfield, IL) unit. This system is a microprocessor-driven device that delivers a rate-controlled infusion of anesthetic solution. The unit accepts standard dental anesthetic glass cartridges. The microprocessor monitors and varies the infusion pressure while maintaining a constant flow rate. An electronically driven plunger contacts the rubber plunger in the cartridge and expels the anesthetic solution at a precisely regulated rate. Sterile tubing connects the cartridge receptor to a pen-like, hand-held plastic wand that is attached to a Luer-Lok needle, together forming a disposable syringe assembly. To prevent cross-contamination, the handpiece, micro tubing, and anesthetic cartridge are designed for single use only. A foot pedal is used to control flow rate, initiation and cessation of flow, and aspiration.

When the disposable syringe assembly was connected to the unit, the foot pedal was depressed once for the unit to purge the air from the tubing, fill the tubing with anesthetic solution, and prepare the unit for injection. A small portion of solution from a standard cartridge was lost during the purge cycle and some of the solution remained in the cartridge and tubing, thus only 1.4 mL of anesthetic solution from a standard cartridge was delivered.

At the first appointment for this experiment, a cartridge of the blinded anesthetic solution was placed into the plastic barrel of the unit’s handpiece assembly which was then placed into the cartridge holder socket with a quarter turn in a clockwise direction. A 25-gauge 5/8-inch Luer Lok needle (Monoject; Sherwood Services, Mansfield, MA) was attached to the opposite end of the tubing. The cap was removed from the needle and the
foot pedal was depressed once to activate the purge cycle to remove air from the plastic tubing and fill the line with anesthetic solution.

The intraseptal injection was done in the following manner: the subject was placed in a supine position. The 25-gauge 5/8-inch Luer-Lok needle was inserted on the buccal side through the center of the intradental papilla on the mesial aspect of the mandibular first molar at an approximate 30-degree angle to the long axis of the tooth in a buccal-lingual plane until bone was contacted. The bevel of the needle faced inferiorly (insertion phase). The investigator slowly pressed the needle into the crestal bone with continuous pressure until it could not be advanced any further. Approximately 0.7 mL of the anesthetic solution was deposited using the slow rate setting of the CCLAD (solution deposition phase) which was approximately 1 drop of anesthetic solution delivered every other second. The CCLAD system was activated to the slow rate by partially depressing the foot pedal for 8 seconds (continuous flow of anesthetic solution at the slow rate). One chime from the CCLAD machine corresponded to one second, allowing audible monitoring of the elapsed time. Visually monitoring the green lights on the unit and audibly monitoring the corresponding chimes determined when the deposition of solution was complete. The time to administer 0.7 mL of anesthetic solution was approximately 2 minutes. The foot pedal was then depressed once again to stop the flow of anesthetic. The researcher waited 10 seconds after the flow of anesthetic was stopped before slowly removing the needle from the injection site. The intraseptal injection was then immediately repeated on the distal aspect of the experimental tooth using the same technique and sequence of steps described above. The amount of anesthetic solution delivered with the distal injection was 0.7 mL.
For both injection sites, the author had direct vision of the injection site to monitor if anesthetic solution was expressed from the papilla or sulcus. If notable solution was identified as escaping, the injection would be stopped and the needle would be rotated with firm apical pressure into the papilla and the injection resumed. However, this did not occur with any of the included subjects. None of the injections were paused before completion and no notable amounts of solution escaped.

Before administration of the injections, the subjects were instructed on how to rate any discomfort during needle insertion and deposition of the anesthetic solution using a Heft-Parker visual analogue scale (VAS). The VAS was divided into four categories. No pain corresponded to 0 mm. Mild pain was defined as greater than 0 mm and less than or equal to 54 mm. Mild pain included the descriptors of “faint,” “weak,” and “mild” pain. Moderate pain was defined as greater than 54 mm and less than 114 mm and included the descriptor “moderate.” Severe pain was defined as equal to or greater than 114 mm. Severe pain included the descriptors of “strong,” “intense,” and “maximum possible.”

The depth of anesthesia of the test teeth was monitored with the electric pulp tester. At 1 minute after completion of the distal intraseptal injection, pulp test readings were obtained for the first molar and contralateral control canine. After these readings were obtained, the subject rated the pain of needle insertion and solution deposition for both the mesial and distal intraseptal injections using the VAS. At 3 minutes, the second molar and second premolar were tested. The testing continued in 2-minute cycles for a period of 60 minutes. Additionally, subjective lip anesthesia was evaluated every 5 minutes for an hour by asking the subject if their lip was numb.
No response from the subject to the maximum output (no response at the 80 reading) of the pulp tester was used as the criterion for pulpal anesthesia. Anesthesia was considered successful when two consecutive no responses at the 80 readings were obtained. Onset of anesthesia was determined to have occurred at the first of two consecutive 80 readings. Duration of anesthesia was determined when the last of two consecutive 80 readings occurred.

All subjects completed post-injection surveys (Appendix I) after each set of intraseptal injections were administered. The subjects rated pain in the injection area, using a similar VAS (Appendix G) as previously described, for three days following the appointment. Patients were also instructed to describe and record any problems, other than pain, that they experienced.

The second appointment was completed at least one week after the first appointment following the protocol outlined above, using the anesthetic solution which was not used at the first appointment.

The data was statistically analyzed. Between anesthetic solution differences in pain of injection, post-injection pain, and pulse rate were analyzed using repeated-measures, factorial analyses of variance. Solution differences in success were evaluated using the chi-square test. Post hoc testing was done using the Tukey-Kramer procedure. With a non-directional alpha risk of 0.05 and a power of 80%, a sample size of 100 subjects was required to demonstrate a difference of ± 15 mm in the VAS pain assessment, ± 30% in anesthetic success, and ± 2 beats per minute for pulse rate changes. Comparisons were considered significant at p < 0.05.
Chapter 3

Results

Table 1 shows that a total of 100 subjects participated in this study, 49 females and 51 males. The average age of the participants was 25.2 years.

The participants’ injection pain ratings categorized as none, mild, moderate, or severe for mesial and distal insertion and deposition of both articaine and lidocaine are found in Table 2. Utilizing the Heft-Parker visual analogue scale (VAS), no pain corresponded to 0 mm. Mild pain was defined as greater than 0 mm and less than or equal to 54 mm. Moderate pain was defined as greater than 54 mm and less than 114 mm. Severe pain was defined as equal to or greater than 114 mm. A total of 53 subjects reported moderate-to-severe pain upon needle insertion on the mesial aspect of the test tooth in the articaine group and only 31 for insertion in the distal papilla. For solution deposition pain of articaine, 20 felt moderate to severe pain with the mesial injection and 14 for the distal injection. Similar results were found for injection of lidocaine, with a total of 52 who felt moderate to severe pain upon mesial needle insertion and 32 upon distal insertion. For deposition of lidocaine, 19 felt moderate to severe pain on the mesial and 14 on the distal. Overall, females reported more pain than males.
Table 3 reports injection pain utilizing VAS values (in millimeters). Mesial needle insertion had the highest pain ratings with $55.3 \pm 27.7$ mm for articaine and $53.6 \pm 28.0$ mm for lidocaine. Distal needle insertion pain ratings were lower with $34.5 \pm 30.3$ mm for articaine and $38.0 \pm 32.5$ mm for lidocaine. No statistically significant differences were found between articaine and lidocaine for needle insertion pain. Solution deposition values were lower than needle insertion pain ratings, with mesial values greater than distal values as well. Mesial solution deposition had an average pain rating of $31.3 \pm 24.7$ mm for articaine and $31.1 \pm 27.0$ mm for lidocaine. Distal solution deposition pain values were $20.8 \pm 25.8$ mm for articaine and $21.9 \pm 25.3$ mm for lidocaine. Only the mesial needle insertion pain ratings were above the mild range, the rest were within the mild range. No statistically significant differences were seen between articaine and lidocaine in any of these groups. Figure 1 illustrates injection pain in VAS values (mm) by solution, phase, and area. For all injection pain ratings, females reported a slightly higher pain level than males, on average.

Anesthetic success, defined as two consecutive 80/80 readings with the electric pulp tester, is summarized in Table 4. For the first molar, articaine had a success rate of 35% and lidocaine 28%. For the second molar, articaine was successful 32% of the time and lidocaine slightly lower with 30%. For the second premolar, the same trend is seen with articaine at 34% and lidocaine at 26%. There were no statistically significant differences found between articaine and lidocaine for any of the teeth. Figures 2, 3, and 4 illustrate percentage of teeth numb by minute for the first molar, second molar, and second premolar. The figures show that anesthesia peaked immediately following injection for all 3 teeth, and began to decline immediately thereafter.
Table 5 shows the calculated onset and duration of pulpal anesthesia and subjective lip numbness for both anesthetic solutions. The N values are less than 100 because only those subjects who achieved pulpal anesthesia or lip numbness were included for the calculations of onset and duration of anesthesia. Onset of anesthesia was defined as the first two consecutive 80 readings with the EPT. Duration of anesthesia was defined as the time from the first two consecutive 80 readings to the last two consecutive 80 readings. Onset of pulpal anesthesia was very quick, ranging from 1.4 to 4.7 minutes. The first molar had the quickest onset and the second premolar the slowest. Duration of pulpal anesthesia was relatively short, ranging from 16.9 to 28.2 minutes, with a slightly longer duration for each tooth with articaine. If lip numbness was achieved, it was felt at the first time period the subject was questioned, which was at 5 minutes, and was maintained for an average of 22.2 to 23.5 minutes. There were no statistically significant difference between articaine and lidocaine for onset or duration of lip numbness or pulpal anesthesia for the mandibular first molar, second molar, or second premolar.

Table 6 summarizes postoperative pain ratings categorized as none, mild, moderate, or severe over a 3-day post-injection period. When given articaine, a total of 22 subjects felt moderate to severe pain on Day 1, followed by 17 on Day 2, and 8 on Day 3. For lidocaine, 18 felt moderate to severe pain on Day 1, 9 on Day 2, and 5 on Day 3. Postoperative pain decreased each day for both anesthetic solutions. Females reported moderate to severe pain more often than males on Day 1 with both articaine and lidocaine and Day 2 with lidocaine. Males reported moderate to severe pain more often than females on Days 2 and 3 with articaine and Day 3 with lidocaine.
Table 7 shows postoperative pain utilizing VAS values. On Day 1, the average pain ratings were 27.9 ± 31.4 mm for articaine and 23.7 ± 32.9 mm for lidocaine. On Day 2, ratings decreased to 19.8 ± 30.0 mm for articaine and 12.2 ± 25.4 mm for lidocaine. On Day 3, ratings decreased yet again with 12.7 ± 25.8 mm for articaine and 7.0 ± 19.9 mm for lidocaine. All of these pain ratings are in the mild category. No statistically significant differences were found between articaine and lidocaine for any of the three days. Figure 5 illustrates postoperative pain in VAS values (mm) by day and solution. On average, females reported slightly higher levels of pain than males for articaine and lidocaine on Day 1 and lidocaine on Day 2. For Days 2 and 3 with articaine and Day 3 with lidocaine, males reported slightly higher levels of postoperative pain.

Table 8 shows a list and frequency of postoperative complications reported by the subjects. Most commonly occurring were injection site soreness or redness, pain or bleeding with eating, chewing, biting, brushing, or flossing, and bruising or gingival discoloration. Day 1 had the most complaints, which decreased each subsequent day.

Table 9 summarizes the mean heart rate readings by period, gender, and anesthetic. Heart rate decreased from baseline values during mesial and distal solution deposition phases, with a slight increase occurring immediately post-injection. This was followed by a further decrease in heart rate during pulp testing. No statistically significant differences were found between males and females for each period or between articaine and lidocaine solutions for each period. Figure 6 illustrates mean heart rate (bpm) by period, solution, and gender.

Table 10 shows the comparison of heart rate between time periods for each solution and by gender. Statistically significant differences were found in every group.
except baseline vs. post-injection with articaine in females, baseline vs. post-injection with lidocaine in males, and mesial deposition vs. distal deposition with lidocaine in males. The differences were due to decreases in heart rate during the injection versus baseline readings. Post-injection heart rates appear to have rebounded back to baseline heart rates.
Chapter 4

Discussion

Participants

Biographical data for all subjects who took part in this study is shown in Table 1. Participants under the age of 18 were excluded from the study since they were not legally able to provide informed consent. Participants over the age of 65 were not included in this study due to shorter onset of anesthesia when compared to a younger population, which was reported by Nordenram and coauthors (66). In order to avoid the influence of this effect, only those under the age of 65 were allowed to participate in the study.

Relatively equal numbers of male (51) and female (49) subjects were included in this study to provide an accurate sample of the general population (Table 1). It has been shown by numerous studies that men and women report pain differently. Females generally report more pain than males (67-70). If unbalanced numbers of males and females were included in the study, it may have biased the results of pain ratings toward the majority gender.

Liddell and Locker (67) compared questionnaires from 2,609 subjects (1,481 female, 1,128 male) regarding dental anxiety, pain remembered from dental visits, and feelings about pain and control in dentistry. They reported that women were more
anxious than men about dental visits. They also found that women were more likely to avoid pain, accept pain less, and fear pain more than men (67).

Keogh and coauthors (68) measured pain threshold, tolerance, and recovery by having 100 participants place their hands in an ice cold water bath for up to two minutes. The data was analyzed for differences between genders; 50 males and 50 females participated in the study. Pain threshold was the point when the participant started to feel pain after placement of their hand into the water bath. Pain tolerance was the point when the participant had to withdraw their hand. Pain recovery was the point at which pain was no longer felt following removal of the hand from the water bath. Participants filled out a pain survey following the experiment. No differences were found between males and females for pain threshold or pain recovery, but a significant difference was found for pain tolerance. Females showed a lower pain tolerance than males. Upon analysis of the pain surveys, females reported significantly more pain than males (68).

Fillingim and coauthors (69) also measured pain threshold and tolerance, but used a heated thermode which was placed on the forearms of 209 subjects (117 female, 92 male). The temperature was raised 1°C per second and subjects pressed a button when they felt warmth, when it became painful, and then again when it became intolerable. Females demonstrated significantly lower warmth threshold, thermal pain threshold, and thermal pain tolerance. Also, both males and females had a lower pain threshold when the experiment was conducted by a female rather than a male (69).

Perry and coauthors (70) evaluated operator gender and its effect on subjects’ reported pain by gender. Two hundred subjects, 100 female and 100 male, participated in the study. Each participant had two appointments at which maxillary infiltrations of 2%
lidocaine with 1:100,000 epinephrine were given, one by a male operator and one by a female operator. At each visit, subjects rated the pain of injection in three parts: pain of needle insertion, pain of needle placement, pain of solution deposition. No significant differences in pain ratings were found between the 4 operator/subject gender combinations for needle insertion or needle placement. For solution deposition, male operator/female subject showed a significantly higher pain rating than the other 3 operator/subject combinations (70).

It has been reported that females accept pain less, fear it more, and tend to avoid it more often than males. Females have also been found to report pain more often and have a lower pain threshold and less pain tolerance than males (67-70). Because gender has an effect on pain ratings, relatively equal numbers of males (51) and females (49) were enrolled in the current study.

Injection Pain

The Heft-Parker visual analog scale (VAS) was used to measure participants’ pain. This graphic rating scale was developed by Heft and Parker (71) to provide a more accurate scale for pain ratings. The VAS includes the categorical descriptors of “faint,” “weak,” “mild,” “moderate,” “strong,” and “intense” to guide participants in reporting their pain, while providing an infinite number of points along the scale which can be marked to correlate to their perceived pain. Heft and Parker (71) determined their VAS to be accurate in their study by comparing the intensity of electrocutaneous shocks and
reported pain ratings with two different word descriptor lists. When the descriptor words were assigned values, there was agreement between the subjects on the non-homogeneous spacing of the descriptors along the scale. Based on their findings, Heft and Parker devised the VAS that is used in many different clinical and research settings today (71).

Injection pain is summarized in Tables 2 and 3. Most participants rated their pain in the mild range (≤ 54 mm), with the exception of the mesial needle insertion phase, which was just into the moderate range (> 54 mm, ≤ 114 mm). Mesial needle insertion was the most painful, followed by distal needle insertion, then mesial solution deposition, and finally distal solution deposition. The distal needle insertion and solution deposition were most likely less painful than the mesial insertion and deposition due to the soft tissue anesthesia which had already set in from the mesial injection. Deposition was most likely less painful than needle insertion due to the very slow injection rate of 0.005 mL/s at which the anesthetic was delivered compared to the sharp pinch associated with the insertion of the 25-gauge needle into the interdental septum. Females reported slightly higher levels of pain of injection for all phases of the injections with both anesthetic solutions; however, the differences in pain ratings between males and females were not significant for any of the phases, solutions, or locations of injections. This slight increase in female pain ratings can be attributed to the fact that females generally report more pain than males (67-70).

Saadoun and Malamed (64) studied the efficacy of intraseptal anesthesia for periodontal surgery. One hundred patients were asked about pain experienced during the injections given prior to periodontal surgery. Intraseptal injections of 2% lidocaine with
1:50,000 epinephrine were administered in the papillae adjacent to the teeth being treated. A range of 4-10 teeth were treated on each patient and an average of 1 1/5 cartridges were used per procedure, ranging from a minimum of 9/10 of a cartridge for 4 teeth to a maximum of 2 cartridges for 10 teeth. It is not clear from the report what method was used to obtain the patients’ pain evaluations, but it appears to have been verbal questioning after the surgery was completed. It was reported that 73% of the patients experienced almost painless needle insertion, but they did report feeling the pressure of the injection. During the injection, 52 patients did not report any pain, 21 reported discomfort, and 27 reported pain (64). The studies on intraseptal anesthesia conducted by Biocanin et al (6) and Brkovic et al (5) did not report on pain of injection.

The supplemental anesthetic techniques most similar to the intraseptal injection are the periodontal ligament (PDL) and intraosseous (IO) injections. Although they use different methods, all three are intraosseous injections as they aim for anesthetic solution to be deposited into the cancellous bone surrounding the tooth. Therefore, the results of this study could be compared to those of studies on asymptomatic patients of similar populations given primary PDL and IO injections on the mandibular first molar (59, 60, 72-74). The pain ratings reported for the intraseptal injection were similar to those of the PDL and IO injections.

Nusstein and coauthors (72) compared pain of injection, heart rate, and postinjection pain of 4% articaine with 1:100,000 epinephrine to 2% lidocaine with 1:100,000 epinephrine in primary intraligamentary injections. As in the present study, 0.7 mL of anesthetic was delivered first on the mesiobuccal aspect of the mandibular first molar, followed by 0.7 mL on the distobuccal aspect of the mandibular first molar using
the slow setting of 0.005 mL/s with the computer-controlled anesthetic delivery (CCLAD) system. Pain was measured using the Heft-Parker VAS following the needle insertion/placement and solution deposition phases. Fifty-one participants completed two appointments each, one for each anesthetic. Most participants rated the needle insertion and solution deposition on the mesial and distal in the mild pain category. Nusstein and coauthors (72) found that for needle insertion on the mesial, 65-69% reported mild pain and 67-78% reported mild pain on the distal. For solution deposition on the mesial, 67-74% reported mild pain and 61-67% reported mild pain on the distal. The current intraseptal injection study showed the same tendency toward mild pain overall, with the exception of the mesial needle insertion pain values, using both articaine and lidocaine, in which 52-53% reported moderate pain. As stated previously, this can most likely be attributed to the mere fact that the mesial injection was given first on every subject. Some measure of soft tissue anesthesia most likely set in before the distal injection was given, making the distal injection less painful. For the PDL injection given in the study by Nusstein and coauthors (72), moderate to severe pain was reported by 27% for mesial needle insertion and 15-16% for distal needle insertion. For solution deposition, 12-18% reported moderate to severe pain on the mesial and 8-12% on the distal (72). With the intraseptal injection given in this study, participants reported moderate to severe pain upon mesial needle insertion 52-53% of the time and only 31-32% of the time for the distal needle insertion. Similarly, moderate to severe pain was reported for solution deposition in 19-20% of the subjects on the mesial and 14% of the subjects on the distal. Needle insertion pain for intraseptal anesthesia was shown to be about double the intensity of needle insertion pain of intraligamentary anesthesia. This could potentially be
due to the existence of the periodontal ligament “space” (a.k.a. gingival sulcus) in which the needle was placed for the PDL injection, versus the need to pierce the attached gingiva in order for the needle to reach the interdental septum for the IS injection. Walton and Garnick (76) gave PDL injections in monkeys and then examined the tissues histologically. On Day 0 they found alterations in the tissues related to the insertion of the needle. The needle path was visible in the gingival fibrous connective tissue and the cervical periodontal ligament in all 8 specimens examined. However, the puncture site of the needle through the sulcular epithelium was detected in only 2 of the 8 examined (76). These findings could indicate that the gingival epithelium may not even be punctured in most PDL injections, thereby making needle insertion a relatively painless part of the injection. Chow and coauthors (77) evaluated dimensions of interdental papillae in 96 adult subjects. They found the average thickness of the papillae to be 1.2-1.5 mm. This means that when an intraseptal injection is given, the needle must traverse at least 1.2-1.5 mm of attached gingival tissue and then ideally pierce cortical bone. The thickness of tissue which must be penetrated for the intraseptal injection could be the cause of the higher injection pain ratings reported in the current study. Nusstein and coauthors (72) used a 27-gauge needle to perform the PDL injections in their study, whereas a 25-gauge needle was used in the present study. In both studies, the needle was advanced until it could not be advanced farther and no topical anesthetic was used. The difference in the gauge of the needle used could have been a factor leading to the higher pain ratings reported in the current study, as compared to those in the study conducted by Nusstein and coauthors (72). However, many studies have shown that needle gauge does not influence pain ratings (78-80). Fuller and coauthors (78) compared 25-, 27-, and 30-
gauge needle penetration in the retromolar fossa. They found no significant differences in perception of pain from needle insertion of the three different needle gauges (78). Brownbill and coauthors (79) compared 30- and 25-gauge needles for IANB in children and found no significant differences in injection pain scores. Flanagan and coauthors (79) compared 25- and 27-gauge needles for IANB and 25-, 27-, and 30-gauge needles for maxillary buccal infiltrations. They found no significant differences in perceived injection pain between the different gauges (80). Therefore, needle gauge may not have played a significant role in this study. Further research using different gauge needles for the IS injection would be needed to determine the effect.

Moore and coauthors (74) compared PDL injections of 1.8 mL of 2% lidocaine with 1:100,000 epinephrine and saline on the mesial and distal aspects of asymptomatic mandibular first premolars in 19 subjects. Using 2% lidocaine with 1:100,000 epinephrine and a 30-gauge short needle, only 1 of 19 subjects reported moderate pain for needle insertion and 4 for solution deposition. Using saline, 4 of 19 subjects reported moderate pain for needle insertion. For solution deposition with saline, 14 reported moderate pain and 2 reported severe pain. The needle insertion pain ratings were reported as the average of the mesial and distal needle insertion pain ratings. No VAS was utilized, but a 0-3 numeric scale. More pain was reported for solution deposition rather than needle insertion when subjects were given saline. This was reported to be due to the fact that saline did not provide any anesthesia during injection (74). Therefore, the results using saline cannot be directly compared to those of the current study. However, the results using lidocaine could be compared to those of the current study, but the low number of subjects in the study by Moore and coauthors (74) make the comparison
difficult. If needle insertion pain ratings are combined for both lidocaine and saline, 14% of subjects reported moderate pain. For solution deposition of lidocaine, 21% reported moderate pain. Although the number of subjects used in the study by Moore and coauthors (74) was small, the injection pain ratings were lower than those in the current study. Again, this could be due to the differences in injection technique related to the amount of tissue penetration required by the injections (PDL versus IS).

Gallatin and coauthors (73) compared injection pain and postoperative pain of intraosseous (IO) injection of 1.8 mL of 2% lidocaine with 1:100,000 epinephrine utilizing the Stabident and X-Tip™ systems in 41 subjects. They reported that 62-100% of subjects experienced mild pain for all parts of a primary intraosseous injection, including bone perforation, needle insertion, and solution deposition. Moderate-to-severe pain was reported by 25-26% of patients (24-35% of females, 21-25% of males) for perforation, 5-12% (0-12% of females, 8-12% of males) for needle insertion, and 24-34% (24-29% of females, 25-37% of males) for solution deposition, using both the Stabident and X-Tip™ systems. There were no significant differences between the two systems or males and females for all three phases of the injections. In the current study, moderate-to-severe pain was reported in 31-53% of the subjects for needle insertion (52-53% on the mesial, 31-32% on the distal) and 14-20% of the subjects for solution deposition (19-20% on the mesial, 14% on the distal). The needle insertion pain ratings in the present study were much higher than the perforation and needle insertion pain ratings reported by Gallatin and coauthors (73) for a primary intraosseous injection. In the study conducted by Gallatin and coauthors (73), the subjects received a supraperiosteal infiltration of 0.6-0.9 mL of 2% lidocaine with 1:100,000 epinephrine at the determined perforation site.
prior to perforation or needle insertion and soft tissue anesthesia was verified by placement of pressure with a periodontal probe at the site. Since the soft tissue at the perforation site was anesthetized before bone perforation and needle insertion, it may have resulted in less reported pain than needle insertion for the intraseptal injection in the present study. In our study, the soft tissue was not anesthetized beforehand via anesthetic infiltration or placement of topical anesthetic. Gallatin and coauthors (73) reported higher pain ratings for the solution deposition phase of the intraosseous injection compared to those of the present study’s intraseptal injection, on both the mesial and distal of the first molars. This could be attributed to the fact that the needle is actually placed within cancellous bone for the intraosseous injection, whereas for the intraseptal injection, the needle is placed in the interdental papilla with the intention of contacting and possibly penetrating the alveolar crestal bone. Perhaps the delivery of anesthetic solution through attached soft tissue produces less pressure than when it is delivered directly into cancellous bone. The volume of anesthetic delivered in the study conducted by Gallatin and coauthors (73) was 1.8 mL, twice than the 0.7 mL delivered at the first injection site (mesial) in the current study. This increased volume could also be a cause of more intense pain.

Replogle and coauthors (60) compared primary intraosseous injections of 2% lidocaine with 1:100,000 epinephrine and 3% mepivacaine in 42 subjects. Similar to the study conducted by Gallatin and coauthors (73), Replogle and coauthors (60) anesthetized the soft tissue at the perforation site with approximately 0.1 mL of either 2% lidocaine with epinephrine or 3% mepivacaine prior to perforation with the Stabident system. Replogle and coauthors (60) reported lower pain ratings than Gallatin and
coauthors (73), with only 0-7% reporting moderate-to-severe pain upon bone perforation, 0-2% upon needle insertion, and 0-7% upon solution deposition. All of these findings were much less than found by this study.

Coggins and coauthors (59) compared intraosseous injections of 2% lidocaine with 1:100,000 epinephrine in maxillary and mandibular first molars and lateral incisors in 40 subjects. Approximately 0.1 mL of 2% lidocaine with 1:100,000 epinephrine was infiltrated at the perforation site prior to bone perforation and needle insertion. For the mandibular first molar, 5% of subjects reported moderate-to-severe pain for bone perforation, 8% for needle insertion, and 15% for solution deposition. These pain ratings were lower than those reported by Gallatin and coauthors (73) and similar to those reported by Replogle and coauthors (60) for primary intraosseous injections. The differences in pain ratings found by Gallatin and coauthors (73) versus Replogle and coauthors (60) and Coggins and coauthors (59) was attributed to variance in operator technique and patient population. All of those studies reported less pain than that found in the current study.

Overall, injection pain in the present study of primary intraseptal anesthesia was in the mild range, with the exception of mesial needle insertion pain, which was in the moderate range. Needle insertion pain ratings in the current study were higher than those reported for the PDL and IO injections (59, 60, 72-75). Solution deposition pain ratings in the current study were similar to those of PDL and IO injections, with most subjects reporting only mild pain (59, 60, 72-75).
Anesthetic Success

Anesthetic success was defined as two consecutive readings of 80/80 on the electric pulp tester (EPT) at any point during the 60-minute testing period. This definition ensured that pulpal anesthesia was achieved and not just a false response from the EPT. This definition of success is also not necessarily predictive for clinical success, since the definition included any two consecutive 80 readings, which could have come at the beginning of the testing period or at the end. If two consecutive 80 readings occurred at the end of 60 minutes, the injection would not be clinically useful; however, it would still be considered a success in this study. If two consecutive readings occurred early in the testing period, it would be somewhat more useful clinically. Ideally, anesthesia would occur immediately following injection of the anesthetic solution. It would be preferable if onset of anesthesia occurred within the first few minutes following injection, similar to findings of the PDL and IO injections (57, 59, 60, 72-75).

Each tooth was tested every 4 minutes. With a definition of success of only two consecutive 80 readings to be achieved, injections may have resulted in pulpal anesthesia for a minimum of 4 minutes (numb right before EPT test and loss of anesthesia seconds after second EPT test) to a maximum of 11 minutes and 58 seconds (numb immediately after EPT, numb for two 4-minute periods, and loss of anesthesia before third EPT test). Clinically, 4-12 minutes would not be much time to complete a dental procedure, especially root canal treatment on a posterior tooth. Perhaps an extraction by a skilled oral surgeon would be possible.
A summary of anesthetic success by tooth type and anesthetic solution is shown in Table 4. Success ranged from 26% for lidocaine in the second premolar to 35% for articaine in the first molar. There were no significant differences in success between articaine and lidocaine for any tooth. The mechanism for the intraseptal injection has been reported to be delivery of the anesthetic under pressure, leading to its penetration through perforations in the cortical bone at the alveolar crest and diffusion into the medullary bone via the interdental septum (3). The low success rate found in this study is likely due to failure of the anesthetic to penetrate the alveolar cortex and reach the cancellous bone. This could have been due to the inability of the needle to perforate the intraseptal bone. During the injection the needle was placed into the papilla at a 30-degree angle to the long axis of the tooth as far as it would go, but there was no way to know its actual depth of penetration and if it did indeed penetrate the bone or periosteum since anatomical differences in soft tissue (papilla) thickness exist between patients (77). The needle may have remained supraperiosteal and therefore was unable to deliver an intraosseous injection. Although no anesthetic was observed leaking from the injection sites, another possible explanation for why the injection failed is that the anesthetic escaped into the buccal vestibule or oral cavity. This may not have been visualized due to the slow injection rate of 0.005 mL/s. It is likely that there was some level of leakage of anesthetic into the oral cavity for most subjects since the majority of participants reported a bad taste in their mouth following the injections, although this was not recorded. The anesthetic solution may also have spread in the soft tissues rather than going into the bone. Blanching of the attached gingiva was observed in most subjects, but also was not recorded.
The intraseptal injection was studied to determine its efficacy in relation to other intraosseous anesthesia techniques. Some dental practitioners are hesitant to perform the perforation required to administer the intraosseous (IO) injection even though it has been shown to have high success rates (59, 60). The periodontal ligament injection (PDL) is a popular injection, but has shown relatively low success rates, possible trauma to the PDL, and potential difficulty with administration due to the need for back pressure in order to achieve successful pulpal anesthesia (72, 76).

When 1.8 mL of 2% lidocaine with 1:100,000 epinephrine was administered in a primary intraosseous injection, success rates ranged from 74-93% (59-61). This is a much higher success rate than the current study found with the intraseptal injection using the same volume and anesthetic.

As compared with PDL injections, the intraseptal injections had a lower success rate as well. Primary PDL injections of 1.4 mL of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine delivered via the CCLAD resulted in success rates of 86% and 74%, respectively (57). Walton (75) discussed the periodontal ligament injection as a primary anesthetic technique. He explained the limitations of the PDL injection and its inability to provide the profound pulpal anesthesia needed for pulp extirpation. Walton also described the unpredictable nature of the PDL injection and its inconsistency in different regions of the mouth (75).

The poor success rate found in the current study for a primary intraseptal injection may indicate that it would be a poor supplemental injection to the IANB as well. However, further study is needed to determine the efficacy of intraseptal anesthesia as a supplemental technique.
Biocanin and coauthors (6) administered 0.4 mL, 0.6 mL, and 0.8 mL of 4% articaine with 1:100,000 epinephrine via the computer-controlled local anesthesia delivery (CCLAD) system as a primary intraseptal injection. One hundred and eighty healthy subjects participated in the single-blind study. Half of the dose of anesthetic was injected on the mesial and distal aspects of the mandibular first premolar. Anesthetic efficacy was determined by use of an electric pulp tester (EPT). Success was defined as 2 or more consecutive 80 readings, similar to this study. Success rates for the volumes of 0.4 mL, 0.6 mL, and 0.8 mL were reported as 73%, 90%, and 90%, respectively (6). In the current study, although 1.4 mL of 4% articaine with 1:100,000 epinephrine was administered, much lower success rates were found. When given articaine, the mandibular first molar was successfully anesthetized in 35% of the subjects. There are a number of differences in study design which may have led to this discrepancy in success rates.

Biocanin et al (6) aimed to anesthetize the mandibular first premolar, injecting half of the anesthetic solution on the mesial aspect of the premolar and the other half on the distal aspect. In the current study, the mandibular first molar was targeted, depositing half of the anesthetic solution on each side. Cone-beam computed tomography images have shown that cortical bone is thicker in the posterior mandible than in the anterior mandible (81). Therefore, the alveolar cortex in the region of the mandibular first premolar is thinner than that of the mandibular first molar. Thinner cortical bone could potentially allow penetration of anesthetic through the cortex more readily in the premolar region as compared to the molar region of the mandible. This could lead to
higher success rates due to the ability of the anesthetic solution to reach the medullary bone surrounding the root of the premolar, resulting in pulpal anesthesia.

Differences in tooth anatomy between the mandibular first premolar and first molar could have also impacted the levels of success reported by Biocanin and coauthors (6) and the current study. Most mandibular premolars have only one root, whereas mandibular molars generally have two roots which are spaced apart. The intraseptal injections given in the study by Biocanin and coauthors (6) were given on both the mesial and distal aspects of the mandibular first premolar, which means that the solution only had to anesthetize one root. In the present study, anesthetic solution was deposited on the mesial and distal aspects of the mandibular first molar, but had to anesthetize two roots in order to achieve pulpal anesthesia. Success on one root and not the other would potentially cause failure. The results found in the study conducted by Biocanin and coauthors (6) cannot be directly compared to those found in the current study due to the fact that the premolar roots in their study received mesial and distal injections, whereas the premolars in our study received anesthetic on only one side each.

In the study reported by Biocanin and coauthors (6), the mandibular first premolar was tested with an EPT every 2 minutes. In the current study, each tooth was tested every 4 minutes. Two teeth (first molar and contralateral canine, second molar and second premolar) were tested as pairs every 2 minutes. The mandibular first molar was tested at 1 minute following completion of the injection and not again until 5 minutes after the injection. As previously discussed, when the definition of success is a minimum of only two consecutive 80 readings, the injections in this study resulted in pulpal anesthesia for a minimum of 4 minutes to a maximum of 11 minutes and 58 seconds. In Biocanin and
coauthors’ study (6), the same definition of success was used as in the present study, requiring 2 consecutive 80 readings with the EPT. Biocanin and coauthors (6) tested the mandibular first premolar immediately following completion of the injection and again at 2 minutes after the injection. This means that the premolar would only have to be numb for 2 minutes to be considered a success in their study. This difference in timing of pulp testing could have led to the higher success rates of pulpal anesthesia reported by Biocanin and coauthors (6). When anesthesia was achieved, it was found to be immediate in both studies. Therefore, initiation of pulp testing immediately following injection and more frequent pulp testing would likely result in higher success rates of pulpal anesthesia when using the same definition as was used in both the current study and the study conducted by Biocanin and coauthors (6).

In the current study, a 25-gauge 5/8-inch needle was used to give the injections. This type of needle was chosen after preliminary testing of various needle sizes on mandibles of cadavers. Smaller gauge needles were found to be too flimsy and seemed to bend or break rather than pierce the bone. The 25-gauge needle was sturdy enough to apply a significant amount of pressure in order to potentially penetrate the cortical bone. Biocanin and coauthors (6) used a 30-gauge short needle. They did not explain why they chose this needle, but it is possible that the smaller gauge was actually better able to penetrate the bone to deliver the anesthetic solution, contrary to what was seen on the cadaver jaws. Use of the 30-gauge needle could have potentially increased success of pulpal anesthesia, as Biocanin and coauthors (6) reported in their study. Malamed (13) recommends the use of a 27-gauge needle. Marin (65) and Woodmansey (3) both report a preference for the use of a 30-gauge short (1/2-inch) needle for administration of
intraseptal injections. Saadoun and Malamed (64) used a 27-gauge short needle in their
study involving intraseptal anesthesia for periodontal surgery. Brkovic and coauthors (5)
reported use of a 27-gauge short needle as well in their study conducted on intraseptal
anesthesia for maxillary lateral incisor extractions. Future studies could involve the use of
different gauges of needles to administer intraseptal anesthesia to determine its effect on
achieving pulpal anesthesia.

Brkovic and coauthors (5) used intraseptal anesthesia for extraction of maxillary
lateral incisors. They administered 0.8 mL of 2% lidocaine with 1:100,000 epinephrine,
0.2 mL on the buccal and palatal side both on the mesial and distal, approximately 2 mm
above the tip of the interdental papilla. A total of 35 patients participated in the study and
23 were able to endure the extractions without additional anesthetic infiltrations, resulting
in a 65.7% success rate. The success rate in the anterior maxilla would be expected to be
higher than that of the posterior mandible due to the difference in density of the bone.
Maxillary bone is less dense than mandibular bone (82). It is difficult to directly compare
the study completed by Brkovic and coauthors (5) to the current study because of the
major differences in study design, including the location of anesthetic deposition, patient
population, and procedure completed. However, what can be noted is the relatively low
success rate of 65.7% reported in the anterior maxilla. An even lower success rate would
be expected in the posterior mandible and was found in the current study. Also, Brkovic
and coauthors (5) did not report how quickly the extractions were initiated and completed
following the administration of anesthesia. It is possible that the oral surgeon completing
the procedures was able to extract the teeth very quickly, given that extraction of
maxillary lateral incisors is relatively simple compared to posterior teeth. This may have
allowed for soft tissue and possibly pulpal anesthesia throughout the short procedure for many patients, resulting in the success rate reported by Brkovic and coauthors (5).

Saadoun and Malamed (64) used intraseptal anesthesia for periodontal surgery. Depending on the number of teeth included in the surgery, they administered 0.9 to 1.43 cartridges of 2% lidocaine with 1:50,000 epinephrine in the centers of the papillary triangles, approximately 2 mm below the tip of the papilla. In 100 surgeries, 22 patients reported pain or discomfort during the procedure, resulting in a 78% success rate. Most of the patients who reported discomfort experienced it during ultrasonic scaling of the tooth roots, indicating a lack of pulpal anesthesia. The surrounding tissues were reported to be anesthetized. It was not reported how long the teeth were scaled or at what time point the scaling was initiated or completed after the injections were given. Again, it is difficult to compare the study by Saadoun and Malamed (64) to the current study due to the many differences in study design. However, one difference to be noted is the use of 2% lidocaine with 1:50,000 epinephrine. The higher concentration of epinephrine could have potentially increased the duration of anesthesia (83). Kammerer and coauthors (83) reported that increased concentration of epinephrine resulted in increased duration of pulpal anesthesia. Also, as soft tissue anesthesia was likely more important during the periodontal surgeries than pulpal anesthesia, the increased concentration of epinephrine may have helped with this. In the current study, soft tissue anesthesia was not tested or recorded; however, blanching of the attached gingival tissue was observed by the operator during and after most injections.

In summary, the intraseptal injection in the current study had very low success rates of 26-35%. A similar study of primary intraseptal anesthesia found 73-90% success,
but differences in study design and methods to determine success may have lead to this discrepancy in success rates (6). Higher success rates of 65.7-90% were reported in clinical treatment studies using intraseptal anesthesia, but these studies were very difficult to compare to the present study due to major differences in methods and procedures performed (5, 64). Much higher anesthetic success rates have been reported for primary PDL and IO injections at 74-86% (57) and 74-93% (59-61), respectively.

Onset of Anesthesia

Anesthetic onset and duration are summarized in Table 5. For those subjects who achieved pulpal anesthesia, onset occurred immediately after injection, ranging on average from 1.4 to 4.7 minutes. The mandibular first molar had the fastest onset time of 1.4 minutes for articaine and 2.3 minutes for lidocaine. There were no significant differences between articaine and lidocaine for onset of anesthesia.

Immediate onset of anesthesia following intraseptal injections was also reported by Biocanin and coauthors (6). In their study, the first EPT test was done immediately after the intraseptal injection. Brkovic and coauthors (5) reported onset times of 20-30 seconds. This was determined with a gingival pinprick test every 15 seconds after injection, using a 27-gauge needle. This definition of anesthetic onset only ensures soft tissue anesthesia, not pulpal anesthesia (5). Saadoun and Malamed (64) reported an immediate onset of anesthesia following completion of the intraseptal injections as well.
They did not report how onset was calculated. They simply stated that the surgical procedure was begun as soon as the injections were finished (64).

When compared to other intraosseous anesthesia techniques, onset for intraseptal anesthesia was very similar. Berlin and coauthors (57) reported an anesthesia onset of 1.3 minutes and 2.2 minutes for PDL injections of 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine, respectively, with no significant difference between the two anesthetic solutions. The same result was found in the current study, with no significant difference between 4% articaine with 1:100,000 epinephrine and 2% lidocaine with 1:100,000 epinephrine for onset of anesthesia. Moore and coauthors (74) did not report anesthesia onset; however, the teeth were tested at 2, 4, 10, 20, 30, and 45 minutes following completion of the PDL injections. The highest percentage of 80 readings was observed at the 2-minute testing interval with 78.9%. This percentage decreased at the 10-minute interval and onward (74). These findings indicate that anesthetic onset occurred within the first 2 minutes following injection of 2% lidocaine with 1:100,000 epinephrine, similar to the findings reported by Berlin and coauthors (57). Walton (75) reported that an advantage of the PDL injection is the rapid onset of anesthesia.

Intraosseous anesthesia has been shown to have an onset of anesthesia within the first several minutes following injection (59-61). Gallatin and coauthors (61) reported onset of pulpal anesthesia at an average of 1.11 minutes for the Stabident technique and 1.57 minutes for the X-Tip™ technique using 1.8 mL of 2% lidocaine with 1:100,000 epinephrine. Coggins and coauthors (59) reported immediate onset, as the highest percentage of 80 readings was at the first testing interval, which was 4 minutes following
the injection of 1.8 mL of 2% lidocaine with 1:100,000 epinephrine. Replogle and coauthors (60) also reported the highest percentage of 80 readings within the first 3 readings, which was 6 minutes, indicating rapid onset following the injection of both 1.8 mL of 2% lidocaine with 1:100,000 epinephrine and 3% mepivacaine plain. These findings are very similar to those found in this study with the intraseptal injection.

Rapid onset of anesthesia is very useful for clinical applications. If onset is immediate, the practitioner is able to begin the procedure without the need to wait for anesthesia to occur.

Duration of Anesthesia

The current study found a duration of pulpal anesthesia of 16.9 to 28.2 minutes. For those who achieved pulpal anesthesia of the mandibular first molar, average duration of anesthesia was 18.4 minutes with 2% lidocaine with 1:100,000 epinephrine and 28.2 minutes with 4% articaine with 1:100,000 epinephrine. The mandibular second premolar and second molar had shorter duration of anesthesia since they only received anesthetic on one side of the tooth: distal for the second premolar and mesial for the second molar. The first molar received anesthetic on both sides and therefore had a longer duration of anesthesia. The standard deviation for anesthetic duration of pulpal anesthesia was very large, ranging from 14.3 minutes to 17.7 minutes. This indicates that the data points were spread over a larger range of values rather than being very close to the mean. Each individual’s duration of pulpal anesthesia differed considerably from the average duration
reported. Therefore, the mean values of anesthetic duration reported in the current study show a high level of variability.

Biocanin and coauthors (6) found that the duration of anesthesia increased in a dose-dependent manner. On average, subjects given 0.4 mL of 4% articaine with 1:100,000 epinephrine experienced pulpal anesthesia for 9.4 minutes. This increased to 14.7 minutes with 0.6 mL, and 24.2 minutes with 0.8 mL. The present study used 1.4 mL 4% articaine with 1:100,000 epinephrine and duration of anesthesia followed the pattern Biocanin and coauthors (6) found.

Brkovic and coauthors (5) reported duration of anesthesia to be an average of 90 minutes on the buccal and 60 minutes on the palatal soft tissue (5). However, duration of anesthesia was measured by pinprick testing every 20 minutes following the extraction. This method only indicated soft tissue anesthesia, not pulpal anesthesia. Testing intervals of 20 minutes did not provide a high level of accuracy for duration of anesthesia.

Saadoun and Malamed reported a duration of pulpal anesthesia of 30-60 minutes, based only on when patients felt sensitivity with the ultrasonic scaler used during the periodontal surgeries (64). This method of determining duration was not very controlled. The time at which patients reported sensitivity was not recorded and this determination of duration of anesthesia was only an estimate at best.

Anesthetic duration found in the current study of the intraseptal injection was similar to that of other intraosseous injection techniques. Berlin and coauthors reported duration of 34 and 31 minutes for articaine and lidocaine, respectively, for PDL injections (57). For intraosseous injections, onset was very rapid, but anesthesia steadily declined over 60 minutes (59-61). Replogle and coauthors (60) reported 52% of subjects
still had pulpal anesthesia at 30 minutes following injection of 2% lidocaine with 1:100,000 epinephrine. Gallatin and coauthors (61) reported that at 30 minutes, 73-76% of subjects still had pulpal anesthesia and at 60 minutes, 39-51% of subjects still had pulpal anesthesia, after given 1.8 mL of 2% lidocaine with 1:100,000 epinephrine.

In the current study, the teeth were pulp tested every 4 minutes, as discussed previously. This allows for the accuracy of calculation of anesthetic duration to be ± 8 minutes. Anesthetic duration in the present study was shorter than that reported in other studies of intraseptal anesthesia (5, 6, 64), which may have been due to discrepancies in methodology of duration determination. Anesthetic duration was also somewhat shorter in the present study of the intraseptal injection than that of other intraosseous techniques, including PDL and IO injections (57, 59-60). This shorter duration of anesthesia could also be attributed to the fact that the anesthetic is not being distributed into the cancellous bone with the intraseptal injection, as well as it is for the PDL and IO injections. As discussed previously, the anesthetic solution could have remained trapped in the gingival soft tissues and/or may have leaked from the injection sites, resulting in a low success rate and short duration of anesthesia. The current study found no significant differences between articaine and lidoaine in onset or duration of anesthesia, with duration being 4.6-9.8 minutes longer for articaine than lidocaine.

In the current study, anesthetic duration was relatively short for those who achieved pulpal anesthesia. Clinically, treatment would need to be performed very fast. An endodontic procedure would be difficult to complete under these time constraints, requiring quick access opening and prompt pulp extirpation, if pulpal anesthesia was achieved (see section on anesthetic success).
Postoperative Pain

Postoperative pain is summarized in Tables 6 and 7. On average, the participants’ postoperative pain was reported to be in the mild range for all 3 days following the injection. Pain levels were highest at Day 1 and decreased with each consecutive day. Articaine and lidocaine did not have a statistically significant difference at any day; however, pain ratings were slightly higher for articaine for all 3 days. When given lidocaine, moderate to severe pain was reported by 18, 9, and 5 participants for Days 1, 2, and 3, respectively. With articaine, 22, 17, and 8 participants reported moderate to severe pain for Days 1, 2, and 3, respectively. Nydegger and coauthors (84) reported that mandibular buccal infiltration of articaine was significantly more painful than lidocaine and prilocaine on the day of the injection after soft tissue anesthesia wore off. However, there were no significant differences in postoperative pain between the 3 solutions on Days 1, 2, and 3 after the injection (84). In the present study, no significant differences were found between males and females in postoperative pain for all days with both solutions.

Postoperative complications are shown in Table 8. The most commonly reported complications were soreness and redness at the papilla where the injection was given, pain and/or bleeding upon eating, chewing, biting, brushing, or flossing, and bruising or discoloration of gingiva. Complications were reported more frequently with articaine than lidocaine. Females reported postoperative complications more often than males. In total, 30 female participants reported any postoperative complications, in comparison to
25 males. This difference can be attributed to the fact that females generally report pain more and tolerate it less than males (67-70).

Biocanin and coauthors (6) reported 3 of 90 participants experienced a hematoma in the area of the papilla after receiving the intraseptal injection. Brkovic and coauthors (5) administered intraseptal anesthesia for maxillary lateral tooth extractions and reported that no side effects or complications were recorded during a 5-day postoperative period. Saadoun and Malamed (64) had trouble evaluating postoperative pain due to the nature of the periodontal surgery performed. However, they reported uneventful healing and healthy gingiva one week after the procedures. In the studies conducted by Brkovic and coauthors (5) and Saadoun and Malamed (64), it would be difficult to determine whether postoperative pain and complications were due to the intraseptal injections or the procedures conducted. Therefore, a direct comparison to this study is not possible.

In comparing the intraseptal injection to the PDL injection, Nusstein et al (72) reported similar findings for postoperative pain. Moderate to severe pain was reported on Day 1 in 31% and 20% for articaine and lidocaine, respectively (72). In the current study, moderate-to-severe pain was reported on Day 1 in 22% and 18% for articaine and lidocaine, respectively. In both studies, there was no significant difference between articaine and lidocaine and pain decreased over the next 2 days. Moore and coauthors (74) did not have their participants record a pain diary, but they did recall them at 21 days for examination and found all pulps and periodontium to be within normal limits following PDL injections. Walton (75) reported discomfort following PDL injections lasting several hours to 2 days. Walton (85) reported that any damage that occurred during the injection was due to the needle itself and not damage that occurred in the
apical region. Upon histologic examination following PDL injections in monkeys, Walton and Garnick (76) determined that disruption of the periodontal ligament was minimal and only occurred in the crestal region. They also reported rapid repair of the damage, which resulted in slight changes in the periodontium (76).

Similar post-injection results were also found with intraosseous injections. Gallatin and coauthors reported moderate to severe pain on Day 1 in 4-25%, on Day 2 in 4-17%, and on Day 3 in 2-12% (73). Coggins and coauthors (59) reported moderate to severe pain postoperatively in 15%, 13%, 10%, and 2% of subjects who received IO injections distal to the mandibular first molar at Days 0, 1, 2, and 3, respectively. Replogle and coauthors (60) reported moderate to severe pain in 2%, 4%, 2%, and 2% at Days 0, 1, 2, and 3 following IO injections, respectively.

In summary, postoperative pain was in the mild range for both solutions, both genders, and all 3 days following the primary intraseptal injections administered in the present study. Other studies of intraseptal anesthesia reported mild postoperative pain as well, although some may have been difficult to determine due to the clinical procedures that were completed following administration of the intraseptal injections (5, 6, 64). Similar postoperative pain ratings, with most participants reporting pain in the mild range, were found in studies conducted using primary PDL and IO injections. Swelling, soreness at the injection site, and sensitivity with chewing were sequelae reported by subjects following intraseptal, PDL, and IO injections (59, 60, 72-75).
Heart Rate

Tables 9 and 10 summarize heart rate during each period measured: baseline, mesial anesthetic deposition, distal anesthetic deposition, immediate post-injection, and during pulp testing. Mean heart rate decreased from baseline during mesial and distal anesthetic deposition for both solutions. Heart rate returned to normal after the injections and then decreased again during pulp testing. There were no significant differences between articaine and lidocaine or between males and females during any of the testing periods. Heart rate was measured to determine if there was an associated increase during or following intraseptal injection of 4% articaine or 2% lidocaine with 1:100,000 epinephrine. As discussed previously, intraseptal anesthesia is a type of intraosseous injection.

Replogle and coauthors (85) measured heart rates during and following intraosseous injection of 2% lidocaine with 1:100,000 epinephrine and 3% mepivacaine plain. In subjects given lidocaine with epinephrine, 67% had an increase in heart rate and 60% of them were able to perceive it. On average, heart rate increased by 28 beats per minute. The time at which the highest heart rate occurred was 1 minute and 36 seconds following the start of solution deposition. The time it took for heart rate to return to within 5 beats of the baseline value was 2 minutes and 27 seconds from the completion of solution deposition. When subjects were given 3% mepivacaine plain, none of them reported a perceived increase in heart rate and only 31% had an actual increase in heart rate, an average of only 4 beats per minute (85). Coggins and coauthors (59) reported a subjective heart rate increase in 78% of participants who were given 2% lidocaine with
1:100,000 epinephrine via an intraosseous injection. No actual heart rate measurements were taken (59). Gallatin and coauthors (73) reported a perceived increase in heart rate in 85% and 93% of subjects receiving intraosseous injections of 2% lidocaine with 1:100,000 epinephrine via the Stabident and X-Tip™ systems, respectively. Gallatin and coauthors (73) attributed this higher percentage of perceived heart rate increase to the higher success rates of pulpal anesthesia achieved in their study compared to previous intraosseous studies. The intraosseous injection has been shown to have a large increase in heart rate, whereas the intraseptal injection given in the current study did not. The increase in heart rate for the intraosseous injection could be attributed to the higher success rate of pulpal anesthesia, meaning that the anesthetic solution containing epinephrine is able to reach the cancellous bone for the intraosseous injection to a much greater degree than for the intraseptal injection. Further research on solution dispersion with the IS injection is needed.

Although the PDL injection is also a type of intraosseous injection, no increase in heart rate (compared to baseline) was found by Berlin and coauthors during or after the injections with both 4% articaine and 2% lidocaine with 1:100,000 epinephrine (57). Heart rate may have been expected to increase due to the fact that the PDL injection is actually an intraosseous anesthetic technique. Histologic studies have shown that the anesthetic solution is pushed through the cribriform plate under heavy back pressure during the PDL injection and into the cancellous bone to surround the root apex (51). The mechanism for the intraseptal injection is similar, only the solution is pushed through the alveolar cortical bone rather than the cribriform plate. The similarity in mechanism of
action of anesthesia can account for the similarity in results between PDL and intraseptal injections regarding heart rate.

Brkovic and coauthors (5) found a significant increase in heart rate following intraseptal injection of 0.8 mL of 2\% lidocaine with 1:100,000 epinephrine for maxillary lateral incisor extractions. Heart rate was measured via monitoring with an electrocardiogram (ECG) monitor. Average baseline heart rate was 92 beats per minute and the highest heart rate was found 15 minutes after injection at 105 beats per minute. This increase in heart rate could have been due to the fact that the anesthetic was able to penetrate the anterior maxilla and the epinephrine could reach the medullary bone. Another consideration is that the authors were performing extractions in their study (5). The patients’ heart rates may have increased simply because they were nervous about the procedure or experienced pain/pressure during treatment.

Biocanin et al (6) reported no significant differences in heart rate before administration of anesthetic, during administration of anesthetic, or 5, 10, 15, or 30 minutes after injection of 0.4 mL, 0.6 mL, and 0.8 mL of 4\% articaine with 1:100,000 epinephrine. An ECG was used to monitor and record heart rate (6). Although Biocanin et al (6) did not report actual values of heart rate for each testing period, they did include a box plot which indicated that heart rate ranged from approximately 63 bpm to 87 bpm throughout the experiment with no significant increase in heart rate during and after the injection. Their results were similar to those found in the current study.

Intraseptal anesthesia does not appear to have a significant effect on heart rate when given in the posterior mandible. Although intraseptal anesthesia is an intraosseous anesthetic technique, it did not increase heart rate significantly, as did intraosseous
injections (59, 73, 85). The PDL injection is also considered an intraosseous technique, but similar to the intraseptal injection in the current study, it did not cause an increase in heart rate (57). The volume of anesthetic (epinephrine) entering the cancellous bone may be the biggest contributor to an increase in heart rate for these three injection techniques.
Chapter 5

Summary and Conclusions

The purpose of this randomized, double-blind, crossover study was to compare the degree of pulpal anesthesia obtained with 1.4 mL of 2% lidocaine with 1:100,000 epinephrine versus 1.4 mL of 4% articaine with 1:100,000 epinephrine as a primary intraseptal injection of the mandibular first molar.

One hundred healthy adult participants enrolled in this study (49 female, 51 male). Every participant presented for the study with asymptomatic test teeth. All participants received an intraseptal injection of either 1.4 mL 2% lidocaine with 1:100,000 epinephrine or 1.4 mL 4% articaine with 1:100,000 epinephrine at two appointments spaced at least one week apart. Injections were administered with the computer-controlled local anesthesia delivery (CCLAD) system. Half of the anesthetic solution (0.7 mL) was administered on the mesial aspect of the mandibular first molar and the other half (0.7 mL) on the distal aspect. A 25-gauge 5/8-inch needle was inserted on the buccal side through the center of the intradental papilla at an approximate 30-degree angle to the long axis of the tooth until bone was contacted and slowly pressed into the crestal bone with continuous pressure until it could not be advanced any further. The mandibular first molar and the control tooth (contralateral canine) were tested every
4 minutes with an electric pulp tester (EPT) beginning at 1 minute following completion of the injection. The mandibular second premolar and second molar were also tested every 4 minutes, beginning at 3 minutes following completion of the injection. Each participant rated the two phases (needle insertion and solution deposition) of the injections for pain experienced using a 170-mm visual analog scale. Postoperative pain was recorded for 3 days after the injections. Participants were also asked to record any associated postoperative complications on each day.

There were no significant differences in the mean pain ratings for needle insertion and solution deposition between lidocaine and articaine. All mean pain ratings for needle insertion and solution deposition were within the “mild” pain category, except for the mesial needle insertion pain ratings for both lidocaine and articaine, which were in the “moderate” pain category. The female participants reported slightly more pain than the male participants during each stage of the injection for both lidocaine and articaine solutions.

Successful pulpal anesthesia was defined as two consecutive 80/80 readings with the EPT within the test period (60 minutes). The lidocaine success rates were 28%, 30%, and 26% for the mandibular first molar, second molar, and second premolar, respectively. The articaine success rates were 35%, 32%, and 34% for the mandibular first molar, second molar, and second premolar, respectively. There were no significant differences in anesthetic success between lidocaine and articaine for the mandibular first molar, second molar, or second premolar.

The time of onset for pulpal anesthesia with articaine was 1.4, 3.7, and 3.2 minutes for the mandibular first molar, second molar, and second premolar, respectively.
The time of onset for pulpal anesthesia with lidocaine was 2.3, 4.7, and 3.6 minutes for the mandibular first molar, second molar, and second premolar, respectively. There were no significant differences between the onset of pulpal anesthesia by anesthetic formulation for any of the test teeth.

The duration of pulpal anesthesia for the articaine solution was 28.2, 23.2, and 21.5 minutes for the mandibular first molar, second molar, and second premolar, respectively. The duration of pulpal anesthesia for the lidocaine solution was 18.4, 18.1, and 16.9 minutes for the mandibular first molar, second molar, and second premolar, respectively. No significant differences were found for duration of pulpal anesthesia between the two anesthetic solutions.

Heart rate was recorded via the use of a pulse oximeter, which was placed on each subject’s forefinger before the injections were given. Mean heart rate decreased from baseline during both the mesial and distal anesthetic deposition phases for both solutions. Heart rate returned to normal following the injections and then decreased again during pulp testing. There were no significant differences between articaine and lidocaine or between males and females during any of the testing periods for heart rate.

All mean postoperative pain ratings were in the “mild” pain category. Postoperative pain decreased each day for both anesthetic solutions. Females reported slightly more pain than males on Day 1 with both articaine and lidocaine and Day 2 with lidocaine. Males reported slightly more pain than females on Day 2 with articaine and Day 3 with both articaine and lidocaine. There were no significant differences in postoperative pain ratings between articaine and lidocaine for any day.
We concluded that neither 4% articaine with 1:100,000 epinephrine nor 2% lidocaine with 1:100,000 epinephrine is significantly better for primary intraseptal anesthesia of the mandibular first molar. The success rates achieved for the mandibular first molar in this study were 35% and 28% for articaine and lidocaine, respectively. These results demonstrate that a primary intraseptal injection does not achieve high enough success rates of pulpal anesthesia to support its use as a primary injection for the mandibular first molar.
References


APPENDIX A

TABLES
<table>
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<th>Number of Subjects</th>
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Table 1. Biographical Data for All Subjects.
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Table 2. Summary of Injection Pain Ratings by Gender Utilizing a Descriptive Scale.
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Table 3. Mean VAS Values (mm) of Injection Pain Ratings by Gender.
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**Table 5. Onset and Duration of Pulpal Anesthesia and Subjective Lip Numbness.**
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Table 6. Summary of Pain Ratings for Postoperative Pain Utilizing a Descriptive Scale.
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Table 7. Summary of Mean Postoperative Pain (mm) by Postoperative Day and Gender.
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Table 8. Frequency of Subject-Reported Postoperative Complications by Day.
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Table 9. Mean Heart Rate Readings (beats per minute) by Period, Gender, and Anesthetic.
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Table 10. Comparison of Heart Rate Between Time Periods with Both Solutions.
Appendix B

Figures
Figure 1. Mean Injection Pain in VAS Values (mm) by Solution, Phase, and Area.
Figure 2. Percentage of Teeth Numb (80/80) by Minute for First Molar by Solution.
Figure 3. Percentage of Teeth Numb (80/80) by Minute for Second Molar by Solution.
Figure 4. Percentage of Teeth Numb (80/80) by Minute for Second Premolar by Solution.
Figure 5. Mean VAS Values (mm) of Postoperative Pain by Day and Solution.
Figure 6. Mean Heart Rate (beats per minute) by Period, Solution, and Gender.
Appendix C

Biographical Data
### Biographical Data

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Appendix D

Medical History
Medical History

1. Do you have or have you had any of the following?
   a. rheumatic fever or rheumatic heart disease………………… NO YES
   b. heart murmur or mitral valve prolapse………………… NO YES
   c. heart disease or heart attack……………………… NO YES
   d. artificial heart valve…………………………… NO YES
   e. irregular heart beat……………………………… NO YES
   f. pacemaker……………………………… NO YES
   g. high blood pressure……………………… NO YES
   h. chest pains or angina…………………………… NO YES
   i. stroke……………………………… NO YES
   j. artificial joint…………………………… NO YES
   k. hepatitis/liver disease……………………… NO YES
   l. tuberculosis…………………………… NO YES
   m. thyroid problem…………………………… NO YES
   n. kidney disease…………………………… NO YES
   o. diabetes (sugar)…………………………… NO YES
   p. asthma……………………………… NO YES
   q. HIV or other immunosuppressive disease…………… NO YES
   r. radiation or cancer therapy……………………… NO YES

1. Do you or have you had any disease, condition, or problem not listed here? NO YES

3. Have you ever been hospitalized? NO YES

4. Have you had excessive or prolonged bleeding requiring special treatment? NO YES

5. Have you had an allergic reaction to any drugs or medications?
   (Circle all that apply: penicillin; codeine; aspirin; anesthetics; other) NO YES

6. Are you currently under the care of a physician (M.D., D.O.)? NO YES
   When were you last seen by a physician? _______________________
   Name of Physician__________________________________________
   Street address_______________________________________________
   City, State, and Zip Code_____________________________________
   Phone____________________________________________________

7. Are you pregnant or nursing? Estimated date of delivery________ NO YES

8. Have you had any trouble associated with previous dental treatment? NO YES
9. How often do you have dental check ups? ________ Date of last Exam________

10. Do you have any lumps or sores in your mouth now? NO YES

11. Do you smoke or use smokeless tobacco? NO YES

12. Are you currently taking any drugs or medications (such as antibiotics, heart medicine, birth control pills?) NO YES

Current Medications

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Summary of Patient’s Medical Status: __________________________________________________________

Medical Risk Assessment

☐ ASA I (healthy individual) ☐ ASA III (severe disease but not incapacitating)
☐ ASA II (mild systemic disease) ☐ ASA IV (incapacitating systemic disease)

Medical Consultation Required

☐ No (healthy and/or stabilized disease)

☐ Yes (ASA III or IV; cardiac murmur; vague hx; recent major disease; recent diagnosis/operation; uncontrolled disease; blood pressure; etc.)

To the best of my knowledge, the above information is correct and complete.

________________________________________ __________________________
Patient’s Signature Date
Appendix E

Consent Form
The Ohio State University Consent to Participate in Research

Study Title: Anesthetic efficacy of articaine and lidocaine in a primary intraseptal injection: a prospective, randomized, double-blind study.

Principal Investigator: Dr. John M. Nusstein

Sponsor: None

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.

- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.

- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.

- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

1. **Why is this study being done?**

   The purpose of this study is to compare two different numbing solutions and see which numbing solution works best when injected into the bone next to the lower back teeth.

2. **How many people will take part in this study?**

   One hundred ten (110) people will take part in this study.

3. **What will happen if I take part in this study?**
I will receive two different injections (shots). The shots will be articaine and lidocaine (numbing solutions like “novocaine”), all with epinephrine, into the bone next to the lower jaw back teeth. The articaine and lidocaine numbing solutions are not experimental. They are routine anesthetics and all have been approved by the FDA for dental use. Prior to the first injection, I will be required to complete a medical history questionnaire. A device called an electric pulp tester will be used to test my teeth for numbness. The electric pulp tester is a battery operated device that delivers a very small amount of current to the tooth resulting in a tingling sensation that might be uncomfortable or cause pain in the tooth being tested and which may last up to one second. It will be used on my teeth before the injections of numbing solutions. Three of my lower back teeth as well as a tooth on the opposite side (control tooth) will be tested with the electric pulp tester to be sure that my teeth respond (are alive). This will take about 6 minutes. I will have two appointments spaced at least one week apart. I will receive two injections at each appointment. My heart rate will be measured before, during, and after the injections using a pulse oximeter attached to my index finger. I will receive 1.4 ml (a little less than one anesthetic cartridge) of either 4% articaine with 1:100,000 epinephrine or 2% lidocaine with 1:100,000 epinephrine, 0.7 mL (half the cartridge) on the front side of the lower first molar and the remaining 0.7 mL on the back side of the lower first molar. The injections will be given using a computer-controlled injection system. My numb teeth will then be pulp tested every 2 minutes for 60 minutes to determine how well the injections (shots) get my teeth numb. In addition, the electric pulp tester will be used on one of my teeth on the opposite side (where I am not numb). Teeth that are not numb or are being used as a control will experience a tingling sensation or discomfort at which time the device will be removed immediately. I will not know which injection, using either the articaine or lidocaine numbing solution, I will receive at each session. The doctor will not know which injection I receive either. An assistant will help prepare the solutions and will know which anesthetic solution I will receive. I will be asked to rate the amount of pain I feel when the injections are being given. I will do this by marking my pain experience on a line graph with a pen. I will be asked to complete a short survey after each appointment to rate any pain or discomfort I have at the injection site over a three-day period following each appointment. I will also report any other side effects not relating to pain or discomfort. This survey will take about one minute to fill out each morning.

4. **How long will I be in the study?**

I am aware that I will have two appointments. Each will last approximately 70 minutes - 10 minutes for baseline pulp testing and filling out health information and receiving the initial injection. My teeth will be pulp tested for a total of 60 minutes. The post-injection questionnaires will take about 1 minute to fill out on the day of the appointment and for each morning for 3 days following each appointment. After completing the questionnaires, I will either mail them in a pre-addressed envelope or personally deliver them to the endodontic clinic front office. This will take about five minutes.
5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

I may have pain associated with the local anesthetic (numbing solution) or soreness at the site of the injections (shots) for approximately two days. Where I receive the injection, I may have swelling (hematoma—a collection of blood in my mouth) or a bruise may develop (1%). I may experience a feeling of anxiety, lightheadedness or fainting (3.2%), and/or a temporary increase in my heart rate (1%). The tingling sensation and/or slight discomfort (pain) produced by the pulp tester may be uncomfortable to me. I may have an allergic reaction to the local anesthetic (itching or hives, very rare), or have an unexpected gum infection (rare, 1%). I may have soreness of my gum tissue for a few days or a possible altered sensation of my lip (1%) that may last up to a few weeks.

If I am a woman able to have children, I will be questioned regarding pregnancy or suspected pregnancy and will not be allowed to participate if pregnant, suspect a pregnancy, trying to become pregnant, or nursing. Additionally, I will be required to take a urine pregnancy test before I can start this study. If I am a woman, I must also be using a reliable method of contraception (oral contraceptives, condoms, diaphragm, or abstinence) during the next 24 hours. The reason for excluding pregnant or potentially pregnant women is an attempt to minimize this population group in the study because the potential risks to the fetus and nursing baby are unknown. There are no adequate and well-controlled studies of articaine and lidocaine in pregnant women. This pregnancy test will be paid for by the study.

7. What benefits can I expect from being in the study?

I will not directly benefit from this study. Society may benefit if one of the anesthetics (numbing solutions) works better at anesthetizing (numbing) the teeth than the other using the intraseptal injection.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled. No dental treatment will be done, so no other choices are available.
9. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;

You may also be asked to sign a separate Health Insurance Portability and Accountability Act (HIPAA) research authorization form if the study involves the use of your protected health information.

10. What are the costs of taking part in this study?

The study will pay for the cost of the study drugs (articaine and lidocaine) and urine pregnancy test. You may need to pay for parking while participating in the study.

11. Will I be paid for taking part in this study?

Yes, I will be paid $75.00 for my participation. I will receive $75.00 for completing all aspects of the study. If I am unable or unwilling to complete both sessions of the study, I will be paid a pro-rated $30.00 per session and an additional pro-rated $5.00 per completed and returned questionnaire form. After completing the questionnaires, I will personally deliver them to the endodontic clinic front office, at which time I will receive payment for the completed parts of the study for which I have not yet received payment. Payment is to compensate me for time and travel expenses.

By law, payments to subjects are considered taxable income.

12. What happens if I am injured because I took part in this study?
If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

13. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of participants in research.

14. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Dr. John Nusstein or Dr. Tera Pandrangi at (614) 292-5399.

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact Ms. Sandra Meadows in the Office of Responsible Research Practices at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study related injury, you may contact Dr. John Nusstein or Dr. Tera Pandrangi at (614) 292-5399.
Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this form.

Printed name of subject

Signature of subject

Date and time

Printed name of person authorized to consent for subject (when applicable)

Signature of person authorized to consent for subject (when applicable)

Date and time

Relationship to the subject

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent

Signature of person obtaining consent

Date and time

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness

Signature of witness

Date and time

Printed name of witness

Signature of witness

Date and time
Appendix F

HIPAA Forms
THE OHIO STATE UNIVERSITY
HIPAA RESEARCH AUTHORIZATION FORM

Beginning April 14, 2003, the new HIPAA Privacy Rule requires that Ohio State University Principal Investigators (PIs) provide research subjects with greater detail than what is currently included in the IRB-approved consent form concerning how a subject’s past, present and future health-related information (collectively, Protected Health Information or PHI) will be used, shared and protected during the research. Specifically, the Privacy Rule now requires that PIs inform subjects of the following: 1) what specific kinds of information will be used or disclosed to others during the course of the research; 2) the specific identities of collaborating investigators, sponsor companies or sponsor agencies that will potentially receive copies of subjects’ PHI during the research; 3) that subjects have a right to review their research-related PHI; and 4) that subjects have the express right to revoke their authorizations for the release of PHI at any time.

To meet these new requirements, PIs using PHI obtained from medical or research records from the Ohio State University Hospitals, The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, OSU & Harding Behavioral Health Care & Medicine, the Ohio State University Hospitals East and the Primary Care Network (the University Health System), or other University operated health centers or clinics, must now complete and receive a signed copy of the University’s “Authorization to Use Personal Health Information in Research” form (the Authorization) below from subjects enrolling in research studies on or after April 14th (or be granted a waiver by a HIPAA Privacy Board) in addition to obtaining a signed IRB-approved consent form. The form will need to be carefully prepared by PIs to ensure that the Authorization covers ALL of the necessary uses and disclosures of personal health information used in clinical research. Failure to do so may violate the Privacy Rule and result in penalties against the University as well as individual civil and criminal penalties against the Principal Investigator.
INSTRUCTIONS TO RESEARCHERS
FOR PREPARING THE RESEARCH AUTHORIZATION FORM

1. Complete the first section of the Authorization form with title of the study, the OSU IRB protocol number, and PI name. Add subject name at the time of authorization. Do not include these instructions as part of the completed Authorization form.

2. “Uses and Disclosures Covered by this Authorization” – List every known non-OSU person, class of persons, or organizations (including the sponsor agency or company, known subsidiaries of the sponsor, cooperative data groups, etc.) that may create, disclose, receive, and/or use the information in connection with the study. Fill in the blanks on the form (and delete the instructions in italics as well as inapplicable bulleted sections) as appropriate. If information will not be disclosed outside of The Ohio State University, delete all bullets and insert “None”. Note: if a person(s) or organization is not listed on the form, they may not create, disclose, receive or use PHI in connection with the study.

3a. “HIPAA Privacy Contact” – If the research involves the use of medical records from the University Health System, where applicable, insert the contact and address: HIPAA Privacy Manager, the Ohio State University Medical Center, 140 Doan Hall, 410 W. Tenth Avenue, Columbus, Ohio 43210.

3b. If the research solely involves the use of personal health records at non-University Health System clinics or health care facilities (for example, the Dental School, Optometry School, Nisonger Center, Younkin Center, Psychological Services Center, Anxiety and Stress Disorder Clinic, Marriage & Family Therapy Clinic, Camera Center or faculty practice group such as OSU-P) insert the name and address of the appropriate Privacy Contact for the center, school, clinic or practice group. If unknown, contact the director of the health center, school, clinic or practice group or the Office of Legal Affairs at (614) 292-0611 for the contact and address of the applicable Privacy Contact.

4. The Authorization must be presented to all newly enrolled or “re-consented” subjects in IRB-approved research beginning April 14, 2003 at the time the IRB-approved consent form is signed. The subject or his/her legally authorized representative must be provided with a copy of this form after it has been signed. The original, signed copy must be retained in the research file for a period of six years from the date the Authorization was signed (or longer, according to sponsor requirements). Prior IRB approval of the Authorization is not required; however, the Privacy Contact and/or HIPAA Privacy Board may conduct audits of the Authorization to ensure completeness.

5a. “Notice of Privacy Practices” – Each subject who receives health care services at the University on or after April 14, 2003 should receive a copy of a Notice of Privacy Practices (NPP) and sign an acknowledgement (NPP Acknowledgement form) that (s)he obtained the NPP.

5b. If the research involves the use of health and/or medical records from the University Health System and the subject has not received a copy of the University Health System’s NPP, provide the subject with a copy of the NPP. The subject should sign a copy of the University Health System’s NPP Acknowledgement form. The original, signed copy of the NPP Acknowledgement form must be retained in the research file for a period of six years from the date the NPP Acknowledgement was signed (or longer, according to sponsor requirements). The
University Health System’s NPP and NPP Acknowledgement form are available in electronic format on the Office of Responsible Research Practices (ORRP) website at http://www.orrp.ohio-state.edu as well as the Medical Center’s website at http://www.osumedcenter.edu.

5c. If the research involves the use of health records at other non-University Health System clinics or facilities (including the sites listed above in item 3b.) and the subject has not received a copy of the facility or clinic’s individual NPP, provide the subject with a copy of the NPP. Contact the director of the applicable health center, school, clinic or practice group to obtain a copy of the NPP and the NPP Acknowledgement form. The original, signed copy of the NPP Acknowledgement form must be retained in the research file for a period of six years from the date the NPP Acknowledgement was signed (or longer, according to sponsor requirements).
The Ohio State University
Authorization to Use
Personal Health Information in Research

Anesthetic efficacy of articaine and lidocaine in a primary intraseptal injection: a prospective, randomized double-blind study.

OSU Protocol Number:

Principal Investigator: Dr. John Nusstein, DDS, MS

Subject Name__________________________________________________________

Before researchers use or share any health information about you as part of this study, The Ohio State University is required to obtain your authorization. This helps explain to you how this information will be used or shared with others involved in the study.

- The Ohio State University and its hospitals, clinics, health-care providers and researchers are required to protect the privacy of your health information.

- You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you. Please carefully review this information. Ask if you have any questions or do not understand any parts of this notice.

- If you agree to take part in this study your health information will be used and shared with others involved in this study. Also, any new health information about you that comes from tests or other parts of this study will be shared with those involved in this study.

- Health information about you that will be used or shared with others involved in this study may include your research record and any health care records at the Ohio State University. For example, this may include your medical records, x-ray or laboratory results. Psychotherapy notes in your health records (if any) will not, however, be shared or used. Use of these notes requires a separate, signed authorization.

Please read the information carefully before signing this form. Please ask if you have any questions about this authorization, the University’s Notice of Privacy Practices or the study before signing this form.

Initials/Date: _______________
Those Who May Use, Share And Receive Your Information As Part Of This Study

- Researchers and staff at The Ohio State University will use, share and receive your personal health information for this research study. Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information. If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic or physician’s office records.

- Those who oversee the study will have access to your information, including:
  - Members and staff of the Ohio State University’s Institutional Review Boards, including the Western Institutional Review Board
  - The Office for Responsible Research Practices
  - University data safety monitoring committees
  - The Ohio State University Research Foundation

- Your health information may also be shared with federal and state agencies that have oversight of the study or to whom access is required under the law. These may include:
  - The Food and Drug Administration
  - The Office for Human Research Protections
  - The National Institutes of Health
  - The Ohio Department of Job and Family Services

These researchers, companies and/or organization(s) outside of The Ohio State University may also use, share and receive your health information in connection with this study:

- None

The information that is shared with those listed above may no longer be protected by federal privacy rules.

Initials/Date_________________
Authorization Period

This authorization will not expire unless you change your mind and revoke it in writing. There is no set date at which your information will be destroyed or no longer used. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

Signing the Authorization

- You have the right to refuse to sign this authorization. Your health care outside of the study, payment for your health care, and your health care benefits will not be affected if you choose not to sign this form.
- You will not be able to take part in this study and will not receive any study treatments if you do not sign this form.
- If you sign this authorization, you may change your mind at any time. Researchers may continue to use information collected up until the time that you formally changed your mind. If you change your mind, your authorization must be revoked in writing. To revoke your authorization, please write to:
  Dr. John Nusstein at the College of Dentistry, 305 W. 12th Avenue, The Ohio State University, Columbus, Ohio 43210 or Dr. Henry Fischbach at the College of Dentistry, 305 W. 12th Avenue, The Ohio State University, Columbus, Ohio 43210
- Signing this authorization also means that you will not be able to see or copy your study-related information until the study is completed. This includes any portion of your medical records that describes study treatment.

Contacts for Questions

- If you have any questions relating to your privacy rights, please contact Dr. Henry Fischbach at the College of Dentistry, 305 W. 12th Avenue, The Ohio State University, Columbus, Ohio 43210
- If you have any questions relating to the research, please contact Dr. John Nusstein at the College of Dentistry, 305 W. 12th Avenue, The Ohio State University, Columbus, Ohio 43210
Signature

I have read (or someone has read to me) this form and have been able to ask questions. All of my questions about this form have been answered to my satisfaction. By signing below, I permit Dr. John Nusstein and the others listed on this form to use and share my personal health information for this study. I will be given a copy of this signed form.

Signature__________________________________________________________
(Subject or Legally Authorized Representative)

Name _____________________________________________________________
(Print name above)
(If legal representative, also print relationship to subject.)

Date___________ Time __________ AM / PM
Appendix G

Primary Intraseptal Injection Pain Rating Form
Clinical Survey

1\textsuperscript{st} Appointment

Mesial (Front) Injection:

Insertion/Placement:

\begin{center}
\begin{tikzpicture}
\draw (0,0) -- (9.5,0);
\foreach \x in {0,1,2,3,4,5,6,7,8,9,9.5}
{\draw (\x,0.1) -- (\x,0.05);}
\foreach \y in {0,1,2,3,4,5,6,7}
\draw (0.5,\y) -- (0.5,\y-0.05);
\node at (0.0,0.2) {None};
\node at (1.0,0.2) {Faint};
\node at (2.0,0.2) {Weak};
\node at (3.0,0.2) {Mild};
\node at (4.0,0.2) {Moderate};
\node at (5.0,0.2) {Strong};
\node at (6.0,0.2) {Intense};
\node at (7.0,0.2) {Maximum Possible};
\end{tikzpicture}
\end{center}

Deposition:

\begin{center}
\begin{tikzpicture}
\draw (0,0) -- (9.5,0);
\foreach \x in {0,1,2,3,4,5,6,7,8,9,9.5}
{\draw (\x,0.1) -- (\x,0.05);}
\foreach \y in {0,1,2,3,4,5,6,7}
\draw (0.5,\y) -- (0.5,\y-0.05);
\node at (0.0,0.2) {None};
\node at (1.0,0.2) {Faint};
\node at (2.0,0.2) {Weak};
\node at (3.0,0.2) {Mild};
\node at (4.0,0.2) {Moderate};
\node at (5.0,0.2) {Strong};
\node at (6.0,0.2) {Intense};
\node at (7.0,0.2) {Maximum Possible};
\end{tikzpicture}
\end{center}
Clinical Survey
1st Appointment

Distal (Back) Injection:

Insertion/Placement:

Deposition:
Clinical Survey

2nd Appointment

Mesial (Front) Injection:

Insertion/Placement:

Deposition:
Clinical Survey
2nd Appointment

Distal (Back) Injection:

Insertion/Placement:

Deposition:
Appendix H

EPT Values Recording Sheet
EPT READINGS

Name ___________________________________________  Code __________________
Pulp Tester _____________________________________  Date __________________

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<th>TIME</th>
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</tbody>
</table>

HEART RATE

P1 (pre-injection): every 1 min for 8 min
8 readings

P2 (M deposition): every 15 s for 2.5 min
10 readings

P3 (D deposition): every 15 s for 2.5 min
10 readings

P4 (post-injection): every 15 s for 2 min
8 readings
Appendix I

Postoperative Survey
Post-Op Survey

Please answer the following questions regarding the injections (shots) that were administered.

DAY 1

A. Please rate the discomfort, soreness, or pain in the area of your mouth where the shots were given. (Place an “X” on the line.”)

_________

B. Please note any additional comments and/or side effects not relating to pain or discomfort. (for example: ulcerations, swelling, bruising, numbness)

_________________________________________________________________________

_________________________________________________________________________

_________________________________________________________________________
Please answer the following questions regarding the injections (shots) that were administered.

**DAY 2**

A. Please rate the discomfort, soreness, or pain in the area of your mouth where the shots were given. (Place an “X” on the line.

| None | Faint | Weak | Mild | Moderate | Strong | Intense | Maximum Possible |

B. Please note any additional comments and/or side effects not relating to pain or discomfort. (for example: ulcerations, swelling, bruising, numbness)

________________________________________________________________________________________
________________________________________________________________________________________
________________________________________________________________________________________
Name___________________  Number_________________

Post-Op Survey

Please answer the following questions regarding the injections (shots) that were administered.

DAY 3

A. Please rate the discomfort, soreness, or pain in the area of your mouth where the shots were given. (Place an “X” on the line.”)

<table>
<thead>
<tr>
<th>None</th>
<th>Faint</th>
<th>Weak</th>
<th>Mild</th>
<th>Moderate</th>
<th>Strong</th>
<th>Intense</th>
<th>Maximum Possible</th>
</tr>
</thead>
</table>

B. Please note any additional comments and/or side effects not relating to pain or discomfort. (for example: ulcerations, swelling, bruising, numbness)

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________