

ANTIBIOTIC SIGNIFICANCE WITH IMMEDIATE IMPLANT PLACEMENT INTO SITES  
WITH APICAL PATHOLOGY OF ENDODONTIC ORIGIN

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## ABSTRACT

Bashir Hosseini: Antibiotic Significance with Immediate Implant Placement into Sites with Apical Pathology of Endodontic Origin.  
(Under the direction of Asma Khan)

Effects of antibiotics on the clinical outcomes of immediate implant placement replacing a tooth with an apical pathology were examined using a double-blind-randomized-controlled trial, antibiotics (N=10) and placebo (N=10). Post-operative pain/discomfort, cone-beam computed tomography and impressions were used to evaluate clinical outcomes. Survival rates of 100% (antibiotics) and 78% (control) were observed. There was no statistical difference in any clinical outcomes except for mid-facial soft tissue changes ( $p=0.02$ ). Antibiotics appear to have little effect on immediate implant treatment outcomes.

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## **CHAPTER 1 REVIEW OF LITERATURE**

### **I. INTRODUCTION**

Placing a dental implant immediately in the fresh extraction socket has demonstrated promising results with comparable implant survival to placing an implant into a healed site (Douglass et al, 2002). However, the immediate placement of an implant to replace a tooth with a periapical lesion has cause for concern. Possible remaining infection and the loss of periodontal architecture can make the ideal placement on an immediate implant challenging (Chrcanovic et al, 2013). Immediate implant therapy is indicated for a tooth with poor restorability but the debate whether a clinician should prescribe antibiotics for implant therapy when replacing a tooth with apical pathology has stirred up much controversy (Wasdroop et al, 2010).

Traditionally, immediate implant therapy was contraindicated in sites with periapical pathology (Novaes et al, 1995). However, recent evidence has moved away from this concept. A systematic review by Waasdrop et al suggest that immediate implant therapy for a tooth with a periapical lesion can be done successfully as long as three clinical parameters are fulfilled. These parameters include thorough debridement of the socket, sufficient primary stability of the implant, and application of antibiotics. While the first two parameters are deem essential, it was suggested there is a need for further investigation on the clinical necessity of antibiotics (Waasdrop et al, 2010).

In an exploratory cohort study by Givens et al, the use of systemic antibiotics with immediate implants was explored. This study also found that immediate implants into sites with apical pathology is a predictable treatment option, but was also able to give some insight into whether or not antibiotics is needed. Although a very small sample size, the findings suggested that systemic antibiotics may not play a role in the post-operative complications or the survival of the dental implant (Given et al, 2013).

While it is our duty as health care providers to prescribe antibiotics properly for the management and treatment of dental infections, there may be some disconnect when dealing with immediate implant placement into sites with apical pathology (Chrcanovic et al, 2013). Preoperative antibiotics are routinely prescribed in connection with many implant surgical procedures (Esposito et al, 2008). It is widely believed that prophylactic antibiotics can prevent implant failure and reduce postoperative complications (Esposito et al, 2008 ). With the growing risk of antibiotic resistant bacterial strains and limited number of new antibiotic development, a future public health care crisis can arise. Exploring the clinical relevant use of antibiotics in immediate implant therapy replacing a tooth with apical pathology may provide additional information on this topic in the field of dentistry.

## **II. REVIEW OF LITERATURE**

Dental implants have been a field of dentistry that has seen tremendous improvements in its design and biology. Although more modern dental implants were introduced in the 1970s (Misch et al, 2007), historically we know the idea has been around for ages. Archeologist have found ancient skulls in which teeth were replaced with various material such as stone, sticks and shells of which fusion to bone was noted (Misch et al, 2007). Dentistry has really made large strides in

the field of implant dentistry in both the design and clinical implications and we continue to make further improvements with research.

When we compare the original blade implants to the recent endosseous implants we can see this vast advancement. The clinical use and indications of these recent endosseous implants has also progressed (Misch et al, 2007). Originally when the tooth in question was removed, a healing period of a few months was allowed. An implant was then placed into the healed edentulous site. A two stage surgery was then recommended where the implant fixture was covered fully by the soft tissue to ensure proper healing and minimize the chance of infection, and later the second stage would be completed to uncover the implant a few months later (Collaert et al, 1998). The uncovered implant would then be left with a healing abutment, which extended above the soft tissue and more time would be allowed to ensure the soft tissue was fully stable and healthy prior to the final restoration.

With further research we started to find that we could in fact move away from the two stage surgery in the right circumstances. In this scenario, a healing abutment would be placed on top of the implant fixture at the time of implant placement (Collaert et al, 1998). This allows shortening of the treatment time. The envelope was further explored with the advancement of immediate implant placement. With time and research we found that in the esthetic zone and under the proper conditions we could remove the involved tooth and immediately place the implant into the extraction socket (Douglass et al, 2002). This treatment modality was very promising to the field of dentistry as we were now able to significantly reduce the treatment time, decrease complications from multiple surgeries, obtain better esthetic outcome by preserving the hard and soft tissues and thus allow patients to be more accepting of the treatment option (Douglass et al, 2002).

One main challenge in immediate implant therapy was when dealing with a tooth that had developed pathology. Traditionally clinicians believed that immediate implant placement into infected sites were contraindicated but current literature has shown this to be a predictable treatment option (Waasdrop et al, 2010). When reviewing the literature on immediate implant therapy to replace teeth with infections we will find that this can be very successful if there is complete debridement of the socket, copious irrigation, proper remaining bone support and although controversial, the use of antibiotics.

This review of the literature will look at the implications and success of immediate implant placement into infected sites and also explore the limited evidence on the need of antibiotics to have a successful outcome. A comprehensive literature review was done on this topic and 16 articles will be discussed.

## **2.1 ANIMAL STUDIES UTILIZING ANBITIBIOTICS**

There have been a number of studies that have explored the placement of immediate implants into an infected site. We will review four animal studies that utilized canines to study this field. A point of significant to mention is the manner in which these sites of induced lesions were treated. The methodology in all studies reports that the sockets were fully curetted and cleaned and also most importantly all of these studies utilized antibiotic coverage following immediate implant placement. The animals in all studies were euthanized at various times and studied to determine if there was a significant difference in immediate implant placement into infected sites versus healthy sites.

In regards to the immediate implant placement into sites with induced periapical lesion, animal studies have shown that this procedure can be a treatment option. In a histomorphometric study by Novaes et al, periapical lesions were induced in premolars of 4 canines, they also used

the same contralateral teeth with no periapical lesions as controls (Novaes et al, 1998). Twenty eight implants were placed, half in the sites with induced periapical lesions, and half for the control teeth with healthy bone. This study had zero failures of all fixtures and both histologically and clinically found there to be no difference in healing and osseointegration of the implants (Novaes et al, 1998). Similarly, Chang et al also looked at immediate implant placement into sites with induced periapical lesions. With the use of 4 canines and 24 implants comparing healthy sites versus sites with periapical lesions, there was no implant failure (Chang et al, 2009).

When looking at immediate implant placement into sites that were induced with periodontitis, similar findings have been reported. Marcaccini et al did a similar study in canines in 2003 with the use of fluorescence microscopy. Here, periodontitis was induced in the mandibular premolar of 5 mongrel dogs with the use of ligatures (Marcaccini et al, 2003). Immediate implants were placed in 20 periodontally induced sites and 20 contralateral teeth as controls. Fluorescence microscopy found that although there was a slower initial healing at the earlier weeks, there was no difference in degree of bone remodeling between the two groups and no significant difference at the final 12 week check (Marcaccini et al, 2003). In regards to bone to implant contact, Novaes et al found no difference when comparing the experimental group to the control group (Novaes et al, 2003). This Novaes study also utilized 5 canines in which periodontitis was induced with ligatures.

All of these animal studies show that immediate implants can be utilized to replace teeth that have a periapical or periodontal lesion, granted that certain precautions are taken. These precautions include: proper curettage of the infected socket and antibiotic coverage following

surgery. Although significant, the major limitations of these studies are the very small sample size and short recall periods.

## **2.2 HUMAN STUDIES UTILIZING ANTIBIOTICS**

There are also numerous human studies that explore the placement of an immediate implant into a site with a periapical or periodontal lesion. Similar to animal studies, most reports provide promising results with high implant survival rate. All of the studies discussed in this section did utilize systemic antibiotics except Given et al 2013.

One of the first clinical trials in this topic was by Novaes et al in 1995 (Novaes et al, 1995). They utilized 3 patients that had a radiographic sign of a periapical lesion. The involved tooth was extracted and an immediate implant was placed and followed up for 7-14 months. The clinical outcome was a 100% survival of all 3 implants. The study was very meticulous in the careful extraction, debridement, copious irrigation of the socket, and the use of pre- and post-operative antibiotics for the subjects. Antibiotic coverage was of main concern as the subjects utilized pre- and post-operative antibiotics for a total of 31 days throughout the study. While there is no control group and a small test group (n=3 sample size), the conclusion made was that these clinical steps are of utmost significance and importance to ensure survival of the dental implant when immediately placed in such conditions.

Villa and Rangart conducted two similar studies in 2005 and 2007 looking at this topic with a large sample size (Villa and Rangart et al, 2005) (Villa and Rangart et al, 2007). The 2005 study utilized 20 patients with 97 total implants placed and 2007 had 33 patients with 100 implants placed. Both studies looked at patients who had immediate implants placed to replace teeth with endodontic lesions, periodontal lesions or root fractures. There was at least a 12 month follow up for all subjects. These authors made sure to take certain precautions for which they

thought would ensure the survival of the implants. The methodology included the extraction of the involved tooth, socket debridement, curettage, use of local antibiotics, cortisone injection and post-operative antibiotic coverage. The survival rate for the 2005 and 2007 studies were again excellent with 100% and 97.4% respectively. However, there was no control group without antibiotic therapy or placebo.

In a prospective clinical study conducted by Lindeboom et al in 2006, the survival of immediate implant placement to replace a tooth with an infection was compared to a delayed implant placement following extraction and 3 month healing of the infected site (Lindeboom et al, 2006). This study also practiced socket degranulation and irrigation and the use of antibiotic coverage. The survival rate of the immediate implant into the site of infection was noted to be 92% while they obtained a 100% survival rate for the control group.

When looking at studies that compared immediate implant placement to replace a tooth with and without a chronic periapical lesion, Crespi et al had a well conducted prospective clinical trial looking exactly at this (Crespi et al, 2010). A total of 30 patients were utilized with a 24 month follow up. There were 15 patients in the experimental and 15 patients in the control groups with all patients obtaining antibiotic coverage. The study reports a 100 % survival for both groups after a 24 month follow up. When comparing the change in probing depths, keratinized mucosa, plaque index, bleeding index, and marginal bone levels, they found no significant difference between the two groups. This study is also relevant because not only did it look at the survival of the dental implants, but also showed that there were also equally favorable soft and hard tissue changes between the two groups.

In a retrospective study by Meltzer et al, immediate implants were placed into sites of infection and also provisionalized. This study utilized both infected extraction sites of both

periodontal and endodontic origin. A total of 63 patients were used with 77 immediate implants. Post-operative antibiotic coverage was given to all subjects. This study found a 98.7% survival rate and made similar conclusion to studies already discussed (Melzer et al, 2012).

The current literature suggests that immediate implant therapy to replace teeth with apical pathology is a predictable treatment option in human subjects. It is not an issue of if it can be done, but more of what precautions and measures must be taken to insure implant survival as well as maintain peri-implant tissue. It appears that the current literature has demonstrated that as long as there is proper debridement of the socket, copious irrigation, and adequate bone support this procedure can be done predictably. The question of antibiotic coverage still remains to be a topic of controversy and not yet clear.

### **2.3 ANTIBIOTIC USE WITH IMPLANT THERAPY**

There is always concern of dental implant failure due to bacterial contamination of the fixture right at or shortly after insertion into the surgical site (Tanner et al, 1997). This concern becomes more elevated when dealing specifically with an infected site. The challenge of dealing with an infected implant can be very devastating and can ultimately result in the loss of the implant (Tanner et al, 1997). The dental profession currently does have specific guidelines for when prophylaxis antibiotics are required such as: patients at risk for infectious endocarditis, patients with artificial joint replacements, patients with reduced host defense, etc (Tong et al, 2000). The concern in the field of implant dentistry is that there are no set guidelines which results in much controversy and ultimately misuse of the drug. Traditionally implant surgeons would always give an initial loading dose prior to implant placement (Esposito et al, 2008 ), and some wish to provide post-operative coverage as well (Esposito et al, 2008 ). This controversial topic has been



and is still an issue today, but ultimately we need to determine if antibiotic coverage is effective in reducing implant failures.

In a meta-analysis looking at two randomized clinical trials, Esposito et al looked at this topic closely (Esposito et al, 2008). They looked at the benefit, versus the negative effect of systemic prophylactic antibiotics for dental implant placement when compared to a placebo group. One of the randomized clinical trials compared 2 g of preoperative Amoxicillin versus placebo in 316 patients, while the other compared 2 g of preoperative Amoxicillin as well as 500 mg 4 times a day for 2 day postop versus a placebo in 80 patients. The results of this study showed that a pre-load dose of 2 g of Amoxicillin given 1 hour prior to surgery can significantly reduce dental implant failures, but the benefits of post-operative antibiotics remain unclear. The final recommendation of this study is to use one dose of prophylactic antibiotic prior to dental implant placement.

Similar to the Esposito study, Laskin et al in a multi-center prospective analysis also found a significantly higher survival rate of dental implants for patients who had received preoperative antibiotics (Laskin et al, 2000). The study group consisted of 387 patients with a total of 1,743 implants who received a preoperative dose of antibiotics, while the placebo group consisted of 315 patients with 1,287 implants who did not receive preoperative antibiotics. They looked at the success at various time intervals of implant surgery. The first time period was when the implant was placed, second time period was during the uncovering of the dental implant, third time period was right before loading the dental implant and the fourth time period was between the loading of the implant to the 36 month follow up. They made specific classifications of what they considered failure of the dental implant and the follow up was for 36 months. When comparing the study group to the placebo group they found a survival rate of 95.4 and 90 %

respectively. This result was statistically significant and the final conclusion was that preoperative antibiotics are beneficial to the survival of the dental implant.

When looking more closely at the need for postoperative antibiotic coverage, Gynther et al were able to study this in a retrospective study (Gynther et al, 1998). The experiment group they looked at consisted of 147 patients with 790 implants placed in which both pre- and post-operative antibiotics were given. The other group they looked at did not receive any pre- or post-operative antibiotics and consisted of 132 patients with 664 implants placed. All implants were placed in edentulous spaces in either the maxilla or mandible. They found no significant difference between the two groups in either the early or late phases. The conclusion of this study was that there is no added advantage to antibiotic coverage for routine dental implants. Morris et al looked at implant placement and the need for preoperative antibiotics and found similar results to Gynther (Morris et al, 2004). With a total of 1500 implants placed with one group obtaining preoperative antibiotics (n=1175) and the other group not receiving antibiotic coverage (n=354) a 96.3% and 95.2% implant survival rate was noted respectively. They found no statistical difference between the two groups.

When looking at immediate implant placement into infected sites and the benefits of antibiotic coverage, the research is very limited and unclear. In an exploratory cohort study by Givens et al, the use of systemic antibiotics with immediate implants was explored. This study found that placement of immediate implants into sites with apical pathology is a predictable treatment option. This study was also able to give some insight into whether or not antibiotics are needed. Although a very small sample size, the findings suggested that systemic antibiotics may not play a role in the survival of the dental implant or the postoperative pain and complications (Givens et al, 2013). This topic continues to be one of controversy and with the limited data, we

must continue to understand this issue better with more relevant research. With the possible risks of antibiotic misuse in our culture, we owe it to our patients, our profession and society to improve the understanding of this field and do what is best for our patients.

## **2.4 DISCUSSION**

The current literature has shown that we can indeed place immediate implants into sites with apical pathology. The high survival rate reported in many of these studies is promising. The survival rate for this situation has been reported in the mid to high nineties, which is similar to convention implant placement into healthy bone or a healed site. It is important that all of the research stresses the importance of properly cleaning the socket of any granulation tissue, proper irrigation, need for sufficient bone to support an immediate implant and until otherwise proven, the need to utilize antibiotic coverage to perform this procedure.

When placing an immediate implant into an infected site one must not forget all the important clinical and biological characteristics of implant dentistry. The use of antibiotics and proper debridement of the socket alone will not insure implant survival. The clinician must still assess the occlusion, soft tissue characteristics, proximity to anatomic structures, quality of bone, ability to obtain primary stability, and so forth to ensure ideal treatment results. If all these factor fall in place then according to our literature, the current train of thought is that antibiotics should be utilized when replacing a tooth with apical pathology.

When looking more closely at the various human studies as they relate to implant dentistry and antibiotics, the controversy continues. There is compelling research that has shown that a preoperative course of antibiotics can be beneficial to implant survival but the need of post-operative antibiotics is still unclear. These studies looked more closely at implants placed in clean healthy bone but the findings can be significant.

We currently do not have sufficient randomized clinical trials that look at the need for antibiotic coverage when replacing a tooth with pathology with an immediate implant. The limited research we do have on this topic are very vague with short follow ups, no clear clarification of type of infection involved, and small sample sizes. The true benefit of antibiotic coverage in such conditions is not yet proven and still unclear. With such little understanding of this topic and with the growing concern of antibiotic resistance in our current population, we must continue to investigate with proper randomized clinical trials with the hope of developing the correct guideline for clinicians to follow. The issue at hand is the lack of a guideline for this aspect of dentistry.

## **2.5 CONCLUSION**

There is compelling evidence in the field of dentistry that suggest an immediate implant can be utilized to replace a tooth that has apical pathology. Unfortunately our confirmation for the need of antibiotic coverage for this circumstance remains unclear and very controversial. The current recommendation when performing this procedure is for adequate curettage of the involved socket, copious irrigation and until otherwise proven, antibiotic coverage. With the growing risk of antibiotic resistance in our population, we must compile more relevant research to study this notorious topic and develop a more clear and precise guideline.

## REFERENCES

1. Chang, Seok-Woo, Seung-Yun Shin, Jong-Rak Hong, Seung-Min Yang, Hyun-Mi Yoo, Dong-Sung Park, Tae-Seok Oh, and Seung-Beom Kye. "Immediate implant placement into infected and noninfected extraction sockets: a pilot study." *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 107, no. 2 (2009): 197-203.
2. Chrcanovic, Bruno Ramos, Maximiliano Delany Martins, and Ann Wennerberg. "Immediate Placement of Implants into Infected Sites: A Systematic Review." *Clinical implant dentistry and related research* (2013).
3. Collaert, Bruno, and Hugo De Bruyn. "Comparison of Brånemark fixture integration and short-term survival using one-stage or two-stage surgery in completely and partially edentulous mandibles." *Clinical Oral Implants Research* 9, no. 2 (1998): 131-135.
4. Crespi, Roberto, Paolo Cappare, and Enrico Gherlone. "Fresh-socket implants in periapical infected sites in humans." *Journal of periodontology* 81, no. 3 (2010): 378-383.
5. Douglass, G. L., and R. L. Merin. "The immediate dental implant." *Journal of the California Dental Association* 30, no. 5 (2002): 362-5.
6. Esposito, Marco, Maria Gabriella Grusovin, Minesh Talati, Paul Coulthard, Richard Oliver, and Helen V. Worthington. "Interventions for replacing missing teeth: antibiotics at dental implant placement to prevent complications." *Cochrane Database Syst Rev* 3 (2008).
7. Givens, Edward, Sompop Bencharit, Warren C. Byrd, Bashir Hosseini, Ceib Phillips, and Donald Tyndall. "Immediate placement and provisionalization of implants into sites with periradicular infection with and without antibiotics: An exploratory study." *Journal of Oral Implantology* (2013).
8. Gynther, Göran W., Per Åke Köndell, Lars-Erik Moberg, and Anders Heimdahl. "Dental implant installation without antibiotic prophylaxis." *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 85, no. 5 (1998): 509-511.
9. Laskin, Daniel M., C. Daniel Dent, Harold F. Morris, Shigeru Ochi, and John W. Olson. "The influence of preoperative antibiotics on success of endosseous implants at 36 months." *Annals of Periodontology* 5, no. 1 (2000): 166-174.
10. Lindeboom, Jérôme AH, Yang Tjiook, and Frans HM Kroon. "Immediate placement of implants in periapical infected sites: a prospective randomized study in 50 patients." *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology* 101, no. 6 (2006): 705-710.

11. Marcaccini, Andréa M., Arthur B. Novaes Jr, Sérgio LS Souza, Mário Taba Jr, and Márcio FM Grisi. "Immediate placement of implants into periodontally infected sites in dogs. Part 2: a fluorescence microscopy study." *International Journal of Oral & Maxillofacial Implants* 18, no. 6 (2003).
12. Meltzer, Alan M. "Immediate implant placement and restoration in infected sites." *International Journal of Periodontics & Restorative Dentistry* 32, no. 5 (2012).
13. Misch, Carl E. *Contemporary implant dentistry*. Elsevier Health Sciences, 2007.
14. Morris, Harold F., Shigeru Ochi, Richard Plezia, Harry Gilbert, C. Daniel Dent, James Pikulski, and Paul M. Lambert. "AICRG, Part III: The influence of antibiotic use on the survival of a new implant design." *Journal of oral implantology* 30, no. 3 (2004): 144-151.
15. Novaes Jr, Arthur B., and Arthur B. Novaes. "Immediate implants placed into infected sites: a clinical report." *International Journal of Oral & Maxillofacial Implants* 10, no. 5 (1995).
16. Novaes Jr, Arthur B., Guaracilei M. Vidigal Jr, Arthur B. Novaes, Marcio FM Grisi, Sergio Polloni, and Adalberto Rosa. "Immediate implants placed into infected sites: a histomorphometric study in dogs." *International Journal of Oral & Maxillofacial Implants* 13, no. 3 (1998).
17. Novaes Jr, Arthur B., Andrea M. Marcaccini, Sergio LS Souza, Mario Taba Jr, and Marcio FM Grisi. "Immediate placement of implants into periodontally infected sites in dogs: a histomorphometric study of bone-implant contact." *International Journal of Oral & Maxillofacial Implants* 18, no. 3 (2003).
18. Tanner, A., M. F. J. Maiden, K. Lee, L. B. Shulman, and H. P. Weber. "Dental implant infections." *Clinical Infectious Diseases* 25, no. Supplement 2 (1997): S213-S217.
19. Tong, Darryl C., and Bruce R. Rothwell. "Antibiotic prophylaxis in dentistry: a review and practice recommendations." *The Journal of the American Dental Association* 131, no. 3 (2000): 366-374.
20. Villa, Roberto, and Bo Rangert. "Early loading of interforaminal implants immediately installed after extraction of teeth presenting endodontic and periodontal lesions." *Clinical implant dentistry and related research* 7, no. s1 (2005): s28-s35.
21. Villa, Roberto, and Bo Rangert. "Immediate and early function of implants placed in extraction sockets of maxillary infected teeth: a pilot study." *The Journal of prosthetic dentistry* 97, no. 6 (2007): S96-S108.
22. Waasdorp, Jonathan A., Cyril I. Evian, and Martine Mandracchia. "Immediate placement of implants into infected sites: a systematic review of the literature." *Journal of periodontology* 81, no. 6 (2010): 801-808.

## **CHAPTER 2 PROSPECTIVE RANDOMIZED CLINICAL TRIAL**

### **III. PROSPECTIVE CLINICAL TRIAL**

#### **3.1 INTRODUCTION**

One common treatment modality when replacing a non-restorable tooth in the esthetic zone is the use of an immediate implant. However, in most instances, the affected tooth has often developed an apical pathology. This can create controversy as to whether clinicians should or should not prescribe antibiotics in conjunction with immediate implant placement into an extraction site with apical pathology. Endodontic treatment of a tooth with an apical pathology does not normally require antibiotics. Fouad et al reported that antibiotics are most of the time not indicated in conjunction with endodontic therapy, and that the infection of endodontic origin is usually resolved with only localized endodontic therapy<sup>1</sup>. Abbott et al further discouraged the use of antibiotics in conjunction with endodontic therapy. They found that antibiotics are often over-prescribed and suggested that there are only a limited number of indications for antibiotics for endodontic infection<sup>2</sup>. Similar recommendations of limited prescription of antibiotics for extraction of a tooth with a chronic apical lesion are widely accepted<sup>3</sup>. In implant dentistry, however, it is almost universally accepted that antibiotics are needed in every case of implant surgery<sup>4</sup>.

Recently, “superbugs” or antibiotic resistant bacteria have become a major public health crisis and a common life-threatening problem for individual patients. Overprescribing antibiotics is known to create new strains of bacteria that resist common antibiotics. Moreover, the manufacturing of new antibiotics has not kept up with the resistant bacteria that are developing<sup>5</sup>.

This increase in antibiotic resistance bacteria has been described as both a threat to global stability and national security<sup>6</sup>. Antibiotic resistance is in many cases an irreversible phenomenon and difficult to manage. The World Health Organization emphasizes that unnecessary use of antibiotics with minor infections is perhaps one of the main etiological factors for antibiotic resistance<sup>6</sup>. The World Health Assembly resolution of 1998 urged health care organizations to develop a protocol for the appropriate use of antibiotics to improve and prevent the spread of resistant bacteria and avoid a potential health care crisis<sup>7</sup>.

Immediate implants traditionally were contraindicated in sites with periapical pathology, but recent trends have moved away from this concept. Recently, the potential benefit of systemic antibiotic therapy to manage surgical complications after implant placement into sites with apical pathology has been a subject of debate. In a systematic review by Waasdorp et al, this issue was explored in both animal and human models. Combining two animal and three human studies, 100% and 98.9 % survival rates of the implant fixtures were found, respectively<sup>8</sup>. Waasdorp et al suggested that “although controversial, the use of systemic antibiotics is recommended for this procedure until future evidence proves otherwise<sup>8</sup>.” Givens et al in a randomized controlled trial compared the survival rate and the clinical outcomes including post-operative pain and discomfort of immediate implants placed in sites with apical pathology<sup>9</sup>. Their findings suggested that systemic antibiotics may not play a role in the survival of the dental implant. However, in this study, there was no direct measurement of soft or hard tissue changes around the implant.

It is a duty of health care providers to prescribe antibiotics properly for the management and treatment of dental infections. There is however some disconnect in clinical understanding when dealing with immediate implant placement into sites with chronic apical lesions. In this



study we explore the need for antibiotic use with immediate implants into sites with apical pathology as well as if antibiotics have any positive effects on clinical outcomes, in particular, the facial alveolar bone and soft tissue.

### **3.2 MATERIALS & METHODS**

#### **Subject recruitment, selection, and randomization**

Subject selection and treatment protocol was similar to our previous study<sup>9</sup>. The study protocol was approved by the University of North Carolina at Chapel Hill (UNC) Institutional Review Board (IRB Study # 10-0286). Written consents were obtained from all subjects. A total of 20 subjects were recruited at the UNC School of Dentistry. All subjects were required to have a current dental provider and to have all active caries and periodontal disease treated and controlled. Subjects were in good periodontal health with proper periodontal recalls. The subject was required to have a current anterior or premolar tooth with an apical radiolucency evident on a periapical radiograph. The tooth in question was deemed to be non-restorable by the subject's current dental providers. A treatment plan for extraction and dental implant was indicated and prescribed by the dental provider. The tooth could be either in the maxillary or mandibular arch with intact adjacent teeth and appropriate opposing dentition.

For each subject, the general health history was thoroughly reviewed to ensure that there was no contraindication for dental implant therapy. Only ASA class 1 or 2 patients were selected. Subjects with a compromised medical history (ASA class 3 or higher) that would require a physician's consultation and alteration to surgical treatment or protocol were excluded. Subjects who were currently taking or require antibiotics, steroids and or any immunosuppressive drugs on a regular basis or in conduction with dental appointments were

excluded. Table 1 shows the inclusion and exclusion criteria that were similar to our previous study.

Periapical radiographs were used for initial screening (Figure 1a). Preoperative small volume cone-beam computed tomography (CBCT) scans, Kodak 9000 (Kodak dental systems, Rochester, NY), were taken for all potential subjects (Figure 1b). The CBCT scans were used to determine if the subject would fit the radiographic criteria for the study (Table 2). Note that the availability and integrity of facial alveolar bone and the extent of the apical lesions that would allow ideal positioning of the implant with minimal or no grafting are used as the major criteria for case selection (Figure 1c). The CBCT scans were also used for the determination of the appropriate implant diameter and length (Figure 1b).

Subjects were randomly allocated to the antibiotic or placebo group. This was a double-blind study in which neither the subject nor the operator knew which group the patient was assigned to. A computer generated randomization sheet was given to the UNC drug investigational pharmacy at the UNC Hospital. The pharmacist was the only person who had access to the allocation of subjects. An initial loading dose of antibiotics or placebo one hour prior to surgery and then four doses per day post-operatively for 7 days were instructed. The antibiotic selection was based on the most commonly used antibiotics in the field of dentistry. Patients were to receive Amoxicillin (n=25 capsules) if they did not have a Penicillin allergy or Clindamycin (n=23 capsules) if they did not report a history of Penicillin hypersensitivity (Table 3).

### **Treatment Protocol**

A written informed consent was obtained from all subjects. All subjects were instructed to take the initial loading dose of either antibiotics (2 g of Amoxicillin or 600 mg of

Clindamycin) or placebo one hour prior to the surgery. Immediately before the surgery, the subject was instructed to rinse for two minutes with 0.12% chlorhexidine. An initial pre-operative impression was made with polyvinyl siloxane (Regisil, Dentsply Caulk, Milford, DE, USA). The patient was properly anesthetized with 2% Lidocaine with 1:100,000 epinephrine (Xylocaine, Dentsply, York, PA, USA). The tooth was extracted using periostomes and small straight elevators to ensure that we did not damage the facial alveolar bone (Figure 2a-b)<sup>9,10</sup>. The socket was thoroughly curetted and all granulation tissue was removed. The socket was irrigated with about 10 ml of 0.12% chlorhexidine and then with copious amounts of normal saline solution (about 20 ml). The socket was then inspected to ensure there was an intact facial plate at least at the cervical ½ of the socket (Figure 1c). Osteotomy was made using the final 1 or 2 drills following the manufacturer's recommended protocol for drill sequence and speeds (Figure 2c). The use of only the final 1-2 drills (large diameter drills) was to control the implant angulation and minimize misalignment for the osteotomy. Copious irrigation with saline was used throughout the drill sequence. A root-form endosseous implant (Tapered-Screw vent (TSV), Zimmer Dental Carlsbad, CA, USA), was placed into the osteotomy (Figure 2d-e). Each implant had good primary stability at about 50 N-cm insertion torque. The implant was then provisionalized with a screw-retained provisional crown fabricated from provisional abutment (Zimmer Dental Carlsbad, CA, USA) and bis-acryl acrylic resin (Integrity, Dentsply, York, PA, USA). The occlusion of the provisional crown was adjusted until there were no contacts in the maximum intercuspal position or in lateral excursive movements (Figure 3a-b). The subject was instructed to continue the use of their antibiotics/placebo for the next 7 days. Over-the-counter analgesics (acetaminophen or ibuprofen) were recommended to the subject to use as needed for pain management. No narcotic prescriptions were given. A postoperative periapical radiograph

was taken immediately after the surgery (Figure 3c). In some cases where the implant was deemed close to the maxillary sinus, the inferior alveolar canal or root of an adjacent tooth, small volume CBCT scans similar to the pre-operative one were also be taken to ensure appropriate implant placement position.

Subjects were seen at one week and then at four weeks following implant surgery. Each subject completed a visual analog scale at each appointment to assess the level of pain and discomfort. The scale was from 0-10, 10 representing the worst pain they have ever experienced. At each appointment the extent and location of inflammation, edema and erythema was noted. The clinical measurement was recorded as none, mild, moderate or severe.

The fabrication of the definitive restoration was performed at least 12 to 16 weeks after the implant was placed (Figure 4a-b). All implants were restored with a custom zirconia abutment (Atlantis, Dentsply, Cambridge, MA, USA) or zirconia prefabricated abutment (Zimmer Dental, Carlsbad, CA, USA). The selection of the abutment was based on the size of the tooth and the angulation of the implant placed. All implants were restored with lithium disilicate with esthetic layered feldspathic porcelain crowns (IPS e.max, Ivoclar Vivadent, Amherst, NY) using CAD-CAM technology. Patients were recalled between 6 to 12 months to assess survival, function and esthetics of the implant. Implant survival criteria similar to those used by Smith and Zarb 1989 were applied<sup>11</sup>.

### **Facial alveolar bone and soft tissue measurements**

Subjects were seen at a 6 month recall after the placement of the implant for a CBCT scan (Kodak 9000, Kodak dental systems, Rochester, NY, USA) and a polyvinyl siloxane impression of the implant area. The vertical change in the alveolar bone was measured by comparing the pre- and post-operative CBCT scans using Simplant software (Materialise Dental,

Waltham, MA, USA). To ensure that the similar linear plane of reference was used in the two different CBCT scans, the long-axis of the tooth mesial to the implant site was used as a reference plane (Figure 5a and 6a). In both CBCT scans, the same panoramic curve was drawn utilizing the center of each tooth at the level of the cement-enamel junction (CEJ). The long axis of the tooth mesial to the implant site was determined from the tip of the incisal edge or the midpoint between the buccal and lingual cusp tips to the apex of the root in the sagittal plane (Figure 5a). This long axis was used as a reference line allowing us to have a common and predictable reference plane to measure the facial alveolar height of the facial plate, preoperatively (Figure 5b) and postoperatively (Figure 6b). A common horizontal line was drawn in the axial view at the root apex of this mesial tooth. This horizontal line was stationary and could be used as a common reference line to measure the facial plate from. The vertical measurement was made of the facial alveolar bone from the mid-facial of the tooth in the preoperative CBCT scans and the implant in the postoperative CBCT scans, to the stationary horizontal line in the axial plane of the apex of the tooth mesial to the implant site (Figure 5b and 6b). The difference between the pre- and post-operative facial bone height was recorded, positive value as a bone resorption and negative value as a bone gain.

The facial soft tissue height was measured using polyvinyl siloxane impressions of the affected tooth preoperatively and the implant at the 6-month follow-up visit. The impressions were digitally scanned using Ortho Insight 3D, (Motion View Software, LLC, Chattanooga, TN, USA) which then allowed for the fabrication of digital three-dimensional casts in a STL format. The digital cast was used to measure the soft tissue changes. Five common reference points were used (Figure 7a-b), including top of the facial-proximal line angle of incisal edges or cusps of adjacent teeth (2 reference points), height of mesial and distal papillae (2 reference points), and

the lowest level of the mid-facial gingival margin of the tooth or implant (1 reference point). The change in the mesial papilla height, distal papilla height and the facial gingival margin was determined. Positive values were used as soft tissue height reduction and negative values were used as soft tissue height gained.

Non-parametric statistical analyses were used to examine the statistical differences between the antibiotic and the placebo group. The Mann-Whitney U statistical test was used to determine if the soft tissue changes as well as the hard tissue changes. The Spearman Rank Correlation coefficient test was used to examine if there was a correlation between the changes of the underlying facial alveolar bone and the mid facial marginal gingiva.

### **3.3 RESULTS**

#### **Implant survival and reported complications**

A total of 20 immediate implants were placed in a total of 20 subjects (1 implant per subject). 10 subjects were in the antibiotic group and 10 subjects were in the placebo group. Nine implants were placed in males and 11 in females. Considering implant site, implants were placed in the central incisor (n=2), later incisor (n=4), canine (n=2) and premolar (n=12) sites. Two implants in the placebo group were determined to have had an early failure. One subject, also in the placebo group, was lost after the 6-month follow up. The overall survival rate is 89.5 %. Table 4 represents the patient distribution and survival rate within each group.

Note that one of the failures was in a subject who did not come back after the second post-surgical visit. The provisional abutment screw became loose which resulted in the provisional crown being in hyper-occlusion and thus the subject overloaded the implant. When the subject came back about 4 months after surgery, the implant was loose. The second failure was noted in a subject when she came back for the final impression visit. We determined that

there was an abscess and the implant was mobile. Once we removed the implant, a fragment of hard tissue debris was found packed between the implant and facial alveolar bone.

In terms of postoperative pain and discomfort, one subject in each group reported mild pain, ( $\geq 3$ ) on the 0-10 visual analog scale, at the 1-week post-surgical visit (Figure 8a-b). However, none of the subjects reported any pain or discomfort at the 4-week post-surgical visit. Note also that clinical inflammation and swelling was not reported in any of the clinical visits. All subjects reported that they no longer used any analgesics at 1-week post-surgical visit or thereafter.

### **Facial alveolar bone and soft tissue changes**

To measure the soft tissue changes, pre- and post-operative digital three-dimensional casts were used to compare the vertical height of the mesial and distal papillae as well as the mid-facial gingiva (Table 5). The tooth mesial to the implant site was used to determine the measurement error. The differences between the pre- and post-operative soft tissue height (standard deviation) for this calibration tooth are on average 0.14 (0.09) mm, 0.19 (0.07) mm, and 0.21 (0.08) for the mid-facial, distal papilla and mesial papilla measurements respectively. The average mesial papilla height change (standard deviation) was 0.6 (+/- 1.08) mm for the antibiotic group and 1.5 (+/- 1.32) mm for the placebo group; however, this difference was not statistically significant. The average distal papilla height change was 0.5 (+/- 0.81) mm for the antibiotic group and 0.2 (+/- 0.44) mm for the placebo group; however, this difference was not statistically significant. When comparing the mid-facial gingival margin change, the average change for the antibiotic group was 0.5 (+/- 0.72) mm while for the placebo group it was 1.7 (+/- 1.06) mm. This difference is noted to be statistically significant ( $p < 0.02$ ). The total average soft

tissue change was 0.5 (+/- 0.71) mm for the antibiotic group and 1.1 (+/- 0.76) mm for the placebo group; however, this difference was not statistically significant.

Regarding the hard tissue changes, the height of the mid-facial alveolar plate was measured from the apex of the tooth mesial to the implant site to determine the measurement error similar to the soft tissue measurement (Table 5). The differences between the pre- and post-operative mid-facial alveolar bone height (Standard deviation) of the tooth mesial to the implant site was on average 0.16 (0.08) mm. The average change of the mid-facial alveolar plate for the antibiotic group was 0.63 (0.46) mm and 1.34 (0.91) mm for the placebo group; however, this was not statistically significant.

To determine if there was a possible correlation between the mid-facial alveolar bone and mid-facial gingival soft tissue changes, the Spearman Rank Correlation coefficient test was used. Our data shows that there is no correlation between the hard and soft tissue changes (Figure 9).

### **3.4 DISCUSSION**

The goal of this study was to address the clinical question of whether antibiotics are needed when replacing a tooth with a periapical lesion with an immediate implant in the esthetic zone. In addition we explored the effects of peri-operative antibiotics for immediate single implants in terms of implant survival, postoperative complications, and most importantly, changes in facial soft and hard tissue. While we share the same clinical protocol (double-blinded randomized controlled trial protocol, antibiotics and implant placement/restoration protocol) with our previous study<sup>9</sup>, we found that the placebo group did show a lower survival rate than the Givens et al results. Note here however, that the two failures in the placebo group were caused by overloading of the implant due to screw loosening in one patient and by the root/bone



fragment wedged between the tooth and the socket in the other patient. Antibiotics likely would not have helped in either case.

The question remains: are antibiotics needed if there is any infection remaining in the extraction socket? In this study, implants were placed into extraction sockets that were thoroughly curetted and irrigated with Chlorhexidine as well as saline. All teeth with lesions were chronic in nature. There were no flap or large grafting procedures performed. We believe that in select cases of replacing a tooth with a chronic apical lesion with an immediate implant, antibiotics are not necessary. This study is however only an exploratory study with a small sample size. A larger study of this type is required to provide us with a more definitive answer. We need to keep in mind that unnecessary use of common antibiotics today may result in both expensive antibiotics in the future, as well as an increase in bacterial resistance. This may pose a significant risk for patients in the future and could possibly develop into a public health crisis for the community at large<sup>6</sup>.

Similar to Givens et al and other studies, we found that immediate implant therapy for single tooth requires little pain management<sup>9,12,13</sup>. In the Givens et al study, narcotic analgesics, acetaminophen/codeine (Tylenol 3), were given to all subjects as our pain management protocol. We realized after that study that most of the patients did not take any narcotics prescribed. In this study, we therefore revised the protocol and none of our subjects were given narcotic analgesics. Only one subject in each group reported mild pain at the 1 week post-surgical visit and none of them reported any pain after that. It is possible that placing an implant into a fresh extraction socket reduces the volume of the socket and creates only a small layer of clot. This would result in a smaller amount of inflammatory mediators. In addition, we fabricated a screw-retained provisional crown that was customized to fit the socket. This permitted primary closure of the

socket thus allowing stabilization of the clot and facilitating healing<sup>14</sup>. While the healing of the extraction socket is known to take up to 3-4 months, we know that the socket mineralization occurs within a few weeks at the periphery of the socket (close to the alveolar bone)<sup>15</sup>. In immediate single implant placement, there is only a 2-4 mm gap between the implant and the facial alveolar bone<sup>16,17</sup>. The gap appears to fill in completely in all cases at the 6-month post-surgical visit. It is plausible that immediate implant placement can facilitate bone healing simply by minimizing the bone healing volume in the extraction socket. In addition, we previously suggest that perhaps antibiotics are not needed in cases of a single tooth immediate implant even with periapical lesion when flap opening and graft were not performed<sup>9</sup>.

One of the factors to consider in our study is the pre-surgery planning of the immediate implant. Using pre-operative CBCT scans, we ideally selected an implant that was slightly longer than the socket. For instance, all implants placed were either 13 or 16 mm in length. We learned from our previous study that shorter implants may contribute to failure due to lack of primary stability<sup>9</sup>. The longer implants and the triple thread design of TSV implants allow sufficient primary stability, which is one of the main requirements for immediate implant placement<sup>8</sup>. We were also careful in placing an implant to keep a small gap (about 3 mm or less) from the implant fixture to the facial alveolar bone<sup>16</sup>. For all subjects except one, we did not place any graft material. It has been suggested that the gap of 3-4 mm between immediate implant and extraction socket does not need grafting<sup>17,18</sup>. We found that the facial bone in all cases regenerates into the gap. However, we also found that the apical fenestration from the previous lesion did not fully mineralize in all cases. This is most likely due to a short 6-month follow up period, and likely at one year we would see more complete healing of the apical fenestration.

When replacing a tooth with an implant in the esthetic zone, the primary goals of the treatment are to replace and restore the esthetics and function of the coronal portion of the tooth. Also we wish to preserve and restore the facial alveolar soft and hard tissues. The contemporary technology allows fabrication of esthetic abutments and crowns to mimic natural adjacent teeth. In our study, we used Zirconia abutments and lithium disilicate crowns (Figure 4a-b). More importantly, this study is one of the few that digitally measured the facial soft and hard tissue for the tooth pre-operatively and the implant post-operatively. We found that only about 0.5 to 2 mm of soft and hard tissue is lost at the 6-month post-surgical recall visit. While this number is similar to other studies<sup>18-21</sup>, we believe that antibiotics have little influence of the hard and soft tissue change. While it is possible that antibiotics can reduce subclinical infection that may in turn reduce inflammation, soft tissue recession, and bone resorption, only the mid-facial soft tissue change was found to be statistically significant in this study. It is also possible that the sample size of this study is too small to see the effects on soft tissue changes.

Both the hard and soft tissue measurement techniques were tested to see the accuracy of our method. For consistency of the measurement, we did not want to use any molars. Thus, we used the tooth mesial to the implant site as our reference because we included anterior and premolar teeth in this study. The measurement was done carefully with one operator. Our measurement error was found to be  $0.18 \pm 0.06$  mm and  $0.16 \pm 0.08$  mm for the soft and hard tissues respectively. This is comparable to other studies<sup>22</sup>. Hermann et al. found precision of their radiograph technique to be 0.1mm.<sup>23</sup> The measuring errors for repeated measurements of the soft and hard tissues were  $0.14 \pm 0.02$  mm and  $0.13 \pm 0.01$  mm, respectively Small volume CBCT scans may be an important research or clinical tool in monitoring facial bone changes<sup>24</sup>.

Interestingly, we found no correlation between the mid-facial soft and hard tissue changes. Several studies have examined the relationship between interproximal bone and inter-implant-dental papilla and suggested that there are certain correlations between the underlying bone and soft tissue. For instance, Tarnow et al reports that if the distance between the interproximal bone and contact is 5 mm or less, the papilla will be present 100% of the time whereas if the distance is 7 mm or less, the papilla will only be present 25% of the time<sup>25</sup>. There is very little information in the literature on the relationship between the facial alveolar bone and facial soft tissue of a dental implant<sup>26,27</sup>. While in a single tooth implant situation, the periodontal health of the adjacent teeth play an important role in maintaining the mesial and distal papilla<sup>19</sup>, the mid-facial gingiva and its relevance to the facial plate is not clear<sup>26,27</sup>. We believe that while the facial alveolar bone may be important for long-term survival of the implant, it plays a limited role in maintaining the soft tissue. We further propose that appropriate contouring of the abutment, in particular the provisional abutment, may have a crucial role in preserving the mid-facial soft tissue of the implant. In our study, we fabricated a provisional abutment that fit into the extraction socket with a concave emergence profile. The customized provisional abutment can potentially provide primary closure and protect the blood clot in the socket. More importantly the provisional abutment also acts as a root contour and therefore preserves the facial soft tissue contour.

### **3.5 CONCLUSION**

The results of this study suggest that the use of peri-operative antibiotics has little influence on replacing a tooth with apical pathology with an immediate implant in the esthetic zone. Furthermore, antibiotics were not shown to have a material effect on either post-operative pain/discomfort or facial alveolar bone preservation. However, antibiotics may have limited

effects on the mid-facial soft tissue. No correlation was observed between the mid-facial alveolar bone and soft tissues. Immediate provisional abutments may play an important role in preserving the mid-facial soft tissue. With careful treatment planning and execution, immediate implant therapy even in a case with a periapical lesion can be done successfully with an optimal esthetic and functional outcome.

## **ACKNOWLEDGEMENTS**

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### **3.6 FIGURE LEGEND**

**Figure 1 Preoperative Radiographs and Immediate implant protocol,** (A) A preoperative periapical radiograph of the tooth with a periapical lesion; (B) An example of CBCT scans of the affected area; and (C) Implant placement protocol showing the placement of an implant by engaging the palatal bone and the bone apical to the extraction socket.

**Figure 2 Clinical Treatment Protocol showing a series of an immediate implant surgery,** (A) Preoperative view of the non-restorable tooth; (B) The extraction socket after curettage and irrigation; (C) The implant drill in the extraction socket showing the angulation of the osteotomy site; (D) The implant in place; and (E) Occlusal view of the implant fixture showing no contact to the facial bone.

**Figure 3 Screw-retained custom provisional abutment/crown,** (A) The provisional screw-retained abutment/crown showing the screw hole near the incisal edge of the crown; (B) The provisional abutment/crown after the screw hole was filled; and (C) Post-operative periapical radiograph taken immediately after the implant placement.

**Figure 4: Definitive restoration,** (A) The definitive prefabricated zirconia abutment in place; and (B) The definitive cement-retained CAD/CAM lithium disilicate crown.

**Figure 5: Preoperative measurement of facial alveolar bone,** (A) Measurements at the reference site, tooth mesial to the implant site, in sagittal plane (upper) and frontal plane (lower); and (B) Measurements at the affected tooth site in sagittal plane (upper) and frontal plane (lower).

**Figure 6: Postoperative measurement of facial alveolar bone,** (A) Measurements at the reference site, tooth mesial to the implant site, in sagittal plane (upper) and frontal plane (lower); and (B) Measurements at the implant site in sagittal plane (upper) and frontal plane (lower);

**Figure 7: Measurements of facial soft tissue**, the same five points of references were used including the top of the line angles of the adjacent teeth, the top of the inter-dental papillae, and the lowest part of the marginal gingiva; (A) preoperative measurements; and (B) postoperative measurement.

**Figure 8: Postoperative pain/discomfort measured by visual analog scale**, (A) at the 1-week postoperative visit; and (B) at 4-week postoperative visit

**Figure 9: Correlation between facial bone and facial soft tissue changes after immediate implant placement**, plot based on the Spearman Rank Correlation Coefficient showing no significant correlation between hard and soft tissue changes.

**Table 1: Inclusion and exclusion criteria based on subjects' health history**

**Table 2: Inclusion and exclusion criteria based on subjects' preoperative CBCT scans**

**Table 3: Prescription protocol**, In the antibiotic group, for patients that are allergic to penicillin, Clindamycin was given; For patients that are not allergic to penicillin, Amoxicillin was given.

**Table 4: Implant survival rates**, the antibiotic group of 10 subjects had a 100% implant survival rate, while the placebo group of 9 subjects had a 78% survival rate.

**Table 5: Average hard and soft tissue changes**, shows the medial, distal, facial, and total average soft tissue changes, (mm) standard deviation values, and statistical significance based on the Mann-Whitney U test for both groups. The average facial hard tissue change is shown for both groups, as well as the standard deviation values and statistical significance based on Mann-Whitney U test. The soft tissue changes on the facial gingival margin were the only significant changes.

Figure 1a:





Figure 1b:

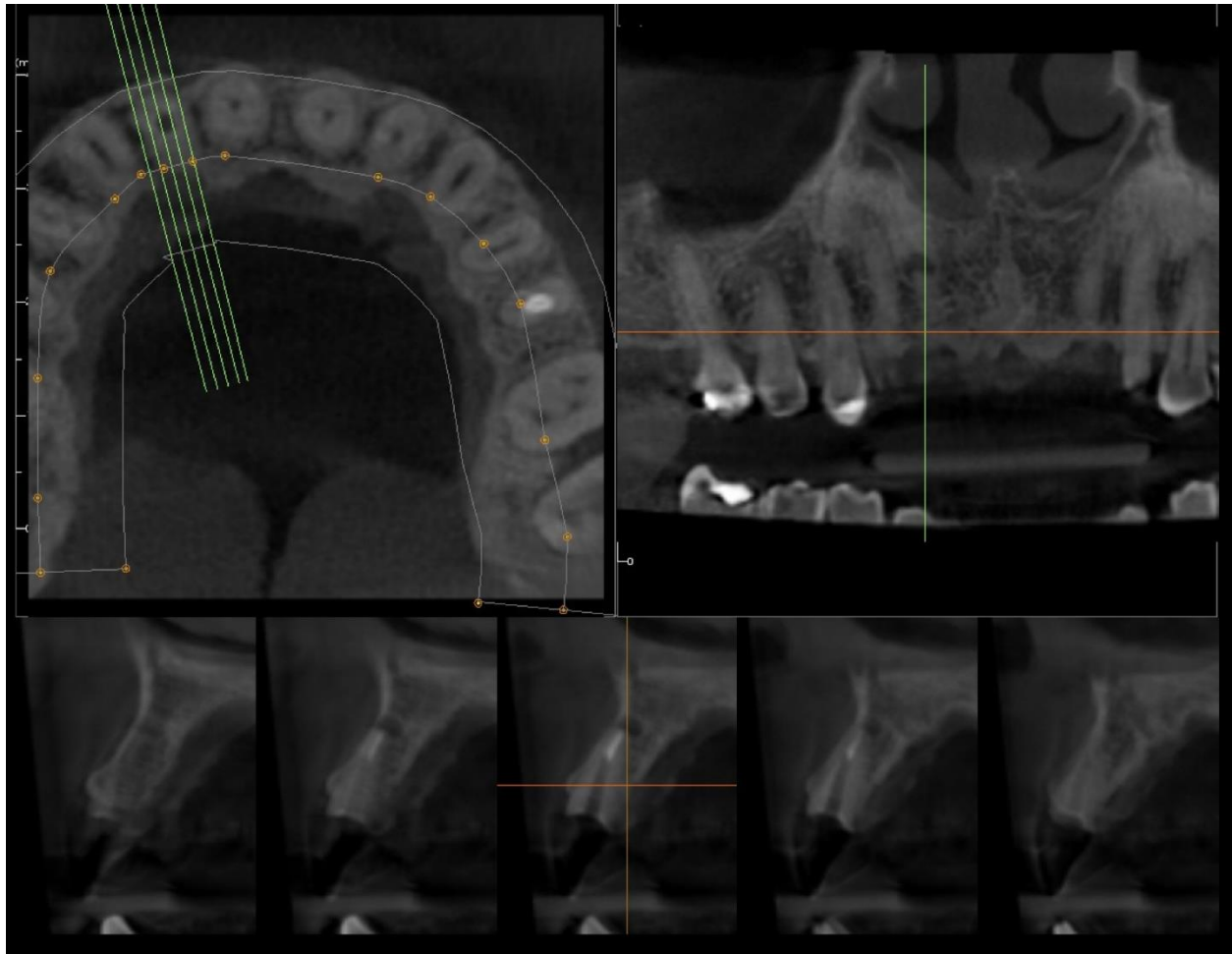


Figure 1c:

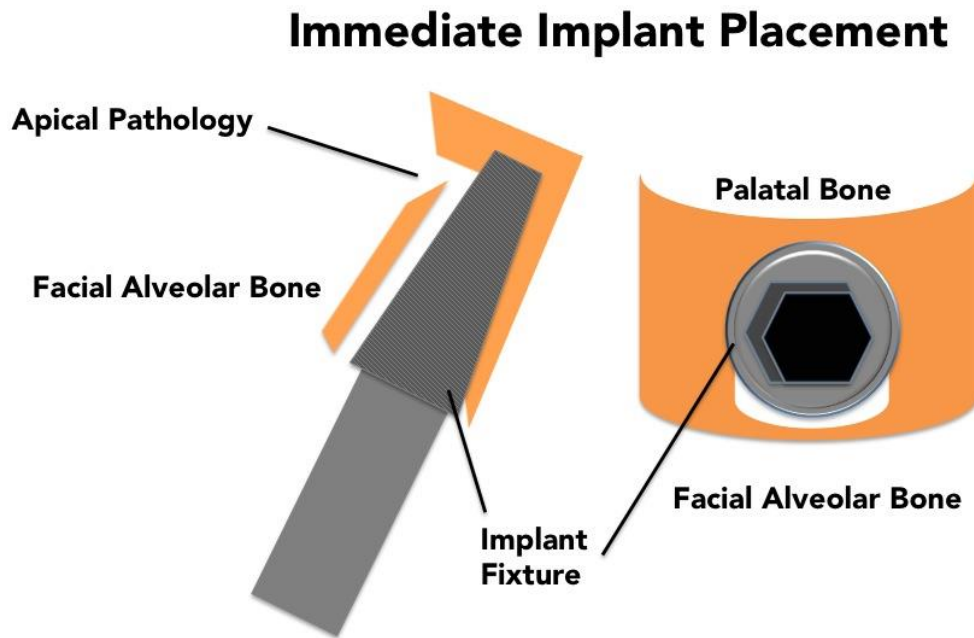


Figure 2a:



Figure 2b:



Figure 2c:

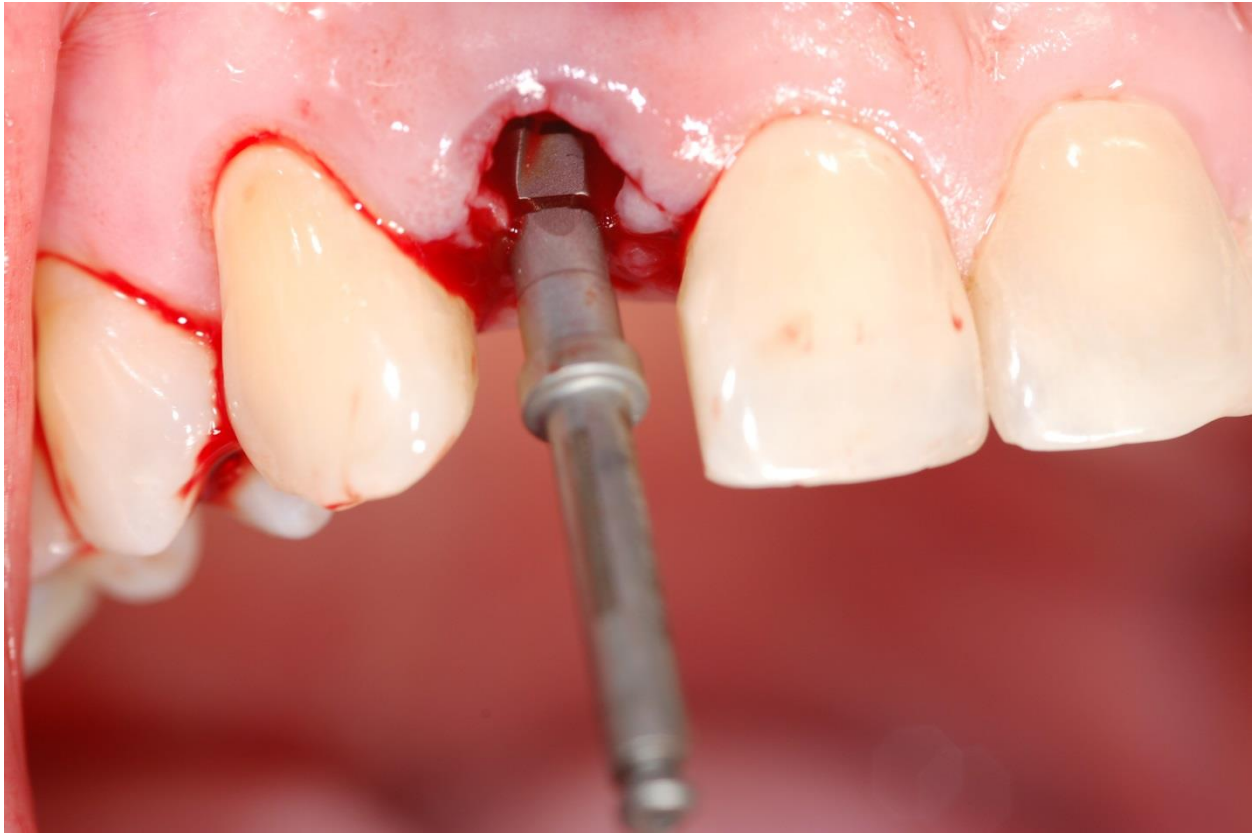


Figure 2d:





Figure 2e:

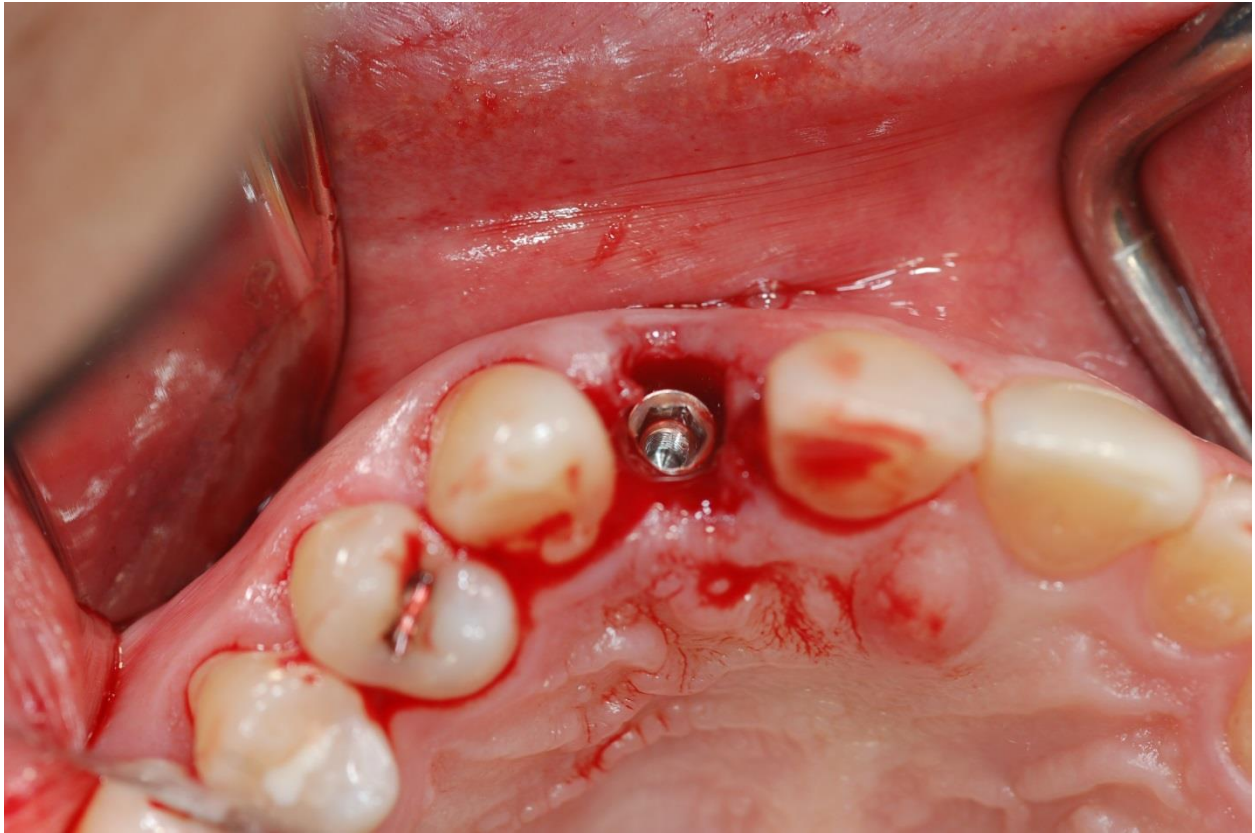


Figure 3a:





Figure 3b:



Figure 3c:

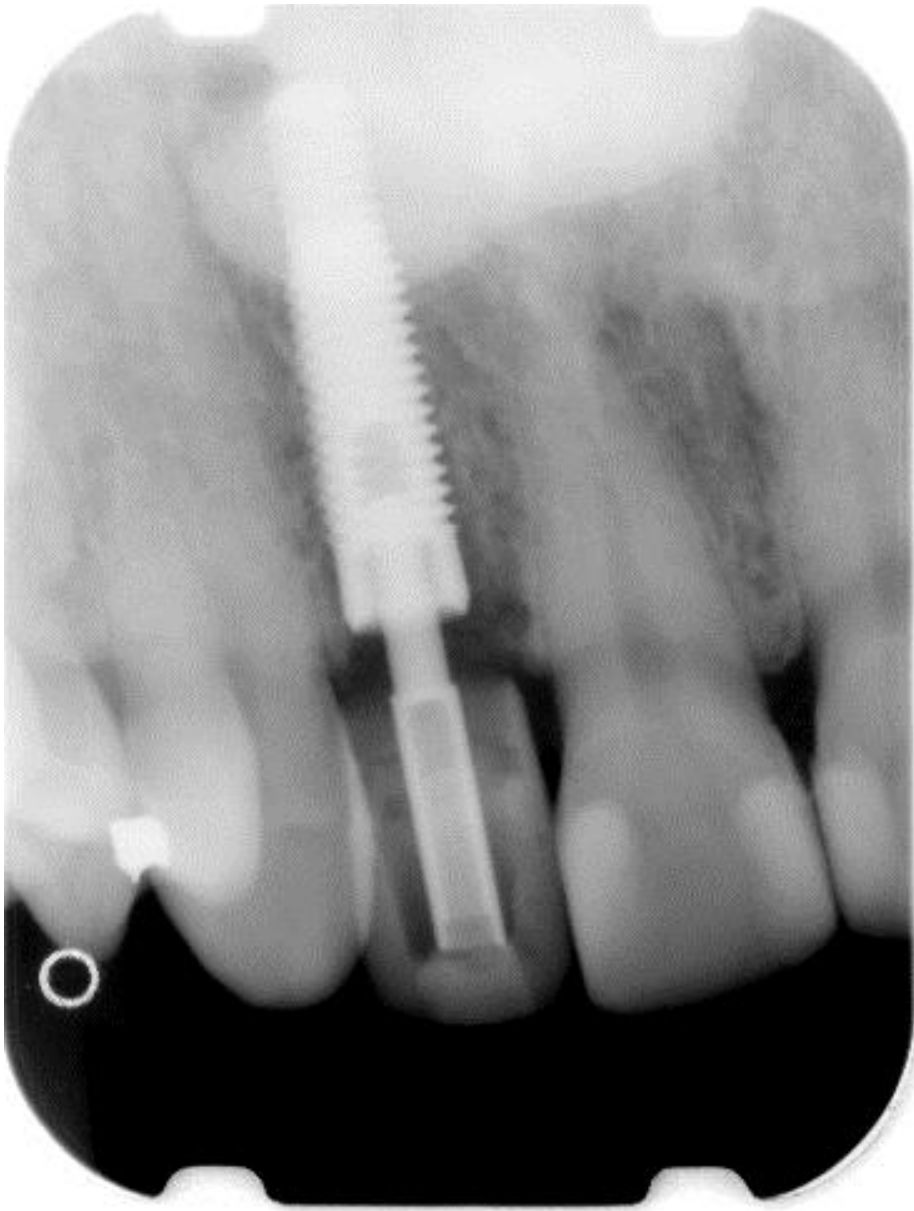


Figure 4a:



Figure 4b:



Figure 5a:

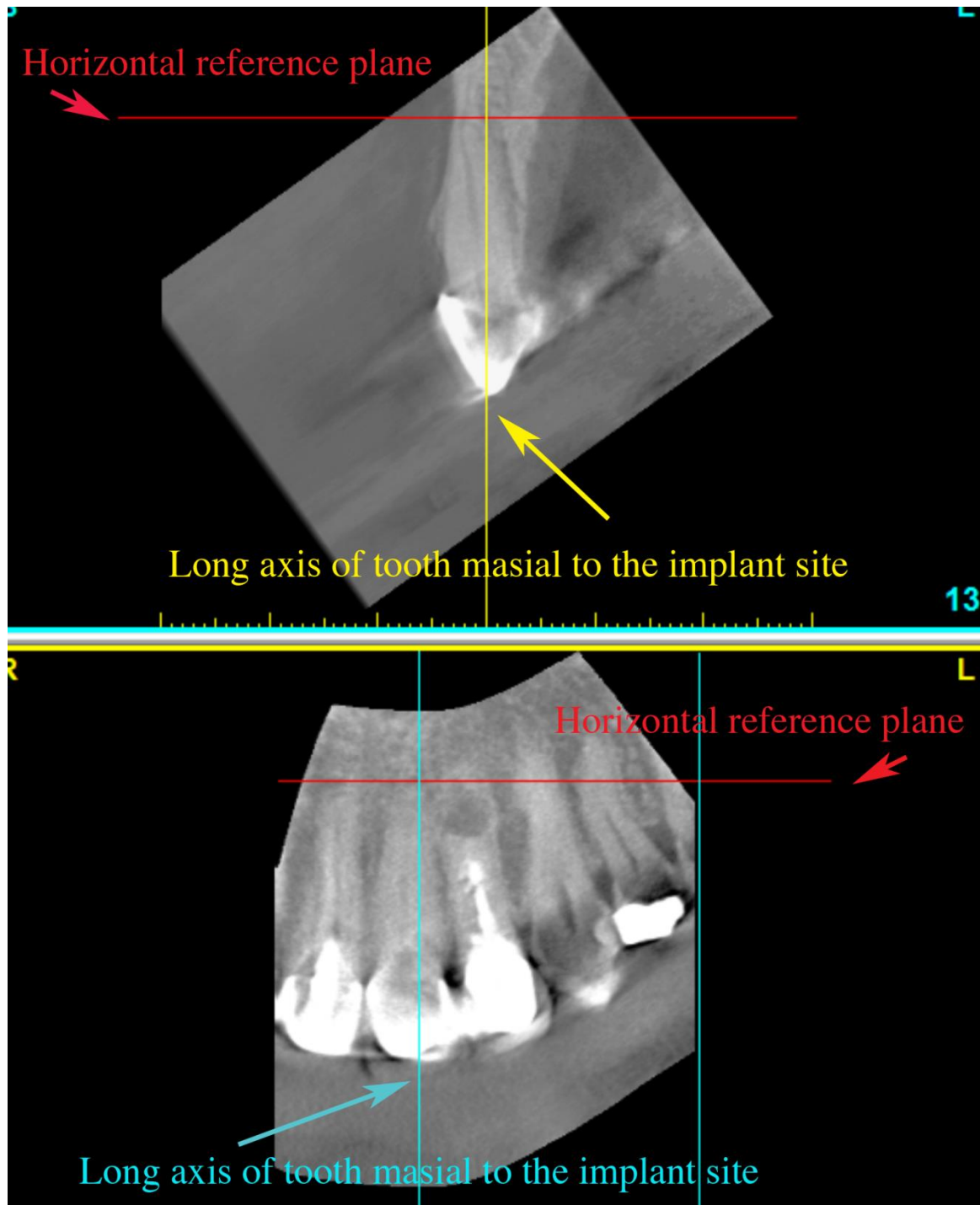


Figure 5b:

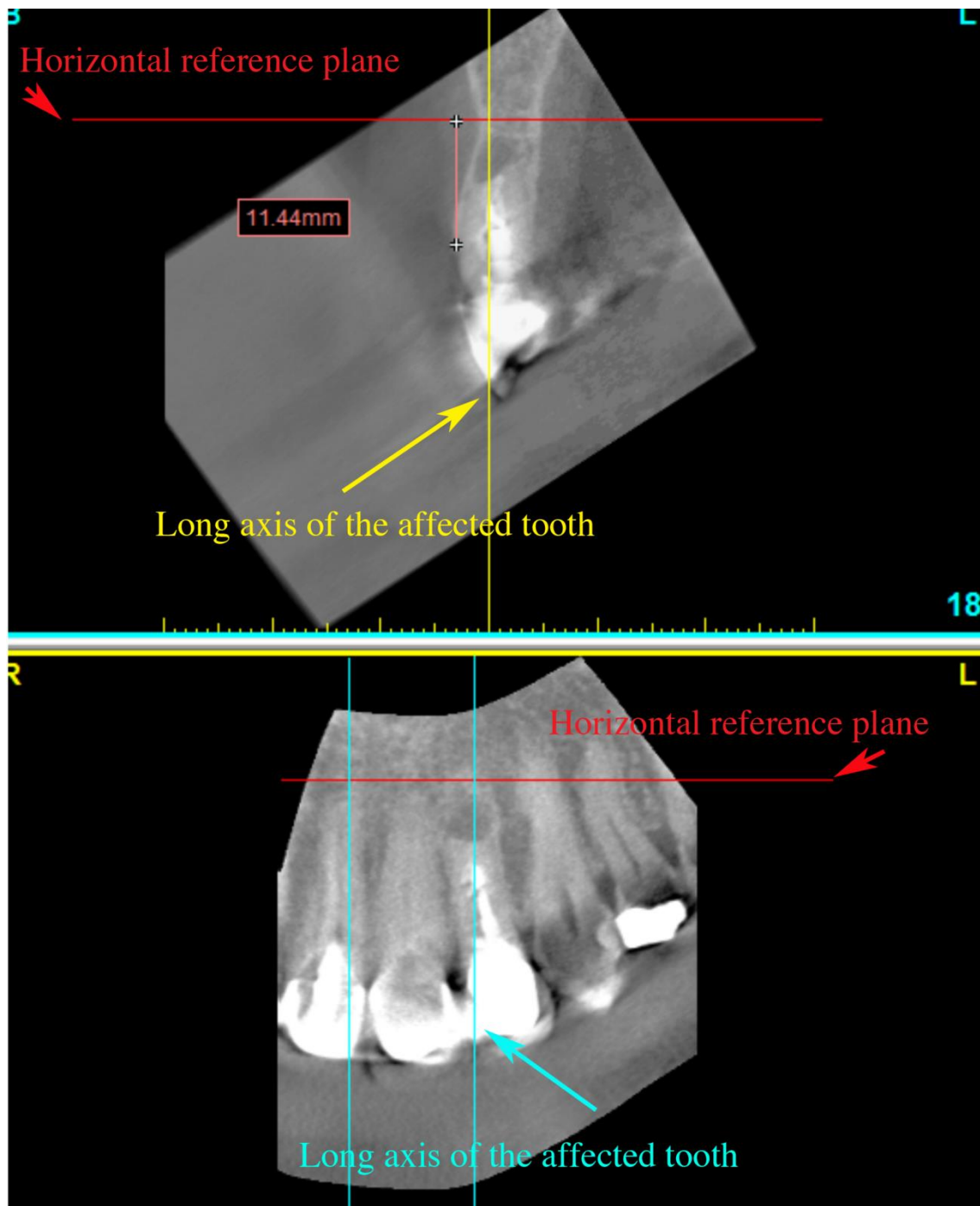


Figure 6a:

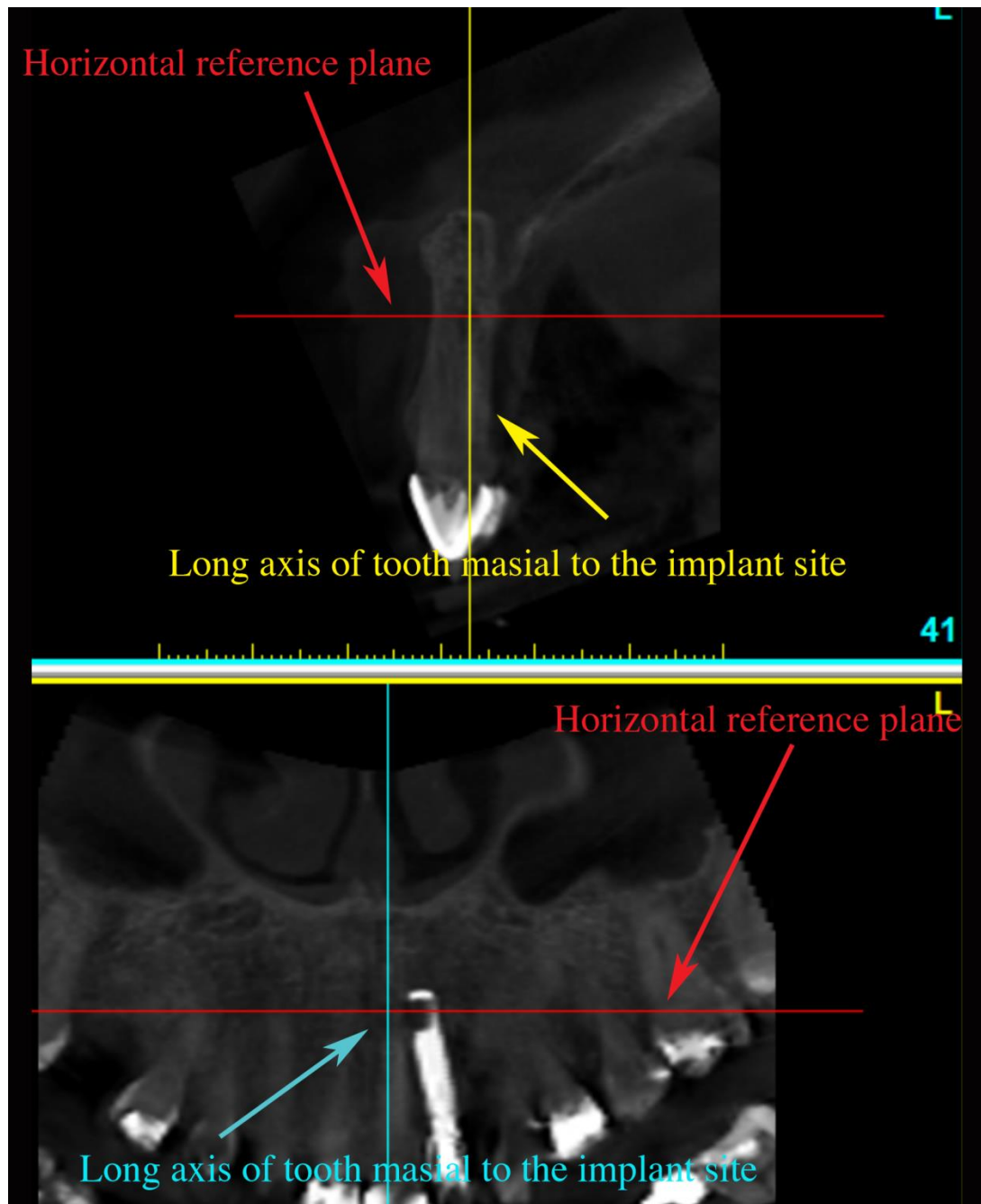




Figure 6b:

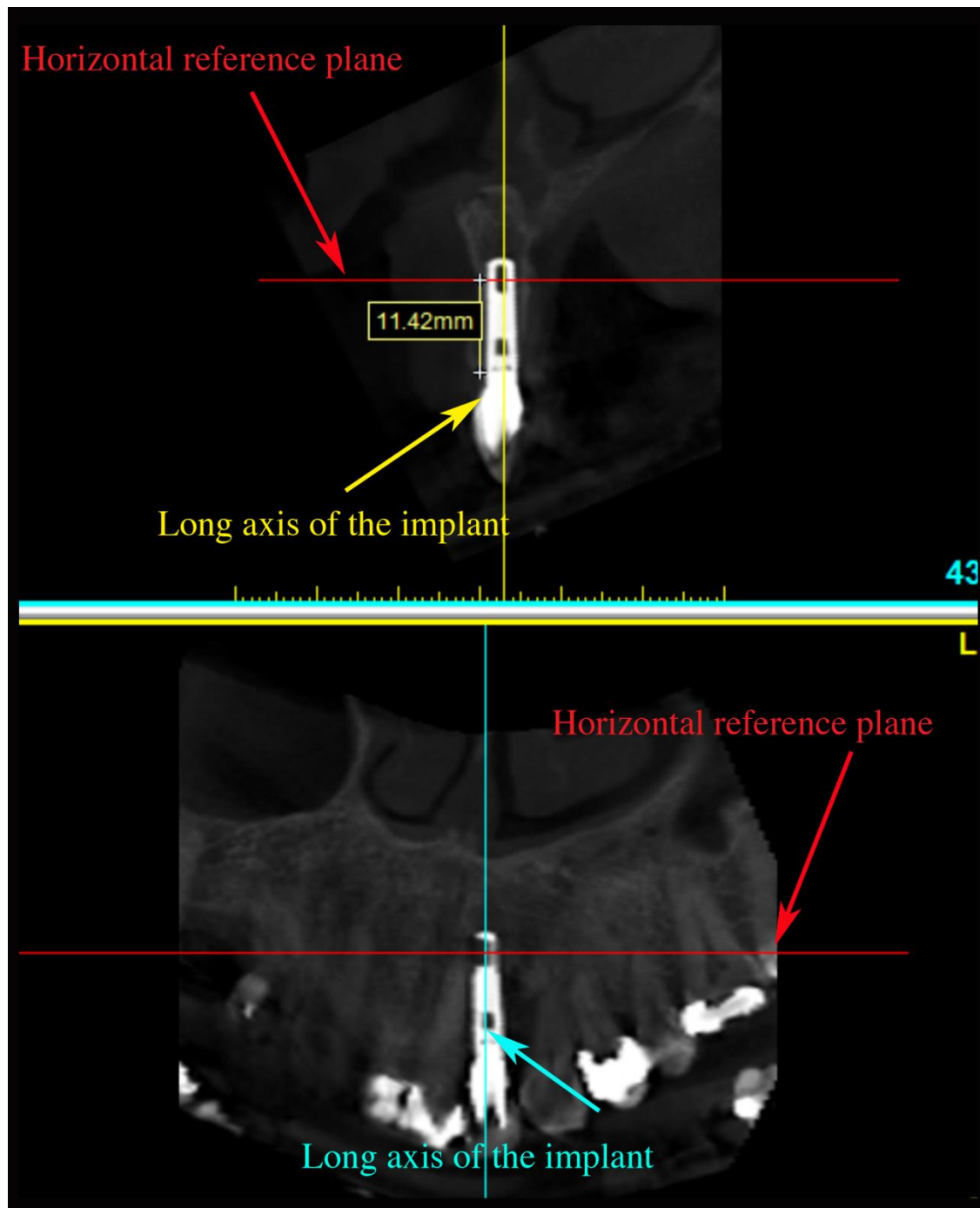




Figure 7a:

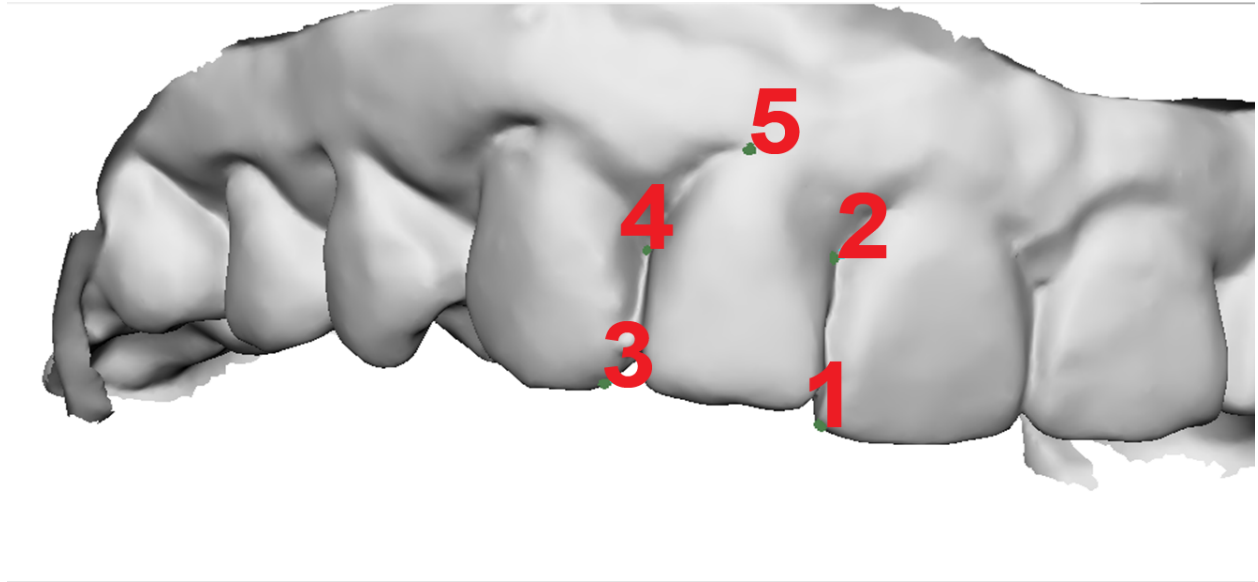


Figure 7b:

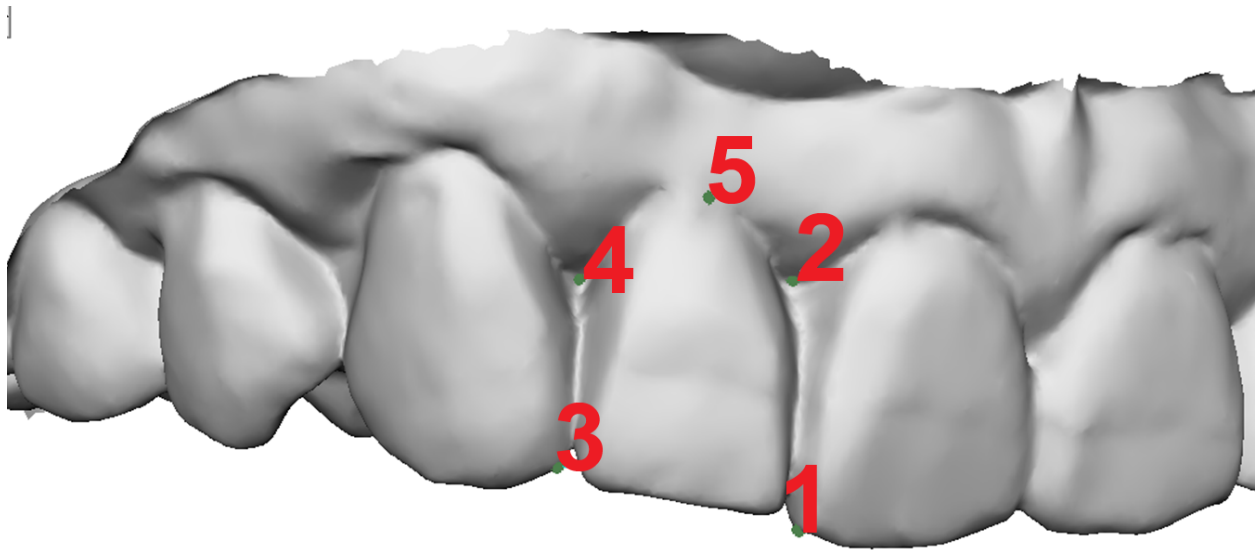


Figure 8a:

## Visual analog scale at 1 week

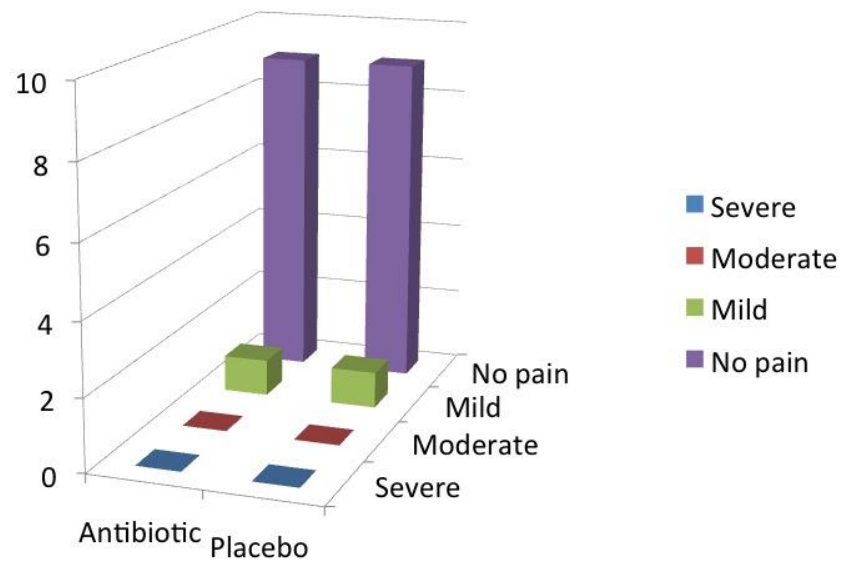


Figure 8b:

## Visual analog scale at 4 weeks

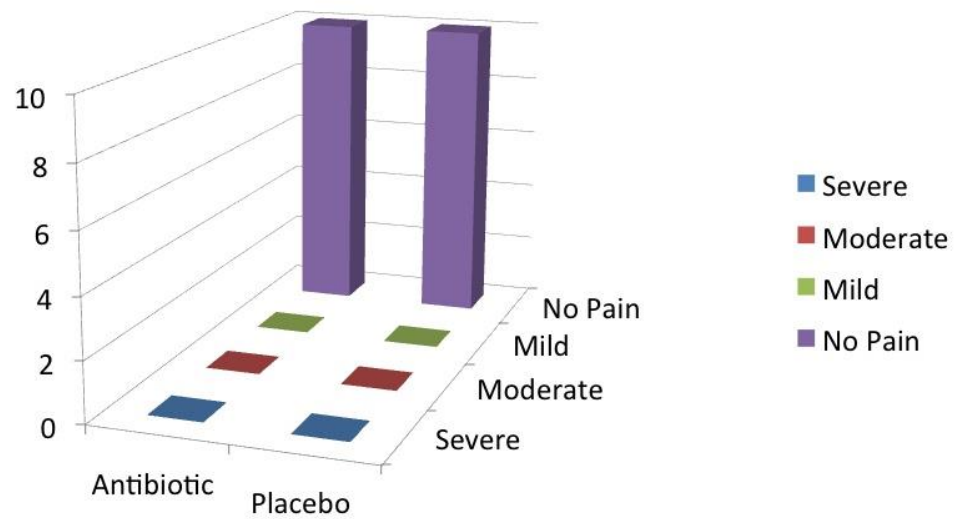
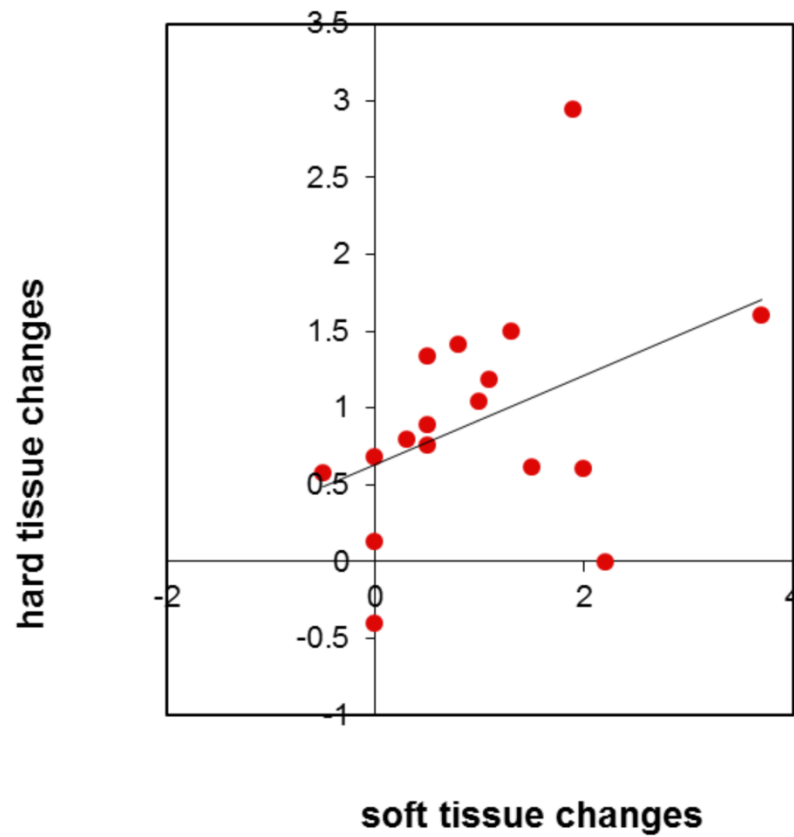


Figure 9:



**Spearman's rho: 0.406**  
**Degree of freedom: 15**  
**P-value: 0.1055**

**Table 1 Inclusion and Exclusion Criteria based on Subject's General Health History**

<b><u>Inclusion Criteria</u></b>	<b><u>Exclusion Criteria</u></b>
<ul style="list-style-type: none"> <li>-ASA Class 1 or 2 individuals, to include those with controlled HTN, diabetes, etc</li> <li>-Female/Male, ages 19-70</li> <li>-Non-smokers or smokers with a reported use of less than 1 pack/day</li> <li>-Not taking any antibiotics or steroids or immunosuppressive drugs</li> <li>-A pre-molar, canine, or incisor tooth with a non-restorable tooth with PA pathology</li> <li>-Patients with sufficient bone quantity for implant placement, irrespective of infective lesion, and as determined by initial exam, preoperative periapical radiograph and CBCT scans</li> </ul>	<ul style="list-style-type: none"> <li>-ASA Class 3 or 4 individuals or have other contraindication for oral surgery</li> <li>-Age less than 19, over 70</li> <li>-Smokers (more than 1 pack/day) or smokeless tobacco users</li> <li>-Patients who are on antibiotic therapy, steroids or immunosuppressive drugs</li> <li>-Patients who exhibit gross infection/facial space infection with purulent discharge</li> <li>-Insufficient alveolar bone for the placement of dental implant, or insufficient primary stability of dental implant during the placement.</li> <li>-Patients unable to tolerate implant placement with local anesthesia</li> <li>-Patients who are unable/unwilling to return for follow-up appointments</li> </ul>

**Table 2 Inclusion and Exclusion Criteria based on preoperative CBCT scans**

<b>CBCT Scan Inclusion / Exclusion Criteria</b>	
<b>Inclusion</b>	<b>Exclusion</b>
<ol style="list-style-type: none"> <li>1. Apical Radiolucency present</li> <li>2. Adequate bone to support dental implant</li> <li>3. Adequate facial plate to allow immediate implant placement</li> <li>4. No anatomic landmarks that would not allow appropriate placement of an immediate implant, e.g. maxillary sinuses, inferior alveolar canals, roots of adjacent teeth.</li> </ol>	<ol style="list-style-type: none"> <li>1. No apical radiolucency present with associated tooth in question</li> <li>2. Extensive apical lesion that has resulted in loss of bone that would not allow for stability of immediate implant</li> <li>3. Not ideal facial plate that would compromise an immediate implant placement and the esthetic outcome.</li> <li>4. Extensive bone loss that would require major bone grafting.</li> </ol>

**Table 3 Prescription protocol**

<b>Antibiotics vs Placebo Selection</b>	
Not Allergic to Penicillin	Allergic to Penicillin
Amoxicillin 0(Placebo)/500 mg Cap Sig: Take 4 capsules by mouth 1 hour before the procedure; then take 1 capsule three times daily for 7 days DSP: 25 Capsules	Clindamycin 0(Placebo)/300 mg Cap Sig: Take 2 capsules by mouth 1 hour before the procedure; then 1 capsule three times daily for 7 days DSP: 23 capsules



**Table 4 Implant survival rate per group**

	<b>Total Subjects</b>	<b>Survival</b>	<b>Failure</b>	<b>Survival Rate</b>
<b>Antibiotic</b>	10	10	0	100%
<b>Placebo</b>	9	7	2	78%

**Table 5: Average hard and soft tissue changes**

<b>Average hard and soft tissue changes</b>					
	Mesial Papilla change (mm)	Distal Papilla change (mm)	Facial Gingival margin change (mm)	Total Average Soft tissue change (mm)	Average change of facial plate (mm)
<b>Antibiotic group</b>	0.6 ± 1.08	0.5 ± 0.81	0.5 ± 0.72	0.5 ± 0.71	0.63 ± 0.46
<b>Placebo Group</b>	1.5 ± 1.32	0.2 ± 0.44	1.7 ± 1.06	1.1 ± 0.76	1.34 ± 0.91
<b>Mann Whitney U-test value</b>	24	31.5	10	21	15
<b>Statistical Significance</b>	p > 0.05	p > 0.05	<b>p ≤ 0.02</b>	p > 0.05	p > 0.05

## REFERENCES

1. Fouad AF, Rivera EM, Walton RE. Penicillin as a supplement in resolving the localized acute apical abscess. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1996;81(5):590-595. Accessed 3/10/2014 9:50:34 AM.
2. Abbott PV. Medicaments: Aids to success in endodontics. part 2. clinical recommendations. *Aust Dent J.* 1990;35(6):491-496. Accessed 3/10/2014 9:55:13 AM.
3. Misch CE. *Contemporary implant dentistry.* St. Louis: Mosby/Elsevier; 2008. <http://search.lib.unc.edu?R=UNCb5326445>. Accessed 3/10/2014 10:02:21 AM.
4. Esposito M, Grusovin MG, Worthington HV. Interventions for replacing missing teeth: antibiotics at dental implant placement to prevent complications. *Cochrane Oral Health Group.* 2013.
5. Bencharit S. Bacterial resistance to antibiotics and implanted medical device. *Advances in Pharmacoepidemiology & Drug Safety.* 2012;1(5).
6. WHO global strategy for containment of antimicrobial resistance. . 2001.
7. Emerging and other communicable diseases: Antimicrobial resistance. . 1998;Agenda item 21.3.
8. Waasdorp JA, Evian CI, Mandracchia M. Immediate placement of implants into infected sites: A systematic review of the literature. *J Periodontol.* 2010;81(6):801-808. Accessed 3/10/2014 11:16:50 AM. doi: 10.1902/jop.2010.090706; 10.1902/jop.2010.090706.
9. Givens E, Bencharit S, Byrd WC, Hosseini B, Phillips C, Tyndall D. Immediate placement and provisionalization of implants into sites with periradicular infection with and without antibiotics: An exploratory study. *J Oral Implantol.* 2013. Accessed 3/10/2014 11:20:09 AM. doi: 10.1563/AAID-JOI-D-13-00002.
10. De Rouck T, Collys K, Cosyn J. Immediate single-tooth implants in the anterior maxilla: A 1-year case cohort study on hard and soft tissue response. *J Clin Periodontol.* 2008;35(7):649-657. doi: 10.1111/j.1600-051X.2008.01235.x; 10.1111/j.1600-051X.2008.01235.x.
11. Smith DE, Zarb GA. Criteria for success of osseointegrated endosseous implants. *J Prosthet Dent.* 1989;62(5):567-572.
12. Cannizzaro G, Leone M, Consolo U, Ferri V, Esposito M. Immediate functional loading of implants placed with flapless surgery versus conventional implants in partially edentulous patients: A 3-year randomized controlled clinical trial. *Int J Oral Maxillofac Implants.* 2008;23(5):867-875. Accessed 3/10/2014 11:50:33 AM.

13. Fortin T, Bosson JL, Isidori M, Blanchet E. Effect of flapless surgery on pain experienced in implant placement using an image-guided system. *The International journal of oral & maxillofacial implants*. 2006;21(2):298-304.
14. Chu SJ, Salama MA, Salama H, et al. The dual-zone therapeutic concept of managing immediate implant placement and provisional restoration in anterior extraction sockets. *Compend Contin Educ Dent*. 2012;33(7):524-32, 534.
15. Tan WL, Wong TL, Wong MC, Lang NP. A systematic review of post-extraction alveolar hard and soft tissue dimensional changes in humans. *Clin Oral Implants Res*. 2012;23 Suppl 5:1-21. doi: 10.1111/j.1600-0501.2011.02375.x; 10.1111/j.1600-0501.2011.02375.x.
16. Covani U, Bortolaia C, Barone A, Sbordone L. Bucco-lingual crestal bone changes after immediate and delayed implant placement. *J Periodontol*. 2004;75(12):1605-1612. doi: 10.1902/jop.2004.75.12.1605.
17. Tarnow DP, Chu SJ. Human histologic verification of osseointegration of an immediate implant placed into a fresh extraction socket with excessive gap distance without primary flap closure, graft, or membrane: A case report. *Int J Periodontics Restorative Dent*. 2011;31(5):515-521.
18. Botticelli D, Berglundh T, Lindhe J. Hard-tissue alterations following immediate implant placement in extraction sites. *J Clin Periodontol*. 2004;31(10):820-828. doi: 10.1111/j.1600-051X.2004.00565.x.
19. Kan JY, Rungcharassaeng K, Umezu K, Kois JC. Dimensions of peri-implant mucosa: An evaluation of maxillary anterior single implants in humans. *J Periodontol*. 2003;74(4):557-562. doi: 10.1902/jop.2003.74.4.557.
20. Kan JY, Rungcharassaeng K, Liddel G, Henry P, Goodacre CJ. Periimplant tissue response following immediate provisional restoration of scalloped implants in the esthetic zone: A one-year pilot prospective multicenter study. *J Prosthet Dent*. 2007;97(6 Suppl):S109-18. doi: 10.1016/S0022-3913(07)60014-6; 10.1016/S0022-3913(07)60014-6.
21. Chen ST, Wilson TG, Jr, Hammerle CH. Immediate or early placement of implants following tooth extraction: Review of biologic basis, clinical procedures, and outcomes. *Int J Oral Maxillofac Implants*. 2004;19 Suppl:12-25.
22. Meijndert L, Meijer HJ, Raghoobar GM, Vissink A. A technique for standardized evaluation of soft and hard peri-implant tissues in partially edentulous patients. *J Periodontol*. 2004;75(5):646-651. doi: 10.1902/jop.2004.75.5.646.
23. Hermann JS, Schoolfield JD, Nummikoski PV, Buser D, Schenk RK, Cochran DL. Crestal bone changes around titanium implants: A methodologic study comparing linear radiographic with histometric measurements. *Int J Oral Maxillofac Implants*. 2001;16(4):475-485.

24. Vera C, De Kok IJ, Chen W, Reside G, Tyndall D, Cooper LF. Evaluation of post-implant buccal bone resorption using cone beam computed tomography: A clinical pilot study. *Int J Oral Maxillofac Implants*. 2012;27(5):1249-1257.
25. Tarnow DP, Magner AW, Fletcher P. The effect of the distance from the contact point to the crest of bone on the presence or absence of the interproximal dental papilla. *J Periodontol*. 1992;63(12):995-996. doi: 10.1902/jop.1992.63.12.995.
26. Chen ST, Darby IB, Reynolds EC. A prospective clinical study of non-submerged immediate implants: Clinical outcomes and esthetic results. *Clin Oral Implants Res*. 2007;18(5):552-562. doi: 10.1111/j.1600-0501.2007.01388.x.
27. Chen ST, Buser D. Clinical and esthetic outcomes of implants placed in postextraction sites. *Int J Oral Maxillofac Implants*. 2009;24 Suppl:186-217.