# Treatment Outcome in Endodontics: The Toronto Study. Phase III: Initial Treatment

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**Abstract**

The 4- to 6-year outcome of initial endodontic treatment was assessed for phase III (1998-1999) of the Toronto Study. Of the 532 teeth treated, 248 were from discontinuers (excluded), 142 from dropouts, 10 extracted, and 132 (50% recall) examined for outcome: healed (no apical periodontitis [AP], signs, symptoms) or diseased. Phase III was analyzed alone and combined with phases I, II ($n = 373$ teeth). Logistic regression performed on the combined phases I-III sample identified significant ($p \leq 0.05$) outcome predictors: preoperative AP (OR = 3.5; CI 1.7-7.2; healed: absent, 93%; present, 80%), number of roots (OR = 2.2; CI 1.0-4.7; healed: 1 - 92%; ≥2 - 83%), and intraoperative complications (OR = 2.2; CI 1.1-4.5; healed: absent, 88%; present, 76%). Treatment technique (OR = 2.8; CI 1.3-6.1; healed: Schilder, 89%; alternative, 73%) was suggested as an outcome predictor in teeth with AP, requiring confirmation from randomized controlled trials. *(J Endod 2006;32:299–306)*

**Key Words**

Apical periodontitis, endodontic treatment, prognosis, root canal therapy, treatment outcome

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Endodontic treatment is performed to prevent or cure apical periodontitis and to retain the treated tooth in function. The predictability of achieving these goals has recently been questioned (1–3), as the inconsistent outcomes reported for endodontic treatment contrast with consistently favorable outcomes reported for implant-supported single-tooth replacement. Thus, the outcome of endodontic treatment has recently come to the forefront as the focus of a debate regarding tooth retention or replacement.

The outcome of initial (first-time) endodontic treatment has been assessed in many studies during the past decades; however, the results have varied considerably (4). This wide variation of the reported outcomes, attributed mainly to differences in methodology (4), has caused considerable confusion in the profession, and it interferes with attempts to establish evidence-based guidelines for endodontic practice. To provide the evidence base to support endodontic treatment, outcome studies must conform to design and methodology criteria consistent with an adequate (at least mid-range) level of evidence (5, 6), e.g. they should be randomized controlled trials or methodologically sound observational cohort studies. A recent review (7) has highlighted the shortage of such studies, identifying only 14 (8–21) that appear to methodologically conform to the mid-range level of evidence. Adding three more recent studies (22–24), the short list now comprises 17 studies. However, because several of these studies (8–12) include treatment techniques that have been modified in the recent years, they may no longer be considered as reflecting the outcome of state-of-the-art endodontic treatment (4, 7). The remaining 12 studies comprise the evidence base for current initial endodontic treatment; clearly, additional studies are required to broaden this evidence base.

Of the current studies, two have reported on phases I (20) and II (21) of the prospective Toronto Study project. This modular project was initiated in 1993 and designed as a continuous investigation of the 4- to 6-year outcome of endodontic treatment performed by graduate endodontics students. Patients have been recalled in 2-year "phases," and the sample size multiplied with each successive phase added, so as to increase the statistical power for assessment of significant outcome predictors. Thus, the analyzed sample for initial treatment has multiplied from 120 teeth in phase I (20) to 242 teeth in phases I and II combined (21). Consequently, the number of significant outcome predictors suggested by a multivariate analysis increased from one (20) to two (21). Preoperative apical periodontitis (AP), shown by the majority of previous studies (8–10, 12–14, 18) to influence the outcome of treatment, was clearly identified as a significant outcome predictor. In addition, treatment technique was highlighted as warranting investigation in randomized controlled trials, with a better outcome observed after flared canal preparation and vertical compaction of warm gutta-percha, as described by Schilder (25, 26), than after step-back canal preparation and lateral compaction of gutta-percha. It was expected that by extending the Toronto Study project onto an additional phase, the increased sample size and statistical power would allow corroboration of the previously identified outcome predictors and the identification of additional ones.

The objectives of this study were 2-fold: (a) to systematically assess the 4- to 6-year outcome of initial endodontic treatment in phase III of the Toronto Study project, and (b) to assess associations between the outcome of treatment and pre-, intra-, and postoperative variables, by combining the phase III sample with those of the previous two phases for increased statistical power.

## Materials and Methods

The protocol of the Toronto Study project was established before subjects were recruited and treated. The study protocol and informed consent forms were approved by the University of Toronto Health Sciences Research Ethics Board. The same methodology as described in the previous reports (20, 21) was followed in this study. It is briefly summarized below.

1. Cohort: The inception cohort comprised all 532 teeth in 468 patients who had received initial endodontic treatment from January 1998 to December 1999.
2. Intervention: Supervised graduate students provided treatment in accordance with two main treatment techniques: (a) step-back/lateral compaction (SBLC), and (b) flared preparation/vertical compaction (FPVC). Ten teeth in total were treated with different root filling techniques, either single gutta-percha cone with a glass-ionomer cement sealer (Ketac-Endo, 3M ESPE, St. Paul, MN), or injectable gutta-percha (Obtura II, Obtura Spartan, Fenton, MO). Each technique was performed only in specific sessions during the week. Allocation of treatment techniques was quasirandomized by allowing patients to select clinical sessions according to their availability and convenience.
   The intervention in the phase III cohort differed from that in phases I and II in three ways: (a) engine-driven NiTi instruments were used routinely rather than hand stainless steel files; (b) The FPVC technique was modified from the classic Schilder technique (25, 26) by treating all canals concurrently rather than in sequence, by using the System B (SybronEndo, Orange, CA) and Obtura II (Obtura Spartan) devices rather than sectional gutta-percha and conventional heat carriers, and by using engine-driven instruments as mentioned above; and (c) operating microscopes were used routinely in all treated cases, rather than loupes.
   All preoperative and intraoperative data were uniformly recorded by the providers of treatment and entered into a database in real time.
3. Recall: All subjects were recalled by letters, invited to attend a follow-up examination, and offered compensation for work time lost and travel expenses incurred by attending. Nonresponders were contacted by telephone and encouraged to attend. When treated teeth were reported to be lost, subjects were questioned and the records of those who received regular care at the Faculty of Dentistry examined, to establish the reasons for extraction.
4. Outcome assessment: All follow-up examinations were performed by the phase III-designated examiner (V.M.). Before examining subjects, he was calibrated for use of the Periapical Index (PAI) (27) in the same manner as the examiners for phases I and II and the co-investigator (S.F.) for the project. Interexaminer and intraexaminer agreement scores were calculated by using weighted Cohen's kappa statistics. PAI scores were dichotomized to reflect absence (PAI $\leq$ 2) or presence (PAI $\geq$ 3) of AP. The evaluated unit was the tooth as a whole, with multirooted teeth assigned the highest score of all roots. All postoperative data recorded at the follow-up examination were immediately entered into the database.

Based on clinical and radiographic measures, the outcome was dichotomized either as "healed" (absence of AP, signs and symptoms other than tenderness to percussion), or as "disease" (presence of either AP, signs or symptoms). Teeth presenting without clinical signs or symptoms were considered "functional" regardless of the PAI score.

### Analysis

Separate statistical analyses were performed on the data of this study (phase III) and on the pooled data from phases I, II, and III. Pooling of the data was justified by the consistency of the methodology for all phases of the Toronto Study project. Univariate analysis (percent frequencies) characterized the data. Bivariate analysis ($\chi^2$ test of proportions and Fisher's exact test) examined associations between the treatment outcome and pre-, intra-, and postoperative variables, to suggest potentially important variables for inclusion in the multivariate analysis. Multivariate analysis (logistic regression) was performed on the pooled data only, incorporating the variables found significant in the bivariate analysis into a prediction model, in order to identify significant outcome predictors. The dependent variable in all analyses was the dichotomous outcome, healed versus disease. All tests were performed as two-tailed and interpreted at the 5% significance level. In addition to the analysis of the complete sample, stratified analyses were performed for teeth treated without or with preoperative radiolucency. Table 1 lists all of the 17 investigated variables.

## Results

Unweighted Cohen's kappa scores for the intraexaminer agreement of the phase III examiner ($\kappa = 0.96$) indicated "very good agreement" (28). The interexaminer agreement between the phase III examiner and the phase I and II examiners ($\kappa = 0.67$ and 0.63, respectively), and the co-investigator ($\kappa = 0.65$) indicated "good agreement" (28).

### Phase III Sample

The inception cohort of 468 patients and 532 teeth was distributed into the following categories: (a) discontinuers (excluded)—248 teeth from 222 relocated subjects who could not be contacted; (b) dropouts—142 teeth from 21 subjects who declined the recall and 105 subjects who did not respond; and (c) attending—142 teeth (50% recall rate after exclusion of discontinuers) from 120 subjects, including 132 teeth examined for outcome (study sample) and 10 extracted teeth (five for restorative considerations, three for fractures, one for advanced periodontal disease, and one for unknown reasons). The examined study sample is compared to the inception cohort in Table 1. Response bias analysis (not shown) suggested that the attending and lost-to-follow-up (dropouts and discontinuers) populations differed significantly with regards to age.

At the end point of the phase III study, 113/132 teeth (86%) were classified as healed. One of these teeth presented with vertical root fracture associated with severe bone loss, and was excluded from further analysis. Nineteen teeth (14%) were classified as having disease. The bivariate analysis (Table 2) suggested only one statistically significant association, with a higher healed rate for teeth without than with preoperative radiolucency. Four additional variables (tooth type, number of treatment sessions, root filling voids, and type of coronal seal material) were associated with healed rate differentials of $\geq$10%, which were not statistically significant.

Of the 112 teeth classified as healed (one fractured tooth excluded), seven teeth (6%) presented with a slight tenderness to percussion. Of the 19 teeth classified as having disease, three teeth (16%) presented signs and symptoms (pain), of which two had a PAI score $\leq$2 (no AP). Thus in total, 121 teeth (105 healed and 16 having disease) of 131 analyzed (92%) were fully functional, without any signs or symptoms and without tenderness to percussion. In the 16 teeth with PAI $\geq$ 3, the lesion was smaller than preoperatively in four teeth (25%), unchanged in five teeth (31%), and increased or new in seven teeth (44%).

Sixty-one of 65 teeth (94%) without preoperative radiolucency healed. Stratified analysis showed no variables associated with statistically significant or large healed rate differentials. Of 66 teeth with preoperative radiolucency, 51 teeth (77%) healed. Stratified

**TABLE 1.** Univariate distribution of investigated factors in the study population

| Prognostic Factor | Phase III | | Phases I-III Pooled | |
|---|---|---|---|---|
| | Inception Cohort % ($n$ = 532) | Study Sample % ($n$ = 132) | Inception Cohort % ($n$ = 1370) | Study Sample % ($n$ = 373) |
| Preoperative | | | | |
| Age | | | | |
| ≤45 yr | 47 | 21 | 50 | 25 |
| >45 yr | 53 | 77 | 50 | 75 |
| Gender | | | | |
| Female | 58 | 59 | 55 | 55 |
| Male | 42 | 41 | 45 | 45 |
| Tooth type | | | | |
| Anterior | 16 | 16 | 18 | 18 |
| Posterior | 84 | 84 | 82 | 82 |
| Tooth location | | | | |
| Maxilla | 50 | 46 | 51 | 50 |
| Mandible | 50 | 54 | 49 | 50 |
| No. of roots | | | | |
| 1 | 27 | 30 | 29 | 31 |
| ≥2 | 73 | 70 | 71 | 69 |
| Signs and symptoms | | | | |
| Absent | 41 | 45 | 37 | 38 |
| Present | 59 | 55 | 63 | 62 |
| Radiolucency | | | | |
| Absent | 46 | 50 | 43 | 43 |
| Present | 54 | 50 | 57 | 57 |
| Pulp status | | | | |
| Responsive | 33 | 42 | 34 | 36 |
| Nonresponsive | 67 | 58 | 66 | 64 |
| Intraoperative | | | | |
| Treatment sessions | | | | |
| 1 | 15 | 17 | 18 | 18 |
| ≥2 | 85 | 83 | 82 | 82 |
| Technique | | | | |
| SBLC | 54 | 55 | 52 | 51 |
| FPVC | 43 | 43 | 45 | 45 |
| Other* | 3 | 2 | 3 | 4 |
| Root-filling length | | | | |
| Adequate | 74 | 73 | 76 | 74 |
| Short | 8 | 10 | 7 | 7 |
| Long | 18 | 17 | 17 | 19 |
| Root-filling voids | | | | |
| Absent | 90 | 86 | 85 | 84 |
| Present | 10 | 14 | 15 | 16 |
| Sealer extrusion | | | | |
| Absent | 38 | 42 | 45 | 46 |
| Present | 62 | 58 | 55 | 54 |
| Complications | | | | |
| Absent | 83 | 79 | 84 | 83 |
| Present | 17 | 21 | 16 | 17 |
| Coronal seal material | | | | |
| Temporary† | 12 | 15 | 15 | 18 |
| Definitive‡ | 82 | 85 | 85 | 82 |
| Postoperative | | | | |
| Restoration at follow-up | | | | |
| Temporary | | 2 | | 5 |
| Definitive filling | | 25 | | 28 |
| Crown | | 73 | | 67 |
| Post | | | | |
| Absent | | 70 | | 58 |
| Present | | 30 | | 42 |

SBLC = Modified step-back preparation, lateral compaction of gutta-percha; FPVC = Flared preparation, vertical compaction of warm gutta-percha.

*Modified step-back preparation, single gutta-percha cone and Ketac-Endo sealer.

†Cavit, ZOE, IRM.

‡Amalgam, composite resin, glass ionomer cement, crown.

analysis (Table 3) suggested only two statistically significant associations, with a higher healed rate for maxillary than mandibular teeth, and for coronal seal with a definitive than a temporary restorative material. Seven additional variables (tooth type, periodontal defect, number of treatment sessions, type of sealer, sealer extrusion, complications, and restoration at follow-up) were associated with healed rate differentials of ≥10% that were not statistically significant.

**TABLE 2.** Bivariate analysis of associations between selected factors[§] and the healed rate 4 to 6 yr after treatment, presented for phase III ($n = 131$) and the pooled phases I–III ($n = 369$)

| Prognostic Factor | Phase III | | | Phase I-III Combined | | |
|---|---|---|---|---|---|---|
| | *n* | Healed (% n) | p Value | *n* | Healed (% n) | p Value |
| Preoperative | | | | | | |
| **Gender** | | | | | | |
| Female | | | | **201** | **89** | **0.041** |
| Male | | | | **168** | **82** | |
| Tooth type | | | | | | |
| Anterior | 21 | 95 | 0.167 | | | |
| Posterior | 110 | 84 | | | | |
| **No. of roots** | | | | | | |
| 1 | | | | **114** | **92** | **0.018** |
| ≥2 | | | | **255** | **83** | |
| **Radiolucency** | | | | | | |
| Absent | **65** | **94** | **0.007** | **160** | **93** | **< 0.001** |
| Present | **66** | **77** | | **209** | **80** | |
| Intraoperative | | | | | | |
| Treatment sessions | | | | | | |
| 1 | 22 | 96 | 0.195* | | | |
| ≥2 | 109 | 84 | | | | |
| Root-filling voids | | | | | | |
| Absent | 113 | 88 | 0.140* | | | |
| Present | 18 | 72 | | | | |
| **Complications** | | | | | | |
| Absent | | | | **306** | **88** | **0.019** |
| Present | | | | **63** | **76** | |
| Coronal seal material | | | | | | |
| Temporary† | 20 | 75 | 0.169* | | | |
| Definitive‡ | 111 | 87 | | | | |

Bold type face highlights statistical significance.

*Fischer's Exact test, $\chi^2$ test otherwise.

†Cavit, ZOE, IRM.

‡Amalgam, composite resin, glass ionomer cement, crown.

§Only factors associated with a healed rate differential of ≥10%, or significant variables, presented.

**TABLE 3.** Bivariate analysis between selected factors[§] and preoperative radiolucency, presented for the pooled phases I-III ($n = 369$)

| Prognostic Factor | Preoperative Radiolucency | | |
|---|---|---|---|
| | Absent n (%) | Present n (%) | p Value[a] |
| Preoperative | | | |
| **Gender** | | | |
| Female | **100 (50)** | **101 (50)** | **0.007** |
| Male | **60 (36)** | **108 (64)** | |
| **Signs and symptoms** | | | |
| Absent | **73 (51)** | **69 (49)** | **0.014** |
| Present | **87 (38)** | **140 (62)** | |
| **Pulp status** | | | |
| Responsive | **104 (78)** | **29 (22)** | **< 0.001** |
| Nonresponsive | **56 (24)** | **180 (76)** | |
| Intraoperative | | | |
| **Treatment sessions** | | | |
| 1 | **47 (70)** | **20 (30)** | **< 0.001** |
| ≥2 | **113 (37)** | **189 (63)** | |
| **Root-filling voids** | | | |
| Absent | **144 (46)** | **167 (54)** | **0.008** |
| Present | **16 (28)** | **42 (72)** | |
| **Sealer extrusion** | | | |
| Absent | **87 (50)** | **86 (50)** | **0.012** |
| Present | **73 (37)** | **123 (63)** | |

Bold type face highlights statistical significance.

§Only factors significantly associated with preoperative radiolucency presented.

a$\chi^2$ test.

**TABLE 4.** Logistic regression model of the outcome of initial endodontic treatment 4 to 6 years after treatment for the pooled phases I-III ($n$ = 369)

| Predictor | Odds Ratio (for disease) | 95% Confidence Interval | p Value |
|---|---|---|---|
| Preoperative | | | |
| **Radiolucency** (0 = absent, 1 = present) | **3.55** | **1.75-7.23** | **<0.001** |
| **No. of roots** (0 = single, 1 = multiple) | **2.17** | **1.00-4.69** | **0.050** |
| Intraoperative | | | |
| **Complications** (0 = absent, 1 = present) | **2.23** | **1.10-4.52** | **0.026** |

Bold type face highlights statistical significance.

### Pooled Phases I, II, and III Sample

The pooled examined sample included 373 teeth (50% recall rate) in 325 patients. Table 1 compares the examined study sample to the inception cohort (1370 teeth in 1151 patients). Response bias analysis (not shown) confirmed that the attending and lost-to-follow-up populations differed significantly only with regards to age.

Of the pooled sample, 317/373 teeth (85%) were classified as healed and 56/373 (15%) as having disease. Four teeth (one healed and three diseased) were found to be fractured; as they could potentially confound the investigation of other variables, they were excluded from further analysis reducing the analyzed sample to 369 teeth. Of the 316 teeth classified as healed (one fractured tooth excluded), 12 teeth (4%) presented with a slight tenderness to percussion. Of the 53 teeth classified as having disease (three fractured teeth excluded), five teeth (9%) presented signs and symptoms (three had pain, one had a sinus tract, and one had pain and swelling), of which three had a PAI score $\leq$2. Thus, in total, 352/369 teeth (95%) (304 healed and 48 having disease) were fully functional, without signs, symptoms, or tenderness to percussion. In 49 teeth with PAI $\geq$ 3, the lesion was smaller than preoperatively in 21 teeth (43%), unchanged in 10 teeth (20%), and increased or new in 18 teeth (37%).

The bivariate analysis (Table 2) suggested only four statistically significant associations, with a higher healed rate for teeth: (a) in females than males, (b) without than with preoperative radiolucency, (c) single-rooted than multirooted, and (d) without than with intraoperative complications. All other variables were associated with healed rate differentials of <10%. A further analysis (Table 3) revealed that the variable "gender" was significantly associated with the variable "preoperative radiolucency," both in the study sample ($p = 0.007$) and in the inception cohort ($p = 0.026$, not shown). Complications, observed in 63 teeth (17%), comprised a variety of preoperative complexities, including aberrant anatomy (20 teeth) and crack observed in the pulp chamber (3 teeth), as well as intraoperative complications, including perforation (18 teeth), file breakage (11 teeth) and apparently calcified canals that could not be negotiated (14 teeth). The four variables were considered potentially important and further assessed in the multivariate analysis.

Multivariate analysis performed on the pooled study sample (Table 4) revealed an increased risk of persistent disease for preoperative radiolucency (OR = 3.55; CI 1.75-7.23), multirooted teeth (OR = 2.17; CI 1.00-4.69), and intraoperative complications (OR = 2.23; CI 1.10-4.52).

Of 160 teeth without preoperative radiolucency, 149 (93%) healed. Stratified analysis did not show any significant associations, and all healed rate differentials were <10%. Of 209 teeth treated with radiolucency present, 167 (80%) healed. Stratified analysis (Table 5) suggested only three statistically significant associations, with a higher healed rate for: (a) single-rooted than multirooted teeth, (b) FPVC than SBLC technique, and (c) teeth without than with intraoperative complications. Two additional variables (tooth type, coronal seal material) were associated with healed rate differentials of $\geq$10% that were not statistically significant. The three variables were further assessed in a stratified multivariate analysis.

Stratified multivariate analysis performed on teeth with preoperative radiolucency (Table 6) revealed an increased risk of persistent disease for the SBLC technique (OR = 2.83; CI 1.31-6.13) and complications (OR = 2.67; CI 1.13-6.32).

## Discussion

### Methodology

Clinical outcome research is intended to support decision-making, such as selecting between tooth retention via endodontic treatment or extraction and replacement. Because the evidence base for current endodontic treatment outcome is limited to only few studies that conform to an adequate level of evidence (13–22, 24), additional studies may add important information to the existing knowledge. On this premise, the Toronto Study project was established in 1993 as a prospective, modular observational cohort study designed to assess the 4- to 6-year outcome of endodontic treatment. The first two phases of the project have been summarized in reports on the outcome of initial endodontic treatment (20, 21), orthograde retreatment (29), and apical surgery (30).

The present study assessed the outcome of initial endodontic treatment in phase III of the Toronto Study project. The methodology and protocol of this study were consistent with those of the previous phases (20, 21) except for a few updates to comply with current endodontic techniques. Furthermore, the univariate analysis suggested that the phase III study sample was comparable to those of phases I and II in regard to size and frequencies. The uniformity allowed the pooling of the study samples from all three phases, previously suggested as a benefit of the Toronto Study design (21). The increased statistical power was expected to facilitate the assessment of outcome associations with variables, particularly in the stratified analyses for which the sample size was roughly half that of the entire study sample. Indeed, in the preoperative presence of AP, the outcome was significantly associated with only one variable (number of roots) in the phase I study (20), two variables (number of roots, treatment technique) in the pooled phases I and II (21), and three variables (number of roots, treatment technique, and complications) as shown herein for the pooled sample of phases I through III. Clearly, a large sample size is essential for assessment of outcome predictors in a multifactorial disease process such as apical periodontitis.

The study methodology has already been discussed in detail in the previous reports (20, 21, 29, 30). Arguably, it conformed to criteria defining an adequate level of evidence in regards to the study cohort, intervention, outcome assessment, and analysis, with the exception of the low recall rate. Despite the monetary compensation offered and numerous attempts to contact discontinuers and to encourage dropouts

**TABLE 5.** Stratified bivariate analysis of associations between selected factors§ and the healed rate in teeth treated with preoperative radiolucency 4 to 6 years after treatment, presented for phase III ($n = 66$) and the pooled phases I-III ($n = 209$)

| Prognostic Factor | Phase III | | | Phases I-III pooled | | |
|---|---|---|---|---|---|---|
| | *n* | Healed (% n) | p Value | *n* | Healed (% n) | p Value |
| Preoperative | | | | | | |
| Tooth type | | | | | | |
| Anterior | 7 | 100 | 0.336* | 40 | 90 | 0.076 |
| Posterior | 59 | 75 | | 169 | 76 | |
| **Tooth location** | | | | | | |
| Maxilla | **25** | **64** | **0.045** | | | |
| Mandible | **41** | **85** | | | | |
| **No. of roots** | | | | | | |
| 1 | | | | **62** | **89** | **0.039** |
| ≥2 | | | | **147** | **76** | |
| Periodontal defect | | | | | | |
| No | 62 | 76 | 0.567* | | | |
| Yes | 4 | 100 | | | | |
| Intraoperative | | | | | | |
| Treatment sessions | | | | | | |
| 1 | 3 | 100 | 1.000* | | | |
| ≥2 | 63 | 76 | | | | |
| **Technique** | | | | | | |
| SBLC | | | | **103** | **73** | **0.005** |
| FPVC | | | | **96** | **89** | |
| Other* | | | | 10 | | |
| Type of sealer | | | | | | |
| ZOE | 65 | 78 | 0.227* | | | |
| Non-ZOE | 1 | 0 | | | | |
| Sealer extrusion | | | | | | |
| Absent | 21 | 86 | 0.353* | | | |
| Present | 45 | 73 | | | | |
| **Complications** | | | | | | |
| Absent | 54 | 82 | 0.125* | **180** | **83** | **0.008** |
| Present | 12 | 58 | | **32** | **63** | |
| **Coronal seal material** | | | | | | |
| Temporary† | **6** | **33** | **0.021*** | 34 | 68 | 0.051 |
| Definitive‡ | **60** | **82** | | 175 | 82 | |
| Postoperative | | | | | | |
| Restoration at follow-up | | | | | | |
| Temporary | 1 | 100 | 1.000* | | | |
| Definitive | 63 | 78 | | | | |

Bold type face highlights statistical significance.

SBLC = modified step-back preparation, lateral compaction of gutta-percha; FPVC = flared preparation, vertical compaction of warm gutta-percha.

§Only factors associated with a healed rate differential of ≥10%, or significant variables, presented.

*Fischer's Exact test, $\chi^2$ test otherwise.

†Cavit, ZOE, IRM.

‡Amalgam, composite resin, glass ionomer cement, crown.

to attend the follow-up examination, the recall rate of 50% in the phase III study was similar to that in the previous two phases (20, 21). The recall rate fell below the guidelines suggested for high level of evidence (6). Theoretically, examination of the lost-to-follow-up population (discontinuers and dropouts) could strongly pull the outcome towards healing or disease, according to this population's characteristics. The recall bias analysis was performed, therefore, to compare the characteristics of the study sample and the lost-to-follow-up population. The analysis revealed that the proportion of young (≤45 yrs) subjects was significantly higher in the latter than in the former; however, because age was not identified as a significant outcome predictor, the study results were unlikely to be impacted by the low recall rate.

The majority of the study cohort comprised a specific dental school population that could differ from that treated in private practice in regards to demographic characteristics or disease severity (6). Because the study cohort did not represent the population at large, the

**TABLE 6.** Logistic regression model of the outcome of initial endodontic treatment in teeth treated with preoperative radiolucency 4 to 6 years after treatment for the pooled phases I-III. ($n = 209$)

| | Predictor | Odds Ratio | 95% Confidence Interval | p Value |
|---|---|---|---|---|
| Intraoperative | | | | |
| **Technique** (0 = Schilder, 1 = alternative) | **2.83** | **1.31-6.13** | **0.008** | |
| **Complications** (0 = absent, 1 = present) | **2.67** | **1.13-6.32** | **0.026** | |

Bold type face highlights statistical significance.

results might not be generalized beyond this specific study cohort. Nevertheless, the Graduate Endodontics Clinic at the Faculty of Dentistry has functioned as a specialty referral clinic; therefore, the scope of clinical conditions treated in this study was considered to be comparable to that in an endodontic specialty practice.

The close supervision of the treatment providers (graduate students) by qualified endodontists as well as the principal treatment protocol, were unchanged from the previous phases. Importantly, however, engine-driven nickel titanium instruments and surgical operating microscopes were introduced during the period when the phase III cohort was treated. The FPVC technique also was modified and adhered less to the specific guidelines established by Schilder (25, 26). Whether or not these changes have influenced the outcome of treatment was expected to be gleaned from comparison of the phase III and the previous phases' results. The overall 86% healed rate in the phase III study was consistent with the 87% rate in phase II (21), and both were higher than the 81% rate in phase I (20). Thus, the aforementioned changes in protocol did not appear to influence the outcome of treatment.

### Overall Outcome and Main Predictors

Adding the third phase to the previous two made it apparent that any significant associations suggested by the bivariate analyses of either single phase, have neither been consistently corroborated by successive phases nor substantiated in the pooled samples. Likewise, not all variables suggested to be significant by the bivariate analyses of the pooled samples were confirmed as significant outcome predictors by the mutivariate analysis. This inconsistency underscored the limitations of the bivariate analysis, which does not take into account confounding effects when assessing any specific variable, but only suggests potential variables for inclusion in logistic regression models. In view of these considerations, only the results in the pooled study sample are discussed below, with greater emphasis placed on the multivariate than the bivariate analyses.

Using both clinical and radiographic outcome measures, the overall healed rate in the pooled sample was 85%. However, as many as 95% of the teeth presenting for follow-up were symptom-free and fully functional. This finding was within the range of 88% to 97% reported in other current studies (14, 17–19). Furthermore, if the sole presence of a slight tenderness to percussion was considered as not hindering function, 99% of the teeth in this study (316 healed and 48 having disease) would be functional. Inasmuch as scientific rigor requires the use of both clinical and radiographic outcome measures, individuals/patients may select to base their treatment preferences exclusively on the chances of eliminating signs and symptoms (7). This concept of patient autonomy in clinical decision-making provides the rationale and supports the relevance of reporting treatment outcomes in regards to both healing and functionality (7). Therefore, patients who are weighing endodontic treatment against tooth extraction and replacement should be advised that, based on this and several other current studies (14, 17–19), the chance of endodontically treated teeth to remain fully functional 4 to 6 years after treatment is 88% to 97%, even if some may present radiographic signs consistent with disease.

The multivariate analysis performed on the entire pooled sample identified three significant outcome predictors, one of which (preoperative AP) was previously identified in phases I (20) and II (21) of the Toronto Study project. Preoperative AP had the strongest predictive ability, in agreement with most previous studies (8–10, 12–14, 18, 23, 24). Without preoperative AP, the 93% healed rate was in the middle of the range (88-97%) reported in previous studies (8–10, 12–14, 18, 20–23). With preoperative AP, the 80% healed rate was in the middle of the range (73-90%) reported in previous studies (8–11, 13–23). Certain aspects of treatment in teeth with AP require consideration. Firstly, healing of AP is a dynamic process that requires different lengths of time for different teeth. In a long-term follow-up study (31), about 6% of teeth that had persistent AP 10 to 17 yrs after initial treatment were completely healed a further 10 yrs later. Notably, of the teeth classified as having disease in the present study, 43% had a smaller lesion than preoperatively, possibly suggesting a slower than usual healing process for at least some of these teeth. This consideration emphasizes the need for extended follow-up when a possible healing process is suggested by reduction of the lesion and absence of clinical signs and symptoms (21). Possibly, in the long term the difference in outcome in teeth treated with or without AP may be less than what is apparent in the shorter term, such as the 4- to 6-yr follow-up reported herein. Secondly, the poorer outcome may be a result of a small proportion of teeth with AP where the infecting bacteria are not situated in the root canal system but rather in the periapical tissues (32, 33) or on the outer surface of the root (32). Even if root canal treatment can effectively control intracanal infection in all teeth where such is present, it is unlikely to curtail extraradicular infection. Thus, even if novel root canal disinfection regimens such as potent irrigants, intracanal medication or lasers are more effective than the conventional ones, and they become widely adopted, the healing rate is unlikely to match that in teeth treated without AP.

The number of roots was identified as a significant outcome predictor, with an overall healed rate differential of 9%. However, the methodology precluded any insight into whether this finding reflected a greater challenge to eliminate root canal infection in multirooted teeth, or the use of the tooth (as opposed to the root) as the evaluated unit with the risk of persisting AP multiplied by the number of roots in any treated tooth (21). Nevertheless, when advising patients of the prognosis for a single-rooted or multirooted tooth, the specific healing rates for either group can be quoted rather than average figures that do not truly represent either group.

Intraoperative complications had a significant negative impact on treatment outcome, particularly in teeth with preoperative AP where the healed rate differential reached 20%. This finding was in agreement with other studies (8, 10, 13). By their nature, all of perforation, file breakage, untreated canals, cracks, and aberrant anatomy can either promote infection or interfere with its elimination; therefore, their impact on the outcome of treatment was expected, and the differential in outcome was already apparent in the pooled phases I and II, but without statistical significance (21). Some of these complications, however, may be much less frequent in the general population treated in private practice (34) than in this university-based study. Thus the impact of complications on the outcome of initial endodontic treatment in the general population might be proportionally lower than observed herein. Importantly, without the complications, the healed rate in teeth with preoperative AP was 83%.

### Suggested Predictors and Clinical Significance

Treatment technique was suggested as a significant outcome predictor, corroborating the phase II study (21) results, but only in teeth with preoperative AP. The association between outcome and treatment technique was not confounded by any other outcome predictor (analysis not shown). As in the phase II study (21), the healed rate after use of FPVC was 16% higher than after use of SBLC. Thus the modification of the original Schilder technique (25, 26) did not appear to notably affect the outcome. The fact that this finding was corroborated by the multivariate analysis in a successive phase of the Toronto Study strengthened its validity. Nevertheless, it should be considered as suggestive at best, because this study was only quasirandomized for treatment technique and other variables were not controlled, as is required for the highest level of evidence (5, 6). In the absence of other studies that compare FPVC and SBLC, the results of this study underlined the need for ran-

domized controlled trials designed specifically to compare the outcome of treatment associated with these two treatment techniques.

Although the sample has grown 3-fold since the phase I study (20), none of the variables significantly influenced the outcome in teeth without preoperative AP. On the contrary, several large healed rate differentials of ≥10%, highlighted in the phase I and II studies (20, 21), have diminished below 10% when the three phases were pooled. These findings suggested that with such small differences in outcome among teeth without preoperative AP, a much larger sample size would be required to identify significant outcome predictors.

As the study sample of the Toronto Study project has increased with more phases added, the multifactorial influences on the outcome of intitial endodontic treatment have become more apparent. Clinicians should take notice of the variables identified as significant outcome predictors. The importance of the preoperative ones (apical periodontitis and number of roots) is that they can be recognized at the stage when prognosis is projected and the patient is weighing treatment of the tooth against extraction. The importance of the intraoperative ones (complications and possibly treatment technique) is that clinicians might be able to control the outcome of treatment by preventing procedural errors and possibly, by making informed choices of treatment techniques. The authors suggest that as more knowledge becomes available on the outcome predictors in endodontic treatment, the greater becomes the onus on the clinicians to apply this knowledge when providing endodontic care to their patients.

In conclusion, in phase III of the Toronto Study project, 113/132 teeth (86%) were classified as healed. The addition of phase III demonstrated the limitations of the bivariate analyses in identifying outcome predictors in endodontic treatment. After combining the data collected from phase III with that collected in the two previous phases, the multivariate analysis identified preoperative radiolucency, number of roots, and intraoperative complications as significant outcome predictors in initial endodontic treatment. The suggested outcome predicting ability of treatment technique in teeth with preoperative apical periodontitis requires confirmation by results of appropriately designed randomized controlled trials.

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