Endodontic Topics

Endodontic Topics 2009, 15, 32–55

ENDODONTIC TOPICS 2009
1601-1538

Repair of perforations with MTA: clinical applications and mechanisms of action

THOMAS CLAUDER & SU-JUNG SHIN

Root perforations may occur due to pathological processes or treatment consequences. Such perforations are severe complications and are associated with dramatically compromised endodontic treatment outcomes, especially when bacterial infection is allowed to establish. A new material, mineral trioxide aggregate (MTA), promotes a favorable environment for regeneration and has been successfully used for perforation repair. This is in contrast to previously-used materials that often led to variable outcomes. Based on the currently-available literature, the guidelines for perforation repair and treatment options need to be re-evaluated and usage parameters for MTA need to be optimized.

Received 25 May 2008; accepted 8 November 2008.

Introduction

Root perforations may arise pathologically, i.e., by resorptive processes or by caries, or may occur iatrogenically as a complication during or after root canal therapy (1) (Figs. 1–6). The American Association of Endodontists (AAE) Glossary of Endodontic Terms defines perforations as mechanical or pathological communications between the root canal system and the external tooth surface (2). The injury to the periodontium results in the development of inflammation, destruction of periodontal fibers, bone resorption, formation of granulomatous tissue, proliferation of epithelium, and ultimately in the development of a periodontal pocket (3–6). Root perforations are significant complications to endodontic treatment and, if not detected and properly treated, the breakdown of the periodontium may ultimately lead to loss of the tooth. A recently-published outcome study on non-surgical re-treatment demonstrated that one of the two factors significantly affecting the success rate of the re-treatment was the presence of a pre-operative perforation (7). The incidence of perforations is quoted in the literature as being between 3 and 10 percent (8–10). Analyzing the success rates of non-surgical re-treatment procedures, perforations were found to be present in 7 to 12 percent of the previous endodontic treatments (7, 11, 12). The following section provides an overview of the occurrence and diagnosis of radicular perforations.

Occurrence and diagnosis of perforations during root canal treatment

Root perforations may occur in any area of radicular tissues and can be divided according to the time a perforation occurs:

A. pre-operative occurrences, typically pathologically, e.g. resorption or decay;
B. peri-operative procedural accidents, e.g. during access or canal instrumentation; or
C. post-operative procedural errors, e.g. during preparation of a post-space.

According to Kvinnsland et al. (13), 53% of iatrogenic perforations occur during insertion of posts (prosthodontic treatment); the remaining 47% are induced during routine endodontic treatment. In 73% of all cases, the complications occur in the maxilla and

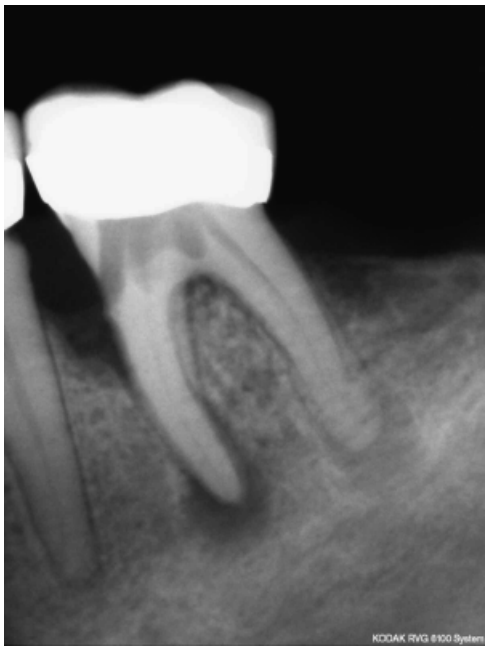

Fig. 1. Radiograph showing different localization for perforation that occurred during access preparation or endodontic treatment. Perforation in the coronal aspect of a lower molar, leading to a periodontal pocket.

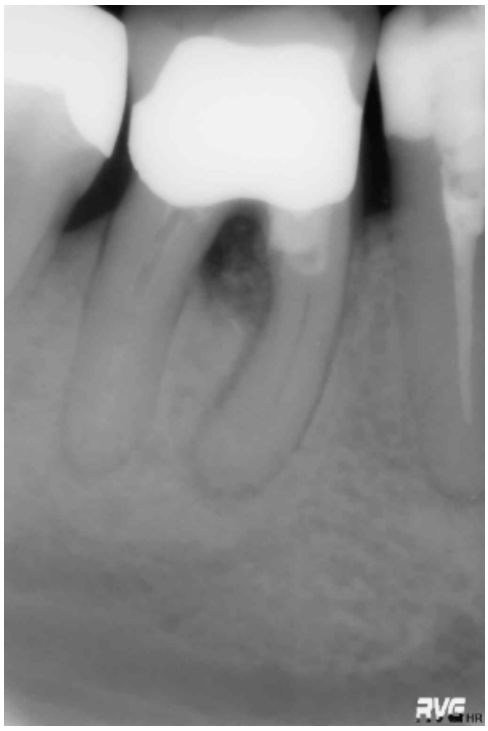

Fig. 2. Radiograph showing different localization for perforation that occurred during access preparation or endodontic treatment. Furcal perforation in a mandibular molar showing bone destruction in the furcal region.

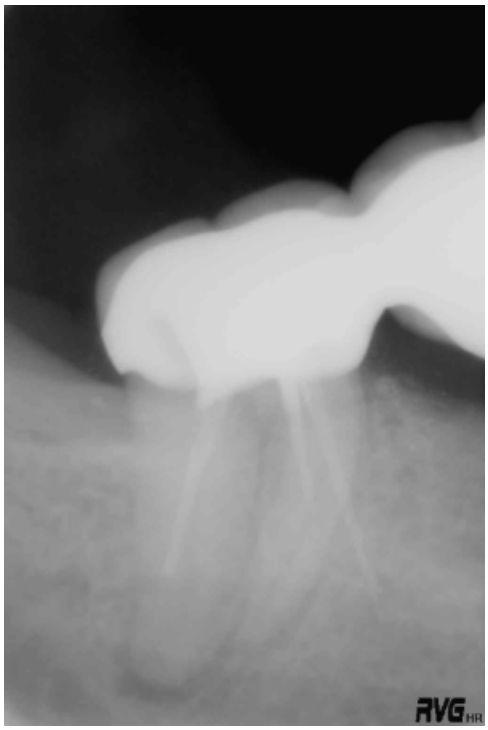

Fig. 3. Radiograph showing different localization for perforation that occurred during access preparation or endodontic treatment. Perforation in the middle aspect of a lower molar with large overextension of the filling material into the bone.

the remaining 27% occur in the mandibular arch. Adequate knowledge is needed of the location and dimensions of the pulp chamber as well as the anatomical variations of the specific tooth treated in order to prevent complications. Kvinnsland et al. (13) found that in maxillary anterior teeth, all perforations were located at the labial root aspect due to the operator's underestimation of the palatal root inclination in the upper jaw. In multi-rooted teeth, furcal perforations can occur when removing dentin from the chamber floor while searching for canal orifices (5). The crowns of many teeth are frequently perforated when anatomical variations are not anticipated during access preparation as a result of misalignment of the bur with the long axis of the root (14). Careful examination of radiographs is important to evaluate the shape and depth of the pulp chamber and width of the furcation floor (6). Significant crown–root angulations, calcifications of the pulp chamber and orifices, anatomical variations, misidentification of canals, and excessive removal of coronal dentin are often the reason for perforations in the coronal part of the tooth. Attempts to locate calcified orifices or excessive flaring

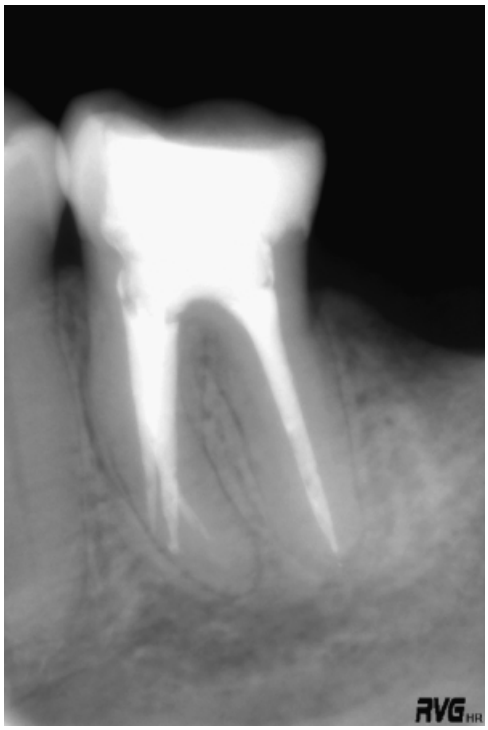

Fig. 4. Radiograph showing different localization for perforation that occurred during access preparation or endodontic treatment. Apical perforations resulting from inadequate cleaning and shaping concepts.

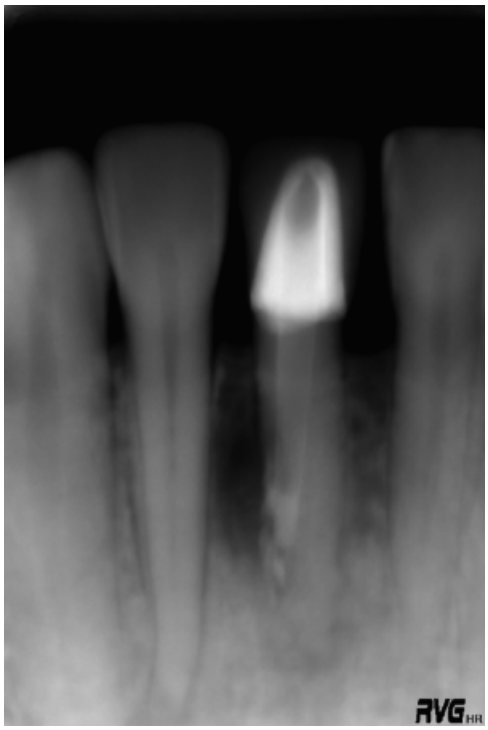

Fig. 5. Radiograph showing different localization for perforation that occurred during access preparation or endodontic treatment. Radiograph showing massive bone destruction after perforation of a glass fiber post in a lower, anterior tooth.

of the cervical portion of curved roots in molars can cause lateral root perforations in the root canal (15). Perforations caused by overzealous instrumentation occur mostly in the coronal or middle aspect of the root, are usually of ovoid shape, and are termed strip perforations. Excessive use of Gates Glidden burs or overzealous canal enlargement can result in these procedural accidents. Perforations in the apical area of roots mainly result from a failure to properly clean and shape the canal, and are often initiated by blocks and ledges (16).

Post-space preparation may result in a perforation due to over-enlargement or misdirected angulations. It has been held that the best way to manage perforations is to prevent them (14) but it is imperative to diagnose and treat a perforation if one has occurred.

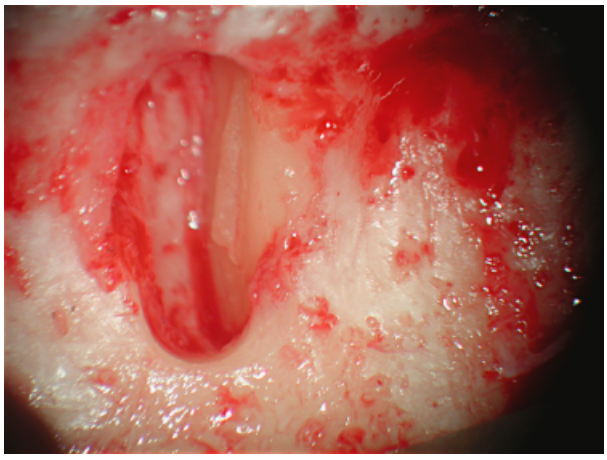

Fig. 6. The surgical site demonstrates a wide strip perforation in the middle region of the tooth.

Diagnosis of perforations

The correct diagnosis of the presence and localization of a perforation, as well as the determination of a treatment plan, can be challenging. As the time lapse between the perforation development and its repair is critical to the prognosis for the tooth, early and accurate determination of the presence of a perforation is of paramount importance (6, 17, 18). The diagnosis should be confirmed by clinical observations including etiological aspects and radiographical findings. The first clinical appearance of a perforation frequently demonstrates profuse bleeding from the injured side

(19, 20). If anesthesia is less than adequate, the patient may experience sudden pain when perforation occurs. Indirect bleeding assessment using paper points have been demonstrated to be helpful to identify smaller perforations or strip perforations. The canals should be cleaned as best achievable and dried. A newly-inserted paper point that shows blood on the lateral aspect indicates a strip perforation. Repeated insertion of paper points demonstrating blood at their tip can indicate apical perforations. Another way to facilitate diagnosis of a perforation is the use of an electronic apex locator. Normally used to determine working length, such an electronic apex locator connected to a file and inserted into the perforation is a reliable tool to detect and confirm the perforation (21, 22).

Multiple, angulated radiographs including bitewing radiographs are also essential for accurate diagnosis. However, the radiographical detection of root perforations, especially on the buccal or lingual root surfaces, is often impractical since the image of the perforation is superimposed on intact root structure. Three-dimensional information acquired from computed tomography (CT) or cone beam CT scans can provide additional and more conclusive information (23) (Figs. 7–12).

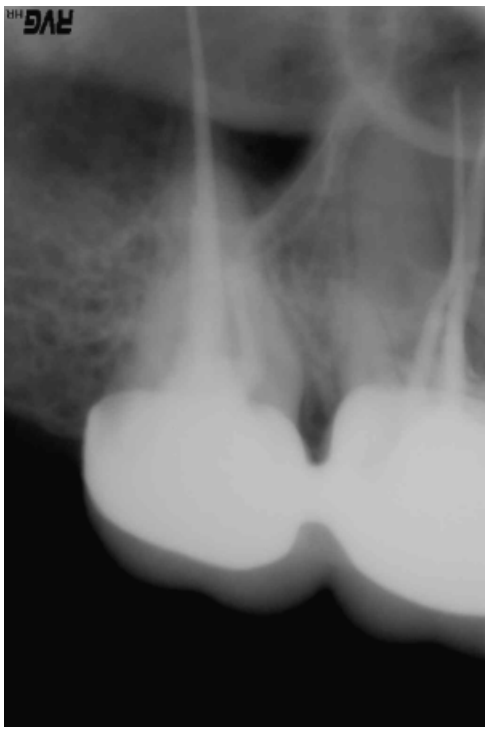

Fig. 7. Multiple perforations shown in all regions of the teeth. Tooth 17 showing gross overextension of the filling material into the maxillary sinus.

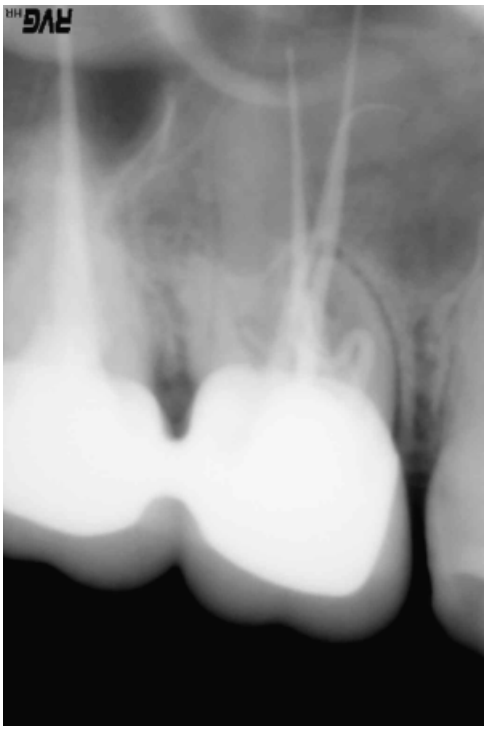

Fig. 8. Multiple perforations shown in all regions of the teeth. Tooth 16 demonstrates a large perforation in the furcal region exhibiting massive overextension into the maxillary sinus.

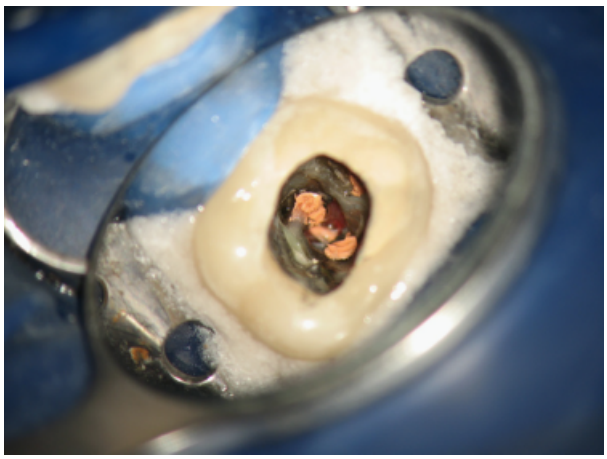

Fig. 9. Multiple perforations shown in all regions of the teeth. The clinical view of tooth 16 shows gutta-purcha points in the furcal perforations.

In existing and probably infected perforations, it is considered important to assess the periodontal status of the tooth in question as cervical and occasionally mid-root perforations are frequently associated with epithelial downgrowth and subsequent periodontal defects, which will compromise the prognosis (3, 24).

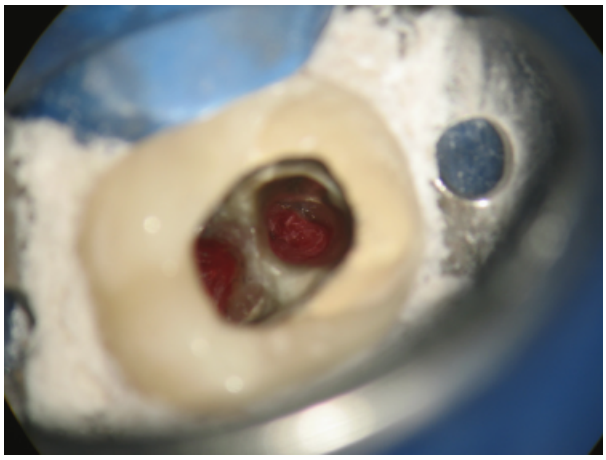

Fig. 10. Multiple perforations shown in all regions of the teeth. After removal of the filling material of the perforation site, massive destruction of the tooth structure is visible.

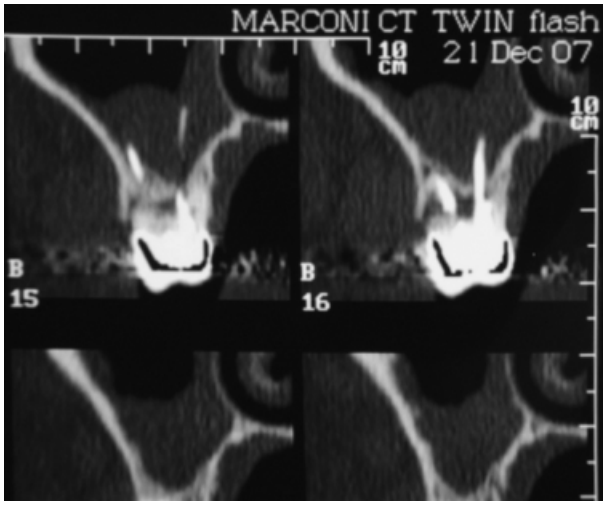

Fig. 11. Multiple perforations shown in all regions of the teeth. A CT scan of that region demonstrate the gutta-percha points extended into the sinus with injury of the sinus membrane, resulting in extended swelling of the mucosa.

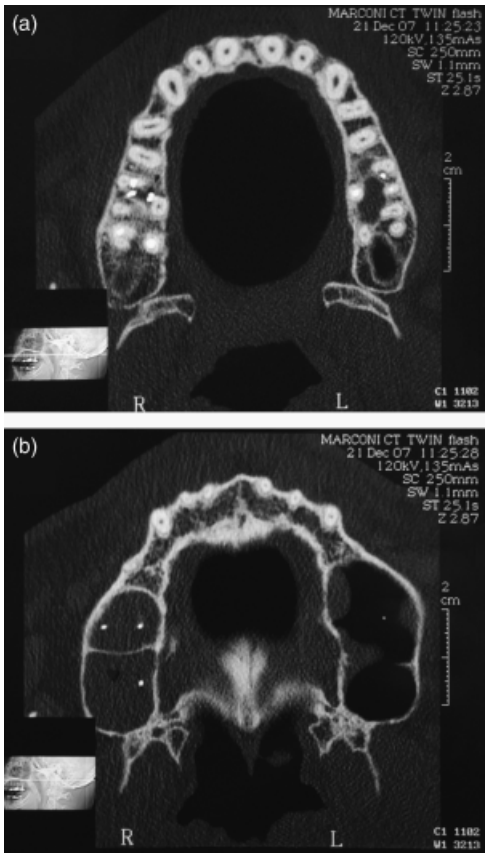

Fig. 12. Multiple perforations shown in all regions of the teeth. The horizontal scans show the exact localization of the filling material in the surrounding bone and sinus area.

Classification of perforations and factors affecting prognosis

The aim of perforation management is to maintain healthy periodontal tissues against the perforation without persistent inflammation or loss of periodontal attachment. In the case of established periodontal tissue breakdown, the aim is to re-establish tissue attachment (25, 26). Successful perforation repair depends on the ability to seal the perforation and to re-establish a healthy periodontal ligament (3). In the past, any attempt to repair perforations exclusively with an orthograde technique was less than predictable (13). Materials used to repair root perforations were associated with the formation of a fibrous connective tissue capsule in contact with the adjacent bone. The formation of a periodontal defect has been a more common finding associated with the majority of previously-used materials (24).

Kvinnsland et al. (13) reported 56% success in the primary treatment of perforations. Their conclusion was that the major problem with a non-surgical approach was the inability to routinely seal the canal and the perforation defect without extruding considerable amounts of filling material through the perforation and into adjacent periodontal structures. They also found a relatively poor prognosis for perforations in the cervical portion of roots and attributed this to the loss of the epithelial attachment resulting in the formation of a permanent periodontal defect. This has been confirmed in experimental studies of the treatment of

furcal perforations, which have invariably produced disappointing results (3, 20, 27–29).

In general, investigators have agreed that the prognosis for root perforations in the apical and middle third of the root is much better than for those in the cervical third of the root or of the pulp chamber floor (26). The prognosis of teeth with root perforations depends on the severity of the initial damage to the periodontal tissues, the size of the perforation, the location of the perforation in relation to the gingival sulcus, the time lapse between injury and repair, the adequacy of the perforation seal, the sterility of the perforation, and the biocompatibility of the material used to repair the perforation (27–34). In the past, many materials were advocated for perforation repair; however, none provided a favorable environment for re-establishing the normal architecture and predictable healing after treatment. The inadequacy of these materials can be attributed to their inability to seal the communication between the oral cavity and the underlying tissues, or their lack of biocompatibility. A characteristic that differentiates MTA (Mineral Trioxide Aggregate) from other materials is its ability to promote regeneration of cementum, thus facilitating the regeneration of the periodontal apparatus (5, 26). Until the advent of MTA, repair materials had not been able to stimulate this regenerative process (24). Histological examination of the periradicular tissues after root-end filling with MTA in dogs has shown that not only is there a re-establishment of normal periodontium, but there is also a cementum build-up over the material (26, 35). Lack of adverse effects after extrusion of MTA into the furcation in both cases indicates biocompatibility (5, 26). Several studies have concluded that MTA establishes an effective seal of root perforations (36–39) and can be considered as a potential repair material that enhances the prognosis of perforated teeth which would otherwise be compromised (24, 26).

To determine an ideal treatment strategy, in 1996 Fuss & Trope introduced a classification based on different factors affecting the prognosis of perforations and their treatment (9) (see Table 1).

Table 1. Factors that affect the treatment prognosis of lateral and furcal root perforation repairs

⇐ Good prognosis	Poor prognosis ⇒
Fresh	Old
Small	Large
Apical/coronal	Crestal

Factors on the left suggest a good prognosis, while factors on the right point towards a poor prognosis.
Redrawn from (9), with permission.

Time of repair

As prevention or treatment of bacterial infection of the perforation site dictates the success of the attempted repair, the time elapsing between perforation and appropriate treatment is extremely important. Immediate repair under aseptic conditions before bacterial contamination and breakdown of the surrounding tissues achieves better results than delayed repair, which promotes a more questionable prognosis. Several histological studies with experimentally-induced perforations show more favorable healing when perforations are sealed immediately (3, 4, 31). Pitt Ford et al. demonstrated that even with the use of MTA in the group with delayed repair, more specimens were associated with inflammation, which appeared to be linked to the presence of infection (26). When examining infected, previously-untreated perforations, epithelial proliferation can often be observed. Successful treatment of infected perforations seems to be attributed to removal of contaminants as well as cleansing of the pulp chamber, perforation and wound site before repairing under aseptic conditions (13, 26, 30).

Size of perforation

The potential for successful reattachment of the periodontal ligament is dependent on the size of the surface area that must be repaired. In small perforations, mechanical damage to tissue is minimal and sealing opportunity is improved in comparison to large perforations. Although often mentioned, Pitt Ford states that there is no substantive evidence in the literature that perforation size affected prognosis (26). Some case reports have shown healing and promising results in large perforations treated with MTA (5), so the effects of perforation size may need re-evaluation. Moreover, most articles refer to problems with the coronal seal in situations with larger defects. Most of

these studies used materials other than MTA, so the potential to achieve regeneration would be increased by using MTA in these cases.

Location of perforation

The location of a perforation is probably the most important factor affecting treatment prognosis (9). In general, investigators have agreed that the prognosis for root perforations in the apical and middle third of the root is much better than those in the cervical third of the root or in the floor of the pulp chamber (30). Fuss & Trope (9) emphasized the importance of the 'critical zone' at the crestal bone level and the epithelial attachment. Perforations above that zone have a good prognosis as they can be sealed properly, using adhesive techniques or being covered by final restorations, without periodontal involvement. In some cases, orthodontic eruption of the tooth or surgical crown lengthening can move the perforation out of the critical zone. Crestal root perforations are sensitive to epithelial migration and quick periodontal breakdown, which can reduce the chance of regeneration and lower success rates, making treatment more complex and less predictable. Perforations apical to the critical zone have a good prognosis, assuming that endodontic treatment can be adequately performed and the perforation sealed tightly.

Although there are claims for a good prognosis apical to the critical zone, the difficulties concerning accessibility increase with the perforation being localized deep in the canal. In these cases, predictable repair may be challenging or provide a compromised result, necessitating a surgical approach. Perforations can occur circumferentially on the buccal, lingual, mesial, or distal aspects of roots. The location of the defect is not as important when non-surgical treatment is selected, but can be critical in a surgical approach to repair (16).

The decision to treat a perforation is also dependent on the periodontal condition of the defect. The presence of periodontal involvement frequently requires additional procedures for management and lowers the prognosis for successful repair. If a defect is not associated with increased probing depths, the treatment method of choice is usually non-surgical perforation repair, which should be done as soon as possible since timing is essential for a successful long-term prognosis. However, if a defect is associated with increased probing depth, the loss of attachment and the risk of epithelial downgrowth decrease the chances of regeneration drastically. When pockets have already formed, any conservative treatment is compromised (26). These defects usually require non-surgical periodontal management or may even need surgical intervention. Surgical treatment of perforations can often lead to the loss of periodontal attachment, chronic inflammation, and furcal pocket formation (33). Based on the probability for regeneration, the treatment options (namely surgical, non-surgical, or a combination of both) require careful consideration. When teeth are of strategic value, perforation repair is clearly indicated.

Mechanisms for action of MTA as a perforation repair material

Various materials have been used to repair root perforations. The requirements for an ideal repair material have been described by several authors (17, 40):
-provide hermetic seal;
-non-resorbable and insoluble;
-not contaminated by hemorrhage;
-'controllable to prevent its extrusion';
-biocompatible;
-induce osteogenesis and cementogenesis;
-non-carcinogenic, non-toxic;
-easily obtainable;
-should not cause inconvenience to the patient or dentist; and
-inexpensive.

The most commonly-used repair materials are amalgam, zinc oxide eugenol cement, calcium hydroxide, gutta-percha, glass ionomer cement, IRM, composite resin, SuperEBA and mineral trioxide aggregate (MTA).

MTA was initially introduced as a root-end filling material for surgical endodontic procedures (35, 41). Since then, its clinical applications have broadened to include perforation repair, pulp capping, pulpotomy, and apexification. During these procedures, the dental filling materials usually come into contact with the underlying tissues. The bond strength of most dental materials is significantly reduced by moisture contamination from the tissue, whereas MTA requires the presence of water for setting. Therefore, set MTA can acquire its optimal strength and produce excellent sealability in the presence of moisture (36).

Physical and chemical properties of MTA

MTA is composed of tricalcium silicate, tricalcium aluminate, tricalcium oxide, silicate oxide, mineral oxide and bismuth oxide. The powder consists of fine hydrophilic particles that harden in the presence of water. Hydration of the powder leads to the formation of a colloidal gel, which then solidifies to a hard structure in approximately 4 h. The characteristics of the aggregate depend on the size of the particles, the powder to water ratio, the setting temperature, the presence of water during setting, and the presence of entrapped air. Lee et al. (41) examined the properties of hydrated MTA by scanning electron microscopy and X-ray diffraction. Upon MTA hydration, crystallization of the hydrates causes it to form an interlocking mass. Crystallization includes the formation of cubic and needle-like crystals. The nucleation rates may differ due to the complexity of the MTA components, and some parts may form hydration products more rapidly than others. Lee et al. (41) also studied the effects of pH on the setting of MTA. Their findings were significant as they discovered that, when used for perforation repair or retrograde filling, the crystallization properties differ when MTA comes into contact with inflammatory tissues with a low pH. Pulpal and periapical inflammation typically lowers the tissue pH to approximately 5.5. When MTA is hydrated at acidic pH, there are no needle-like crystal structures formed because the large surface areas of such crystals provides a large number of reaction sites for rapid dissolution under those conditions. The micro-hardness test of the specimens taken at pH 5 revealed a significantly lower hardness than the samples examined at higher pH. The authors hypothesized that the needle-like crystals might be important for interlocking the entire mass of the material and their disappearance caused a decrease in material hardness. Torabinejad et al. (42) compared the setting time and compressive strength of four different materials: amalgam, SuperEBA, IRM, and MTA. Amalgam had the shortest setting time (4 min) and MTA had the longest (2 h and 45 min). MTA showed the lowest compressive strength (40 MPa at 24 h) but the strength increased to 67 MPa after 21 days.

Tronstad et al. (43) claimed that the highest cytotoxicity for most dental materials occurs during the setting period. Consistent with the findings reported by Tronstad et al., Saidon et al. (44) found denatured proteins and dead cells in the area immediately below fresh MTA in cell culture studies. They also noticed that the total number of cells grown on fresh MTA was significantly lower than the preset MTA. Freshly-mixed MTA has a pH of 10.2, which increases to 12.5 during setting (43). It is possible that the high surface pH of freshly-mixed MTA contributes to the denaturation of proteins and cell death. The cytotoxicity of freshly-mixed MTA appears to be more pronounced *in vitro* than *in vivo*. Apaydin et al. (45) compared the effect of fresh MTA with set MTA on hard tissue healing after periradicular surgery in dogs. They found no significant differences in cementum or osseous healing between the freshly-mixed and set MTA (see Fig. 13).

Many studies have examined the sealing ability of MTA (15, 46, 47). Indeed, the excellent ability of MTA to seal has lead to its introduction as a root-end filling material. Torabinejad et al. (47) compared the sealing ability of MTA, amalgam and Super EBA in root-end fillings and showed that MTA leaked significantly less

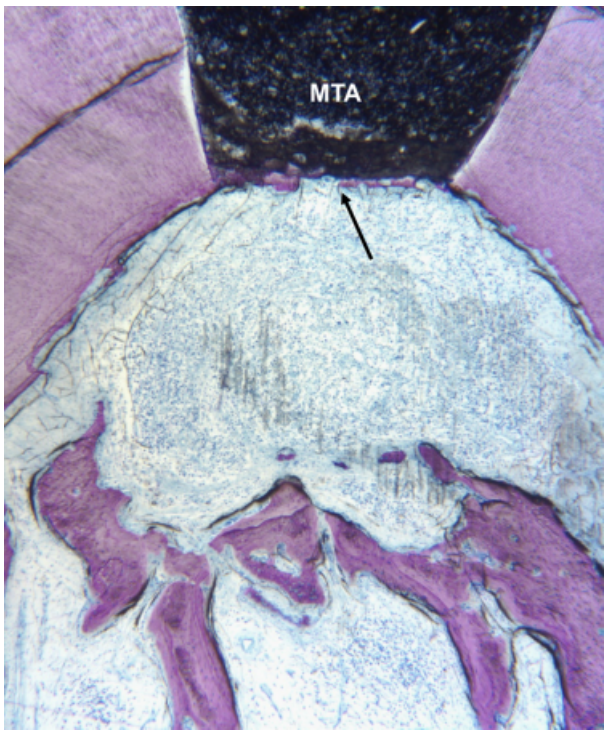

Fig. 13. Cementum-like material deposition of the MTA perforation repair (arrow). Artificial furcal perforation on Beagle dog's tooth was created and MTA applied for repair. 4 months later, histological section showed no signs of inflammation and possible regrowth of cementum (unpublished data, courtesy of Seung-Ho Back at Seoul National University).

than the other materials. According to Lee et al. (15), MTA also had superior sealing ability compared to amalgam or IRM when used for perforation repair.

MTA was originally made in the form of a gray powder and has been associated with the occasional discoloration of teeth when used in pulpotomy or pulp capping (48). White MTA was developed later by Dentsply Inc. to overcome this concern. Based on studies thus far (49, 50), white MTA mainly differs from the original gray MTA by the absence of iron. Asgary et al. (49) performed electron probe micro-analysis which indicated that CaO, SiO_2 and Bi_2O_3 were the major compounds in gray and white MTA. Significantly-increased components in gray MTA compared to white MTA were Al_2O_3, MgO and FeO. Similar results were reported by Song et al. (50). Based on their results using X-ray diffraction (XRD) analysis, gray MTA contained significant amounts of iron. They also analyzed the chemical components of gray MTA-Angelus (Angelus Soluções Odontológicas, Londrina, Brazil) and found that it contained smaller amounts of bismuth oxide compared with the original gray MTA.

Biological effects of MTA

Biocompatibility

The most critical property of any dental material that comes into contact with periapical, pulpal or periodontal tissues is its biocompatibility. Several *in vivo* animal studies (51–53) have reported that MTA is a biocompatible material with no adverse effects on the dental tissues. Little or no inflammation was observed with MTA when it was used as a root-end filling material in dogs (35) and monkeys (53) or as a pulp-capping agent in monkeys (51). Furthermore, these studies identified cells lined along the MTA surface, further supporting that MTA has little or no cytotoxicity (see Fig. 14).

The biocompatibility of MTA was also tested in *in vitro* cell culture studies. Zhu et al. (54) reported that human osteoblast-like Saos-2 cells attach and spread well on the surface of MTA after 1 day in culture. Balto (55) demonstrated that human periodontal ligament fibroblasts were well attached and grew on MTA. A few previous studies examined whether there were any differences in biocompatibility between the gray and white MTA. Holland et al. (56) evaluated the reaction of rat subcutaneous connective tissue to the implantation of dentin tubes filled with white MTA. They showed similar results to those reported for gray MTA. This indicates that white and gray MTA have similar mechanisms of action. However, a cell culture study by Perez et al. (57) showed that osteoblasts behave differently on white MTA and suggested that this might be due to the surface morphology of the materials. Camilleri et al. (58) and Ribeiro et al. (59) reported no difference in biocompatibility between the two variants. Therefore, more studies are needed to fully characterize the biological effects of white and gray MTA.

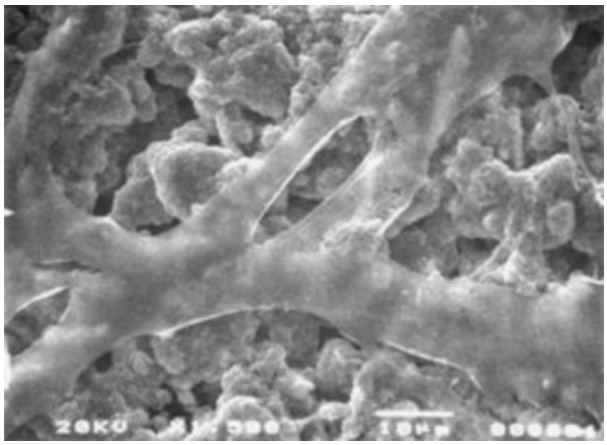

Fig. 14. Scanning electron microscopy of human cementum-derived cells (HCDCs) grown on white MTA. Cells were stretched and tightly attached when they were grown on MTA for 72 h (unpublished data).

Mineralized tissue inductive property

MTA has the capacity to promote hard tissue formation. In an animal study, Tziafas et al. (60) showed that pulp capping with MTA induces cytological and functional changes in pulpal cells, which result in the formation of fibrodentin and reparative dentin at the surface of mechanically-exposed dental pulp. Torabinejad et al. also showed that MTA was covered with a cementum layer when used as a root-end filling material in dogs (35) and monkeys (53). The dog study showed that cementum was present on MTA in all of their 10 samples. Pitt Ford et al. (26) reported continuous hard tissue formation around excess MTA material when it was used to repair a perforation.

Baek et al. (61) performed a histology study using amalgam, SuperEBA, and MTA as root-end filling

materials in dogs. They concluded that MTA had the most favorable periapical tissue response, with neoformation of cemental coverage over MTA.

Moretton et al. (62) rebutted the mineral tissue inductive property of MTA. In their study, a subcutaneous implant of MTA elicited severe initial reactions with coagulation necrosis and dystrophic calcification, which later subsided. Based on this finding, they suggested that MTA is osteoconductive rather than osteoinductive.

Potential cellular mechanisms underlying osteoinductive and dentinoinductive properties of MTA

Cell proliferation

Cell proliferation is essential for increased bone, dentin and cementum formation during wound healing. Bonson et al. (63) reported the enhanced proliferation of periodontal ligament (PDL) fibroblasts on MTA compared with other root-end filling materials. Interestingly, gingival fibroblasts failed to proliferate on MTA even though they survived. This suggests that MTA may stimulate only a subset of cell types.

The mechanisms for the stimulatory effect of MTA on PDL cell proliferation are unknown. However, given that calcium ions are a major component of MTA, it is quite plausible that the calcium ions released from MTA may play an important role in cell proliferation. More recently, Takita et al. (64) demonstrated that MTA stimulates human pulp cell proliferation, whereas a calcium hydroxide containing cement (Dycal, Sybron Kerr, Orange, CA) had no such effect. They hypothesized that one of the main reasons for the MTA-induced cell proliferation might be the continuous release of calcium ions from MTA. It was reported that elevating the calcium level from 1.2 to 1.8 or 2.5 mM in a culture medium increases the rate of osteoblastic cell proliferation by 1.1 and 1.3 fold, respectively (65).

Cell differentiation

The functional competency of a cell is achieved through differentiation, and the process of cell differentiation is characterized by the expression of tissue-specific genes. Bonson et al. (63) showed that MTA increases the expression of alkaline phosphatase, osteonectin, and osteopontin genes in PDL fibroblasts. This suggests that MTA induces bone formation by stimulating osteogenic cell differentiation. Andelin et al. (66) reported that rat pulps capped with MTA formed hard tissue that was immunostained with a dentin sialoprotein-specific antibody, indicating that some pulpal cells differentiate to odontoblasts in response to MTA. However, Koh et al. (67) and Mitchell et al. (68) reported a more complex mechanism for the potential role of MTA in bone formation. These studies show that MTA increases the level of interleukin-6 (IL-6), IL-8, and osteocalcin expression. Osteocalcin is a bone-specific marker which supports the role of MTA in osteogenic cell proliferation. However, IL-6 stimulates osteoclast formation and recruitment (69). Therefore, MTA may actually promote bone turnover by increasing the osteoclastic and osteoblastic activity.

Alternative materials for perforation repair in specific indications

An attempt was made to take advantage of the excellent biological properties of MTA in periodontal regenerative therapy. However, freshly-mixed MTA was washed out whenever there was significant communication between the oral cavity and MTA, which has limited its applications in periodontal procedures. In order to circumvent this problem, MTA was used in combination with a bone graft material to repair external resorption and osseous defects (70). This approach was successful in reducing the pocket depth without causing any clinical symptoms.

Another material class, resin-modified glass ionomers such as Geristore (DenMat, Santa Maria, CA, USA), may be used for perforation repair, specifically when there is communication between the perforation site and the oral cavity. Geristore is a resin ionomer that was introduced relatively recently to treat perforations and resorptive defects. Several case studies using Geristore in perforation sites have reported promising results. Breault et al. (71) reported sustained tissue health and a minimal probing depth at the surgical site when a root perforation was repaired with Geristore. There have only been a few studies examining the biocompatibility of Geristore. Al-Sabek et al. (72) reported that human gingival fibroblasts attached and spread well on Geristore, which demonstrates that Geristore might

be less toxic than IRM (Sybron Kerr) and Ketac-Fil (Espe, Seefeld, Germany).

Techniques and considerations to clinically repair perforations

If careful judgement favors retaining the tooth and repairing the perforation, other factors further influence the choice of treatment procedure. Good visibility of the damaged site is essential to achieve the treatment goals. The microscope is now an indispensable tool to facilitate the delicate techniques and improves the management of procedural errors (73). Two factors appear to be most important in relation to clinical perforation repair: an appropriate material selection and the use of a matrix.

Appropriate material selection

As stated before, an important factor in a non-surgical as well as a surgical perforation repair is to achieve a fluid-tight seal between the tooth and the repair material. This can be affected by the location and size of the perforation, operator skill, and by the physical and chemical characteristics of the repair material (15). The choice of restorative repair material is based on the technical access to the defect, the ability to control moisture, and aesthetic considerations (16). As previously discussed, in most cases MTA is the restorative material of choice. In some specific indications, MTA has disadvantages and preference should be given to different materials. The main disadvantage of currently-available MTA is a setting time of approximately 3 to 4 h (42), compromising the application in supracrestal cases. The possibility of being washed out during setting time needs to be considered. Another disadvantage, especially of the gray MTA, is the potential for discoloration of the treated tooth (48). Esthetic demands also have to be considered in the anterior region, especially when treating patients with a high lip line. Careful consideration is necessary as to whether the optimal red and white esthetics can be achieved. The application of adhesive materials can provide an adequate seal and a faster setting time (74). To restore subgingival defects, a resin-bonded material such as Geristore is also recommended. This material has been shown to be an acceptable material for repair of root caries and cervical erosions in a number of clinical studies (75–78). However, some authors (79) have reported the use of MTA in supracrestal areas in the posterior region.

Use of a matrix

The two main challenges a clinician faces when attempting to repair a perforation are hemostasis and the controlled placement of a restorative material. Most materials used for repair are sensitive to moisture, frequently compromising the seal of the repair material and resulting in unfavorable outcomes; controlling hemostasis is of major importance in achieving a tight seal. MTA sets in the presence of moisture and blood does not affect its sealing ability (36). Sluyk et al. demonstrated that the presence of moisture in perforations during the placement of MTA increased its adaptation to perforation walls (80). For that reason, it is suggested that MTA does not require the use of an internal matrix when sealing furcal perforations (5, 80).

As previously mentioned, a perforation can lead to breakdown of the attachment and the surrounding bone, which is then replaced by granulation tissue. Repair of the perforated defect is then complicated by the fact that the defect allows extrusion of the repair material into surrounding structures. This usually occurs during condensation of the filling material into the perforation side and can cause traumatic injury to the surrounding periodontal ligament. The extrusion of repair materials should be expected in cases of delayed repair compared to immediate repair (81). During immediate repair of smaller perforations, the periodontal ligament and surrounding hard tissue will act as a barrier if it has not been instrumented during the development of the perforation itself.

Alhadainy & Himel reported a 60% incidence of extrusion of resin-modified glass ionomer, producing additional inflammation and a foreign body reaction (19). The extrusion of material beyond the confinement of the root may preclude success regardless of the material used (81). In the past, attempts have been made to control extrusion and to increase the sealing ability of the repair materials with internal biocompatible barriers (17, 82–85). Internal matrices such as calcium sulphate did prevent extrusion of the material used for repair into the surrounding area (74, 81, 85).

MTA is known to be biocompatible and to cause new cementum formation (26, 35, 86, 87) with regenera-

tion of the entire periodontal apparatus, despite its extrusion into the periradicular tissues (26, 35), similar to when used in root-end fillings (25). Arens & Torabinejad (5) demonstrated that cementum not only forms in continuance with the existing root cementum but also attaches itself directly to MTA even when the material has been extruded into furcal defects. It has been stated that extrusion of MTA into the alveolar bone does not pose a problem (26, 35).

In a recent histological study on the healing response of contaminated perforations repaired with MTA with or without internal matrices, Al-Daafas & Al-Nazhan (81) demonstrated that the success rate when using only MTA (without a barrier) was excellent and comparable to previous results. The use of calcium sulphate as an internal matrix with MTA did prevent extrusion of the repaired material into the contaminated perforated area but it caused an unfavorable inflammatory reaction. When MTA was accidentally extruded into the interradicular area, deposition of hard tissue over the material with the presence of a healthy periodontium was observed. Al-Daafas & Al-Nazhan concluded that placement of MTA alone shows a better healing response compared to other groups, and using calcium sulphate as an internal matrix for MTA is not recommended (81).

However, several publications have also shown excellent clinical results with barriers using calcium sulphate or collagen (88, 89). A variety of resorbable barriers exist (e.g., collagen, freeze-dried demineralized bone allograft, hydroxy apatite, Gelfoam (Pfizer, New York, NY, USA), or calcium sulphate) (1, 16); if the use of a barrier is required, collagen and calcium sulphate materials are best employed because of ease of handling, research, and observed clinical results (16). Collagen, such as Collacote (Sulzer Dental, Carlsbad, CA, USA), is biocompatible, easy to handle, provides quick hemostasis (2–5 min), and is resorbable in 10 to 14 days. The material is cut into small pieces and placed one after the other in the bony crypt until it reaches the periodontal ligament. As the material will be absorbed, collagen should stay within the limits of the bone. The use in conjunction with adhesive dentistry is not recommended as it adsorbs moisture and contaminates the restorative interface (16).

Calcium sulphate is biocompatible, has a predictable haemostatic effect, and is bioresorbable in about 4 weeks (16, 90–93), depending on the density of the material. It is delivered with a plugger or the MTA Gun System (Dentsply Maillefer, Ballaigues, Switzerland) to the bony defect. After the material is set, it is important to clean the dentinal walls of the perforation, for example with ultrasonic tips. As it sets hard, it can be cleaned and used for dentin bonding procedures, improving the seal (94).

Non-surgical management of perforations

Crown, pulpal floor and furcation areas

The first step is to isolate the defect and provide ideal visualization. The major difference between coronal one-third and furcal-floor perforations is the shape of the resultant root defect. Mechanical perforations that occur in the furcal floor are generally round whereas those occurring in the lateral aspects of roots are ovoid by nature of occurrence (16). Repair of furcal perforations should be attempted through a non-surgical intra-coronal approach as surgical treatment can often lead to loss of periodontal attachment, chronic inflammation, and furcal pocket formation (5, 33). Prior to debriding the defect, root canals should be instrumented to allow proper intra-canal medication and closure of the orifices. For canal medication, syringeable calcium hydroxide materials simplify the procedure. The orifices can be covered with an easily-removable filling material such as Cavit. Another option is to use gutta-percha points, paper points or cotton pellets. The lapse of time between development of a perforation and the moment of repair is critical for prognosis, as previously discussed. Repairing a non-contaminated perforation immediately in that session after achieving hemostasis prevents breakdown of the periodontal attachment. For an older, chronic, and probably infected perforation, proper cleaning and preparing is needed before restoring the defect, which creates greater treatment challenges (16).

Success in the treatment of infected perforations seems to be attributed to removal of contaminants before repairing under aseptic conditions (5, 13, 26, 30). If dentin structure must be removed, this can be accomplished ideally with slight enlargement using burs or ultrasonic under magnification. Ultrasonic tips should be the preferred choice, as they are gentler to the adjacent tissues. In their protocol, Arens & Torabinejad (5) described further enlargement and cleaning of the infected perforation and the wound site with copious irrigation of 2.5% sodium hypochlorite before placement of the repair material. The use of a

disinfecting solution such as sodium hypochlorite can improve antimicrobial interaction and is helpful, but it should be used carefully, with the awareness of the increased risk of severe complications (see article by Hülsmann et al. in the next issue). In cases of large lesions, proximity to sensible structures, or to control bleeding, sterile saline can be advantageous. These cases frequently present with hyperplastic and hypervascular granulation tissue which protrudes into the defect; the removal of these tissues is necessary and sometimes makes hemostasis challenging. The use of non-specific intravascular clotting agents (e.g., ferric sulphate: stasis (21% ferric sulphate), Gingi-Pak, Camarrilo, CA, USA; Astringedent (15.5% ferric sulphate), Ultradent, South Jordan, UT, USA) commonly used to control bleeding should not be used as these chemicals can irreversibly damage delicate alveolar bone and delay healing (95, 96). Although the delay in healing can be prevented by copious irrigation with sterile saline and adequate curettage of the defect (97), the use in perforations is not advantageous. Hemostasis should be achieved using collagen, calcium sulphate, or calcium hydroxide. When the bleeding has been controlled, an easily-removable material should be placed over the entrances to the deeper portion of the canals, preventing the repair material from blocking re-access to the apical terminus (98) if not done prior to cleaning the defect.

The next important factor is the degree of bone destruction and the resulting defect surrounding the perforation. If there is no intraosseus defect, no barrier is needed. In cases with larger osseous defects, the careful use of a barrier can facilitate proper placement and adaptation of the filling material as well as prevent overcontouring. No force should be used to prevent damage of adjacent vital structures (98). The location of the perforation dictates different techniques for accessing and closing the perforation. Supracrestal perforations require a different approach than most subcrestal perforations for several reasons. The defects have a periodontal involvement as they communicate with the oral environment, so the demands required of the material used are slightly different than in subcrestal perforations without periodontal involvement. Generally, in supracrestal perforations, preference should be given to adhesive materials and in subcrestal regions, to MTA.

MTA, as the restorative material of choice, is placed either directly on the bone or on the previously-placed matrix. The easiest way to apply MTA is to use an appropriate carrier (MTA Gun System; MAP–Micro Apical Placement System, Produits Dentaires SA, Vevey, Switzerland; Dovgan MTA Carrier, G. Hartzell & Son, Concord, CA, USA). Pluggers (Schilder-Plugger e.g. Dentsply Maillefer, Ballaigues, Switzerland) or micro-spatulas (West Perforation Repair Instruments, Sybron Endo, Orange, CA, USA) are used for effective condensation. The technique of ultrasonic activation i.e., condensation by vibrating MTA into place to achieve a tight seal, is helpful when placing the material in difficult anatomical situations. Although ultrasonic activation is frequently used in this context by clinicians, its benefit has been not verified in outcome studies (99, 100).

After placing the initial portion of MTA precisely, the use of a blunt paper point can be helpful in removing excess moisture and such to solidify the material (98). Since MTA needs moisture during setting, after placement is complete, a wet cotton pellet is placed on top of the material, allowing the MTA to set. For temporary closure of the access cavity, a tight and solid seal is necessary, preferably using materials which increase the fracture resistance of the tooth. Recommendations for placing the final restorations vary from 1 day to 1 week after the repair procedure (5, 26). Sluyk

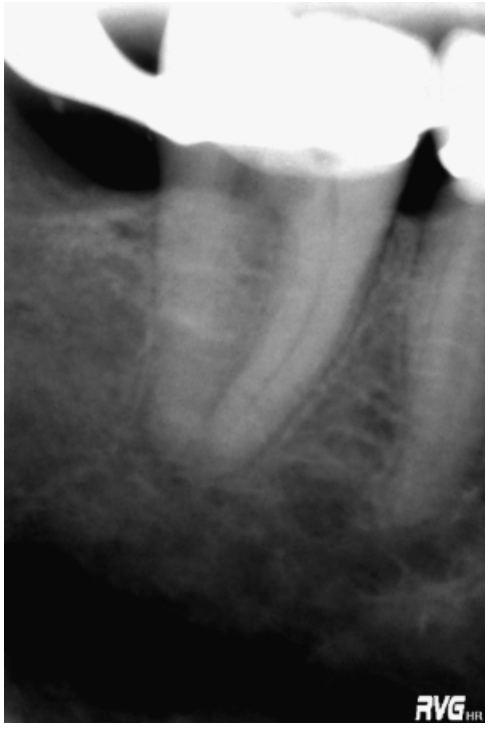

Fig. 15. Repair of a furcal perforation. The radiograph demonstrates extended loss of tooth stucture in the furca after access preparation.

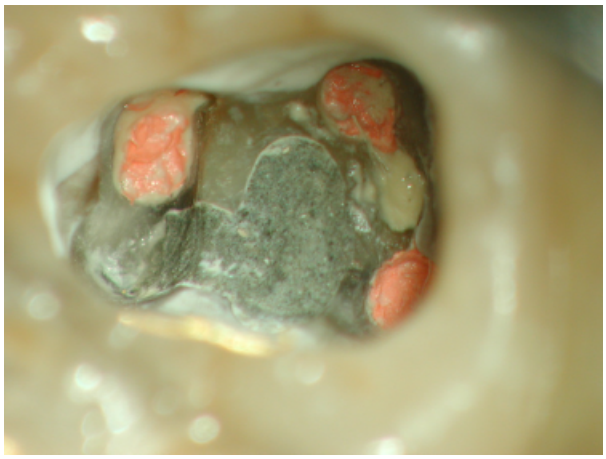

Fig. 16. Repair of a furcal perforation. After cleaning the perforation and reparing with MTA, the obturation is accomplished in a second visit, checking hardness of the repairing material.

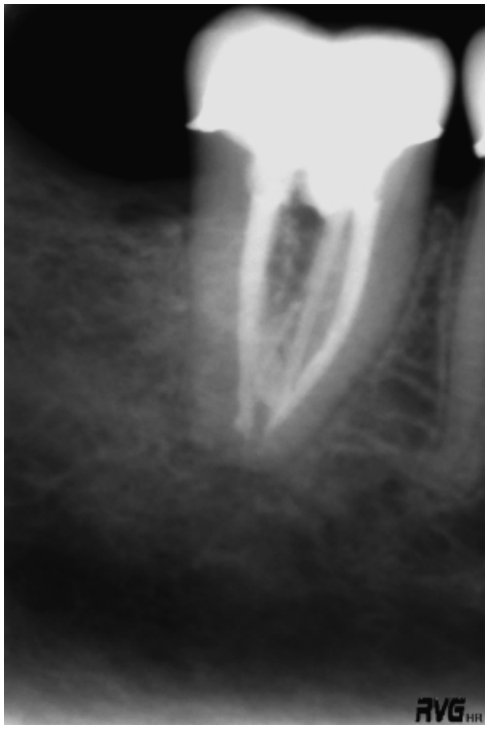

Fig. 17. Repair of a furcal perforation. After thermoplasic obturation of the canals, multiple communications in the canals are visible.

et al. (80) showed that at a time range of 72 h, the resistance to dislodgement improves significantly. At the next visit, the material should be checked to determine if it has set hard and remains positioned in the perforation site (80). If the MTA has set and perforation repair has been accomplished, cleaning and

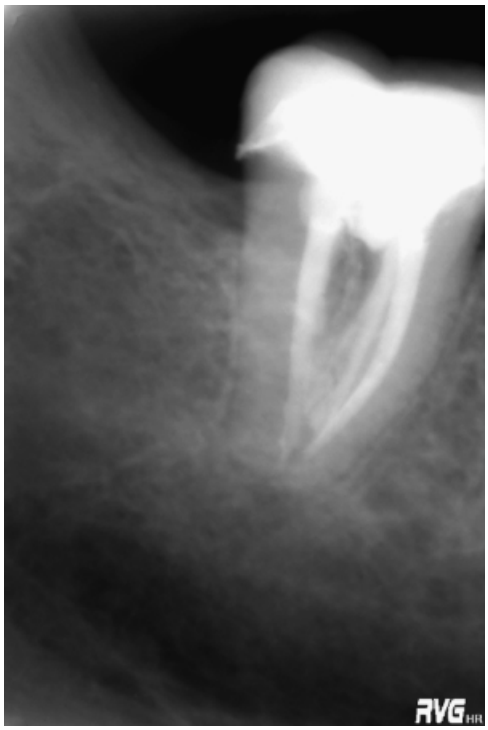

Fig. 18. Repair of a furcal perforation. A 4-year recall shows complete healing in the furcal region.

shaping should to be finalized, followed by root canal filling (Figs. 15–18). Immediate adhesive reconstruction of the tooth provides less possibility for coronal leakage and strengthens the tooth. Perforations in the cervical region, especially in anterior teeth with loss of dentinal structure, weaken the tooth in a strategically important area. In selected indications, placement of an adhesively-luted post may be advantageous (101).

Middle one-third of the root canal

Iatrogenic perforations in the middle one-third of roots are generally caused by endodontic files, Gates Glidden drills, or large, misdirected posts. By nature of occurrence, these defects are ovoid in shape and typically represent relatively large surface areas to seal (16) (Figs. 19–22). Strip perforations are frequent problems in thin and concave roots (102). The use of an operating microscope facilitates technically-demanding treatments in this more restricted area. Before closing the defect, the original canal should be instrumented to at least a size that allows accurate protection of the canal, thus preventing blockage.

Ideally the canal is instrumented as close to final apical size and shape as possible. Caution is necessary to

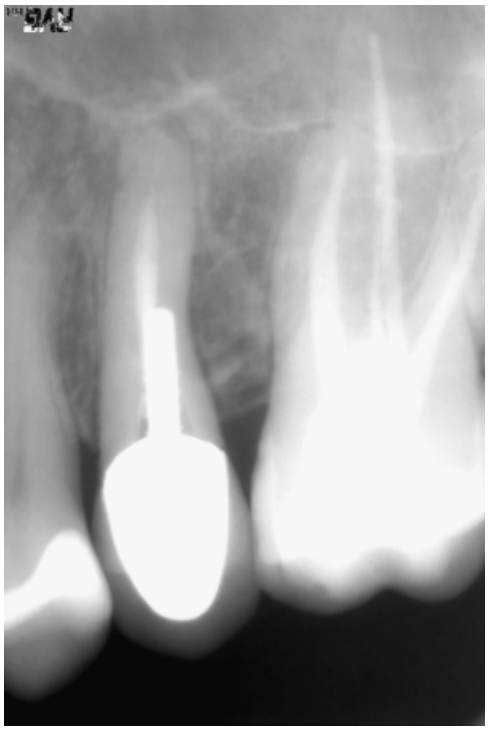

Fig. 19. Repair of perforations in the middle third. The perforation in this case occurred during post-preparation.

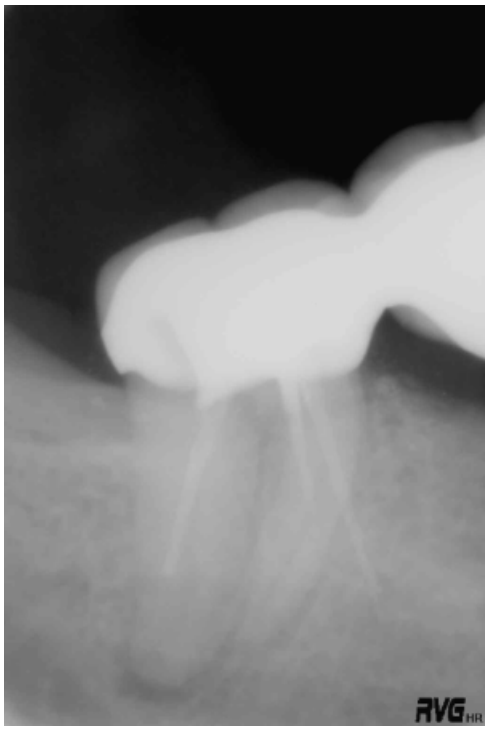

Fig. 21. Repair of perforations in the middle third. The two perforations in the mesial root of the lower molar occurred during instrumentation.

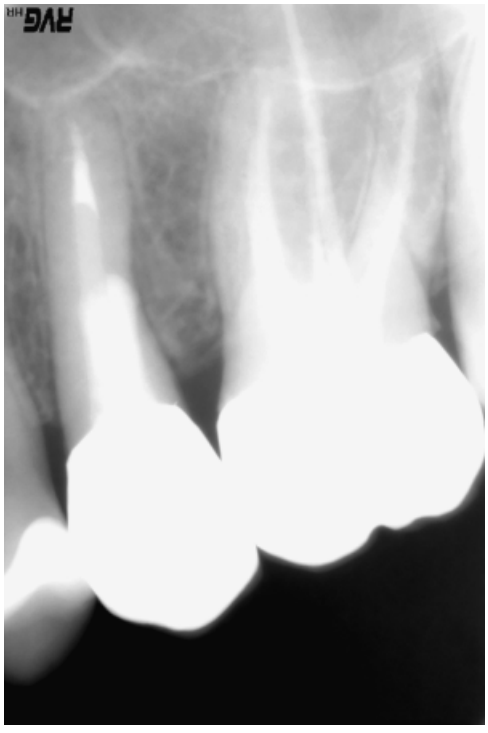

Fig. 20. Repair of perforations in the middle third. A 3-year recall shows resolution of the osseous defect.

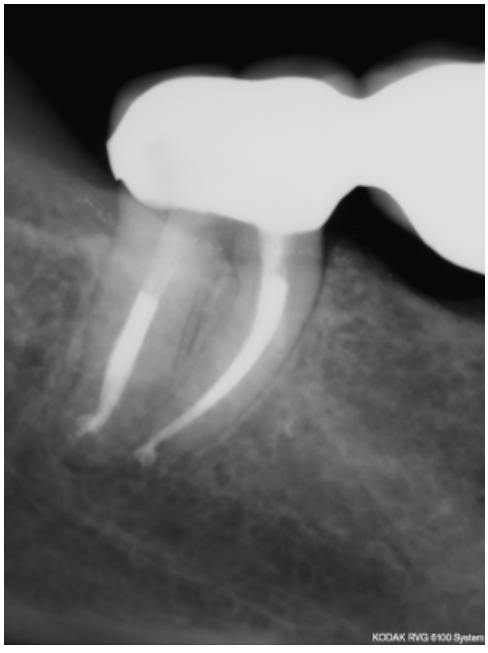

Fig. 22. Repair of perforations in the middle third. A 6-month recall shows lack of inflammation in the perforation area.

place instruments in the original canal and not the perforation. This is facilitated by pre-bending root canal instruments and ensuring good visibility of the defect. For closure, basically two techniques can be recommended. After initial 3-dimensional obturation of the canal apical to the perforation, the defect and the rest of the canal can be obturated with MTA. The disadvantage of this technique is the potential extrusion of obturation material into the perforation.

The other option is to use a 'space-maintainer' after hemostasis has been achieved. After the final canal shape is almost accomplished, some material is then placed into the canal and used to maintain patency and the original canal outlines. It must be placed deeper than the perforation. That way, almost no instrumentation is required after perforation repair and when the material is set, thus minimizing the risk of disturbing the seal. Different materials can achieve that goal. Roda & Gettleman (98) recommend the use of a severed file, which prevents canal blockage and can be used as an indirect carrier for transmitting ultrasonic energy to the MTA when attempting to achieve good adaptation. This can be helpful when direct condensation is difficult or not possible.

Another technique using a space maintainer is to fit a gutta-percha cone into the canal and melt it with heat to the dentinal wall of the root. The gutta-percha point should be placed against the canal wall opposing the perforation so that proper application of the repair material is possible. MTA is then placed at the level of the defect and condensed by hand or with ultrasonic activation of the condensing instrument.

When a file was used as a space-maintainer, it needs to be loosened with careful manipulation after finishing the repair procedure so that it can easily be removed after the MTA is fully set. Closure of the access cavity should be accomplished as previously mentioned.

Apical one-third root canal

Perforations occurring in the apical one-third of roots primarily result from breakdowns that occur during cleaning and shaping procedures (16). Management of these perforations is quite difficult: access is limited and therefore finding, negotiating, cleaning, shaping, and obturating the frequently-blocked and ledged original canal provides a challenge. If the canal can be located and instrumented, obturation can be accomplished with gutta-percha and sealer (Figs. 23 and 24). This

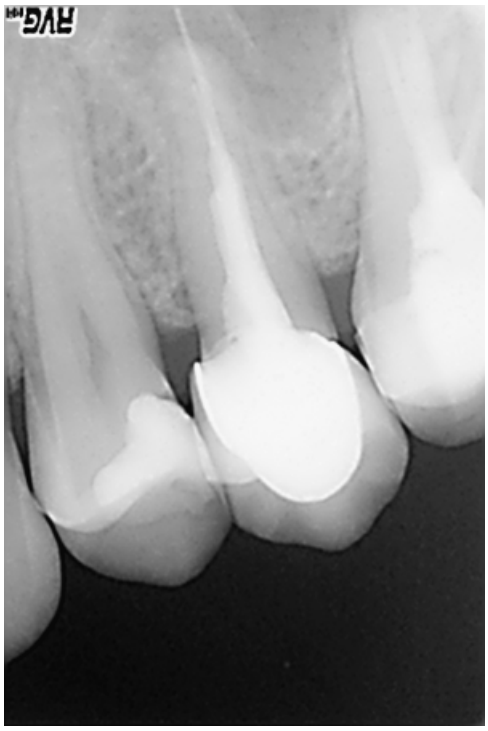

Fig. 23. Repair of perforations in the apical third. In this case, lack of apical control caused an apical perforation.

Fig. 24. Repair of perforations in the apical third. As the perforation was small in this case and apical control achievable, the perforation repair was done with a warm vertical compaction technique.

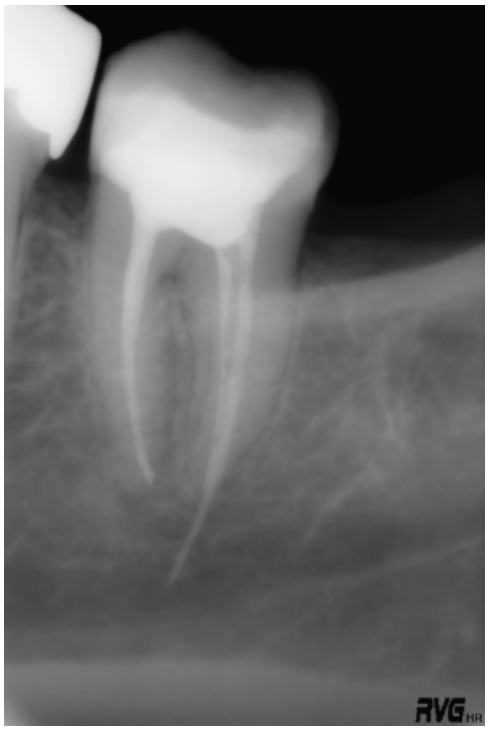

Fig. 25. Repair of perforations in the apical third. The overextension of filling material in this case is in close proximity to the mandibular canal.

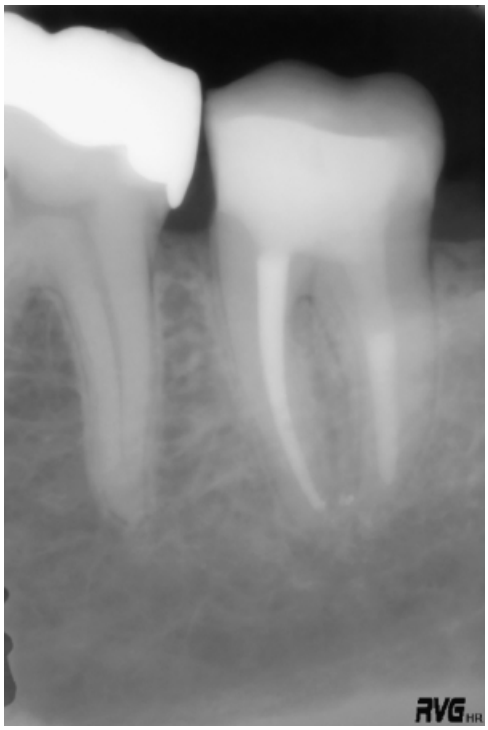

Fig. 26. Repair of perforations in the apical third. A 1-year recall shows that the apical perforation in the distal root was extensive and obturated using MTA for perforation repair and a warm vertical compaction technique for the mesial root.

approach is advantageous when the perforation tends to be small or behind a curve and the handling of MTA, even with ultrasonic vibration, is difficult. MTA is the material of choice, especially when it is hard to dry the canal. Sometimes it can be helpful to place a pre-bent file into the original canal, which stays as a space maintainer. After MTA is placed in the perforation site, the file must be loosened before MTA sets in order to be able to negotiate the original canal in the next visit. MTA can also be used to fill the perforation and the original canal (Figs. 25 and 26). Apical perforations cannot be managed successfully in all cases and apical surgery or extraction of the tooth may sometimes be better options for a stable outcome (98).

Surgical management of perforations

In the past, perforations were often managed surgically but in recent years, non-surgical perforation repair (1) has been facilitated by the use of improved magnification and illumination, providing better visualization and access to the defect. Currently, a non-surgical approach is indicated whenever possible. Surgical intervention is reserved for cases not amenable to, or

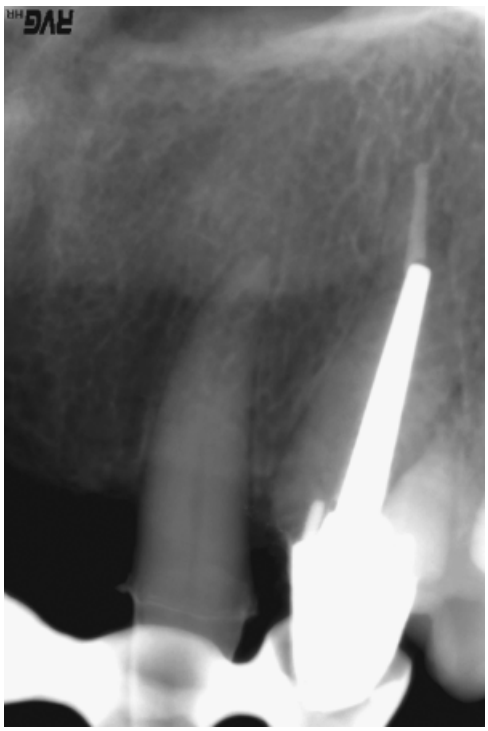

Fig. 27. Repair of perforations using a surgical approach. The radiograph of tooth 23 does not allow the diagnosis of an apical perforation.

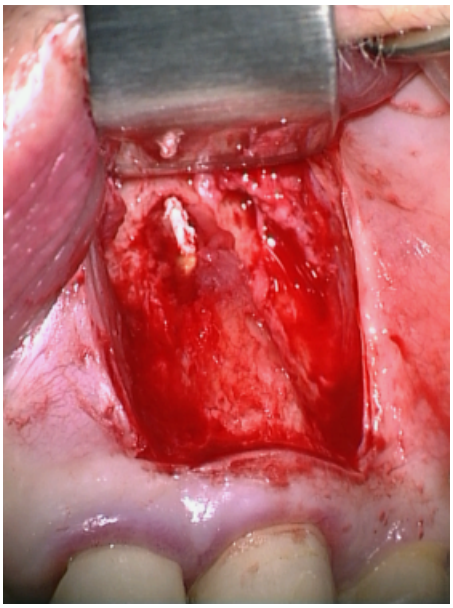

Fig. 28. Repair of perforations using a surgical approach. After surgical access, the buccal perforation becomes obvious.

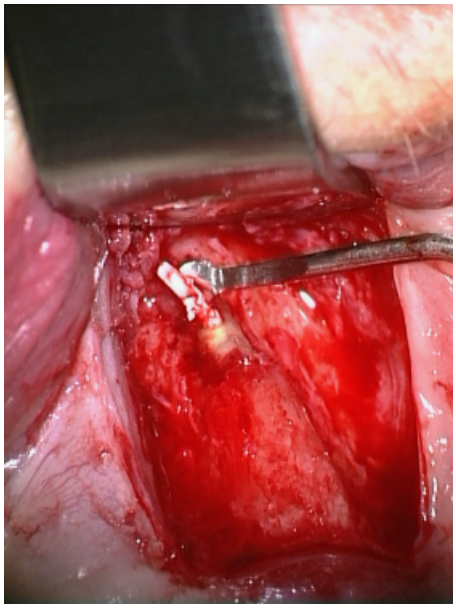

Fig. 29. Repair of perforations using a surgical approach. The obturation material is protruding into the periradicular tissues.

which have not responded to, non-surgical treatment, or in which the concomitant management of the periodontium is indicated (18). Apical perforations especially complicate conventional instrumentation and obturation of root canals. Surgical repair of root perforations has been performed by reflecting a flap at the perforation site and packing a repair material into

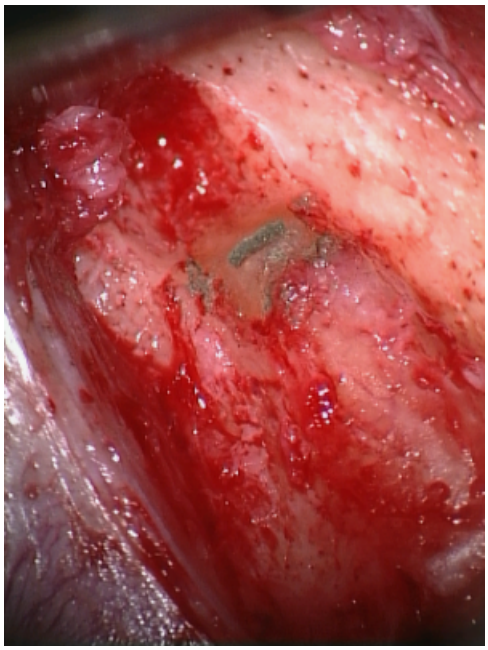

Fig. 30. Repair of perforations using a surgical approach. After careful resection of the root to the peforation area, an apical retrofilling with MTA was placed.

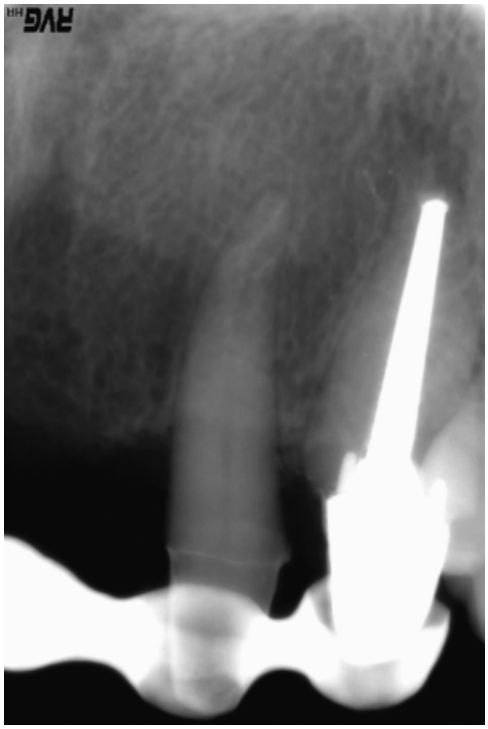

Fig. 31. Repair of perforations using a surgical approach. The post-operative radiograph shows the difficulties in this case due to lack of space for an adequate apical retrofill.

the cleaned and usually mechanically-prepared defect (74) (Figs. 27–31). Surgical intervention may also be needed in the treatment of a perforating resorption. Internal resorption is characterized by resorption of radicular dentin by clastic cells originating from the pulp (103). A communication between the pulp space and the periodontal structures can occur as a result of an extensive resorptive process if it has been given an adequate time (74).

Andreasen stated that the progression of internal resorption depends on vital tissue (104). Thus immediate root canal treatment with the removal of blood supply to the clastic cells would be the only treatment necessary for cases without external perforation (105). However, the complex irregularities of the root canal system, especially in internal resorption defects, pose technical difficulties for the thorough cleaning and obturation of the root canal (106). The persistence of organic debris and bacteria in these irregularities may interfere with the long-term success of the endodontic treatment (107). Treatment of a perforating internal resorption calls for using either surgical correction techniques or calcium hydroxide or another suitable material in an effort to form a hard tissue matrix against which a permanent root canal filling is condensed (108). Benenati (109) reported a case with a perforating internal resorption and, despite calcium hydroxide therapy for 10 months and clinical inspection, there was overextension of the filling material. If the resorption repair is surgically accessible, the combination of non-surgical and surgical interventions may provide a more favorable outcome (Figs. 32–37).

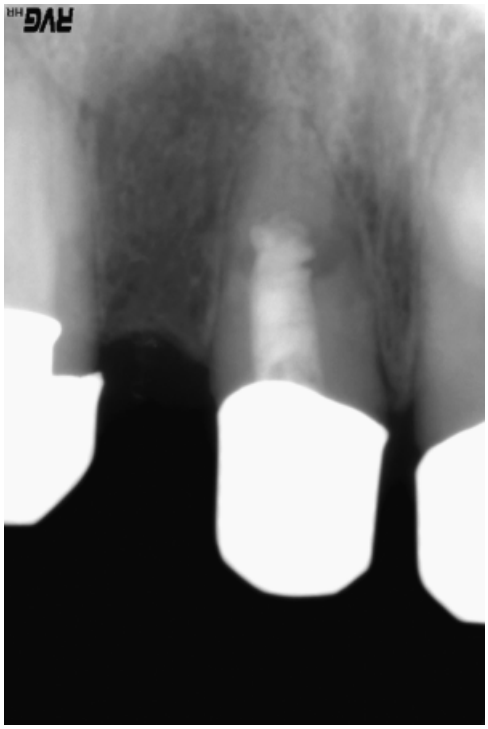

Fig. 32. Repair of a perforating internal resorption using a surgical approach. In this case, an ideal seal through the orthograde approach was not achievable, so a combined treatment was accomplished.

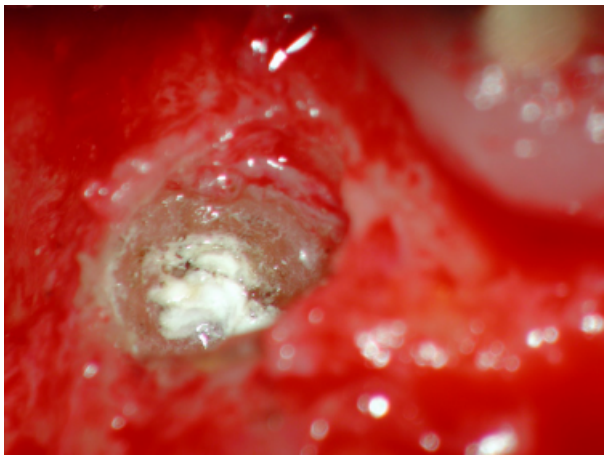

Fig. 33. Repair of a perforating internal resorption using a surgical approach. After surgical access, the extended resorption defect is visble.

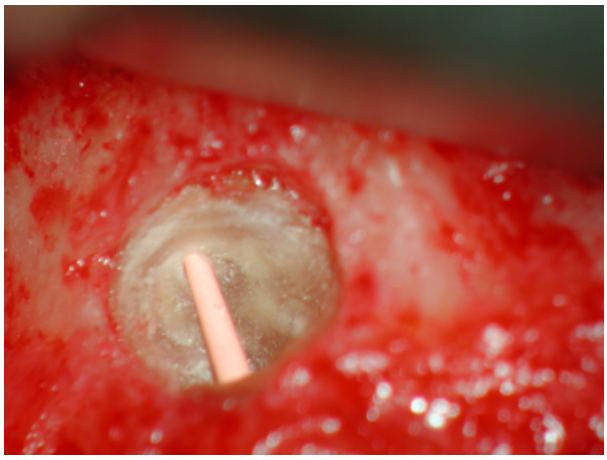

Fig. 34. Repair of a perforating internal resorption using a surgical approach. After cleaning the resorption area, negotiation, and shaping the original canal, a gutta-percha point is placed as a 'space-maintainer'.

Clinical outcomes

A number of case reports have demonstrated consistent healing of perforations treated with MTA (5, 24, 48,

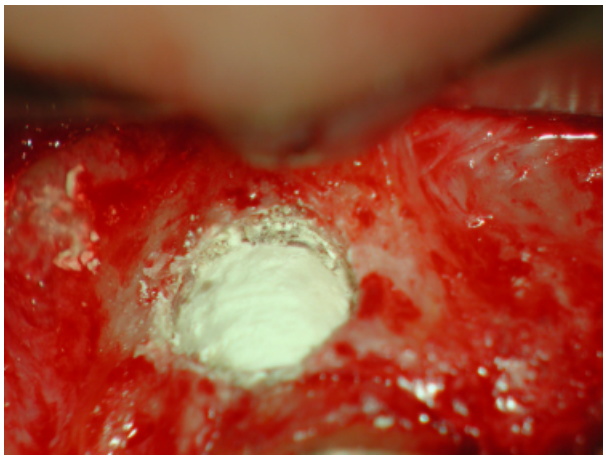

Fig. 35. Repair of a perforating internal resorption using a surgical approach. The resorption defect is restored with MTA.

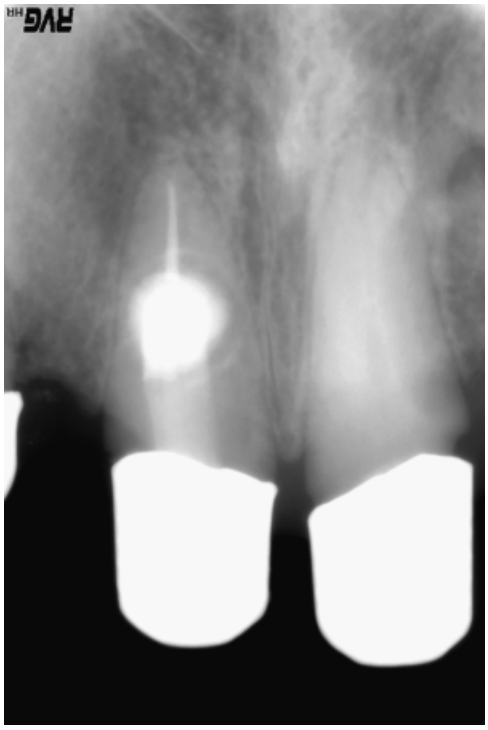

Fig. 36. Repair of a perforating internal resorption using a surgical approach. After the MTA had set, the 'space-maintainer' was removed and cleaning, shaping, and obturation of the canal was completed.

79, 88, 89, 105, 106, 110). The results reported with MTA are promising and support the use of this material for root perforation repair. Main et al. (24) showed 16 cases with normal tissue architecture adjacent to the repair site independent of the location of the defect at the recall visit. Teeth with existing lesions showed resolution of the lesion, and teeth without pre-operative lesions continued to demonstrate absence of lesion formation at the recall visit. In a prospective, observational cohort study with 4 to 6 year recall (Phases 1 and 2 of the Toronto Study), the outcome in teeth with pre-operative perforation was significantly worse than without (7). Healing occurred in only 42% of the teeth with perforations. Most of the perforations were infected and the results were consistent with previous studies.

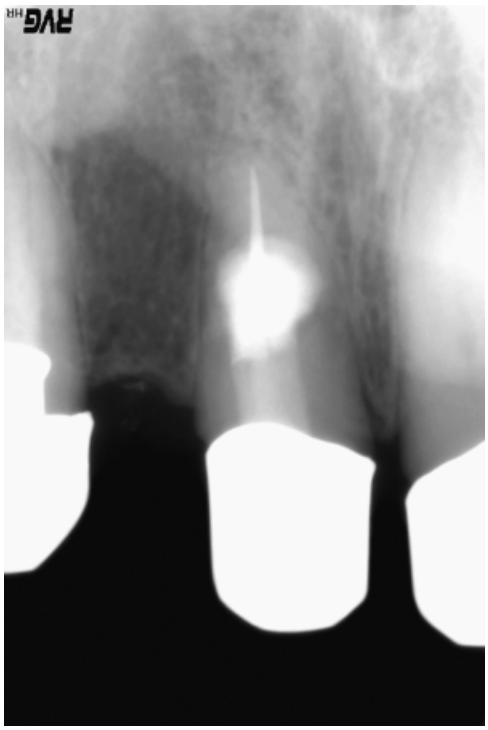

Fig. 37. Repair of a perforating internal resorption using a surgical approach. A 3-year recall shows no sign of inflammation.

Most of those defects were repaired with resin-modified glass ionomer cement. In further phases of the project, the repair protocol was changed and perforation defects were repaired with MTA. Collecting the pooled data from phases 1 to 4, the prognosis is still clearly affected by the presence of a perforation (56% vs. 87% healing). Using data from phases 3 and 4, where all 4 teeth with perforations were repaired with MTA, all cases showed healing. Possibly, the addition of subsequent phases of the Toronto Study (in which MTA has been exclusively used) might further reduce the impact of pre-operative perforations on the outcome of orthograde re-treatment (12).

In conclusion, root perforations are severe complications which lower the prognosis of endodontic

procedures. Treatment can be challenging and sometimes requires certain creativity. MTA seems to be an excellent and promising material for the repair of perforations. More research is needed to evaluate clinical procedures and outcomes in human subjects.

References

1. Roda RS. Root perforation repair: surgical and nonsurgical management. *Pract Proced Aesthet Dent* 2001: **13**: 467–472.
2. *Glossary of Endodontic Terms*. Chicago, IL: American Association of Endodontists, 2003.
3. Seltzer S, Sinai I, August D. Periodontal effects of root perforations before and during endodontic procedures. *J Dent Res* 1970: **49**: 332–339.
4. Beavers RA, Bergenholtz G, Cox CF. Periodontal wound healing following intentional root perforations in permanent teeth of Macaca mulatta. *Int Endod J* 1986: **19**: 36–44.
5. Arens DE, Torabinejad M. Repair of furcal perforations with mineral trioxide aggregate: two case reports. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996: **82**: 84–88.
6. Tsesis I, Fuss Z. Diagnosis and treatment of accidental root perforations. *Endodontic Topics* 2006: **13**: 95–107.
7. Farzaneh M, Abitbol S, Friedman S. Treatment outcome in endodontics: the Toronto study. Phases I and II: Orthograde retreatment. *J Endod* 2004: **30**: 627–633.
8. Ingle JI. A standardized endodontic technique utilizing newly designed instruments and filling materials. *Oral Surg Oral Med Oral Pathol* 1961: **14**: 83–91.
9. Fuss Z, Trope M. Root perforations: classification and treatment choices based on prognostic factors. *Endod Dent Traumatol* 1996: **12**: 255–264.
10. Eleftheriadis GI, Lambrianidis TP. Technical quality of root canal treatment and detection of iatrogenic errors in an undergraduate dental clinic. *Int Endod J* 2005: **38**: 725–734.
11. Gorni FG, Gagliani MM. The outcome of endodontic retreatment: a 2-yr follow-up. *J Endod* 2004: **30**: 1–4.
12. de Chevigny C, Dao TT, Basrani BR, Marquis V, Farzaneh M, Abitbol S et al. Treatment outcome in endodontics: the Toronto study. Phases III and IV: Orthograde retreatment. *J Endod* 2008: **34**: 131–137.
13. Kvinnsland I, Oswald RJ, Halse A, Gronningsaeter AG. A clinical and roentgenological study of 55 cases of root perforation. *Int Endod J* 1989: **22**: 75–84.
14. Gutmann JL, Dumsha TC, Lovdahl PE. *Problem Solving in Endodontics*. Mosby, 2006.
15. Lee SJ, Monsef M, Torabinejad M. Sealing ability of a mineral trioxide aggregate for repair of lateral root perforations. *J Endod* 1993: **19**: 541–544.
16. Ruddle CJ. *Nonsurgical Endodontic Retreatment*, 8th Edn. Mosby: St. Louis, MO, 2002.
17. Lemon RR. Nonsurgical repair of furcation defects (Internal matrix concept). *Dent Clin North Am* 1992: **36**: 439–457.
18. Regan JD, Witherspoon DE, Foyle D. Surgical repair of root and tooth perforations. *Endodontic Topics* 2005: **11**: 152–178.
19. Alhadainy HA, Himel VT. An *in vitro* evaluation of plaster of Paris barriers used under amalgam and glass ionomer to repair furcation perforations. *J Endod* 1994: **20**: 449–452.
20. Bryan EB, Woollard G, Mitchell WC. Nonsurgical repair of furcal perforations: a literature review. *Gen Dent* 1999: **47**: 274–278.
21. Kaufman AY, Fuss Z, Keila S, Waxenberg S. Reliability of different electronic apex locators to detect root perforations *in vitro*. *Int Endod J* 1997: **30**: 403–407.
22. Kaufman AY, Keila S. Conservative treatment of root perforations using apex locator and thermatic compactor–case study of a new method. *J Endod* 1989: **15**: 267–272.
23. Tsurumachi T, Honda K. A new cone beam computerized tomography system for use in endodontic surgery. *Int Endod J* 2007: **40**: 224–232.
24. Main C, Mirzayan N, Shabahang S, Torabinejad M. Repair of root perforations using mineral trioxide aggregate: a long-term study. *J Endod* 2004: **30**: 80–83.
25. Pitt Ford TR, Torabinejad M, Hong CU, Kariyawasam SP. Assessment of mineral trioxide aggregate as a retrograde root filling. *J Dent Res* 1994: **73**: 804, abstract #141.
26. Pitt Ford TR, Torabinejad M, McKendry DJ, Hong CU, Kariyawasam SP. Use of mineral trioxide aggregate for repair of furcal perforations. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1995: **79**: 756–763.
27. ElDeeb ME, ElDeeb M, Tabibi A, Jensen JR. An evaluation of the use of amalgam, Cavit, and calcium hydroxide in the repair of furcation perforations. *J Endod* 1982: **8**: 459–466.
28. Aguirre R, ElDeeb ME, ElDeeb ME. Evaluation of the repair of mechanical furcation perforations using amalgam, gutta-percha, or indium foil. *J Endod* 1986: **12**: 249–256.
29. Balla R, LoMonaco CJ, Skribner J, Lin LM. Histological study of furcation perforations treated with tricalcium phosphate, hydroxylapatite, amalgam, and Life. *J Endod* 1991: **17**: 234–238.
30. Nicholls E. Treatment of traumatic perforations of the pulp cavity. *Oral Surg Oral Med Oral Pathol* 1962: **15**: 603–612.
31. Lantz B, Persson PA. Periodontal tissue reactions after root perforations in dog's teeth. A histologic study. *Odontol Tidskr* 1967: **75**: 209–237.
32. Frank AL. Resorption, perforations, and fractures. *Dent Clin North Am* 1974: **18**: 465–487.
33. Oswald RJ. Procedural accidents and their repair. *Dent Clin North Am* 1979: **23**: 593–616.
34. Jew RC, Weine FS, Keene JJ, Smulson MH. A histologic evaluation of periodontal tissues adjacent to

root perforations filled with Cavit. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1982: **54**: 124–135.
35. Torabinejad M, Hong CU, Lee SJ, Monsef M, Pitt Ford TR. Investigation of mineral trioxide aggregate for root-end filling in dogs. *J Endod* 1995: **21**: 603–608.
36. Torabinejad M, Higa RK, McKendry DJ, Pitt Ford TR. Dye leakage of four root end filling materials: effects of blood contamination. *J Endod* 1994: **20**: 159–163.
37. Weldon JK, Pashley DH, Loushine RJ, Weller RN, Kimbrough WF. Sealing ability of mineral trioxide aggregate and super-EBA when used as furcation repair materials: a longitudinal study. *J Endod* 2002: **28**: 467–470.
38. Hamad HA, Tordik PA, McClanahan SB. Furcation perforation repair comparing gray and white MTA: a dye extraction study. *J Endod* 2006: **32**: 337–340.
39. Hashem AA, Hassanien EE. ProRoot MTA, MTA-Angelus and IRM used to repair large furcation perforations: sealability study. *J Endod* 2008: **34**: 59–61.
40. Himel VT, Brady J, Weir J. Evaluation of repair of mechanical perforations of the pulp chamber floor using biodegradable tricalcium phosphate or calcium hydroxide. *J Endod* 1985: **11**: 161–165.
41. Lee YL, Lee BS, Lin FH, Yun Lin A, Lan WH, Lin CP. Effects of physiological environments on the hydration behavior of mineral trioxide aggregate. *Biomaterials* 2004: **25**: 787–793.
42. Torabinejad M, Hong CU, McDonald F, Pitt Ford TR. Physical and chemical properties of a new root-end filling material. *J Endod* 1995: **21**: 349–353.
43. Tronstad L, Wennberg A. *In vitro* assessment of the toxicity of filling materials. *Int Endod J* 1980: **13**: 131–138.
44. Saidon J, He J, Zhu Q, Safavi K, Spangberg LS. Cell and tissue reactions to mineral trioxide aggregate and Portland cement. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003: **95**: 483–489.
45. Apaydin ES, Shabahang S, Torabinejad M. Hard-tissue healing after application of fresh or set MTA as root-end-filling material. *J Endod* 2004: **30**: 21–24.
46. Mangin C, Yesilsoy C, Nissan R, Stevens R. The comparative sealing ability of hydroxyapatite cement, mineral trioxide aggregate, and super ethoxybenzoic acid as root-end filling materials. *J Endod* 2003: **29**: 261–264.
47. Torabinejad M, Watson TF, Pitt Ford TR. Sealing ability of a mineral trioxide aggregate when used as a root end filling material. *J Endod* 1993: **19**: 591–595.
48. Bortoluzzi EA, Araujo GS, Guerreiro Tanomaru JM, Tanomaru-Filho M. Marginal gingiva discoloration by gray MTA: a case report. *J Endod* 2007: **33**: 325–327.
49. Asgary S, Parirokh M, Eghbal MJ, Brink F. Chemical differences between white and gray mineral trioxide aggregate. *J Endod* 2005: **31**: 101–103.
50. Song JS, Mante FK, Romanow WJ, Kim S. Chemical analysis of powder and set forms of Portland cement, gray ProRoot MTA, white ProRoot MTA, and gray MTA-Angelus. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2006: **102**: 809–815.
51. Pitt Ford TR, Torabinejad M, Abedi HR, Bakland LK, Kariyawasam SP. Using mineral trioxide aggregate as a pulp-capping material. *J Am Dent Assoc* 1996: **127**: 1491–1494.
52. Torabinejad M, Hong CU, Pitt Ford TR, Kaiyawasam SP. Tissue reaction to implanted super-EBA and mineral trioxide aggregate in the mandible of guinea pigs: a preliminary report. *J Endod* 1995: **21**: 569–571.
53. Torabinejad M, Pitt Ford TR, McKendry DJ, Abedi HR, Miller DA, Kariyawasam SP. Histologic assessment of mineral trioxide aggregate as a root-end filling in monkeys. *J Endod* 1997: **23**: 225–228.
54. Zhu Q, Haglund R, Safavi KE, Spangberg LS. Adhesion of human osteoblasts on root-end filling materials. *J Endod* 2000: **26**: 404–406.
55. Balto HA. Attachment and morphological behavior of human periodontal ligament fibroblasts to mineral trioxide aggregate: a scanning electron microscope study. *J Endod* 2004: **30**: 25–29.
56. Holland R, de Souza V, Murata SS, Nery MJ, Bernabe PF, Otoboni Filho JA et al. Healing process of dog dental pulp after pulpotomy and pulp covering with mineral trioxide aggregate or Portland cement. *Braz Dent J* 2001: **12**: 109–113.
57. Perez AL, Spears R, Gutmann JL, Opperman LA. Osteoblasts and MG-63 osteosarcoma cells behave differently when in contact with ProRoot MTA and White MTA. *Int Endod J* 2003: **36**: 564–570.
58. Camilleri J, Montesin FE, Papaioannou S, McDonald F, Pitt Ford TR. Biocompatibility of two commercial forms of mineral trioxide aggregate. *Int Endod J* 2004: **37**: 699–704.
59. Ribeiro DA, Duarte MA, Matsumoto MA, Marques ME, Salvadori DM. Biocompatibility *in vitro* tests of mineral trioxide aggregate and regular and white Portland cements. *J Endod* 2005: **31**: 605–607.
60. Tziafas D, Pantelidou O, Alvanou A, Belibasakis G, Papadimitriou S. The dentinogenic effect of mineral trioxide aggregate (MTA) in short-term capping experiments. *Int Endod J* 2002: **35**: 245–254.
61. Baek SH, Plenk H Jr, Kim S. Periapical tissue responses and cementum regeneration with amalgam, SuperEBA, and MTA as root-end filling materials. *J Endod* 2005: **31**: 444–449.
62. Moretton TR, Brown CE Jr, Legan JJ, Kafrawy AH. Tissue reactions after subcutaneous and intraosseous implantation of mineral trioxide aggregate and ethoxybenzoic acid cement. *J Biomed Mater Res* 2000: **52**: 528–533.
63. Bonson S, Jeansonne BG, Lallier TE. Root-end filling materials alter fibroblast differentiation. *J Dent Res* 2004: **83**: 408–413.
64. Takita T, Hayashi M, Takeichi O, Ogiso B, Suzuki N, Otsuka K et al. Effect of mineral trioxide aggregate on proliferation of cultured human dental pulp cells. *Int Endod J* 2006: **39**: 415–422.

65. Duarte MA, Demarchi AC, Yamashita JC, Kuga MC, Fraga Sde C. pH and calcium ion release of 2 root-end filling materials. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003: **95**: 345–347.
66. Andelin WE, Shabahang S, Wright K, Torabinejad M. Identification of hard tissue after experimental pulp capping using dentin sialoprotein (DSP) as a marker. *J Endod* 2003: **29**: 646–650.
67. Koh ET, Torabinejad M, Pitt Ford TR, Brady K, McDonald F. Mineral trioxide aggregate stimulates a biological response in human osteoblasts. *J Biomed Mater Res* 1997: **37**: 432–439.
68. Mitchell PJ, Pitt Ford TR, Torabinejad M, McDonald F. Osteoblast biocompatibility of mineral trioxide aggregate. *Biomaterials* 1999: **20**: 167–173.
69. Franchimont N, Canalis E. Platelet-derived growth factor stimulates the synthesis of interleukin-6 in cells of the osteoblast lineage. *Endocrinology* 1995: **136**: 5469–5475.
70. White C, Bryant N. Combined therapy of mineral trioxide aggregate and guided tissue regeneration in the treatment of external root resorption and an associated osseous defect. *J Periodontol* 2002: **73**: 1517–1521.
71. Breault LG, Fowler EB, Primack PD. Endodontic perforation repair with resin-ionomer: a case report. *J Contemp Dent Pract* 2000: **1**: 48–59.
72. Al-Sabek F, Shostad S, Kirkwood KL. Preferential attachment of human gingival fibroblasts to the resin ionomer Geristore. *J Endod* 2005: **31**: 205–208.
73. Daoudi MF, Saunders WP. *In vitro* evaluation of furcal perforation repair using mineral trioxide aggregate or resin modified glass lonomer cement with and without the use of the operating microscope. *J Endod* 2002: **28**: 512–515.
74. Alhadainy HA. Root perforations. A review of literature. *Oral Surg Oral Med Oral Pathol* 1994: **78**: 368–374.
75. Behnia A, Strassler HE, Campbell R. Repairing iatrogenic root perforations. *J Am Dent Assoc* 2000: **131**: 196–201.
76. Nakazawa Y, Mitsui K, Hirai Y, Takahashi K, Ishikawa T. Histo-pathological study of a glass-ionomer/resin (Geristore) restoration system. *Bull Tokyo Dent Coll* 1994: **35**: 197–205.
77. Dragoo MR. Resin-ionomer and hybrid-ionomer cements: part I. Comparison of three materials for the treatment of subgingival root lesions. *Int J Periodontics Restorative Dent* 1996: **16**: 594–601.
78. Dragoo MR. Resin-ionomer and hybrid-ionomer cements: part II. Human clinical and histologic wound healing responses in specific periodontal lesions. *Int J Periodontics Restorative Dent* 1997: **17**: 75–87.
79. Menezes R, da Silva Neto UX, Carneiro E, Letra A, Bramante CM, Bernadinelli N. MTA repair of a supracrestal perforation: a case report. *J Endod* 2005: **31**: 212–214.
80. Sluyk SR, Moon PC, Hartwell GR. Evaluation of setting properties and retention characteristics of mineral trioxide aggregate when used as a furcation perforation repair material. *J Endod* 1998: **24**: 768–771.
81. Al-Daafas A, Al-Nazhan S. Histological evaluation of contaminated furcal perforation in dogs' teeth repaired by MTA with or without internal matrix. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007: **103**: e92–e99.
82. Auslander WP, Weinberg G. Anatomic repair of internal perforations with indium foil and silver amalgam: outline of a method. *N Y J Dent* 1969: **39**: 454–457.
83. Imura N, Otani SM, Hata G, Toda T, Zuolo ML. Sealing ability of composite resin placed over calcium hydroxide and calcium sulphate plugs in the repair of furcation perforations in mandibular molars: a study *in vitro*. *Int Endod J* 1998: **31**: 79–84.
84. Jantarat J, Dashper SG, Messer HH. Effect of matrix placement on furcation perforation repair. *J Endod* 1999: **25**: 192–196.
85. Rafter M, Baker M, Alves M, Daniel J, Remeikis N. Evaluation of healing with use of an internal matrix to repair furcation perforations. *Int Endodon J* 2002: **35**: 775–783.
86. Holland R, Filho JA, de Souza V, Nery MJ, Bernabe PF, Junior ED. Mineral trioxide aggregate repair of lateral root perforations. *J Endod* 2001: **27**: 281–284.
87. Bernabe PF, Gomes-Filho JE, Rocha WC, Nery MJ, Otoboni-Filho JA, Dezan-Junior E. Histological evaluation of MTA as a root-end filling material. *Int Endod J* 2007: **40**: 758–765.
88. Kratchman SI. Perforation repair and one-step apexification procedures. *Dent Clin North Am* 2004: **48**: 291–307.
89. Bargholz C. Perforation repair with mineral trioxide aggregate: a modified matrix concept. *Int Endod J* 2005: **38**: 59–69.
90. Pecora G, Kim S, Celletti R, Davarpanah M. The guided tissue regeneration principle in endodontic surgery: one-year postoperative results of large periapical lesions. *Int Endod J* 1995: **28**: 41–46.
91. Pecora G, Baek SH, Rethnam S, Kim S. Barrier membrane techniques in endodontic microsurgery. *Dent Clin North Am* 1997: **41**: 585–602.
92. Murashima Y, Yoshikawa G, Wadachi R, Sawada N, Suda H. Calcium sulphate as a bone substitute for various osseous defects in conjunction with apicectomy. *Int Endod J* 2002: **35**: 768–774.
93. Yoshikawa G, Murashima Y, Wadachi R, Sawada N, Suda H. Guided bone regeneration (GBR) using membranes and calcium sulphate after apicectomy: a comparative histomorphometrical study. *Int Endod J* 2002: **35**: 255–263.
94. Zou L, Liu J, Yin SH, Tan J, Wang FM, Li W et al. Effect of placement of calcium sulphate when used for the repair of furcation perforations on the seal produced by a resin-based material. *Int Endod J* 2007: **40**: 100–105.

95. Carr G. Endodontic retreatment. In: Cohen S, Burns RC, eds. *Pathways of the Pulp*, 7th edn. Mosby: St. Louis, MO, 1998: 791–834.
96. Lemon RR, Steele PJ, Jeansonne BG. Ferric sulfate hemostasis: effect on osseous wound healing. Left *in situ* for maximum exposure. *J Endod* 1993: **19**: 170–173.
97. Jeansonne BG, Boggs WS, Lemon RR. Ferric sulfate hemostasis: effect on osseous wound healing. II. With curettage and irrigation. *J Endod* 1993: **19**: 174–176.
98. Roda RS, Gettleman BH. Nonsurgical retreatment. In: Cohen S, Hargreaves KM, eds. *Pathways of the Pulp*, 9th edn. Mosby: St. Louis, MO, 2006.
99. Aminoshariae A, Hartwell GR, Moon PC. Placement of mineral trioxide aggregate using two different techniques. *J Endod* 2003: **29**: 679–682.
100. Yeung P, Liewehr FR, Moon PC. A quantitative comparison of the fill density of MTA produced by two placement techniques. *J Endod* 2006: **32**: 456–459.
101. Schwartz RS, Robbins JW. Post placement and restoration of endodontically treated teeth: a literature review. *J Endod* 2004: **30**: 289–301.
102. Allam CR. Treatment of stripping perforations. *J Endod* 1996: **22**: 699–702.
103. Trope M, Blanco L, Chivian N, Sigurdsson A. The role of endodontics after dental traumatic injuries. In: Cohen S, Burns RC, Hargreaves KM, eds. *Pathways of the Pulp*, 9th edn. Mosby: St. Louis, MO, 2006: 610–649.
104. Andreasen JO. *Traumatic Injuries to the Teeth*, 2nd edn. Copenhagen: Munksgaard, 1981.
105. Hsien HC, Cheng YA, Lee YL, Lan WH, Lin CP. Repair of perforating internal resorption with mineral trioxide aggregate: a case report. *J Endod* 2003: **29**: 538–539.
106. Sari S, Sonmez D. Internal resorption treated with mineral trioxide aggregate in a primary molar tooth: 18-month follow-up. *J Endod* 2006: **32**: 69–71.
107. Goldberg F, Massone EJ, Esmoris M, Alfie D. Comparison of different techniques for obturating experimental internal resorptive cavities. *Endod Dent Traumatol* 2000: **16**: 116–121.
108. Frank AL, Weine FS. Nonsurgical therapy for the perforative defect of internal resorption. *J Am Dent Assoc* 1973: **87**: 863–868.
109. Benenati FW. Treatment of a mandibular molar with perforating internal resorption. *J Endod* 2001: **27**: 474–475.
110. Meire M, De Moor R. Mineral trioxide aggregate repair of a perforating internal resorption in a mandibular molar. *J Endod* 2008: **34**: 220–223.