Assessment Of Periapical Bone Healing After Endodontic Microsurgery Using Cone-Beam Computed Tomography

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THESIS

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LIST OF ABBREVIATIONS

CBCT - Cone Beam Computed Tomography

CT - Computed Tomography

DOM - Dental Operating Microscope

EMS – Endodontic Microsurgery

FOV - Field Of View

GTR - Guided tissue regeneration

MRI - Magnetic Resonance Imaging

NS-RCT - Non-Surgical Root Canal Treatment

PAI - Perapical Index

PAIchange - Periapical Index Change

PARL - Periapical Radiolucency

PDL - periodontal ligament

Post-PAI- Post-treatment Periapical Index

Pre-PAI – Pre-treatment Periapical Index

TAS – Traditional Endodontic Surgery

RCT - Root Canal Treatment

ReTx – Root Canal Retreatment

US – Ultrasonic

SUMMARY

The purpose of this study was to evaluate the outcome of endodontic microsurgery (EMS) using Cone Bean Computed Tomography (CBCT) technology. The study also examined the success rate of EMS when bone graft and membranes used in patients who had undergone EMS for a bone defect using CBCT. It was hypothesized that patients who underwent the bone and membrane graft procedures would have better healing outcomes than those that did not undergo the bone and membrane grafts. The study was conducted using retrospective CBCT records of patients who had undergone endodontic microsurgery from October 2011 - July 2015 at a local Endodontic specialty practice. CBCT scans with a recall period of at least 6 months were selected. Preoperative and postoperative CBCTs were evaluated for healing outcomes.

From the total surgeries performed in the clinic, 56 teeth (65 roots) were selected and were eligible for the study. EMS was divided into two groups dependent on the use of bone graft/membrane during the procedure. In Group A: bone graft/membrane was used during EMS. In Group B: bone graft/membrane was not used during EMS. Post-operative follow-up ranged from 6 months to 36 months and subjects were further divided into two sub-groups; one with a 6-12 month follow-up examination and one with a 13-36 month follow-up.

Outcomes were categorized as complete healing, incomplete healing, unsatisfactory healing or persistent disease using the CBCT periapical index modified by Estrela in 2008. The results of the study failed to find a statistically significant difference. The reasons for this failure are suspected to be a small sample size and the inability to account for co-morbid factors that could have influenced healing after the EMS.

I. INTRODUCTION

A. Background:

Several factors are responsible for increasing tooth retention in older adults. Over the past several decades, improvements in community water fluoridation, the inclusion of fluoride in toothpaste, along with improved patient and provider attitudes regarding oral hygiene, regular use of dental services and advances in dental technology are thought to be responsible for this trend (U.S. Department of Health and Human Services, 2000, Center for Disease Control and Prevention, 2002). Endodontics has experienced many new advancements over the last 20 years. One of the most notable advancement was the development of the dental operating microscope (DOM). This allows clinicians to have better illumination and magnification during dental procedures. In addition, new technologies such as rotary instrumentation, electronic apex locators, improved irrigation techniques, ultrasonic (US) tips, CBCT, and biocompatible root-end filling materials such as MTA have all contributed to better patient outcomes and the ability to retain teeth for a longer time (Paredes-Vieyra, 2012).

During this time, the success rate of non-surgical endodontic therapy (NS-RCT) has remained within the same range of 86%-96%. However, new available technology and materials allows the ability to achieve this rate more consistently and with fewer visits (Paredes-Vieyra, 2012). The biggest advancement in terms of predictability and outcome comes from EMS. Traditional apical surgery (TAS) outcome ranged between 19%-59%. In contrast, EMS outcome studies indicate a success rate of 94%-96% (Setzer, 2000). Furthermore, the introduction of CBCT to endodontics offers an in-depth view of the periradicular tissues compared to periapical radiographs (PA). This is especially beneficial when treatments planning and assessing healing following EMS (Petel, 2014; American Association of Endodontists Position Statement 2015).

There are very few CBCT studies that assess the healing of bone defects after EMS. In 2013, the first clinical study that used volumetric measurement of periapical lesions on CBCT to assess the result was published (van der Borden, 2013). In the study, 50 teeth with 71 roots that had evidence of periapical bone loss were recalled for examination at about 10-37 months after treatment. The study evaluated the initial size of the lesion on both the periapical radiographs and CBCT images after EMS. Findings suggest that 11 of 71 roots (15.5%) showed complete healing of the lesion on CBCT as opposed to 32 of 71 (45.1%) on periapical radiograph. Overall findings noted that 55 of 71 roots (77.5%) demonstrated a reduction in the size of the lesion as opposed to 63 of 71 roots (88.7%) on periapical radiograph. In conclusion, the study showed that changes in the lesion after root canal treatment assessed with 3D volumetric CBCT data and 2-dimensional PA data did not show the same outcome. This indicates that the outcome would be assessed differently, depending on the imaging technique.

B. <u>Statement of the Problem and its Significance:</u>

Modern imaging has been able to establish evidence of the healing of periapical lesions after EMS, but there is limited research on assessment and evaluation of the outcome of EMS using CBCT technology and examination of prognostic factors that relate to bone healing. Several studies have observed that the use of bone grafts and membranes in periodontal surgery can lead to improved patient outcomes. This has led to the development of a bone grafts and membranes that allow the cellular regrowth of bone defects caused by pathosis (Wang and MacNeil, 1998). Likewise, academic studies have demonstrated that this grafting technique can also be successfully applied during EMS (Abramowitz, 1994; Tobon, 2002; and Dietrich, 2003). A comparison of outcomes of academic research suggests that the success rate of grafting techniques in periapical lesions might not yield statistically significant results. This study will help to provide further insight into the usefulness of bone graft/membrane in EMS to repair periapical defects.

C. Purpose of the Study:

The purpose of this retrospective study was to evaluate the outcome of endodontic microsurgery using CBCT technology. The study also evaluated the success in terms of patient outcome of the use of a bone graft and membrane during EMS. The purpose of this study was to support evidence-based practice in the use of bone graft/membranes in EMS for the repair of apical bone defects.

D. Significance of the Study:

This study aims to improve clinical understanding of the changes that occur in the periapical bone, where periapical lesions are reduced after using CBCT technology to evaluate the success of repair of the bone using bone graft/membrane during EMS. The most important outcome of the study was to determine if bone graft/membranes during EMS improved patient outcomes. This will help clinicians to recommend the most appropriate treatment that is more likely to result in improved patient outcomes.

E. Hypothesis:

The purpose of this research study is two-fold. The first aim of the study is to further develop the use of CBCT technology to assess bone healing after EMS. The second outcome is to assess the effectiveness of bone graft and membrane techniques for the repair of periapical lesions. In order to accomplish this task, the following hypotheses will be examined as part of the study.

The use of bone graft/membrane in EMS will result in statistically significant improvement in patient outcomes, as opposed to EMS using no bone graft/membrane.

II. CONCEPTUAL FRAMEWORK AND LITERATURE REVIEW

Prior to conducting this research study, a literature review was conducted that examined EMS, techniques, and imaging for successful patient assessment both before and after surgery. The literature review included both recent and seminal works in the field. Research in this area established state-of-the-art in the field and the need for the current research study. It also formed the conceptual framework for the research study.

A. Endodontic microsurgery

Endodontic microsurgery is a procedure that is effective in treating apical periodontitis; particularly in cases where either non-surgical retreatment (ReTx) or initial root canal treatment (RCT) were not successful in treating the disease (Safi, 2015). Situations where there is refractory or persistent intracanal infection after iatrogenic changes are observed in the canal anatomy, or microorganisms that is close to the area of constriction as well as the apical foramen may be included. In extraradicular infection there might be changes detected such as bacterial plaque found on the apical surface of the root or there might be bacteria found in the lesion (Safi, 2015).

Before the introduction of surgical operating microscopes, endodontic surgery had success rates that ranged from 43% to 75% lower than nonsurgical retreatments (Song, 2013). Traditionally endodontists were using amalgam for root-end filling and surgical burs for root-end preparation. These approaches have been employed for many years, but have now been replaced with the use of DOM, US instruments, MTA or other biocompatible filling materials. In addition, endodontic microsurgical approaches have produced predictable outcomes of the healing of endodontic lesions (Kim, 2006).

Recently, endodontic microsurgery includes the use of magnification and high-power illumination, US root-end preparation, as well as biocompatible root-end filling materials that have produced outcomes that are more favorable than previous techniques. Many authors have engaged in the analysis of individual variables and their effects on the outcome of endodontic surgery. Predictable preoperative prognostic factors in most studies reviewed included the quality and length of existing root fill, the presence of a post and the lesion size, and the presence of a preoperative lesion (Song, 2013). The placement of a root-end filling, the root-end preparation methods, the root-end filling materials, and the operator's skill are all considered intraoperative factors that could affect the outcome of surgical treatment (Song, 2013).

Within the past ten years, numerous studies have reported on the clinical outcomes of EMS. At the same time, few of these reports discussed the relationship between prognostic factors and the outcome of endodontic microsurgery. Von Arx et al (2015) evaluated the influence of several factors on the outcome of healing 1 year after EMS in a study using a sample of 194 teeth. In another study, tooth position (anterior), lesion type (isolated endodontic lesion), root-end filling material (ProRoot MTA and Super EBA), and sex (female) were positive prognostic factors for endodontic microsurgery (Song, 2013). Anterior tooth position was a predictor of healing. At the same time, rarely have these prognostic factors been reported for endodontic microsurgery, and more research is needed in this area (Song, 2013).

Bioceramics is a new product that has been used recently in clinical dentistry. MTA was first used in 1993. It was introduced to endodontic community by Dr. Torabinejad. MTA has the same composition as Portland cement, but bismuth oxide for radio-opacity has been added. It also contains dicalcium silicate, tricalcium silicate, small proportions of tricalcium aluminate and calcium sulfate, as well as bismuth oxide. This compound is a significant improvement over older materials.

No studies were found that addressed the CBCT methods and its efficiency in evaluating success (Safi, 2015). Mead et al, (2005) conducted an investigation on the quality of various clinical investigations on the outcome or success rates of endodontic surgery. He found few research studies that exist, which indicate valid and reliable clinical studies and that were acceptable as a source upon which to base clinical decisions.

Nowadays CBCT is used widely to facilitate pre-surgical planning for endodontic microsurgery. Limited field CBCT has been used as an effective predictor to buccal cortical plate perforations caused by endodontic lesions. Ha (2013) observed 35 roots that underwent microsurgical root-end resection in his study. Pre-operative, there were 90 voxel CBCTs that were taken using a Carestream 9300. The scans that were produced were analyzed by both an oral radiologist and endodontic resident with the objective of determining if a perforation in the buccal plate was present. Findings derived from the scans were compared to how the bone appeared in the clinical environment (Ha, 2013). In addition, there was notable significance in the relationship between judgment of perforation that is made on the basis of CBCT as opposed to the actual perforation that was clinically observed. Prediction made by CBCT were accurate 83% of the time. In

88% of the instances a predicted perforation was validated and in 75% of instances a non-perforation was predicted (Ha, 2013).

Endodontists must be familiar and knowledgeable regarding the dimensions of the anatomy at the site where the surgery will be performed (Lavasani, 2016). If CBCT technology is not available due to the cost and location, then it is imperative for the clinician to consult a base of knowledge for the site of the surgery (Lavasani, 2016). It is critical to know and understand the prognostic predictors when making a decision between alternative treatment methods and EMS.

Tooth-related and patient-related factors were reviewed in numerous studies that may have an impact on the outcome of EMS (Safi, 2015). Barone (2010) in his study examined and assessed the outcome of 134 teeth where EMS was performed. The follow-up period ranged from 4-10 years. Results showed that 74% of the teeth had healed and three outcome predictors were identified: preoperative root-filling length, age of patient, and size of the surgical crypt. Patients who were older than 45 years old, surprisingly healed better than younger patients. Root filling lengths were seen as either adequate or inadequate, where adequate lengths showed exceptional healing. Better healing was also identified in a 10mm or less size operative crypt. Other factors such as absence or presence of perforation, root-end filling depths, lesion size, post-operative restoration did not show significant impact on the results and outcome (Safi, 2015). These factors could also affect the outcome of this research study.

Setzer (2010) published a meta-analysis that investigated prognostic factors related to EMS. Thirty-eight articles were evaluated for prognostic factors. Those factors were divided into categories: 1. patient-related, tooth-related and 2. treatment related factors. Patient-related factors are factor such as age and sex, but in the investigation neither factor was deemed as a significant predictor of outcome. Significant predictors of healing in the tooth-related factors are maxillary and mandibular anterior teeth, absence of pre-operative signs and symptoms, and size of the lesion. First-time EMS, US root-end preparation, using an endoscope, and root-end filling with MTA are treatment-related factors and have been identified as significant predictors of result and outcome. In none of the studies reviewed was CBCT technology used to achieve outcome prediction. In a meta-analysis conducted by Setzer (2010), a 94% weighted pooled success rate for EMS was observed over a period of 6 months.

The results of this portion of the literature review found that only a few studies investigated the use of CBCT imaging in EMS. Differences patient outcomes were identified. In addition, a number of factors, other than the surgery were found to affect patient outcomes. Further studies need to be conducted in this area in order to improve the clinical reliability of EMS procedures.

B. Bone defect healing

Healing constitutes a restoration of damaged and lost tissue of the tooth that the patient had before the injury occurred (Kumar, 2010). There are four phases to healing: hemostasis, inflammation, proliferation, and tissue remodeling. There is a simultaneous integration to each phase (Gosain and DiPietro, 2004). The healing of apical periodontitis progresses from peripheral tissues toward the center of the lesion. The new trabecular bone for the most part is endosteal in origin. If the disease affected the cortical plate then the periosteum will participate in regeneration of a new cortical bone. It is possible that the last tissue to experience repair or healing is the periodontal ligament to cover the areas where cementum was either lost on the root end or damaged (Michaelson and Holland , 2002).

Ricucci (1998), demonstrated that the steps in healing are somewhat hypothetical since no study has shown all stages/events actually existing. Currently, the information is largely derived from studies and observations involving the repair of tissue after apical surgery and tooth extraction in addition to cross-sectional observations in human being whose teeth that had healing lesions were extracted for prosthetic planning, and animal studies (Michaelson and Holland, 2002). However, at this point, no clinical research supports these observations.

After therapeutic interventions have been completed histological data is not available, which is critical in helping the clinician determine whether or not healing has occurred. As a result, the radiograph has been instrumental in evaluating the size of lesions after surgery. In the absence of swelling, sinus tracts, complete restitution of lamina dura, symptoms, and periodontal ligament (PDL) space on the radiograph after surgery has been deemed the best method for determining patient outcome after nonsurgical root canal therapy (Michaelson and Holland , 2002). Strindberg (1956) published strict criteria to determine successful endodontic treatment, and it included a radiographic resolution of the entire apical lesion.

In a study conducted by Orstavik (1996) an evaluation of 599 endodontically treated teeth demonstrated that peak of healing of apical periodontitis typically occurs after one year of treatment. Orstavik (1996) also noted that four years or more might be necessary for complete healing in some cases, as evidenced and determined by the radiographs. This study created the basis for the recommendation set forth by the European Society of Endodontology that suggests that after one year of treatment, the first-follow-up examination should be conducted to see if the lesion has failed or succeeded. Furthermore, periodic should occur each year for a period of four years as per the recommendation (European Society of Endodontology, 2006). The Society also suggested that if there were a persistence of radiolucency for four years or more, then the case would be considered a failure, even if clinical signs and symptoms were absent. This guidance will be useful in determining the follow-up periods for this research study.

C. Bone graft and membrane

Bone grafts replacement grafts are used to help form bone and periodontal regeneration (Reynolds, 2010). Surgical approaches that are conventional, like open flap debridement, are critical in accessing the evaluation and detoxification of root surfaces and to establish architecture and improved periodontal form, but these surgical techniques are limited in restoring or reconstruction of periodontal tissues (Reynolds, 2010). These materials for bone grafting function partially as structural scaffolds and matrices for proliferation and attachment of anchorage-dependent osteoblasts (Reynolds, 2010). There is a wide range of bone grafting materials, such as bone grafts and bone graft substitutes, which have been applied and clinically evaluated that include autografts, allografts, xenografts, and alloplasts, and synthetic/semisynthetic materials, (Lee, 2012). Not all bone grafting materials can support the creation of a new apparatus for periodontal attachment, but there is definite evidence that periodontal regeneration is possible with bone replacement grafts in humans (Lee, 2012).

Guided tissue regeneration (GTR) techniques have been used in addition to endodontic surgery to promote bone healing (Tsesis, 2011). Studies have shown the additional benefits that GTR has for the outcome of endodontic surgery in treatment protocols that are varied on terms of inclusion criteria and follow-up periods. This caused the generation of confusing and inconsistent results (Tsesis, 2011). Evaluations conducted in studies show that GTR is extremely influential on the outcome of surgical endodontic treatment. Better outcomes have been observed in a trend when control cases were compared to GTR, however the results were not statistical significant (Tsesis, 2011).

The size and type of lesion, as well as the type of membrane, were identified as significant factors that affect the outcome of control cases vs GTR. GTR techniques favorably affected the outcome of surgical endodontic treatments in cases where there are large periapical lesions as well as through-and-through lesions (Tsesis, 2011). When using a resorbable membrane over using a non-resorbable membrane or graft alone, a favorable outcome was found.

Surgical endodontic treatment is an option for teeth that have apical periodontitis and could indicate teeth with periapical pathology when it is not practical to undergo nonsurgical retreatment, when improvement is unlikely compared to previous results, or when a practitioner needs to perform a biopsy (Tsesis, 2011). DOMs are used in modern endodontic surgical techniques, as well as US root-end preparation to a depth of 3 to 4 mm, minimal root resection bevel and new forms of biocompatible root-end filling materials (Tsesis, 2011). GTR has a success rate of over 90%, and the final histological results of the healing of the wound in endodontic surgery may repair or regenerate depending on the nature of the wound, availability of progenitor/stem cells, growth/differentiation factors as well as microenvironmental cues such as extracellular matrix and associated non-collagenous protein adhesion molecules (Tsesis, 2011). The GTR techniques are used and have been offered as an addition to EMS to promote bone healing. Many studies on the effectiveness of GTR techniques to improve the success and promote healing of EMS have been published recently. The significant variability in the designs of the studies as well as treatment protocols, inclusion and exclusion criteria, and follow-up periods generated inconsistent results (Tsesis, 2011).

The primary goal of endodontic surgery is predicting the regeneration of periapical tissues that include the complete repair of osseous defects (Beak and Kim, 2001). A main concern in administering endodontic treatment to an infected tooth with a through-and-through osseous defect is that healing will be certain (Precheur, 2007). In spite of the fact that most canal systems and periapical areas are void of microorganisms after endodontic treatment, not always does bone healing occur due to an ingrowth present in connective tissue that has an osseous defect. Periapical scarring can occur, which is misdiagnosed often as a pathologic condition and may lead to unnecessary surgical reentry (Precheur, 2007).

Synthetic bone substitutes, bone grafts and membranes have been used to prevent the regrowth of cellular periodontal defects that were caused by surgical trauma during EMS. Nyman et al. (1982) presented and defined a new principle of biology relating to the regenerative healing of wound, which Beak and Kim (2001) described as guided tissue regeneration. GTR, as applied to bone healing, focuses on the prevention of connective tissue from entering the defect of the bone during the healing phase. The slower bone-producing cells are allowed through GTR to migrate and reproduce into the defect of the bone (Beak and Kim, 2001).

Previous studies that used polytetrafluoroethylene (PTFE) membrane on defects of the mandibular bone in rats and monkeys shows evidence of repair within 3 weeks (Beak and Kim, 2001). Similarly, Lundengren et al (1997) used the GTR technique to test whether or not polyglactin, which is a resorbable membrane, can be used to accomplish actual bone regeneration in through-and-through bone defects observed in rabbit skulls. Regeneration of bone extending from the edge of the defect to the other was evident and control groups only contained soft tissue repair. Pecora et al (1995) also demonstrated the use of GTR principles as effective in enhancing the quantity and quality of bone regeneration in human periapical lesions and the procedure of GTR procedure, which accelerates bone growth and bone cavities after endodontic surgery (Precheur, 2007).

D. Literature Review of Radiography:

Numerous methodologies have been used to evaluate the healing of the bone including, but not limited to, techniques of radiographic subtraction techniques (Grondahl, 1983), ultrasound (Cotti, 2003), MRI (Patel, 2009), tuned aperture computed tomography (Nair, 2001), Computed Tomography (CT) (Velvart, 2001), and CBCT (Patel, 2007; Cotton, 2007). In endodontics, PA radiographs are the most common way to assess healing of periapical lesions after an endodontic treatment. In this technique, the affected tooth or areas will be exposed to one or more radiographs by the dental practitioner (Glickman, 2009).

Radiography is an adjunct to clinical examination, but it is irreplaceable and is determined to be the only way that a practitioner can determine the presence of a disease such as cystic lesions with bone resorption, periradicular inflammation, and other diseases that typically can only be detected through radiography (Syrjanen, 1982). To determine the location and extent of the infection and to diagnose pathosis, radiographic images have been used by clinicians since the later part of the nineteenth century (Syrjanen, 1982). Today, the standard for radiological diagnosis of the existence of infection and persistence of healing of apical periodontitis is conventional intraoral PA radiography. Since the 1980s digital radiography became more prominent because it was responsible for the reduction of patient radiation dose, as well as eliminating the development time of the disease (Lalonde, 1970). Since the 1990's cone beam computed tomography (CBCT) has become widespread in endodontics. In order to determine whether the endodontic treatment of apical pathosis is effective or not radiographic imaging is done to see evidence of healing in lesions. Radiographic techniques observe changes in the apical radiolucencies, which largely determine the success of endodontic treatment (Peters & Peters, 2012).

D.1. Conventional Radiography

Currently, in the clinical setting, PA radiographs are used to evaluate PA lesions (Patel, 2015). A lesion will be recognized through radiolucency at the apex on a PA radiograph. PA radiographs taken before surgeries are typically used to estimate the extent and the size of PA lesions. After surgery these PA radiographs are instrumental in detecting the change in size of lesions (Tanomaru-FIlho, 2015). If the lesion disappears completely or there is a decrease in size endodontic treatment, it indicates healing, but an increase in size of the lesion might be an indication of non-healing due to the persistence of the disease (Patel, 2015). When the lesion is the same size after surgery as it was before surgery, then the results are undetermined (Tanomaru-FIlho, 2015). This can be a result of the radiograph after the surgery is taken earlier on in the healing process. If PA radiographs are taken prior to 6-12 months following the endodontic procedure, dimensional changes in periapical lesions cannot be detected (Murphy, 1991). This means that the result of the endodontic treatment results, such as the lesion healing may not be known for up to a year or more following the end of the treatment. CBCT is efficient in overcoming numerous limitations of PA radiographs. CBCT has been hypothesized as being able to detect dimensional changes in lesions earlier than PA radiographs (Tanomaru-FIlho, 2015).

Murphy (1991) published a study in which he evaluated the healing of periapical radiolucencies after nonsurgical endodontic therapy by using conventional PA radiographs. In his retrospective chart review, he evaluated 89 patients who were healing and concluded that an estimated 41 (46.1%) of the PA lesions resolved by the time the patient attended follow-up treatment and close to 43 (48.3%) had experienced partial radiographic resolution, which means that there was a reduction observed in their PA radiolucency. In addition, the length of the follow-up was a vital factor according to the study. The results clearly noted that the measurement of the lesion in two dimensions, using PA radiographs, was a major source of error (de Paula-Silva, 2009). The study also identified the impossibility of evaluating the extent of bucco-lingual structures. It was noted that the clinician was limited it two-dimensional images as part of the evaluation.

D.2. <u>MRI and CT</u>

Both MRI and CT are widely used in the medical field. Their main advantage is offering information in three dimension, which allows for a more accurate evaluation to be conducted of the captured area by assessing the sections that are acquired in all three of the orthogonal planes (axial, sagittal and coronal) (Ruprecht and Lam, 2009). Primarily CT is used to examine the hard tissues, and MRI is excellent as it offers the depiction of soft tissue, which also allows it to examine neoplasms. These modalities have allowed for the evaluation of exact extent of lesions and their spatial relationships that are important to anatomical structures (Cotti, 1999). Superior visualization of the nasal cavities, paranasal sinuses, and ostiomeatal complex are offered by CT in comparison to conventional forms of radiography (Selden, 1999) . With CT scans, both bone and soft tissues in thin sections as well as in multiple views can be visualized, which is a major advantage.

There are shortcomings with both CT and MRI making them less practical for use in dental offices. Both devices require lengthy times to scan and are expensive. In addition, a high dose of radiation is required with CT scanning. As a result, CT devices are not readily available in the field of dentistry as they are in other areas of the medical field.

D.3. <u>CBCT</u>

CBCT is a three-dimensional imaging technique that has been developed and serves as a response to the limitations of PA radiographs (Velvart, 2001). CBCT is capable of detecting lesions that PA radiographs, cannot detect, such as small size lesions that are primarily confined to cancellous bone (Lofthag-Hansen, 2007). CBCT yields comparable diagnostic quality and with lower dosage of radiation as MRI and other radiographic techniques. Recently, CBCT has become the standard to assess dental and PA tissues using imaging as a modality (Mozzo, 1998).

Images of CBCT visualized lesions allow for measurement of the area of low density (PARL), and offer images in three dimensions in order to accurately estimate the size of the lesion (Ahlowalia, 2013). Since the 1980's cone-beam technology has been widely used in the medical field. A new tomographic scanner that is known as cone beam computed tomography, was developed in the late 1990's to be used specifically for dental and maxillofacial purposes (Patel, 2007). In March 2001, the Food and Drug Administration first approved CBCT unit to be used for dental purposes in the United States. Since then, the use of CBCT technology has been widely embraced globally and use in endodontics grown substantially. Cotton et al (2007) submitted recommendations that training in CBCT technology should be incorporated in training of graduate endodontic programs. Patel et al (2015) also reiterated these recommendations in their review article. It is seen as the technology that will have long-standing impact on the future of Endodontics.

D.3.a. Advantages of CBCT

CBCT has recently been introduced as a method that is able to gain an unblocked view of the anatomy of teeth, eliminating the most prevalent dental problems such as distortion and superimposition. CBCT is said to be quickly replacing other radiographic techniques in diagnosis, outcome assessment, and quality control of treatment techniques and methods. Healing assessments using newer three-dimensional images and conventional images include but are not limited to conditions of the maxillary sinus, status after EMS, hard tissue development in regeneration procedures, and horizontal root fractures (Kumar, 2010).

High contrasting structures are captured by CBCT machines, so they are well-suited for dental and osseous structures examination in the maxillofacial area (Patel, 2009). In comparison to conventional medical CT, CBCT machines are much smaller, which makes them more practical to be used in the field of dentistry. Also, these CBCT machines are much lower cost, require a shorter time to scan, and produce less radiation than medical CT (Patel, 2009). CT machines emit constant radiation as the patient goes through multiple rotations throughout the scanning process. However, CBCT machines use sequential planar projections throughout the length of one rotation, reducing the patient's exposure time significantly. Raw data or projection images only need computer software to reconstruct and assemble a three-dimensional image (Scarfe, 2013). CBCT scanner produces an x-ray beam that is cone-shaped that comes straight from the source directly to the x-ray detector that passes throughout the area of interest (Scarfe, 2013). A cylindrical volume of data is produced, which is called the field of view (FOV). Various factors such as the size and shape of the detector, beam collimation and its projection geometry have an influence on the dimensions of the FOV. Overall, the smaller the FOV is, the smaller the exposure and greater the spatial resolution will be. These FOV's are either limited/localized with FOV 5 cm or less, or a single arch with (FOV 5-7 cm), an inter-arch with (FOV 7-10 cm), maxillofacial with (FOV 10-15 cm) and craniofacial that has a FOV>15 cm (Scarfe, 2013).

Among the various scanners the size of the FOV is different, with some machines that offer the chance to select the FOV, which depends on the needs of the practitioner. A voxel size of 0.4mm and a size as low as 0.076mm produces scans that are spatially accurate and accommodates precise assessment and measurement. The Kodak 9000 produces the CBCT radiation dose produced by the limited FOV device. This is the model used in most studies and equates to about 1-5 days of background radiation. By comparison the posterior bitewing radiograph is the same as 3 days of background radiation (Scarfe, 2013). The extra benefit of limited FOV's is that there is a decreased dose of radiation to the patient.

The images can either be viewed in the coronal (or facial), sagittal planes, three-dimensional reconstructions and axial with the help of computer software. A focused view of CBCT in endodontics is said to be the preferred FOV because it largely improves diagnostic accuracy, and decreases the amount of radiation patients are exposed to (Scarfe, 2006). The earliest PA findings on radiographs is the widening of the periodontal ligament space, which suggests apical pathosis. On an average the width observed of the PDL space is about 200µm. So it has been the suggested optimal resolution for any CBCT imaging system that is used in endodontics that does not exceed 200µm (Kaffe & Gratt, 1988).

In radiation dosimetry, there are three basic dose units. First the radiation absorption dose is considered the energy that has been absorbed from radiation beam per unit mass of tissue (Patel, 2007). The measurement is in joules per kilogram. Secondly, the equivalent dose is acquired through the multiplication of radiation–absorbed dose with a weighting factor using radiation-quality. In addition, this factor accounts for the different amounts of tissue that are damaged that can result from the same amount as well as different types of radiation (Patel, 2007). Lastly, the effective dose is acquired by multiplying the equivalent dose with different tissue weighting factors. Tissue weighting factors accommodate for the different levels or radio sensitivity that different tissues have (Patel, 2007).

The micro Sievert [10^{-6} Sieverts : µSv] in maxillofacial imaging is often used to quantify the dose of radiation. An effective dose of radiation is comparable to different imaging modalities. In neck and head region, the exposure of radiation to the bone marrow, thyroid, esophagus, skin, bone surface, salivary glands, and brain are of particular interest (Barnett, 2011).

One day of background radiation at sea level is 7-8 µSv (Barnett, 2011) is estimated to be one digital PA radiograph, which has an estimated effective dose of 6 μSv (Barnett, 2011). So one digital PA radiograph then is equivalent to approximately one day's exposure to background radiation (Barnett, 2011). The images produced by CBCT technology are not the same based upon multiple factors including the exposure settings of the CBCT scanner, the size of the FOV, exposure time, tube current and the energy/potential, in the effective dose of radiation (Patel, 2007). In addition, the effective dose is also dependent upon the area of oral cavity in the FOV (Patel, 2007). The effective dose is estimated to be 4.7 μSv or 21.7 μSv, respectively in the focused field CBCT in the maxillary or mandibular anterior (Ludlow, 2008). In the maxillary posterior for an effective dose for a focused field CBCT, there is an estimation of 9.8 μSv (Ludlow, 2008). A focused field CBCT effective dose in the mandibular posterior is estimated at is estimated to be 38.3 μSv (Ludlow, 2008).

D.3.b. Limitations of CBCT

CBCT still subjects the patient to higher radiation than conventional intraoral radiographs in spite of relatively lower dosage of radiation dose in comparison to medical CT (Patel, 2009). Scans that have a larger FOV, CBCT machines emit dosage of radiation that is the same as 5-33 PA radiographs. The radiation dosage is equivalent to limited FOV scans seen in a single panoramic film (Patel, 2009). In addition, CBCT is known to yield inferior spatial resolution in comparison to conventional intraoral radiographs. Digital and conventional radiography has a 15-20-line pairs mm spatial resolutions while CBCT scans are only 2-line pairs mm (Patel, 2009). CBCT shows inferior soft tissue resolution when compared to medical CT, for this reason still medical CT is the highest diagnostic modality available in three-dimensional medical radiography (Patel, 2009). The occasional presence of artifacts can compromise the interpretation and quality as with medical CT. Metallic structures are present in the areas that are scanned, which cause cupping effect, which is produced absorption of x-ray photons that is differential; this results in the distortion of images, known as beam hardening (Scarfe, 2013). Streaks of dark bans can appear between two dense objects in beam hardening (Scarfe, 2013). Even the slightest movement by a patient during a scam can create artifacts that can render a scan that has little diagnostic value (Scarfe, 2013). These factors can affect the quality of the CBCT image.

D.4. Application of of CBCT in Endodontics

There are three-dimensional scans of the maxilla-facial skeleton that CBCT produces that uses an extra-oral system. The source of radiation as well as the detector rotates anywhere between 180 and 360 degrees around the head of the patient in order to get an image (Patel, 2009). 3-D cubes of information, called voxels, represent a value of three-dimensional space on a regular grid (Von Arx, 2015). These voxels are all isotropic meaning they are perfect three-dimensional cubes. They allow the objects in the scan volume to be measured accurately in many different planes (Cotton, 2007).

CBCT is now the superior form of imaging to detect PA bone loss. In cases where there was no detection of pathosis on PA radiographs, CBCT was able to detect it (Guo and Dipietro, 2010). Both surgical and non-surgical treatment for root canal in cases where PA pathosis were detected, the results were predicated with high amounts of success based on the healing evident in the osseous lesion (Orstavik, 1996). There are limitations as well as abilities evident in techniques associated with radiography to detect both resolution and presence of PA periodontitis, with special emphasis on CBCT and a superior imaging technique.

A lack of well-designed clinical trials and meta-analysis regarding CBCT technology and its use in endodontics, suggests that current decisions regarding the use of CBCT for in different endodontic situations are primarily theoretical (Patel, 2007). In order to provide clinicians with the most available and scientifically based guidelines, the American Association of Endodontists (AAE) and the American Academy of Oral and Maxillofacial Radiology (AAOMR) jointly released a statement in 2015, where the recommendations included the consideration of CBCT as the choice for imaging modality in the evaluation of endodontic patients as well as imaging before ReTx and EMS. Patel (2015) suggested specifically that any future clinical research trials should use small FOV CBCT scans, and it should be done in such a way so as to assess the healing of lesions that are associated with apical periodontitis. It has been suggested that volumetric measurements of lesions could possibly be the way to assess dimensional change in a lesion since CBCT is capable of allowing assessment of lesions in three dimensions (Ahlowalia, 2013). Numerous authors have mentioned that volumetric measurements are correlated with actual physical volumes of bone lesions that were artificially created (Liang, 2013). Van der Borden (2013) published the first clinical study, where he assessed 3-D volumetric changes of PA lesions after RCT. Later on Liang et al (2013) and Metska et al (2013) in their investigations also used CBCT with volumetric measurements in order to assess the healing of lesions of apical periodontitis.

Metska (2013) was the first scientist to use volumetric assessment of lesion size on CBCT in cases where the patients were treated by orthograde retreatment. About 45 root filled teeth with persistent apical periodontitis that required non-surgical retreatment were assessed in the study. For each patient, two CBCT images were obtained, the first taken before treatment and a second was taken a year after retreatment. In 20 teeth (57%) of the teeth, the volume of the PA lesions decreased, 8 (23%) remained unchanged and increase was observed in in 7 (20%).

C.5. <u>Application of CBCT for evaluation of EMS outcome</u>

CBCT has been used in a number of applications. In the assessment of root-end surgery, certain criteria for the outcome have been defined for evaluation using 2-dimensional radiography. The same criteria do not necessarily apply to 3-dimensional radiography such as CBCT (Von Arx, 2016). One of the criteria that must be met, regardless of the radiography technique used is that the technique must produce both reliable and repeatable results in order to be useful for clinicians. To measure this factor requires a consistency in readings between two different clinicians, and repetition across a number of samples, in this case roots. Intraobserver agreement can be used to measure repeatability, and interobserver consistency reflects reproducibility (Von Arx, 2016). Congruence between these factors is necessary to develop CBCT as a radiographic technique for the assessment of EMS (Von Arx, 2016).

CBCT represents a major accomplishment in the ability to improve modern endodontic techniques. The development of CBCT is essential in the diagnosis, assessment, and outcome assessment when microsurgery of roots is indicated. Several recent clinical articles have documented the use of CBCT as a means of postoperative evaluation in EMS (Christiansen, 2009; Tanomaru, 2015 and Von Arx, 2015). These articles established radiographic healing based on whether radiolucencies were present after the procedure was performed.

Current assessment of apical surgery is based on studies that were conducted in 1972 and in 1987, and are based on 2-dimensional radiographic techniques (Molven, 1987; Rud, 1972). These criteria have remained valid since that time. However, recent studies suggest that these techniques may no longer be applicable to EMS.

Von Arx et al (2016) examined the applicability of assessment criteria to CBCT by examining group of patients that had been evaluated, and surgery performed. In this study, the surgical techniques used were identical. Patients were evaluated one year after the surgical process. Images were taken of the patients and examined by two separate observations by the same clinician, and by three different clinicians. This allowed the researcher to determine if results were consistent in both intra-and inter clinician observations. To be useful clinically, consistency must be able to be obtained when viewing the same set of images. If different clinicians arrive at different conclusions based on the same image, it may indicate that there are issues or artifacts in the images that cause them to interpret them differently. The same could be said if results are different when the same operator evaluates the same image more than one time. The study by Von Arx et al (2016) was not intended to evaluate the surgical technique or procedure, but rather to examine consistency of post-surgery radiography techniques.

The observers in the Von Arx (2016) study were asked to evaluate the radiography images using a set of predetermined criteria. This allowed direct comparison of the results obtained by the different observers. Three different indices regarding various parameters of the image were used as a source of comparison. These were the R index, which is the resection plane. The A index is the apical area. The C index is the cortical plate. The B index refers to the bone. Using this methodology, it was found that scores by the same observer on consecutive observations never differed by a value greater than one. This demonstrates that the results obtained have a high degree of repeatability. The B index demonstrated the highest intraobserver agreement at 72.1%.

The results of the study conducted by Von Arx et al (2016) indicates that there is a high degree of variance in judgment of the healing process by different observers. This indicates that stricter criteria need to be developed for the use of 3-dimensional radiography. The authors concluded that the use of the B index and R index, apical and cortical defects, along with the healing of the resection produced results that are sufficient to be used in the clinical setting, or to design future studies. The study supported the need for the development of new techniques using CBCT and other 3-dimensional techniques that are currently being used. The study supports the need for future studies to help develop a more consistent evaluation criteria for the use of CBCT in the evaluation of this healing process after microsurgery.

III. MATERIALS & METHODS

The protocol for the research project "Assessment Of Periapical Bone Healing After Endodontic Microsurgery Using Cone-Beam Computed Tomography" was submitted to the University of Illinois at Chicago Institutional Review Board (IRB) for exemption. The IRB responded that the research did not involve human subjects and did not require IRB approval (see Appendix).

A. Case Selection:

CBCT scans that were previously taken at a local Endodontic specialty practice before and after endodontic microsurgery were reviewed and assessed for periapical bone healing. All scans were deidentified prior to evaluation.

A.1. Inclusion Criteria

- CBCT scans of patients who received EMS and who have at least 6 months recall scans.
- Pre- and post-operative CBCT of high diagnostic value in all three planes.

A.2. Exclusion Criteria

- Non-diagnostic CBCT scans.
- Teeth that have received surgical endodontic treatment but didn't have recall images.

B. Surgical procedure

All EMS procedures in this endodontic practice were performed by an experienced endodontist (M.F.) and followed the same guidelines and principles for root-end surgery as outlined by Kim and Kratchman (2006). All surgical procedures were performed using an operating microscope (OPMI PICO; Carl Zeiss, Gottingen, Germany). The flap was reflected after local anesthesia, and the osteotomy was performed. After removing the soft-tissue debris, an additional 3 to 4 mm of root tip was resected with a 0 to 10 degree angle bevels with a tapered fissure bur under copious water irrigation. The resected root surfaces were then stained with methylene blue and inspected with micromirrors (ObturaSpartan, Fenton, MO) under 20 X magnification to examine the cleanness of the root-end preparation and to search for other anatomic details. The root-end preparation extended 3 mm into the canal space along the long axis of the root using KIS ultrasonic tips (ObturaSpartan) driven by a Piezoelectric ultrasonic unit (Spartan MTS, ObturaSpartan). The root-end filling material used was ProRoot MTA (Dentsply, Tulsa, OK). In selected cases, bone graft and membrane were used. The wound site was closed and sutured with 6X0 sutures, and a postoperative CBCT was taken to check for correct placement and an absence of excess material in the surgical site. A postoperative mouthwash (0.12% chlorhexidine gluconate) was routinely prescribed, and the sutures were removed 4 to 7 days later.

C. **CBCT Analysis:**

All CBCT images were obtained using a Kodak 9000 3D Extraoral Imaging System (Kodak Dental Systems, Atlanta, GA) using limited field of view (5 cm x 5 cm) with voxel size of 76 microns. Using the Kodak Imaging Software, the CBCT images were evaluated on axial, coronal and sagittal sections. An endodontist and a second-year endodontic resident evaluated the scans.

Pre-operative scans were evaluated and CBCT PAI was recorded. Post-operative scans were evaluated for any changes in CBCT PAI.

The dimensions of the periapical lesion were measured on the CBCT by measuring the longest distance in length and in width of the periapical radiolucency. When more than one root had a PARL, the root with the largest PARL was selected.

Presence of a periapical lesion was recorded and classified according to the CBCT-PAI scoring system developed by Estrela et al (2008). (0): intact periapical tissues, (1): diameter of periapical radiolucency =0.5–1 mm, (2): diameter of periapical radiolucency =1–2 mm, (3): diameter of periapical radiolucency =2–4 mm, (4): diameter of periapical radiolucency =4–8 mm, (5): diameter of periapical radiolucency >8 mm (Estrela, 2008).

A total of 65 pre- and post-operative resected roots were evaluated in this study, which were further divided into 2 groups based on use of bone graft/membrane: Group 1 - bone graft/membrane was used (n=41). Group 2 - bone graft/membrane was used (n=24). Further, based on recall period, roots were divided into 2 subgroups: Subgroup 1 - recall of 6 to 12 months (n=25), Subgroup 1 – recall of 13 to 36 months (n=40).

D. <u>Outcome Measures</u>

The following information was recorded for each of the 65 roots included in this study from the pre- and post-operative scans: sex of the patient, date of the preoperative scan, date of the postoperative scan, dimensions of the PARL if present, use of bone graft and membrane during EMS.

IV. STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS Statistics software package (Version 21; IBM Corp, Armonk, NY). First, the associations between the dependent variable, the use of a bone graft,/membrane and the independent variables were described using descriptive statistical techniques. The independent variables included preoperative PAI, postoperative PAI, and the change in the PAI over time. Another factor in the independent variable was the patient's sex. These factors were evaluated using Fisher's exact test and chi-square. The Wilcoxon Signed-Rank test was used to evaluate changes in the presurgery PAI and postoperative PAI. A significance level of p=/< 0.05 was used for the evaluation of this study sample.

One of the most important factors in any clinical study is the ability to apply the results obtained to a larger population. To be applicable in a clinical setting, the study must use a sample population that is sufficiently large to be applied to the general clinical setting. A confidence level of 95% corresponds to a Z score of 1.96. This was used in the calculation of the appropriate sample size. Using a standard deviation of .5 and a margin of error of .05, it was determined that the size of 384.16 (385) respondents were needed for a valid study. The following calculation was used to determine the appropriate sample size.

$$\text{Sample Size} = (\text{Z-score})^2 * \text{StdDev}*(1-\text{StdDev}) / (\text{margin of error})^2$$

In this case, one sample is equal to one root. In this study, evaluation of only 65 roots obtained. These roots were spread over 41 patients and 56 teeth. Of the sample, 41 roots were treated using bone graft/membrane, and 24 roots were treated without the bone/membrane graft. The actual sample population was only 1/6 the size needed to be considered applicable to the general population of patients needing EMS. This suggests that these results only represent a preliminary study on both the effectiveness of the bone graft/membrane technique and on the ability to use CBCT to evaluate it. These results suggest that a study be conducted at a later time that uses a sample population of at least 385 patients. A larger sample population would help to confirm the results obtained in this study. It would be possible to decrease the confidence level or increase a margin of error to obtain a sample size that was more manageable, but this would significantly affect reliability of the results. Therefore, this is not suggested, as it is not in alignment with the goal of developing valid clinical techniques for CBCT radiography. Even though the results of this study are not clinically reliable due to its sample size, it is still suggestive of the direction that future research needs to take and is of value to the research community.

V. RESULTS

In keeping with the results obtained by Von Arx (2016), which indicated that bone structures were the most reliable indices used in the assessment of EMS results, bone alterations were used in the assessment of patients in the study. Bone alterations in mineral structures were used to assign a score ranging from 0 to 5. Radiolucency was used to rate the bone structures. A score of zero represented and intact periapical bone structure whereas a score of five indicated radiolucency with a diameter of greater than 8 mm. The diameter of the radiolucency determined the score of the bone structure. This method meets with the goal of developing a standard technique for the evaluation of 3-dimensional radiography.

Using this evaluation criteria, complete healing was indicated as a CBCTPAI of zero. Incomplete healing was indicated as a CBCTPAI that is smaller than the pre-op score, but is not a 0. Unsatisfactory healing is a post-op CBCTPAI that is the same or larger than the pre-op CBCTPAI. This allowed a rating scale to be developed that can be easily translated into clinical assessment and results for future planning of the case. The development of this rating scale allows CBCT to be used in a way that can be easily interpreted by the clinician.

The results of the bone graft/membrane and no bone graft/membrane groups included 41 roots that were repaired using bone grafts, and 24 roots that were not repaired using bone grafts. The overall results demonstrated that out of 65 roots, 44 roots (67.7%) demonstrated complete healing. Incomplete healing was found on 13 roots (20%) and 8 roots demonstrated unsatisfactory healing (12.3%). This demonstrates that overall the healing of the majority of the roots were satisfactory.

	Bone graft/membrane group	No bone graft/membrane group	Two groups together
Complete healing	73.2%	58.4%	67.7%
Incomplete healing	19.5%	20.8%	20%
Unsatisfactory healing	7.3%	20.8%	12.3%

Table 1: Percentages of the healing results in between two groups (bone graft/membrane vs no bone graft/membrane)

The success rates of the two groups were determined by combining those that had complete healing and incomplete healing. Those that had unsatisfactory healing were considered a failure. The inclusion of incomplete healing is based on the assumption that the healing will continue to occur in a similar fashion in the future. This means that eventually those patients should achieve complete healing, but this is not certain. The success rate for those in the bone graft group was 97%, which translates into 38 out of 41 of the roots. This means that three in that group had unsatisfactory healing outcomes. In the patients that received no bone graft, 79.2% achieved success, which translates into 19 out of 24 roots. This means that five patients had an unsatisfactory outcome. In this study, those that received a bone graft/membrane had a clinically significantly higher success rate than those that did not receive a bone graft. However, the statistical analysis determined that there was no significant difference (p=0.134).

	Bone graft/membrane group	No bone graft/membrane group	Two groups together
Success	92.7%	79.2%	87.7%
Failure	8.3%	21.7%	12.3%

Table 2: Percentages of the success and failure in between two groups (bone graft/membrane vs no bone graft/membrane)

Overall, 12.3% of the roots, which is eight out of 65, demonstrated unsatisfactory healing. Of the 8 roots that did not achieve satisfactory healing, a bone graft/membrane was used for three of the roots and no bone graft/membrane was used for five or the roots. Of the patients with unsatisfactory results, two were female and six were male ($p=0.076$). It might also be noted that of the unsatisfactory roots, seven had an over one-year recall interval and one had a less than one-year recall interval ($p=0.139$). This is significant because it demonstrates that many of the patients with an unsatisfactory result had even more time to achieve healing. All the results presented above failed to reach statistical significance ($p<0.05$).

	Female	Male	Two groups together
Success	94.6%	78.6%	87.7%
Failure	5.4%	21.4%	12.3%

Table 3: Percentages of the success and failure related to the sex of the patient (female vs male)

	> 1 yr recall	< 1 yr recall	Two groups together
Success	82.5%	96%	87.7%
Failure	17.5%	4%	12.3%

Table 4: Percentages of the success and failure related to recall period (> 1 yr recall vs < 1 yr recall)

Overall, of the entire sample population, 87.7% achieved complete or incomplete healing of bone defects. The average recall was 14.8 months, with lower and upper limits of six and 36 months. Due to the small sample size, it cannot be determined that bone graft/membrane during EMS had a statistically significant effect on the healing of bone defects, even though the results look promising when one examines the raw data. The results of this study are inconclusive due to the small sample size and disparities in the number of patients in the two groups. However, they are suggestive that future research with a larger sample size may yield positive results for the use of bone grafts/membrane in the healing of the bone defects after EMS.

VI. DISCUSSION

This study accomplished two important tasks in the further development of research into this field. The first is that it is examined a test group of patients who needed similar surgery, on which two different surgical techniques were used. In this way, the study is similar to a traditional clinical study in that it compares the results of one treatment protocol with another. However, in accordance with research found in the literature review that indicated that CBCT could be used to assess pre-and post-op bone defects, the study demonstrated that a scale could be developed that meets the requirements in this area of clinical research.

The first area of clinical contribution is that this study examined a group of patients who needed EMS to repair defective root structures. In this regard, the number of patient records received was determined to be too small for a clinically valid study. The overall results suggest that bone graft/membrane may be more effective in achieving complete healing of the bone structure based upon a one-year follow-up. However, the sample sizes were unequal in the two clinical groups, therefore this cannot be considered a clinically valid result. Nonetheless, it sets the stage for future research in the area using a larger sample size. When one considers the proportions of the number patients with unsatisfactory healing results in the two groups, the group with 41 patients only had three unsatisfactory results. Whereas the smaller sample size group that did not receive the bone graft had only 24 patients and had five that did not heal satisfactorily. This is a significantly higher portion in the no bone graft/membrane group that did not achieve satisfactory healing as compared to those that received bone graft/membrane.

Upon preliminary examination, it would first appear that those that did not receive bone graft/membrane demonstrated a significantly higher level of unsatisfactory healing, compared to those that received bone graft/membrane. However, the group that did not receive a bone graft/membrane was an extremely small sample size and cannot be used to make clinical determinations of the success of these two surgical techniques. Therefore, no statistically significant difference was observed ($p=0.134$).

Perhaps the more important contribution of this study was the use of CBCT and the development of a standardized evaluation technique that results in a measurable scale that can be used to determine pre-op and post-op evaluation of the structures. This study developed a scale that was based on the lesion size as represented by radiolucency in the image. This provides a parameter that can be easily measured using quantitative techniques. Based on this measurement, clinicians can then quantify and assess the severity of the lesion. It also provides them with a quantitative measurement that can be used to compare pre-op and post-op size of the lesion. This method is highly preferred over qualitative methods where the clinician simply makes a judgment on the results of the radiography.

The analysis technique developed in this study will allow clinicians to make measurements based on a feature of the image that is easily identifiable, and easily measured. Von Arx et al, (2016) demonstrated that the same clinician would be likely to make the same assessment of an image based on two occasions that are temporally separated. However, the study found that when different people read the same image, they could interpret the results differently. The study suggested that a method needed to be developed that would allow consistency when two different people read the imaging results. The technique developed in this research study is one step to achieving this goal. It demonstrated that structures can be easily identified on the 3-D imaging and can be measured in a quantitative manner, thus producing results that will be more consistent when different clinicians read the same image. This was one of the goals of the research.

The development of the scale used to evaluate bone lesions both preoperatively and postoperatively demonstrated the ability to determine quantitative differences in the bone structure. This study demonstrated that the clinician is able to determine if healing has occurred completely, incompletely, or whether the condition has worsened. Not only can the clinician make the determination of the direction of the healing process, they could also use this to develop a method for determining the healing rate. While this was not a part of the current research study, it is possible that in the future the same quantitative technique could be developed into a measurement for the rate of bone healing. This would allow surgical techniques to be developed that not only improve the prognosis of the patient long-term, but it would allow surgeons to develop techniques that demonstrate faster short-term results in healing of the bone. This would have the overall effect of improving outcomes of the procedure over the entirety of the general patient population.

The literature indicated that bone graft/membrane helps to improve periodontal regeneration. Several surgical techniques have been developed with success for bone grafting in patients with advanced periodontal disease. Membrane grafts have also been demonstrated to have an effect on helping the teeth to regenerate, as well is the tissue surrounding them. This literature was the basis of the techniques used in conducting the surgical techniques used in this study. In the current study, the surgeon who performed the technique was an experienced endodontist. This could represent a factor that could account for differences in the success of the surgical procedures. In clinical settings, it is often difficult to obtain results based on surgery that was performed by the same surgeon on a number of patients, but this can have an effect on the perceived statistical effectiveness of the treatment. There may also be physical conditions, or health habits of the patient that could affect the results obtained by the graft technique. Due to considerations that are beyond the scope of the research methodology used in this study, the effectiveness of bone graft and membrane techniques cannot be used as clinical indications of future actions regarding patients.

The most valuable contribution of this study is that it demonstrated that a quantitative technique for the evaluation of patients can be developed with a considerable degree of success. In this study, lesions were measured at their widest point. This can easily be quantitatively determined with a reasonably reliable degree of accuracy. The skull is a 3-D facial structure. Until the invention of 3-dimensional techniques such as MRI and CBCT, this 3-dimensional structure could only be examined using 2-dimensional radiographic techniques. Examining a 3-dimensional structure using 2-dimensional images has the potential to produce errors due to the inability to see structures that are behind the structures closest to the camera lens. The ability to adapt 3-D imaging to see what lies beyond the structures will improve both the ability to evaluate patients, and the ability to perform EMS with greater accuracy as well. This ability eliminates the need to “guess” about the relational properties of the structures. This research agrees with the literature about the need to upgrade current protocols used in radiography due to new advances in technology. It demonstrates that it is possible to develop accurate, quantitative methods for the use of 3-dimensional imaging technology.

The theoretical framework of this study was based on reliance on techniques for endodontic surgery and research on the treatment and evaluation of periodontal disease. It was also dependent on the current state of technology in radiographic techniques. The study by Von Arx et al, (2016) formed the main theoretical foundation of this research. These researchers determined that evaluation techniques based on 2-dimensional imaging are no longer valid for the evaluation of patients using newer 3-D technology. It demonstrated that standardized techniques need to be developed that reflect advances in technology, rather than relying on evaluation techniques based on out of date technology.

If surgeons in the dentistry field wish to use state-of-the-art technology, they must also reevaluate their techniques in relation to these technological changes. This research demonstrates that this new technology has the potential to revolutionize surgical evaluation of patients both before and after surgery. It also demonstrates that the problems found by Von Arx et al (2016) can be resolved in a way that demonstrates the development of clinical criteria based on quantitative, rather than qualitative assessment of radiographic images. However, at present, this research also indicates that there is much more work to be done before these techniques can be used in clinical practice. This research is one step in the development of these techniques and opens the way for future research in this area.

VII. LIMITATIONS

There are many factors that can influence the outcome of a clinical study. A comparison of studies on EMS and radiographic techniques found that it is difficult to isolate the dependent variable in many cases. This can limit the ability to draw valid conclusions from the clinical study. In this case, one of the key limitations was sample size. It was determined that a valid sample size would be six times larger than the sample used for this study. Until the study can be repeated using a larger sample size, the results of this study can only be considered speculative, at best. However, this does not reduce the value of the study and guiding the development of more valid studies using a larger sample size, but it cannot be considered evidence-based research for the guidance of technique and policy development.

This study only divided the sample population according to the surgical technique that was used and according to whether they were male or female. There may be factors that affect the outcome of the surgery that are based on demographics. For instance, lower income patients may not have access to proper nutrition were here healthcare resources which could influence their ability to heal from the surgical procedure. Certain conditions such as diabetes, high blood pressure, or a compromised immune system could also compromise the ability to heal. Smoking and exercise habits could also be a factor.

In this study, some of the patient's healed more rapidly than others, while other patients failed to heal at all, or their condition worsened after surgery. This brings into question many factors that could limit the ability to apply this study to the clinical setting. The surgeon performing the technique, as well as the exact procedures used may have an effect on the outcome of the study. In addition, the patient's general overall health could also affect their ability to heal both from the original disease and from the surgical procedure. These factors were not taken into account in the design of this research study.

One of the difficulties with clinical research such as this is that there are only a limited number of patients available to take part in the study. If one begins eliminating factors that could affect the results, such as overall health, or demographics, it reduces the sample size even more. However, it would be helpful to conduct an assessment of these factors so that they can be analyzed statistically to see if they had effect on the outcome of the study. Sample population bias is always a consideration in any research study. Information was not collected that would help to determine if bias exists in the sample population. For instance, the clinical results may have been a result of a sample population that was generally healthy, and therefore was able to heal more effectively than would be represented in the general population.

In order to conduct a research study that accurately reflects the overall population of EMS patients will require enlisting a larger sample population, and the collection of more data to determine if comorbid, or overall health conditions could account for the results that were obtained. The focus of this research study was not on developing clinically valid results, but to use a quantitative method to help obtain a more consistent evaluation of clinicians. In this regard, the study achieved this goal. However, this area of the study to could benefit from a larger patient sample population, and a group of clinicians evaluating the same image. Using the standard established by Estrela et al (2008) would further contribute to validation of CBCT as a method for evaluating EMS patients. These factors limit the ability of this research to draw valid conclusions, based on the research technique used and the small sample size of this study.

This study did not specify when and why bone graft/membrane was used. According to the literature the use of bone graft and membrane beneficial in cases were periapical lesions are bigger than 10mm, also for through and through defects (Tsesis, 2011).

This is a retrospective study. This can be considered as a limitation due to the lack of random assignment to bone graft/membrane and no bone graft/membrane groups. The fact that curtain patents were selected for bone graft/membrane, and others not, based on clinical judgment of each specific case, is a big limitation of this study. Therefore, the bone graft/membrane versus no bone graft/membrane groups had different and possible important variables at time of surgery that were not measured.

VIII. FUTURE RESEARCH

This study was a result of foundational research that indicated that a 3-dimensional technique needed to be developed that reflected current technology, rather than relying on 2-dimensional techniques based on technology that was decades out of date. This research successfully took the next step in the development of these techniques, but there is still much more to be done in this field.

The first area of research that needs to be developed is to determine whether certain bone graft/membrane techniques are superior over no bone graft/membrane. This area of research needs to be conducted with sample populations that will produce clinically valid results and can result in evidence-based practice in the clinical field. In addition, it needs to be determined if demographics play a role in the healing process of the patient. Sample populations need to be examined in terms of income, diet, comorbid conditions, and general health. Another factor that needs to be considered in future research studies in this topic area is age. The average age of patients in the study was 54 years old. A younger or older population may produce different clinical results.

In terms of the development of radiographic techniques using CBCT, research needs to be conducted that able to reproduce results when data analyzed by different clinicians. In addition, studies need to be conducted that evaluate the patient’s more frequently after the surgical procedure. This study, and research found in the literature review, typically evaluated patients one year after the surgical procedure. Studies need to be conducted that consider both the short, medium, and long-term results of the procedure on the rate of healing. This research demonstrated that quantitative methods using CBCT can be used to develop methods for determining the rate of healing among various patient groups. This is the next step in the research that needs to be undertaken.

IX. CONCLUSION

The study aimed to provide information that would be helpful in understanding the changes that occur in the periapical bone when EMS is performed to reduce defects in the bone.

The results of this study, although promising upon first examination, failed to produce clinically significant results. The reasons for this failure were a small sample size and the inability to account for factors that could have influenced healing after EMS.

EMS success rate of 87.7% achieved when root-ends observed after 6 to 36 months recall periods.

The null hypothesis was rejected: the use of bone graft/membrane in EMS did not show statistically significant improvement in patient outcomes, as opposed to EMS using no bone graft/membrane.

This work extended the work conducted by others in the literature review and helps fill the gap indicated by Von Arx et al (2016) regarding the need to develop methods that would lead to better consistency in the evaluation of images by different clinicians. This research study helped fill the gap by developing a quantitative method that can provide more consistent results. The next step of this research is to evaluate consistency using this technique and the evaluation of images by several different clinicians. This work advanced the body of research by providing insight into the next step that needs to be taken. The limitations of this study need to be considered in the design of future research in this area of study, but this research study helped to provide insight into the direction and considerations that future researchers must consider in their studies.

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APPENDIX

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UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
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Notice of Determination of Human Subject Research

November 25, 2015

20151223-93876-1

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RE: **Protocol # 2015-1223**
"Assessment of periapical bone healing after Endodontic Microsurgery using Cone Beam Computed Tomography"

Sponsor: None

Dear Andok Barseghyan:

The UIC Office for the Protection of Research Subjects received your "Determination of Whether an Activity Represents Human Subjects Research" application, and has determined that this activity **DOES NOT meet the definition of human subject research** as defined by 45 CFR 46.102(f).

You may conduct your activity without further submission to the IRB.

If this activity is used in conjunction with any other research involving human subjects or if it is modified in any way, it must be re-reviewed by OPRS staff.

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