Contemporary endodontics – part 1

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VERIFIABLE CPD PAPER

IN BRIEF

- Emphasises the importance of case selection and assessment of restorability.
- Highlights contemporary special tests, including cone beam computed tomography.
- Discusses preservation of the pulp as the best root filling and the potential future of endodontics in regeneration of the pulp.

PRACTICE

This is the first of two review papers which aim to update the general dental practitioner on contemporary endodontic practice. This first paper reviews advancements in knowledge of endodontic infections, case selection and diagnosis. An overview is given of contemporary pulp therapy and the role of antibiotics in endodontics. The second paper assesses the recent developments in root canal treatment, restoration of the endodontically treated tooth, and advanced endodontic procedures, ie root canal retreatment and surgical endodontics.

INTRODUCTION

The aim of endodontic treatment is to treat or prevent apical periodontitis.[1] Endodontics encompasses the differential diagnosis and management of oro-facial pain, pulp therapy to preserve the health of the pulp, root canal treatment, root canal retreatment, and surgical endodontics.

Investigations in the 1960s confirmed that infection within the tooth is essential for apical periodontitis to occur.[2] The 1970s and 1980s increased understanding of the microbiology of infected root canals[3-5] and the ways in which irrigants, agitation of irrigants, and medicaments can disinfect the root canal.[6-10] Over the past two decades knowledge of the nature of endodontic disease has improved including microbial biofilms, the causes of persistent infection, and the factors which influence the outcome of endodontic treatment. There have also been advancements in materials, equipment and techniques including nickel-titanium files, newer generations of electronic apex locators, dental operating microscopes, alternative root filling materials, and endodontic microsurgery. These technical advancements have improved the delivery, consistency and efficiency of endodontic treatment as well as improving patient comfort.

ENDODONTIC INFECTIONS AND BIOFILMS

The detection and identification of microbes in endodontic infections has continued to improve. It was traditionally thought that there were up to 12 taxa of bacteria in any untreated endodontic infection.[5] Contemporary culture-independent molecular techniques have revealed a more diverse microflora with up to 20 taxa of bacteria per untreated endodontic infection.[11] It has also been shown that the microflora of endodontically treated teeth with persistent infection differs from that of untreated infected teeth, with *Enterococcus faecalis*[12] and *Candida albicans*[13] being found more frequently in the root canals of endodontically treated teeth. Several viruses, including cytomegalovirus and Epstein-Barr virus, have been detected in periapical lesions. The role of these viruses in apical periodontitis is yet to be confirmed.

It is now widely accepted that the vast majority of microbes exist as biofilms and not in 'free-floating' planktonic form. A biofilm is a complex community of microbes embedded in an exopolysaccharide matrix that tenaciously adheres to a surface or each other, and the cells exhibit phenotypic differences with respect to growth rate and gene transcription.[14] In nature and industry, biofilms exist on the surface of a pond or the inner surface of oil pipes. In dentistry, biofilms are present in dental unit water lines and as dental plaque on the surfaces of teeth. In endodontics, biofilms have been visualised within accessory canals,[15] at the apical foramen,[16] and within isthmuses.[17] Biofilms are usually multispecies with each species bringing their own beneficial function including adaptive survival mechanisms and resisting adverse environmental changes, host defences and antimicrobial agents (Fig. 1). A simple analogy is a country where humans and other animals coexist and depend on each other for survival.[18] All aspects of contemporary endodontics are aimed at disrupting and killing these well adapted microbial coatings in order to disinfect teeth and allow healing of apical periodontitis.

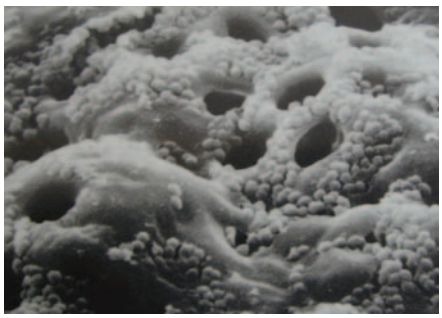

Fig. 1 Scanning electron microscope section of a microbial biofilm on a root canal wall surface; the aim of chemo-mechanical debridement is to disrupt these tenacious microbial coatings

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PREREQUISITES FOR CONTEMPORARY ENDODONTICS

Rubber dam

Rubber dam remains mandatory for contemporary non-surgical endodontic procedures (Fig. 2). The advantages of rubber dam are protection of the patient's oropharynx, infection control, patient comfort and improving treatment efficiency.[19,20] With increasing numbers of patients and health care professionals reporting allergy to latex, it is recommended that clinicians use alternatives to latex, such as silicone-based dams. Some non-latex dams are very flexible and should be avoided as they may encourage saliva leakage.

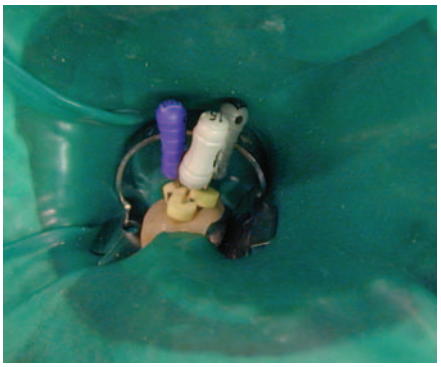

Fig. 2 Rubber dam is essential for carrying out endodontic treatment

Magnification and coaxial illumination

Traditionally, the clinician relied largely on tactile sensation to 'blindly' locate root canal orifices and navigate root canals. Contemporary endodontic diagnostic and treatment procedures utilise magnification, such as dental loupes, dental operating microscopes and endoscopes (Fig. 3). Magnification of up to ×6 may be achieved with standard dental loupes; higher magnifications of ×25 can be achieved with dental operating microscopes. Dental loupes and operating microscopes should be used with coaxial lighting to provide constant illumination in the same plane as the clinician's vision. A front surface mirror is also a prerequisite to prevent secondary reflections. Endoscopes are gaining popularity for use in surgical endodontics with several advantages over the operating microscope, including non-fixed field of vision, direct viewing, and faster focusing and zooming.[21] Without magnification, it would be difficult to:

- Detect subtle signs of microleakage around existing restorations
- Visualise incomplete tooth fractures ('cracks') on the outer surface of teeth
- Visualise fractures running across the pulp chamber floor or into root canals
- Locate and negotiate root canals, especially partially calcified root canals
- Remove fractured instruments
- Perform endodontic microsurgery.

DIAGNOSIS – SPECIAL TESTS

An accurate diagnosis is the first and most important aspect of endodontics. Special tests are essential aids to arriving at the correct diagnosis. Ideally, several tests should be used in conjunction to give an overall picture. It is not sufficient to rely on a single diagnostic test, for example a crude percussion test using a dental mirror handle, to arrive at a diagnosis.

Assessment of pulp status

There are many ways to assess the status of the pulp. Conventional special tests assess conduction of nerves in the pulp and are therefore not strictly vitality tests but rather sensibility tests. These include cold thermal, heat thermal and electrical tests.

It is generally accepted that cold tests are more reliable than heat tests, and the colder the test the better.[22] Ethyl chloride (boiling point -4°C) and ice are relatively ineffective in assessing the status of the nerves in the pulp, yet they are the most commonly used cold tests in general dental practice. More effective cold tests include carbon dioxide snow (boiling point -72°C) or refrigerant spays (boiling point -50°C). The latter is easily available from most dental suppliers, eg Endo-Frost (Coltène/Whaledent, Langenau, Germany) (Fig. 4). Thermal tests are subjective and it is not possible to objectively compare results. The advantage of electric testing is that a numerical value is obtained from the electric pulp tester. This result can be compared to previous readings. It should be remembered that results from thermal and electric tests are not quantitative and do not indicate the level of health or disease of the pulp.

Physiometric special tests assess pulpal blood flow, eg laser Doppler flowmetry, or oxygen saturation levels in the blood, eg pulse oximetry. These are currently technique sensitive, time consuming to assess data, and the equipment is expensive. Nevertheless, these are true vitality tests, and are potentially the future of pulp testing.

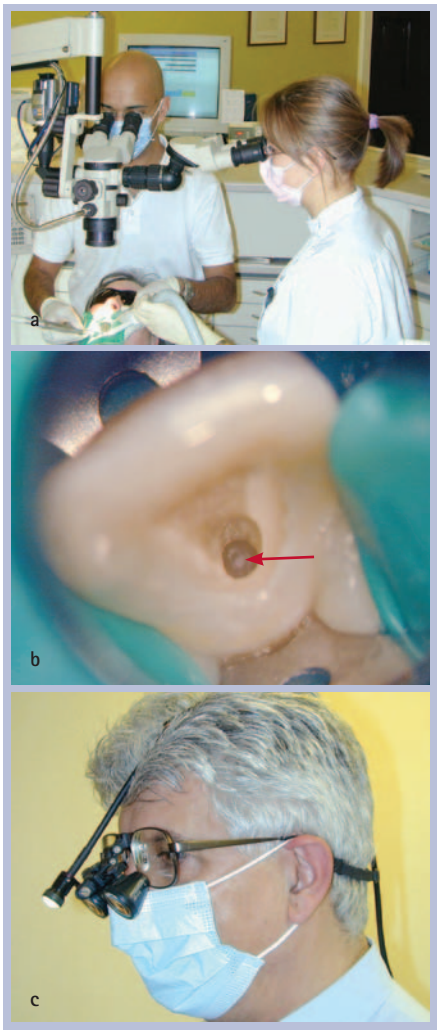

Fig. 3 (a) Dental operating microscope, the additional observer scope for the dental assistant facilitates four-handed close support dentistry. (b) A calcified canal is easily detectable with the aid of magnification. (c) Dental loupes with a fibre optic light are also useful

Radiology

Over the past decade image quality from digital radiography has improved considerably, the diagnostic yield of digital image receptors (eg phosphor plates, solid-state digital sensors connected to Charge Coupled Devices) is equal to conventional film-based radiographs. The main benefit of digital radiography is reduced radiation dose to the patient. Other advantages include quicker viewing of images (immediate with solid-state sensors); ability to enhance images using computer software; data storage benefits; elimination of a dark room and developing/fixing solutions, and

Fig. 4 (a) Electric pulp tester. (b) Refrigerant aerosol spray for cold sensibility testing. (c) The refrigerant is sprayed on a cotton pellet and then applied to the tooth

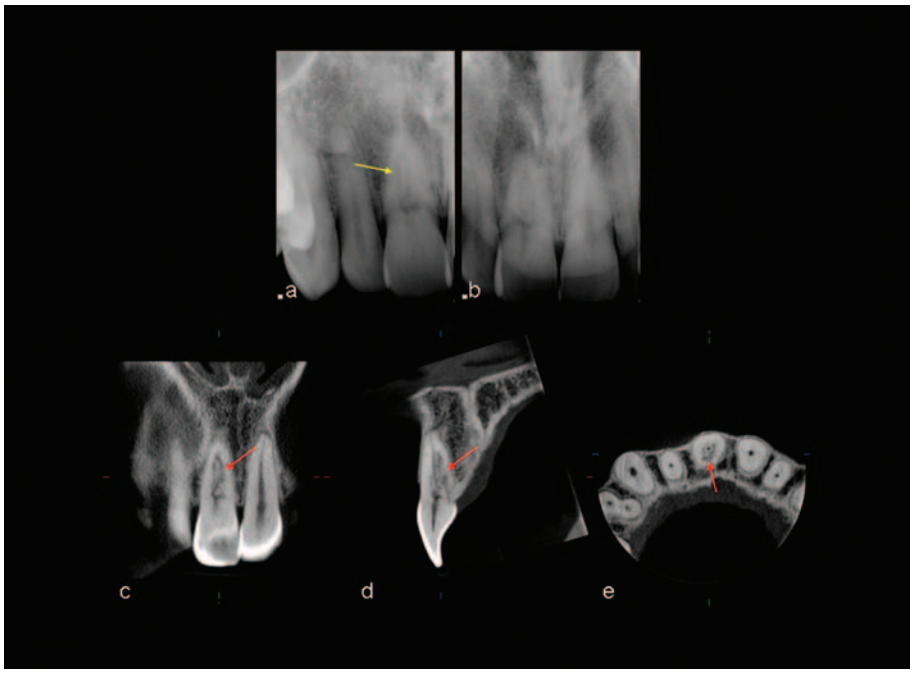

Fig. 5 (a) Periapical radiographs reveals a mottled appearance in the mid-third of tooth 11; provisional diagnoses of either internal resorption or external cervical resorption are reached from these two-dimensional images. Reconstructed CBCT (b) coronal, (c) sagittal and (d) axial images confirm a diagnosis of external cervical resorption, and also reveal the true nature of the resorptive defect. Courtesy of Patel S, Dawood A, Wilson R, Horner K, Mannocci F. The detection and management of root resorption lesions using intraoral radiography and cone beam computed tomography – an in vivo investigation. *Int Endod J* 2009; 42: 831–838.

the associated environmental problems; images can be easily sent electronically to other health care professionals; and improved patient communication with computer-screen sized images.[23] Despite these advantages, conventional images, whether captured digitally or on film, have several limitations including the compression of three-dimensional anatomy, anatomical noise, and geometric distortion.[24]

Cone Beam Computed Tomography (CBCT) is a three-dimensional imaging technique which has been specifically designed for imaging the maxillofacial skeleton and overcomes the limitations of radiographs.[25,26] A succession of 'basis images' are taken of the region of interest as the X-ray source and scanner simultaneously rotate once around the patient's head.[27] Sophisticated software is used to convert this series of two-dimensional basis images into a three-dimensional data set. This data set may then be reconstructed in three orthogonal planes (axial, sagittal and coronal) which are then displayed simultaneously. These images can be scrolled through in real time (Fig. 5).[28,29]

The effective radiation dose to the patient is of the same order of magnitude as conventional radiography.[30,31] The operator is not constrained by predetermined views, instead, they may select virtually any view they wish, thus maximising the diagnostic value of the scan. Several studies have confirmed that CBCT produces undistorted and accurate images of the area under investigation. The compact size of the CBCT scanner and its ease of use has resulted in its rapid uptake in dental practices.[32,33]

Clinical and laboratory studies have concluded that CBCT detects endodontic lesions before they become visible on conventional radiographs.[34-38] This should improve diagnosis, and may also result in a more objective assessment of healing of endodontically treated teeth.[33] Three-dimensional imaging with CBCT is extremely useful for planning apical surgery. Recently, CBCT has been shown to be very useful for accurately diagnosing and managing external cervical and internal resorption lesions, as well as teeth with complex anatomy, for example, dens invaginatus and moderately-severely curved canals in the bucco-lingual planes.[39] CBCT is not without its limitations, these include scatter caused by metallic restorations, the resolution (2-3 lines/mm) is inferior to conventional radiography (15-20 lines/mm) and the cost of the scanner.

CASE SELECTION

Heroic endodontics is futile when the overall prognosis of a tooth is not predictable. Sometimes it is in the patient's best interest to opt for extraction and consider restoration of the resulting space, ideally with a crown retained implant. Implants have a high survival rate and are a viable alternative in certain cases.[40] The decision-making process should be based on a logical and structured assessment including:[41]

- Prosthodontic factors. The clinician should identify incomplete tooth fractures or root fractures after removing the existing coronal restoration. The clinician must ask themselves 'Can I restore this tooth

Fig. 6 (a) The restorability, type and design of the post-endodontic crown can only be assessed (b) when the restoration has been dismantled and (c) the tooth has been provisionally restored with an orthodontic band and glass ionomer cement to prevent fracturing of the remaining cusps before definitive restoration

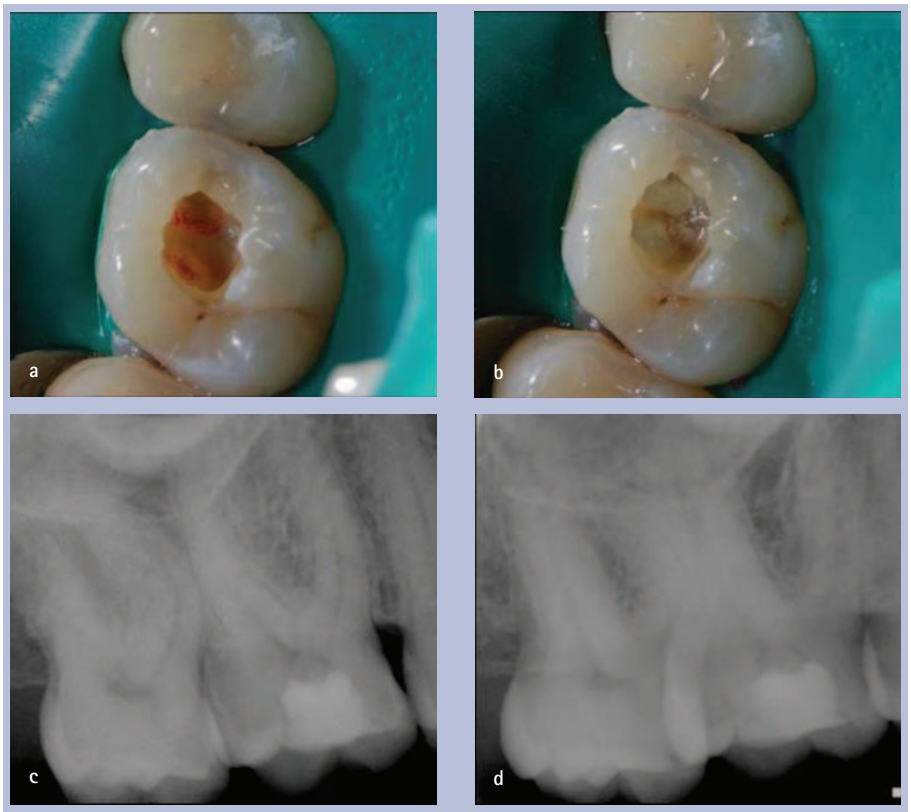

Fig. 7 (a) A pulp exposure in a permanent molar tooth. (b) The exposure has been sealed with MTA and a permanent plastic coronal restoration. (c) Immediate postoperative radiograph. (d) Four year follow-up radiograph, the tooth responds to sensibility testing and is functional. The patient has avoided root canal treatment and a crown

reliably and predictably after root canal treatment is complete?'

- Periodontal factors
- Endodontic factors. The clinician should be assessing adequate mouth opening, ease of isolation, and ability to locate, negotiate, disinfect and fill all root canals
- Psychosocial factors, including the patient's motivation and financial implications
- The clinician's own abilities. Referral to a specialist in endodontics may be warranted.

Microbes are the cause of apical periodontitis. Microbes may enter the pulp via several 'avenues', eg caries, incomplete tooth fractures, marginal breakdown of restorations, or poorly adapted restorations. It is desirable to dismantle the existing restoration to ensure that the coronal portion of the tooth is completely disease free,[42] and to assess the overall restorability of the tooth (Fig. 6). The authors recommend that in the majority of cases the entire restoration is removed, before commencing endodontic treatment. If the caries is extensive or there is a catastrophic crack, then the patient should be advised to have the tooth extracted. The exception to this is when a well-adapted cast restoration has recently been fitted and the pulp subsequently becomes irreversibly inflamed. The patient should still be warned that it may be necessary to remove this restoration once treatment has commenced. Patients should always be informed of the necessity and rationale of assessing the restorability of the tooth treatment planned for endodontics before embarking upon treatment.

PRESERVING AND REGENERATING THE PULP

In developing teeth, the pulp plays a role in dentine formation, thus allowing radicular dentine to thicken and root length to continue. In mature teeth, the pulp provides sensory protection so that catastrophic forces are not applied to teeth during function; a maintenance role whereby an intact blood supply provides nutrients to and removes breakdown products from cells; and a defence role whereby the pulp has the ability to produce tertiary dentine to

protect itself from irritants. A healthy pulp maintains healthy periapical tissues and is therefore the ideal root filling. The clinician should always consider performing pulp therapies to preserve the vitality of the pulp rather than root canal treatment for cases of reversibly inflamed pulps. Pulp therapies include biological caries removal, pulp capping and pulpotomies. As with root canal treatment, the success of pulp therapies is dependent on removal of infected dentine, and prevention of re-infection through good coronal seal.

Traditionally, pulp capping involved the use of self-setting calcium hydroxide. This has been superseded by calcium silicate cement, eg mineral trioxide aggregate (MTA), which is now considered the material of choice for direct pulp capping (Fig. 7). MTA has better sealing characteristics, biocompatibility and stimulates the release of bioactive endogenous factors which induce a more predictable reparative dentine bridge than self-setting calcium hydroxide.[43] More recently, a new calcium silicate cement, Biodentine (Septodont, Saint Maur des Fosses, France), has become available which has improved handling compared to MTA. Biodentine is prepared by placing a capsule of powder and liquid in a high-speed mixing device. The material is then applied to the pulpal exposure using a suitable carrier/gun and left to set. The total preparation, placement and setting time is approximately 12 minutes.

An exciting emerging field is regenerative endodontics, which aims to biologically replace diseased, missing or traumatised pulp, as well as dentine, through revascularisation or other approaches such as stem cell therapy and tissue engineering.[44] Revascularisation allows normal wound healing and continued root formation by utilising existing mesenchymal stem cells in the dental papilla. The protocol for revascularisation includes disinfecting the root canal with sodium hypochlorite and an interappointment medicament, usually a mixture of antibiotic pastes (ciprofloxacin, metronidazole and/or minocycline). At the next visit, bleeding is mechanically induced by overinstrumenting the periapical tissues and a calcium silicate cement is placed over the blood clot followed by an adhesive plastic restoration. It should be emphasised that current evidence for revascularisation is based on case reports/series[45-47] and there are no established guidelines. It has been recommended that regenerative endodontic procedures in traumatised non-vital immature permanent teeth should only be performed if the tooth is not suitable for apexogenesis, apexification and root canal treatment.[48] It has been proposed that regenerative endodontic procedures may include the delivery of stem cells, growth factors and tissue scaffolds into the root canal to guide appropriate tissue differentiation.[49] In the future, regenerative endodontics may be used instead of root canal treatment for selected cases.

ANTIBIOTICS

Historically, systemic antibiotics were required for patients considered at risk of infective endocarditis. Current national guidelines in the United Kingdom do not recommend antibiotic prophylaxis against infective endocarditis.[50] In contemporary endodontics, systemic antibiotics are indicated as an adjunct to treatment when there is evidence of severe disease with cellulitis or if there are systemic features of infection;[51] or after re-implantation of an avulsed tooth.[52,53] Local antibiotics may have a role as interappointment dressings to eradicate endodontic infections in immature teeth that are undergoing regenerative endodontic procedures.

CONCLUSION

Our understanding of and ability to diagnose endodontic disease continues to improve. Several contemporary diagnostic special tests are available to assist clinicians in arriving at the correct diagnosis. It is essential to look at the overall picture and select cases carefully for endodontic treatment to have a favourable outcome. Just because a tooth can be endodontically treated does not necessarily mean that it should be. In certain cases, clinicians should also consider contemporary endodontic procedures to preserve or regenerate the pulp.

1. Ørstavik D, Pitt Ford T. Apical periodontitis: microbial infection and host response. *In* Ørstavik D, Pitt Ford T (eds) *Essential endodontology: prevention and treatment of apical periodontitis.* 2nd ed. pp 1–9. Oxford, UK: Blackwell Munksgaard Ltd, 2008.
2. Kakehashi S, Stanley H R, Fitzgerald R J. The effects of surgical exposures of dental pulps in germ-free and conventional laboratory rats. *Oral Surg Oral Med Oral Pathol* 1965; **20:** 340–349.
3. Sundqvist G. *Bacteriological studies of necrotic pulps.* Umeå, Sweden: Umeå University, 1976. PhD Thesis.
4. Möller A J, Fabricius L, Dahlén G, Ohman A E, Heyden G. Influence on periapical tissues of indigenous oral bacteria and necrotic pulp tissue in monkeys. *Scand J Dent Res* 1981; **89:** 475–484.
5. Fabricius L, Dahlen G, Holm S E, Möller Å J R. Influence of combinations of oral bacteria on periapical tissues of monkeys. *Scand J Dent Res* 1982; **90:** 200–206.
6. Byström A, Sundqvist G. Bacteriologic evaluation of the efficacy of mechanical root canal instrumentation in endodontic therapy. *Scand J Dent Res* 1981; **89:** 321–328.
7. Tronstad L, Andreasen J O, Hasselgren G, Kristerson L, Riis I. pH changes in dental tissues after root canal filling with calcium hydroxide. *J Endod* 1981; **7:** 17–21.
8. Moorer W R, Wesselink P R. Factors promoting the tissue dissolving capability of sodium hypochlorite. *Int Endod J* 1982; **15:** 187–196.
9. Byström A, Sundqvist G. Bacteriologic evaluation of the effect of 0.5 percent sodium hypochlorite in endodontic therapy. *Oral Surg Oral Med Oral Pathol* 1983; **55:** 307–312.
10. Byström A, Sundqvist G. The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy. *Int Endod J* 1985; **18:** 35–40.
11. Munson M A, Pitt-Ford T, Chong B, Weightman A, Wade W G. Molecular and cultural analysis of the microflora associated with endodontic infections. *J Dent Res* 2002; **81:** 761–766.
12. Molander A, Reit C, Dahlén G, Kvist T. Microbiological status of root-filled teeth with apical periodontitis. *Int Endod J* 1998; **31:** 1–7.
13. Waltimo T M, Sirén E K, Torkko H L, Olsen I, Haapasalo M P. Fungi in therapyresistant apical periodontitis. *Int Endod J* 1997; **30:** 96–101.
14. Donlan R M, Costerton J W. Biofilms: survival mechanisms of clinically relevant microorganisms. *Clin Microbiol Rev* 2002; **15:** 167–193.
15. Nair P N, Sjögren U, Krey G, Sundqvist G. Therapy-resistant foreign body giant cell granuloma at the periapex of a root-filled human tooth. *J Endod* 1990; **16:** 589–595.
16. Nair P N, Pajarola G, Luder H U. Ciliated epithelium-lined radicular cysts. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; **94:** 485–493.
17. Nair P N, 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:** 231–252.
18. Costerton J W. Overview of microbial biofilms. *J Ind Microbiol* 1995; **15:** 137–140.
19. Bhuva B, Chong B S, Patel S. Rubber dam in clinical practice. *Endo* 2008; **2:** 131–141.
20. Ahmad I A. Rubber dam usage for endodontic treatment: a review. *Int Endod J* 2009; **42:** 963–972.
21. Taschieri S, Del Fabbro M, Testori T, Weinstein R, Del Fabbro M. Microscope versus endoscope in root-end management: a randomized controlled study. *Int J Oral Maxillofac Surg* 2008; **37:** 1022–1026.
22. Pitt Ford T R, Patel S. Technical equipment for assessment of dental pulp status. *Endodontic Topics* 2004; **7:** 2–13.
23. Christensen G J. Why switch to digital radiography? *J Am Dent Assoc* 2004; **135:** 1437–1439.
24. Patel S, Dawood A, Mannocci F, Wilson R, Pitt Ford T. Detection of periapical bone defects in human jaws using cone beam computed tomography and intraoral radiography. *Int Endod J* 2009; **42:** 507–515.
25. Arai Y, Tammisalo E, Iwai K, Hashimoto K, Shinoda K. Development of a compact computed tomographic apparatus for dental use. *Dentomaxillofac Radiol* 1999; **28:** 245–248.
26. Mozzo P, Procacci C, Tacconi A, Martini P T, Andreis I A. A new volumetric CT machine for dental imaging based on the cone-beam technique: preliminary results. *Eur Radiol* 1999; **8:** 1558–1564.
27. Scarfe W C, Farman A G, Sukovic P. Clinical applications of cone-beam computed tomography in

dental practice. *J Can Dent Assoc* 2006; **72:** 75–80.
28. Patel S, Dawood A, Ford T P, Whaites E. The potential applications of cone beam computed tomography in the management of endodontic problems. *Int Endod J* 2007; **40:** 818–830.
29. White S C. Cone-beam imaging in dentistry. *Health Phys* 2008; **95:** 628–637.
30. Ludlow J B, Davies-Ludlow L E, Brooks S L, Howerton W B. Dosimetry of 3 CBCT devices for oral and maxillofacial radiology: CB Mercuray, NewTom 3G and i-CAT. *Dentomaxillofac Radiol* 2006; **35:** 219–226.
31. Loubele M, Bogaerts R, Van Dijck E *et al.* Comparison between effective radiation dose of CBCT and MSCT scanners for dentomaxillofacial applications. *Eur J Radiol* 2009; **71:** 461–468.
32. Thomas S L. Application of cone-beam CT in the office setting. *Dent Clin North Am* 2008; **52:** 753–759, vi.
33. Patel S. New dimensions in endodontic imaging: Part 2. Cone beam computed tomography. *Int Endod J* 2009; **42:** 463–475.
34. Low M T L, Dula K D, Bürgin W, von Arx T. Comparison of periapical radiography and limited cone beam tomography in posterior maxillary teeth referred for apical surgery. *J Endod* 2008; **34:** 557–562.
35. Estrela C, Bueno M R, Leles C R, Azevedo B, Azevedo J R. Accuracy of cone beam computed tomography and panoramic radiography for the detection of apical periodontitis. *J Endod* 2008; **34:** 273–279.
36. Stavropoulos A, Wenzel A. Accuracy of cone beam dental CT, intraoral digital and conventional film radiography for the detection of periapical lesions: an ex vivo study in pig jaws. *Clin Oral Investig* 2007; **11:** 101–106.
37. Tyndall D A, Rathore S. Cone-beam CT diagnostic applications: caries, periodontal bone assessment, and endodontic applications. *Dent Clin North Am* 2008; **52:** 825–841, vii.
38. Patel S, Dawood A, Whaites E, Pitt Ford T. New dimensions in endodontic imaging: part 1. Conventional and alternative radiographic systems. *Int Endod J* 2009; **42:** 447–462.
39. Cohenca N, Simon J H, Mathur A, Malfaz J M. Clinical indications for digital imaging in dento-alveolar trauma. Part 2: root resorption. *Dent Traumatol* 2007; **23:** 105–113.
40. Hannahan J P, Eleazer P D. Comparison of success of implants versus endodontically treated teeth. *J Endod* 2008; **34:** 1302–1305.
41. Bhuva B. The restorability of broken down teeth: the decision-making process. *In* Mannocci F, Cavalli G, Gagliani M (eds) *Adhesive restoration of endodontically treated teeth.* pp 101–125. London, UK: Quintessence Publishing Co Ltd, 2008.
42. Abbott P V. Assessing restored teeth with pulp and periapical diseases for the presence of cracks, caries and marginal breakdown. *Aust Dent J* 2004; **49:** 33-39.
43. Nair P N, Duncan H F, Pitt Ford T R, Luder H U. Histological, ultrastructural and quantitative investigations on the response of healthy human pulps to experimental capping with mineral trioxide aggregate: a randomized controlled trial. *Int Endod J* 2008; **41:** 128–150.
44. Murray P E, Garcia-Godoy F, Hargreaves K M. Regenerative endodontics: a review of current status and a call for action. *J Endod* 2007; **33:** 377–390.
45. Iwaya S I, Ikawa M, Kubota M. Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. *Dent Traumatol* 2001; **17:** 185–187.
46. Banchs F, Trope M. Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? *J Endod* 2004; **30:** 196–200.
47. Petrino J A, Boda K K, Shambarger S, Bowles W R, McClanahan S B. Challenges in regenerative endodontics: a case series. *J Endod* 2010; **36:** 536–541.
48. Garcia-Godoy F, Murray P E. Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. *Dent Traumatol* 2011; doi: 10.1111/j.1600–9657.2011.01044.x.
49. Hargreaves K M, Giesler T, Henry M, Wang Y. Regeneration potential of the young permanent tooth: what does the future hold? *J Endod* 2008; **34:** S51–56.
50. National Institute for Health and Clinical Excellence. *Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures.* London, UK: National Institute for Health and Clinical Excellence, 2008. Clinical Guideline 64.
51. Joint Formulary Committee. *British National Formulary.* 60th ed. London, UK: British Medical Association and Royal Pharmaceutical Society, 2010.
52. Flores M T, Andersson L, Andreasen J O *et al.* International Association of Dental Traumatology. Guidelines for the management of traumatic dental injuries. II. Avulsion of permanent teeth. *Dent Traumatol* 2007; **23:** 130–136.
53. Hinckfuss S E, Messer L B. An evidence-based assessment of the clinical guidelines for replanted avulsed teeth. Part II: prescription of systemic antibiotics. *Dent Traumatol* 2009; **25:** 158–164.