

One-appointment endodontic therapy

Biological considerations

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A debate is ongoing among researchers and clinicians concerning the effectiveness of one-appointment versus multiple-appointment endodontic therapy for asymptomatic teeth with apical periodontitis. In a recent systematic review of the literature, Sathorn and colleagues¹ reported no statistically significant difference in periapical wound healing between one- and multiple-appointment endodontic therapy for asymptomatic teeth with apical periodontitis.

In their systematic review, Sathorn and colleagues¹ reported that only three studies²⁻⁴ were eligible for meta-analysis, and the sample size in each study was relatively small. In addition, the results of one study² conflicted with the results of the other two studies. If the methodologies of independent studies are similar, the results should be reproducible.

Meta-analysis has several purposes when the literature contains studies with conflicting results, or when the studies have relatively small sample sizes. By combining the data of several independent studies regarding a specific topic, researchers can increase the statistical power by increasing the sample size. However, the process is not without its critics. If the study

ABSTRACT

Background. The authors conducted a literature review to present the best available biological evidence concerning one-appointment endodontic therapy for asymptomatic teeth with apical periodontitis.

Types of Studies Reviewed. Because of recent advances in technology, such as rotary engines and nickel-titanium instruments, some practitioners are performing one-appointment endodontic therapy for asymptomatic teeth with apical periodontitis. The authors reviewed the literature, which revealed only a small number of randomized, controlled clinical trials that have been conducted on one-appointment versus multiple-appointment endodontic therapy.

Results. As the apical canal preparation is enlarged, a greater percentage of bacteria is eradicated from infected root canals. In addition, sufficiently large apical root canal enlargement facilitates the delivery of antimicrobial irrigant to the apical portion of the canal. However, an association between positive or negative preobturation root canal culture results and the outcome of endodontic treatment has not been well-established.

Clinical Implications. The best available evidence, based on a systematic literature review, indicates that one-appointment endodontic therapy may be feasible in selected cases of apical periodontitis in asymptomatic teeth. However, additional randomized, controlled clinical trials are required.

Key Words. One-appointment endodontic therapy; apical periodontitis; treatment outcome.

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protocols of the individual studies are different, the conclusion drawn from the meta-analysis may not be completely accurate.

The question that we consider in this review article focuses on the quality of the evidence in the literature concerning one- and multiple-appointment endodontic therapy for teeth with apical periodontitis. Increasing the number of independent studies with high levels of evidence in a meta-analysis should increase the predictability of the treatment's effectiveness. Accordingly, more randomized, controlled clinical studies are required to determine accurately the effectiveness of one-appointment endodontic therapy for teeth with apical periodontitis.

Rather than debate the effectiveness of endodontic treatment on the basis of the number of appointments, we should focus on the biological aspects of treatment effectiveness. The purpose of this article is to review the existing literature regarding the biological aspects of endodontics that must be evaluated when performing one-appointment endodontic therapy for asymptomatic teeth with apical periodontitis.

BIOLOGICAL CONSIDERATIONS

Apical periodontitis is caused primarily by microorganisms in the root canal system.⁵⁻⁸ The primary goal of root canal therapy is to reduce or eliminate intracanal microorganisms and their by-products from the root canal system. If one-appointment therapy for asymptomatic teeth with apical periodontitis is to be performed, satisfactory root canal disinfection in one visit is necessary because intracanal medication cannot be used as an adjunct to further disinfect the root canal system, as it is in multiple-appointment therapy. The clinician relies on adequate working length control, mechanical instrumentation, antimicrobial irrigation and removal of the smear layer to eliminate intracanal bacteria. In addition, the clinician must achieve a bacteria-tight seal of the root canal system with obturating materials to prevent reinfection of the root canal and communication between the root canal and the periradicular tissues.

WORKING LENGTH CONTROL

Adequate working length control is important in treating teeth with apical periodontitis,^{9,10} because bacterial contamination may extend to the apical few millimeters of the root canals.¹¹⁻¹³ Leaving critical numbers of microorganisms in

the root canal could result in persistent periradicular inflammation after endodontic therapy.^{11,14} The biological limit of root canal instrumentation and obturation ideally should be at the apical root canal constriction or the dentinocemental junction.^{15,16} Conventional radiographic measurements can be deceiving,¹⁷ because the apical foramen is not located at the apex in more than 60 percent of teeth.^{15,18,19} In addition, neither the apical root canal constriction nor the apical foramen is identifiable radiographically or clinically. Modern electronic apex locators have been shown to be reliable in measuring the root canal length within 0.5 millimeters from the apical foramen.²⁰⁻²³

In contemporary endodontic therapy, both electronic apex locators and radiographic measurements should be used to obtain the best estimation of working length. Sjögren and colleagues²⁴ found that instrumentation and obturation more than 2 mm short of the radiographic apex in teeth with apical periodontitis resulted in poorer treatment outcomes than those in other teeth. Chugal and colleagues¹⁰ reported that a 1-mm loss in working length increased the incidence of treatment failures by 14 percent in teeth with apical periodontitis. In addition, instrumentation and filling of the root canal beyond the apical foramen violate the periapical tissues and could result in poor treatment outcomes.²⁴

MECHANICAL INSTRUMENTATION AND ANTIMICROBIAL IRRIGATION

Mechanical instrumentation and irrigation with copious amounts of an antimicrobial are important factors in reducing the intracanal bacterial level. Several authors demonstrated that teeth with apical periodontitis have a poorer prognosis than those without apical periodontitis after root canal therapy.²⁴⁻²⁶ This is due, in part, to the difficulty of completely chemomechanically débriding infected root canal systems associated with apical periodontitis. Infected root canals usually harbor more microorganisms than root canals associated with irreversible pulpitis or partially vital pulp tissue.^{27,28} Therefore, the root canals associated with apical periodontitis must be enlarged chemomechanically to larger sizes than those not associated with apical periodontitis.

In their investigation of one-appointment

ABBREVIATION KEY. EDTA: Ethylenediamine tetraacetic acid. PCR: Polymerase chain reaction.

endodontic therapy for asymptomatic teeth with apical periodontitis, Sjögren and colleagues²⁹ instrumented the root canals to a no. 40 Hedstrom file and irrigated them with 0.5 percent sodium hypochlorite. The results of 31 (58 percent) of 53 root canal cultures obtained before obturation were negative. In their one-visit study, Peters and Wesselink⁴ instrumented infected necrotic root canals by using no. 35 to no. 60 FlexoFiles (Dentsply Maillefer, Tulsa, Okla.) and irrigated them with 2 percent sodium hypochlorite. Eleven (67 percent) of 21 root canal cultures obtained before obturation had negative results. The latter study probably was able to attain a slightly higher percentage of negative preobturation culture results than the former study because of larger apical root canal preparations. The available evidence indicates no significant difference in antibacterial activity between 0.5 percent and 2.0 percent sodium hypochlorite in vivo.³⁰⁻³² Therefore, the size of the apical root canal preparation probably accounts for the slightly different percentage of negative preobturation root canal culture results.^{4,29}

Apical root canal enlargement. Several textbooks suggest that the apical root canal should be enlarged to at least three sizes larger than the first file binding at the apical constriction during root canal preparation.³³⁻³⁶ However, Wu and colleagues³⁷ demonstrated that the first file to bind in the apical root canal does not necessarily reflect the true root canal diameter at the working length, because the apical portion of the root canal system is an ovoid, not round, configuration. Preparing the apical root canal to only three sizes larger than the first binding file does not ensure removal of the inner layer of dentin from all apical root canal walls or all infected necrotic pulp tissue.³⁷

Intracanal bacterial level. A systematic review of the literature by Baugh and Wallace³⁸ indicated that the larger the apical root canal preparation, the higher the percentage of bacteria that is eliminated from the infected root canals. In addition, a sufficiently enlarged apical root canal facilitates the delivery of copious amounts of antimicrobial irrigants to the apical portion of the root canals to kill microorganisms.^{39,40} Nevertheless, conflicting studies show that a larger

apical root canal preparation does not necessarily result in an increased bacterial reduction in the infected root canals.^{25,26,41-43} Mechanical instrumentation in combination with repeated irrigation with copious amounts of an antimicrobial agent is the most effective way to reduce the intracanal bacterial level.³² Dentists can use more flexible nickel-titanium instruments to enlarge the apical portion of the root canals.

As mentioned above, controversy exists regarding the antimicrobial activity of various concentrations of sodium hypochlorite solution. Differences concerning the effectiveness of various concentrations of sodium hypochlorite against intracanal microorganisms and biofilm may be explained by the use of different in vitro

research methodologies. For example, investigators recently reached contrasting results in their evaluations of various concentrations of sodium hypochlorite as an endodontic irrigant in in vitro studies.^{44,45} In a comprehensive literature review of root canal irrigants, Zehnder³² concluded that there was no rationale for using sodium hypochlorite solutions at concentrations of more than 1 percent weight per volume. In fact, we could find no evidence-based outcome studies that clearly pointed to a statistically valid outcome benefit derived from

the use of one concentration compared with another.

ROOT CANAL DISINFECTION

Because of the complexity of the root canal anatomy (such as lateral/accessory canals, apical ramifications, isthmuses and fins), complete root canal disinfection may be impossible to achieve in teeth with apical periodontitis regardless of the number of dental visits. In a histobacteriologic study, Nair and colleagues⁴⁶ examined mesiobuccal or mesiolingual root canals of infected mandibular molars. They instrumented the canals with hand files (K-Files, SDS, Orange, Calif.) or NiTi rotary files (LightSpeed LSX, Discus Dental, Culver City, Calif.) to an apical size of no. 40. The canals were irrigated with 5.25 percent sodium hypochlorite and rinsed with 10 milliliters of 17 percent ethylenediamine tetraacetic acid (EDTA) to remove the smear layer. The authors obturated the canals with zinc

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oxide–eugenol cement and gutta-percha. Fourteen (88 percent) of 16 root canals still contained bacteria after one-appointment endodontic therapy. They concluded that contemporary instruments and irrigation alone could not remove biofilms in inaccessible areas of the root canal system in one-visit treatment, because of the anatomical complexity of the root canal system.

ROOT CANAL CULTURE RESULTS

Some investigators have found that a negative result of a preobturation culture of the root canal system appears to improve the outcome of endodontic therapy for teeth with apical periodontitis.^{24,29,47} However, a negative culture result does not necessarily imply a bacteria-free root canal system, because bacteria may be retained in complex areas of the system or embedded inside a biofilm and are inaccessible to bacterial sampling techniques.⁴⁸

Card and colleagues⁴⁹ conducted a study that indicated that negative results of cultures from infected root canals might be obtained after increasing the size of the apical root canal preparation and by irrigating with copious amounts of an antimicrobial. However, because of variations in root canal anatomy and varying thicknesses of dentinal walls,⁵⁰⁻⁵² not all root canals can be enlarged to no. 60 or no. 80 K-Files.^{49,53} Excessive removal of dentin by instrumentation may weaken the apical portion of the root canal and cause root fracture or perforation, thus compromising the treatment outcome. There is no consensus among investigators concerning the final file size of apical root canal preparations. Clinicians should determine the final file size for each root canal system according to the root canal morphology and periradicular status.^{54,55}

Positive or negative culture results simply indicate the presence or absence of culturable bacteria in the root canal system. However, culturing does not indicate the true bacterial count and/or virulence factors, which might be more important than the culture findings in relation to the development of apical periodontitis. In addition, anaerobic culturing is impractical in private practice, because it is expensive and time-consuming. Although polymerase chain reaction (PCR), a molecular technique, is more sensitive than the culturing technique in detecting intracanal bacteria, PCR cannot determine whether target DNA is from live or dead bacteria.⁴⁸

Some studies have concluded that satisfactory

root canal disinfection can be completed in one visit for teeth with apical periodontitis, because the differences in outcomes were not statistically significant between one- and multiple-appointment endodontic therapy or between negative and positive preobturation root canal culture results.^{3,4} However, other studies found that it was difficult to achieve satisfactory root canal disinfection in one appointment, and intracanal medication, such as calcium hydroxide, was necessary to kill bacteria remaining in the root canals.^{2,29,47} Endodontic studies have reached different conclusions regarding the value of culturing, the need for interappointment intracanal medication and the optimal number of treatment visits.^{2,3,4,29,47}

The differences in findings may be attributable to variations in research methodologies, small sample sizes and inconsistent recall periods, as well as differing outcome criteria. However, it is clear that the presence of bacteria in the root canal system, especially in an incompletely obturated root canal system, is the central factor determining the ultimate outcome of endodontic therapy.^{11,14}

COMPLEX ROOT CANAL SYSTEMS

Unfortunately, available instrumentation and irrigation techniques, as well as intracanal medication are not able to eradicate intracanal bacteria in a complex root canal system regardless of the number of visits. Because root canal infection is the primary cause of apical periodontitis and some intracanal bacteria are inaccessible to the host's innate and adaptive immune defense mechanisms, and antimicrobial agents may not be able to reach bacteria in the lateral/accessory canals, isthmuses and dentinal tubules, continuous improvement in root canal disinfection methodologies is needed to ensure the maximum reduction in intracanal microorganisms before root canal obturation.⁵⁶

SMEAR LAYER REMOVAL

The smear layer of dentin is a microfilm produced by the filing or reaming action of endodontic instruments. It is composed of organic and inorganic debris and may harbor microorganisms.⁵⁷ The smear layer can prevent penetration of antimicrobial irrigants and intracanal antimicrobial medicaments into the dentinal tubules to kill microorganisms.^{31,58} Bacteria are known to penetrate into the dentinal tubules in teeth with

apical periodontitis.⁵⁹⁻⁶¹ Removing the smear layer may be advantageous because bacteria remaining inside the dentinal tubules may constitute an important reservoir from which root canal infection or re-infection may occur during or after endodontic therapy.^{62,63} Several agents have been used to remove the smear layer, including EDTA, citric acid and a mixture of tetracycline, acid and a detergent.^{32,64} However, we could find no evidence of a relationship between smear layer removal or retention and the outcome of endodontic therapy.

ROOT CANAL OBTURATION

The major function of root canal obturation is to completely seal the root canal system with filling materials, thus preventing bacterial microleakage and protecting the periradicular tissues from developing disease. Dentists commonly use gutta-percha and sealer/cement as root canal obturation materials. In vitro and in vivo studies have shown that gutta-percha and sealer are unable to create a bacteria-tight seal of the root canal system and prevent bacterial penetration along the root canal walls in teeth without adequate coronal restoration.⁶⁵⁻⁶⁸ However, in teeth with adequate coronal restoration, bacteria remaining in the root canal system after endodontic therapy may become entombed or cut off from communication with the periapical tissues by obturating materials.

Sjögren and colleagues²⁹ studied 22 teeth with positive preobturation root canal culture findings; 15 (68 percent) of these teeth healed satisfactorily after one-appointment endodontic therapy. Peters and Wesselink⁴ examined eight teeth with positive preobturation root canal culture results; seven (87.5 percent) of these teeth also healed satisfactorily after one-appointment endodontic therapy. The results of these studies suggest that some bacteria in the root canals with positive preobturation culture results might have been killed, entombed or cut off from communication with periapical tissues by antimicrobial treatment and/or the physical properties of root canal obturating materials.⁶⁹

Using bacteriologic culturing, Molander and colleagues⁷⁰ recovered bacteria from nine (45 percent) of 20 teeth with filled root canals without clinical signs or symptoms of periapical disease or

radiographic evidence of periradicular lesions. The authors concluded that as long as no pathway to the periapical tissues existed for remaining intracanal bacteria, a periapical tissue response would not develop. Nonetheless, the likelihood of intracanal bacteria being entombed or cut off from communication with periradicular tissues by root canal obturating materials is unpredictable.

Existing evidence shows that mineral trioxide aggregate, dentin bonding/resin-based composite and intermediate restorative materials can be used to seal the root canal orifices of obturated teeth to prevent bacterial penetration into the root canals.^{71,72} Because coronal leakage may be a factor in failed endodontic treatment,⁷³ effective coronal restoration is important immediately after endodontic therapy.⁷⁴⁻⁷⁷

CONCLUSION

The results of a recent systematic review of the literature¹ suggest that one-appointment endodontic therapy may be feasible in selected

cases of teeth with apical periodontitis. Teeth appropriate for one-appointment endodontic therapy should be free of clinical signs and/or symptoms, such as pain, swelling or draining sinus tract. The root canal anatomy should permit a sufficiently large apical root canal preparation that enables the dentist to remove intracanal bacteria effectively and deliver

antimicrobial irrigants to the apical portion of the root canal and achieve optimum disinfection without causing perforation or transportation.

Regardless of the number of appointments, effective bacteriologic control of the root canal system is critical in endodontic therapy. Although endodontic treatment failures may be due to multiple factors—including root canal transportation, perforations, incomplete instrumentation and/or obturation, coronal leakage, vertical root fracture, presence of foreign bodies or host resistance—the primary etiology is bacterial infection in the root canal system.^{5-8,11}

Increasing the size of the apical root canal preparation and irrigating with copious amounts of sodium hypochlorite have been shown to significantly reduce the intracanal bacterial level^{49,53,78,79} and, presumably, will result in better treatment outcomes for asymptomatic teeth with

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apical periodontitis. Nevertheless, limited evidence is available concerning the relationship between increasing the size of the apical root canal preparation and the outcome of endodontic therapy.^{25,26}

Only a small number of randomized, controlled clinical trials have been conducted regarding one-appointment endodontic therapy. Therefore, more randomized controlled clinical trials using contemporary treatment procedures are required to establish an evidence-based decision regarding one-appointment endodontic therapy for asymptomatic teeth with apical periodontitis.⁸⁰ ■

- Sathorn C, Parashos P, Messer HH. Effectiveness of single- versus multiple-visit endodontic treatment of teeth with apical periodontitis: a systematic review and meta-analysis. *Int Endod J* 2005;38(6):347-55.
- Trope M, Delano EO, Orstavik D. Endodontic treatment of teeth with apical periodontitis: single vs. multiple treatment. *J Endod* 1999;25(5):345-50.
- Weiger R, Rosendahl R, Löst C. Influence of calcium hydroxide intracanal dressings on the prognosis of teeth with endodontically induced periapical lesions. *Int Endod J* 2000;33(3):219-26.
- Peters LB, Wessellink PR. Periapical healing of endodontically treated teeth in one and two visits obturated in the presence or absence of detectable microorganisms. *Int Endod J* 2002;35(8):660-7.
- Kakehashi S, Stanley HR, Fitzgerald RJ. The effects of surgical exposures in dental pulps in germ-free and conventional laboratory rats. *Oral Surg Oral Med Oral Pathol* 1965;20:340-9.
- Sundqvist G. Bacteriologic studies of necrotic dental pulp. Odontology dissertation no. 7 (dissertation). Umea, Sweden: University of Umea; 1976:1-94.
- Moller AJ, Fabricius L, Dahlen G, Ohman AE, Heyden G. Influence on periapical tissues of indigenous oral bacteria and necrotic pulp tissue in monkeys. *Scand J Dent Res* 1981;89(6):475-84.
- Lin LM, Di Fiore PM, Lin J, Rosenberg PA. Histological study of periradicular tissue responses to uninfected and infected devitalized pulps in dogs. *J Endod* 2006;32(1):34-8.
- Simon JH. The apex: how critical is it? *Gen Dent* 1994;42(4):330-4.
- Chugal NM, Clive JM, Spångberg LS. Endodontic infection: some biologic and treatment factors associated with outcome. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;96(1):81-90.
- Nair PN, Sjogren U, Krey G, Kahnberg KE, Sundqvist G. Intraradicular bacteria and fungi in root-filled, asymptomatic human teeth with therapy-resistant periapical lesions: a long-term light and electron microscopic follow-up study. *J Endod* 1990;16(12):580-8.
- Molven O, Olsen I, Kerekes K. Scanning electron microscopy of bacteria in the apical part of root canals in permanent teeth with periapical lesions. *Endod Dent Traumatol* 1991;7(5):226-9.
- Baumgartner JC, Falkler WA Jr. Bacteria in the apical 5 mm of infected root canals. *J Endod* 1991;17(8):380-3.
- Lin LM, Pascon EA, Skribner J, Gandler P, Langeland K. Clinical, radiographic, and histologic study of endodontic treatment failures. *Oral Surg Oral Med Oral Pathol* 1991;71(5):603-11.
- Kuttler Y. Microscopic investigation of root apexes. *JADA* 1955;50(5):544-52.
- Ricucci D, Langeland K. Apical limit of root canal instrumentation and obturation, part 2: a histological study. *Int Endod J* 1998;31(6):394-409.
- Williams CB, Joyce AP, Roberts S. A comparison between in vivo radiographic working length determination and measurement after extraction. *J Endod* 2006;32(7):624-7.
- Dummer PM, McGinn JH, Rees DG. The position and topography of the apical canal constriction and apical foramen. *Int Endod J* 1984;17(4):192-8.
- Blasković-Subat V, Marčić B, Sutalo J. Asymmetry of the root canal foramen. *Int Endod J* 1992;25(3):158-64.
- Shabahang S, Goon WW, Gluskin AH. An in vitro evaluation of Root ZX electronic apex locator. *J Endod* 1996;22(11):616-8.
- Dunlap CA, Remeikis NA, BeGole EA, Rauschenberger CR. An in vivo evaluation of an electronic apex locator that uses the ratio method in vital and necrotic canals. *J Endod* 1998;24(1):48-50.
- Fouad AF, Reid LC. Effect of using electronic apex locators on selected endodontic treatment parameters. *J Endod* 2000;26(6):364-7.
- Hor D, Attin T. The accuracy of electronic working length determination. *Int Endod J* 2004;37(2):125-31.
- Sjogren U, Hagglund B, Sundqvist G, Wing K. Factors affecting the long-term results of endodontic treatment. *J Endod* 1990;16(10):498-504.
- Strindberg LZ. The dependence of the results of pulp therapy on certain factors: an analytic study based on radiographic and clinical follow-up examination. *Acta Odontologica Scand* 1956;14(supplement 21):1-174.
- Kerekes K, Tronstad L. Long-term results of endodontic treatment performed with a standardized technique. *J Endod* 1979;5(3):83-90.
- Sundqvist G. Taxonomy, ecology, and pathogenicity of the root canal flora. *Oral Surg Oral Med Oral Pathol* 1994;78(4):522-30.
- Lin L, Shovlin F, Skribner J, Langeland K. Pulp biopsies from the teeth associated with periapical radiolucency. *J Endod* 1984;10(9):436-48.
- Sjogren U, Figdor D, Persson S, Sundqvist G. Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. *Int Endod J* 1997;30(5):297-306.
- Cvek M, Nord CE, Hollender L. Antimicrobial effect of root canal debridement in teeth with immature root: a clinical and microbiologic study. *Odontol Revy* 1976;27(1):1-10.
- Bystrom A, Sundqvist G. The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy. *Int Endod J* 1985;18(1):35-40.
- Zehnder M. Root canal irrigants. *J Endod* 2006;32(5):389-98.
- Grossman LI. Endodontic practice. 8th ed. Philadelphia: Lea & Febiger; 1974:188-221.
- Ingle JI, Bakland LK, eds. Endodontics. 5th ed. Hamilton, Ontario, Canada: Decker; 2002:405-570.
- Weine FS. Endodontic therapy. St. Louis: Mosby; 1996:164-239.
- Walton RE, Torabinejad M. Principles and practice of endodontics. 3rd ed. Philadelphia: Saunders; 2002:206-38.
- Wu MK, Barkis D, Roris A, Wessellink PR. Does the first file to bind correspond to the diameter of the canal in the apical region? *Int Endod J* 2002;35(3):264-7.
- Baugh D, Wallace J. The role of apical instrumentation in root canal treatment: a review of the literature. *J Endod* 2005;31(5):333-40.
- Ram Z. Effectiveness of root canal irrigation. *Oral Surg Oral Med Oral Pathol* 1977;44(2):306-12.
- Chow TW. Mechanical effectiveness of root canal irrigation. *J Endod* 1983;9(11):475-9.
- Yared GM, Dagher FE. Influence of apical enlargement on bacterial infection during treatment of apical periodontitis. *J Endod* 1994;20(11):535-7.
- Coldero LG, McHugh S, MacKenzie D, Saunders WP. Reduction in intracanal bacteria during root canal preparation with and without apical enlargement. *Int Endod J* 2002;35(5):437-46.
- Hoskinson SE, Ng YL, Hoskinson AE, Moles DR, Gulabivala K. A retrospective comparison of outcome of root canal treatment using two different protocols. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;93(6):705-15.
- Clegg MS, Vertucci FJ, Walker C, Belanger M, Britto LR. The effect of exposure to irrigant solutions on apical dentin biofilms in vitro. *J Endod* 2006;32(5):434-7.
- Dunavant TR, Regan JD, Glickman GN, Solomon ES, Honeyman AL. Comparative evaluation of endodontic irrigants against *Enterococcus faecalis* biofilms. *J Endod* 2006;32(6):527-31.
- Nair PN, Henry S, Cano V, Vera J. Microbial status of apical root canal system of human mandibular first molars with primary apical periodontitis after 'one-visit' endodontic treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005;99(2):231-52.
- Waltimo T, Trope M, Haapasalo M, Orstavik D. Clinical efficacy of treatment procedures in endodontic infection control and one year follow-up of periapical healing. *J Endod* 2005;31(12):863-6.
- Sathorn C, Parashos P, Messer HH. How useful is root canal culturing in predicting treatment outcome? *J Endod* 2007;33(3):220-5.
- Card SJ, Sigurdsson A, Orstavik D, Trope M. The effectiveness of increased apical enlargement in reducing intracanal bacteria. *J Endod* 2002;28(11):779-83.
- Kerekes K, Tronstad L. Morphometric observations on the root canals of human anterior teeth. *J Endod* 1977;3(1):24-9.
- Kerekes K, Tronstad L. Morphometric observations on the root canals of human premolars. *J Endod* 1977;3(2):74-9.
- Kerekes K, Tronstad L. Morphometric observations on the root canal of human molars. *J Endod* 1977;3(3):114-8.
- Shuping GB, Orstavik D, Sigurdsson A, Trope M. Reduction of intracanal bacteria using nickel-titanium rotary instrumentation and

various medications. *J Endod* 2000;26(12):751-5.

54. Vertucci F. Root canal morphology and its relationship to endodontic procedures. *Endod Topics* 2005;10:3-29.

55. Hulsman M, Peters OA, Dummer PM. Mechanical preparation of root canals: shaping goals, techniques and means. *Endod Topics* 2005;10:30-76.

56. Bystrom A, Happonen RP, Sjogren U, Sundqvist G. Healing of periapical lesions of pulpless teeth after endodontic treatment with controlled asepsis. *Endod Dent Traumatol* 1987;3(2):58-63.

57. Pashley DH. Smear layer: overview of structure and function. *Proc Finn Dent Soc* 1992;88(supplement 1):215-24.

58. Orstavik D, Haapasalo M. Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules. *Endod Dent Traumatol* 1990;6(4):142-9.

59. Ando H, Hoshimo E. Predominant obligate anaerobes invading the deep layers of root canal dentine. *Int Endod J* 1990;23(1):20-7.

60. Peters LB, Wesselink PR, Buijs JF, van Winkelhoff AJ. Viable bacteria in root dentinal tubules of teeth with apical periodontitis. *J Endod* 2001;27(2):76-81.

61. Love RM, Jenkinson HF. Invasion of dentinal tubules by oral bacteria. *Crit Rev Oral Biol Med* 2002;13(2):171-83.

62. Oguntebi B. Dentine tubule infection and endodontic therapy implications. *Int Endod J* 1994;27(4):218-22.

63. Peters LB, Wesselink PR, Moorer WR. The fate and the role of bacteria left in root canal dentinal tubules. *Int Endod J* 1995;28(2):95-9.

64. Torabinejad M, Handysides R, Khademi AA, Bakland LK. Clinical implications of the smear layer in endodontics: a review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002;94(6):658-66.

65. Swanson K, Madison S. An evaluation of coronal microleakage in endodontically treated teeth, part I: time periods. *J Endod* 1987;13(2):56-9.

66. Madison S, Wilcox LR. An evaluation of coronal microleakage of endodontically treated teeth, part III: in vivo study. *J Endod* 1988;14(9):455-8.

67. Torabinejad M, Ung B, Kettering JD. In vitro bacterial penetration of coronally unsealed endodontically treated teeth. *J Endod* 1990;16(12):566-9.

68. Friedman S, Torneck CD, Komorowski R, Ouzounian Z, Syrtash P, Kaufman A. In vivo model for assessing the functional efficacy of endodontic filling materials and techniques. *J Endod* 1997;23(9):557-61.

69. Orstavik D. Materials used for root canal obturation: technical, biological and clinical testing. *Endodontic Topics* 2005;12:25-38.

70. Molander A, Reit C, Dahlén G, Kvist T. Microbiological status of root-filled teeth with apical periodontitis. *Int Endod J* 1998;31(1):1-7.

71. Mah T, Basrani B, Santos JM, et al. Periapical inflammation affecting coronally-inoculated dog teeth with root fillings augmented by white MTA orifice plugs. *J Endod* 2003;29(7):442-6.

72. Yamauchi S, Shipper G, Buttke T, Yamauchi M, Trope M. Effect of orifice plugs on periapical inflammation in dogs. *J Endod* 2006;32(6):524-6.

73. Saunders WP, Saunders EM. Coronal leakage as cause of failure in root-canal therapy: a review. *Endod Dent Traumatol* 1994;10(3):105-8.

74. Safavi KE, Dowden WE, Langeland K. Influence of delayed coronal permanent restoration on endodontic prognosis. *Endod Dent Traumatol* 1987;3(4):187-91.

75. Ray HA, Trope M. Periapical status of endodontically treated teeth in relation to the technical quality of the root filling and the coronal restoration. *Int Endod J* 1995;28(1):12-8.

76. Tronstad L, Asbjørnsen K, Døving L, Pedersen I, Eriksen HM. Influence of coronal restorations on the periapical health of endodontically treated teeth. *Endod Dent Traumatol* 2000;16(5):218-21.

77. Hommez GM, Coppens CR, De Moor RJ. Periapical health related to the quality of coronal restorations and root fillings. *Int Endod J* 2002;35(8):680-9.

78. Byström A, Sundqvist G. Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scand J Dent Res* 1981;89(4):321-8.

79. Orstavik D, Kerekes K, Molven O. Effects of extensive apical reaming and calcium hydroxide dressing on bacterial infection during treatment of apical periodontitis: a pilot study. *Int Endod J* 1991;24(1):1-7.

80. Molander A, Warfvinge J, Reit C, Kvist T. Clinical and radiographic evaluation of one- and two-visit endodontic treatment of asymptomatic necrotic teeth with apical periodontitis: a randomized clinical trial. *J Endod* 2007;33(10):1145-8.