Mishaps and serious complications in endodontic obturation

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There are numerous examples reported in the literature that cite and document many disabling complications to the alveolar bone, neurovascular anatomy and maxillary sinus following overextension of root canal filling materials. Neural complications as a consequences of endodontic obturation as well as other server outcomes to overfill are a serious problem. These injuries require a thoughful strategy for prevention during endodontic procedures as well as a responsible systematic approach to management, should the outcome of endodontic therapy produce an injury. This monogrph will focus on measures that can prevent obturation mishaps which occur under the most vulnerable of circumstances during the course of endodontic therapy. This paper will also critically review the toxicity of materials used in endodontic obturation and seek to identify those principal factors which affect prognosis after injury.

I have nerve damage to the inferior alveolar nerve that was done during a root canal procedure. To make matters worse, the root canal filling spilled out into the mandible (sic) canal on the nerve that was injured. I have shooting pain in almost all of my teeth which is unbearable. I also have other types of constant aching pain. My teeth are so super-sensitive at times, that even air bothers them. I don't think I am going to make it. I can't find the right kind of help. I have seen a pain specialist who has me on special drugs but it hasn't helped. Is there anyone out there who can help me find a specialist who has expertise dealing with this type of problem?

Is there a dental practitioner, reading the above comment posted to an Internet website for patients with facial pain, who would not empathize with the suffering of this patient? Unfortunately, there are numerous examples reported in the literature that cite and document many disabling complications to the alveolar bone, neurovascular bundle and maxillary sinus following inadvertent overextension of root canal-filling materials. Paresthesia as a consequence of endodontic obturation as well as other severe neural complications must be considered as a serious problem. These injuries require a thoughtful strategy for prevention during endodontic procedures as well as a responsible systematic approach to management, should the outcome of endodontic therapy produce an overfill injury.

This monograph will focus on measures that can prevent and/or minimize accidents, which can occur under the most vulnerable of circumstances during the course of endodontic therapy. The identification of those principal factors that can affect prognosis after injury will also be an important focus of this article. Many of the root-filling materials used today are either chemically neurotoxic or can be mechanically destructive to surrounding structures via compression injury. In addition, overinstrumentation errors in shaping root canal spaces may produce an abnormal overenlargement of the apical constriction allowing overfill or instrument damage to structures through direct manipulation or rotation that severs susceptible tissues. With the use of rotation during instrumentation and heated obturation devices becoming increasingly available to all practitioners in the last decade, the introduction of endodontic filling materials into periapical tissues is quite common. This is of major concern when the teeth being treated are in close proximity to anatomically important structures such as the maxillary sinus or inferior alveolar canal. Overextension of the root canal-filling material risks injurious consequences if the underlying inferior alveolar nerve or sinus structures are initially penetrated with files. A pathway of entry into the inferior alveolar nerve or sinus space can more likely result when the pathway is created by overinstrumentation (Fig. 1).
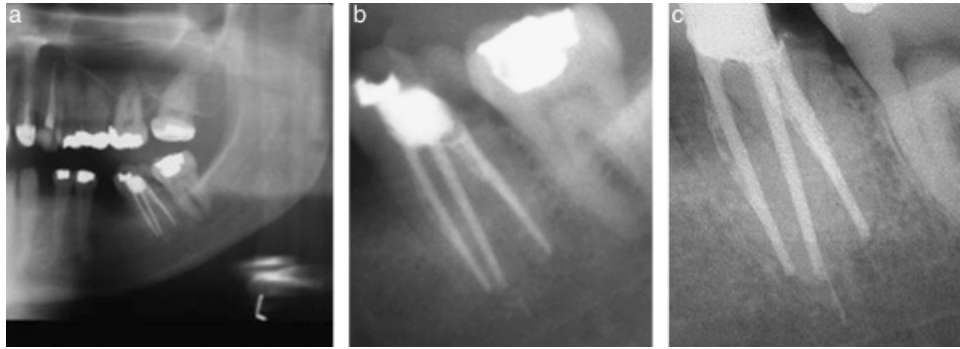
Fig. 1. (A) Panoramic radiograph of completed root canal therapy of the lower left second molar. Radiograph shows proximity to the inferior alveolar canal; **(B)** isolated image of the second molar shows radiopaque material beyond the mesial root and root shapes that have transported the original canal positions; **(C)** magnification identifies an overinstrumented root canal providing a pathway for injury by instruments and/or sealer. Patient experienced permanent paresthesia in the inferior alveolar distribution on the face.

The importance of accurate radiographic imaging

You don't know . . . what you don't know.

This common admonition by educators to many students in the medical sciences, as they are learning the principles and practice of diagnostic assessment, is a fundamental truth. 'You don't know . . . what you don't know.' For the practitioner embarking on therapy for a molar or bicuspid tooth in the anatomical vicinity of the maxillary sinus, mental foramen or inferior alveolar nerve, this caveat is vital. Understanding the proximity of roots to these important structures must be recognized and accurate radiographic imaging is the most direct route to that knowledge. When a radiographic examination is performed or needed, the practitioner assumes the responsibility to make accurate interpretations from good discernable images of diagnostic quality. It is a common understanding that both large and small lesions as well as anatomical entities are routinely missed in radiographic surveys both by the operator and the limitations of the technology when encountering differences in anatomic variation (1).

Thus, viewing the radiographs as part of a routine and standardized diagnostic sequence requires the following principles be carefully observed (1, 2).

1. Interpretations should only be made from properly exposed and processed radiographs (Fig. 2).
2. Use multiple views and imaging modalities (panographic) as often as necessary to demonstrate important radiographic features in three dimensions.
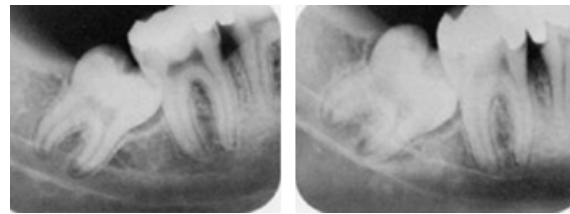

Fig. 2. Traditional radiographic images with slight angulation changes identifying the two-dimensional relationship of the molar roots to the inferior alveolar canal.

3. Use magnification and other optimal viewing modalities to enhance all images.
4. Obtain special imaging studies if necessary (2).

These viewing principles, whether the images are rendered on traditional film or digital, are critical to extracting the maximum information for the purpose of diagnostic interpretation (2). When special imaging is required, dentistry is making rapid strides in the areas of digital radiography and computed tomography (CT).

Digital Radiography

Digital imaging of dental structures has become a common diagnostic modality in the last decade in offices around the world. A charged sensor and associated computer hardware and software are the new paradigm in dental imaging, often replacing traditional film in a number of applications. The sensor can be positioned once and the cone adjusted for several angulations,

offering the possibility of multiple images, rendering a better assessment of the third dimension. This affords the practitioner instant processing and enhanced understanding via computer manipulation. Although concerns still linger regarding image quality compared with traditional film, these concerns are lessened by improving technology, magnification possibilities (3, 5), digital subtraction (4), reduced radiation exposures, real-time images, and archival benefits (2). The ability to control the image that is on the computer screen is what allows digital imaging its genuine power to aid in identification and diagnosis. Some of the real brilliance associated with these images are the so-called 'smart technologies' associated with the software. One of these smart technologies can evaluate radiographs for anatomy as well as pathology that are not visible to the human eye. This smart technology software analyzes changes in radiographic density to find hidden structures such as the inferior alveolar canal, mental foramen or undetectable caries, and apical pathology (2) (Fig. 3).
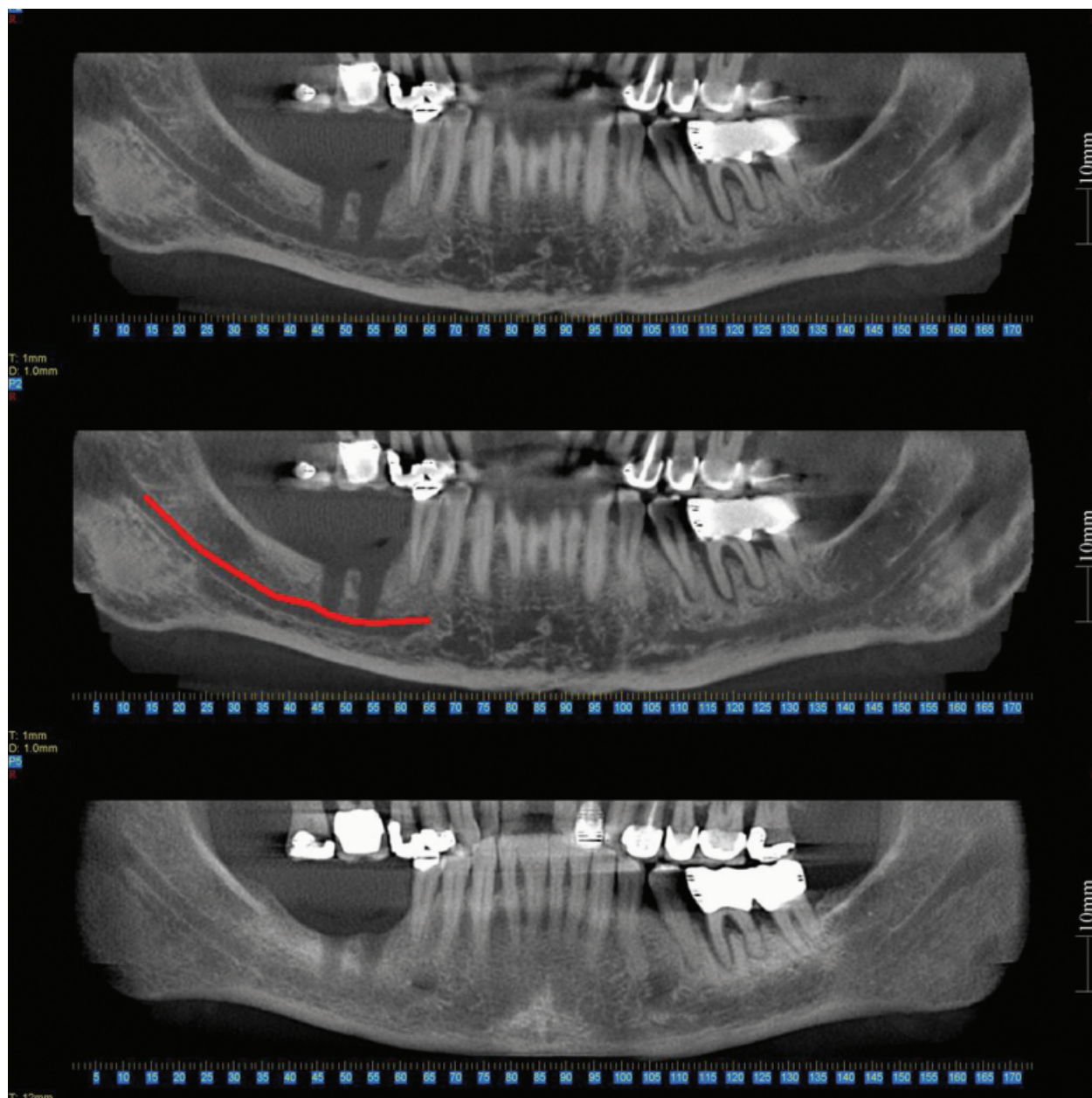

Fig. 3. NewTom™ cone beam CT imaging (Aperio Services, Sarasota, FL) with 'smart software' outlining the inferior alveolar canal as the scan provides 1 mm cross-sectional slices through the mandible.

Computed Tomography

While tomography can best be defined as a radiographic slicing of a specific structure in thin millimeter sections on any desired axis, CT offers the reality of three-dimensional images. The safe placement of implants around neurovascular danger and sinuses that course deep around roots where implants are desired has made the use of tomography and CT an indispensable special imaging technique. In the United States, while CT imaging is widely available for medical diagnosis, it is slowly making its way into dental radiology. In other countries of Europe and Asia, this technology has been in use in dentistry for over a decade and the research and development of applications in this area has made significant advances in traditional CT and the three-dimensional cone beam CT (6).

In the clinical scenario for cone beam CT, the patient is positioned to the scanner. A small conical X-ray beam is exposed to a high sensitivity Image Intensifier (sensor), whereas the X-ray arm is rotating 360° around the region. The digital image is transmitted to a computer.

Images are generated by a reconstruction algorithm, after mathematical data processing and displayed on a PC monitor, which generates a three-dimensional image of the oral and maxillofacial region of interest (7). Regions that are required to be compared over time need not be radiographed in exactly the same way as in traditional radiography (6) (Figs 4 and 5).

Anatomic and Imaging Characteristics of the Maxillary Sinus

The maxillary sinus or antrum is an air-filled cavity lined by respiratory mucosa. The inferior border of the sinus lies in the alveolar process of the maxilla and is situated above or often between the apices of the maxillary posterior teeth. The sinus may also be separated by bony walls into several compartments. Proper visualization of the maxillary sinuses is critical for interpretation of location and distances of root apices from the sinus space (8).

Fig. 4. *XYZ* **axis slices through the inferior alveolar canal of an edentulous mandible with the Accuitomo™, three-dimensional cone beam imager (J. Morita Mfg. Co., Kyoto, Japan).**

Fig. 5. *XYZ* **axis slices showing the relationship of the apices of the lower left first molar to the inferior alveolar canal (Accuitomo™, J. Morita Mfg.Co., Kyoto, Japan).**

Often a panoramic projection provides a clearer imaging of the sinus than do periapical films. A standard panoramic projection provides very good information about the dimensions of the sinus space notwithstanding the superimposition of the nasal and zygomatic structures in a panographic image. The size and configurations of the sinuses vary greatly; in some individuals there is considerable bone between the apices of the teeth and the sinus cavity, whereas in others the roots directly project into the sinus with minimal or no bony covering (9–13). Information derived from cone beam CT was reported very useful in a case involving surgical access to an upper molar. The course of the sinus and its relationship to the roots of the first molar as well as potential sinus pathology were assessed (14).

Neural distribution to the sinus is diagnostically important. The nerve supply is from the maxillary division of the trigeminal nerve, with branches coming from the posterior, middle, and anterior superior portions. The inflammatory effects of overfilled endodontic materials as well as dental sepsis can affect the differential diagnosis of

pain localized to the sinuses. High contrast three-dimensional CT will greatly facilitate the evaluation of the sinuses and determine the position of foreign materials and their relation to the apices of teeth (8). The inflammatory effects induced by irrigants, medicaments, and endodontic-filling materials will extend a pathway to the sinus if proximity allows; more than the usual care and discretion in the use of these products is indicated in root canals that adjoin the sinus (9, 10).

Anatomic and Imaging Characteristics of the Inferior Alveolar Canal and Mandibular Nerve

The inferior alveolar canal starts at the mandibular foramen on the inner aspect of the ramus and passes in a downward and forward direction through the mandible. As it passes forward, it also moves from the lingual side of the body of the mandible in the third molar area

to the buccal side in the premolar area. In traditional radiography and panographic films as well as digital images, it appears as a narrow, radiolucent ribbon between two radiopaque lines representing the canal walls. It has been reported that CT imaging was highly reliable when attempting to determine the relation between periapical lesions and the mandibular canal before endodontic surgery (15).

In the region of the mental foramen, the mandibular nerve bifurcates into its two branches, the incisive and mental nerves. The exact location of the inferior alveolar canal and its mental branch is important in the placement of implants, surgical extractions, and endodontic therapy of roots within close proximity.(16) In a series of investigations on 75 human skulls to identify the radiographic position of the mental foramen on periapical and panographic film, the authors found that the foramen could be seen on only 75% of the horizontal periapical radiographs.(17) Visualization of the mental foramen was increased and enhanced when a panoramic radiograph was available because of a 23% magnification factor that occurs in a panographic film.(18)

Interruptions in the protective wall of the canal by dental manipulations can have serious and calamitous effects on the patient's sensibility in the distribution of the nerve. The mandibular nerve is a peripheral nerve consisting of an outer epineurium that encloses it as it courses through the inferior alveolar canal. As an anatomic structure, it is composed of bundles (fascicles) of nerve fibers. The fascicles are wrapped by the perineurium, and within each fascicle are the individual axons ensheathed by Schwann cells and surrounded by a delicate packing of loose vascular supporting tissue called endoneurium (19, 20) (Fig. 6). Peripheral nerves receive a rich blood supply via numerous penetrating vessels from surrounding tissues and accompanying arteries. In research that assessed the spatial relationship between the posterior teeth and the mandibular canal in 22 mature dried human skulls accounting for 264 specimen sections; second premolars and second molars had the closest distances to the canal with a mean distance of 4.7 and 3.7 mm, respectively. The mandibular canal was directly inferior to the root apices of the posterior teeth 5% of the time. The data also determined that as the mandibular height decreased, the distance between the canal and root apices also decreased (21). In prior studies, investigators have found that 60% of mandible specimens contained canals whereas 40% of the dissec-
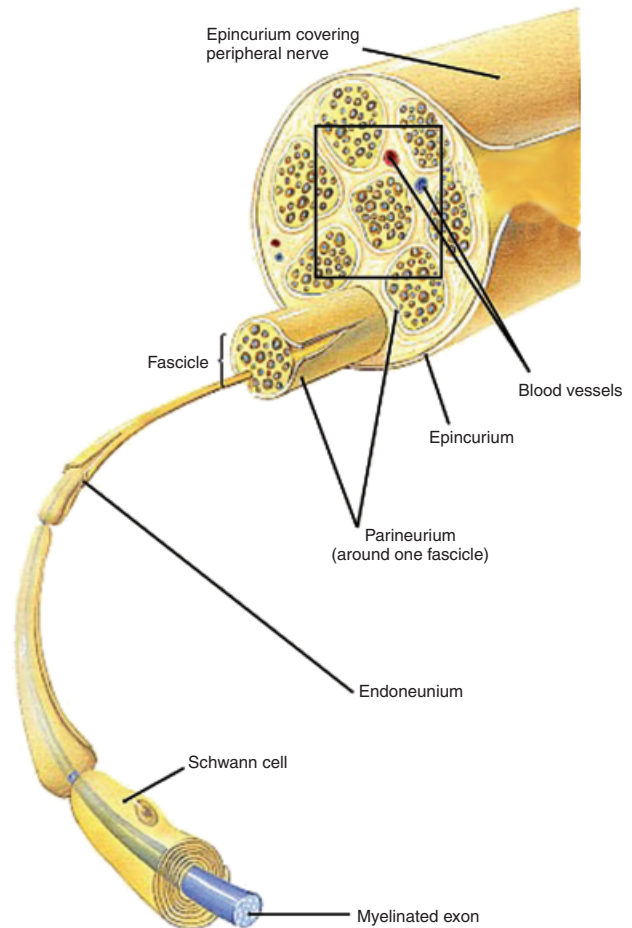

Fig. 6. Graphic illustration of the crossectional anatomy of the neurovascular complex of a peripheral nerve. The boxed area represents the macroscopic relationship of the vasculature to the neural elements (reproduced from Martini et al. (19); reprinted by permission of Pearson Education, Inc).

tion samples had no distinct canals. Often branches of the nerve showed significant morphologic variability and occupied only a space in the bone as opposed to residing within a distinct tunnel-like structure (22). This finding has significant implications as we investigate the scientific literature regarding the effects of endodontic medicaments, sealers, and materials on bone, connective tissue and specifically the neurovascular elements found in the antrum and inferior alveolar canal.

Inflammatory and Neurotoxic Effects of Root Canal Materials

In a decade old consensus report of the European Society of Endodontology regarding quality guidelines

for endodontic therapy, it is clearly recommended that 'the objective of any (endodontic) technique used should be to apply a *biocompatible* hermetically sealing canal filling that obturates the prepared canal space from pulp chamber *just to* its apical termination'(23).

Currently, there is an important body of convincing biologic literature that gives confidence to the science describing host tissue reaction to many endodontic obturation materials. The following conclusions regarding endodontic sealers have stood the test of time in the last 50 years (24).

1. All obturation sealers are irritants in their freshly mixed states.
2. After setting or curing, some sealers lose their irritant components and become relatively inert.
3. All sealers are absorbable
4. Components of sealers will be managed by the immune system in the process of absorption (24, 25).
5. Pastes intended to fill the entire root canal system will be absorbed more rapidly than solid core obturations with sealer (26).
6. A minimum amount of sealer should be exposed to periapical tissue (Fig. 7).

In endodontic therapy, sealers and cements are primarily used to fill any irregularities at the interface between the solid core root canal-filling material and the walls of the canal system, ideally rendering the system bacteria impervious. Endodontic failures caused by a continued re-growth and proliferation of micro-organisms because of apical percolation of blood-borne

Fig. 7. Large zinc-oxide-eugenol sealer overfill was tolerated by the patient for many years and remains asymptomatic today. There was no neurovascular involvement. Radiograph courtesy Dr. Roxanne Benison.

proteins can still occur even within properly cleaned and shaped teeth if the apical foramen is poorly sealed. It has been reported that even in the absence of microbial factors, root-filling substances can evoke a foreign body reaction leading to the development of periapical lesions that may be refractory to endodontic therapy (27).

Many sealers, when used properly, are recognized to have antimicrobial activity as well as the potential to stimulate fibroblastic, osteoblastic, or cementoblastic activity. Sealers can be grouped based on their primary constituents, such as zinc oxide–eugenol, calcium hydroxide, resins, glass ionomers, or resin-/composite-based sealers.

The biological and irritational properties of root canal sealing materials can be evaluated in a number of ways. These have included tissue and cell culture studies (28–30), bone and soft-tissue reactions to set and unset implanted materials in experimental animals (31–33), experimental and clinical studies on animals and humans (34–36) and new assessments involving histochemical analysis and X-ray microanalysis (37–39).

Early investigations into the absorbability of root canal sealers in animal models showed that very hard and compact sealers with low solubility became encapsulated by fibrous connective tissue (26). Less dense and more soluble sealers were dispersed and absorbed more rapidly. Large quantities of excess filling materials in the periapical tissues caused necrosis of bone followed by bone resorption and then absorption of the filling materials. Most root canal sealers produce an initial acute inflammatory reaction in the connective tissues (24). This is followed by the production of a chronic foreign body reaction in which phagocytosis is a recognized feature. As the material disintegrates in tissue fluids, macrophages are a predominant element in the removal of the foreign body. Such evidence suggests that the presence of foreign material in large quantities in the periapical tissues causes persistence of breakdown and that persistence is fueled by the toxicity of the engulfed material. In particular, the breakdown products may have an adverse effect on the proliferation and viability of periradicular cell populations that are necessary for repair (39).

It is the sealers and components of sealers that are recognized by the scientific literature as neurotoxic or highly irritating that warrants more scrupulous attention and an equally careful recognition of their potential for serious injury.

Gutta-percha:

The most common core material worldwide is gutta-percha. It has a history of usage in dentistry of well over a century and is chemically considered a polyisoprene (a crystalline polymer). In its clinical formulations, it comprises approximately 20% of total volume with the remainder mostly zinc oxide and proprietary additives. Gutta-percha has a low degree of toxicity when compared with other components used in endodontic obturation and has withstood the test of time in clinical usage (40).

Eugenol:

Eugenol is a phenol derivative and a major component of the numerous formulations of sealers that incorporate this liquid into a zinc oxide powder for placement with a solid core obturation. Most ZOE sealer cements are cytotoxic and invoke an inflammatory response in connective tissues. As a component, the liquid exhibits an inhibition of sensory nerve activity. Because of its long-time use as a sedative or anodyne in dentistry, eugenol has been an integral component in modern dental therapeutics. It is also currently recognized that if misused, eugenol can be highly inflammatory and destructive.

In a study to determine the effects of eugenol on evoked nerve impulse transmission, using a standard experimental model, concentrations of eugenol as low as 0.05%, were applied to frog's sciatic nerve. All concentrations were found to reduce and finally eliminate the amplitude of the nerve's evoked compound action potential. The author concluded unequivocally, eugenol is toxic to nerve (41). It was further recommended that eugenol can be a dangerous substance when used improperly in endodontic therapy, and that the practice of placing eugenol with a paper point into the periapical tissues to sedate an acute apical periodontitis, is fraught with hazard to neural structures in the vicinity of mandibular teeth (41). Other researchers have shown similar neurotoxic effects of eugenol in sealers using other experimental animal models (42).

Calcium hydroxide:

Calcium hydroxide sealers are relatively new to the marketplace and have been promoted for their ability to stimulate repair. These claims have yet to be proven. Rather, the inclusion of calcium hydroxide should be assessed for its efficacy in creating a long-term seal of the root canal space and its inflammatory effects on periapical tissues. In one study, calcium hydroxide root canal sealers produced irreversible blockade of rat phrenic nerve conduction upon 30 min application (43). In another, the investigators found complete inhibition of rat sciatic nerve after 50 min of exposure with calcium hydroxide sealer. They observed partial recovery after perfusion with a saline solution (44).

In a detailed study of the effects of an intentionally injected calcium hydroxide sealer that penetrated the mandibular canal in dogs, both the tissue reactions to the material and changes in the alveolar nerve tissue were observed (37, 38). Tissue reactions to the calcium hydroxide paste were examined by radiography, histopathology, and electron microscopy. The alveolar nerve tissue was examined by light and electron microscopy. The paste was phagocytized by macrophages and foreign body giant cells and absorbed over time (37) and tissue damage was found in sites of direct contact with the calcium hydroxide (38). The connective tissue was observed to be compressed by the injected paste and both degeneration and regeneration were observed at the same time during the experimental period (38). Another study showing the cytotoxic effects of calcium hydroxide sealers on human fibroblasts showed early severity in the first 48 h with significant reduction in toxicity between the third and fifth day (30).

Paraformaldehyde:

The use of paraformaldehyde pastes depends on the acceptance of concepts and therapies related to the principles of mummification and fixation of pulp tissue (45). In 1959, Sargenti and Richter introduced a method for endodontic therapy that included filling the root canal system with a paraformaldehyde paste (N2). Sargenti and other proponents for a number of paraformaldehyde paste formulations have touted the consistent antimicrobial activity of the paste when used in endodontic therapy (46). Although traditional zinc oxide and eugenol sealers are used in conjunction with solid core materials such as gutta-percha, N2, RC2B, endomethosone, and other paraformaldehyde paste formulations are recommended as the sole-filling material, greatly increasing the volume of material used in the canal system. Thus, absorbability and toxicity are serious considerations with paraformaldehyde pastes. In a large number of reports published regarding paresthesia and other complications of the inferior alveolar nerve following penetration of root canal-filling material into the mandibular canal, in most cases, damage to the nerve was specifically attributed to the highly irritating components of various paraformalde-

hyde pastes (47–53). Brodin (54) and other investigators (36, 55–59), have experimentally and convincingly demonstrated the neurotoxicity of these paraformadehyde compounds. Furthermore, Brodin et al. (60) have shown that N2, among other root-filling materials with paraformaldehyde as a component, produced permanent disruption of nerve conduction *in vitro*. Others have demonstrated the systemic distribution of radioactively labeled paraformaldehyde incorporated within formocresol in pulpotomized dogs (61). Disintegration products were found in periapical and periodontal tissues remote from the pulpal wound site. The radiolabeled paraformaldehyde was additionally found in blood, regional lymph nodes, kidney and liver. It had been recognized early on by researchers that every effort should be made to confine these materials to the canal (49, 55–57), as more and more clinical reports of extreme complications were published (36, 50, 53, 62).

Because of the higher risks associated with paraformaldehyde-containing endodontic materials, the use of N2 or similar type pastes are contraindicated as permanent injury risk is substantially less with traditional-filling materials. When a safer, less hazardous alternative therapy exists, it is unreasonable to elect an unsafe methodology. This fact is highly relevant because it is contrary to patient safety to require an individual to assume inherently more dangerous treatment risks that are reasonably avoidable, with safer and more predictable methodologies.

Polymers, Resins, and Other Sealer Options

A number of currently available sealers are variations on a resin/polymer formulation. This makes them options in their own right, or they are a choice when resin bonding within the canal is proposed, and the effects of eugenol on dentin are not desired as a contaminant in the bonding process.

The most commonly know sealer within this category is AH26, AH26 Plus (Caulk/Dentsply, Milford, DE, USA). The sealer is reported to have good handling characteristics, seals well to dentin, and can be used effectively with heat during obturation. The sealer has been reported to be very toxic upon initial mixing (29, 63). This toxicity resolves rapidly during the setting process, and after 24 h the sealer is reported to have a relatively low toxicity. Spångberg et al. (63) have

reported this initial toxicity was due to the formation of a very small amount of formaldehyde as a result of the chemical setting process. They described the release of formaldehyde as thousands of times lower than conventional formaldehyde containing sealers such as N2, and stated that after setting there was little toxic effect.

Diaket (ESPE, Seefeld, Germany) is a polyketone compound containing vinyl polymers that mixed with zinc oxide and bismuth phosphate, forms an adhesive sealer. It has been demonstrated that it is relatively toxic during setting and these effects are persistent (29, 39).

Resorcinol-formalin resin is a paste-filling material that is commonly used in Russia, China, and India for the treatment of pulpitis. Although there are many variations of the resin pastes that are used, the main ingredients are resorcinol and formaldehyde. The principle behind 'resinifying therapy' is that of a liquid phenolic resin being used which will solidify by polymerization after being placed into the root canal. The residual pulpal remnants are claimed to be 'resinified' and to be 'rendered harmless' (64). However, when set, this material creates an almost impenetrable barrier and renders the tooth structure a deep brownish to red color. Owing to remaining pulp tissue in the apical part of the canal, complete absence of cleaning and shaping procedures, and/or failure of the resinifying agent to reach the apical portions of the canal, this treatment may eventually fail, making retreatment of these teeth necessary. Using pastes as a sole root canal filling is generally not the treatment of choice. It has many disadvantages which include the lack of apical length control, inability to obtain a compact obturation, frequent presence of voids and possible severe toxicity if the paste material is extruded beyond the apical foramen. A specific disadvantage of resorcinol paste is the inability to retreat failed cases because of the hardness of the material once it has set (65). In the event of an overfill into the sinus or neurovascular bundle, loss of the retreatment option and the potential for severe irreversible damage makes this choice unreasonable in the year 2006.

Arsenical pastes:
In the last century, arsenic played an important role in the treatment of pulpitis at a time when anesthesia was either unavailable or rudimentary. Its use was usually accompanied by severe but short-lived pain. Danger to the periodontal membrane and surrounding bone was warned in textbooks of the time, and contained the serious admonishment to contain the material within

the tooth. Even in our modern times, however, there is the occasional report of the serious and damaging consequences of using an arsenical paste (66).

Length Determination and Instrumentation Controversies in Endodontics

One of the major controversies in root canal treatment is the apical end point of the working length. It is a paradigm in modern endodontics that instrumentation beyond the apical foramen should be avoided because it is so often associated with a reduced success rate (67–71) and exposes the patient to the potential for injury (72).

Generally most clinicians prefer to end the biomechanical instrumentation at the apical constriction (narrowest point in the canal at approximately the dentin-cemental junction) (73), where the contact between root canal-filling material and the apical tissues is minimal. In addition, many dentists practice apical patency with small files in order to maintain communication with the apical tissues and prevent canal blockage and ledging coronal to the determined end point.

Despite the limited three-dimensional information provided by a conventional radiograph, radiography remains the commonly used standard for working length determination (74, 75). However, the acceptance of apex locators is widely increasing with the introduction of devices well into their fourth generation. In addition, many clinicians use paper points to help determine the juncture of the canal confines from the serum of periapical tissues. Generally, a distance of 0-2 mm between radiographic apex and the obturation material marking the end point of root canal instrumentation has been designated as acceptable when evaluating postoperative radiographs. Accordingly, in a retrospective study that investigated the influence of the level of apical obturation on the treatment outcome (69), a root canal filling was considered satisfactory, if among other factors its apical level was 0–2 mm short of the radiographic apex; this apical level contributing to the highest success rates.

Stein and Corcoran (76) discussed the possibility of unintentional overinstrumentation when radiographs alone were used for working length determination. They reported that the position of a file placed for working length determination appeared radiographically 0.7 mm shorter than its actual position. The

results of another investigation suggest that a working length which ends radiographically 0–2 mm short of the radiographic apex does not guarantee that instrumentation beyond the apical foramen will be avoided in premolars and molars. The authors conclude that radiographic measurements should be combined with electronic working length determination using modern apex locators to better help identify the apical end point of root canal preparation and avoid overinstrumentation (77).

In a recent review of the literature on the role of apical instrumentation in root canal treatment (73), Baugh and Wallace concluded that because the apical dimensions of root canals range from very large to very small, the clinician should seek instruments and techniques that can help determine when instrumentation to the correct apical size has been achieved and that additional research was necessary given the controversy that still lingers regarding final apical size. Other researchers have shown the importance of combining therapies such as rotary instrumentation using larger apical sizes with the use of calcium hydroxide to reduce the numbers of bacteria in root canals and increase long-term success (78). In a recent meta-analysis of studies performed over the last three decades on optimal obturation length, the results demonstrated that obturating materials extruding beyond the radiographic apex correlated with a decreased prognosis for repair (79). When faced with the possibility of inadvertent overinstrumentation into neurovascular danger, the research provides a substantial number of appropriate caveats.

A Recipe for Disaster

Gross overextension of obturation materials usually indicates faulty technique. However, as long as the overextension is not in contact with vital structures, such as the inferior alveolar nerve or sinuses, and the apical terminus is well filled in three dimensions, permanent harm is potentially small, unless the obturation materials contain paraformaldehyde.

On the other hand, overextension of the root canal-filling material risks serious and possibly permanent consequences should the underlying inferior alveolar nerve be adjacent to the root terminus or initially penetrated with files. To create a mishap scenario that includes the possibility for severe injury:
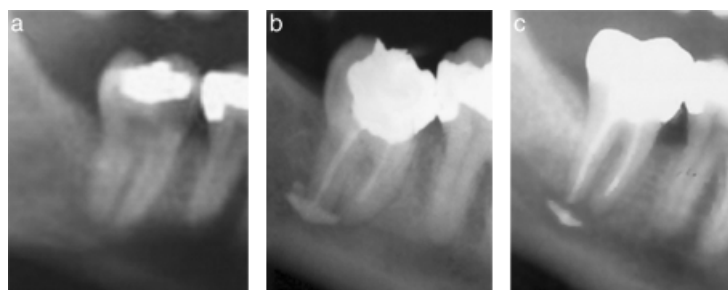
Fig. 8. (A) A section of a pre-operative panoramic radiograph showing the relationship of the inferior alveolar canal to the lower right second molar; (B) post-operative periapical film of overfill into the inferior alveolar canal; this magnification identifies the large mass of sealer (ZnOE) overfill exposing the patient to chemical toxicity and mechanical compression of the neurovascular anatomy; (C) the decision to 'watch and wait' for 3 years was misguided. The patient exhibits continued anesthesia in the distribution of the nerve and minimal absorption of sealer is apparent over time.

- Take one part ignorance of the proximity of the root end to the sinus or mandibular canal by inadequate imaging.
- Add one part overinstrumentation, because of inaccuracy about length of the root canal for lack of electronic apex location.
- Add one part accidental extrusion of endodontic pastes or sealers into neurovascular tissue; because the hydraulics of flow is unpredictable and all materials are initially toxic.
- Mix in one part compression of vital structures by the overfill mass.
- And you have a *recipe for disaster* (Fig. 8).

Techniques for Obturation Control

There are a number of contributions to the literature which assess techniques for apical control of obturation materials. Tronstad (80) assessed the apical plug of dentin chips in monkeys and showed that a plug of clean dentin fillings could provide an apical matrix that was well tolerated by the tissues and would provide an apical barrier that would allow the canals to be well sealed yet protect against impingement of filling materials on the periodontal tissues. In a comprehensive study comparing the apical plugs of dentin versus calcium hydroxide to prevent overfilling, when the apical foramen had been intentionally overinstrumented in cats, the investigators found plugs of calcium hydroxide or dentin to work equally well (81). However, the calcium hydroxide plugs were less durable and produced foramina mineralization that was less complete than the dentinal plugs. Periapical healing was similar for both calcium hydroxide and dentin. In another study that looked at foramen size as it

affected apical extrusion of thermoplasticized gutta-percha, it was noted that overfills and the extrusion of material occurred proportionately to the area of the apical opening. An opening the size of a 40 (0.40 mm) diameter file was found to be twice as likely to allow extrusion of material than an apical diameter sized at 20 (0.20 mm)(82). When the sealing ability of laterally condensed gutta-percha was compared with injection molded thermoplasticized gutta-percha in straight and curved canals, only the thermoplasticized technique produced overextensions (83). It has also been shown that great differences in flowability exist between gutta-percha brands when used in a thermocompaction technique (84). The recommendation to consider a hybrid technique when using thermoplasticized materials has often involved a cold condensation of gutta-percha apically followed by a thermomechanical compaction, providing a safer barrier for limiting the extrusion of material (82).

Thermoplasticized Gutta-Percha and the Effects of Heat

In a series of investigations *in vitro* (85) and on dogs (86), the heat of thermoplasticized gutta-percha was assessed for its potential injurious effects. Levels of heat generated by the plasticized gutta-percha did not appear to be at clinically deleterious levels and no apparent irreversible tissue destruction was evident (86). Similar results have been obtained in other in-vitro and in-vivo studies when manufacturer's protocols for usage have been followed (87–91). Where deleterious effects are seen either experimentally or in clinical situations, the lessons need to be

heeded. Bailey et al. in a study utilizing ultrasonic condensation of gutta-percha found that the combination of a high power setting and a 15 s application of activation energy resulted in temperature rise on the root surface beyond the recognized deleterious threshold of 10° centigrade (92). The use of heat and the potential for injurious heat transfer to dentin and bone has been investigated for a number of different devices used in endodontics and associated restorative procedures (93–97). It is generally accepted that external root temperature increases that exceed 10°C produce irreversible bone and attachment damage as well as dehydration effects on dentin often resulting in resorption (93, 94). Only a small number of investigators and authors have cautioned that ultrasonic energy can be harmful through heat generation (92, 95).

Clinical case reports involving overfill with heat softened gutta-percha are increasing in the literature (98, 99). The current practice of maintaining apical patency and the popularity of thermoplastic gutta-percha-filling techniques have increased the likelihood that overfills can involve the neurovascular anatomy. Fanibunda et al. (99) warn of the lesser-known danger of thermal and mechanical insult from chemically 'safer' materials other than paraformaldehyde, being extruded into the inferior alveolar canal. They report a case of thermally compacted gutta-percha having a severe affect on patient sensory loss after gross overfill into the mandibular canal. In this case they identified a mechanical (compression), chemical (calcium hydroxide sealer) and thermal insult (molten gutta-percha) to the nerve (99).

Carrier-Based Gutta-Percha

Carrier-based gutta-percha was first introduced as Thermafil™ (Dentsply Tulsa Dental, Tulsa, OK.) (100). The Thermafil™ obturator currently consists of a plastic carrier and is covered in a uniform layer of gutta-percha. The carrier is constructed from a special radiopaque plastic similar to a manual or rotary endodontic instrument. The obturator is heated in a special oven where the gutta-percha it carries assumes a softened state with unique adhesive and flow characteristics. The ideal canal preparation for a carrier-based obturator must allow sufficient space for the flow of cement and gutta-percha (101). Carrier-based

obturators use techniques that caution against the use of excess cement because of the increased likelihood of overfilling because of the piston-like effect of the obturator during placement. As the risk of overfilling is considered the only true limitation of carrier-based obturators, authors and manufacturers' caution against the following major errors in technique:

- incorrect canal preparation including overinstrumentation and laceration of the apical terminus,
- excessive cement or gutta-percha,
- excessive force and velocity during insertion,
- improper obturator selection (101).

Damage to the Neurovascular Anatomy: Causes and Outcomes

Reports in the literature involving serious injury to the inferior alveolar nerve have included paresthesia or anesthesia associated with overfill of N2 and similar paraformaldehyde pastes, (47, 48, 50, 52, 53), Endomethasone, (49, 62), AH26 (102–105), calcium hydroxide (99, 106), zinc-oxide and eugenol, and gutta-percha (72, 104). There is almost no current obturation material that has not been reported in the literature to produce paresthesia when overfilled into the neurovascular anatomy. If a new material(s) is not currently cited, it is almost assured the mishap will eventually find itself in the literature.

Ørstavik et al. (36) reviewed 24 published cases of paresthesia involving the mandibular nerve. It was reported that there was no indication of healing in 14 of the 24 patients during the observation periods which ranged from 3 months to 18 years after initiation of the injury. They described the characteristic deficits of the inferior alveolar nerve as unilateral loss of sensitivity of the lip and gums; numbness, a tingling sensation and dryness of the affected mucosa, often preceded by intense pain in the affected area (36). All of the reported cases were molars or involved the lower second premolar. There were numerous materials involved all of which are cited in this manuscript. Paraformaldehyde pastes were well represented in the materials cited but were not exclusive. They concluded that neurotoxic and compressive effects are the most frequent causes of paresthesia after endodontic overfill into the mandibular canal and that the use of syringes and rotary paste fillers should not be used to insert

root-filling pastes or cements in teeth susceptible to neurovascular damage.

A serious case of calcium hydroxide overfill has been reported through a lower second molar causing severe vasospasm and a resulting facial ischemia (107). The ischemia caused cyanosis and necrosis on the face as well as a total absence of function in the mandibular and mental nerve. Again, the authors cautioned in this case report, against the use of a syringe in applying the calcium hydroxide with a known level of toxicity and a high pH (12.4) (107).

It is difficult to ascertain with absolute certainty the primary etiology for paresthesia when assessing the sequelae and future prognosis for repair from overfill into neurovascular tissue. The clinician, therefore, must consider the following critical factors in all cases of overfill: the chemical neurotoxicity of the materials involved; the possibility of direct damage of files (crushing and mechanical injury) (48, 104); the compression damage of solid materials such as gutta-percha (the pressure on the nerve bundle is directly proportional to the amount of material pushed into the canal) (99, 104); the possibility of epineural fibrosis resulting in neuroma (50) (Fig. 9). In a clinical report that suggests the use of corticosteroids may be helpful in countering the injurious compression effects resulting in epineural and intraneural edema, Gatot and Tovi (108) have reported that prednisone therapy may limit the severity of injury as well as aid in the prevention of fibrosis. Others also report the pharmacologic use of corticosteroids in the treatment of paresthesia related to overfill (109).

Inflammatory edema with resulting ischemia, that compresses and compromises blood supply to soft tissues and nerves in confined spaces such as the inferior alveolar canal, is termed *compartment syndrome* (110).

Compartment syndromes are a group of conditions that result from increased pressure within a limited anatomic space, acutely compromising the circulation and ultimately threatening the function of the tissue within that space. Compartment syndrome occurs from an elevation of the interstitial pressure in a closed osseous compartment that results in microvascular compromise. The pathophysiology of compartment syndrome is an insult to normal local tissue homeostasis that results in increased tissue pressure, decreased capillary blood flow, and local tissue necrosis caused by oxygen deprivation. Compartment syndrome is caused by localized hemorrhage or post-ischemic swelling resulting in fibrosis that obstructs axonal regeneration. The clinician should have a high index of suspicion whenever a closed bony nerve compartment has the potential for bleeding or swelling. Compartment syndromes are characterized by pain beyond what should be experienced from the initial injury. Also, diminished sensation may be noted in the distribution of the nerve within a compartment that is being compressed (110).

Diagnosis of Inferior Alveolar Nerve Injury

Nerve recovery subsequent to an endodontic mishap is unpredictable. Because of this unpredictability, the clinician is responsible for making a timely diagnosis and monitoring neurosensory changes. Careful follow-up evaluations and appropriate referral is our responsibility to the patient (111–114).

Neurosensory function can be divided into two basic categories based on the specific receptors that are either stimulated or injured: mechanoreceptive and nociceptive. The mechanoreceptive aspect of sensory perception
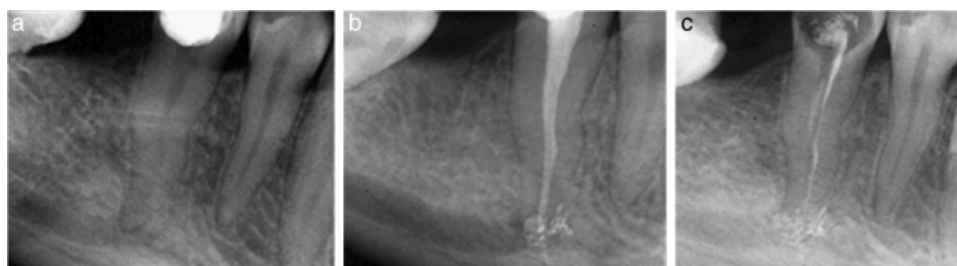

Fig. 9. (A) Pre-operative radiograph of lower right second premolar, (B) Radiograph reveals ZnOE sealer into the mental foramen and nerve; patient was anesthetic in the distribution of the mental nerve 24 h after obturation and the decision was made to remove the obturation in an attempt to decompress the mass of the overfill and remove as much sealer as possible; (C) patient exhibited signs of anesthesia for approximately 30 more days. After 30 days the character of the deficit showed a 'recovering profile'. Patient was symptom free in 6 months.

can be further divided into two-point discrimination and brush directional stroke. The nociceptive path can be subdivided into pinprick and thermal discrimination. Each type of nerve fiber varies with respect to diameter, conduction speed and physiologic function. Each afferent nerve end offers a distinct receptor terminal that is specific for warmth, cold, pain, and touch. The first phase of any peripheral nerve regeneration is the degeneration of the axon and its myelin sheath along the nerve fiber at the site of injury. These changes along the nerve are known as Wallerian degeneration and lead to degeneration of the entire axon terminal over several weeks following a severe injury. Neural injuries are most commonly classified using the Seddon classification system (115). Seddon's classification is derived from the extent of nerve injury. **Neurotemesis** is the most severe nerve injury because conduction is completely disrupted resulting in the loss of anatomic integrity of the endoneurium, perineurium and epineurium. **Axonotemesis**, a less severe injury results in damage to the axons, but the endoneurial and epineurial sheaths are preserved. Neuropraxia occurs when a nerve is injured and conduction is blocked but this does not lead to Wallerian degeneration.

Clinically neurotemesis leads to anesthesia with a loss of feeling or sensation. It can also produce dysesthesia, an abnormal unpleasant sensation often burning in character. Recovery is unlikely or limited. Axonotemesis causes paresthesia, an abnormal altered sensation, which can show some degree of sensory recovery after several months. Neuropraxia is usually a transient paresthesia where recovery is complete from days to weeks.

The clinical evaluation of a patient who suffers a sensory loss in the oral or maxillofacial region subsequent to an endodontic obturation should begin by identifying the patient's subjective assessment of these alterations. The clinician should distinguish between anesthesia, dysesthesia and paresthesia. Often considerable variability will exist within the descriptions outlined above and few patients will fit perfectly within the Seddon categories (111). However, it is important that any patient with anesthesia or a painful dysesthesia be evaluated in a systematic fashion (111, 112). The dentist should assess the chronologic history of the area even if that history has only been in the last several hours and note the patient's chief complaint; the nature, frequency and severity of the symptoms and how they might be changing for better or worse as well

Fig. 10. Mapping of paresthesia deficits on a young man associated with the overfill of a lower left second molar into the inferior alveolar canal.

as the loss of function that is occurring. If the initial symptom is anesthesia, the area of anesthesia should be mapped and placed in the patient's record. Any return of sensation should be noted (113) (Fig. 10).

The physical evaluation should also include pin prick for deep pain (small-myelinated A δ fibers), brush stroke for directional discrimination (mediated by large-myelinated A α nerve fibers), and two-point discrimination for proprioception (large-myelinated A α fibers). The small myelinated fibers of the A delta group and the smaller unmyelinated axons of the C group are responsible for sensations of temperature (111).

Should anesthesia and painful dysesthesia be consequences of overfilling, the practitioner must understand when the referral to a surgeon (oral-maxillofacial or neurosurgeon) who is experienced in the surgical therapies for relief and healing, may be required to resolve the patient's problem (114). The final management of such a case depends on several factors. Even the most acceptable materials can cause serious injury if extruded in large volumes into sensitive structures. Pastes and sealers that contain paraformaldehyde or known safer materials are difficult to control and may
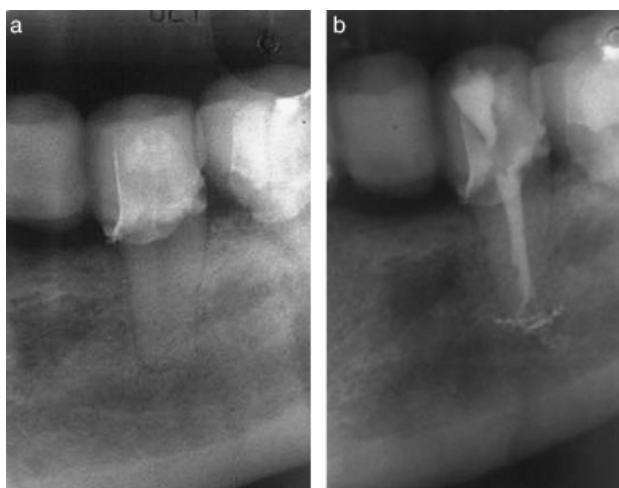
Fig. 11. (A) Pre-operative periapical radiograph demonstrating the close proximity of a lower right second premolar to the mental nerve; **(B)** post-operative radiograph reveals sealer in the mental nerve. The decision to 'watch and wait' left the patient exhibiting paresthesia deficits in the mental distribution 5 years later. These deficits are considered permanent.

additionally create injuries to the maxillary division of the trigeminal nerve when extruded through maxillary teeth or into the sinus membranes (116). While paraformaldehyde-containing materials should never be used because of the dangers of chemical injury they present, all obturation materials should be used with extreme caution in all circumstances, especially in teeth intimately related to the inferior alveolar canal.

When presented with the extrusion of endodontic obturation materials into the neurovascular tissues, and after careful and systematic assessment of the nature and course of the injury and its effects, a decision to intervene surgically or delay and observe has to be made (Fig. 11).

Management of Inferior Alveolar Nerve Injuries

The oral surgery literature describes most inferior alveolar nerve injuries as neuropraxias and thus they resolve spontaneously within a 6-month time frame. These are often lingual nerve injuries as well as mandibular trauma subsequent to tooth removal. It is reported that inferior alveolar nerve injuries heal better than lingual nerve injuries because of the guidance provided by the bony mandibular canal (113). This fact

has relevance if oral surgical procedures are likely and decortication procedures and removal of overfill are contemplated. The clinical examination that results in a diagnosis of anesthesia or increasing painful dysesthesia unresponsive to non-surgical therapy should help guide this decision (111, 112). It is suggested that the decision to intervene surgically should include the high suspicion of injury resulting in the loss of conduction within the nerve because of suspected chemical toxicity and mechanical compression.

The favorable results for long-term spontaneous recovery require thoughtful considerations for taking a 'wait and observe' approach. When a peripheral nerve is injured, a non-surgical management that supports spontaneous neurosensory recovery and promotes patient tolerance of the sensory loss is a viable option (113). The most compelling reason to wait is that a majority of injuries are known to recover spontaneously to some degree. Higher levels of recovery can also be expected when the patient is young and healthy. In addition, a 'recovering patient profile' with improving levels of function, detection abilities and sensory symptoms argues for restraint in management (111, 113).

In the final analysis, the decision of whether and when to intervene surgically in the removal of overfill should be based on objective criteria and a comprehensive assessment of each individual patient. The current guidelines for intervention are unfortunately not based on satisfactory evidence-based science, and this leaves a troublesome vacuum in our knowledge of effective therapies, making prevention of this injury critical to treatment planning before initiating root canal therapy.

Prevention of Obturation Mishaps and Concluding Remarks

This manuscript has offered a number of remedies to provide a safe and prudent approach to the obturation of posterior teeth in close proximity to the vulnerable tissues of the sinus or inferior alveolar nerve. In summary, the clinician is recommended to observe the following counsel:

- It is essential to image and identify radiographically the sensitive neural structures of the jaws in order to clearly understand the proximal risk.
- It is critical to use obturation materials that are well tolerated by the body after therapy, rather than paraformaldehyde formulations that can cause

irreversible sensory nerve damage and should not be used in the good and safe practice of endodontics.

- The clinician must practice careful and judicious shaping strategies that use multiple confirmations of working length and take serious precaution against overinstrumentation.

- It is important to use 'resistance form' in controlling overfills. This 'resistance form' can be imparted during canal preparation by producing funnelform, tapered preparations and by selecting guttapercha cones to match those canal shapes which will resist the obturation forces which promote extrusion.

- When using thermoplastic techniques, it is important to respect the flow characteristics of the materials and the heat energy used.

- The use of paste-fillers and syringes for applying endodontic sealers should be cautioned when there is close proximity to neural structures and control is compromised.

- In cases of extreme proximity to the neurovascular anatomy, the importance of creating a clean dentin plug or material barrier at the patent apical terminus should be carefully planned when the risk of extrusion is considerable.

Each endodontic procedure has a variable degree of inherent risk. The standards of good practice require that the clinician avoid unreasonable risks that may harm the patient. Treatment is deemed negligent when a reasonably careful clinician should have foreseen and prevented unreasonable risk of harm to the patient.

The mishap of overfill that could cause permanent sensory loss for a patient is disconcerting for any practitioner to consider. We must recognize that these injuries should encourage reflection on the safe and prudent practice of endodontics that promotes safeguards. Our ethical obligation to protect patients from harm is met when we as a profession can provide advanced and sophisticated therapies in a safe and controlled manner with patient safety as an overriding priority.

References

1. Langlais RP, Rodriguez IE, Maselle I. Principles of radiographic selection and interpretation. *Dent Clin North Am* 1994: **38**: 1–12.

2. Benjamin D. Digital radiography: more than meets the eye. *Compendium* 2005: **26**: 464–467.

3. Lavelle CLB. The role of direct intraoral sensors in the provision of endodontic services. *Endod Dent Traumatol* 1999: **15**: 1–5.

4. Tyndall DA, Kapa SF, Bagnell CP. Digital subtraction radiography for detecting cortical and cancellous bone changes in the periapical region. *J Endod* 1990: **16**: 173–178.

5. Ellingsen MA, Harrington GW, Hollender LG. Radiovisiography versus conventional radiography for detection of small instruments in endodontic length determination. In vitro evaluation. *J Endod* 1995: **21**: 326–331.

6. Gröndahl H-G, Huumonen S. Radiographic manifestations of periapical inflammatory lesions. *Endod Topics* 2004: **8**: 55–67.

7. *www.jmoritaeurope.de/3d_accuitomo_eng.html*

8. Van Dis ML, Miles DA. Disorders of the maxillary sinus. *Dent Clin North Am* 1994: **38**: 155–166.

9. Selden HS. The interrelationship between the maxillary sinus and endodontics. *Oral Surg* 1974: **38**: 623–629.

10. Watzek G, Bernhart T, Ulm C. Complications of sinus perforations and their management in endodontics. *Dent Clin North Am* 1997: **41**: 563–583.

11. Dodd RB, Dodds RN, Holcomb JB. An endodontically induced maxillary sinusitis. *J Endod* 1984: **10**: 504–506.

12. Selden HS. Endo-antral syndrome and various endodontic complications. *J Endod* 1999: **25**: 389–393.

13. Selden HS. The Endo-antral syndrome. *J Endod* 1977: **3**: 462–464.

14. Rigolone M, Pasqualini D, Bianchi L, Berutti E, Bianchi SD. Vestibular surgical access to the palatine root of the superior first molar: 'low-dose cone-beam' CT analysis of the pathway and its anatomic variations. *J Endod* 2003: **29**: 773–775.

15. Velvart P, Hecker H, Tillinger G. Detection of the apical lesion and the mandibular canal in conventional radiography and computed tomography. *Oral Surg Oral Med Oral Path Oral Radiol Endod* 2001: **92**: 682–688.

16. Phillips JL, Weller N, Kulild JC. The mental foramen: Part 1. Size, orientation, and positional relationship to the mandibular second premolar. *J Endod* 1990: **16**: 221–223.

17. Phillips JL, Weller N, Kulild JC. The mental foramen: Part 2. Radiographic position in relation to the mandibular second premolar. *J Endod* 1992: **18**: 271–274.

18. Phillips JL, Weller N, Kulild JC. The mental foramen: Part 3. Size and position on panoramic radiographs. *J Endod* 1992: **18**: 383–386.

19. Martini FH, Timmons MJ, McKinley MP. *Human Anatomy*, 3rd edn. New Jersey: Prentice-Hall, 2000: 359.

20. Young B, Heath JW. *Wheater's Functional Histology, A Text and Colour Atlas*, 4th edn. Edinburgh: Churchill Livingstone, 2000: 130.

21. Denio D, Torabinejad M, Bakland LK. Anatomical relationship of the mandibular canal to its surrounding structure in mature mandibles. *J Endod* 1992: **18**: 161–165.

22. Carter RB, Keen EN. The intramandibular course of the inferior alveolar nerve. *J Anat* 1971: **108**: 433–440.

23. European Society of Endodontology Consensus Report of the European Society of Endodontology on Quality Guidelines for Endodontic Treatment. *Int Endod J* 1994: **27**: 115–124.

24. Langeland K. Root canal sealants and pastes. *Dent Clin North Am* 1974: **18**: 309–327.

25. Block RM, Lewis RD, Hirsch J, Coffey J, Langeland K. Systemic distribution of [^{14}C]-labeled paraformadehyde incorporated within formocresol following pulpotomies in dogs. *J Endod* 1983: **9**: 176–189.

26. Branstetter J, von Fraunhofer JA. The physical properties and sealing action of endodontic sealer cements: a review of the literature. *J Endod* 1982: **8**: 312–316.

27. Nair PNR, Sjogren 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.

28. Briseno BM, Willershausen B. Root canal sealer cytotoxicity on human gingival fibroblasts. I. Zinc oxide-eugenol-based sealers. *J Endod* 1990: **16**: 383–386.

29. Briseno BM, Willershausen B. Root canal sealer cytotoxicity on human gingival fibroblasts: II. silicone- and resin-based sealers. *J Endod* 1991: **17**: 537–540.

30. Briseno BM, Willershausen B. Root canal sealer cytotoxicity with human gingival fibroblasts: III. Calcium hydroxide-based sealers. *J Endod* 1992: **18**: 110–113.

31. Curson I, Kirk EEJ. An assessment of root canal-sealing cements. *Oral Surg Oral Med Oral Pathol* 1968: **26**: 229–236.

32. Friend LA, Browne RM. Tissue reactions to some root filling materials. *Br Dent J* 1968: **125**: 291–297.

33. Zmener O. Tissue response to a new methacrylate-based root canal sealer: preliminary observations in the subcutaneous connective tissue of rats. *J Endod* 2004: **30**: 348–351.

34. Muruzabal M, Erausquin J, Devoto FCH. A study of periapical overfilling in root canal treatment in the molar of rat. *Arch Oral Biol* 1966: **11**: 373–383.

35. Rowe AHR. Effect of root filling materials on the periapical tissues. *Br Dent J* 1967: **122**: 98–102.

36. Ørstavik D, Brodin P, Aas E. Paraesthesia following endodontic treatment: survey of the literature and report of a case. *Int Endod J* 1983: **16**: 167–172.

37. Kawakami T, Nakamura C, Eda S. Effects of the penetration of a root canal filling material in to the mandibular canal.1. Tissue reaction to the material. *Endod Dent Traumatol* 1991: **7**: 36–41.

38. Kawakami T, Nakamura C, Eda S. Effects of the penetration of a root canal filling material into the mandibular canal. 2. Changes in the alveolar nerve tissue. *Endod Dent Traumatol* 1991: **7**: 42–47.

39. Ørstavik D, Mjör IA. Histopathology and X-ray microanalysis of the subcutaneous tissue response to endodontic sealers. *J Endod* 1988: **14**: 13–23.

40. Spångberg L. Biologic effects of root canal filling materials. 7. Reaction of bony tissue to implanted root canal filling material in guinea pigs. *Odontol Tidskr* 1969: **77**: 133–159.

41. Kozam G. The effect of eugenol on nerve transmission. *Oral Surg* 1977: **44**: 799–805.

42. Holland GR. A histological comparison of periapical inflammatory and neural responses to two endodontic sealers in the ferret. *Arch Oral Biol* 1994: **39**: 539–544.

43. Boiesen J, Brodin P. Neurotoxic effect of two root canal sealers with calcium hydroxide on rat phrenic nerve in vitro. *Endod Dent Traumatol* 1991: **7**: 242–245.

44. Serper A, Üçer O, Onur R, Etikan I. Comparative neurotoxic effects of root canal filling materials on rat sciatic nerve. *J Endod* 1998: **24**: 592–594.

45. Seidler B. Irrationalized endodontics: N2 and us too. *J Am Dent Assoc* 1974: **89**: 1318–1331.

46. Sargenti A, Richter S. *Rationalized Root Canal Treatment.* New York: AGSA Scientific Publications, 1959.

47. Montgomery S. Paresthesia following endodontic treatment. *J Endod* 1976: **2**: 345–347.

48. Forman GH, Rood JP. Successful retrieval of endodontic material from the inferior alveolar nerve. *J Dent* 1977: **5**: 47–50.

49. Kaufman AY, Rosenberg L. Paresthesia caused by endomethasone. *J Endod* 1980: **6**: 529–531.

50. LaBlanc JP, Epker BN. Serious inferior alveolar nerve dysesthesia after endodontic procedure: report of three cases. *J Am Dent Assoc* 1984: **108**: 605–607.

51. Fanibunda KB. Adverse response to endodontic material containing paraformadehyde. *Br Dent J* 1984: **157**: 231–235.

52. Allard KUB. Paraesthesia – a consequence of a controversial root-filling material? A case report. *Int Endod J* 1986: **19**: 205–208.

53. Kleier DJ, Averbach RE. Painful dysesthesia of the inferior alveolar nerve following use of a paraformadehyde-containing root canal sealer. *Endod Dent Traumatol* 1988: **4**: 46–48.

54. Brodin P. Neurotoxic and analgesic effects of root canal cements and pulp- protecting dental materials. *Endod Dent Traumatol* 1988: **4**: 1–11.

55. Barker BCW, Lockett BC. Periapical response to N2 and other paraformadehyde compounds confined within or extruded beyond the apices of dog root canals. *Dent Practitioner* 1972: **22**: 370–379.

56. Cohler CM, Newton CW, Patterson SS, Kafrawy AH. Studies of Sargenti's technique of endodontic treatment: short-term response in monkeys. *J Endod* 1980: **6**: 473–478.

57. Newton CW, Patterson SS, Kafrawy AH. Studies of Sargenti's technique of endodontic treatment: six-month and one-year responses. *J Endod* 1980: **6**: 509–517.

58. Lewis BB, Chestner SB. Formaldehyde in dentistry: a review of mutagenic and carcinogenic potential. *J Am Dent Assoc* 1981: **103**: 429–434.

59. Tagger E, Tagger M. Pulpal and periapical reactions to glutaraldehyde and paraformadehyde pulpotomy dressing in monkeys. *J Endod* 1984: **10**: 364–371.

60. Brodin P, Røed A, Aars H, Ørstavik D. Neurotoxic effects of root filling materials on rat phrenic nerve in vitro. *J Dent Res* 1982: **61**: 1020–1023.

61. Block RM, Denby Lewis R, Hirsch J, Coffey J, Langeland K. Systemic distribution of [^{14}C]-labeled paraformaldehyde incorporated within formocresol following pulpotomies in dogs. *J Endod* 1983: **9**: 176–189.

62. Rowe AHR. Damage to the inferior dental nerve during or following endodontic treatment. *Br Dent J* 1983: **153**: 306–307.

63. Spångberg LSW, Barbosa SV, Lavigne GD. AH26 releases formaldehyde. *J Endod* 1993: **19** : 596–598.

64. Schwandt NW, Gound TG. Resorcinol-formaldehyde resin 'Russian Red' endodontic therapy. *J Endod* 2003: **29**: 435–437.

65. Vranas R, Hartwell GR, Moon PC. The effect of endodontic solutions on resorcinol-formalin paste. *J Endod* 2002: **29**: 69–72.

66. Smart ER, Barnes IE. Tissue necrosis after using an arsenical endodontic preparation: a case report. *Int Endod J* 1991: **24**: 263–269.

67. Seltzer S, Soltanoff W, Sinai I, Goldenberg A, Bender IB. Biologic aspects of endodontics: Part III. Periapical tissue reactions to root canal instrumentation. *Oral Surg Oral Med Oral Pathol* 1968: **26**: 534–546.

68. Seltzer S, Soltanoff W, Sinai I, Smith J. Biologic aspects of endodontics: part IV. Periapical tissue reactions to root-filled teeth whose canals had been instrumented short of their apices. *Oral Surg Oral Med Oral Pathol* 1969: **28**: 724–738.

69. Sjörgen U, Hägglund B, Sundqvist G, Wing K. Factors affecting the long-term results of endodontic treatment. *J Endod* 1990: **16**: 498–504.

70. Smith CS, Setchell DJ, Harty FJ. Factors influencing the success of conventional root canal therapy – a five year retrospective study. *Int Endod J* 1993: **26**: 321–333.

71. Ricucci D, Langeland L. Apical limit of root canal instrumentation and obturation. Part 2. A histological study. *Int Endod J* 1998: **31**: 394–409.

72. Neaverth EJ. Disabling complications following inadvertent overextension of a root canal filling material. *J Endod* 1989: **15**: 135–139.

73. Baugh D, Wallace J. The role of apical instrumentation in root canal treatment: a review of the literature. *J Endod* 2005: **31**: 333–340.

74. Olson AK, Goerig AC, Cavataio RE, Luciano J. The ability of the radiograph to determine the location of the apical foramen. *Int Endod J* 1991: **24**: 28–35.

75. Powell-Cullingford AW, Pitt Ford TR. The use of E-speed film for root canal length determination. *Int Endod J* 1993: **26**: 268–272.

76. Stein TJ, Corcoran JF. Radiographic working length revisited. *Oral Surg Oral Med Oral Pathol* 1992: **74**: 796–800.

77. ElAyouti A, Weiger R, Löst C. Frequency of over-instrumentation with an acceptable radiographic working length. *J Endod* 2001: **27**: 49–52.

78. McGurkin-Smith R, Trope M, Caplan D, Sigurdsson A. Reduction of intracanal bacteria using GT rotary instrumentation, 5.25% NaOCl, EDTA, and Ca(OH)$_2$. *J Endod* 2005: **31**: 359–363.

79. Schaeffer MA, White RR, Walton RE. Determining the optimal obturation length: a meta-analysis of literature. *J Endod* 2005: **31**: 271–274.

80. Tronstad L. Tissue reactions following apical plugging of the root canal with dentin chips in monkey teeth subjected to pulpectomy. *Oral Surg* 1978: **45**: 297–304.

81. Pitts DL, Jones JE, Oswald RJ. A histological comparison of calcium hydroxide plugs and dentin plugs used for the control of gutta-percha root canal filling material. *J Endod* 1984: **10**: 283–293.

82. Ritchie GM, Anderson DM, Sakumura JS. Apical extrusion of thermoplasticized gutta-percha used as a root canal filling. *J Endod* 1988: **14**: 128–132.

83. Mann SR, McWalter GM. Evaluation of apical seal and placement control in straight and curved canals obturated by laterally condensed and thermoplasticized gutta-percha. *J Endod* 1987: **13**: 10–17.

84. Tagger M, Gold A. Flow of various brands of gutta-percha cones under in vitro thermomechanical compaction. *J Endod* 1988: **14**: 115–120.

85. Gutmann JL, Creel DC, Bowles WH. Evaluation of heat transfer during root canal obturation with thermoplasticized gutta-percha. Part I. In vitro heat levels during extrusion. *J Endod* 1987: **13**: 378–383.

86. Gutmann JL, Rakusin H, Powe R, Bowles WH. Evaluation of heat transfer during root canal obturation with thermoplasticized gutta-percha. Part II. In vivo response to heat levels generated. *J Endod* 1987: **13**: 441–448.

87. Saunders EM. In vivo findings associated with heat generation during thermomechanical compaction of gutta-percha. Part I. Temperature levels at the external surface of the root. *Int Endod J* 1990: **23**: 263–267.

88. Saunders EM. In vivo findings associated with heat generation on during thermomechanical compaction of gutta-percha. Part II. Histological response to temperature elevation on the external surface of the root. *Int Endod J* 1990: **23**: 268–274.

89. Barkhordar RA, Goodis HE, Watanabe L, Koumdjian J. Evaluation of temperature rise on the outer surface of teeth during root canal obturation techniques. *Quint Int* 1990: **21**: 585–588.

90. Weller RN, Koch KA. In vitro radicular temperatures produced by injectable thermoplasticized gutta-percha. *Int Endod J* 1995: **28**: 86–90.

91. Romero AD, Green DB, Wucherpfennig AL. Heat transfer to the periodontal ligament during root obturation procedures using an *in vitro* model. *J Endod* 2000: **26**: 85–87.

92. Bailey GC, Cunnington SA, Ng Y-L, Gulabivala K, Setchell DJ. Ultrasonic Condensation of gutta-percha: the effect of power setting and activation time on temperature rise at the root surface – An in vitro study. *Int Endod J* 2004: **37**: 447–454.

93. Eriksson AR, Albrektsson T. Temperature threshold levels for heat-induced bone tissue injury: a vital-microscopic study in the rabbit. *J Prosth Dent* 1983: **50**: 101–107.

94. Atrizadeh F, Kennedy J, Zander H. Ankylosis of teeth following thermal injury. *J Periodont Res* 1971: **6**: 159–167.

95. Satterthwaite JD, Stokes AN, Frankel NT. Potential for temperature change during application of ultrasonic vibration to intra-radicular posts. *Eur J Prosthodon Restor Dent* 2003: **11**: 51–56.

96. Kreisler M, Haitham AH, d'Hoedt B. Intrapulpal temperature changes during root surface irradiation with an 809-nm gaaias laser. *Oral Surg Oral Med Oral Pathol* 2002: **93**: 730–735.

97. Sweatman TL, Baumgartner JC, Sakaguchi RL. Radicular temperatures associated with thermoplasticized gutta-percha. *J Endod* 2001: **27**: 512–515.

98. Blanas N, Kienle F, Sàndor GKB. Injury to the inferior alveolar nerve due to thermoplastic gutta percha. *J Oral Maxillofac Surg* 2002: **60**: 574–576.

99. Fanibunda K, Whitworth J, Steele J. The management of thermomechanically compacted gutta percha extrusion in the inferior dental canal. *Br Dent J* 1998: **184**: 330–332.

100. Johnson WB. A new gutta-percha technique. *J Endod* 1978: **4**: 184–188.

101. Cantatore G, Johnson WB. The Thermafil System. In: Castellucci A. *Endodontics*, **Vol. II**. Florence: Edizioni Odontoiatriche Il Tridente S.r.l, 2006: 702.

102. Spielman A, Gutman D, Laufer D. Anesthesia following endodontic overfilling with AH26. *Oral Surg Oral Med Oral Pathol* 1981: **52**: 554–556.

103. Tamse A, Kaffe I, Littner MM, Kozlovsky A. Parethesia following overextension of AH-26: report of two cases and review of the literature. *J Endod*, **8**: 88–90.

104. Nitzan DW, Stabholz A, Azaz B. Concepts of accidental overfilling and overinstrumentation in the mandibular canal during root canal treatment. *J Endod* 1983: **9**: 81–85.

105. Barkhordar RA, Nguyen NT. Paresthesia of the mental nerve after overextension with AH26 and gutta-percha: report of case. *J Am Dent Assoc* 1985: **110**: 202–203.

106. Ahlgren FKEK, Johannessen AC, Hellem S. Displaced calcium hydroxide paste causing inferior alveolar nerve paraesthesia: report of a case. *Oral Surg Oral Med Oral Pathol* 2003: **96**: 734–737.

107. Lindgren P, Eriksson K-F, Ringberg A. Severe facial ischemia after endodontic treatment. *J Oral Maxillofac Surg* 2002: **60**: 576–579.

108. Gatot A, Tovi F. Prednisone treatment for injury and compression of inferior alveolar nerve: report of a case of anesthesia following endodontic overfilling. *Oral Surg* 1986: **62**: 704–706.

109. Morse DR. Endodontic-related inferior alveolar nerve and mental foramen paresthesia. *Compend Contin Educ Dent* 1997: **18**: 963–987.

110. Schwartz SI, Shires GT, Spencer FC. *Principles of Surgery*, 7th ed. New York: McGraw-Hill, 1999.

111. Fleisher KE, Stevens MR. Diagnosis and management of inferior alveolar nerve injury. *Compend Contin Educ Dent* (1995): **16**: 1028–1040.

112. Donoff RB. Surgical management of inferior alveolar nerve injuries (Part I): the case for early repair. *J Oral Maxillofac Surg* 1995: **53**: 1327–1329.

113. Gregg JM. Surgical management of inferior alveolar nerve injuries (Part II): the case for delayed management. *J Oral Maxillofac Surg* 1995: **53**: 1330–1333.

114. Pogrel MA, Thamby S. The etiology of altered sensation in the inferior alveolar, lingual, and mental nerves as a result of dental treatment. *CDA J* 1999: **27**: 531–538.

115. Seddon HJ. Three types of nerve injuries. *Brain* 1943: **66**: 237–288.

116. Yaltirik M, Berberoglu HK, Koray M, Dulger O, Yildirim S, Bariş AA. Orbital pain and headache secondary to overfilling a root canal. *J Endod* 2003: **29**: 771–772.