Post-endodontic neuropathy of the trigeminal nerve: part one

In the first of two articles, **Tara Renton** presents a literature review for the post-endodontic neuropathy of the trigeminal nerve

Sensory disturbances or peripheral neuropathies such as anaesthesia, hypoesthesia, hyperaesthesia, and paraesthesia may present in the trigeminal system, due to many local and systemic factors. Spontaneous neuropathy must always be regarded with suspicion (red flag) and neoplasia excluded. However, if the neuropathy coincides with recent dental treatment then exclusion of post-traumatic neuropathy must be excluded first.

The inferior alveolar nerve (IAN) is at risk from a variety of dental procedures, in that the IAN is contained within a bony canal predisposing it to ischaemia, trauma and subsequent injury in relation to dental procedures. This may also result in a higher incidence of permanent damage for inferior alveolar nerve injuries compared with lingual nerve injuries (Pogrel, 2007). Causes of inferior alveolar nerve injury include local anaesthetic injections, third molar surgery, implants, endodontics, ablative surgery, trauma and orthognathic surgery.

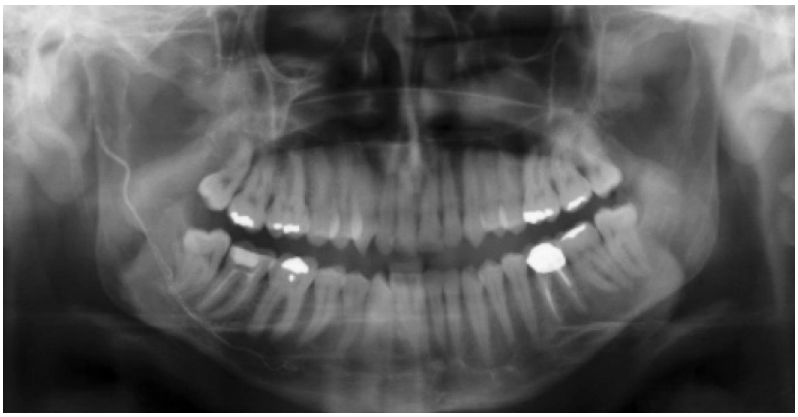

Figure 1: Abducent and inferior alveolar nerve injury due to endodontic overfill of mandibular molar (image courtesy of S Ruggiero)

TURN TO PAGE 00

CPD

CPD AIMS AND OBJECTIVES

This clinical article aims to provide a review of endodontic-related nerve injuries using the literature.

EXPECTED OUTCOMES

Correctly answering the questions on page 39, worth one hour of verifiable CPD, will demonstrate that the reader understands and recognises the risk factors and consequences of post-endodontic neuropathy of the trigeminal nerve.

Endodontists and dentists take for granted the rather unusual characteristics of the dental pulp (the only organ in health to display allodynia [pain] to all stimuli) and to respond innocuously to caustic high pH chemicals that would destroy and burn tissues elsewhere in the body. Thus, many compounds and chemicals routinely used in dentistry can cause severe irreversible tissue damage in structures close to the treated tooth.

Iatrogenic trigeminal nerve injuries remain a significant and complex clinical problem. Altered sensation and pain in the orofacial region may interfere with speaking, eating, kissing, shaving, applying make-up, tooth brushing and drinking – in fact, just about every social interaction we take for granted. Thus, these injuries have a significant negative effect on the patient's quality of life and the iatrogenesis of these injuries lead to significant psychological effects (Smith et al, 2013).

Incidence endodontic nerve injuries

The most common nerve affected by endodontic procedures is the inferior alveolar nerve (IAN) (Alves, Coutinho, Gonçalves, 2014). Maxillary branches of the trigeminal nerve can also be damage-related endodontic treatment usually due to sodium hypochlorite leakage (Pelka, Petschelt, 2008) (Figure 1).

In one retrospective study examining cases of paraesthesia related to endodontic treatment of mandibular premolars, the incidence was 0.96% (8/832) (Knowles, Jergenson, Howard, 2003). In a survey of 2,338 patients, 7% sustained chronic neuropathic pain after a single endodontic procedure (Klasser et al, 2011).

Most reports of endodontic-related nerve injuries are case reports with very little analysis of the clinical impact for the patient, risk factors or management issues and are solely case

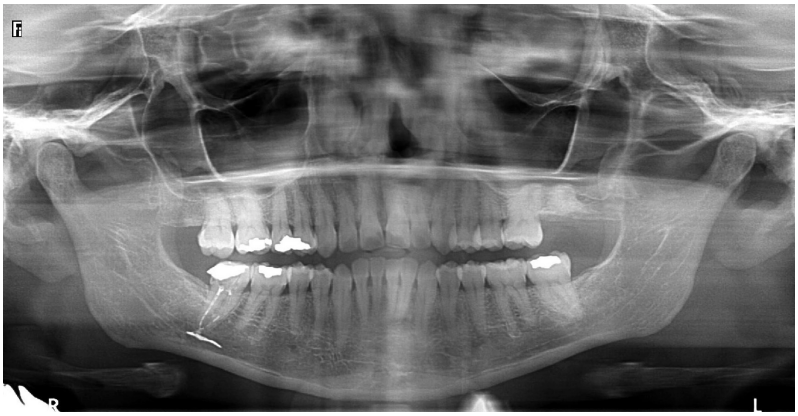

Figure 2: Panoral X-ray illustrating overfill and leakage of endodontic material into inferior dental canal

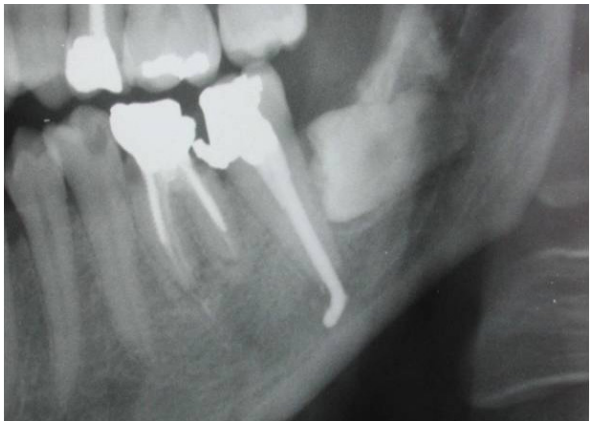

Figure 3: Panoral X-ray illustrating cases of extruded endodontic materials into the inferior dental canal

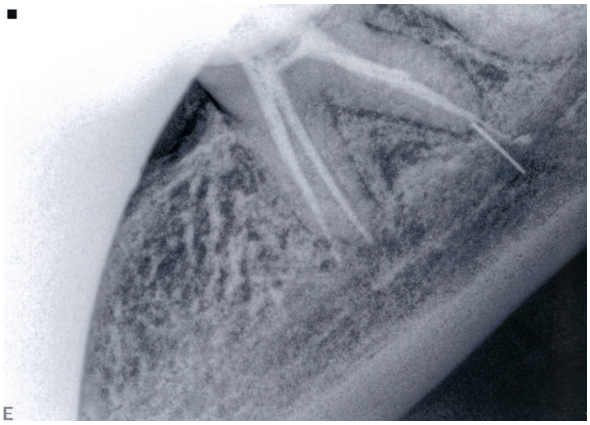

Figure 4: Panoral X-ray illustrating overinstrumentation of LL6 resulting in inferior alveolar nerve injury

reports. These case reports solely focus on over-instrumentation and loss of apical seal leading to endodontic material extrusion into the inferior dental canal (IDC) resulting in 'mechanical' damage to the IAN (Figures 2-5). (Rowe, 1983; Yaltirik, Ozbas, Erisen, 2002; Gallas-Torreira et al, 2003; Tilotta-Yasukawa et al, 2006; Scolozzi, Lombardi, Jaques, 2004; Zmener, 2004; Vasilakis, Vasilakis, 2004; Poveda et al, 2006; Pogrel, 2007; von Ohle, ElAyouti, 2010; Gonzalez-Martin et al, 2010; Gambarini et al, 2011; Marques, Gomes, 2011; Lopez-Lopez et al, 2012; Orr, 1987; 1985; Dempf, Hausamen, 2000; Forman, Rood, 1977; Gallas-Torreira et al, 2003; Tilotta-Yasukawa, 2006; Qrstravik, Brodin, Aas, 1983; Vasilakis, Vasilakis, 2004).

To date, there are four case series reports on inferior alveolar nerve injuries (IANIs) related to root canal treatment (RCT) including 61 cases (Pogrel, 2007), eight cases (Knowles, Jergenson, Howard, 2003) four cases (Scolozzi, Lombardi, Jaques, 2004) and one case series reported on the treatment of 11 cases (Grötz et al, 1998). These case series predominantly focus on the outcomes surgical exploration and irrigation of damage nerves.

Consequences of endodontic-related nerve injuries

The largest series of endodontic-related trigeminal nerve injuries in 61 patients over an eight-year period (Pogrel, 2007) reported that eight patients (12.5%) were asymptomatic, which is the only report to proactively highlight that overfilling and extrusion of endodontic materials into the IDC will not always cause neuropathy.

However, the majority of the patients reported symptoms (87.5%); 42 exhibited only mild symptoms (three-month-old injuries), 10 patients experienced some resolution, 11 patients were symptomatic and underwent surgical exploration – five of these within 48 hours and others up to 10 days to three months (four experienced partial resolution and two no recovery) (Pogrel, 2007). More recently, in a personal communication, Dr Pogrel has undertaken a further eight cases as urgent cases (within 24 hours) and reports significantly improved resolution of neuropathy and pain in these patients.

Neuropathic pain

Persistent pain after endodontics has been reported to occur in 3-13% of patients (Marbach et al, 1982; Lobb, Zakariasen, McGrath, 1996) while surgical endodontics resulted in chronic neuropathic pain in 5% of patients (Campbell, Parks, Dodds, 1990). In a previous study of 135 patients with IANI caused by dental treatment or malignancy, 22% presented with dysaesthesia, which was significantly associated with the female gender (Caissie et al, 2005). In another study the significant factors associated with persistent post-endodontic pain included prolonged preoperative pain, female gender and previous chronic pain symptoms (Polycarpou et al, 2005).

Two recent reviews of chronic post-endodontic pain (Nixdorf et al, 2010; Nixdorf, Moana-Filho, 2011) propose persistent dentoalveolar pain (PDAP) occurs in 1.6-3.6% of

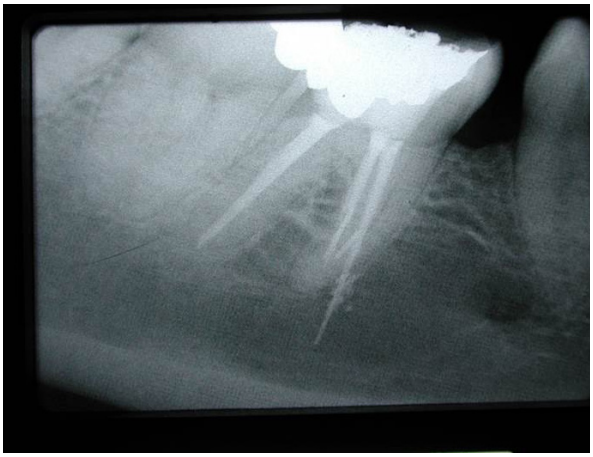

Figure 5: Radiograph illustrating case of over-instrumentation of LR6 into inferior dental canal

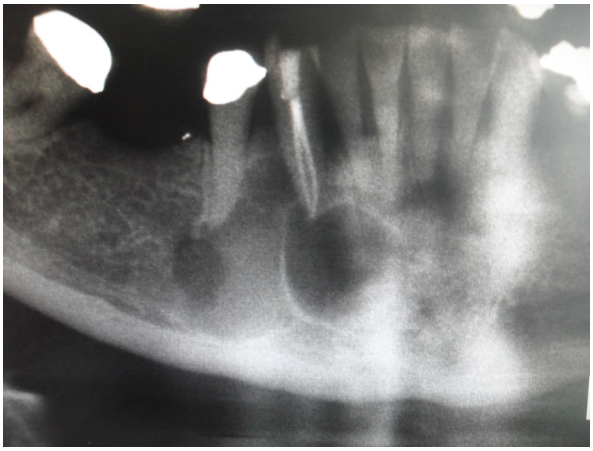

Figure 6: Panoral X-ray of case of LR3 root canal treatment resulting in leakage of endodontic chemicals causing inferior alveolar nerve injury via cystic lesion adjacent to the inferior dental canal

cases. The average pain reported as 7.2 on a visual analogue scale (where zero is no pain and 10 is pain as severe as it could be). The neuropathic pain was more common in middle-aged (mean 50.6 years of age) individuals with no sex predilection and occurred more frequently in the mandibular arch without any differences attributable to the number of canals treated. Also, the majority of subjects most frequently endorsed their pain experiences as abnormal sensitivity to touch and pain when the area is pressed or rubbed.

Persistent pain after routine surgery is an emerging entity; in a recent study of 221 patients with trigeminal nerve injuries related to dentistry, 70% are reported to have chronic neuropathic post-traumatic pain in patients attending a nerve injury clinic (Renton, Yilmaz, 2011). Another study confirmed this phenomenon in 91 patients (Benoliel et al, 2012). Neuropathic pain (NP) syndromes are chronic pain disorders that develop after a lesion of the peripheral nervous structures that are normally involved in signalling pain. Mechanisms for this process have been investigated but as yet elude us (Fried et al, 2001; Benoliel, Kahn, Eliav, 2012; Forssell et al, 2007). There are increasing reports of persistent pain post-dental surgery, likely to be related to post-traumatic neuropathy due to nerve injury (Queral-Godoy et al, 2006; Rodriquez-Lozano et al, 2010; Renton et al, 2012). This increased recognition of chronic persistent pain after surgery is also occurring in general surgery (Kehlet et al, 2007), reaffirming that a large proportion of patients attending chronic pain management clinics do in fact have post-surgical neuropathic pain.

There are relatively few reports of persistent pain subsequent to endodontic procedures (Nixdorf et al, 2010). Persistent pain after endodontics has been reported to occur in 3-13% of patients (Polycarpou et al, 2005). Surgical endodontics are reported to result in chronic neuropathic pain in 5% of patients (Campbell, Parks, Dodds, 1990). Groltze et al reported on 11 patients with endodontic associated neuropathy and their management. They similarly reported that the neurological findings were dominated by hypaesthesia and dysaesthesia with 50% of patients reporting pain. Eleven of 61 patients with endodontic NI presented with significant pain and only 40% responded to surgery (Pogrel, 2007). Ninety per cent of the 10 patients in a later study reported chronic pain with 50% experiencing allodynia (pain evoked to non-noxious stimuli) and hyperalgesia (increased pain to noxious stimuli, for example, a pinprick or partners bristles on kissing).

The characteristics of NP differ substantially from those of other chronic pain states, ie, chronic nociceptive pain, which develops while the nervous system that is involved in pain processing is intact. As well as the existence of negative somatosensory signs (deficit in function) there are other features that are characteristic of neuropathic conditions. Paraesthesias are symptoms typically described by patients that are bothersome but not painful. Furthermore, NP states require different therapeutic approaches such as anticonvulsants, which are not effective in nociceptive pain, according to NICE guidance. Thus, symptoms experienced by patients with post-traumatic neuropathy of the trigeminal nerve can range from next to no symptoms, such as minimal anaesthesia in a small area to devastating effects on the patient's quality of life (Renton, Yilmaz, 2011).

There is a lot of confusion in terminology used for chronic pain related to surgical interventions. Chronic pain after

Table 1: Commonly used endodontic medicaments have very high or low pHs

• **Formocresol**	pH 12.45 +/- 0.02
• **Sodium**	hypochlorite pH 11-12
• **Calcium hydroxide (Calyxl)**	pH 10-14
• **Antibiotic-corticosteroid paste (Ledermix)**	pH 8.13 +/- 0.01
• **Neutral**	pH 7.35-7.45
• **Eugenol**	pH 4.34 +/- 0.05
• **Iodoform paste**	pH 2.90 +/- 0.02
• **EDTA**	pH 8.0 with NaOH
• **MTA**	pH 10.2, increasing to 12.5 after 3h then constant

Table 2: CBCT radiography may assist in risk assessment for nerve injury related to endodontic treatment chemical leakage

Predisposing tooth factor that may result in an adverse incident during root canal treatment	*Potential adverse incident if tooth factor not recognised*
Resorption defects where extent is not identified such as internal/external communicating with root canal and external surface of the root	*Extrusion of endodontic filler/hypochlorite accident*
Suspicion of a perforation communicating with the external root surface	*Extrusion of endodontic filler/hypochlorite accident*
Root fracture where there could be a potential communication of the root canal with external root surface	*Extrusion of endodontic filler/hypochlorite accident*
Sclerosed root canal	*Possible perforation with subsequent hypochlorite accident*
Dens invaginatus	*Possible perforation with subsequent hypochlorite accident*
Periapical lesions and other pathology (cysts)	*Neurological injury (may occur if lesion close to inferior dental canal)*
Lower molar teeth where root apices are is close proximity to the Inferior dental canal and or mental foramen	*Neurological injury (over-instrumentation, overfilling with obturation materials or sealer)*

surgery has too many names, including: surgically induced neuropathic pain (SNIP), chronic post-surgical pain (CPSP), post-traumatic neuropathy (PTN), postoperative neuropathic pain (PPNP) and phantom limb pain. There are two main types of chronic pain relating to surgery

- Induced intractable neuropathic pain post-surgery (new or worsening pain)
- Persistent neuropathic pain pre- and post-surgery (persistent dentoalveolar pain [PDAP] or pre-existing neuropathic pain before the surgery).

The criteria for diagnosing CPSP (Macrae, 2008) include:

- Pain developed after surgery
- Minimum two-month duration
- Other causes of pain have been excluded (infection, persistent malignancy, misdiagnosis)
- Excluded preoperative pain from other cause.

For CPSP, a neuropathy does not have to be demonstrated in these cases, where as if post-traumatic neuropathy is present a neuropathy will be present, however, other features of neuropathic post-surgical pain will be present including;

- Pain
- Hyperaesthesia
- Allodynia pain with non-noxious stimulus
- Pain on touch/cold/hot
- Hyperalgesia increased pain to painful stimulus
- Altered sensation
- Paraesthesia – pins and needles, formication, many descriptions
- Dysaesthesia – uncomfortable sensations, often burning
- Numbness – hypoaesthesia

Chronic pain induced by surgery results in significant functional and psychological implications for the patients (Smith et al, 2013; Renton, Yilmaz, 2011). Therefore, holistic assessment and management is imperative to manage these patients. Optimal management of chronic pain will help the patient move forward with support from Liaison Psychiatry Service (Renton, Yilmaz, 2012). Lifelong chronic pain is a likely outcome with endodontic-related IANIs, and can mean that patients are on long-term medications. This reinforces the emphasis on prevention of these IANIs as they are so difficult to manage.

As a result of these severe consequences complaints and litigation often ensue. In a review of 16 medicolegal claims related to persistent altered sensation following endodontic treatments, the typical profile of a claim was a female patient who underwent an endodontic treatment at a second mandibular molar, which was associated with overfilling. None of the claims were reported by the practitioners, and all cases were identified as a result of the patient's demand for financial compensation, either directly or by legal actions (Givol et al, 2011).

Mechanism of nerve injury related to endodontic treatment

All trauma-sensitive neural tissues will result in various neurophysiological effects as the IAN is contained within a bony canal, which predisposes it to compression and possible ischaemic type injury. Compression of peripheral sensory nerves over six hours can evoke nerve fibre atrophy (Shimpo et al, 1987). Ischaemia alone without direct nerve damage will cause sufficient neural inflammation and damage to cause permanent nerve injury (Park, Kim, Moon, 2012). Three months after the IAN injury, permanent central and peripheral changes occur within the nervous system subsequent to injury, which are unlikely to respond to surgical treatment intervention (Yekta et al, 2010).

IANIs related to RCTs can be due to local anaesthesia, which is rare and usually associated with acute pain during block injections. IANIs related to endodontic treatment can be due to mechanical, chemical and haemorrhagic insults. The injury may be to the nerve itself (extraneural or intraneural) of varying sites and or associated vessels.

- Mechanical direct reamer/indirect scarring – excessive root canal preparation often causes enlargement of the apical foramen and loss of constriction, which favours extravasation of irrigation products or filling material beyond the apex, which, in turn, may cause neural injury of chemical or mechanical origin. The diameter of bone lesions of endodontic origin may also influence the occurrence of paraesthesia, especially when associated with the premolars and lower molars (Koseoglu et al, 2006). Rowe argued that mechanical damage to the nerve caused by an endodontic instrument can

be repaired during the healing process and that this form of paresthesia is generally temporary (Rowe, 1983). Figures 2-4 are examples of post-endodontic radiographic overfills in our patient sample

- Dental materials may exert damaging effects on nerve conduction as a result of their physical and chemical properties (Table 1)
- Even chemically bland materials such as gutta-percha may cause irreversible neural injury following their entry to the inferior dental canal in a molten, thermoplastic state, partially resulting from direct thermal damage, and partly from nerve compression as the material cools and contracts (Fanibunda, Whitworth, Steele, 1998)
- Pressure ischaemia from bleed or endodontic preparation
- Periapical infection may also cause IANI (Morse, 1997). The possibility of paraesthesia due to extrusion of microorganisms should be considered, given the potential for biological aggression, although this mechanism has not been explored in the literature (Table 1)
- Chemical toxicity and mechanical pressure produced by leakage of sealers into areas close to the mandibular canal are other potential mechanisms for nerve injury related to endodontic procedures, with the IAN and mental nerve being most affected. The materials most commonly associated with these complications are those containing paraformaldehyde (Ahonen, Tjaderhane, 2011). However, most endodontic materials have very high pHs resulting in immediate nerve damage likely to be permanent (Brodin et al, 1982; Brodin, 1988; Serper et al, 1998; Kozam, Newark, 1977)
- Haemaglobin irritates nerve tissue due to the iron content.

Risk factors

Tilotta-Yasukawa and colleagues (2006) determined the proximity of the apex of the premolars and molars in relation to the mandibular canal, as well as the relationship between the IAN and its corresponding artery, with the goal of understanding how endodontic filling material spreads through the bone to penetrate the mandibular canal. They observed that the distance between the dental apex and the mandibular canal was more variable (and generally greater) for the first molar than for the second and third molars (1–4mm vs less than 1mm [35 cases in 40 mandibles examined]). The authors concluded that, in the posterior region, the mandibular bone is not very dense and has a greater amount of trabecular bone. In addition, the presence of numerous vacuoles in the mandibular bone in the molar region facilitates the spread of irrigation products and filling material toward the inferior alveolar neurovascular set (Knowles, Jergenson, Howard, 2003).

In a study of 135 patients with inferior alveolar nerve injuries caused by dental treatment or malignancy, 22% presented with dysaesthesia that was significantly associated with the female gender and previous chronic pain (Oshima et al, 2009).

GDP inadequacies

GDP inadequacies of GDP root canal treatments was highlighted by Jenkins, Hayes and Dummer (2001).

Chemical nerve injuries

Chemical nerve injuries from leakage through the apex, such as sodium hydroxide – there are several reports of extreme pain and swelling resulting from endodontic irrigation with sodium hypochlorite, with a multitude of associated complications including neuropathy. Kleier, Averbach and Mehdipour (2008) surveyed 342 diplomates of the American Board of Endodontics. Of the diplomates who responded, 132 reported experiencing a sodium hypochlorite accident. The risk factors included: women compared with men ($p < 0.0001$); maxillary teeth compared with mandibular teeth ($p < 0.0001$); posterior more than anterior teeth ($p < 0.0001$); a diagnosis of pulp necrosis with radiographic findings of periradicular radiolucency were positively associated with such accidents ($p < 0.0001$). Table 2 lists potential risk factors for sodium chlorite and other chemical leaks that may contribute to nerve injury.

Technical detectable overfill

Technical detectable overfill (Figures 2-3) occurred in 60% of cases and over-instrumentation during preparation. Any tooth requiring endodontic therapy, which is in close proximity to the IAN canal, should require special attention, including: sodium hypochlorite (as irrigation) and calcium hydroxide (as sealant; calcium hydroxide medicaments breach the canal roof, precipitating a vascular bleed resulting in haemoglobin irritation of the nerve due to the iron content) (Escoda-Francoli et al, 2007; Blanas, Kienle, Sándor, 2004).

Over-instrumentation (Figures 4-5)

The practitioner should be trained in root length assessment and root canal preparation. If the apex is proximal to the IAN canal, and if the canal is over-instrumented, there is increased risk of damage to the nerve. If the canal is overprepared and the apex opened, the nerve may be damaged by preparatory files, overfilling using pressurised thermal filling, and pressure and ischaemia due to intracanal haemorrhage.

Dental factors

Many studies report the most likely teeth related to IANI are first molar and second premolars. A previous study reported a significant correlation between the tooth location and the suggested cause of nerve injury was found (Chikvashvili, 2011). Other dental factors can be found in Table 2.

Periapical lesions (Figure 6)

In one retrospective study, the incidence of mental paraesthesia resulting from periapical infection or pathology was 0.96%. In another, 0.24% of cases in the same study, mental paraesthesia was a complication of root canal treatment (caused by severe overfill in one case and iatrogenic perforation of mechanical instrumentation through the root and into the mental nerve in the second case). Neuritis neuropathy may be induced by local inflammatory factors related to the periapical lesions and, if persistent, can cause permanent IAN neuropathy. Many case reports that document neuropathies associated with apical periodontitis are scant, but usually involve premolars, and sensory disturbance in the distribution of the mental nerve (von Ohle, ElAyouti, 2010; Shadmehr, Shekarchizade, 2015). There is every expectation that carefully conducted root canal treatment that limits instruments and materials within the tooth, or indeed tooth

extraction will allow symptoms to resolve (Ahonen, Tjäderhane, 2011).

Proximity

Proximity of tooth to the IDC is a risk factor reported in all studies, including teeth apices close to the IDC and premolars adjacent to the mental loop (Scarano et al, 2007; Köseoğu et al, 2006). Mandibular teeth proximal to the IAN canal may have the apex of the tooth and may be adjacent or intruding into the IDC canal, and any small degree of leakage or overfilling may compromise the IAN. Assessment of the proximity of the tooth apex to the IAN canal has become significantly improved with cone beam CT scanning (CBCT) with the attendant risk of additional radiation, and may not provide significantly more information than a plane long cone radiograph. Most CBCT assessment of tooth positioning in relation to the IAN canal is based on M3M prior to extraction (Tilotta-Yasukawa et al, 2006).

It is a concern that several reports are emerging that some endodontic programmes are training delegates to overfill past the apex by 1-2mm for optimal results. Firstly, there is insufficient evidence to support this recommendation and no mention of pre-surgical safety zone assessment to avoid nerve injuries in those teeth with apices close to the IDC.

Part two

Part two of this article will examine CBCT guidance in endodontic-related nerve injuries, as well as the diagnosis, assessment and management in practice. ■

AUTHOR

TARA RENTON is a specialist in oral surgery with a particular interest in trigeminal nerve injuries and pain. After completing her oral and maxillofacial surgical training in Melbourne in 1991, Tara undertook a PhD in trigeminal nerve injury at King's College London in 1999. She was later appointed senior lecturer at Queen Mary University of London and was then awarded her chair in 2006 at King's College London. Over the past seven years Tara has lead the teaching of dental students, modernising the oral surgical teaching with minimal access approach and modern local anaesthesia techniques. She has established an academic training programme, and in collaboration with the Institute of Psychiatry, Psychology & Neuroscience at King's College London and Imperial College, Tara has established an international leading programme of trigeminal nerve injury and orofacial pain research.

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