LONG-TERM EVALUATION OF PERIAPICAL HEALING FOLLOWING ENDODONTIC TREATMENT OF TEETH WITH APICAL PERIODONTITIS

Deborah A. Conner, MDiv, DDS

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Approved by:

Advisor: Martin Trope, DMD

Readers: Daniel J. Caplan, DDS, PhD

Valerie A. Murrah, DMD, MS

Mary T. Pettiette, DDS, MS

Fabricio B. Teixeira, DDS, MS, PhD

ABSTRACT

DEBORAH A. CONNER: Long-term evaluation of periapical healing
following endodontic treatment of teeth with apical periodontitis
(Under the direction of Fabricio B. Teixeira, DDS, MS, PhD; Daniel J. Caplan, DDS, PhD;
Valerie A. Murrah, DMD, MS; Mary T. Pettiette, DDS, MS; Martin Trope, DMD)

The purpose of this investigation was to evaluate long-term healing of teeth with apical periodontitis treated by dental students according to the protocol of UNC School of Dentistry, Department of Endodontics. A total of 49 patients returned for follow up (N= 55 teeth). Healing was assessed radiographically using two methods: the Periapical Index (PAI) and a Clinical Impression of Healing (CIH). Overall, favorable healing was found in 69% (PAI) and 90.3% (CIH) of teeth. Of the independent variables assessed, only patient history of tobacco use significantly affected healing in the presence of a preoperative periapical lesion (Chi Square=4.27; p=0.038) although clear differences in healing emerged based on patient diabetic status.

Conclusion: Teeth with chronic apical periodontitis treated close to the radiographic apex, with adequate apical enlargement, and with calcium hydroxide as an interappointment, intra-canal medicament had a success rate comparable to outcomes reported in the endodontic literature.

DEDICATION

To my father: educator, athlete, optimist.

To my mother: in honor of your life of service.

To my partner: for her sense of humor and ability to shine in a crisis.

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LIST OF ABBREVIATIONS

Abbreviation	
CAP	chronic apical periodontitis
CDC	Center for Disease Control
CIH	clinical impression of healing
EPT	electric pulp test
F	follow up
HTN	hypertension
IgG	immunoglobin G
IPO	immediate post operative
IRM	intermediate restorative material
IT	initial treatment
mm	millimeter(s)
MMP	matrix metalloproteinase
NiTi	nickel titanium
PAI	periapical index
PMN	polymorphonuclear leukocytes
PTH	parathyroid hormone
SS	stainless steel
UNC	University of North Carolina

CHAPTER 1
LONG-TERM EVALUATION OF PERIAPICAL HEALING IN DIABETICS AND NON-DIABETICS FOLLOWING ENDODONTIC TREATMENT OF TEETH WITH APICAL PERIODONTITIS

Abstract

The purpose of this investigation was to evaluate long-term healing of teeth with apical periodontitis from diabetic patients versus non-diabetic patients treated according to the protocol of UNC School of Dentistry, Department of Endodontics. A total of 55 teeth from 49 patients returned for follow up: 38 (67.2%) teeth from non-diabetics and 17 (32.8%) teeth from diabetic patients. Healing was assessed radiographically using two methods: the Periapical Index (PAI) with one calibrated examiner (kappa=0.81) or by a Clinical Impression of Healing (CIH) with three examiners. There were clear differences in healing based on diabetic status (74% healing in non-diabetics vs. 58% healing in diabetics), although not statistically significant, when assessed by the PAI. Differences in other independent variables were nonsignificant. The CIH showed a substantially higher outcome overall average with little difference in healed or healing of the same teeth from diabetics (94%) vs. non-diabetics (88.6%).

Introduction

Diabetes mellitus is a collection of diseases characterized by disorders with carbohydrate, protein, and lipid metabolism involving the hormone, insulin, that affects the macro- and micro- vasculature and other organ systems of diseased patients (American Diabetes Association, 1997) (Table 1). Its prevalence in the U.S. in 2005 was at least 7% (14.6 million diagnosed; 6.2 million undiagnosed) (www.niddk.nih.gov). Diabetes is found to be the leading cause of blindness, amputation, and renal failure in the U.S. It is the third leading cause of death and diabetics carry a 2-5 times greater risk of myocardial infarction and stroke than non-diabetics. Damage to the systemic health of patients is reported to be inversely proportional to glycemic control (ADA, 1997; DCCRTG, 1993).

Given its profound systemic health impact on microvasculature and resulting end-organ disease, relatively little research has been reported in the endodontic literature about the outcome of endodontic treatment - specifically healing of periapical lesions associated with apical periodontitis in diabetics. One Scandinavian epidemiological study found a greater prevalence of periapical lesions in women with long duration adult insulin-dependent diabetics (Falk, et al, 1989). Further, a case report-based evaluation observed healing of periapical rarefactions in diabetics to be similar to non-diabetics when the systemic disorder was controlled with proper therapy (Bender, et al, 1963). Yet another study of 540 endodontic treatment cases found diabetics with preoperative periradicular lesions to have a significantly reduced successful outcome compared to non-diabetics (approximately 15% versus 53%) (Fouad & Burleson, 2003). These studies have only begun to associate endodontic pathology with this systemic disease.

By contrast, the relationship between periodontal disease and diabetes has been well investigated (Taylor, et. al., 2004; Graves, et al, 2006). Recent periodontal study speculated that the break down of tissue (via cytokine dysregulation (especially TNF) and formation of advanced glycation end-products (AGEs) potentiating inflammation) may not be as decisive a factor in diabetic healing potential as the failure of adequate repair due to the loss of matrix-producing cells (fibroblasts and osteoblasts) via the mechanism of apoptosis (Graves, et al, 2006).

Irrespective of the mechanism, it is this failure of adequate repair that is most readily evidenced radiographically as periapical lesions. The Periapical Index (PAI) is one method of quantifying lesion change subsequent to endodontic therapy. Using this technique, a single, blinded, calibrated examiner scored 110 individual, randomly sequenced radiographs on a 5 point scale where 1 represents teeth with a normal periapex and 5 represents a periradicular radiolucency with radiating expansions of bone structural changes (Orstavik, et al, 1986). This method was juxtaposed to interpretation by three examiners who formed a Clinical Impression of Healing (CIH) by viewing 55 immediate post operative (IPO) and follow up (F) radiographic pairs.

The aim of this study was to evaluate long-term (1.7-5.6 year) healing of teeth from diabetic patients versus non-diabetic patients with apical periodontitis treated according to the protocol of the Department of Endodontics at UNC School of Dentistry to test the null hypothesis that there is no difference in healing of teeth with apical periodontitis on the basis of the patient's diabetic status at the 0.05 level of significance.

Materials & Methods

The material consisted of 1,009 teeth treated by 3rd and 4th year dental students at the UNC School of Dentistry, Department of Endodontics between July, 1998 and August, 2002. Teeth treated in the student clinic received nonsurgical, primary endodontic treatment and were screened preoperatively by faculty to rule out teeth with complex anatomy. There were 858 patients involved in treatment and 271 students. Of the 1,009 treated teeth, the research sample of teeth was reduced by the following sequential inclusion criteria: a) selection of only patients with necrotic pulps and chronic apical periodontitis (CAP) (N=398 teeth); then b) selection of patients for whom bite registration stents were made and could be located (N=150 teeth); and then c) random availability of remaining patients (N=55 teeth).

Given the above criteria, patients were contacted for radiographic and clinical follow-ups with financial incentives. Efforts made to recall patients for post-treatment evaluation were limited to phone calls. Three attempts were made for each in-service phone number with a message left on an answering machine or with a person, if the individual patient was unavailable. For phone numbers no longer in service, the chart was searched for other contact information and/or on-line phone directories were searched by patient name. Nonparticipation was primarily due to inability to contact the patient (phone number not in service/disconnected, no one there by that name/wrong number, left message that was never returned, no answer, patient had moved).

A total of 55 teeth from 49 patients were involved in this study. Of this total, 17 (31%) were teeth from diabetics and 38 (69%) were teeth from non-diabetics (Table 2A). Two diabetic patients had more than one tooth treated, whereas three non-diabetics had multiple teeth involved. Only one tooth from a Type 1 diabetic patient was involved in the study; sixteen teeth were from type 2 diabetics. Extracted teeth were excluded from the study. Table 2B identifies study teeth by arch, position, and diabetic status of the patient. Table 2C presents the distribution of teeth by gender vs. diabetic status.

Working diagnoses were established at the beginning of treatment with standard pulp and periapical tests: cold, percussion, palpation, probing, EPT, initial treatment (IT) radiograph with bite registration, history of present illness. And definitive diagnoses were established upon access. Patients with diabetes (and hypertension) were identified on the basis of self disclosure on UNC Dental School health history forms and confirmed that these systemic health conditions were “controlled” by medication or diet. No blood work was taken to confirm long-term glycemic control (HbA1c) nor were diabetic logs consulted to confirm daily glycemic status.

For the purposes of the study, diabetics reported the last three home monitoring readings of their blood sugar at the follow up (F) exam.

All patients included in the study had a custom bite stent made at the initial treatment (IT) or immediate post-operative (IPO) radiograph to insure a reproducible angulation of the follow up (F) radiograph. Stents were made using Rinn XCP precision instrument (Rinn Corp., Elgin, IL) bite tabs coated with adhesive and Regisil 2x (Dentsply Caulk, Milford, DE) impression material to capture an initial reproducible orientation of film to the pathological tooth and periradicular tissue.

At the time of this study, the UNC protocol for biomechanical treatment of necrotic teeth at UNC School of Dentistry Department of Endodontics required:

1. Endodontic access under rubber dam isolation with betadine or chlorhexidine disinfection of the field
2. Canal patency with #10-20 SS K-files
3. Crown-down instrumentation technique using
    - NiTi rotary orifice shapers in the coronal third;
    - NiTi rotary .06 tapers in the middle third (Profile Series 29, Tulsa Dental Products, Tulsa, OK); and
    - NiTi hand .04 tapers in the apical third to a predetermined size (Table 3)
4. Teeth irrigated with 1.25% sodium hypochlorite and RC Prep (Stone Pharmaceuticals, Philadelphia, PA) as lubricant
5. Interappointment calcium hydroxide/chlorhexidine (0.12%) dressing placed with a lentulo spiral for a minimum of 7 days
6. Asymptomatic teeth root filled with gutta percha and Roth sealer (Roth International Ltd., Chicago, IL) by lateral condensation
7. Cotton pellet and IRM (Dentsply Caulk, Milford, DE) or Cavit (3M ESPE, St. Paul, MN) temporary restoration with at least 3mm thickness
8. 6-12 month post operative follow up exams

The long-term healing rate of the teeth was determined radiographically by measuring the periapical destruction of bone. Immediate post operative (IPO) and follow up (F) radiographs of each tooth were assessed using the Periapical Index (PAI) (Orstavik, 1986), a scoring index based on histologic analysis by Brynoff, 1967. The criteria for scoring under this system are:

1 = normal apical periodontium

2 = bone structural changes indicating, but not pathognomonic for, apical periodontitis

3 = bone structural changes with some mineral loss characteristic of apical periodontitis

4 = well-defined radiolucency

5 = radiolucency with radiating expansions of bone structural changes (Figure 1)

One examiner (FT) read two randomly sequenced radiographs (IPO and F) for each tooth (a total of 110 radiographs) within 24 hours of calibration (kappa=0.81) as described by Huumonen, et al, 2003. Radiographs were scanned and presented in a PowerPoint format to be scored by the calibrated examiner (FT) based on healing of the most diseased root (in a multirooted tooth) as defined by the PAI system above. Each radiograph received a single PA score by the examiner who was blinded to prevent identification of the patient or phase of treatment (F or IPO reading). Another examiner (DAC) subsequently entered those scores in an Excel spreadsheet. Also, similar to the procedure followed in the Huumonen, 2003 investigation, improvement in periapical status was declared for a tooth when the follow up (F) radiograph reading revealed a lower score than the IPO reading.

To facilitate analyses and discussion, the change in periapical status was evaluated in two ways using the PAI. First, changes were evaluated on a point-by-point basis. For instance, if a tooth had been given an IPO rating of 3 and a F rating of 2, it was given a +1; that is, it "improved" one point (Table 4A). Second, the seemingly continuous data of the PAI scores were dichotomized such that a score of 1 or 2 was classified as "absence of disease," while a score of 3, 4, or 5 was classified as "diseased." According to this classification, change in periapical status was evaluated by movement between categories and was defined as (Table 4B):

Disease to absence-of-disease (from 5-3 at IPO to 1-2 at F)

Stayed absent (1-2 at IPO and 1-2 at F)

Stayed diseased (5-3 at IPO and 5-3 at F)

Absence-of-disease to disease (1-2 at IPO to 3-5 at F)

"Disease to absence-of-disease" and "stayed absent" were considered favorable healing while "stayed diseased" and "absence-of-disease to disease" were viewed as unfavorable. These changes were then analyzed bivariately by 7 independent variables: age, length of follow up, presence of hypertension, voids in root filling, number of treatment appointments, history of tobacco use, and sensitivity to percussion using Chi Square and the two-tailed Fisher Exact at an 0.05 level of significance (Procedure StatCalc from EpiInfo, Version 3.3.2).

In addition to the use of the Periapical Index in which radiographs were viewed randomly with individual IPO films unpaired from its F film, three individual examiners read the IPO-F paired films for a second measure deemed Clinical Impression of Healing (CIH). The Clinical approach did not require calibration; rather observers were provided information on the evaluation process and the three types of ratings to be assigned. In this second system, the readers viewed the IPO-F film pairs (with a known restoration status) to replicate clinical impression of whether a tooth had “healed,” was “healing,” or was “neither healed nor healing.”

Results

Overall, healing was found in 58% of teeth from diabetics vs. 74% of teeth from non-diabetics in the PAI (Table 4B). This difference was not statistically significant. There was no significant bivariate relationship observed between healing of teeth of diabetics or non-diabetics and any of seven independent variables: age (Table 5), follow up time (Table 6), hypertension status (Table 7), voids in root filling (Table 8), the number of treatment appointments (Table 9), history of tobacco use (Table 10), percussion sensitivity (Table 11) using Chi Square ($p>0.05$).

The CIH showed an average of 94% of teeth in diabetics (94%, 88%, and 100% from examiner 1, 2, and 3 respectively) to be “healed” or “healing” while an average of 89% of teeth in non-diabetics were judged to be “healed” or “healing” (Table 12, 13, 14).

Discussion

Diabetes mellitus is a groups of diseases associated with the lack of insulin production or a defect in the insulin molecule or cell membrane receptors for insulin. The result is a hyperglycemia with classical systemic complications: impaired wound healing, macrovascular disease, nephropathy, neuropathy, retinopathy. Diabetes mellitus also increases the pace, severity, and incidence of these complications. Conversely, control of hypergly-cemia has been associated with reduced morbidity or slowed progression among insulin dependent diabetes mellitus (IDDM) (DCCRTG, 1993).

In the current study, the material (55 teeth) received standardized primary endodontic root canal therapy from dental students, in conjunction with faculty supervision, and were diagnosed as necrotic with CAP on the basis of clinical and radiographic presentation. While this university-based study supports the hypothesis that there is no statistical difference in healing between diabetics and non-diabetics, the trends evidenced by this research support the findings of Fouad & Burleson, 2003 which demonstrated significantly fewer successful cases in patients with diabetes who demonstrate preoperative lesions.

In this study two systems of measurement were juxtaposed: the PAI and the CIH. While the Periapical Index (PAI) (Orstavik, et al, 1986), is a research tool and scoring index based on histologic analysis by Brynoff, 1967 and the Clinical Impression of Healing (CIH) is a technique more germane to clinicians. These approaches varied in three ways. First, the PAI required evaluator reliability be established through a calibration process prior to rating experimental radiographs (in this study the evaluator received a training calibration kappa of 0.81). The Clinical approach did not require calibration; rather observers were provided information on the evaluation process and the types of ratings to be assigned. Secondly the PAI observer was blinded to the phase of endodontic treatment and restoration status and viewed randomly ordered, individual radiographs. Conversely, three Clinical observers made direct comparison of IPO-F pairs. Thirdly, the scoring system for the PAI was based on a five point scale. Diagrammatic and radiographic guideline were provided (Figure 1) as well as written descriptors for each value on the PAI scale where a value of 1 represented teeth with a normal apical periodontium and 5 represented teeth with a radiolucency and radiating expansions of bony structural changes. The CIH required one of three ratings (healed, healing, or neither healed nor healing) based on the presence or absence of a periapical lesion and lamina dura. In a clinical setting, radiographic findings would be considered one diagnostic factor used in conjunction with standard clinical endodontic tests (palpation, percussion, etc.). But in a scholarly context, the PAI is an important tool to strictly assess radiographic information regarding healing on its own merits.

One of the major concerns in conducting research that requires judgements on the part of an observer, even a calibrated observer, is the reliability of ratings assigned. While the Periapical Index makes stringent efforts to standardize findings (calibration kappa must be >0.61), it is based on radiographic measures that differ from clinical tests and perceptions. One evidence of this is the discrepancy between apparent evaluations of “improvement” between the two scoring systems presented in this study. Healing in teeth of diabetic patients evaluated by a single calibrated examiner vs. three uncalibrated examiners differed widely between the two measurement systems. Fewer teeth from diabetics were classified as healed or healing in PAI versus clinical impression (58% vs. 94%) as were teeth in non-diabetics (74% vs. 89%). A second expression of this issue of reliability is in the original diagnosis of teeth included in the study. While all teeth were diagnosed clinically as having necrotic pulps with chronic apical periodontitis based on clinical tests and initial treatment (IT) radiographs, a more stringent, calibrated examiner looking at a later IPO film found that 29% of teeth from diabetics and 27% of teeth from non-diabetics were found to be “absent of disease” at baseline (PAI 1 or 2). In the case where CAP exists, all teeth should start in the 3 - to - 5 PAI category of “disease.” Conversely, since the PAI is a research tool and radiographic measure of periapical healing, it is blinded to variables available to clinicians (such as multiple angulations of radiographs) or demonstrated by other studies to affect healing: restoration status, voids in root filling, history of tobacco use, etc.

Another issue is the sample size. While it has been suggested that the validity of the study could be improved by increasing the number of calibrated examiners, it may be even more important to increase the size of the sample. One of the major drawbacks of this study was insufficient sample size to evaluate all of variables for which data was collected, for instance, the impact of final restoration and the length of root filling - variables found to be significant by some research (Ray & Trope, 1995; Sjogren, et al, 1990; Chugal, et al, 2001) but not significant in others (Ricucci & Bergenholtz, 2003).

Although 109 items of data were collected for each tooth, analysis by Chi Square was limited to variables in which cell sizes were large enough to show marginals with non-zero numbers. Although no significant differences were found between diabetics and non-diabetics and any of the other variables, several patterns emerged among diabetic patients: they were older (all >40 years of age) and predominately male; they had a longer follow up interval; there was a greater incidence of concurrent hypertension; there were a larger number of teeth with voids in the root filling; they had similar number of treatment appointments with less healing; they had a greater reported history of tobacco use (10 out of 17 vs. 8 out of 38 non-diabetics); there was more reported percussion sensitivity among diabetics (41% vs. 23% in non-diabetics). None of these comparisons were statistically significant.

Age was an interesting variable in that diabetic patients who contributed teeth were all over the age of 40. In order to “control” for this factor, only teeth from non-diabetics age 40 or more were analyzed. Hence in this study, 5 of 17 teeth (29.4%) from diabetics moved from “disease to absence-of-disease” while among non-diabetics 13 of 27 (48.1%) did so. Falk, et al, 1989 used age- and sex- matched long- and short-duration IDDM and NIDDM vs. non-diabetics to describe prevalence of diabetes in a segment of the Scandinavian population. A similar stratification would strengthen analysis of both age and hypertensive statuses since both variables are so closely associated with diabetes mellitus.

In the current study, time to follow up demonstrated a longer interval in diabetic than in non-diabetic patients. This is telling in that longer follow up intervals are associated with more definitive healing patterns by some research (Strindberg, 1956; Kerekes & Tronstad, 1979) although others find that signs of initiated healing are discernible in at least 89% of all healing roots after 1 year (Orstavik, 1996). This at least suggests that greater potential exists among teeth from non-diabetics to resolve lesions if a longer follow up interval were available thereby improving success among non-diabetics.

While some studies report gender differences in healing outcome (Chugal, et al, 2001 women had significantly higher success: 82:2% vs. 73.2%) or prevalence (Falk, et al, 1989 demonstrated greater prevalence of lesions among long-duration IDDM), the current study had insufficient sample size from which to draw conclusions. And while the size of pre-operative lesion size has been found to be significantly related to healing time for teeth with acute exacerbation of chronic apical periodontitis (AE/CAP) in some studies (Chugal, et al, 2001), the PAI does not directly measure lesion size and so results from this study cannot confirm those conclusions.

Any infection in any patient can affect carbohydrate metabolism, and therein glycemic control - indirectly, by hormones secreted during infection that are antagonistic to insulin (glucagon, cortisol, etc.), or directly, through destruction of islet cells (mumps, Coxsackie virus, rubella virus) (Rayfield, et al, 1982; Drobny, et al, 1984). Medical and periodontal research has worked to define specific morbidity associated with diabetes mellitus based on a number of factors including patient age, diabetes type, duration of diabetes, level of glycemic control; and Loe goes so far as to suggest periodontitis be considered a sixth complication of diabetes mellitus (Loe, 1993). The Diabetes Control and Complications Trial Research Group (1993) found significantly reduced development and progression of retinopathy, nephropathy, and neuropathy in an “intensive” therapy group of IDDM over a mean of 6.5 years. Under similar plaque conditions, Seppala, et al, 1993 found greater severity of disease among long duration, poorly controlled IDDM than among long duration, controlled IDDM while Taylor et al 1998 also suggest that the level of glycemic control is associated with risk and progression of periodontal disease in type 2 diabetics. On the other hand, Taylor et al 1996 suggested that severe periodontitis may increase the risk of poor glycemic control while Grossi, et al, 1997 demonstrated a positive association between treatment of periodontal disease and reduction in glycosylated hemoglobin.

In light of the morbidity associated with diabetes, treatment strategies in endodontics should be informed by the relative role of various factors at play in diabetic healing: leukocyte (especially PMN) dysfunction in adhesion, diapedesis, chemotaxis, phagocytosis in these immune compromised individuals; defects in host response (via mechanisms of hyperinflammatory response); and defects in repair potential due to apoptosis of blastic cells (Graves, et al, 2006). While the effect of immune compromise has been more thoroughly considered in endodontics, the role of pharmacological agents with regard to inflammatory mediators is developing. Advanced glycosylation end products (AGEs) are known to hyper-stimulate phagocytes in the presence of gram-negative bacterial challenge. This results in an increased production of pro-inflammatory mediators which stimulates matrix metalloproteinases (MMPs) like MMP-1 (fibroblast-derived), MMP-8 (neutrophil-derived), and MMP-13 (osteoclast-derived) (Ryan, et al, 1994; Vernillo, et al, 1994). While periodontal application of low dose doxycycline (Crout, et al, 1996) appears to inhibit host response (production of MMP-8 collagenase), it is also antibacterial. In a rat model, Ryan et al 1994 found chemically modified (non-antimicrobial) tetracyclines (CMTs) to be even more effective than doxycycline with regard to reduced incidence of long-term diabetic consequences related to altered collagen metabolism: cataract development, proteinuria (the first manifestation of diabetic nephropathy), and tooth loss in type 2 diabetic rats. A similar antibiotic solution that could inform treatment regime in endodontics associated with osseous healing (osteoclast-derived MMP-13) has not been studied. However, other research has considered the effect of exogenous PTH on bone mass in diabetics that may be associated with the inhibition of osteoblast apoptosis (Jilka, et al, 1999; Stanislaus, et al, 2000). If defects in repair potential due to differential apoptosis of blastic cells are substantiated, incorporating either antibiotic or hormonal solutions into treatment protocols may improve diabetic outcome with regard to endodontic therapy.

The current study poses questions about differential healing among diabetics with chronic infection. Although non-statistically significant differences were observed in healing of necrotic teeth with chronic apical periodontitis in diabetics and non-diabetics, the data in this study suggest the need for multivariate analysis which controls for factors of age, hypertensive status, diabetic status and history of tobacco use (effect on severity of disease and host healing response) (Grossi, et al, 1996). Apart from the independent variables suggested in this study, genetically linked hyperinflammatory response traits (hyperresponsive monocytes (Salvi, et al, 1997)), may be a factor in the destruction/repair coupling for diabetics. This should be incorporated as a variable that impacts healing in future studies (Mattson & Cerutis, 2001). Further study should also classify subjects according to degree of glycemic control by a definitive parameter such as fasting blood glucose for non-diabetics (normal <110mg/dL) or glycosylated hemoglobin levels (HbA1c) for diabetics (Murrah, 1985; Grossi, et al, 1996). One endodontic study concerned with PCR-based identification of endodontic pathogens in necrotic teeth with apical periodontitis provided such definitive measures but these findings were not directly related to healing outcome

(Fouad, et al, 2002). Incorporating both measures in further research would more precisely establish what association, if any, exists between this systemic disease in an immune compromised environment, glycemic control, and endodontic healing outcome.

In conclusion, this study identified clear differences in healing outcome according to the research measurement instrument (PAI) between non-diabetics (74%) and diabetics (58%) in 55 necrotic teeth with chronic apical periodontitis. This is a significant observation in spite of the fact that it lacks statistical significance due to low power of the study.

Acknowledgements

The authors thank radiographic examiners Dr. Daniel Oliveira and Dr. Joao Vincente Barbizam for their assistance.

TABLES

Table 1
Etiologic classification of diabetes mellitus

(adapted from American Diabetes Association,
Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997)

1. Type 1 diabetes (beta-cell destruction, usually leading to absolute insulin deficiency)
    - A. Immune related
    - B. Idiopathic
2. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
3. Other specific types
    - A. Genetic defects of beta-cell function
    - B. Genetic defects in insulin action
    - C. Diseases of the exocrine pancrease
    - D. Endocrinopathies
    - E. Drug- or chemical-induced
    - F. Infections
    - G. Uncommon forms of immune-mediated diabetes
    - H. Other genetic syndromes sometimes associated with diabetes
4. Gestational diabetes mellitus (GDM)

Table 2A
Number and percent of teeth by diabetic status

	Number	Percent
Diabetic teeth	17	31
Non-diabetic	38	69
Total	55	100

Table 2B
Number and percent of teeth by arch and position by disease category

Arch and position		Total		Disease category				
		#	%	Disease -to-absent	Stayed absent	Absent-to -disease	Stayed diseased	% success
Upper	anterior	24	43.6	10	4	2	8	58.3
	premolar	12	21.8	7	4	0	1	91.6
	molar	5	9.0	1	2	0	2	60
Lower	anterior	2	3.6	1	0	0	1	50
	premolar	6	10.9	5	1	0	0	100
	molar	6	10.9	1	2	0	3	50
Total		55	100	25	13	2	15	

Table 2C
Number of teeth by gender and by diabetic status

Gender	Diabetics	Non-diabetics
Male	14	12
Female	3	26
Total	17	38

Table 3
Minimum sizes of the last apical instrument in root canal instrumentation
Department of Endodontics, UNC School of Dentistry, 2001

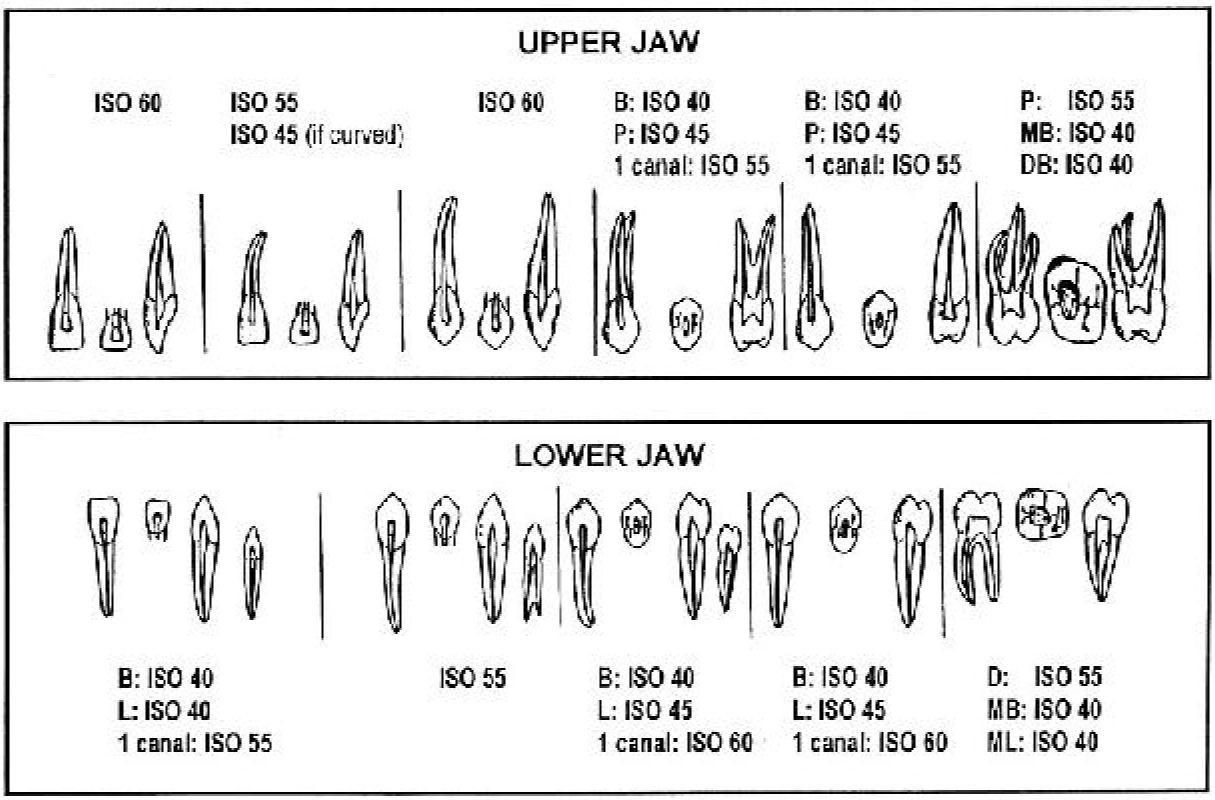


Table 4A
Number and percent of teeth by change in ordinal disease scale and by diabetic status

Degree of Change	Diabetics		Non-diabetics		Total	
	#	%	#	%	#	%
Negative change	1	6	3	8	4	7
No change	5	29	9	24	14	25
One point improvement	8	47	9	24	17	31
Two point improvement	1	6	8	21	9	16
Three point improvement	2	12	7	18	9	16
Four point improvement	0	0	2	5	2	4
Total	17	100	38	100	55	100

Note: A positive change of one point or more was observed in 37 (67%) of the total number of teeth. The number and percent of diabetic and non-diabetic patients with teeth showing one or more points of positive change were 11 (65%) and 26 (68%) respectively. Using this format for measuring progress, little difference was observed between teeth of diabetics (65%) and non-diabetics (68%). Also, the improvement rate for each group was relatively low.

Table 4B
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by diabetic status

Nature of Change	Diabetic		Non-diabetic		Total	
	#	%	#	%	#	%
Disease-to-Absence (from 5-3 to 2-1)	5	29	20	53	25	45
Stayed Disease (from 5-3 to 5-3)	7	42	8	21	15	27
Stayed Absent (from 1-2 to 1-2)	5	29	8	21	13	24
Absence-to- Disease (from 1-2 to 3-5)	0	0	2	5	2	2
Total 17	100	38	100	55	100	

Note: A total of 38 (69%) of the total number of teeth either moved from disease to absence or stayed absent of disease. For the diabetics, 10 (58%) of the teeth moved from disease to absence or stayed absent; for the non-diabetics 28 (74%) moved from disease to absence or stayed absent.

Table 5
Number and percent of teeth by age groups at follow up (F) and by diabetic status

Age Group	Diabetic		Non-diabetic		Total	
	#	%	#	%	#	%
≤19	0	6	1	3	1	2
20-29	0	0	2	5	2	4
30-39	0	0	8	21	8	15
40-49	1	6	11	29	12	22
50-59	6	35	7	18	13	24
60-69	3	18	5	13	8	15
70+	7	41	4	11	11	20
Total	17	100	38	100	55	100

Note: Over 94% of teeth in patients with diabetes were over the age of 50, whereas only 42% of the non-diabetics were 50 or over. For the total group, 58% were over 50.

Table 6
Number and percent of teeth by time to follow up (F) and by change in category of disease (dichotomous PAI scale) according to diabetic status

Recall (years)	Diabetic								Non-diabetic							
	Disease to Absence		Stayed Disease		Stayed Absent		Absence to Disease		Disease to Absence		Stayed Disease		Stayed Absent		Absence to Disease	
	#	%	#	%	#	%	#	%	#	%	#	%	#	%	#	%
<2	0	0	0	0	0	0	0	0	3	15	1	13	0	0	0	0
2-3	0	0	2	29	0	0	0	0	7	35	3	37	1	13	1	50
3-4	2	40	4	57	2	40	0	0	7	35	2	25	4	50	1	50
4 plus	3	60	1	14	3	60	0	0	3	15	2	25	3	37	0	0
Total	5	100	7	100	5	100	0	0	20	100	8	100	8	100	2	100

Table 7
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by diabetic and hypertensive status

Nature of Change	**Hypertension**							
	Diabetic				**Non-diabetic**			
	Yes		**No**		**Yes**		**No**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	5	36	0	0	3	37	17	56
Stayed Disease (from 5-3 to 5-3)	6	43	1	33	2	26	6	20
Stayed Absent (from 1-2 to 1-2)	3	21	2	67	3	37	5	17
Absence-to- Disease (from 1-2 to 3-5)	0	0	0	0	0	0	2	7
Total	14	100	3	100	8	100	30	100

Note: HTN was reported in approximately 82% of diabetics vs 21% of non-diabetics.

Table 8
Number and percent of voids in root fillings in teeth by diabetic status (dichotomous PAI scale) and by change in category of disease

Nature of Change	**Void In Root Fillings**							
	Diabetic				**Non-diabetic**			
	Yes		**No**		**Yes**		**No**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	1	34	4	29	3	100	17	48
Stayed Disease (from 5-3 to 5-3)	1	33	6	42	0	0	8	23
Stayed Absent (from 1-2 to 1-2)	1	33	4	29	0	0	8	23
Absence-to- Disease (from 1-2 to 3-5)	0	0	0	0	0	0	2	6
Total 3	100	14	100	3	100	35	100	

Note: Voids were reported in 18% of teeth in diabetics (2 were absent of disease at follow up (F)) vs. 8% of non-diabetics (all 3 were absent of disease at follow up (F)).

Table 9
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by number of treatment appointments according to diabetic status

	Diabetic								Non-diabetic							
Appointments	**Two**		**Three**		**Four**		**Five**		**Two**		**Three**		**Four**		**Five**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	1	14	2	25	2	100	0	0	15	56	3	38	1	50	1	100
Stayed Disease (from 5-3 to 5-3)	3	43	4	50	0	0	0	0	6	22	2	25	0	0	0	0
Stayed Absent (from 1-2 to 1-2)	3	43	2	25	0	0	0	0	4	15	3	38	1	50	0	0
Absence-to- Disease (from 1-2 to 3-5)	0	0	0	0	0	0	0	0	2	7	0	0	0	0	0	0
Total	7	100	8	100	2	100	0	0	27	100	8	100	2	100	1	100

Note: In diabetics 7/17 (41%) teeth were completed in 2 appointments vs 27/38 (71%) in non-diabetics.

Table 10
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by history of patient tobacco use according to diabetic status

Nature of Change	**History of Patient Tobacco Use**							
	Diabetic				**Non-diabetic**			
	Yes		**No**		**Yes**		**No**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	3	30	2	28	4	50	17	57
Stayed Disease (from 5-3 to 5-3)	7	70	0	0	2	25	6	20
Stayed Absent (from 1-2 to 1-2)	0	0	5	72	1	13	6	20
Absence-to- Disease (from 1-2 to 3-5)	0	0	0	0	1	13	1	3
Total	10	100	7	100	8	100	30	100

Note: Approximately 81% of the patients who had no history of tobacco use registered disease to absence or stayed absent PAI rating. 59% of teeth from diabetics had a tobacco use history (with only 30% absence of disease at follow up (F)) vs non-diabetics, 21% (8 out of 38) (with 63% absence of disease at follow up (F)).

Table 11
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by sensitivity to percussion according to diabetic status

Nature of Change	**Tooth Percussion**							
	Diabetic				**Non-diabetic**			
	Yes		**No**		**Yes**		**No**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	1	14	4	40	4	58	16	52
Stayed Disease (from 5-3 to 5-3)	2	28	5	50	1	14	7	23
Stayed Absent (from 1-2 to 1-2)	4	58	1	10	2	28	6	19
Absence-to- Disease (from 1-2 to 3-5)	0	0	0	0	0	0	2	6
Total	7	100	10	100	7	100	31	100

Note: Sensitivity to percussion was observed in 7/17 (41%) of diabetics vs 7/38 (23%) non-diabetics.

Table 12
Number and percent of teeth by clinical perception of healing and by diabetic status (Reader 1)

Clinical perception	Diabetic # (%)	Non-diabetic # (%)	Total # (%)
Healed	11 (65)	22 (58)	33
Healing	5 (29)	13 (34)	18
Not healed/healing	1	3	4
Total	17	38	55

Note: Reader 1 identified a total of 51 teeth (93%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs

Table 13
Number and percent of teeth by clinical perception of healing and by diabetic status (Reader 2)

Clinical perception	Diabetic # (%)	Non-diabetic # (%)	Total # (%)
Healed	9 (53)	21 (55)	30
Healing	6 (35)	12 (32)	18
Not healed/healing	2	5	7
Total	17	38	55

Note: Reader 2 identified a total of 48 teeth (87%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs

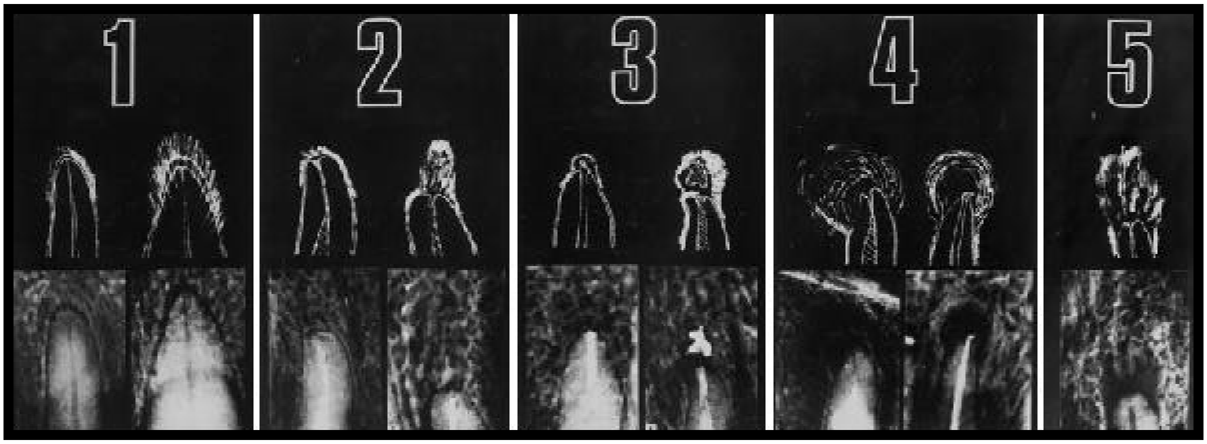
Table 14
Number and percent of teeth by clinical perception of healing and by diabetic status (Reader 3)

Clinical perception	Diabetic # (%)	Non-diabetic # (%)	Total # (%)
Healed	10 (59)	17 (45)	27
Healing	7 (41)	16 (42)	23
Not healed/healing	0	5	5
Total	17	38	55

Note: Reader 3 identified a total of 50 teeth (91%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs.

FIGURES

Figure 1
PAI diagrammatic & radiographic reference



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CHAPTER 2
PERIAPICAL HEALING FOLLOWING ENDODONTIC TREATMENT OF TEETH WITH APICAL PERIODONTITIS USING A STANDARD PROTOCOL

Abstract

The purpose of this investigation was to evaluate long-term (1.7-5.6 year) healing of teeth from patients with apical periodontitis treated in the undergraduate clinic according to the protocol of UNC School of Dentistry, Department of Endodontics. The protocol included crown-down close to working length and apical enlargement to a predetermined size and distance from the radiographic apex for each canal, copious irrigation with 1.25% hypochlorite, and calcium hydroxide as an intracanal medicament. A total of 55 teeth from 49 patients returned for follow up. Healing was assessed radiographically using two methods: the Periapical Index (PAI) with one calibrated examiner (kappa=0.81) and by a Clinical Impression of Healing (CIH) with three examiners. Overall, the PAI assessment demonstrated favorable healing in 69% of necrotic teeth with apical periodontitis. A second CIH measure (of the same teeth) among three examiners showed a substantially higher outcome with “healed” or “healing” teeth averaging 90.3% when immediate post-operative (IPO) and follow up (F) radiographic pairs were viewed in a side-by-side comparison (examiner 1, 2, and 3: 93%, 87%, and 91% respectively) (Table 13, 14, 15).

Conclusion: Teeth with chronic apical periodontitis treated close to the radiographic apex, with adequate apical enlargement, and with calcium hydroxide as an interappointment, intra-canal medicament have a success rate comparable to outcomes reported in the literature.

Introduction

Outcome studies of primary endodontic treatment have consistently found teeth with preoperative radiographic lesions to have a poorer prognosis than teeth without periapical pathology (Strindberg, 1956; Kerekes & Tronstad, 1979; Bystrom, et al, 1987; Sjogren, et al, 1990; Chugal, et al, 2003). Success has ranged as much as

20% less than treatment of teeth without apical periodontitis. However, definitions of success have been based on a variety measurement systems: clinical and radiographic examination (Strindberg, 1956; Sjogren, et al, 1997); histologic and radiographic (Brynolf, 1967; Orstavik, et al, 1986); and tooth survival (Dammaschke, et al, 2003; Stoll, et al, 2005) among others.

As well, many additional factors have been found to be significant in the determination of success including: length of follow up interval (Strindberg, 1956; Bystrom, et al, 1987); length of instrumentation and fill (Strindberg,1956; Sjogren, et al, 1990; Chugal, et al, 2003); quality of the root filling and presence of a definitive coronal restoration (Ray & Trope, 1985); bacteriological status at the time of root fill (Sjogren, et al, 1997); host metabolic disorders (Fouad & Burleson, 2003).

While determination of endodontic treatment success has varied based on the factors considered and the method of evaluation, most studies include some radiographic measure by which healing (or its absence) is measured. The Periapical Index (PAI) (Orstavik, et al, 1986) is one such method of quantifying degrees of healing subsequent to endodontic therapy.

The aim of this outcome study was to evaluate long-term (1.7-5.6 year) healing of teeth in patients with apical periodontitis treated according to the standardized protocol of the Department of Endodontics at UNC School of Dentistry in order to provide additional evidence-based treatment protocols and prognosis. This investigation radiographically evaluated long-term periapical healing of chronically infected teeth (necrotic pulps, chronic apical periodontitis) treated by novice practitioners.

Hypothesis: Teeth with chronic apical periodontitis treated close to but not through the apex, with adequate apical enlargement, and with calcium hydroxide intracanal, interappointment medicament will have a comparable success rate compared to outcomes reported in the literature (Table 1).

Materials & Methods

The material is comprised of 1,009 teeth treated by 3rd and 4th year dental students at the UNC School of Dentistry, Department of Endodontics between July, 1998 and August, 2002. Teeth treated in the student clinic received nonsurgical, primary endodontic treatment and were screened preoperatively by faculty to rule out teeth with complex anatomy. There were 858 patients involved in treatment; 271 students. Of the 1,009 treatment teeth, the research sample of teeth was further reduced by the following sequential inclusion criteria: a) selection of only patients with necrotic pulps and chronic apical periodontitis (CAP) (N=398 teeth); then b) selection of patients for whom bite registration stents were made and could be located (N=150 teeth); and then c) random availability of remaining patients (N=55 teeth; 49 patients).

Given the above criteria, patients were invited for follow ups with financial incentives. Efforts made to recall patients for post-treatment evaluation were limited to phone calls. Three attempts were made for each in-service phone number with a message left on an answering machine or with a person if the individual patient was unavailable. For phone numbers no longer in service, the chart was searched for other contact information and/or on-line phone directories were searched by patient name. By far, nonparticipation was most frequently due to an inability to contact the patient (phone number not in service/disconnected, no one there by that name/wrong number, left message that was never returned, no answer, patient had moved).

A total of 55 teeth from 49 patients were involved in this outcome study. Extracted teeth were excluded from the study. Table 2 identifies study teeth by arch and position. Table 3 presents the distribution of teeth by gender and by change in PAI category of disease (from the IPO score to the F score).

Working diagnoses were established at the beginning of treatment with standard pulp tests (cold, percussion, palpation, probing, EPT, initial treatment (IT) radiograph with bite registration, history of present illness) with definitive diagnoses established upon access. Patients with systemic health considerations (e.g., diabetes) were identified on the basis of self disclosure on UNC Dental School health history forms and reported (but not confirmed by blood work) that systemic health conditions were “controlled” by medication or diet.

All patients included in the study had a custom bite stent made at the initial treatment (IT) or immediate post-operative (IPO) radiograph to insure a reproducible angulation of the follow up (F) radiograph. Stents were made using Rinn XCP precision instrument (Rinn Corp., Elgin, IL) bite tabs coated with adhesive and Regisil 2x (DENTSPLY Caulk, Milford, DE) impression material to capture an initial reproducible orientation of film to the pathological tooth and periapex.

At the time of this study, the UNC protocol for biomechanical treatment of necrotic teeth at UNC School of Dentistry Department of Endodontics required:

1. endodontic access under rubber dam isolation with betadine or chlorhexidine disinfection of the field
2. canal patency with #10-20 SS K-files
3. crown-down instrumentation technique using
   - NiTi rotary files orifice shapers in the coronal 1/3;
   - rotary .06 tapers in the middle 1/3 (Profile Series 29, Tulsa Dental Products, Tulsa, OK); and
   - hand .04 tapers in the apical 1/3 to a predetermined size (Table 4)

4. irrigation with 1.25% sodium hypochlorite; RC Prep (Stone Pharmaceuticals, Philadelphia, PA) available as a lubricant

5. interappointment calcium hydroxide with 0.12% chlorhexidine dressing placed with a lentulo spiral for a minimum of 7 days

6. asymptomatic teeth root-filled with gutta percha, lateral condensation, Roth sealer (Roth International Ltd., Chicago, IL)

7. cotton pellet and ≥3mm IRM (DENTSPLY Caulk, Milford, DE) or Cavit (3M ESPE, St. Paul, MN) temporary restoration

8. 6-12 month post operative follow up exam

The long-term healing rate of the teeth was determined radiographically by measuring the periapical status. Immediate post operative (IPO) and follow up (F) radiographs of each tooth were read and assessed using the Periapical Index (PAI) (Orstavik, et al, 1986), a scoring index based on histologic analysis by Brynoff, 1967. With the PAI system, the calibrating examiner (FT) read and scored a set of one hundred individual training radiographs (controls) provided on a CD using radiographic and diagrammatic guides (Figure 1) in conjunction with the following written descriptors of each of 5 PAI categories:

1 = normal apical periodontium

2 = bone structural changes indicating, but not pathognomonic for, apical periodontitis

3 = bone structural changes with some mineral loss characteristic of apical periodontitis

4 = well-defined radiolucency

5 = radiolucency with radiating expansions of bone structural changes

A second investigator (DAC) graded the training results according to a “true” score assigned by gold standard examiners who developed the system. Training radiographs were read on day 1, 2, and 5; when the calibrating examiner deviated from the gold standard, discussion and retesting occurred. By day 5, however, the intra- observer reproducibility (kappa) was required to be greater than 0.61 in order to proceed to the experimental radiographs read on day 6.

Following the example of several studies (Huumonen, et al, 2003; Friedman, et al, 2003; Farzaneh, et al, 2004) only one examiner (FT) read two radiographs (IPO and F) for each tooth (a total of 110 radiographs) within 24 hours of calibration (kappa=0.81). Treatment radiographs were scanned and prepared digitally (by DAC) for review by an endodontist (FT). Randomly sequenced radiographs were then presented in a

PowerPoint presentation and scored by a blinded, calibrated examiner (FT) based on osseous healing (of the most periapically involved root in a multirooted tooth) defined by the PAI system above. Each radiograph received a single PA score by the examiner who was blinded to prevent identification of the patient or phase of treatment (IPO or F radiograph). Another investigator (DAC) subsequently entered those scores in an Excel spreadsheet such that an individual tooth could be analyzed for the rate of change for IPO-F pairs.

To facilitate analyses and discussion, the change in periapical status was evaluated in two ways using the PAI. First, changes were evaluated on a point-by-point basis. Similarly to the procedure followed in the Huumonen, 2003 investigation, improvement in periapical status was declared for a tooth when the follow up (F) radiograph reading revealed a lower score than the IPO reading. For instance, if a tooth had been given an IPO rating of 3 and a F rating of 2, it was given a +1; that is, it "improved" one point. Secondly, the seemingly continuous data of the PAI scores were dichotomized such that a score of 1 or 2 was classified as "absence of disease," while a score of 3, 4, or 5 was classified as "diseased." According to this classification, change in periapical status was evaluated by movement between categories at two different time periods and were defined as:

Disease to absence-of-disease (from 5-3 at IPO to 1-2 at F)

Stayed absent (1-2 at IPO and 1-2 at F)

Stayed diseased (5-3 at IPO and 5-3 at F)

Absence-of-disease to disease (1-2 at IPO to 3-5 at F)

"Disease to absence-of-disease" and "stayed absent" were considered favorable healing while "stayed diseased" and "absence-of-disease to disease" were viewed as unfavorable. These changes then were analyzed bivariately by 8 independent variables: age, length of follow up, presence of systemic factors, voids in root filling, number of treatment appointments, history of tobacco use, sensitivity to percussion, length of root filling using Chi Square and the two-tailed Fisher Exact ($p<0.05$) (Procedure StatCalc from EpiInfo, Version 3.3.2).

In addition to the use of the Periapical Index in which radiographs were viewed randomly with individual IPO films unpaired from their F films, three individual examiners 1, 2, and 3 (FT, DO, RW) read the IPO-F paired films for a second measure deemed Clinical Impression of Healing (CIH). In this second system, the readers viewed the IPO and F film pairs side-by-side in a PowerPoint presentation to replicate clinical impression of whether a tooth had "healed," was "healing," or was "neither healed nor healing."

Data was collected on 109 items of treatment data on each case. Students treating each case completed Proctor Sheets which were then transcribed into Microsoft Access for later export into Microsoft Excel by a single investigator (DAC). Tables provided univariate and bivariate relationships between dependent (healing) and independant variables while tests for statistical significance were based on Chi square and two-tailed Fischer extact ($p<0.05$).

Results

Two methods were used to assess outcome in this study: PAI and CIH. The PAI stringently defined disease or its absence on a 1-to-5 scale. When teeth were analyzed by change in PAI score on a point-by-point basis, 67.2% of teeth “improved” while 7.2% “got worse” and 25.4% had no change in their IPO-to-F score (Table 5A).

When the change in periapical status was evaluated in terms of dichotomous categories, 69% of teeth demonstrated favorable healing overall (Table 5B). When teeth from patients with known systemic factors (hypertension, diabetes mellitus, history of tobacco use) were excluded, percentage of healing in teeth improved to 73.8%. Healing (PAI categories of “disease to absence” and “stayed absent”) was evaluated in terms of 9 independent variables: tooth arch and position (Table 2), gender (Table 3), age (Table 6), length of follow up (Table 7), voids in root filling (Table 8), the number of treatment appointments (Table 9), history of tobacco use (Table 10), percussion sensitivity (Table 11), length of root filling (Table 12). A significance difference in healing was found under only one circumstance. Teeth that started with disease as defined by the PAI classification (i.e, teeth that had an immediate post op PAI reading in the 3 - to - 5 category) were 4.07 times less likely to heal than teeth that started without disease if there was a reported history of tobacco use (Chi Square=4.27; p=0.038).

In contrast to the PAI, three examiners formed a clinical impression of healing in which an average of 90.3% of necrotic teeth with apical periodontitis were found to be “healed” or “healing” when IPO and F radiographic pairs were viewed in a side-by-side comparison (examiner 1, 2, and 3: 93%, 87%, and 91% respectively) (Table 13, 14, 15).

Discussion

In the current study, the material (55 teeth) received standardized primary endodontic root canal therapy from dental students, in conjunction with faculty supervision. Teeth included in the study were diagnosed as necrotic with chronic apical periodontitis (CAP) on the basis of clinical and radiographic presentation at the time of initial treatment. The study sample was reduced sequentially from 1,009 teeth by excluding teeth 1. which had initial treatment diagnoses other than necrotic with chronic apical periodontitis, 2. for which bite stents could not be located; 3. from patients who not could be contacted by telephone. This resulted in a potential sample of 150 teeth for which reproducible radiographic angulation could be expected and an actual sample of 55 teeth (36.6%) from patients who could be contacted and agreed to come for a follow up exam with financial incentive. This recall rate reflects the highly transient nature of the Triangle area of NC from which University patients are drawn and compares favorably with another recent outcome study which recalled 18.7% - 20% of patients at 4 or more years (Chugal, et al, 2001; Friedman, et al, 2003; Farzaneh, et al, 2004).

Of nine major outcome studies that form the basis of comparison for this study, no other study reports the use of a custom bite stent to aid in reproducible angulation of radiographs at the follow up exam. As well, only 3 of these studies report treatment by dental students (Kerekes & Tronstad, 1979; Molven & Halse, 1988; Sjogren, et al, 1990). One study (Bystrom, et al, 1987) based their findings on single rooted teeth only. Only two other studies used teeth as the unit of measurement (Strindberg, 1956; Seltzer, et al, 1963); others used the root as the basis of measurement (Kerekes & Tronstad,1979; Molven & Halse, 1988; Sjogren, et al, 1990; Chugal, et al, 2001; Friedman, et al, 2003; Farzaneh, et al, 2004). Follow up times varied from 6 months (Seltzer, et al, 1963) to 17 years (Molven & Halse, 1988). Two studies reported the use of radiographic series to determine radio-graphic end points rather than using single IPO and F films (Bystrom, et al, 1987; Molven & Halse, 1988). All report following Strindberg or modified Strindberg criteria of success except one (Seltzer, et al, 1963) but criteria for calibration tend to be oblique with the exception of Molven & Halse, 1988; Sjogren, et al, 1990; Friedman, et al, 2003; Farzaneh, et al, 2004.

One of the major concerns in conducting research which requires judgements on the part of an observer, even a calibrated observer, is the reliability of ratings assigned. In this study there is a seeming discrepancy in outcome between the two systems of evaluation. On the one hand, the Periapical Index requires stringent standardization from its examiners (calibration kappa must be >0.61) with analysis of randomized, individual radiographs. In the current study the calibrating examiner (FT) scored a kappa of 0.82, 0.9, 0.83 on sequential readings prior to proceeding to 110 experimental radiographs. Based on this intensive standardization, overall success was found to be 69% (Table 5B). But because teeth from patients with systemic factors were found to contribute 58.2% of the data, separate calculations were made for teeth from patients with and without reported history of systemic factors that could influence healing potential: hypertension, diabetes mellitus, history of tobacco use. Success was found to be 65.6% with and 73.8% without the presence of these factors (Table 16). As well, it was found that teeth that started with disease as defined by the PAI classification (i.e., teeth that had an immediate post op PAI reading in the 3 - to - 5 category) were 4.07 times less likely to heal than teeth that started without disease if there was a reported history of tobacco use (Chi Square=4.27; p=0.038).

While the PAI is a radiographic measure correlated with histologic findings, the CIH method was performed by dentists who read IPO and F radiographs in side-by-side pairs to assess whether a tooth had healed, was healing, or was neither healed nor healing. Outcomes from this method were substantially more favorable averaging 90.3%. Unlike a Strindberg-based methodology, however, it was beyond the scope of this study to account for clinical examination data regarding patient signs and symptoms from the follow up evaluation.

One aspect of reliability is the above mentioned variation in outcome based on two different methods of assessment. A second issue regarding reliability centers on an inclusion criterion: diagnosis. While all teeth included in the study were preoperatively diagnosed clinically as necrotic with chronic apical periodontitis based on pulp tests and initial treatment (IT) radiographs, a more stringent, calibrated examiner looking at baseline IPO films judged 26% of the teeth to lack periapical lesions (PAI scores of 1 or 2) typically associated with CAP (Table 5B). By convention in the case where CAP exists, all teeth should start in the 3 - to - 5 PAI category of "disease" for inclusion in this study. However, since the PAI is a solely radiographic measure of osseous healing, it is blinded to variables available to initial treatment (IT) clinicians (such as multiple angulations of radiographs, findings upon endodontic access) or variables demonstrated by other studies to affect healing: the status of coronal seal, voids in root filling, history of tobacco use, length of follow up, etc. Examiners in the clinical impression of healing methodology were also blinded to these variables but they had the advantage of direct visual comparison of IPO and F pairs. In agreement with Strindberg, 1956 and Bystrom, et al, 1987, this visual comparison allowed the examiners to not judge a tooth as an outcome failure where there was decrease in the size of the lesion at the 5 year or less follow up.

Another issue relating to reliability is the small sample size. Although 109 items of data were collected for each tooth, analysis by Chi Square and Fischer extact was limited to bivariate analysis of variables in which cell sizes were large enough to show marginals with non-zero numbers (see Table 17). While it has been suggested that the validity of the current study could be improved by increasing the number of calibrated examiners, it may be even more important to increase the size of the sample in order to analyze data multivariately. This is especially true when the sample seems skewed toward teeth from patients in whom we would suspect compromised health and healing:

- 58.2% of the data was contributed by patients with systemic factors (hypertension (HTN), diabetes mellitus, history of tobacco use) that may affect healing. **HTN**, with its associated atherosclerotic vascular disease, has been associated increased mortality and morbidity - increased vascular resistance in the form of end-organ disease: stoke, myocardial infarction, kidney failure, blindness, etc. Pathophysiologically, atherosclerotic lesions develop in the intimal layer of large vessels from smooth muscle cell proliferation, insudation of lipid, endothelial injury, encrustation and thrombosis. Some authors speculate that T lymphocytes present in the plaque reflect an autoimmune response important for lesion progression (Rubin & Farber, 1995). In light of the morbidity associated with **diabetes**, expectations concerning endodontic outcome should be informed by the relative role of various factors at play in diabetic healing: leukocyte (especially PMN) dysfunction in adhesion, diapedesis, chemotaxis, and phagocytosis in these immune compromised individuals; defects in host response (via mechanisms of hyperinflammatory response); and defects in repair potential due to differential apoptosis of blastic cells (Graves, et al, 2006). Although it is widely accepted that **smoking** impairs wound healing due to decreased blood flow, hypoxia (increased carbon monoxide), and damage to the microcirculation (Freiman, et al, 2004), recent in vitro research proposed one mechanism by which nicotine may impair the ability of fibroblasts to adhere to and communicate with one another and with the extracellular matrix (Snyder, et al, 2002). Other research associates smoking with decreased immune response by altering neutrophil function, decreased IgG production, and impaired lymphocyte proliferation (Savage, et al, 1991; Johnson & Hill, 2004).
- 40% of the sample teeth were from patients 50 years old or more. Immune senescence is a term used with reference to age-related changes in immune function reported in many studies. These changes may include impaired neutrophil response (reduced numbers and bacteriocidal activity) (innate immune system) with corresponding increased incidence of infectious disease, qualitative changes in antibody function and affinity, enhanced inflammation, atrophy of the thymus (adaptive immune system) with restricted production of naive T cells (Lord, et al, 2001; LeMaoult, et al, 1997; Gavazzi & Krause, 2002; McGlauchlen & Vogel, 2003; Effros, 2001).
- Only 27% (15/55 teeth) had greater than 4 year follow up associated with more definitive healing (Strindberg, 1956; Kerekes & Tronstad, 1979). Further, time to follow up demonstrated a shorter average interval in teeth from patients without known systemic factors (3.19 years) vs. those with known systemic factors

(3.68 years). This is telling in that shorter follow up intervals are associated with less definitive healing patterns by some research (Strindberg, 1956; Kerekes & Tronstad, 1979) although others find that signs of initiated healing are discernible in at least 89% of all healing roots after 1 year (Orstavik, 1996). This at least suggests that greater potential exists among teeth from patients without known systemic factors to resolve lesions if a longer follow up interval were available thereby improving success among that group.

Since the sample in this study seems skewed toward teeth from patients in whom we would suspect compromised health and healing, multivariable regression would shed light on the relative impact of the independent variables. However, sample size limits discussion to bivariate analysis. While some studies report **gender** differences in healing outcome (Chugal, et al, 2001 women had significantly higher success: 82:2% vs. 73.2%) or prevalence (Falk, et al, 1989 demonstrated greater prevalence of lesions among long-duration IDDM), the current study found a non-significant difference in which 76% women vs. 62% men demonstrated favorable results (Table 3). And while pre-operative **lesion size** has been found to be significantly related to healing time for teeth in some studies (Chugal, et al, 2001), the PAI does not directly measure lesion size and so results from this study cannot confirm those conclusions.

The relative impact of **final restoration** and **the length of root filling** on outcome could not be analyzed. While these variables were found to be significant by some research (Ray & Trope, 1995; Sjogren, et al, 1990; Chugal, et al, 2001) they were not significant in others (Ricucci & Bergenholtz, 2003). In the current study, all teeth except four in the follow up group had a definitive restoration. Of 3 teeth with IRM, 2 “stayed diseased;” 1 moved from “disease to absence-of-disease.” One tooth with no restoration “stayed absent” of disease. Of the 15 (27%) teeth that “stayed diseased” in the PAI system of evaluation, 12 were filled within 0-2mm of the apex; 3 were reported as flush radiographically with the apex (Table 12).

Similarly, neither the relative impact of **number of treatment appointment**s nor the presence of voids in the root filling on outcome could be assessed. While 61.8% of teeth were completed in 2 appointments and 90.9% had been completed by 3 appointments, approximately 2/3 of the failures were from the 2 appointment group (11 teeth) and 1/3 were from the 3 appointment group (6 teeth) (Table 9). While only 6 **root filling voids** were observed in the 55 treated teeth, 5 teeth were found to be absent of disease radiographically (Table 8) although other literature suggests that the presence of voids contributes to failure (Ray & Trope, 1985). Lastly, while the literature has attested to the difficulty of associating clinical signs and symptoms with histological state of pulpal disease (Seltzer, et al, 1963; Dummer, et al, 1980), 10 of 13 teeth judged by the PAI to be without disease at follow up reported **percussion sensitivity** (Table 18). Table 11 demonstrates a clear though non-significant relationship between tooth sensitivity and age: 69% (9/13) teeth reporting sensitivity to percussion were in patients over 50 years old. Only 6 of 13 teeth with percussion sensitivity were from diabetics, contrary to trends evidenced by Fouad & Burleson, 2003.

Because of the relatively small number of teeth that were available for study in this investigation, analyses were limited to exploring the relationship between only one independent variable and the dependent variable (healing) at a time. Results of this study lead to the conclusion that, were the sample large enough, multivariate analyses would demonstrate the relative import of independent factors. Toward that end, a multicenter study with standardized data collection and data base would address the issue of size and regional idiosyncracies or bias in the sample. Given the percentage of patients involved in this study with systemic factors (e.g., HTN, diabetes mellitus, history of tobacco use), further study should specifically evaluate the impact of systemic health and habits on treatment protocols and outcome related to the healing of apical periodontitis.

Based on the UNC standardized technique, one finding in this healing outcome study stands out: it was found that teeth that started with radiographic disease as defined by the PAI classification (i.e, teeth that had an immediate post op PAI reading in the 3 - to - 5 category) were 4.07 times less likely to heal than teeth that started without disease if there was a reported history of tobacco use (Chi Square=4.27; p=0.038) (Figure 2). The overall success by the research standard (PAI) was found to be 69% (see Table 5B). But because teeth from patients with systemic factors were found to contribute 58.2% of the data, separate calculations were made for teeth from patients with and without reported history of systemic factors that could influence healing potential: hypertension, diabetes mellitus, history of tobacco use. Success was found to be 65.6% with and 73.8% without the presence of these factors (Table 16). This was consistent with endodontic healing outcome literature in which treatment was rendered by dental students using the same radiographic instrument of measurement (Friedman et al 2003; Farzaneh et al 2004). As well, the finding of the CIH measure (90.9% healed or healing teeth) was consistent with endodontic literature in which treatment was rendered by dental students using methods of radiographic analysis with similar definitions of success or calibration strategies (Kerekes & Tronstad, 1979; Sjogren et al 1990).

In light of non-endodontic treatment alternatives, it is essential to use endodontic techniques which consistently achieve the highest healing outcome. The UNC model provides one such technique. But given an increasing number of patients with compromising systemic health and habits, research on intracanal pharmacological strategies (e.g., corticosteriods, antibiotics) and root filling materials promise even more glowing results for endodontic healing outcome.

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TABLES

Table 1
Literature-based success rates (NSRCT) of teeth with a periapical lucency

Strindberg, 1956	68%
Seltzer, et al, 1963	76%
Kerekes & Tronstad, 1979	85%
Bystrom, et al, 1987	85%
Molven & Halse, 1988	66%
Sjogren, et al, 1990	86%
Chugal, et al, 2001	63%
Friedman, et al, 2003	74%
Farzaneh, et al, 2004	81%

Table 2
Number and percent of teeth by arch and position by disease category

Arch and position		**Total**		**Disease category**				
		#	**%**	**Disease -to-absent**	**Stayed absent**	**Absent-to -disease**	**Stayed diseased**	**% success**
Upper	anterior	24	43.6	10	4	2	8	58.3
	premolar	12	21.8	7	4	0	1	91.6
	molar	5	9.0	1	2	0	2	60
Lower	anterior	2	3.6	1	0	0	1	50
	premolar	6	10.9	5	1	0	0	100
	molar	6	10.9	1	2	0	3	50
Total		55	100	25	13	2	15	

Table 3
Number and percent of teeth by change in dichotomized category of disease (PAI) and by gender

Nature of Change	Female #	Female %	Male #	Male %	Total #	Total %
Disease-to-Absence (from 5-3 to 2-1)	16	55	9	35	25	45
Stayed Disease (from 5-3 to 5-3)	7	24	8	30	15	27
Stayed Absent (from 1-2 to 1-2)	6	21	7	27	13	24
Absence-to-Disease (from 1-2 to 3-5)	0	0	2	8	2	4
Total	29	100	26	100	55	100

Note: Favorable healing was found in 22/29 (76%) of females versus 16/26 (62%) of males

Table 4
Minimum sizes of last apical instrument in root canal instrumentation
Department of Endodontics, UNC School of Dentistry 2001

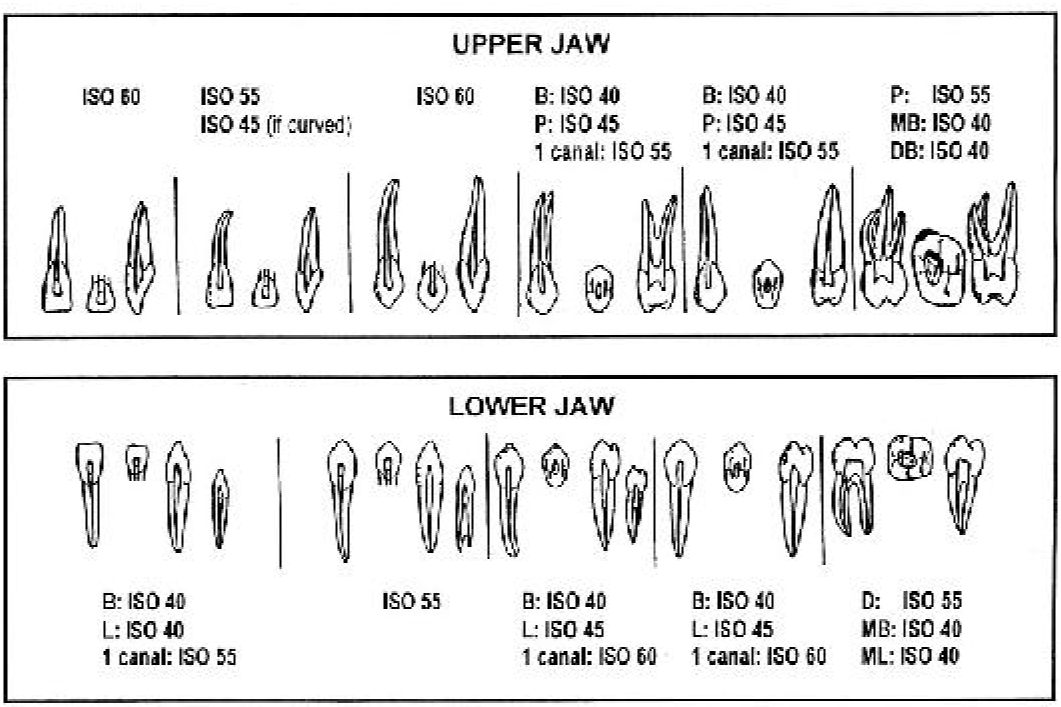


Table 5A
Number and percent of teeth by change in ordinal disease scale (PAI)

Degree of Change	#	%
Negative change	4	7
No change	14	25
One point improvement	17	31
Two point improvement	9	16
Three point improvement	9	16
Four point improvement	2	4
Total	55	100

Note: A positive change of one point or more was observed in 37 (67%) of the total number of teeth. In teeth with no change, 7 teeth "stayed absent" of disease; 7 "stayed diseased"

Table 5B
Number and percent of teeth by change in dichotomized category of disease (PAI)

Nature of Change	#	%
Disease-to-Absence (from 5-3 to 2-1)	25	45
Stayed Disease (from 5-3 to 5-3)	15	27
Stayed Absent (from 1-2 to 1-2)	13	24
Absence-to-Disease (from 1-2 to 3-5)	2	2
Total	55	100

Note: A total of 38 (69%) of the total number of teeth either moved from disease-to-absence or stayed absent of disease.

Table 6
Number and percent of teeth in the total sample by age group and by change in category of disease (dichotomous PAI scale)

Age Group	Disease-to-Absence (5-3 to 2-1)		Stayed Disease (5-3 to 5-3)		Stayed Absent (1-2 to 1-2)		Absence-to-Disease (1-2 to 3-5)		Total	
	#	%	#	%	#	%	#	%	#	%
<20	0	0	1	7	0	0	0	0	1	2
20-29	0	0	1	7	1	8	0	0	2	4
30-39	7	28	1	7	0	0	0	0	8	15
40-49	5	20	5	32	1	8	1	50	12	22
50-59	3	12	3	20	6	45	1	50	13	24
60-69	6	24	1	7	1	8	0	0	8	15
70+	4	16	3	20	4	31	0	0	11	20
Total	25	100	15	100	13	100	2	100	55	100

Note: 58% were over 50 years of age. 38/55 = 69% absent of disease at follow up (F)

Table 7
Number and percent of teeth by length of follow up (F) and by change in category of disease (dichotomous PAI scale)

Followup (years)	Disease-to-Absence		Stayed Disease		Stayed Absent		Absence-to-Disease	
	#	%	#	%	#	%	#	%
<2	3	12	1	7	0	0	0	0
2-3	7	28	5	33	1	8	1	50
3-4	9	36	6	40	6	46	1	50
4 plus	6	24	3	20	6	46	0	0
Total	25	100	15	100	13	100	2	100

Table 8
Voids in root fillings in teeth by change in category of disease (dichotomous PAI scale)

Nature of Change	Yes		No		Total	
	#	%	#	%	#	%
Disease-to-Absence (from 5-3 to 2-1)	4	66	21	43	25	45
Stayed Disease (from 5-3 to 5-3)	1	17	14	29	15	27
Stayed Absent (from 1-2 to 1-2)	1	17	12	24	13	24
Absence-to-Disease (from 1-2 to 3-5)	0	0	2	4	2	4
Total	6	100	49	100	55	100

Table 9
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by number of treatment appointments

Nature of Change	Two		Three		Four		Five	
	#	%	#	%	#	%	#	%
Disease-to-Absence (from 5-3 to 2-1)	16	47	5	31	3	75	1	100
Stayed Disease (from 5-3 to 5-3)	9	26	6	38	0	0	0	0
Stayed Absent (from 1-2 to 1-2)	7	21	5	31	1	25	0	0
Absence-to-Disease (from 1-2 to 3-5)	2	6	0	0	0	0	0	0
Total	34	100	16	100	4	100	1	100

Table 10
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by patient history of tobacco use

Nature of Change	Yes		No		Total	
	#	%	#	%	#	%
Disease-to-Absence (from 5-3 to 2-1)	7	39	19	51	26	47
Stayed Disease (from 5-3 to 5-3)	9	50	6	16	15	27
Stayed Absent (from 1-2 to 1-2)	1	6	11	30	12	22
Absence-to-Disease (from 1-2 to 3-5)	1	6	1	3	2	4
Total	18	100	37	100	55	100

Note: Approximately 81% of the patients who had no history of tobacco use registered disease to absence or stayed absent PAI rating.

Table 11
Number and percent of teeth by age and positive percussion sensitivity

Age Group	#	%
≤19	1	8
20-29	1	8
30-39	1	8
40-49	1	8
50-59	4	30
60-69	1	8
70+	4	30
Total	13	100

Table 12
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by length of root filling from radiographic apex

Nature of Change	**>2mm inside the canal**		**0-2mm inside the canal**		**Flush**		**Long**	
	#	**%**	**#**	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	0	0	21	38	1	2	3	5
Stayed Disease (from 5-3 to 5-3)	0	0	12	22	3	5	0	0
Stayed Absent (from 1-2 to 1-2)	1	2	11	20	0	0	1	2
Absence-to-Disease (from 1-2 to 3-5)	0	0	2	4	0	0	0	0
Total	1	2	46	84	4	7	4	7

Table 13
Number and percent of teeth by clinical perception of healing (Reader 1)

Clinical perception	Total # (%)
Healed	33 (60)
Healing	18 (32.7)
Not healed/healing	4 (7.3)
Total	55

Note: Reader 1 identified a total of 51 teeth (93%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs

Table 14
Number and percent of teeth by clinical perception of healing (Reader 2)

Clinical perception	Total # (%)
Healed	30 (54.5)
Healing	18 (32.7)
Not healed/healing	7 (12.7)
Total	55

Note: Reader 2 identified a total of 48 teeth (87%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs

Table 15
Number and percent of teeth by clinical perception of healing (Reader 3)

Clinical perception	Total # (%)
Healed	27 (49.1)
Healing	23 (41.8)
Not healed/healing	5 (9.1)
Total	55

Note: Reader 3 identified a total of 50 teeth (91%) as healed or healing in a subjective side-by-side evaluation of IPO and F radiographs

Table 16
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by systemic factors

Nature of Change	HTN w/o D	HTN + D	D w/o HTN	Tobacco w/o D or HTN	Total systemic		Total no known systemic factors	
	#	#	#	#	#	%	#	%
Disease-to-Absence (from 5-3 to 2-1)	3	5	0	4	12	37.5	13	56.5
Stayed Disease (from 5-3 to 5-3)	2	6	1	1	10	31.3	5	21.7
Stayed Absent (from 1-2 to 1-2)	3	3	2	1	9	28.1	4	17.3
Absence-to-Disease (from 1-2 to 3-5)	0	0	0	1	1	3.1	1	4.3
Total	8	14	3	7	32 (58.2%)		23 (41.8%)	

Note: 32/55 (58.2%) of the teeth were from patients with known systemic factors related to healing. Disease-to-absence of disease among those with systemic factors vs. none were 38% and 57% respectively. Among teeth from patients with systemic factors vs. none a total of 21 (65.6%) vs. 17 (73.8%) either moved from disease-to-absence or stayed absent of disease.

Table 17
Summary of extent of healing in relationship to independent variables

Variable	**N**	**Percent Favorable Healing**	**Probability of Difference (p<=0.05)**
Total group	55	69	na
Age			
< 60	36	64	ns*
=>60	19	79	ns
Follow up time			
<3	18	61	ns
=>3	37	73	ns
Hypertension			
Y	22	64	ns
N	33	73	ns
Voids in root filling			
Y	6	83	ns
N	49	67	ns
Percussion sensitivity			
Y	14	78	ns
N	41	66	ns
History of tobacco use			
Y	18	44	**significant**
N	37	81	**significant**
# of treatment appointments			
2	34	68	ns
>=3	21	71	ns
Diabetes			
Y	17	59	ns
N	38	74	ns
Gender			
M	26	62	ns
F	29	76	ns

*ns = not significant

Table 18
Number and percent of teeth by change in category of disease (dichotomous PAI scale) and by sensitivity to percussion

Nature of Change	**Yes**		**No**		**Total**	
	#	**%**	**#**	**%**	**#**	**%**
Disease-to-Absence (from 5-3 to 2-1)	4	7	21	38	25	45
Stayed Disease (from 5-3 to 5-3)	3	5	12	22	15	27
Stayed Absent (from 1-2 to 1-2)	6	11	7	13	13	24
Absence-to-Disease (from 1-2 to 3-5)	0	0	2	4	2	4
Total	13	23	42	76	55	100

FIGURES

Figure 1
PAI diagrammatic & radiographic reference

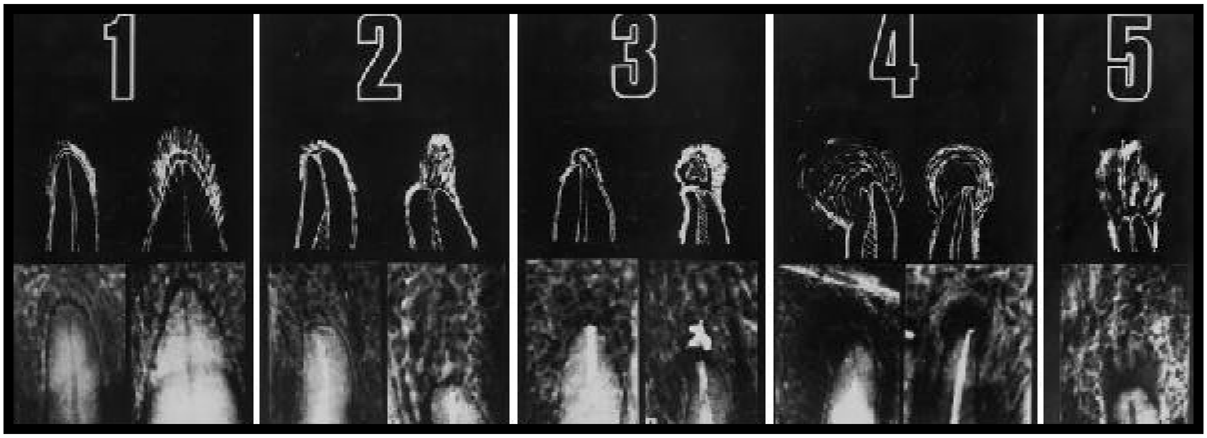
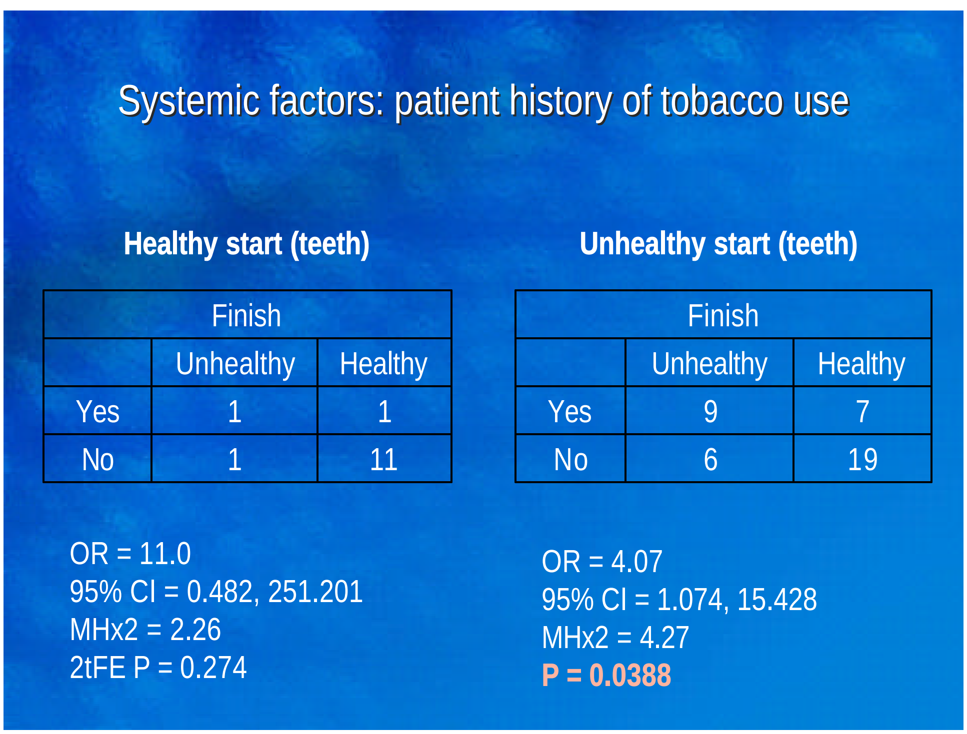


Figure 2
Systemic factors: patient history of tobacco use



Systemic factors: patient history of tobacco use

Healthy start (teeth)

	Finish	
	Unhealthy	Healthy
Yes	1	1
No	1	11

OR = 11.0
95% CI = 0.482, 251.201
MHx2 = 2.26
2tFE P = 0.274

Unhealthy start (teeth)

	Finish	
	Unhealthy	Healthy
Yes	9	7
No	6	19

OR = 4.07
95% CI = 1.074, 15.428
MHx2 = 4.27
P = 0.0388

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