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Dynamic Navigation for Endodontic Access in Calcified Maxillary Molars

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Submitted in fulfilment of the requirements for the Degree of Master of Science (MSc) by Research

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Abstract

Rationale

Endodontic access on teeth with calcified canals is challenging, time consuming and requires significant expertise. Dynamic navigation (DN) is a recent advancement within endodontics that provides real-time guidance during endodontic access. Dynamic navigation may improve the accuracy of canal location in teeth with calcified canals compared to freehand (FH) access.

Aim 1

To carry out a systematic review of existing literature to assess the accuracy of canal location using DN in teeth with pulp canal obliteration when compared to FH and static navigation (SN) and to inform the design of an in vitro study.

Methods 1

The systematic review eligibility criteria included 3D-printed or human teeth with pulp canal obliteration (PCO), endodontic access performed using DN and comparison to FH and/or SN. Embase, MEDLINE and CENTRAL and clinical trial registries were last searched on 31 March 2023. Additional searches included leading endodontic journals, conference proceedings and contact with manufacturers. The risk of bias was assessed using a modified Joanna Briggs Institute (JBI) checklist. Study characteristics and outcomes were tabulated and outcomes were explored as a narrative synthesis.

Results 1

Systematic review identified three eligible articles for inclusion with a total of 172 teeth. All studies were of in vitro design on human and 3D-printed anterior and premolar teeth with varying levels of PCO. No studies included teeth with multiple canals or roots. The overall risk of bias was low in two studies and moderate in one study. Meta-analysis was not performed due to heterogeneity and the results presented as a narrative synthesis. Dynamic navigation improved

accuracy of canal location in teeth with PCO in all three studies when compared to FH access. No studies compared DN to SN.

Aim 2

To perform an in vitro study to compare the tooth volume loss following DN and FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals, performed by two operators with differing levels of experience.

Methods 2

The in vitro study utilised a custom 3D-printed, anatomically accurate maxillary molar with four simulated calcified canals. A total of 40 identical teeth were accessed, 20 using the Navident Dynamic Navigation System (ClaroNav, Toronto, Canada) and 20 FH, by two operators with different levels of endodontic experience. The primary outcome measure was total tooth volume loss, while secondary outcome measures included the incidence of successful canal location, incidence of perforation and procedural time. Volume loss was assessed using pre- and post-operative cone-beam computer tomography, automatic segmentation and volume analysis software.

Results 2

There was no significant difference in tooth volume loss between DN and FH endodontic access in 3D-printed maxillary molars with simulated calcified canals (53.824 vs. 48.144mm³, p=0.085). However, DN significantly reduced the median procedural time (6 minutes 52 seconds vs. 21 minutes 56 seconds, p<0.05).

Conclusions

The systematic review suggested that DN may increase the accuracy of canal location in teeth with PCO when compared to FH access. However, the findings should be interpreted with caution due to the small number of included studies, all of which were of in vitro design.

The in vitro study was the first to compare endodontic access of multiple canals using DN and FH methods. It demonstrated that while DN does not significantly impact tooth volume loss in 3D-printed maxillary molars with simulated canal calcification, it significantly reduces procedural time and enhances consistency.

Further research should involve a range of multi-rooted teeth to validate the findings of the current in vitro study, as well as clinical studies to evaluate the clinical application of DN and address the inherent limitations of in vitro and ex vivo study designs.

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Abbreviations

2D Two-Dimensional

3D Three-Dimensional

AAE American Association of Endodontists

AAOMR American Academy of Oral and Maxillofacial Radiology

CAD/CAM Computer-Aided Design and Computer-Aided Manufacturing

CariesAC Caries-driven access cavity

CBCT Cone Beam Computed Tomography

CEJ Cemento-Enamel Junction

ConsAC Conservative access cavity

DB Disto-buccal

DICOM Digital Imaging and Communications in Medicine

DN Dynamic Navigation

DNS Dynamic Navigation System

DOM Dental Operating Microscope

EPT Electric Pulp Testing

ESE European Society of Endodontology

FH Freehand

FOV Field of View

FWJ Floor-Wall Junction

GE Guided Endodontics

IEJ International Endodontic Journal

JBI Joanna Briggs Institute

JOE Journal of Endodontics

MB1 Mesio-buccal 1

MB2 Mesio-buccal 2

MIE Minimally Invasive Endodontic

mm Millimetre

mm³ Cubic millimetres

P Palatal

PCD Pericervical Dentin

PCO Pulp Canal Obliteration

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-

Analyses

RestoAC Restorative-driven access cavity

s Second

SLA Stereolithography

SN Static Navigation

STL Stereolithography or Standard Tessellation language

TradAC Traditional access cavity

TrussAC Truss access cavity

Ultra-Conservative access cavity

UV Ultraviolet

μm Micrometre

Author's Declaration

I declare that the work described in this thesis is my own work, unless otherwise acknowledged or referenced.

This body of work has not been submitted as part of any other degree.

Chapter 1 Literature review

1.1 Background

1.1.1 General introduction

Advancements in digital dentistry, driven by research, enable us to provide endodontic treatment with increasing predictability. These innovations offer alternative treatment strategies with enhanced precision and efficiency, potentially improving outcomes. This thesis will focus on the use of Dynamic Navigation (DN) in endodontics for the location of calcified canals. Firstly, it is worth considering the dentine-pulp complex, pathogenesis of endodontic disease and its treatment.

1.1.2 Vital pulp response

The healthy tooth has an outer layer of enamel coronally, surrounding the underlying dentine. The dentine encloses the dental pulp which is contained within the pulp chamber located in or just below the anatomic crown and extends into the root canal(s) located in the anatomic root (Figure 1-1) (Berman and Hargreaves 2020). The dental pulp is a highly innervated and vascular connective tissue containing odontoblasts, fibroblasts and immune cells. The dentine and dental pulp are often referred to as the 'dentine-pulp complex' due to their close structural and functional relationship (Berman and Hargreaves 2020). Odontoblasts lie at the periphery of the pulp-dentine junction and are responsible for dentinogenesis (the process of dentine formation). Following primary dentine production during tooth development, secondary dentine is gradually deposited throughout life as part of the normal ageing process. The dentine-pulp complex has an ability to respond to microbial, chemical or physical stimuli through a combination of dentine sclerosis, tertiary dentine formation, and inflammation and immune reactions in the pulp (Cooper et al. 2014). Tertiary dentine is laid down beneath the dentinal tubules adjacent to the stimulus, allowing the pulp to retreat. This acts as a protective mechanism, allowing maintenance of pulp vitality. Tertiary dentine produced by surviving odontoblasts in response to a mild stimulus is referred to as reactionary dentine (Figure 1-2) (Smith et al. 1995). Reparative dentine is formed by odontoblastlike cells that differentiate from mesenchymal stem cells in response to a strong stimulus following destruction of the original odontoblasts (Figure 1-2) (Cooper et al. 2014; Farges et al. 2015).

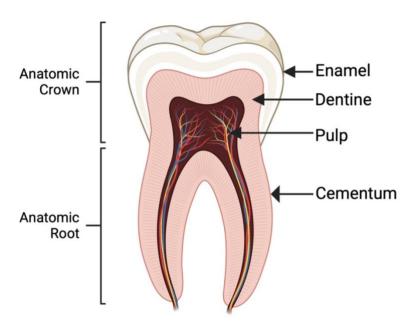


Figure 1-1 - Normal tooth anatomy.

Demonstrates the structure of a healthy tooth. The enamel surrounds dentine within the anatomic crown, while the dentine encloses the pulp. The pulp is divided into the pulp chamber (located in and just below the anatomic crown) and the root canals (located within the anatomic root). This figure was created with BioRender.com.

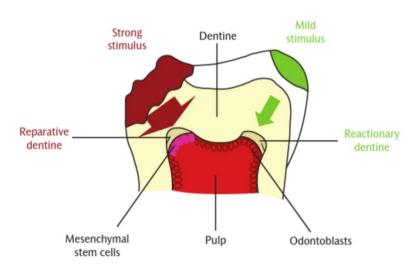


Figure 1-2 - Tertiary dentine formation in response to a stimulus.

Demonstrates reactionary dentine formation in response to a mild stimulus and reparative dentine formation in response to a strong stimulus. Reproduced with permission of The Licensor through PLSclear. The Principles of Endodontics (Oxford Publishing Limited).

1.1.3 Endodontic disease

Where a noxious stimulus persists and remains untreated, pulp necrosis and bacterial colonisation of the root canal system may result (Kakehashi et al. 1965;

Möller et al. 1981; Nair 2004; Nair 2006; Ricucci and Siqueira 2010). This leads to inflammation and destruction of the periodontium, usually apically although lateral destruction can occur. This is known as apical periodontitis, the aetiology of which is well-established to be bacterial. Apical periodontitis results from bacteria and their by-products exiting via the apical and lateral foramina into the peri-radicular tissues resulting in inflammation (Nair 2004). In their landmark study, Kakehashi et al. (1965) exposed the pulps of conventional and germ-free rats to the oral flora. Pulp necrosis, peri-radicular inflammation and abscess formation developed in conventional rats, while dentine bridge formation was seen in the germ-free rats (Kakehashi et al. 1965). These findings were later supported by Möller et al. in a further animal study (Möller et al. 1981). These works have been highly influential in shaping modern endodontic practice. Apical periodontitis poses a significant global health burden, with half the world's adult population having at least one tooth with apical periodontitis (Tibúrcio-Machado et al. 2021). If left untreated, apical periodontitis is known to negatively impact quality of life (Liu et al. 2014).

1.1.4 Root canal treatment

Root canal treatment (also known as endodontic treatment) encompasses procedures that prevent or treat apical periodontitis (European Society of Endodontology 2006). The aim is to adequately disinfect the root canal system and to prevent reinfection through obturation and the provision of a coronal seal (European Society of Endodontology 2006; British Endodontic Society 2022). A recent systematic review found that root canal treatment is highly successful, with an estimated success rate of 92% according to 'loose criteria' (reduction in size of the periapical lesion) and 82% according to 'strict criteria' (complete resolution of periapical lesion) (Burns et al. 2022). Tooth survival after root canal treatment is 87% after an 8-10-year follow-up period (Ng et al. 2010). Retention of natural teeth through root canal treatment is not only more cost-effective than prosthetic replacement but enhances quality of life (Pennington et al. 2009; Liu et al. 2014; Block et al. 2022; Schwendicke and Herbst 2023).

The following sections will provide an overview of traditional endodontic access cavity principles, discuss the contemporary literature on minimally invasive endodontic access cavities, explore the aetiopathogenesis, epidemiology, and

diagnostic and treatment challenges of pulp canal obliteration (PCO), and introduce guided endodontics (GE).

1.2 Traditional endodontic access cavity principles

Endodontic access cavity preparation is considered a key stage of root canal treatment. The main objective is to gain entry to the root canal system to facilitate subsequent chemo-mechanical preparation and obturation (American Association of Endodontists 2020). Traditionally, this involves complete deroofing of the pulp chamber and achieving straight-line access (Berman and Hargreaves 2020). A poorly designed access cavity may hinder subsequent stages, increasing the risk of complications and failure.

Endodontic access relies upon a good knowledge of the tooth's external and internal anatomy. Pre-operative planning involving a detailed clinical and radiographic examination is a prerequisite to any root canal treatment. Krasner and Rankow described a series of laws to aid systematic location the pulp chamber and root canals (Krasner and Rankow 2004). The first three laws describe the relationship between the clinical crown and pulp chamber emphasising the importance of careful visualisation of the external outline of the tooth at the level of the Cemento-Enamel Junction (CEJ) taking note of the tooth's orientation. The CEJ was found to be the most consistent fixed landmark for location of the pulp chamber ('law of the CEJ'). The pulp chamber is always found within the centre of the tooth ('law of centrality') and the walls are of equal distance from the external surface at the level of the CEJ ('law of concentricity'). Deutsch and Musikant found that the roof of the pulp chamber was at the level of the CEJ in 98% of maxillary and 97% of mandibular molars in a sample of 200 molars, emphasising the consistency of the CEJ as a key anatomical landmark (Deutsch and Musikant 2004). In the average molar, the roof of the pulp chamber exists just over 6 millimetres (mm) from the buccal cusp. Careful radiographic examination of each case including taking measurements from the occlusal aspect of the tooth to the pulp chamber roof and floor acts as a good guide and should reduce the risk of perforation. In most cases, knowledge of these laws and measurements results in an uncomplicated access with the clinician experiencing a sudden 'drop' when entering the pulp chamber with a bur.

Once the pulp chamber is located, the access cavity outline is prepared and the orifices located using knowledge of the laws of the pulp chamber floor (Krasner and Rankow 2004). Except for in maxillary molars, the orifices are located equidistant and perpendicular to a line drawn in a mesio-distal direction ('law of symmetry' 1 and 2). Orifice location is further enhanced using the laws of colour change and orifice location. The floor of the pulp chamber is always darker than the walls and creates an intersection known as the Floor-Wall Junction (FWJ) and the orifices are located at the angles of the FWJ at the termination of the root development fusion lines.

1.3 Minimally invasive endodontic access cavities

Traditional endodontic access cavity principles, as described in section 1.2, endorsed straight-line access to the canal orifices and complete deroofing of the pulp chamber. However, more recently there has been a shift towards minimally invasive endodontic (MIE) treatment, a concept focused on maximum preservation of tooth structure, aiming to reduce the incidence of tooth fracture. Clark and Khademi (2010) were pioneers in MIE access cavity preparation and recognised the value of dentine preservation. They are two of many proponents of the concept of the 'endorestorative' interface, that describes the critical relationship between endodontic treatment and the restoration of the tooth. They advocated maintenance of the pulp chamber roof, referred to as the 'soffit' and the 'pericervical dentin' (PCD) where possible. The concept of PCD describes the critical zone of dentine 4mm above and below the alveolar crest, essential for load transfer to the root and fracture resistance (Clark and Khademi 2010). Historic literature demonstrates the most common reason for extraction of an endodontically treated tooth is structural failure, highlighting the significance of the 'endorestorative' interface (Vire 1991). Recent research corroborates this, showing that endodontically treated teeth with greater than 30% of their original tooth structure remaining have a 4-year survival rate three times higher than teeth with less than 30% remaining (Al-Nuaimi et al. 2020).

While the concepts developed by Clark and Khademi were not originally evidence-based, MIE access cavities are gaining increasing popularity, with efforts being made to study their impact. The following sections will outline the

classification of MIE access cavities and discuss the benefits and drawbacks of such approaches, as supported by more recent literature.

1.3.1 Classification

The terminology used to describe access cavity design is inconsistent across the literature. Consequently, Silva et al. proposed a new classification (Silva et al. 2020b). Six main categories were described as follows and are represented in posterior teeth in Figure 1-3:

- Traditional access cavity (TradAC): complete removal of the pulp chamber roof and straight-line access to all canal orifices with smoothly divergent axial walls where all orifices can be seen within the cavity outline.
- 2) Conservative access cavity (ConsAC): starts at the central fossa (posterior teeth) or towards the incisal edge (anterior teeth) with smooth convergent axial walls to the occlusal surface as far as necessary to detect the canal orifices, while preserving part of the pulp chamber roof. A modification of this access cavity design, ConsAC.DW, is performed with divergent walls.
- 3) Ultra-conservative access cavity (UltraAC) (often referred to as 'ninja' access) (Plotino et al. 2017): starts at the central fossa (posterior teeth) or towards the incisal edge (anterior teeth) with no further extensions, maintaining the pulp chamber roof as far as possible.
- 4) Truss access cavity (TrussAC): preserves the dentinal bridge between two or more small access cavities to access the canal orifice(s) in each root of multi-rooted teeth.
- 5) Caries-driven access cavity (CariesAC): access to the pulp chamber is performed by removing caries and preserving all remaining tooth structure, including the soffit.

6) **Restorative-driven access cavity (RestoAC)**: access to the pulp chamber is performed by partially or totally removing existing restorations while preserving all possible remaining tooth structure.

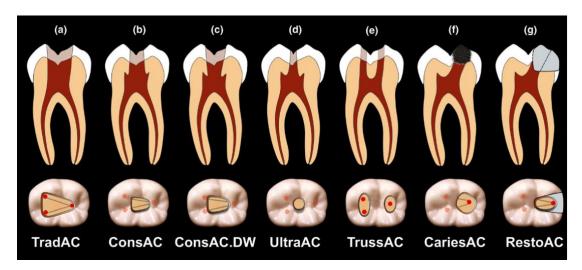


Figure 1-3 - Classification of access cavities.

Categories of access cavity design proposed by Silva. Used with the permission of
Blackwell Publishing Ltd from 'Current status on minimal access cavity preparations: a
critical analysis and a proposal for a universal nomenclature' (Silva et al. 2020, Volume 53,
Issue 12) copyright 2020; permission conveyed through Copyright Clearance Center Inc.

1.3.2 Impact on tooth fracture resistance

The concept of MIE access is supported by the notion that it effectively reduces the incidence of tooth fracture. Krishan et al. were the first to evaluate this in their in vitro study assessing load at fracture using continuous compressive forces with a universal testing machine in a range of extracted teeth (Krishan et al. 2014). They found the fracture resistance in premolars and molars to be significantly higher (2.5-fold and 1.8-fold, respectively) in teeth with ConsAC, compared to TradAC. Plotino et al. (2017) performed a study with a similar design comparing TradAC, ConsAC and UltraAC. In keeping with Krishan's findings, the fracture resistance was significantly greater for ConsAC and UltraAC compared to TradAC and no difference was found between intact teeth (control group), ConsAC and UltraAC (Plotino et al. 2017). Subsequent studies have employed similar loading protocols, with some incorporating thermocycling and fracture testing with dynamic loading followed by static loading to simulate the conditions within the oral cavity, with similar results (Abou-Elnaga et al. 2019; Santosh et al. 2021). Finite element analysis studies have demonstrated a reduction in stress concentration areas on the occlusal surface and cervical

region with ConsAC and UltraAC, when compared to TradAC (Yuan et al. 2016; Zhang et al. 2019).

Although some studies report improved fracture resistance, the literature remains inconsistent regarding the impact of endodontic access cavity design. Several studies comparing TradAC to ConsAC, UltraAC and TrussAC using continuous compressive forces in molars and premolars have demonstrated no difference in fracture resistance (Moore et al. 2016; Rover et al. 2017; Corsentino et al. 2018; Augusto et al. 2020; Barbosa et al. 2020; Silva et al. 2020a; Lima et al. 2021; Silva et al. 2021a).

In an attempt to address the conflicting evidence, systematic reviews have been performed to address the impact of MIE access cavities on the fracture resistance of endodontically treated teeth. Silva's systematic review included six studies and, while no meta-analysis was performed, the majority (four out of six) demonstrated no difference in fracture resistance between MIE access and TradAC (Silva et al. 2018). A more recent systematic review and meta-analysis performed by Rahnamo Nobar et al., which included twenty studies incorporating all those by Silva et al., concluded that conservative access cavities significantly improved the fracture resistance of endodontically treated premolars and molars (Rahbani Nobar et al. 2023). There appears to be emerging evidence suggesting that MIE access cavities improve fracture resistance, when compared to TradAC.

1.3.3 Impact on canal location

Minimally invasive endodontic access cavities may impact the ability to detect all root canal orifices successfully. Saygili et al. compared the detection rate of the MB2 in maxillary molars following TradAC, ConsAC and UltraAC designs performed using the DOM, demonstrating rates of 60%, 53.3% and 31.6% respectively (Saygili et al. 2018). It is well known that the presence of a missed canal is often responsible for persistent apical periodontitis and reduced treatment outcomes (Costa et al. 2019). Nonetheless, Rover et al. found that when the DOM and ultrasonic troughing was employed, no difference in detection rates were found in maxillary molars (Rover et al. 2017). Similarly,

Mendes et al. found no differences in detection rates of the middle mesial canal in mandibular molars (Mendes et al. 2020).

1.3.4 Impact on chemo-mechanical preparation

It should be considered that MIE access may impair subsequent endodontic stages. Lima et al. demonstrated through micro-CT evaluation that UltraAC significantly increases the proportion of untouched canal walls compared to TradAC, independent of the instrument type used (Lima et al. 2021). In addition, Alovisi et al. investigated the impact of TradAC and 'contracted endodontic cavities', a design in keeping with Silva's ConsAC, on the preservation of the original root canal anatomy in mandibular molars using the ProGlider and WaveOne Gold file systems (Alovisi et al. 2018). Analysis of micro-CT images demonstrated that ConsAC resulted in less preservation of the original canal anatomy and increased apical transportation compared to TradAC, potentially due to coronal interferences. However, it should be noted that the difference in centroid shift was around 0.2mm, the clinical significance of such a difference is uncertain. Neelakantan et al. adopted a different approach, using histologic evaluation to assess remaining pulp tissue with both TradAC and TrussAC approaches (Neelakantan et al. 2018). Although no significant differences were observed in the root canals or isthmus, the TrussAC group showed a significantly greater amount of remaining pulp tissue in the pulp chamber. Similarly, Silva et al. found an increase in accumulation of hard-tissue debris after canal preparation in teeth with UltraAC compared to TradAC (Silva et al. 2020a). However, in both studies, no enhanced irrigation measures were used to improve disinfection, which appear to be necessary in teeth with MIE access cavities. Chemo-mechanical preparation has been shown to take significantly longer in MIE access compared to TradAC (Marchesan et al. 2018; Silva et al. 2020a).

There is also a body of evidence indicating that the access cavity design does not affect mechanical preparation. Krishan et al. were the first to compare root canal preparation in TradAC and ConsAC using micro-CT (Krishan et al. 2014). They assessed instrumentation efficacy using WaveOne reciprocating files in extracted human maxillary incisors, mandibular premolar and mandibular molars. By comparison of pre-operative and post-operative micro-CT images, they determined the proportion of unprepared canal walls and volume of

dentine removed within the canal. Their results indicated no significant impact on mechanical preparation, with no difference in the proportion of untouched walls except within the apical third of the distal canal in molars, where teeth with ConsAC had a greater proportion of untouched walls (57.2% vs 36.7%). There were no instrument fractures in either group. Similarly, other studies have reported no difference in unprepared canal walls, canal transportation or centring ability in both molars and premolars (Moore et al. 2016; Rover et al. 2017; Augusto et al. 2020; Barbosa et al. 2020; Silva et al. 2020a; Wang et al. 2021a).

There is ongoing debate in the literature on the impact of MIE access cavities on chemo-mechanical preparation. A systematic review aiming to address this issue found that the majority of studies (11 out of 17) identified a negative impact of MIE access on instrumentation efficacy (Shroff et al. 2023). Significant canal transportation and ledging was found in five out of eleven studies. Three of the four studies assessing the degree of pulp debridement demonstrated incomplete pulp removal.

1.3.5 Impact on instrument fracture

Minimally invasive endodontic access may also influence instrument cyclic fatigue resistance due to an increase in both the angle and curvature, resulting in greater stress along the instrument. Silva et al. demonstrated a reduced cyclic fatigue resistance of Reciproc and Reciproc Blue files when used with an UltraAC compared to TradAC in mandibular molars (Silva et al. 2021b). Furthermore, another study which also used Reciproc Blue in incisors and premolars confirmed the same findings when comparing ConsAC to TradAC (Spicciarelli et al. 2020). Given these findings, and to limit risk of instrument failure, heat treated files with improved cyclic fatigue resistance are recommended.

1.3.6 Summary

Despite a growing body of evidence supporting the use of MIE access to improve fracture resistance of teeth, this still remains a subject of debate. Although there are a significant number of in vitro studies, these carry methodological flaws and do not accurately reflect intra-oral conditions. Additionally, there is a

lack of clinical data to confirm that MIE access cavities can improve fracture resistance. The potential for negative effects on subsequent chemo-mechanical preparation cannot be ruled out. Undoubtedly, chemo-mechanical preparation in teeth with MIE access requires a skilled and experienced clinician utilising the DOM and employing technological advancements in instrumentation and irrigation. In summary, the current evidence supporting MIE access is limited, conflicting and insufficient to guide clinical decision making. While the precise threshold of dentine removal which impacts tooth survival is unclear, minimising unnecessary dentine removal, where feasible, seems sensible provided that it does not compromise effective chemo-mechanical preparation.

As discussed in section 1.1.2, the dentine-pulp complex is a dynamic structure capable of responding to stimuli. As a result of such responses, the dimensions of the pulp chamber and root canals can become contracted. This can have a significant impact on endodontic access. A consideration of this will be made in the following section.

1.4 Pulp canal obliteration

1.4.1 Aetiopathogenesis

Pulp canal obliteration, also referred to as pulp canal calcification or calcific metamorphosis, occurs due to increased deposition of dentine within the root canal system, primarily as a response to trauma (American Association of Endodontists 2020). Calcific changes within the root canal system may also occur in response to caries, tooth wear, restorative procedures, and as a physiological response in older patients.

As mentioned, PCO is most commonly seen in response to dental trauma, occurring within the first-year post-trauma (Andreasen 1970; Jacobsen and Kerekes 1977; Andreasen et al. 1987; Nikoui et al. 2003). Holcomb and Gregory examined periapical radiographs from 881 senior midshipmen. Of those patients demonstrating radiographic signs of PCO, almost 80% recalled a history of significant dental trauma during childhood to the affected tooth (Holcomb and Gregory 1967). Of course, it must be acknowledged that the retrospective nature of this study may be subject to recall and response bias. The mechanism of PCO

remains uncertain, but it is thought to be related to the process of revascularisation of the pulp following a luxation injury (Andreasen et al. 2018). Histological examination of obliterated pulp chambers has revealed calcified tissue in concentric layers with a lack of tubular pattern surrounded by reparative dentine (Piattelli and Trisi 1993). Studies on primary teeth with PCO have shown that the calcified tissue within the pulp space may resemble dentine, bone or fibrotic tissue (Robertson et al. 1997). The variable appearance may result from entrapment of pulpal cells during the rapid and irregular deposition of calcified tissues, sometimes giving a bone-like appearance. The remaining pulpal tissue shows a variable increase in collagen content but is virtually inflammation free. Teeth with a marked increase in collagen show a marked decrease in cell number (Lundberg and Cvek 1980).

Aside from dental trauma, PCO is seen in response to other external insults such as caries, tooth wear and restorative intervention (Bjørndal and Darvann 1999; Fleig et al. 2017). The pathogenesis is discussed in the 'Vital pulp response' section, 1.1.2. Fleig and colleagues conducted a study using Cone Beam Computed Tomography (CBCT) to compare teeth that were crowned or filled with contralateral unrestored and caries-free controls. They found that the root canal space was significantly narrower in restored teeth compared to the controls, particularly within the coronal third (Fleig et al. 2017). Similarly, Gonçalves' study demonstrated that decayed and restored posterior teeth have a significantly higher prevalence of pulp calcification when assessed using Two-Dimensional (2D) and Three-Dimensional (3D) imaging techniques (Gonçalves et al. 2024). Similarly, pulp horn obliteration and pulp calcifications are commonly seen following partial pulpotomy procedures (Mass and Zilberman 2011).

Pulp canal obliteration may also be observed in older patients as a physiological response to ageing. It is well known that secondary dentine deposition occurs throughout life resulting in a reduced pulp chamber and root canal space. In addition, there is an increase in peri-tubular dentine, dentinal sclerosis and the number of dead tracts, while the pulp shows a decrease in cellularity (Murray et al. 2002; Johnstone and Parashos 2015; Carvalho and Lussi 2017). Murray and coworkers undertook a histological study of 147 teeth from 60 patients ranging from 10 to 59 years of age. Their findings confirmed an increase in dentinal thickness and decrease in cellular density, including odontoblasts, sub-

odontoblasts and pulp fibroblasts, with increasing age (Murray et al. 2002). Vera's CBCT study of anterior teeth on a general adult population revealed that the only significant factor related to the presence of PCO was the patient's age. The odds ratio of PCO in the over 60 group was 2.6 (Vera et al. 2022). In this study, PCO was defined as ≥4mm from the CEJ to the visible canal. However, the study design meant that previous dental experience could not be determined as radiographs were not linked to patient records. The higher prevalence in older patients may be attributable to other confounding factors resulting from pathological changes including a cumulative history of trauma, tooth wear, caries or restorative intervention, rather than exclusively physiological changes. Nonetheless, the findings were corroborated by Zahran and Alamoudi who found PCO was more common in individuals over the age of 40 (Zahran and Alamoudi 2024). With an ageing population and patients seeking to retain their natural dentition, the prevalence of PCO due to ageing is likely to increase.

1.4.2 Epidemiology

There is a wealth of epidemiological data on the prevalence of PCO in the permanent dentition dating back over 50 years, particularly in relation to the anterior dentition. Holcomb and Gregory demonstrated an overall prevalence of 3.85% in their study of the anterior teeth of 881 senior shipmen (Holcomb and Gregory 1967). Similarly, a more recent retrospective study, examining over one thousand small and medium field of view (FOV) CBCT scans of anterior teeth taken for other purposes from a database of adult patients, revealed an overall prevalence of 4.7% (Vera et al. 2022). The prevalence of PCO in posterior teeth is more ambiguous since the literature often focuses exclusively on pulp stones or does not differentiate between pulp stones and PCO. The combined prevalence of coronal calcification (pulp stones and PCO) is reported to be 45% (Gonçalves et al. 2024). The authors recorded instances of calcification where there was partial or total "obliteration of the pulp chamber/root canal" or "pulp chamber/root canal narrowing", although these categories were not clearly defined. Taken together, the prevalence of PCO in anterior teeth is approximately 4%, while the prevalence in posterior teeth remains uncertain but is probably greater.

The incidence of PCO in traumatised anterior teeth is much higher than the general population, ranging from 15% to 40% (Andreasen 1970; Jacobsen and Kerekes 1977; Andreasen et al. 1987; Nikoui et al. 2003). Andreasen followed up 189 permanent teeth with luxation injuries, namely subluxation, intrusion and extrusion, over a mean period of 3.4 years and reported an incidence of 22% (Andreasen 1970). A subsequent larger study of 637 luxated permanent teeth, including concussion, subluxation, extrusion, lateral luxation and intrusion injuries, over a similar observation period, showed a lower incidence of 15% (Andreasen et al. 1987). Nikoui and colleagues studied 58 permanent maxillary incisors in 42 patients following lateral luxation injuries over a mean follow-up period of 4 years and found an incidence of 40% (Nikoui et al. 2003). More recently, a study of 427 luxated teeth, including lateral luxation, subluxation, extrusion and concussion followed up for a median period of 1.4 years demonstrated an incidence of 12.9% (Coste et al. 2024).

The variable incidence of PCO in traumatised permanent teeth can be attributed to the type of injury and the stage of root development (Andreasen 1970; Andreasen et al. 1987; Coste et al. 2024). While PCO may be seen with all types of luxation injuries, it is ultimately related to the nature of injury to the pulp and the resultant degree of pulpal damage. Pulp canal obliteration is most common with injuries that result in a 'moderate' degree of pulpal damage, such as extrusion and lateral luxation (Andreasen 1970; Andreasen et al. 1987; Coste et al. 2024). Milder injuries, such as concussion and subluxation, where there is less stimulus for tertiary dentine deposition, results in a lower incidence of PCO (Andreasen et al. 1987). Severe injuries, such as intrusion, also have a lower PCO incidence, this can be explained by the high incidence of pulp necrosis (Andreasen et al. 1987). In fact, PCO is not observed following intrusion of teeth with closed apices, since 100% of these teeth experience pulp necrosis (Andreasen et al. 1987). Studies have consistently demonstrated a significant relationship between an immature apex and increased incidence of PCO and therefore age at the time of injury is an important predictor of PCO (Andreasen 1970; Andreasen et al. 1987; Coste et al. 2024).

1.4.3 Diagnostic challenges

Accurate diagnosis in teeth with PCO can be challenging. Pulp canal obliteration is often asymptomatic and is more commonly an incidental finding following clinical and radiographic examination (Robertson et al. 1996). Teeth with PCO may present clinically with yellow discolouration due to the increased thickness of dentine and lack of translucency (Patterson and Mitchell 1965). The incidence of discolouration varies significantly across studies, ranging from as low as 3% to as high as 79% when reduced transparency is also considered (Jacobsen and Kerekes 1977; Andreasen et al. 1987). Discolouration often goes unnoticed by patients and is not commonly an aesthetic concern (Jacobsen and Kerekes 1977). While Jacobsen and Kerekes noted the highest incidence (79%), only 5% of teeth with PCO in their study were 'severely discoloured'. Other studies have found the incidence of 'marked' discolouration to be around 20% (Holcomb and Gregory 1967; Andreasen 1970). The lack of consistent criteria likely accounts for the wide variation in the incidence of discolouration, making it difficult to draw meaningful conclusions. Robertson et al. demonstrated that of all teeth with PCO and a normal periapical radiographic appearance, 69% had yellow discolouration (Robertson et al. 1996). Whilst yellow discolouration is most commonly reported, grey discolouration can occasionally be seen (Andreasen et al. 1987; Robertson et al. 1996; Oginni et al. 2009). While one may suspect teeth presenting with a grey discolouration would have pulp necrosis, Robertson et al. demonstrated that the three teeth with grey discolouration all had a normal or 'high normal' response to Electric Pulp Testing (EPT) and no periapical radiolucency (Robertson et al. 1996). A more recent study found that among teeth with PCO, only 38% of grey teeth and 33% of yellow teeth exhibited a periapical lesion and a negative response to EPT (Oginni et al. 2009). Therefore, it was concluded that coronal discolouration is not a reliable indicator of pulp necrosis.

Pulp testing in PCO is an unreliable measure of pulp vitality with only 36-56% of teeth showing a normal positive response and 27-30% showing no response (Holcomb and Gregory 1967; Robertson et al. 1996; Oginni et al. 2009). A 'high normal' response to EPT is also commonly seen (Andreasen 1970; Robertson et al. 1996; Oginni et al. 2009). Response to EPT is said to decrease over time as PCO progresses and a negative response to EPT is significantly more likely in

cases of total PCO compared to partial (Patterson and Mitchell 1965; Oginni et al. 2009). The incidence of pulp necrosis secondary to PCO over long-term follow-up ranges between 1% and 27% and does not match pulp testing outcomes (Andreasen et al., 1987, Oginni et al., 2009). In fact, many studies would suggest that the incidence is less than 10% (Holcomb and Gregory 1967; Andreasen 1970; Andreasen et al. 1987; Robertson et al. 1996). Pulp necrosis is more common in cases of total obliteration, compared to partial obliteration (Jacobsen and Kerekes 1977). The literature suggests that the incidence of pulp necrosis increases over time (Robertson et al., 1996). The increased incidence of late pulp necrosis appears to be associated with severe injuries in teeth with complete root formation (Jacobsen and Kerekes 1977). According to Holcomb and Gregory, of those with a negative response to pulp testing, only one quarter had a periapical lesion (Holcomb and Gregory 1967). It can be concluded from these studies that pulp testing in teeth with PCO has little diagnostic value.

Patterson and Mitchell suggested that PCO is a pathological process and a potential focus of infection and should be treated with endodontic treatment or extraction (Patterson and Mitchell 1965). Rock and Grundy were also of the opinion that endodontic treatment should be commenced as soon as PCO is first seen in traumatised teeth (Rock and Grundy 1981). Their rationale was to avoid perforation during post preparation and to avoid the need for surgery. Subsequent publications have disputed this and there is now agreement that PCO is not a pathological response, prophylactic endodontic treatment is not appropriate and treatment should only be commenced where there are clear signs of pulp necrosis (Robertson et al. 1996). The consensus is that a diagnosis of pulp necrosis in teeth with PCO should primarily be based on a combination of the presence of a periapical radiolucency and confirmed by a negative response to EPT (Holcomb and Gregory 1967; Jacobsen and Kerekes 1977; Robertson et al. 1996; Oginni et al. 2009). Most recently, the European Society of Endodontology (ESE) published a position statement on the endodontic management of traumatised permanent teeth which supports this position (Krastl et al. 2021).

1.4.4 Treatment challenges

Pulp canal obliteration presents radiographically as a narrowed or nondiscernible pulp space (Jacobsen and Kerekes 1977; Oginni et al. 2009). Once a diagnosis of pulp necrosis is made, endodontic access presents further challenges. The American Association of Endodontists (AAE) recognise these challenges, classifying root canals that are indistinct or not visible as 'high difficulty' demonstrating that a predictable outcome will be challenging for even the most experienced clinicians (American Association of Endodontists 2019). There are cases where the canal cannot be successfully located (Patterson and Mitchell 1965; Schindler and Gullickson 1988). However, it should be remembered that while PCO may present radiographically with total obliteration of the pulp space, a canal will always be present histologically and a patent canal is often found clinically (Patterson and Mitchell 1965; Schindler and Gullickson 1988; Kuyk and Walton 1990). During endodontic access, the operator will not experience a sudden 'drop' into the pulp chamber and, if a traditional axis is continued, perforation will occur (Amir et al. 2001). Cvek and colleagues established that procedural errors, including perforation and instrument separation, during endodontic treatment of teeth with PCO secondary to trauma are common (Cvek et al. 1982). In fact, Kvinnsland and colleagues in their study of 55 root perforations found that 65% of perforations occurred while attempting to locate or negotiate calcified canals (Kvinnsland et al. 1989).

To avoid iatrogenic damage and successfully locate canals with PCO, systematic pre-operative planning and the basic principles of access cavity design and canal location as discussed in 'Traditional endodontic access cavity principles', section 1.2, should be applied. To reduce the risk of perforation when accessing anterior teeth, McCabe suggests a modified access with a more incisal approach, rather than the traditional lingual approach (McCabe 2006). Tertiary dentine covering the canal orifices may be identified by its whiter appearance compared to secondary dentine which is more yellow in colour (Patel and Rhodes 2007). Ultrasonics may be used with a gentle brushing action to remove the overlying dentine (Patel and Rhodes 2007). A DG-16 probe is an essential piece of armamentarium for the location of canal orifices and will "stick" in the pulp chamber floor if firmly probed where a canal orifice is present (Amir et al. 2001). The sodium hypochlorite "champagne bubble" test can also prove a useful tool to locate calcified canals (Berman and Hargreaves 2020).

Modern endodontic techniques, including the use of CBCT, the Dental Operating Microscope (DOM) and ultrasonic instrumentation, especially in combination,

allow successful location of calcified canals when performed by a specialist where conventional approaches have failed (Coelho De Carvalho and Zuolo 2000; Wu et al. 2011; Yang et al. 2016). In particular, the use of a DOM has been shown to be superior to the naked eye or loupes by providing greater magnification and lighting (Coelho De Carvalho and Zuolo 2000; Omergorduysus et al. 2001; Baldassari-Cruz et al. 2002; Buhrley et al. 2002; Schwarze et al. 2002; Wu et al. 2011; Yang et al. 2016). Notably, Schwarze et al. conducted an in vitro study and found that using the DOM resulted in a success rate for locating the mesio-buccal 2 (MB2) canal orifice more than twice as high when compared to loupes (93.7% vs. 41.3%) (Schwarze et al. 2002). In a clinical setting, endodontists were able to locate the MB2 canal in the maxillary first molar with frequencies of 71.1% using the DOM, 62.5% using loupes and 17.2% with no magnification (Buhrley et al. 2002).

Cone beam computed tomography in cases of PCO facilitates examination of the tooth in 3D, assisting with pre-operative planning. Cone beam computed tomography uses a fixed cone-shaped X-ray beam and detector which rotates around the region of interest (Whaites and Drage 2013). The acquired data is then reconstructed allowing cross-sectional images to be viewed in various anatomical planes (Whaites and Drage 2013). While CBCT is not routinely used in endodontics, the AAE and American Academy of Oral and Maxillofacial Radiology (AAOMR) joint position statement for use of CBCT in endodontics 2015 update, recommended limited FOV CBCT as the imaging modality of choice for treatment of teeth with suspected complex morphology (AAOMR 2015). The ESE position statement on the use of CBCT in endodontics supports this approach, recommending CBCT in cases where a conventional radiograph does not provide adequate information and where it is likely to assist diagnosis and treatment planning or clinical management, including for the location of extensively obliterated canals (Patel et al. 2019). The effective dose of CBCT varies but a small FOV for endodontic purposes has been reported to be as low as 7.3µSv (Patel 2009). However, the effective dose for a CBCT is greater than that of an intra-oral periapical and, as a result, every CBCT should be justified with the additional benefits outweighing the higher radiation exposure. Doses should be kept ALARA ('as low as reasonably achievable') by utilising a small FOV and voxel size in addition to a low mA setting and exposure time (AAOMR 2015; Patel et al. 2019).

Nonetheless, freehand (FH) canal location in cases of PCO can prove to be time consuming, even in the hands of a specialist. Kiefner et al. reported 7% of canals taking between 30 and 45 minutes and another 7% taking between 45 and 60 minutes to locate (Kiefner et al. 2017). In addition, while these studies demonstrate the ability of a specialist to consistently locate calcified canals, they fail to consider the amount of dentine removal during FH canal location.

Although a historic study, the success rate of endodontic treatment on teeth with PCO, when procedural errors are excluded, has been reported to be equivalent to teeth without PCO (Cvek et al. 1982). Akerblom and Hasselgren found the overall success based on clinical and radiographic examination to be 89%, but 62.5% in teeth with a preoperative radiolucency (Akerblom and Hasselgren 1988). A more recent study found a success rate, based on radiographic follow-up only, of 80% after 3 years following endodontic treatment of calcified teeth in their elderly study population (Kiefner et al. 2017). However, where procedural errors occur, Cvek identified a significant detrimental impact on the success of endodontic treatment (Cvek et al. 1982). This agrees with more recent studies which have shown an impact on both success and tooth survival (Ng et al. 2011b; Ng et al. 2011a). Nevertheless, a systematic review has demonstrated that non-surgical perforation repair has a success rate of over 70% (Siew et al. 2015). Overall, endodontic treatment of teeth with PCO appears to have a reasonable outcome when performed by the most experienced operators using a DOM.

Guided endodontics technology may be employed to enhance canal location in cases that present with PCO, allowing dentine preservation. GE will be explored in the following section.

1.5 Guided endodontics

1.5.1 Background

Guided endodontics for location of root canals is a relatively new concept, first described in 2015 and formally named in 2016 (Zubizarreta-Macho et al. 2015; Krastl et al. 2016; Zehnder et al. 2016). Guided endodontics enables MIE access while reducing the risk of procedural errors and enhancing efficiency in challenging cases, such as PCO. Originating from the success in guided implantology, this technique encompasses both Static Navigation (SN) and DN. A prerequisite for GE is a high-resolution CBCT and a Stereolithography (STL) file, often obtained from a digital surface scan. The ESE position statement on the use of CBCT in endodontics recognises the use of CBCT in GE (Patel et al. 2019). However, due to the increased radiation dose of CBCT compared to plain film, GE should be limited to challenging endodontic cases where FH access carries a risk of significant tooth structure loss or iatrogenic damage. A small FOV and voxel size are recommended to minimise the effective dose while improving spatial resolution (Patel et al. 2019). The literature would suggest that the FOV and voxel size do not have a significant impact on the accuracy of GE (Wang et al. 2023; Martinho et al. 2024a). Navident's user manual suggests a maximum voxel size of 400µm (ClaroNav 2021). Digital Imaging and Communications in Medicine (DICOM) is the standard file format used for CBCT data. The DICOM file is segmented and aligned with the STL file using reference landmarks on appropriate implant planning software (Leontiev et al. 2022). An ideal endodontic access cavity is virtually planned by setting the target point, the point at which the canal first becomes visible, and virtual drill path all while maintaining centrality within the root. Where canal curvatures are present, guided access is limited to the first curvature within the straight portion of the canal (Connert et al. 2018). Small diameter drills are used, typically no greater than 1mm diameter (Kinariwala and Samaranayake 2021). The virtual plan is implemented through the use of SN using a 3D printed guide or DN using realtime guidance via a stereoscopic camera.

The effectiveness, accuracy, tooth structure removal and efficiency of SN and DN will be explored through a review of existing literature, which includes case reports, case series, ex vivo and in vitro studies. The majority of the research in

this area is derived from in vitro studies using 3D printed teeth (Kulinkovych-Levchuk et al. 2022; Martinho et al. 2022).

1.5.1.1 Endodontic applications of GE

While this thesis focuses on GE for the location of root canals, it should be mentioned that GE does have a range of applications with the field of endodontology. Its success has been demonstrated by laboratory studies, case reports and case series in endodontic microsurgery (Pinsky et al. 2007; Giacomino et al. 2018; Gambarini et al. 2019; Dianat et al. 2021b), fibre post removal (Bardales-Alcocer et al. 2021; Janabi et al. 2021; Alfadda et al. 2022) and post space preparation (Martinho et al. 2024c; Shervani et al. 2024). However, it is not suitable for all endodontic applications. A single study reported on the use of GE for retrieval of separated endodontic files, but found the microscope-guided group to have a greater success, efficiency, fewer deviations and reduced tooth volume loss than that of the DN group (Karim and Faraj 2023).

1.5.2 Static navigation

1.5.2.1 Guide construction

Static navigation for location of root canals utilises Computer-Aided Design and Computer-Aided Manufacturing (CAD/CAM) technology. This involves a 3-stage process: (1) data acquisition, (2) data processing and (3) manufacturing (Van Noort 2012). Data is acquired from a CBCT and digital surface scan, as described in the previous section (1.5.1). Computer-aided design is used to design the guide ensuring support from adjacent teeth and a matching drill sleeve to guide the position and angulation of the bur. Computer-aided manufacturing uses either additive or subtractive techniques. Additive manufacturing, also known as '3D printing', is predominantly used for creating endodontic guides. The process involves incremental deposition of material layer upon layer to create a 3D object (Anderson et al. 2018; Reis et al. 2022). Various 3D printing technologies exist, including Stereolithography (SLA), digital light processing, fused deposition modelling, MultiJet printing, PolyJet printing, ColourJet printing and selective laser sintering. Stereolithography is the most commonly used technology and involves a bath of Ultraviolet (UV) sensitive liquid resin and a UV laser which

selectively and sequentially cures the material within each cross-section, typically 25-100 micrometre (µm) thickness, printing the object layer-by-layer (Anderson et al. 2018; Reis et al. 2022). After printing, the object undergoes postprocessing, which involves rinsing to remove any liquid resin, followed by post-curing to polymerise any uncured resin (Van Noort 2012; Kinariwala and Samaranayake 2021).

1.5.2.2 Procedural steps

The SN procedure begins with multi-tooth rubber dam isolation to allow seating of the guide. It is crucial to test the guide for stability prior to commencing access to ensure the planned access is accurately reproduced and to avoid procedural errors (Leontiev et al. 2022). It is advisable to mark the starting point of the access through the guide with a bur and initiate FH access preparation through enamel, without the guide (Leontiev et al. 2022). Once the dentine is reached, the guide should be placed and guided access commenced with an intermittent drilling technique and copious water coolant to avoid over-heating (Leontiev et al. 2022). In certain cases, the drill path may be shorter than the radiographic obliteration length and, therefore, an attempt to scout the root canal space should be performed when half the planned length is reached. If the canal is not found, a check radiograph may be taken. Guided access is continued until the bur contacts the sleeve, indicating that the planned depth has been achieved. It should be acknowledged that a limitation of SN is the inability to alter the planned access during treatment. Once the canal is located, the guide may be removed and chemo-mechanical preparation commenced.

1.5.2.3 Case reports and case series

Case reports and case series have confirmed the successful clinical application of SN for root canal location in single rooted teeth. The first publication was a single case report by Zubizarreta-Macho and colleagues demonstrating successful completion of a conservative access on a maxillary lateral incisor with Dens Invaginatus (Zubizarreta-Macho et al. 2015). Stainless steel sleeves with 1.3mm internal diameter were utilised, along with a diamond bur with a 1.2mm diameter. Krastl and colleagues were the first to publish the use of SN in a case of PCO (Krastl et al. 2016). At that time, guided endodontic drill sleeves and

matching drills were unavailable, so implant drills and sleeves with a larger diameter of 1.5mm were used. An attempt to locate the canal was performed after each 2mm depth progression and the canal was successfully located 1mm before the target depth. Subsequent to these first publications, multiple authors have demonstrated successful and conservative access using SN in single rooted teeth with PCO using a similar approach (van der Meer et al. 2016; Connert et al. 2018; Fonseca Tavares et al. 2018; Lara-Mendes et al. 2018b; Buchgreitz et al. 2019; Hegde et al. 2019; Torres et al. 2019; Ishak et al. 2020; Llaquet Pujol et al. 2021; Todd et al. 2021; Dąbrowski et al. 2022). The most extensive case series was published by Buchgreitz et al. who presented fifty consecutive clinical cases of SN for canal location in single rooted teeth, the majority presenting with PCO. Location of the canal was achieved in all cases (Buchgreitz et al. 2019). Similarly, Llanquet Pujol et al. presented seven consecutive cases of PCO all successfully accessed with SN (Llaquet Pujol et al. 2021). More recent cases have used smaller diameter burs (<1mm) and sleeves, often specifically designed for endodontics and sometimes custom made, to produce a more conservative access (Connert et al. 2018; Torres et al. 2019; Ishak et al. 2020; Llaquet Pujol et al. 2021). The successful use of SN has also been demonstrated in cases of PCO with previous iatrogenic damage, including root perforations. For example, Loureiro and colleagues published a case of a maxillary central incisor with PCO into the apical third presenting with a middle third root perforation created during previous failed attempts at canal location. They successfully repaired the perforation and located the true root canal, demonstrating a satisfactory outcome at six-month follow-up (Loureiro et al. 2021). Similarly, Casadei et al. demonstrated successful canal location using SN on an upper premolar following a previous deviation from the true root canal and apical perforation (Casadei et al. 2020).

1.5.2.4 Accuracy of canal location

Buchgreitz and colleagues in 2016 were the first to publish a study on the use of SN for the location of root canals and considered it to be a promising technology, particularly for PCO (Buchgreitz et al. 2016). This was closely followed by Zehnder et al. who's ex vivo study confirmed SN could be used to accurately locate canals in the apical third of the root with low deviations between the planned and prepared access, when performed by experienced

operators (Zehnder et al. 2016). They utilised single rooted human extracted teeth and demonstrated a mean horizontal deviation between the planned and prepared access cavities at the tip of the bur of 0.29mm (range 0-1.34mm) in a mesial-distal direction and 0.47mm (range 0-1.59mm) in a buccal-palatal direction with a mean angular deviation of 1.81°. Similar results were observed in research conducted by Connert and colleagues who found low mean linear deviations of 0.14mm in a mesial-distal direction, 0.34mm in a buccal-palatal direction and 0.12mm in an apical-coronal direction with a mean angular deviation of 1.59° when using SN in extracted human teeth (Connert et al. 2017). The same group have published an in vitro study comparing SN to FH access cavity preparations on 3D printed anterior teeth with simulated calcified root canals where the orifice was located 5mm from the apex (Connert et al. 2019). This was the first study to use SN for location of canals in teeth with PCO. They found that SN significantly increased the predictability of canal location when compared to FH with 41.7% versus 91.7% of canals being identified. Unlike earlier studies, they assessed tooth volume loss rather than linear deviation establishing that SN resulted in significantly less tooth structure removal with a mean tooth structure loss of 9.8mm³ versus 49.9mm³. In addition, these studies have consistently shown that while FH access is related to the operator's experience, SN is not influenced by the operator (Zehnder et al. 2016; Connert et al. 2017; Connert et al. 2019). Connert et al. found that the success rate of canal location in 3D printed teeth with PCO for their inexperienced operator (new dental school graduate) was 0/8 using FH, compared to 8/8 using SN (Connert et al. 2019). Although the experienced and specialist operators also benefitted from SN, the improvement was less pronounced. Moreover, a single study has demonstrated that SN performed on extracted incisors and canines by a general dentist was comparable to FH access performed by an Endodontist, in terms of tooth volume loss and time (Hildebrand et al. 2023). Taken together, these findings suggest that SN is beneficial for operators of all levels of experience, but is particularly beneficial for those with less experience in complex endodontics.

While the majority of studies on the use of SN for canal location involve single rooted anterior teeth, SN has been used in multi-rooted teeth. A systematic review of SN up to July 2022, reported that despite some studies including

posterior teeth, most studies focus on anterior teeth (Peña-Bengoa et al. 2023). Loureiro and colleagues in their ex vivo study demonstrated a greater benefit of SN in molars compared to incisors. Mean volume loss was significantly less using SN compared to FH access in molars (45.7mm³ vs 62.5mm³), while in incisors there was no significant difference when performed by an experienced endodontist (Loureiro et al. 2020). This perhaps reflects the more challenging nature of molar endodontic access, again, demonstrating the benefits of SN even for experienced clinicians. These findings from Loureieo et al. parallel those reported by Kostunov et al. who found the mean tooth volume loss to be almost half following SN when compared to FH (51.8 mm³ vs. 99.3 mm³), with a greater benefit demonstrated in molars compared to premolars and incisors (Kostunov et al. 2021). Nonetheless, the mean linear and angular deviation has been found to be significantly higher in molars compared to all other tooth types, 0.64mm and 4.00° respectively (Su et al. 2021). The authors suggested the lack of interocclusal space in the molar region may have resulted in interference between the handpiece and opposing teeth. However, Haarmann and colleagues found the opposite to be true, where molars demonstrated reduced linear and angular deviation when compared to premolars (Haarmann et al. 2023). Angular and linear deviations at the tip of the bur in molars were 1.34°, 0.30mm (mesiodistal) and 0.27mm (bucco-lingual), thus demonstrating greater accuracy than the study by Su et al. (2021). Further research is required to establish the accuracy of SN in molar teeth.

1.5.2.5 Efficiency of canal location

Efficiency is an important consideration for SN, yet few studies report procedural time. Connert et al. reported the time required for each workflow step and as well as the total time (Connert et al. 2017). While access cavity preparation took on average 30 seconds (s), the whole treatment time including the surface scan and digital planning took over 10 minutes per tooth when performed by operators highly experienced in GE. Their subsequent study compared SN and FH access and found SN was more efficient, reducing average access cavity preparation time by almost half (11.3 minutes vs. 21.8 minutes) across three operators with a range of experience, although there was no mention of planning time (Connert et al. 2019). Hildebrand reported an average access time of 4.4 minutes when performed by a general dentist (Hildebrand et

al. 2023). Few case reports and case series report on the time taken for endodontic access. Dąbrowski et al. reported that their first case took 50 minutes, while their consecutive three cases took 10, 15 and 10 minutes from the point of administration of local anaesthetic to confirming of the working length (Dąbrowski et al. 2022). This demonstrates a high level of efficiency and minimal learning curve required for SN.

1.5.2.6 Limitations and failure

The problem of inter-occlusal space, especially in the posterior region, has already been touched upon. This limitation is acknowledged in multiple publications recognising that the inter-occlusal space required for accommodation of the guide and endodontic drills can be problematic, especially in patients with limited mouth opening (Connert et al. 2017; Connert et al. 2018; Lara-Mendes et al. 2018a). Another limitation identified in the literature is the access of multi-rooted teeth where multiple guides may be required, significantly increasing the cost (Loureiro et al. 2020). To negate this limitation, some case reports on multi-rooted teeth have reserved the guide for location of the most challenging canal (Lara-Mendes et al. 2018a; Maia et al. 2019). Although other case reports have accessed multiple canals using SN in multi-rooted teeth, they have failed to describe the guide design (Krug et al. 2020). Shi and colleagues designed a sleeveless guide allowing the location of all canals with a single guide (Shi et al. 2018). However, they performed the entire access with an ultrasonic, which would not be practical in most cases of PCO due to the time-consuming nature of the process and significant heat generation. Excessive heat generation, which can be harmful to the periodontal ligament and alveolar bone, should be considered with all cases of SN due to limited space for the passage of irrigants within the sleeve (Moreno-Rabié et al. 2020).

Despite most publications demonstrating significant success with SN, it should be acknowledged that SN can also fail, potentially resulting in iatrogenic damage. Tavares presented a case with deviation of the prepared access from the planned access resulting in an apical root perforation and the need for corrective endodontic microsurgery (Tavares et al. 2022). While the reason for the failure was uncertain, it was assumed to be as a result of design inaccuracies and failure to verify the fit and stability of the guide prior to commencing

access. In addition, the in vitro pilot study published by Kostunov demonstrated two perforations within the SN group, compared to no perforations within the FH group (Kostunov et al. 2021). They suspected that this was due to movement of the guide or bur during treatment. Errors may occur at each stage of the process, which can have a compounding effect. However, in context, a systematic review revealed only 2 of 43 studies reported accidents or failures, demonstrating that such events are rare (Peña-Bengoa et al. 2023).

1.5.2.7 **Summary**

In summary, ex vivo and in vitro studies, along with case reports and case series, demonstrate safe, reliable, accurate and efficient use of SN in challenging endodontic situations. However, it must be acknowledged that the level of evidence is low. Care is necessary during the design, manufacture and use to avoid errors. Several limitations have been acknowledged, including the need for adequate inter-occlusal space, multiple guides for multi-rooted teeth, potential lack of adequate cooling and the inability to alter the planned access during treatment. Dynamic navigation addresses these technical limitations.

1.5.3 Dynamic navigation

The application of DN in endodontics was first described in an in vitro study published in 2019 (Chong et al. 2019). While DN is relatively new in the field of endodontics, it is not a novel concept. In fact, it was first described in neurosurgery almost 40 years ago and was referred to as 'Neuronavigation' (Enchev 2009). Dynamic navigation provides real-time guidance using an optical tracking system. Common systems for DN, originally developed for guided implant placement, include Navident (ClaroNav, Toronto, Canada) and X-Guide (X-Nav Technologies, Lansdale, PA, USA).

In contrast to SN, no physical guide is required allowing for intra-operative adjustments, application in cases of limited inter-occlusal space and improved irrigation (Dianat et al. 2021a; Wu et al. 2022). Dynamic navigation also opens up the possibility of same-day treatment which is particularly useful in cases of acute symptoms (Stefanelli et al. 2020; Dianat et al. 2021a; Wu et al. 2022).

However, while the cost per procedure is reduced, the initial investment in the DN system (DNS) is high.

1.5.3.1 Procedural steps

Dynamic navigation should be performed as per the manufacturer's instructions, which typically involves four main steps: scan, plan, register and treat (ClaroNav 2021). The first two steps have already been covered. For registration, optically marked tags are attached to the patient ('Jaw Tracker' or 'Head Tracker') and handpiece ('Drill Tag') allowing the camera to track their relative positions. There are four registration methods available, one of which is called 'Trace Registration'. Trace registration matches the CBCT with the patient by selecting three or more visible landmarks on the CBCT and tracing these on the patient. The handpiece and drill tip are calibrated using the Calibrator tool. Optical triangulation of the optically marked tags on the patient and handpiece with the stereoscopic camera produce a real-time image of the handpiece head and tip of the bur superimposed over the CBCT on the monitor. This allows the operator to follow the displayed target in real-time during access preparation, providing live feedback on the location, angulation and depth of the bur. This is something of a departure from normal clinical practice, as the operator looks at the screen rather than the patient.

1.5.3.2 Accuracy of canal location

The study of the accuracy of DN for root canal location is an emerging area of research, particularly for teeth with PCO. It is crucial to study since, as described in section 1.4.4, FH endodontic access on teeth with PCO is exceedingly difficult and is fraught with challenges including the risk of procedural errors. Notably, none of the studies described in section 1.4.4 investigated dentine removal following FH access in teeth with PCO, an important factor which may affect the tooth's fracture resistance, as discussed in section 1.3.2. An initial literature review of DN revealed few studies and an absence of systematic reviews exclusively on teeth with PCO. Therefore, a systematic review was performed to analyse the existing literature and identify research gaps on the accuracy of DN for root canal location in teeth with PCO

when compared to FH and SN. The systematic review is presented in the next chapter.

Chapter 2 Accuracy of dynamic navigation for locating canals in teeth with pulp canal obliteration: A systematic review

2.1 Introduction

Pulp canal obliteration occurs due to the deposition of hard tissue within the root canal system. Pulp canal obliteration is a frequently seen in dental trauma, heavily restored teeth and as a physiological response in older patients (Andreasen et al. 1987; Carvalho and Lussi 2017; Fleig et al. 2017). Endodontic access on teeth with PCO is challenging and time consuming requiring a high degree of expertise and experience (Kiefner et al. 2017; American Association of Endodontists 2019). Freehand access cavity preparations may result in excessive tooth structure removal, compromising the structural integrity of the tooth. Additionally, FH access in teeth with PCO has been shown to carry a high risk of procedural errors including file fracture and perforation significantly increasing the risk of post treatment disease (Cvek et al. 1982).

Guided endodontics is a relatively new concept in endodontics with the use of this terminology first introduced in 2016 (Zehnder et al. 2016). It allows virtual planning using a CBCT scan and digital surface scan on appropriate software. The virtual plan may be implemented through the use of SN using a 3D-printed stent or DN using real-time visualisation of the drill position and angulation through tracking the movements of the handpiece and patient using motion-tracking cameras (Zehnder et al. 2016; Chong et al. 2019).

In vitro studies using DN for canal location in human and 3D-printed teeth without PCO have demonstrated a high success rate (Chong et al. 2019; Gambarini et al. 2020; Zubizarreta-Macho et al. 2020). Dynamic navigation has been shown to have a greater accuracy than FH with significantly less linear and angular deviation from the planned access (Gambarini et al. 2020; Zubizarreta-Macho et al. 2020). This is likely to increase the conservation of tooth structure and reduce the risk of procedural errors. Dynamic navigation and SN have been shown to have no significant difference in their accuracy of canal location (Zubizarreta-Macho et al. 2020). The procedural time for DN and FH is reported to be similar (Gambarini et al., 2020).

There are a limited number of published systematic reviews on the use of DN in non-surgical endodontics. While they provide information on the overall accuracy of DN, none focus exclusively on teeth with PCO (Zubizarreta-Macho et al. 2021; Jonaityte et al. 2022; Vasudevan et al. 2022; Mekhdieva et al. 2023). It is uncertain whether the success and improved accuracy of the DN extends to endodontic access in teeth with PCO, which present a higher degree of difficulty. Further investigation is warranted to guide clinicians in the management of non-surgical endodontics in teeth with PCO. The aim of this systematic review was to analyse the available literature on the accuracy of DN for root canal location in teeth with PCO when compared to FH and SN.

2.1.1 Objectives

The objective of this systematic review was to assess the accuracy of canal location using DN in teeth with PCO when compared to SN and/or FH access. The PICO elements are listed below.

Population = teeth with PCO

Intervention = endodontic access using a DNS

Comparison = FH access and/or SN

Outcome = accuracy of canal location

2.2 Methods

This systematic review was conducted and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al. 2021). The protocol was conducted according to PRISMA-P (for protocols) guidelines (Shamseer et al. 2015) and registered with the PROSPERO (International prospective register of systematic reviews) under registration number: CRD42023401261. There were no amendments to the protocol following registration.

2.2.1 Eligibility criteria

Studies were selected according to the following inclusion criteria: (i) 3D-printed or human teeth with PCO; (ii) endodontic access performed using a DNS; (iii) comparison to FH and/or SN; (iv) randomised controlled trials, controlled trials, in-vitro studies, case series (of at least 10 cases). Non-randomised studies were included since it was anticipated that these would form the majority of the current evidence base due to the relatively recent introduction of DN in endodontics. There were no restrictions applied to outcomes of interest, date of publication or publication status. Exclusion criteria were: (i) non-English language.

2.2.2 Information sources

Two independent reviewers searched the following electronic databases from inception: Embase (Ovid interface), MEDLINE (Ovid interface) and The Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley interface). The WHO International Clinical Trials Registry Platform (ICTRP) and ClinicalTrails.gov trial registries were searched. Hand searching was performed of the International Endodontic Journal (IEJ) and Journal of Endodontics (JOE) by manually screening the contents pages of each published issue on the publisher's website. The hand searching of the IEJ and JOE was restricted to publications from January 2019 given that the first cited paper on DN in endodontics was published in March 2019. Conference proceedings from the ESE congresses since 2019 were searched by screening published abstract booklets published on the congress website. The manufacturers of Navident and X-Guide were contacted to request any unpublished experimental data. Databases, trial registries, journals and conference proceedings were last searched on 31 March 2023. Reference searching was subsequently undertaken by manually screening the reference list of eligible studies. Citation searching of eligible studies was undertaken on 19 April 2023 using the Web of Science platform.

2.2.3 Search strategy

The search strategies were developed by two independent reviewers (H.B. and D.R.). The search strategies for the electronic databases are listed in

Table 2-1. The search was peer reviewed by a librarian not associated with the project by using the Peer Review of Electronic Search Strategies (PRESS) 2015 guideline (McGowan et al. 2016). Trial registries were searched using the advanced search function and the terms 'pulp canal obliteration' and 'dynamic navigation'. No limits on date or language were applied to the searches.

Table 2-1 - Electronic database searches.

Search strategy for MEDLINE (Ovid interface):

- Dental pulp calcification/
- 2. ((canal* adj4 (calcifi* or obliterat* or scleros*)) or (Pulp* adj3 (calcifi* or obliterat* or scleros*)) or Calcific metamorphosis).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- Surgery, Computer-Assisted/
- 4. ((Dynamic* adj2 (navigat* or guide*)) or (Navigat* adj2 (system* or access*)) or (Guided adj2 (endodontic* or access*)) or Image-guided or Real-time tracking or (Computer adj1 (assisted or aided)) or X-Guide or Navident).mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]
- 5. 1 or 2
- 6. 3 or 4
- 7. 5 and 6

Search strategy for Embase (Ovid interface):

- ((canal* adj4 (calcifi* or obliterat* or scleros*)) or (Pulp* adj3 (calcifi* or obliterat* or scleros*)) or Calcific metamorphosis).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
- 2. surgical navigation system/ or computer assisted surgery/
- 3. ((Dynamic* adj2 (navigat* or guide*)) or (Navigat* adj2 (system* or access*)) or (Guided adj2 (endodontic* or access*)) or Image-guided or Real-time tracking or (Computer adj1 (assisted or aided)) or X-Guide or Navident).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword heading word, floating subheading word, candidate term word]
- 4. 2 or 3
- 5. 1 and 4

Search strategy for CENTRAL (Wiley interface):

- 1. Dental pulp calcification
- 2. (canal* near/4 (calcifi* or obliterat* or scleros*)) or (Pulp* near/3 (calcifi* or obliterat* or scleros*)) or Calcific metamorphosis
- 3. Surgery, computer-assisted
- (Dynamic* near/2 (navigat* or guide*)) or (Navigat* near/2 (system* or access*)) or (Guided near/2 (endodontic* or access*)) or Image-guided or Real-time tracking or (Computer near/1 (assisted or aided)) or X-Guide or Navident
- 5. #1 or #2
- 6. #3 or #4
- 7. #5 and #6

2.2.4 Selection process

Covidence systematic review software (Covidence, Melbourne, Australia) automatically removed duplicate records. Initial screening of titles and abstracts against the eligibility criteria was undertaken by two independent reviewers (H.B and W.M.) facilitated by Covidence. Any disagreements were identified by Covidence and resolved through discussion between H.B. and W.M. Full papers were obtained for those meeting the eligibility criteria. Two reviewers (H.B and D.R.) independently performed full text screening for inclusion using Covidence. The justification for any excluded papers was documented.

2.2.5 Data collection process and data items

Data extraction was carried out manually by a single reviewer (H.B.) with verification by another reviewer (D.R.) using a predetermined standardised data extraction form created in Covidence using the headings listed under 'data items' below. No contact with study investigators was required to confirm relevant data. The data extraction form was piloted by three independent individuals, one reviewer (H.B.) and two other individuals not associated with the project, on a small sample of studies prior to implementation.

The following data items were extracted from included studies: (i) study characteristics: title of article, journal, first author, year of publication, funding sources, conflicts of interest; (ii) methods: study design, sample size (total and per method), type of tooth (human or 3D-printed / incisor or canine or premolar or molar / maxilla or mandible / jaw material), degree of PCO (distance in mm measured from either the incisal edge, CEJ or apex), DNS, comparison group (FH and/or SN), details of CBCT, details of optical scanner, planning software, handpiece and bur used, number of operators and level of experience, details of training undertaken on DNS; (iii) outcomes: coronal linear deviation (mm), apical linear deviation (mm), angular deviation (°), incidence of successful canal location (n), incidence of perforation (n), tooth structure removal (mm³), time (s), other outcomes, key conclusions. Successful canal location was defined by the authors as location of the canal in the absence of a perforation. All results compatible with each outcome were recorded. None of the included studies report on all the above methods and outcomes and therefore 'not reported' (NR)

was recorded where appropriate. Alternative outcomes not previously considered by the authors were listed under 'other outcomes'.

2.2.6 Study risk of bias assessment

Risk of bias at a study level was assessed using a modified JBI checklist for quasiexperimental studies (non-randomized experimental studies) (Joanna Briggs Institute 2020). According to Vasudevan et al., the JBI checklist is modified by removing the 'follow up' domain which is irrelevant to in-vitro studies (Vasudevan et al. 2022). A total of eight domains, listed in Table 2-2, were assigned a 'low' or 'high' risk of bias judgement or 'unclear' where there was insufficient information reported to make a judgement. This assessment was undertaken independently by two reviewers (H.B. and D.R.) and subsequently any disagreements were resolved through discussion. Both assessors are experienced researchers in the field and have participated in training in carrying out systematic reviews. The reviewers were not blinded to the study being assessed. Each domain was considered independently in addition to determining an overall risk of bias judgement. The overall score was determined by calculating the percentage of 'low' risk of bias domains and using a classification previously described by Vasudevan et al. with high risk of bias scoring <50%, moderate risk 50-69% and low risk >70% (Vasudevan et al. 2022).

Table 2-2 - Eight domains within the modified JBI checklist.

- 1. Is it clear in the study what is the 'cause' and what is the 'effect'?
- 2. Were the participants included in any comparisons similar?
- 3. Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?
- 4. Was there a control group?
- 5. Were there multiple measurements of the outcome both pre and post the intervention/exposure?
- 6. Were the outcomes of participants included in any comparisons measured in the same way?
- 7. Were outcomes measured in a reliable way?
- 8. Was appropriate statistical analysis used?

2.2.7 Synthesis methods

A preliminary evaluation of the included studies revealed the presence of heterogeneity and therefore it was not appropriate to undertake meta-analysis. Extracted data was summarised for all included studies using summary tables

presenting all data items in order of study characteristics, methods and outcomes predefined in the methods. A separate narrative synthesis of quantitative data explores and interprets study findings and relationships and is presented as recommended by published guidance on narrative synthesis in systematic reviews (Popay et al. 2006).

2.3 Results

2.3.1 Study selection

The PRISMA flow diagram is shown in Figure 2-1. Initial searches identified 250 articles. After automatic removal of 70 duplicates by Covidence, 180 were available for title and abstract screening. Six articles were selected for full-text screening. One article (Buchgreitz et al. 2019) was excluded due to the wrong intervention (SN rather than DN) and 2 articles (Jain et al. 2020a; Torres et al. 2021) were excluded due to the lack of a comparison group. Three articles were eligible for inclusion.

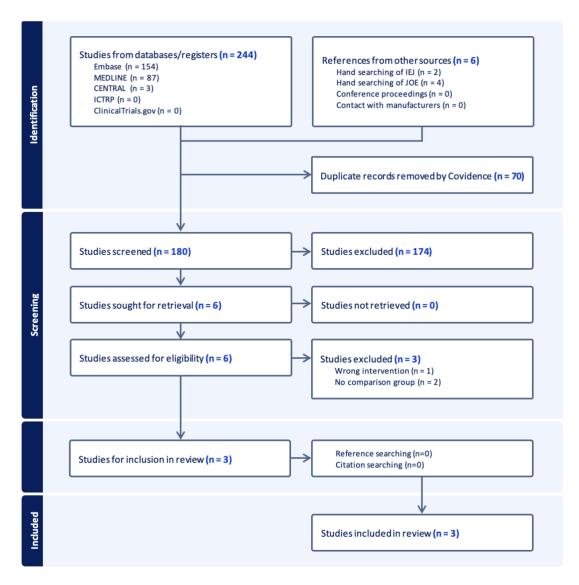


Figure 2-1 - PRISMA 2020 flow diagram. Illustrates the number of studies identified, screened and included in the systematic review.

2.3.2 Study characteristics

The characteristics and methods of the included studies are detailed in Table 2-3 and Table 2-4. The three included studies were all in-vitro studies published in 2020 and 2021 in the JOE. Two studies (Dianat et al. 2020; Jain et al. 2020b) were supported by a research grant and there were no conflicts of interest reported. A total of 172 teeth were included. All teeth were single rooted incisors, canines or premolars. Dianat et al. (Dianat et al. 2020) used extracted human teeth placed in dry cadaver jaws while Jain et al. (Jain et al. 2020b) and Connert et al. (Connert et al. 2021a) used 3D-printed teeth. The degree of PCO differed between studies with Dianat et al. (Dianat et al. 2020) selecting teeth with varying PCO levels of ≥ 9 mm from the incisal edge or occlusal plane while

Jain et al. and Connert et al. simulated a fixed level of PCO; 16mm from the incisal edge for maxillary central incisors (Jain et al. 2020b), 13mm from the incisal edge for mandibular central incisors (Jain et al. 2020b) and 2mm below the lowest point of the CEJ (Connert et al. 2021a). Studies used X-Guide, Navident and DENACAM DNS compared to FH. None of the studies compared DN to SN. All studies used a limited FOV CBCT with a voxel size ranging from 75-125µm. Two studies assessed the impact of operator experience by including two operators with varying levels of experience in endodontics (Dianat et al. 2020; Connert et al. 2021a). Only Dianat et al. reported training on the DNS prior to the experiment (Dianat et al. 2020).

Table 2-3 - Characteristics of included studies.

	Title, journal, first author, year of publication	Funding sources	Conflicts of
			interest
1 (Dianat et al. 2020)	Dianat et al. 2020. Accuracy and Efficiency of a Dynamic Navigation System	Research grant from the Foundation for	No
	for Locating Calcified Canals. JOE	Endodontics	
2 (Jain et al. 2020b)	Jain et al. 2020. Dynamically Navigated versus Freehand Access Cavity	Virginia Commonwealth University School of	No
,	Preparation: A Comparative Study on Substance Loss using Simulated	Dentistry faculty grant (Sameer D. Jain) and	
	Calcified Canals. JOE	the AAE Foundation for Endodontics	
3 (Connert et al. 2021a)	Connert et al. 2021. Real-Time Guided Endodontics with a Miniaturized	No	No
	Dynamic Navigation System Versus Conventional Freehand Endodontic		
	Access Cavity Preparation: Substance Loss and Procedure Time. JOE		

Table 2-4 - Methods of included studies.
(IV = in-vitro, NR = not reported, CBCT = Cone Beam Computed Tomography, FOV = field of view)

	Study	Sample	Type of	Jaw	Degree of	DNS	Comparis	Details of CBCT	Details of	Planning	Handpiece	Number of	Details of
	design	size	tooth	material	PCO		on		optical	software	and bur	operators	training
									scanner			and level of	undertaken
												experience	on DNS
1	IV	60;	Human	Dry	2	X-Guide	FH	Single-arch	NR	X-Guide	Round	2;	40 teeth
			maxillary	cadaver	categories:	(X-Nav)		CBCT scan (CS		software	diamond bur		without
		30 DN,	and	maxillae	9-13 mm			9300;		(X-Nav)	using a high-	Operator 1 =	canal
	30 FH	,	mandibular		and >13 mm			Carestream LLC,			speed	A board-	calcifications
		30 111	single		from the						handpiece	certified	
			_									certified	

		rooted incisors, canine and premolars	and mandibles	incisal edge/occlus al plane			Atlanta, GA), 90μm voxel size			followed by a size #1 (0.8 mm) Munce bur using a	endodontist (A.N.) Operator 2 = A third-year	(20 per operator)
										slow-speed handpiece at 5000 RPM	endodontic resident (O.D.)	
2 IV	40; 20 DN, 20 FH	3D-printed maxillary and mandibular incisors	ModuPRO Endo model (Acadental , OverlandP ark, KS)	Maxillary central incisors 16mm from the incisal edge, mandibular central incisors 13mm from the incisal edge	Navident (ClaroNav)	FH	Limited FOV CBCT scan (CS 8100 3-Dunit; Carestream Health Inc, Rochester, NY), 60-kV peak, 2.0 mA, 15.0s, 75µm voxel size	NR	Navident software (ClaroNav)	A surgical length #2 round bur (Coltene), an 859 FGSL bur (Komet), and an EndoZ bur (Dentsply Sirona) using a high-speed handpiece	1; Second-year endodontic resident	NR
3 IV	72;	3D-printed maxillary	NR	2mm below the lowest	DENACAM (Mininavid ent AG)	FH	Accuitomo 170 (Morita Manufacturing Corp, Kyoto,	TRIOS 3 (3Shape A/S, Copenhag	coDiagnost iX (Dental Wings)	A standard cylindrical diamond bur with a	2; Operator 1 = 12 years of	NR

36 D	DN,	incisors and	point of the		Japan), 6x6cm	en,	diameter of	professional	
36 F	FH	canines	CEJ		FOV, 90 kV, 6	Denmark)	1.0 mm	experience	
					mΑ, 125μm		(Intensiv SA)	in the field	
					voxel size		using a	of	
							contra-angle	endodontics	
							handpiece		
							(T1 Classic S	Operator 2 =	
							200 L;	2 years of	
							Dentsply	professional	
							Sirona)	experience	
								in the field	
								of	
								endodontics	
								chaodontics	

2.3.3 Risk of bias in studies

Overall, two studies (Jain et al. 2020b; Connert et al. 2021a) were judged as low risk of bias while one (Dianat et al. 2020) was judged to have a moderate risk of bias. Details of the risk of bias according to the modified JBI checklist are detailed in Figure 2-2 and Figure 2-3. The reviewers had some concerns over Dianat et al. attributable to differences in baseline levels of PCO and different end-points used for DN and FH when measuring access time (Dianat et al. 2020). All three studies failed to adequately describe or quantify the reliability of the outcome assessors due to a lack of information on assessor training and reliability coefficients and hence it was judged unclear if outcomes were measured in a reliable way. Both Connert et al. and Jain et al. failed to include a sample size calculation and, while the statistical test was stated, it was not clear if the data was tested for normality and therefore it was unclear if the test was appropriate (Jain et al. 2020b; Connert et al. 2021a).

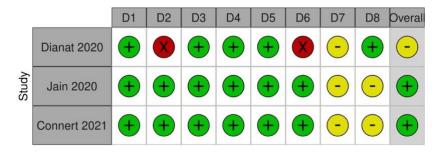


Figure 2-2 - Risk of bias traffic light plot.

This figure presents the risk of bias for each domain and overall for each study, assessed using the modified JBI checklist. Risk of bias judgements were categorised as follows: [+] low risk of bias, (-) unclear risk of bias, (X) high risk of bias.

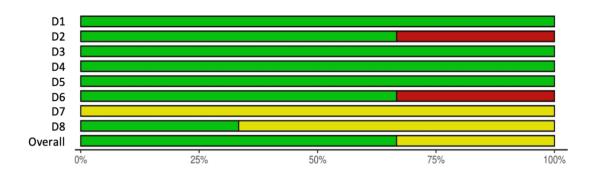


Figure 2-3 - Risk of bias summary plot.

This figure summarises of the risk of bias for each domain within the modified JBI checklist.

Risk of bias judgements were categorised as follows: (+) low risk of bias, (-) unclear risk of

bias, (x) high risk of bias.

2.3.4 Narrative synthesis

A summary of the reported outcomes is listed in Table 2-5 and are explored and interpreted in the form of a narrative synthesis grouped by outcome measure.

2.3.4.1 Linear and angular deviation

No studies reported on coronal linear deviation. Dianat et al. was the only study to report on apical linear and angular deviation (Dianat et al. 2020). Dynamic navigation was found to have a reduced mean bucco-lingual and mesio-distal apical deviation when compared to FH; 0.19mm vs. 0.81mm and 0.12mm vs. 0.31mm, respectively (Dianat et al. 2020). However, the large standard deviations indicate a high degree of variability in the data. Dynamic navigation showed a reduced mean angular deviation when compared to FH (2.39 ° vs 7.25°) (Dianat et al. 2020).

2.3.4.2 Incidence of successful canal location

All three studies reported on the incidence of successful canal location. Although no studies were able to successfully locate the canals 100% of the time, DN performed consistently and was able to successfully locate an average of 90-97% of canals whereas FH showed a greater variability of 85-97% (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a). Dianat et al. and Jain et al. showed an improved average success rate with DN compared to FH whereas Connert et al. demonstrated comparable high success rates for both techniques (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a). The improved success with use of DN was seen across both the experienced and the inexperienced operators (Dianat et al. 2020). Outcomes appeared comparable for human and 3D-printed teeth.

2.3.4.3 Incidence of perforation

Two studies (Dianat et al. and Jain et al.) demonstrated DN had a reduced incidence of perforations when compared to FH, whereas Connert et al. demonstrated comparable results (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a). The highest incidence of perforation was seen by Dianat et al. in their FH group which is surprising considering these were human teeth with

anatomical landmarks, compared to homogenous 3D-printed teeth. While DN completely eliminated the risk of perforation in one study, it was not able to eliminate this risk completely in the remaining two studies.

2.3.4.4 Tooth structure removal

Two studies (Jain et al. 2020b; Connert et al. 2021a) reported on the volume of tooth structure removal. Both studies demonstrated that access with DN reduced the mean tooth structure removal when compared to FH. Jain et al. found that mandibular incisors had a reduced average volume loss compared to maxillary incisors which could be explained by their smaller starting volume and reduced simulated distance to the pulp. Average tooth structure removal was remarkably similar in the mandible for DN and FH access whereas in the maxilla DN resulted in less tooth structure removal (35.5mm³ vs 62.2mm³) (Jain et al. 2020b). Connert et al. found the greatest benefit from DN, with FH removing on average over 2.8 times as much tooth structure (Connert et al. 2021a). This supports the findings from Jain et al. where the benefits of DN were most marked in maxillary teeth. Following FH access, the less experienced operator showed greater tooth structure removal compared to the more experienced operator (39.4 mm³ vs 19.9mm³) while following DN access both operators showed comparable tooth structure removal (Connert et al. 2021a). Therefore, it appears that endodontic access using DN relies less upon operator experience and may allow MIE access cavities to be performed by less experienced operators.

2.3.4.5 Time

All included studies reported on the endodontic access time. Dianat et al. and Jain et al. found that overall DN was more efficient than FH, while Connert et al. found the efficiency to be comparable (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a). The results from Dianat et al. should be interpreted with caution considering the high risk of bias due to differing end points when measuring timing in the DN and FH group. On average, access time with DN ranged from 136 to 227s (2 minutes 16s to 3 minutes 47s). The maxillary teeth appeared to take longer to access than mandibular teeth, consistent with the volume loss and increased distance to the pulp (Jain et al. 2020b). Access took the longest in Dianat's study and, while it is not clear why this may be the case,

one plausible explanation could be the variable presentation of human teeth compared to 3D-printed which may have prevented the operator from learning the location of the canals (Dianat et al. 2020). In both studies comparing two operators, the more experienced operator was more efficient in both techniques, reflective of their experience and confidence level (Dianat et al. 2020; Connert et al. 2021a). However, on average, the efficiency of both operators was improved with DN, with the exception of Connert et al. where operator 2 took longer with DN when compared to FH (Connert et al. 2021a).

2.3.4.6 Other outcomes

Gouging, defined as linear deviation greater than 1mm at the end drilling point, was evaluated by Dianat et al. (Dianat et al. 2020). The total incidence of gouging was three times lower (1/30 vs. 3/30) with DN access compared to FH and was more common with the less experienced operator. However, the authors do not appear to justify the selection of a 1mm deviation cut-off point. Dynamic navigation was shown to have a smaller reduction in dentine thickness when compared to FH (Dianat et al. 2020). As well as assessing the accuracy of DN quantitively, Jain et al. also introduced a qualitative assessment determined by two endodontists who rated (independently and blinded) access as 'optimal' (central drill path, canals negotiable), 'suboptimal' (deviation of drill path, canals negotiable) or 'unacceptable' (perforation, tooth rendered unrestorable or canals not identified/negotiable) (Jain et al. 2020b). Dynamic navigation was found to have a greater number of 'optimal' and a lower number of 'unacceptable' access cavities when compared with FH access.

Table 2-5 - Outcomes of included studies.
(NR = not reported, BL = bucco-lingual, MD = mesio-distal)

		Coronal linear deviation (mm) +/-SD (95% CI)	Apical linear deviation (mm) +/-SD (95% CI)	Angular deviation (°) +/-SD (95% CI)	Incidence of successful canal location (n)	Incidence of perforation (n)	Tooth structure removal (mm³) +/- SD (95% CI)	Time (s) +/- SD (95% CI)	Other outcomes +/- SD (95% CI)	Key conclusions
1	DN	NR	BL = 0.19 +/-0.21 MD = 0.12 +/-0.14	2.39 +/-0.85	29/30; Operator 1 = 15/15 Operator 2 = 14/15	0/30; Operator 1 = 0/15 Operator 2 = 0/15	NR	Mean = 227 +/-97 Operator 1 = 210 +/-80 Operator 2 = 244 +/-112	Gouging (defined as linear deviation >1 mm at the end drilling point): Total = 1/30 Operator 1 = 0/15 Operator 2 = 1/15 Reduced dentine thickness: CEJ = 1.06 +/-0.18mm End drilling point = 1.18 +/-0.17mm	"The DNS was more accurate and more efficient in locating canals in calcified human teeth compared with the FH technique. This novel system resulted in significantly less tooth structure removal and a shorter operation time."
	SN	NR	NR	NR	NR	NR	NR	NR	NR	
	FH	NR	BL = 0.81 +/-0.74 MD = 0.31 +/-0.35	7.25 +/-4.2	25/30; Operator 1 = 12/15 Operator 2 = 13/15	5/30; Operator 1 = 3/15 Operator 2 = 2/15	NR	Mean = 405 +/-246 Operator 1 = 242 +/-83 Operator 2 = 568 +/-248	Gouging: Total = 3/30 Operator 1 = 1/15 Operator 2 = 2/15 Reduced dentine thickness: CEJ = 1.55 +/-0.55mm End drilling point = 1.47 +/-0.49mm	
2	DN	NR	NR	NR	18/20	1/20	Mean = 27.2 (22.0-32.5) Maxilla = 35.5 (29.3- 41.7) Mandible = 19.0 (12.8- 25.2)	Mean = 136.1 (101.4-170.8) Maxilla = 164.8 (101.1-228.4)	Quantitative precision independently and blindly analysed by 2 board-certified endodontists: Optimal = 75%, 15/20 Suboptimal = 15%, 3/20 Unacceptable = 10%, 2/20	"Within the limitations of this in vitro study, overall dynamically navigated access preparations led to significantly less substance loss with optimal and efficient precision in locating simulated anterior

	SN FH	NR NR	NR NR	NR NR	NR 17/20	NR 2/20	NR Mean = 40.7 (29.1-52.2) Maxilla = 62.2 (56.0-38.4) Mandible = 19.1 (13.0-25.3)	Mandible = 107.5 (76.6-138.4) NR Mean = 424.8 (289.4-560.2) Maxilla = 598.8 (370.0-827.6) Mandible = 250.8 (190.6-311.0)	NR Qualitative precision: Optimal = 45%, 9/20 Suboptimal = 40%, 8/20 Unacceptable = 15%, 3/20	calcified root canals in comparison with freehand access preparations."
3	DN	NR	NR	NR	35/36; Operator 1 = 18/18 Operator 2 = 17/18	1/36; Operator 1 = 0/18 Operator 2 = 1/18	Mean = 10.5 (7.6-13.3) Operator 1 = 10.3 (6.4- 14.2) Operator 2 = 10.6 (6.0- 15.2)	Mean = 195 (135-254) Operator 1 = 90 (62-118) Operator 2 = 305 (209- 402)	NR	"Within the limits of this in vitro study, it can be concluded that the investigated method of RTGE using a miniaturized DNS leads to more accurate access cavity
	SN	NR	NR	NR	NR	NR	NR	NR	NR	preparation with
	FH	NR	NR	NR	35/36; Operator 1 = 18/18 Operator 2 = 17/18	1/36; Operator 1 = 0/18 Operator 2 = 1/18	Mean = 29.7 (24.2-35.2) Operator 1 = 19.9 (13.9- 25.9) Operator 2 = 39.4 (32.4- 46.4)	Mean = 193 (164-222) Operator 1 = 124 (100- 150) Operator 2 = 265 (242- 288)	NR NR	significantly less substance loss than CONV. Moreover, using the described experimental setup, an endodontically less experienced operator accomplished minimally invasive access cavity preparations that were comparable with a more experienced operator."

2.4 Discussion

The findings of this systematic review suggest that DN may increase the accuracy of canal location in teeth with PCO when compared to FH. These findings and conclusions were consistent across the included studies. Our findings are in line with published vitro studies performed on teeth without PCO where a mean angular deviation of 4.8° (DN) versus 19.2° (FH) and maximum distance from the planned access of 0.34mm (DN) versus 0.88mm (FH) have been reported (Gambarini et al. 2020). Similarly, a recent systematic review and meta-analysis assessing the use of DN in surgical and non-surgical endodontics found that DN improved the accuracy of endodontic access compared to FH with significant differences in time, angular, coronal and apical deviation, although no significant differences in substance loss were found (Mekhdieva et al. 2023). Likewise, Zubizarreta-Macho et al. in their systematic review found that DN improved the odds of successful canal location when compared to FH (Zubizarreta-Macho et al. 2021). The use of DN is more widely reported in implant dentistry and results consistently demonstrate superior accuracy of DN compared to FH (Jorba-García et al. 2021; Schnutenhaus et al. 2021; Wang et al. 2021b; Wei et al. 2021; Yu et al. 2023).

Existing systematic reviews fail to exclusively address the benefits of DN in nonsurgical endodontics for teeth with PCO, which appears to be the most clinically relevant use for DN technology in non-surgical endodontics. Partial or complete PCO is classified as 'moderate difficulty' or 'high difficulty' requiring a competent experienced practitioner (American Association of Endodontists 2019). With further support from in vitro and clinical studies, it is possible that DN may allow more challenging cases to be undertaken by practitioners with less experience. Our findings would support this idea, particularly with respect to tooth structure removal assessed by Connert et al. where volume loss was comparable between the experienced and less experienced operator; the most dramatic improvement compared to FH being seen with the less experienced operator (Connert et al. 2021a). It should also be considered that use of DN requires a CBCT which should be appropriately justified. The European Society of Endodontology position statement identifies an appropriate justification as the "identification of the spatial location of extensively obliterated canals, also taking into account the possibilities of guided endodontics" (Patel et al. 2019).

This further supports the use of DN in teeth with PCO and need for more targeted studies to support its use.

2.4.1 Limitations of evidence

The findings of this systematic review are based on three in vitro studies limiting the external validity of the findings. A meta-analysis was not possible due to heterogeneity of the included studies, including differences in the tooth type, degree of PCO and reported outcomes. The application of DN within non-surgical endodontics is still at an early stage with a lack of randomised controlled trials and clinical studies. It is hoped this will change in the near future, particularly considering a protocol for a randomised controlled trial for use of DN in endodontic microsurgery has already been published in 2022 (Han et al. 2022). The included studies failed to address all objectives of the review with no studies reporting on the accuracy of DN compared to SN. A similar study on teeth without PCO has demonstrated SN has comparable results with DN (Zubizarreta-Macho et al. 2020). Within implant dentistry, some studies have concluded comparative accuracy (Schnutenhaus et al. 2021; Wang et al. 2021b) while others concluded that DN is superior (Jorba-García et al. 2021; Yu et al. 2023).

Efficiency is an important consideration when introducing new technology and while access time was reported, the clinical applicability of this should be interpreted with caution since there was no measurement of the planning, set-up, trace registration or calibration time. Furthermore, training in DN is essential due to the learning curve required to master the technique. Evidence supports that there is a significant increase in efficiency after 12 procedures and that operators become efficient after 20 procedures (Block et al. 2017; Wang et al. 2022). Only Dianat et al. reported training their operators prior to the study which involved 20 teeth per operator (Dianat et al. 2020).

The findings of this review cannot be extended to all tooth types since no molar teeth were included. An alternative study by Jain et al. found the accuracy of DN in molars to be reduced when compared to anteriors and premolars (Jain et al. 2020a).

The overall risk of bias at a study level was judged as low in two studies (Jain et al. 2020b; Connert et al. 2021a) and moderate in one (Dianat et al. 2020). The 3D-printed teeth are least likely to simulate clinical circumstances due to the absence of anatomic landmarks used for canal location. Whilst Dianat's study perhaps has the greatest generalisability to clinical practice considering their use of human teeth, this study has a moderate risk of bias and therefore their results should be interpreted with caution.

2.4.2 Limitations of review processes

A strength of the methods used in this systematic review is the use of a clearly focused question and robust inclusion criteria which ensured validity of the findings. On the other hand, a potential limitation was the use of strict inclusion criteria which resulted in few included studies. A number of case reports and case series have been published demonstrating successful canal location using DN for teeth with PCO but were not included due to inadequate number of cases (Dianat et al. 2021a; Villa-Machado et al. 2022; Wu et al. 2022; Panithini et al. 2023).

Searching for published and unpublished studies ensured that all relevant studies were included. However, while grey literature was searched through conference proceedings and contact with manufacturers, it was not possible to identify any unpublished studies which presents the risk of publication bias. Exclusion of non-English language studies may have resulted in the exclusion of potentially relevant studies.

2.4.3 Implications for practice, policy and future research

The results of this systematic review should be interpreted with caution due to the limited number of included studies. All included studies were of in vitro design limiting the external validity. Gaps identified in the research were clinical studies, molar teeth with PCO and comparison to SN. Future research is suggested to address these gaps in the literature.

2.5 Conclusion

Within the limitations of this systematic review, DN appears to increase the accuracy of canal location in teeth with PCO when compared to FH access in an in vitro setting. The findings should be interpreted with caution due to the limited number of included studies. Gaps identified in the research were clinical studies, molar teeth with PCO and comparison to SN. Future research is suggested to address these gaps in the literature.

Chapter 3 Insights from the broader DN research literature

To capture and consider relevant literature that was excluded from the systematic review due to methodological criteria, a wider consideration of the literature must be made. By incorporating this broader body of work, it is possible to provide a more comprehensive understanding of the topic, highlight potential gaps in the evidence base, and identify areas for future research that may not be visible through the systematic review alone.

3.1 Case reports and case series

The systematic review applied strict inclusion criteria, resulting in the exclusion of case reports and case series. Given that DN is relatively new within the field of endodontics, there are few published case reports and case series on its use for canal location in teeth with PCO. While the quality of the evidence is low, they represent the only published research demonstrating clinical implementation of DN, making them important to consider. Dianat et al. published the first case report using DN for canal location and it remains the only documented clinical application of DN for molar access (Dianat et al. 2021a). They demonstrated successful location of a partially calcified distobuccal (DB) canal in a maxillary molar using the X-Guide DNS, where previous FH access was unsuccessful, even with CBCT and the DOM. A full-arch pre-operative CBCT was performed with a 120µm voxel size. Access was performed with a #1 Munce bur. A 6-month follow-up periapical radiograph demonstrated healing of the periapical radiolucencies. It should be noted that the operator was highly experienced and widely published in the field of DN and had completed 40 prior DN cases. Villa-Machado et al. presented successful canal location of a maxillary and mandibular central incisor with PCO using the Navident DNS (Villa-Machado et al. 2022). A pre-operative CBCT was performed with a 5x4cm FOV and a 75µm voxel size. An Endoguide EG4 precision micro endodontic bur was used for access. A 12-month follow-up CBCT demonstrated normal periapical structures. Subsequent case reports have utilised a similar protocol to the studies described above. Panithini et al. presented the access of a maxillary central incisor with PCO using the Navident DNS, where a FH attempt had previously failed (Panithini et al. 2023). A full-arch pre-operative CBCT was taken (10x10cm) with a 130µm

voxel size. Access was performed with a #1 Munce bur. A post-operative CBCT was performed to evaluate the linear and angular deviations, demonstrating deviations of 1.46mm mesio-distally, 0.01mm bucco-palatally and 4° at the drill tip. Wu et al., Xue et al. and Yang et al. used the DCARER (Suzhou, China) DNS to access maxillary and mandibular incisors with PCO (Wu et al. 2022; Xue et al. 2024; Yang et al. 2024). Wu et al. performed a full-arch pre-operative CBCT (11x8cm) with a 250µm voxel size. Access was performed with a 1.5mm diameter drill (Wu et al. 2022). All canals were successfully located facilitating the completion of endodontic treatment. Yang et al. performed a pre-operative CBCT with a 16x6cm FOV and a 250µm voxel size (Yang et al. 2024). Initial access through enamel was performed using a round bur, followed by the use of a long-shank fissure bur to access through dentine. However, specific bur details were not provided. Xue et al. conducted a pre-operative CBCT with an 8x8cm FOV and a 300µm voxel size (Xue et al. 2024). The CBCT revealed complete PCO and therefore the drill path was planned according to the principle of centralisation, following the long-axis of the tooth, to successfully locate the canal. One-year review demonstrated healing or healed outcomes in all cases on CBCT or periapical radiographs. Within the cases reported above, two out of fourteen teeth experienced complications during DN, which will be described further in section 3.4.

3.2 Accuracy of canal location

The systematic review included three studies meeting the eligibility criteria. Studies excluded from the systematic review due to the absence of a comparison were Jain et al. and Torres et al. and will be reviewed below (Jain et al. 2020a; Torres et al. 2021). Since conducting the systematic review and while preparing this thesis, one further in vitro study has been published which meets the eligibility criteria (Huth et al. 2024). Unlike the included studies, Huth et al. also compared DN to FH and SN. For completeness, a summary of the methods and outcomes presented by Huth et al. are summarised in Table 3-1 and Table 3-2. Other studies on the use of DN for canal location in teeth without PCO have been published and these will be touched upon.

Table 3-1 - Huth et al. 2024 summary of methods. (IV = in-vitro, NR = not reported, CBCT = Cone Beam Computed Tomography, FOV = field of view)

Study design	Sample size	Type of tooth	Jaw material	Degree of PCO	DNS	Comparison	Details of CBCT	Details of optical scanner	Planning software	Handpiece and bur	Number of operators and level of experience	Details of training undertaken on DNS
IV	144; 48 DN, 48 SN, 48 FH	3D-printed maxillary and mandibular canines and molars	Nissin jaw model (Nissin Dental Products inc. Kyoto, Japan)	Upper canine obliterated till the middle apical third, Upper molar with an obliterated MB2, Lower molar with a pulp chamber containing pulp stones with the distal root to be found, Lower canine having a second lingual canal which needed access	DENACAM (Mininavident AG)	SN, FH	CBCT Carestrea m CS9300 (Carestrea m Dental, Atlanta, USA), 90 µm voxel size	Activity 885 Mark 2, (Pluradent GmbH. & Co. KG, Germany)	coDiagnostiX (Dental Wings)	Spiralbur Endo diameter 1mm, working length 21mm (Steco- system- technik GmbH & Co. KG), using a contra-angle handpiece	4; All operator possessed over 5 years of experience in general dentistry including endodontics	Theoretical and practical tutorial on Denacam and drilling templates. 5 test teeth per operator

Table 3-2 - Huth et al. 2024 summary of outcomes. (NR = not reported, BL = bucco-lingual, MD = mesio-distal)

	Coronal linear	Apical linear	Angular	Incidence of	Incidence of	Tooth structure removal	Time (s) +/-SD (95%	Other	Key conclusions
	deviation	deviation	deviation (°)	successful	perforation (n)	(mm ³) +/-SD (95% CI)	CI)	outcomes	
	(mm) +/-SD	(mm) +/-SD	+/-SD (95% CI)	canal location				+/-SD (95%	
	(95% CI)	(95% CI)		(n)				CI)	
DN	1.62 +/-0.70	1.65 +/-0.79	2.82 +/-1.8	46/48	1/48	Mean = 9.43 +/-9.02	Mean = 252 +/-110	NR	"Guided endodontic access may aid in
SN	0.77 +/-0.37	0.86 +/-0.38	1.12 +/-0.85	47/48	0/48	Mean = 17.60 +/-10.66	Mean = 142+/-58	NR	precise root canal localization and
FH	1.85 +/-0.89	1.52 +/-0.90	9.53 +/-6.36	45/48	2/48	Mean = 31.90 +/-19.78	Mean = 137+/-67	NR	save tooth structure."

3.2.1 Linear and angular deviation

Jain et al. performed an in vitro study using the Navident DNS on 3D-printed anterior teeth, premolars and molars with PCO (Jain et al. 2020a). The orifice was 5mm above the apex for anterior teeth and 2mm below the CEJ for premolars and molars. In teeth with multiple canals, each canal was accessed through its own opening. The endodontist undertook training sessions using the DNS on over twenty teeth. In a similar study, Torres et al. investigated the use of the Navident DNS on 3D-printed teeth with simulated PCO by placing the canal 15mm from the incisal edge or occlusal surface (Torres et al. 2021). Rather than a single operator, they used three operators with varying levels of experience: a final-year dental student, an endodontist with over five years of experience and an endodontist with more than thirty years of experience. Similarly, their operators also undertook rigorous training by preparing twenty-eight access cavities using the DNS.

Comparing studies reporting on access deviation is challenging due to the inconsistency of outcome measures used, including 2D and 3D deviation. Jain et al. found a mean 2D horizontal deviation at the canal orifice of 0.9mm and Torres et al. reported a mean of 0.63mm, slightly greater than reported in the systematic review by Dianat et al. (Dianat et al. 2020; Jain et al. 2020a; Torres et al. 2021). Three-dimensional deviation is consistently greater; Huth et al. reported on 3D deviation with a mean of 1.65mm, which is similar to the 1.60mm deviation reported by Torres et al., while Jain et al. reported a slightly lower deviation of 1.3mm (Jain et al. 2020a; Torres et al. 2021; Huth et al. 2024). These reported deviations are greater than those observed in teeth without PCO, as minor angular deviations become magnified the deeper the access cavities (Gambarini et al. 2020). While the systematic review demonstrated that DN reduced the deviation compared to FH, Huth et al. did not support this (Huth et al. 2024). They found that DN and FH had similar deviation, while SN had significantly less deviation and greater predictability. This could be explained by the rigorous training with at least twenty practices performed by other studies, except Huth et al who only performed five practices (Huth et al. 2024). The findings from Huth et al. appear to be an outlier, since studies on teeth without PCO have also demonstrated DN has significantly less deviation compared to FH (Gambarini et al. 2020; Zubizarreta-Macho et al.

2020). In fact, Zubizarreta-Macho found DN and SN to be superior to FH, while no difference was observed between DN and SN (Zubizarreta-Macho et al. 2020). Torres et al. explored the impact of operator experience and found that the two endodontists had less 3D deviation compared to the dental student. For 2D deviation, the endodontist with over five years of experience performed better than the final-year dental student but no differences were identified between the most experienced endodontist and the student (Torres et al. 2021). Dianat et al. did not present accuracy comparisons between operators (Dianat et al. 2020). In summary, mean 2D deviation tends to be less than 1mm, whereas 3D deviations are typically around 1.6mm. Dynamic navigation demonstrates less deviation than FH, but training on the DNS a minimum of 20 times is recommended.

Jain et al. reported a mean angular deviation of 1.7° and Torres et al. a mean of 2.81°, which both appear to be in keeping with other studies (Dianat et al. 2020; Jain et al. 2020a; Torres et al. 2021; Huth et al. 2024). Similar to the systematic review, Huth et al. demonstrated a reduced angular deviation of DN compared to FH (Huth et al. 2024). This is in agreement with in vitro studies on anterior and posterior teeth without PCO (Gambarini et al. 2020; Zubizarreta-Macho et al. 2020). Huth et al. found that SN exhibited the smallest angular deviation and variability, which was significantly less than that of DN and FH (Huth et al. 2024). Again, this may be due to lack of appreciation of the learning curve required with DN. Nonetheless, a study on teeth without PCO found no significant difference between DN and FH, although there was a trend for reduced angular deviation with DN (Zubizarreta-Macho et al. 2020). However, this study did not perform a sample size calculation and therefore the findings should be interpreted with caution.

Linear and angular deviation may be calculated via an indirect method through the placement of drills in the access cavities during the post-operative CBCT or directly through sophisticated analysis software. The latter method is preferred to avoid errors due to bur positioning (Jain et al. 2020a). In multi-rooted teeth, linear and angular deviation may only be possible to calculate where the access is of a TrussAC design, such as that performed by Jain et al. (Jain et al. 2020a). TradAC, ConsAC or UltraAC designs may prohibit linear and angular deviation calculations on multi-rooted teeth.

3.2.2 Incidence of successful canal location

Torres et al. and Huth et al. found success rates of 93% and 96%, consistent with the range identified in the systematic review of 90-97% (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a; Torres et al. 2021; Huth et al. 2024). Similarly, they also observed that none of the methods were successful in locating the canals with 100% success. In addition, according to Huth et al., there was no statistically significant differences in success rates between the DN, FH and SN groups (Huth et al. 2024). Operator experience does not seem to impact success rate of DN (Dianat et al. 2020; Torres et al. 2021). While the majority of studies reported on the details of operator training, Torres et al. was the only study to report on success rates before and after training on the DNS (Torres et al. 2021). For most operators, training leads to a substantial improvement in success, demonstrating the importance of training and the inherent learning curve.

3.2.3 Incidence of perforation

Torres et al. and Huth et al. reported incidences of perforation of 4% and 2%, respectively (Torres et al. 2021; Huth et al. 2024). These findings are consistent with the range of rates (0-5%) reported in the systematic review (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a). While two studies (Dianat et al. and Jain et al.) found that DN reduced the incidence of perforations when compared to FH, two studies (Connert et al. and Huth et al.) demonstrated no significant difference (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). In addition, SN did not significantly influence the incidence of perforation (Huth et al. 2024).

3.2.4 Tooth structure removal

Tooth volume loss is calculated by first performing semi-automatic segmentation of the tooth from the pre- and post-operative CBCT scans, followed by automatic subtraction of the two scans using medical imaging software (Connert et al. 2021a). Tooth volume loss is an important outcome measure to consider, particularly following FH access of multi-rooted teeth, as it may be one of the only feasible outcome measures when determination of linear and angular deviation is not possible.

Although numerous studies report on tooth volume loss, comparing these studies is difficult owing to the different starting volumes (Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). However, general trends can be explored. All studies which compared DN to FH endodontic access found significantly less tooth structure loss with DN. In fact, Huth et al. found the mean tooth substance loss following FH access was over 3 times greater than DN, similar to Connert's findings (Connert et al. 2021a; Huth et al. 2024). In addition, the variability of the data with DN was lower than FH, suggesting that DN is a more predictable treatment. Contrary to findings when considering linear and angular deviation, Huth et al. found that DN performed better than SN when volume loss was considered (Huth et al. 2024). As highlighted in the systematic review, while DN benefits all operators, it is especially advantageous for those with less experience (Connert et al. 2021a).

3.3 Efficiency of canal location

Jain et al. reported an average drilling time of 57.8s per canal when using DN, which is less than half the time reported in other studies (Jain et al. 2020a; Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). This was also faster than the same group's subsequent study, despite maintaining many of the same study characteristics. A plausible explanation for this discrepancy is the difference in operator experience; the first study was performed by a board-certified endodontist while the second was performed by an endodontic resident. The range of mean access times amongst studies for DN was 58-252s per canal and for FH was 137-425s (Jain et al. 2020a; Jain et al. 2020b; Huth et al. 2024). Contrary to the systematic review where the majority of studies found DN to be quicker and predictable, Huth et al. found FH and SN to be significantly quicker, with less variability than DN (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). The authors suggested this was due to the operators having only performed practice on five test teeth, markedly less than other studies, again demonstrating the importance of rigorous training. Not surprisingly, studies on teeth without PCO have demonstrated quicker access times than in teeth with PCO (Gambarini et al. 2020). However, the study did not provide specific start and end times, so this comparison should be interpreted cautiously.

The majority of studies report on access cavity preparation time, which is commonly defined as the time from initial preparation of tooth structure to the point of successful canal negotiation (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). While Jain et al. included molars, they presented the access time per canal only (Jain et al. 2020a). Total access time, including the time required to select the appropriate canal from the targeted guidance selection menu on the software, is important to consider in multirooted teeth and has not yet been reported. In addition, no DN studies report on total treatment time, unlike Connert et al. who reported the time for each workflow step and as well as the total time in their SN study (Connert et al. 2017).

3.4 Limitations and failure

The case series presented by Yang et al. demonstrated that two out of seven teeth experienced significant deviation from the planned drill path using DN (Yang et al. 2024). The authors suggested this was due to inaccuracy of path design and failure to re-calibrate and re-register following intra-operative redesign of the drill path. In both cases, an intra-operative CBCT was performed and the operator corrected the access FH using the DOM. This demonstrates that a high level of experience is required to identify and correct errors as they arise. In vitro studies have also shown instances of DN failures and iatrogenic damage, including perforations. As detailed above in section 3.2.2 and 3.2.3, no in vitro studies have demonstrated successful canal location 100% of the time and perforations do occasionally occur. The authors have suggested plausible explanations including errors during trace registration, altering the planned access path mid-treatment or loss of the stability of the jaw tracker (Jain et al. 2020b). The original DN study canal location also experienced failure in 10% of cases and all were attributable to tracking failures (Chong et al. 2019). The true incidence of complications occurring during DN, especially in a clinical setting, remains unclear and is it likely that there is significant publication bias.

Chapter 4 Research rationale and justification

4.1 Study design

Within the limitations of the available literature, SN appears to be an accurate and efficient method of locating canals in teeth with PCO. However, the majority of literature focuses on single-rooted anterior teeth. Several limitations have been acknowledged in the literature when using SN in posterior teeth, including the lack of inter-occlusal space for the guide and drill, as well as the need for multiple guides when accessing multiple canals in close proximity. Dynamic navigation offers a promising solution to these challenges, as well as facilitating intra-operative adjustments to the planned access and providing improved access for irrigation compared to SN. Therefore, further research is warranted on the use of DN for locating calcified canals in posterior teeth.

The systematic review carried out within this thesis has highlighted the need for a direct comparison between DN and SN, which has since been addressed in the literature (Huth et al. 2024). In addition, the systematic review identified an absence of studies using multi-rooted teeth with PCO. While the subsequent publication by Huth et al. included an upper and lower molar, DN was used to locate only a single canal (Huth et al. 2024). Jain et al. reported accessing multiple canals in molars, however, there was no comparison to SN or FH, and outcomes were listed per canal rather than per tooth (Jain et al. 2020a). Additionally, there is only one case report documenting the use of DN for canal location in a molar, and this was utilised to access a single canal. The benefit of DN for location of multiple canals in teeth with PCO compared to FH or SN remains unknown and warrants further investigation.

Almost all laboratory-based studies described, have employed 3D-printed teeth, all with varying degrees of PCO. These studies utilise a limited FOV CBCT and voxel sizes ranging from 75 and 125µm. Case reports and case series have used voxel sizes between 75 and 300µm, all falling within the recommended range suggested by ClaroNav. Various DNS have been utilised. The literature consistently suggests that operator training on the DNS is highly recommended on a minimum of 20 teeth, given the inherent learning curve. These described

parameters validated by previous studies will assist in establishing and standardising a reliable methodology.

4.2 Outcome measures

Important outcomes assessed are linear and angular deviation, the incidence of successful canal location, incidence of perforation, tooth structure removal and time.

Linear and angular deviation are reported by a number of studies and DN appears to reduce the deviation when compared to FH. However, it is acknowledged that the access cavity design in multi-rooted teeth may prohibit linear and angular deviation measurements and therefore tooth structure removal appears a more appropriate outcome measure.

While studies have demonstrated that DN may reduce access cavity preparation time compared to FH, none have reported the total treatment time considering other aspects of the DNS workflow. Time taken for trace registration and calibration remains unreported. In addition, no studies have reported the time to access multiple canals, taking into consideration the time required to select the appropriate canal from the targeted guidance selection menu in the software. Further research is required to gain a more accurate understanding of the efficiency of DN for accessing multi-rooted teeth.

The impact of operator experience is a recurring theme in the literature, with DN demonstrating benefits for operators of all levels of experience in terms of both accuracy and efficiency. Experienced operators tend to be more efficient when using either FH and DN compared to inexperienced operators. Notably, DN seems particularly beneficial for inexperienced operators, potentially enabling them to achieve outcomes comparable to an experienced operator. The possibility that outcomes are independent of operator experience warrants further investigation, particularly in multi-rooted teeth.

Considering the gaps in the literature outlined above, the focus of this study is to investigate the use of DN for locating multiple canals in posterior teeth with PCO in comparison to FH access. The impact of operator experience will also be

investigated. Key outcome measures will include tooth structure removal and time, including aspects of the DNS workflow.

Chapter 5 Tooth volume loss following dynamic navigation and freehand endodontic access in calcified maxillary molars: An in vitro analysis

5.1 Research aims

5.1.1 Primary research aim

 To compare the tooth volume loss following DN and FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

5.1.2 Secondary research aims

- To compare the time taken for DN and FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.
- (a) To assess the impact of operator experience on tooth volume loss following DN endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.
 - (b) To assess the impact of operator experience on tooth volume loss following FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.
- 3) (a) To assess the impact of operator experience on time taken for DN endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.
 - (b) To assess the impact of operator experience on time taken for FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

5.2 Null hypotheses

5.2.1 Primary research aim

 There is no difference in tooth volume loss between DN and FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

5.2.2 Secondary research aims

- There is no difference in the time taken for DN and FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.
- (a) Operator experience does not influence tooth volume loss following DN endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.
 - (b) Operator experience does not influence tooth volume loss following FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.
- 3) (a) Operator experience does not influence time taken for DN endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.
 - (b) Operator experience does not influence time taken for FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

5.3 Objectives

The objective was to undertake an in vitro study to compare DN using the Navident DNS and FH endodontic access on anatomically accurate 3D-printed maxillary molars with simulated calcified canals performed by two operators with differing levels of experience by analysing:

- 1) Total volume of tooth structure loss
- 2) Incidence of successful canal location
- 3) Incidence of perforation
- 4) Procedural time

5.4 Funding

The materials for this in vitro study were funded by a British Endodontic Society Grant for Research Work - 2023 award.

5.5 Ethical approval

Ethical approval was not required since the research did not involve human or animal subjects, material or data.

5.6 Methods

5.6.1 Study design

This study was designed as an in vitro analysis to compare DN and FH endodontic access in anatomically accurate 3D-printed teeth. Operator blinding was not feasible, and volume loss analysis was performed automatically by the software, eliminating the need for examiner blinding.

5.6.1.1 Tooth optimisation

The optimisation of the 3D-printed teeth was performed in two stages: (1) suitability screening and (2) suitability assessment. Potential sources of 3D-printed teeth with simulated calcified canals were identified through internet searching and contacting individuals within the field. To proceed to the suitability assessment stage, a tooth needed to meet the four screening criteria listed below.

1) Maxillary molar

- 2) Absence of a pulp chamber
- 3) Canals reduced to the level of the CEJ or just apical to the CEJ
- 4) Canals visible on CBCT

Following the application of the screening criteria by operator 1 and verification by operator 2, each tooth was categorised as either 'suitable' or 'unsuitable'. Samples of teeth classified as 'suitable' were then obtained and evaluated by operator 1 using the suitability assessment criteria listed below.

Clinical examination criteria:

- 1) Absence of significant surface defects (such as altered crown morphology and root morphology)
- Full length of canals patent with small hand files (08, 10 and 15 stainless steel K file)

CBCT examination criteria:

- 1) Simulated canal calcification to the level of the CEJ or below
- Canals clearly visible and well differentiated from the surrounding tooth structure
- 3) Canals continuous to the apex

The CBCT was obtained using the KaVo OP 3D Vision (KaVo Dental, Biberach, Germany) with a field of view of 8x5cm, 120Kvp, 5mA and voxel size 125µm.

The results of the tooth optimisation process are detailed later in Table 5-1. The tooth determined to be suitable following the suitability assessment was selected as the definitive tooth for this study. The custom-made tooth was developed by Newcastle University and was derived from an STL file of an anatomically accurate maxillary left second molar (UL7) with four canals: mesio-buccal 1 (MB1), MB2, DB and palatal (P). The STL image was customised for this

study using MeshMixer (Autodesk Inc., San Rafael, CA, USA) to ensure that the pulp chamber was completely obliterated and the root canal orifices started 2mm below the CEJ level (Figure 5-1). Resection of the root ends allowed any unset resin to drain during the printing process. The modified STL file was subsequently 3D-printed in resin using the Form 3 3D printer (FormLabs, Somerville, MA, USA) with a margin of error of 25µm, producing a series of identical maxillary molars with simulated obliterated pulp chambers, one of which is demonstrated in Figure 5-2.

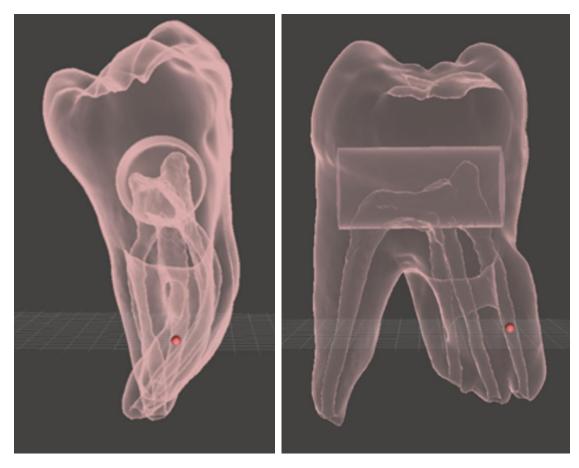


Figure 5-1 - Modification of the STL file in MeshMixer to simulate canal calcification. The 3D cylinder represents the area of the pulp chamber and root canal orifices removed to simulate calcification.



Figure 5-2 - Photograph showing a sample of the selected 3D-printed tooth for the study. Demonstrates the perpendicular root section which allowed drainage of resin following 3D printing.

Each tooth obtained for the main study was evaluated by operator 1 according to the same pre-defined suitability assessment criteria to determine its eligibility for inclusion. Initially, a clinical examination was conducted, and if the tooth was considered suitable, a CBCT examination was performed. To enhance efficiency, CBCT scans were undertaken with 16 teeth per scan (Figure 5-3). The results of the individual tooth assessment were independently verified by operator 2. Teeth that did not meet the criteria for inclusion in the main study were repurposed as 'practice teeth'.



Figure 5-3 - CBCT set-up for the tooth-by-tooth suitability assessment prior to inclusion within the study.

5.6.1.2 Navident optimisation

Operator 1 initially developed the study protocol by consulting the Navident user manual (ClaroNav 2021). The methods were refined through repeated experiments. Given the in vitro study design and the endodontic application of software originally designed for implants, several methodological challenges were encountered and addressed before achieving consistent access to all canals.

Firstly, although the tooth was secured in the jaw model with ribbon wax, movement was still observed. To address this, the tooth was splinted to the adjacent buccal, palatal and interproximal surfaces to prevent movement during the access procedure. Despite these measures, minor errors occurred in tooth positioning persisted, even when using the positioning jig. Consequently, the model was removed from the phantom head for replacement of the tooth to check for debris and to accurately confirm the correct positioning between each access procedure.

Next, the software's 'targeted guidance selection' feature became disabled, displaying an error message "guidance disabled for this implant by user". This

occurred because the software's safety mechanism, designed to ensure adequate inter-implant distance, was triggered by the proximity of the canal accesses converging on the occlusal surface. An update recommended by the manufacturers was not possible due to ongoing experiments by other users. Instead, each access was modified so that the planned 'implant' started below the occlusal surface, avoiding interaction of the individual 'implants'.

Finally, during access cavity preparation, the bur occasionally became trapped apically within the resin. This issue was resolved by using a new bur for each tooth to maintain maximum cutting efficiency and a speed increasing handpiece was employed.

5.6.1.3 Pilot study

A pilot study was undertaken by operator 1 using a sample size of six teeth. The teeth were randomly assigned by means of computer-generated random numbers produced using GraphPad software (GraphPad Software, Boston, MA, USA) into two groups, three in the DN group and three FH.

A pre-operative CBCT of a single unmounted tooth and a post-operative CBCT of each accessed tooth was obtained using the KaVo OP 3D Vision, with the same parameters outlined previously. The Digital Imaging and Communications in Medicine (DICOM) files were converted to STL format using InVesalius version 3.1.1 (Centre for Information Technology Renato Archer, Campinas, Brazil) software, enabling the automatic analysis of total tooth volume (mm³). The total volume loss (mm³) was determined by calculating the difference between the pre-operative and post-operative volumes on Microsoft Excel version 16.93.1 (Microsoft Corp., Redmond, WA, USA).

5.6.1.4 Sample size calculation

Since no previous research had compared tooth volume loss following DN and FH access in multi-rooted teeth, data from the pilot study was utilised. A sample size calculation using Piface software (Lenth 2006) was performed based on the primary outcome measure, tooth volume loss, using a power of 0.8, alpha level of 0.05, effect size of 10.304mm³ and standard deviations of 10.685 mm³ and

11.098mm³, according to the pilot study data. A sample size of twenty teeth per group (DN, FH) was selected.

5.6.2 Experimental methods

The experimental groups involved access with the Navident DNS and FH access, performed by two different operators: a specialty trainee (operator 1) and a specialist endodontist (operator 2).

The study included four experimental subgroups groups, as outlined below:

- 1) Subgroup A: DN operator 1 (n=10)
- 2) Subgroup B: DN operator 2 (n=10)
- 3) Subgroup C: FH operator 1 (n=10)
- 4) Subgroup D: FH operator 2 (n=10)

The 3D-printed maxillary molars were randomly assigned into the four experimental subgroups using computer-generated random numbers using GraphPad software. Each operator accessed a maximum of three teeth per session, with at least one week between sessions to prevent the operator from learning the location of the canals.

5.6.2.1 Dynamic navigation access cavity preparation

Dynamic navigation was performed according the Navident user manual, following the four recommended stages (ClaroNav 2021): scan, plan, register and treat. These stages were performed as detailed below:

1) Scan

A pre-operative CBCT of a single unmounted 3D-printed tooth was performed using the same parameters as previously outlined to enable pre-operative volume analysis (Figure 5-4). The tooth was then mounted in a maxillary Nissin jaw model (Nissin Dental Products Inc., Kyoto, Japan) in its correct anatomical

position and secured with ribbon wax (Metrodent Limited, Huddersfield, United Kingdom) to simulate clinical conditions. A positioning jig was constructed using acrylic resin (Pattern Resin LS, GC America Inc., Alsip, IL, USA) to ensure reproducibility of the tooth position (Figure 5-5). A pre-operative CBCT of the tooth mounted in the jaw model was performed using the same parameters (Figure 5-6). A surface scan was performed using the CARES Visual laboratory scanner (Straumann Holding AG, Basel, Switzerland).

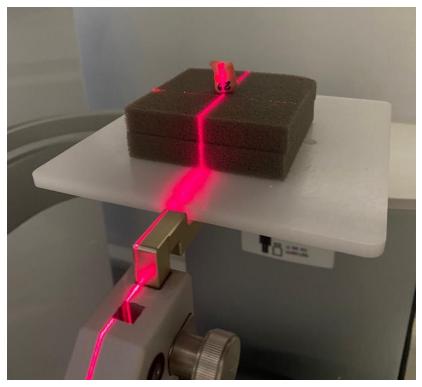


Figure 5-4 - Pre-operative CBCT set-up.

Demonstrates central positioning and use of foam support to avoid artifacts. The CBCT facilitated pre-operative volume analysis.



Figure 5-5 - Positioning jig.

Demonstrates acrylic resin positioning jig cut out over the adjacent teeth to confirm accuracy of fit.



Figure 5-6 - CBCT set-up with the 3D-printed tooth mounted in the Nissin jaw model. Demonstrates anatomic and raised positioning of jaw model to prevent any tooth displacement between use of the jig and the CBCT. The CBCT facilitated planning on the Navident software.

2) Plan

The CBCT was exported in DICOM format, and the surface scan was exported as an STL file. The DICOM file was imported into the Navident DNS software. During the 'Jaw Selection' phase, 'Plan Upper' was selected to initiate a plan in the maxilla. The jaw centreline curve was then placed in the axial section, at around the mid-root level by selecting points around the arch starting posteriorly at the distal aspect of the second molar and including the midpoint of the second premolars and canines and the midline to produce the panoramic view (Figure 5-7). The surface scan, in STL format, was imported and aligned to the CBCT using surface registration by selecting and matching eight structures (ClaroNav recommend between three and eight points) (Figure 5-8). In a clinical setting, fixed structures should be selected; however, the use of a rigid model allowed for the selection of any easily visualised structure.



Figure 5-7 - Jaw centreline curve.

Demonstrates the teeth centrally positioned within the jaw centreline curve allowing production of the panoramic view.

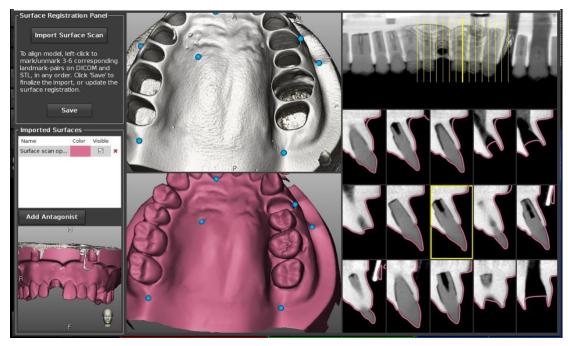


Figure 5-8 - Surface registration.

Demonstrates the selection of matched points on the CBCT (upper middle image) and the surface scan (lower middle image) to facilitate accurate superimposition. Alignment may be visually verified on the right of the screen.

The endodontic access was planned by operator 1 and verified by operator 2. The ideal drill entry point, angle and depth to the level of the canal orifice was planned with a drill diameter of 1.2mm corresponding to the width of the bur (Figure 5-9). Each canal was labelled with its respective name: MB1, MB2, DB and P. While each canal had a distinct entry point on the occlusal surface, accesses were convergent to minimise total volume loss (Figure 5-10).

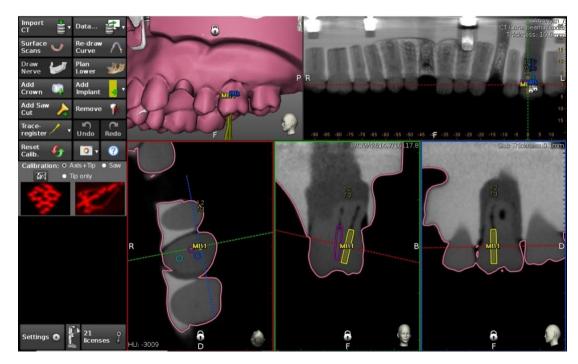


Figure 5-9 - Navident endodontic access plan.

Demonstrates straight-line access to the MB1 canal orifice superimposed on the CBCT in multiple planes.

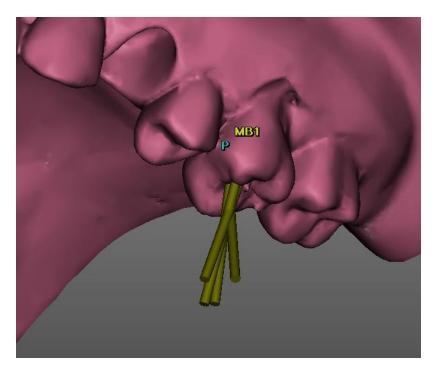


Figure 5-10 - Navident endodontic access plan.

Demonstrates convergence of each individual access centrally on the occlusal surface to minimise tooth structure loss.

3) Register

Each experimental tooth was reproducibly mounted in the Nissin jaw model using the previously constructed positioning jig. The tooth was stabilised with OpalDam (Ultradent, South Jordan, UT, United States), splinted to the adjacent buccal, palatal and interproximal surfaces to prevent any movement during the access procedure (Figure 5-11). The Nissin jaw model was then placed in the dental mannequin to simulate clinical conditions. The Navident cart, along with the laptop and camera box, was positioned in close proximity to the dental mannequin in a fixed and consistent position (Figure 5-12). The laptop screen faced the operator, while the camera was directed towards the mannequin. The case was loaded, and the barcode on the 'DrillTag', 'Tracer' and 'Calibrator tool' did not need to be rescanned since they had been previously scanned. The 'Jaw Tracker-U' was attached to the Nissin jaw model on the contralateral side of the same arch, over the premolars and molars using bite registration material (Regisil Rigid, Dentsply Sirona, Charlotte, NC, USA) within the U-shaped clip. The tracker was positioned with its optical markers facing the MicronTracker Camera.



Figure 5-11 - Splinting of the tooth to prevent movement during endodontic access.

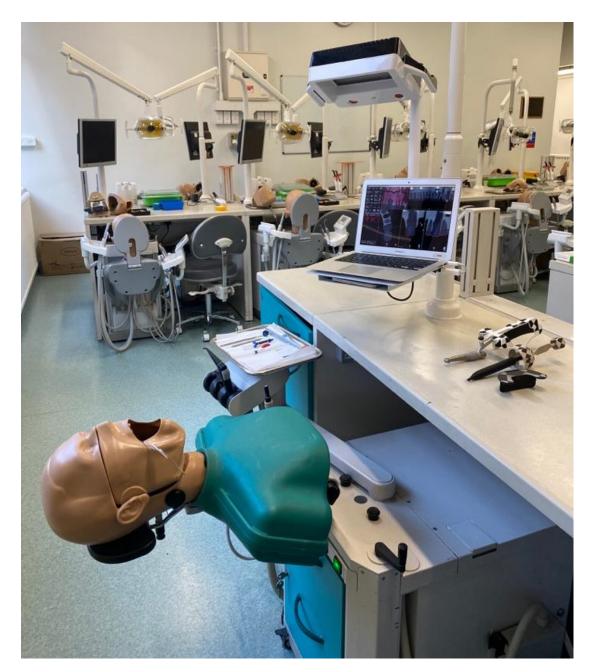


Figure 5-12 - Positioning of dental mannequin, Navident cart, camera and laptop.

The CBCT was registered with the mounted tooth using a process known as 'Trace Registration'. Firstly, the 'Tracer-3' was calibrated by positioning its tip onto the Calibration tool dimple, ensuring that the optical markers were visible to the MicronTracker. Following selecting the 'Trace Registration' icon, the 'surface-based registration' option was chosen. A series of five landmarks visible on the surface scan, including the tooth mesial and distal to the tooth of interest, were selected for tracing (ClaroNav recommend a minimum of three landmarks). For each landmark, the Tracer-3 was placed in contact with the selected landmark and then the tooth surface was traced, using the Jaw Tracker as a reference (Figure 5-13). The movement of the Tracer-3 in relation to the Jaw Tracker was tracked by the MicronTracker, a stereoscopic video camera,

which automatically registers the surface to the CBCT based on selected landmarks and tracing points. The accuracy of Trace Registration was verified visually by both operator 1 and operator 2 by positioning the Tracer-3 on multiple locations and tracing across all tooth surfaces, including buccal/palatal, mesial/distal and occlusal. An example of what was considered an acceptable trace registration is demonstrated in Figure 5-14.

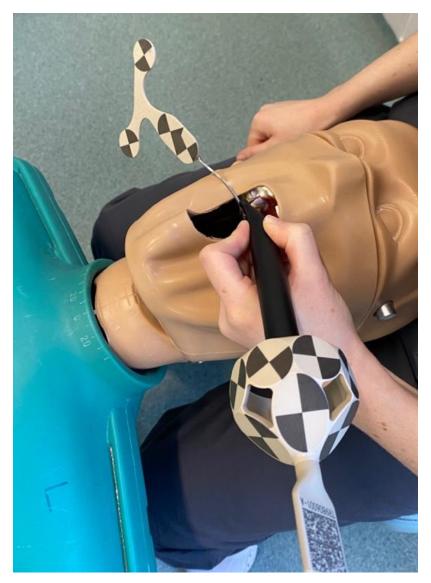


Figure 5-13 - Trace Registration.

Demonstrates the Jaw Tracker (right side of mannequin) and the Tracer-3 in contact with the tooth surface during Trace Registration.

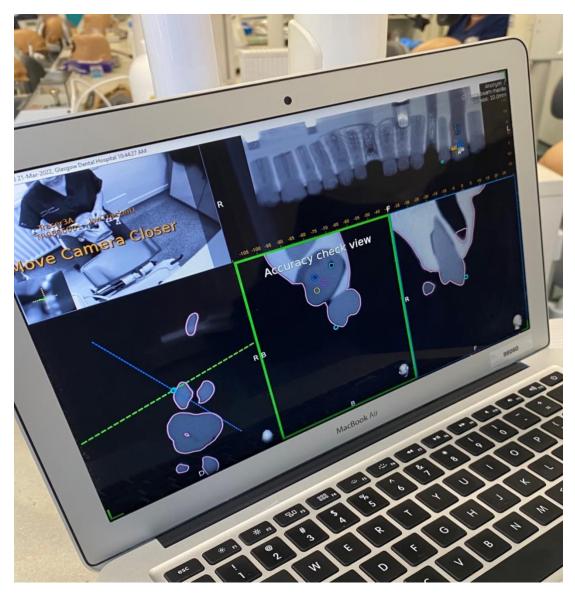


Figure 5-14 - Verification of the Trace Registration.

Demonstrates the tip of the Tracer-3 in contact with the tooth surface in all planes.

4) Treat

Prior to commencing access, the speed-increasing handpiece (W&H, Bürmoos, Austria) was calibrated through a two-stage process. The first stage, known as 'Axis Calibration', involved attaching the 'DrillTag' to the handpiece via the high-speed 'Tag Adapter' and securing the handpiece to the 'Calibrator tool' pin (labelled "4"), both of which carry optical markers (Figure 5-15). The handpiece was then rotated with the optical markers facing the MicronTracker to calibrate the drill axis. After this, the handpiece was detached from the Calibrator tool and the 1.2mm diameter cylinder bur (Wrights, Dundee, United Kingdom) was inserted. The second stage, known as 'Drill-tip Calibration', required placing the tip of the bur onto the Calibrator tool dimple (labelled "2") (Figure 5-16). Once

complete, the accuracy of the drill tip calibration was verified visually by both operators by positioning the bur on multiple tooth surfaces, similar to the verification process for Trace Registration as described above.

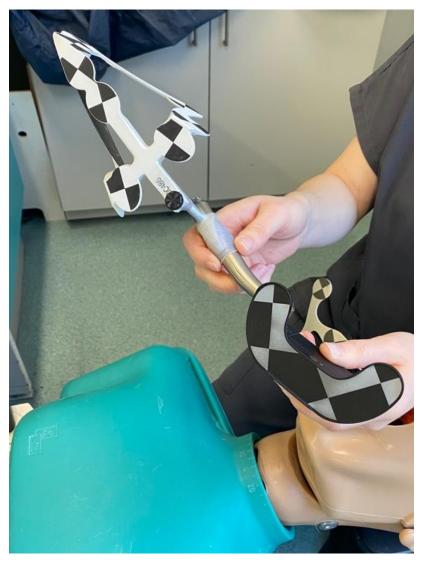


Figure 5-15 - Axis calibration.

Demonstrates the DrillTag secured to the handpiece (held with right hand) and the Calibrator tool used to calibrate the drill axis.

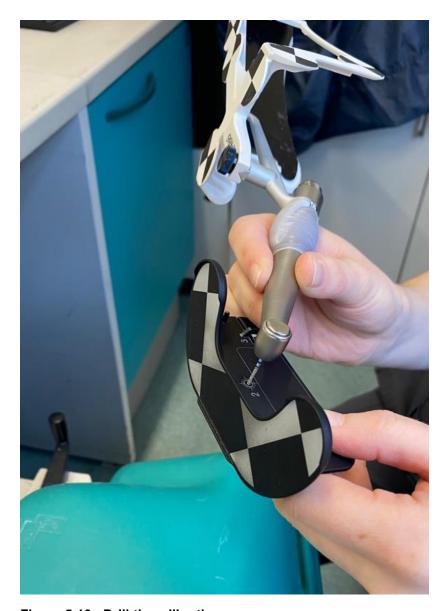


Figure 5-16 - Drill-tip calibration.

Demonstrates the bur secured in the handpiece with the tip of the bur placed onto the Calibrator tool dimple to calibrate the drill tip.

Triangulation of the DrillTag and Jaw Tracker with the MicronTracker generated a real-time image on the Navident laptop, showing the position of the handpiece and bur superimposed on the CBCT. A 'target view' displayed the horizontal deviation, angular deviation and depth in relation to planned endodontic access. The MB1 canal was accessed first by selecting it from the 'Targeted Guidance Selection' menu to avoid switching guidance between adjacent access paths during navigation (Figure 5-17). The operator performed the access cavity by precisely following the displayed target in real time, making corrections for any misalignment before continuing. Drilling stopped once the target drill depth was reached (Figure 5-18). The target depth was indicated by a colour change of the depth indicator: from green through to yellow when within 1mm of the planned

drill depth and turning red once the target depth was achieved. The same process was repeated for each subsequent canal, MB2, followed by DB and P, using the targeted guidance selection menu. Successful canal location was verified after access using a DG16 probe and if required, a 10K stainless steel file (VDW Dental, Munich, Germany). Where further confirmation was required, the DOM was used to visualise the canal orifice.

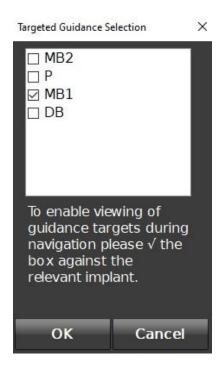


Figure 5-17 - Target guidance selection menu.

Demonstrates selection of the MB1 canal to avoid switching guidance between adjacent access paths during navigation.

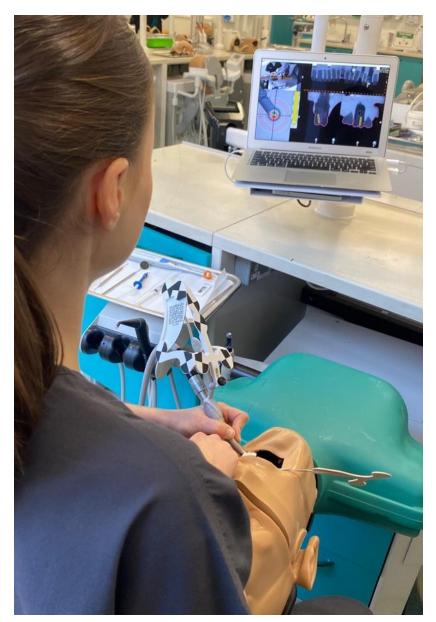


Figure 5-18 - Operator performing DN.

Demonstrates the operator following the displayed target on the laptop screen. The yellow depth indicator demonstrates the operator was within 1mm of the planned drill depth.

Once access was completed, the tooth and bur were replaced, and the protocol was repeated. To ensure accurate tooth positioning, the Nissin jaw model was removed from the phantom head before the tooth was replaced and secured using the previously described method. Trace registration and drill-tip calibration were repeated before commencing the next access.

5.6.2.2 Freehand access cavity preparation

Each tooth was secured in the same Nissin jaw model as previously described. Access was performed using the 1.2mm diameter cylinder bur and speed-increasing handpiece, as described in the DNS group. A DOM was used to

simulate the operator's usual clinical conditions. During FH access cavity preparation, CBCT imaging was available to aid the operator with canal location. Operators were instructed to access each canal aiming for minimal volume loss. The operator was permitted to stop or proceed to the next canal if there was a suspected perforation or the canal could not be located.

5.6.3 Experimental measurements

The primary outcome measure was:

1) Total 3D volume loss (mm³)

The secondary outcome measures were:

- 1) Incidence of successful canal location (n)
- 2) Incidence of perforation (n)
- 3) Time (s)

The total 3D volume loss was calculated using automatic segmentation and volume analysis software. A pre-operative CBCT of a single unmounted tooth and a post-operative CBCT of each accessed tooth were obtained using the KaVo OP 3D Vision, with the same parameters previously outlined. The DICOM files were then converted to STL format using InVesalius 3.1.1 software. Following automatic segmentation and volume analysis, the total volume loss (mm³) was calculated by comparison of the pre-operative and post-operative volumes.

The incidence of successful canal location and perforation were assessed and recorded according to predefined criteria by two examiners, operator 1 and operator 2. Successful canal location was defined as location of the canal in the absence of a perforation. The examiners used a 10K stainless steel file in the canal orifice and observed its exit through the 'apex' to confirm canal location. Blinding was not required due to the binary nature of this outcome measure.

The time taken for access using DN and FH was measured to the nearest second using a digital stopwatch, starting once the bur contacted the tooth and finishing

once access of all canals was confirmed with a DG16 probe or 10K stainless steel file. In the DN group, the time required for trace registration and drill tip calibration for each tooth was also recorded using a time lapse, to provide a more accurate indication of the efficiency.

5.6.4 Statistical methods

All statistical analyses of the study data were undertaken using IBM SPSS Statistics (version 29.0.2.0) (IBM Corp., Armonk, NY, United States). Descriptive statistics were provided for total volume loss, the incidence of successful canal location, the incidence of perforation and the time taken for each group (DN, FH) and subgroup (A, B, C and D). The normality of the data was assessed both visually using histograms and statistically using the Shapiro-Wilk test and was found to be non-normally distributed. These data were summarised using the median and interquartile range (Q1-Q3). The two-tailed Mann-Whitney U test with a significance level set at 0.05 was utilised for group comparisons. For categorical data, a two-tailed Pearson Chi-Square with a significance level set at 0.05 was utilised.

5.7 Results

5.7.1 Tooth optimisation results

The results of the tooth optimisation process, encompassing both the suitability screening and suitability assessment are listed in Table 5-1. A total of five teeth underwent suitability screening and four met the criteria for suitability assessment, ultimately leading to the selection of one tooth for inclusion within the study.

Table 5-1 - Tooth optimisation results: suitability screening and assessment.

Tooth number	Source	Description	Suitability screening outcome	Suitability assessment outcome	Reason for exclusion
1	Plan B Dental	Prefabricated moderately sclerosed maxillary molar	Unsuitable		Pulp chamber present
2	DRSK	Custom maxillary left molar	Suitable	Excluded	Full length of canals not patent clinically Canals poorly visible and differentiated from the surrounding tooth structure on CBCT
3	Newcastle University	Custom maxillary right molar with apices removed at right angles	Suitable	Excluded	Full length of MB1 & DB canals not patent clinically MB & DB canals poorly visible and differentiated from the surrounding tooth structure on CBCT
4	Newcastle University	Custom maxillary right molar with apices removed and oblique cut of MB and DB roots	Suitable	Excluded	Oblique cut across MB & DB roots close to CEJ inappropriately altered root morphology
5	Newcastle University	Custom maxillary left molar with root apices removed at right angles	Suitable	Included	

PlanB Dental (Goleta, CA, USA) was identified as a supplier of prefabricated maxillary molars with calcified pulp chambers (referred to as 'tooth 1'). These teeth failed to meet the suitability screening criteria due to the presence of a pulp chamber and the extension of the pulp coronal to the CEJ. Therefore, it

was determined that custom teeth would be necessary to fulfil the suitability criteria. Custom teeth available commercially were sourced from DRSK (DRSK Group AB, Hassleholm, Sweden). This tooth (referred to as 'tooth 2') had canals that were not patent clinically along their entire length. An axial CBCT section (Figure 5-19) demonstrated the absence of clear patent canals and poor differentiation from the surrounding tooth structure.

It was concluded that commercially available 3D-printed teeth did not meet the defined suitability criteria. To address this, a custom tooth was developed in collaboration with the 3D printing team at the School of Dental Sciences, Newcastle University. The initial sample provided by Newcastle University (referred to as 'tooth 3') had a patent P canal on both clinical and CBCT examination. However, the MB1 and DB canals were not patent, as demonstrated in Figure 5-20 and Figure 5-21, due to retained resin within the canals.

To resolve this, the STL file was modified by introducing an oblique cut over the MB and DB roots to increase the apical aperture diameter, enabling the drainage of unset resin (referred to as 'tooth 4') (Figure 5-22). Although clinical and CBCT examination revealed three patent canals, the oblique root resection was in close proximity to the CEJ, creating the risk of an artificial perforation during endodontic access, even with minimal deviation from the MB canal (Figure 5-23).

Finally, a second STL file of a maxillary molar was obtained that satisfied all the suitability criteria (referred to as 'tooth 5'). The perpendicular root resection allowed any unset resin to drain during the printing process Figure 5-2. The canals were clearly visible and patent along the entire root length, as demonstrated in Figure 5-24 and Figure 5-25.

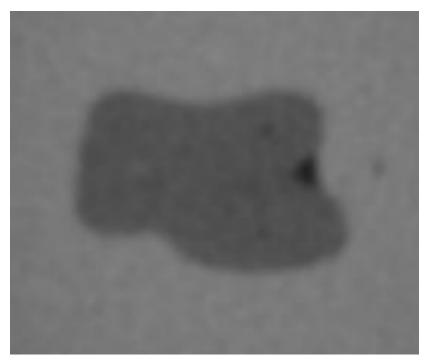


Figure 5-19 - Axial CBCT view of tooth 2. Demonstrates the tooth mounted in silicone putty with a lack of clear patent canals and poor differentiation from the surrounding tooth structure.



Figure 5-20 - Photograph of tooth 3. Demonstrates a visible and patent P canal but absence of the MB and DB canals.

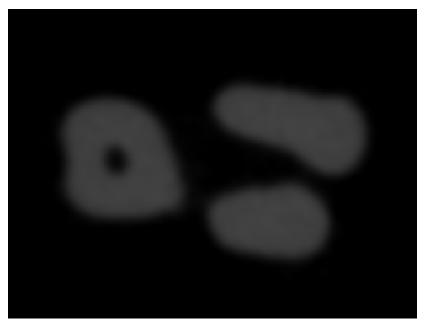


Figure 5-21 - Axial CBCT view of tooth 3. Demonstrates a patent P canal but lack of patency of the MB and DB canals.



Figure 5-22 - Photograph of tooth 4. Demonstrates the oblique resection across the MB and DB roots in close proximity to the CEJ.

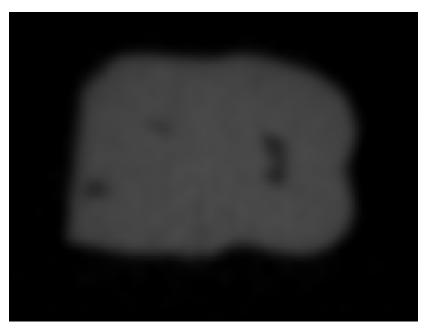


Figure 5-23 - Axial CBCT view of tooth 4.

Demonstrates MB canal in close proximity to oblique root resection.

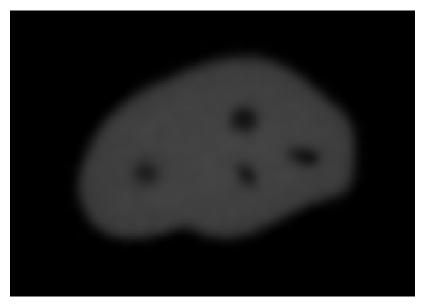


Figure 5-24 - Axial CBCT view of the coronal root third of tooth 5. Demonstrates patent MB1, MB2, DB and P canals which are clearly differentiated from the surrounding tooth structure.

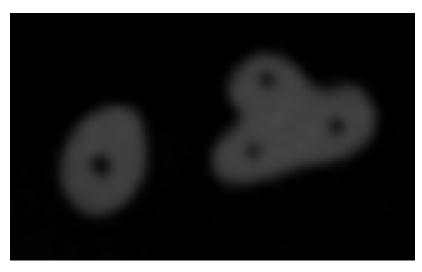


Figure 5-25 - Axial CBCT view of the apical third of tooth 5. Demonstrates patent MB1, MB2, DB and P canals which are clearly differentiated from the surrounding tooth structure.

A summary of the tooth-by-tooth suitability assessment results prior to inclusion within the main study are detailed in Table 5-2. Just under half the sample of teeth obtained were considered suitable for inclusion within the main study. Examples of teeth excluded following clinical examination are presented in Figure 5-26, Figure 5-27, Figure 5-28 and Figure 5-29. Additionally, Figure 5-30 represents an example of a CBCT scan taken during the tooth-by-tooth suitability assessment.

Table 5-2 - Tooth optimisation results: tooth-by-tooth suitability assessment.

Demonstrates the number of teeth excluded following clinical and CBCT examination and the total number of teeth suitable for inclusion within the main study.

Reason for exclusion	Number of teeth excluded
Clinical examination (n=	120)
Altered crown/root morphology or one or more canals not patent with hand instrumentation	45
CBCT examination (n=	75)
One or more canals not visible or continuous	20
Total suitable for inclusion	(n=55)



Figure 5-26 - Tooth excluded due to altered crown morphology. Demonstrates a flat MB cusp tip, in addition to other surface defects.



Figure 5-27 - Tooth excluded due to altered root morphology. Demonstrates a horizontal groove across the middle third of the roots.



Figure 5-28 - Tooth excluded due to altered root morphology. Demonstrates a vertical groove along the palatal root.



Figure 5-29 - Tooth excluded due to lack of patent canals present clinically. Demonstrates the MB1, MB2 and P canals are filled with resin.

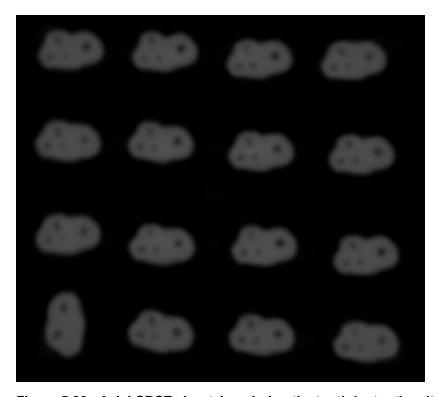


Figure 5-30 - Axial CBCT view taken during the tooth-by-tooth suitability assessment prior to inclusion within the main study.

Demonstrates tooth position 1 (lower left) does not have a patent MB1 and MB2 canal and therefore was excluded from the study.

5.7.2 Pilot study results

All root canals were successfully located without any perforations. The results of the volume loss are detailed in Table 5-3. On average, the volume loss was 10.304mm³ less with DN compared to FH. The results were used to inform the sample size calculation for this study.

Table 5-3 - Pilot study results.

Demonstrates the pre-operative volume, post-operative volume and volume loss for the six pilot teeth and the mean volume loss each group (DN, FH).

Group	Tooth	Pre-op	Post-op	Volume	Mean
	number	volume (mm³)	volume (mm³)	loss (mm³)	volume loss
					(mm³)
					(standard
					deviation)
DN	1	1072.795	1022.624	50.171	46.611
	3	1072.795	1017.734	55.061	(10.685)
		10-0-0-	1000 105	2.4.400	
	6	1072.795	1038.195	34.600	
		1070 707	1000 011	10.010	
FH	2	1072.795	1003.946	68.849	56.915
	4	1072 70F	1025 904	46 004	(11 000)
	4	1072.795	1025.891	46.904	(11.098)
	5	1072.795	1017.804	54.991	
	5	10/2./95	1017.004) 4 .771	

5.7.3 Main study results

A total of 164 canals in 41 teeth were included in this in vitro study. Tooth 21 from group B was excluded due to dislodgement of the bur from the handpiece during drilling. Therefore, two additional teeth (teeth 41 and 42) were added to group B during the study, totalling 41 teeth.

5.7.3.1 Total 3D volume loss

The total volume loss (mm³) was calculated by comparison of the pre-operative and post-operative volume. Total volume loss for DN and FH groups was plotted graphically on a histogram depicted in Figure 5-31 and the results of the Shapiro-Wilk test are illustrated in Table 5-4. For the DN group, p>0.05 indicated a normal distribution, whereas for the FH group, p<0.05 indicating a non-normal

distribution. Therefore, statistical tests appropriate for non-normal data were used.

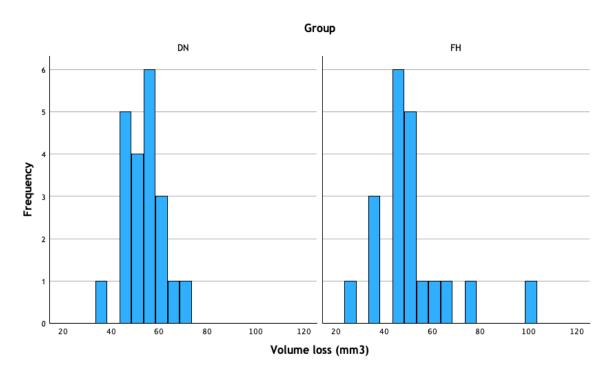


Figure 5-31 - Histogram showing total volume loss by group (DN, FH).

Table 5-4 - Results for Shapiro-Wilk test of normality for tooth volume loss. (df = degrees of freedom, Sig. = significance (p-value))

Group	Statistic	df	Sig.
DN	0.967	21	0.659
FH	0.866	20	0.010

The results for volume loss for each group (DN, FH) are detailed in Table 5-5 and the data are presented graphically in the box plot (Figure 5-32). No significant difference was observed in the median volume loss between the DN and FH groups (53.824 vs 48.144mm³, p=0.085). Examples of typical DN and FH access cavities are demonstrated in Figure 5-33 and Figure 5-34.

Table 5-5 - Results for total volume loss by group (DN, FH).

The corresponding P-value is shown from the two-tailed Mann-Whitney U test.

Group	N		Volume loss (mm³)	P-value (DN vs FH)
DN	21	Median (Q1-Q3)	53.824 (48.144-58.316)	0.085
		Minimum-maximum	36.369-69.656	
FH	20	Median (Q1-Q3)	48.144 (44.129-56.027)	
		Minimum-maximum	25.350-99.825	

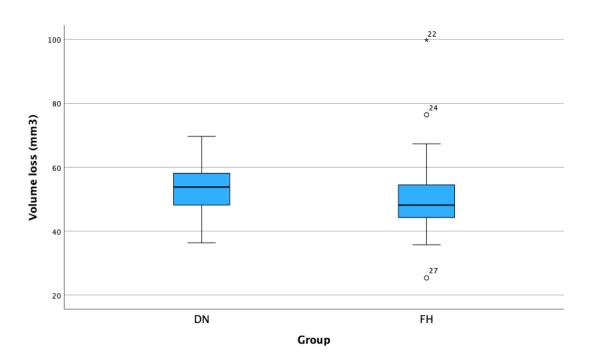


Figure 5-32 - Box plot showing volume loss per group (DN, FH). The box plot displays the median total time (median line within the box), the interquartile range (box) and the minimum and maximum times (whiskers), excluding outliers (points labelled tooth 22, 24, 27).

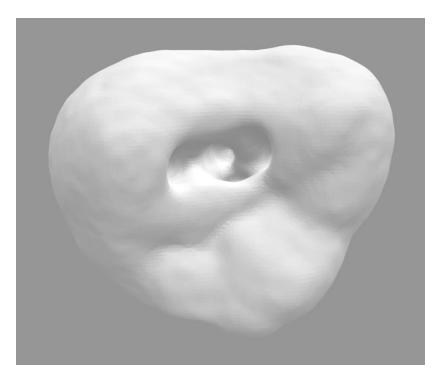


Figure 5-33 - STL file of tooth 16 (DN; subgroup A). Demonstrates a typical DN access cavity.

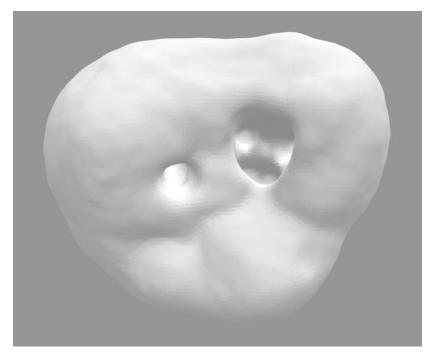


Figure 5-34 - STL file of tooth 19 (FH; subgroup D). Demonstrates a typical FH access cavity.

The results for volume loss for each subgroup (A, B C, D) are detailed in Table 5-6, with the data also presented graphically in the box plot (Figure 5-35). In the DN group, operator 1 (subgroup A) demonstrated significantly less volume loss than operator 2 (subgroup B) (p<0.001), although the study was not powered to

assess this. In the FH group, there was no significant difference in volume loss between the operators, though there was a trend towards operator 2 demonstrating a lower volume loss. Additionally, when examining overall trends, operator 1 performed marginally better with DN, while operator 2 performed marginally better with FH.

Subgroup C (FH; operator 1) demonstrated the highest interquartile range. The smallest volume loss, observed in tooth 23 (FH; subgroup C), was 25.350mm³, which was 30.3% less than the minimum volume loss observed in the DN groups (Figure 5-36). However, the same subgroup also observed the largest volume loss of 99.825mm³, 43.3% greater than the maximum volume loss in the DN group (Figure 5-37).

Table 5-6 - Results for total volume loss by subgroup (A, B, C, D). The median time for each operator and the corresponding P-value from the two-tailed Mann-Whitney U test comparing operator 1 and operator 2 for the DN and FH groups is displayed.

Group	Subgroup	N		Volume loss (mm³)	P-value
DN	Α	10	Median	48.144	<0.001
			(Q1-Q3)	(46.693-50.361)	
			Minimum-maximum	36.369-53.824	
	В	11	Median	58.120	
			(Q1-Q3)	54.885-62-826	
			Minimum-maximum	49.881-69.656	
FH	С	10	Median	49.209	0.393
			(Q1-Q3)	44.096-69.611	
			Minimum-maximum	25.350-99.825	
	D	10	Median	45.049	
			(Q1-Q3)	(42.366-52.261)	
			Minimum-maximum	(36.160-59.660)	

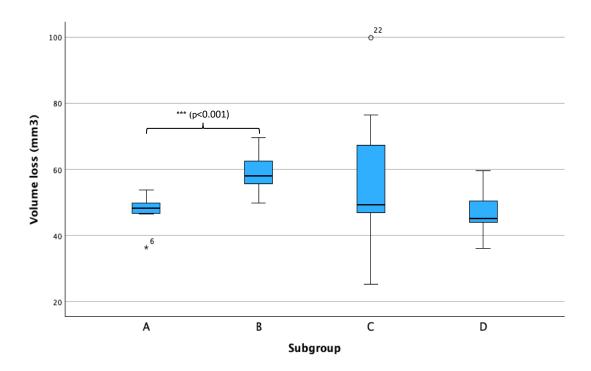


Figure 5-35 - Box plot showing volume loss per subgroup (A, B, C, D). The box plot displays the median total time (median line within the box), the interquartile range (box) and the minimum and maximum times (whiskers), excluding outliers (points labelled tooth 6, 22). *** (p<0.001) demonstrating statistically significant difference between subgroups A and B.

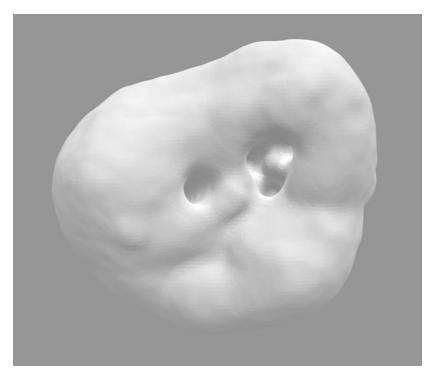


Figure 5-36 - STL file of tooth 23 (FH; subgroup C). Demonstrates the tooth with the lowest volume loss in the study following access cavity preparation.

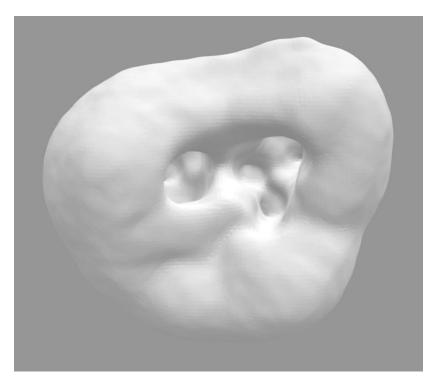


Figure 5-37 - STL file of tooth 3 (FH; subgroup C)
Demonstrates the tooth with the greatest volume loss in the study following access cavity preparation.

5.7.3.2 Incidence of successful canal location

The results for the incidence of successful canal location are detailed in Table 5-7. A total of 160/164 canals were successfully located. The success rates were 95.2% for the DN group and 100% for the FH group, resulting in an overall success of 97.6%. There was no significant difference between the groups, although the study was not powered to assess this. In the DN group, 4 canals (2 DB, 2 P) were not located, with these being distributed across two teeth (tooth 17 and tooth 29), one per operator.

Table 5-7 - Results for incidence of canal location by group (DN, FH) and subgroup (A, B, C, D).

The table presents the incidence of successful canal location for the groups and subgroups, along with the corresponding P-value from the two-tailed Pearson Chi-Square test comparing DN to FH.

Group	Incidence of successful canal location	P-value	Subgroup	Incidence of successful canal location
DN	80/84	0.157	В	38/40 42/44
FH	80/80		C D	40/40

5.7.3.3 Incidence of perforation

The incidence of perforation is detailed in Table 5-8. A single perforation occurred in the DN group (DB canal, tooth 17; subgroup B), demonstrated in Figure 5-38.

Table 5-8 - Descriptive statistics for incidence of perforation by group (DN, FH) and subgroup (A, B, C, D).

Group	Incidence of perforation (n)	Subgroup	Incidence of perforation (n)
DN	1/84	A	0/40
		В	1/44
FH	0/80	С	0/40
		D	0/40

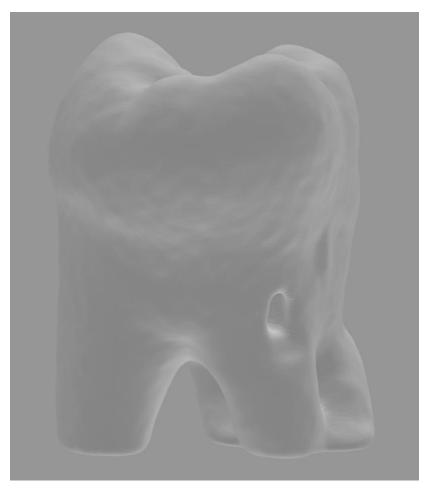


Figure 5-38 - Perforation of the DB canal in tooth 17, subgroup B (operator 2, DN).

5.7.3.4 Time

The total time was recorded for DN and FH, with registration and calibration times also reported separately for DN. Total time for DN and FH groups was plotted graphically on a histogram depicted in Figure 5-39 and the results of the Shapiro-Wilk test are illustrated in Table 5-9. For the DN group, p<0.05 indicated a non-normal distribution, whereas for the FH group, p>0.05 indicating a normal distribution. Therefore, statistical tests appropriate for non-normal data were used.

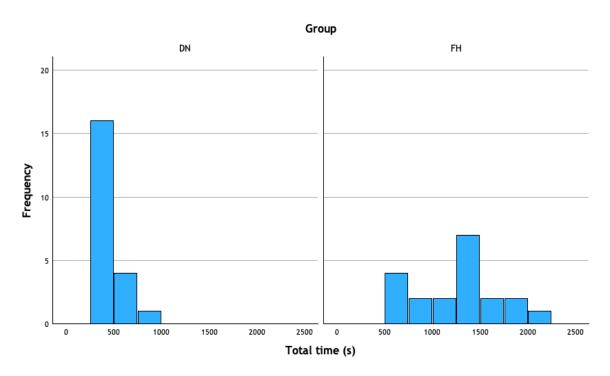


Figure 5-39 - Histogram displaying total time per group (DN, FH).

Table 5-9 - Results for Shapiro-Wilk test of normality for total time. (df = degrees of freedom, Sig. = significance (p-value))

Group	Statistic	df	Sig.
DN	0.853	21	0.005
FH	0.995	20	0.450

The results for the total time for each group (DN, FH) are detailed in Table 5-10 and the data are presented graphically in the box plot (Figure 5-40). Root canal location time was significantly less for DN compared to FH, even when registration and calibration time were considered (p<0.001). It is important to note that the study was not designed with time as the primary outcome measure. The median total time for DN was 6 minutes 52 seconds, while for FH was 21 minutes 56 seconds. The DN group showed a lower interquartile range compared to the FH group.

Table 5-10 - Results for total time by group (DN, FH). The table presents the time for registration/calibration and navigation for the DN group, as well as the total time for both DN and FH groups. The corresponding P-value is shown from the two-tailed Mann-Whitney U test.

Group	N		Time for	Time for	Total time	P value
			registration and	navigation	(s)	(DN vs
			calibration (s)	(s)		FH)
DN	21	Median	179	229	412	<0.001
		(Q1-Q3)	(163-246)	(214-279)	(337-506)	
		Minimum-	144-422	189-407	349-765	
		maximum				
FH	20	Median	n/a	n/a	1316	
		(04.00)			(055 454 4)	
		(Q1-Q3)			(855-1514)	
		Minimum-	n/a	n/a	506-2148	
		maximum				

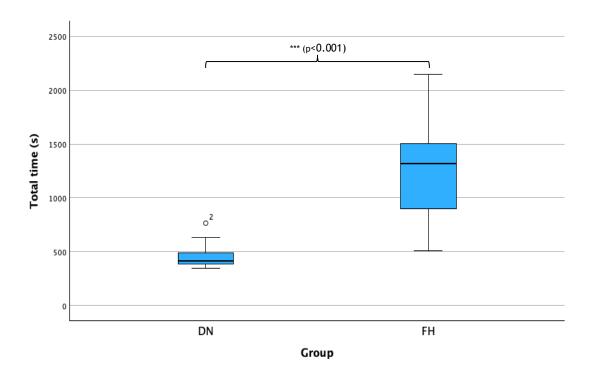


Figure 5-40 - Box plot showing total time per group (DN, FH). The box plot displays the median total time (median line within the box), the interquartile range (box) and the minimum and maximum times (whiskers), excluding the outlier (circle labelled tooth 2). *** (p<0.001) demonstrating statistically significant difference between DN and FH groups.

The results for total time for each subgroup (A, B C, D) are detailed in Table 5-11, with the data also presented graphically in the box plot (Figure 5-41). In the DN group, there was no significant difference between operators (p=0.051), while in the FH group the total time was significantly less for operator 1 (subgroup C) compared to operator 2 (subgroup D) (p=0.043). Again, it is important to note the study was not powered to assess differences between operators. In the DN group, operator 1 (subgroup A) showed a lower interquartile range compared to operator 2 (subgroup B) while in the FH group, operator 2 (subgroup D) showed a lower interquartile range compared to operator 1 (subgroup C).

Table 5-11 - Results for total time by subgroup (A, B, C, D).

The table presents the time for registration/calibration and navigation for the DN group (subgroups A and B) and the total time for all subgroups. The median time for each operator and the corresponding P-value from the two-tailed Mann-Whitney U test comparing operator

1 and operator 2 for the DN and FH groups is displayed.

Group	Subgroup	N		Time for	Time for	Total time	P-value
				registration and	navigation	(s)	
				calibration (s)	(s)		
DN	Α	10	Median	165	227	395	0.051
			(Q1-Q3)	(149-196)	(210-251)	(361-460)	
			Minimum- maximum	144-273	194-278	349-524	
	В	11	Median	208	260	453	
			(Q1-Q3)	(179-252)	(214-343)	(405-599)	
			Minimum- maximum	162-422	189-407	368-765	
FH	С	10	Median	n/a	n/a	980	0.043
			(Q1-Q3)			(582-1467)	
			Minimum- maximum	n/a	n/a	506-1756	
	D	10	Median	n/a	n/a	1451	
			(Q1-Q3)			(1244-1640)	
			Minimum- maximum	n/a	n/a	988-2148	

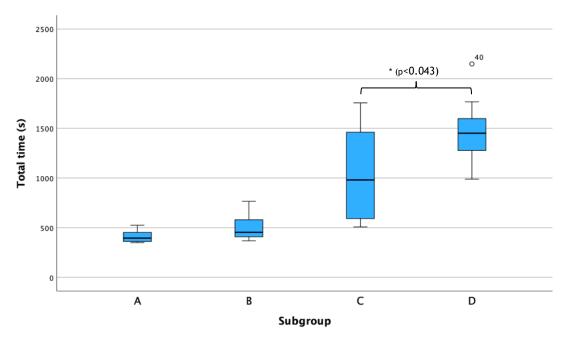


Figure 5-41 - Box plot showing total time per subgroup (A, B, C, D). The box plot displays the median total time (median line within the box), the interquartile range (box) and the minimum and maximum times (whiskers), excluding the outlier (circle labelled tooth 40). * (p<0.043) demonstrating statistically significant difference between subgroups C and D.

5.7.3.5 Summary of study results

This study compared DN and FH endodontic access for locating simulated calcified canals, using anatomically accurate 3D-printed maxillary molars.

Primary research aim

 To compare the tooth volume loss following DN and FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: There is no difference in tooth volume loss between DN and FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was accepted. There was no significant difference in tooth volume loss between DN and FH access.

Secondary research aims

 To compare the time taken for DN and FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: There is no difference in the time taken for DN and FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was rejected. Dynamic navigation significantly reduced the time required to locate canals compared to FH access.

2) (a) To assess the impact of operator experience on tooth volume loss following DN endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: Operator experience does not influence tooth volume loss following DN endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was rejected. Operator 1 (less experienced) demonstrated significantly less volume loss than operator 2 (more experienced) when using DN.

2) (b) To assess the impact of operator experience on tooth volume loss following FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: Operator experience does not influence tooth volume loss following FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was accepted. There was no statistically significant influence of operator experience on volume loss with FH.

3) (a) To assess the impact of operator experience on time taken for DN endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: Operator experience does not influence time taken for DN endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was accepted. Operator experience had no significant influence on the time taken for DN access.

3) (b) To assess the impact of operator experience on time taken for FH endodontic access for locating simulated calcified canals in anatomically accurate 3D-printed maxillary molars.

Null hypothesis: Operator experience does not influence time taken for FH endodontic access in anatomically accurate 3D-printed maxillary molars with simulated calcified canals.

Results: The null hypothesis was rejected. Operator 1 (less experienced) was significantly quicker than operator 2 (more experienced) when performing FH access.

Other results

1) Incidence of successful canal location

No significant differences were observed between DN and FH groups.

2) Incidence of perforation

One perforation occurred in the DN group, while no perforations occurred in the FH group.

Chapter 6 Discussion and conclusions

6.1 Accuracy of dynamic navigation for locating canals in teeth with pulp canal obliteration: A systematic review

The aim of the systematic review carried out as part of this thesis was to analyse the available literature on the accuracy of DN for root canal location in teeth with PCO, in comparison to FH access and/or SN. At the time of conducting the literature review, no systematic reviews had been published that exclusively addressed the benefits of DN in this context. It was determined that there was a need for a systematic review to synthesise the available evidence and identify research gaps that could be addressed.

One of the key advantages of conducting a systematic review was the clearly defined and transparent methodology, which helped to minimise the risk of reviewer bias. A clearly focused research question was developed alongside robust inclusion and exclusion criteria. Furthermore, the search strategy was both comprehensive and systematic, incorporating unpublished studies and grey literature. Given the apparent limited number of published studies in the main databases, this potentially provided the opportunity to capture additional relevant studies from a wider dataset. The approach also enabled a structured assessment of the quality of the included studies, allowing for a degree of caution when interpreting the findings, where appropriate.

A limitation of the systematic review process was that the strict inclusion and exclusion criteria resulted in the inclusion of only three studies. Case reports and case series were excluded, which although of low quality, may have provided valuable insights given that DN is a relatively new technology in endodontics. In addition, all included studies were in vitro, with no clinical studies fulfilling the eligibility criteria, thereby limiting the external validity and generalisability of the findings. A meta-analysis was not feasible due to heterogeneity among the studies, including differences in the tooth type, degree of PCO and reported outcomes. Instead, a narrative synthesis was conducted, facilitating a structured and transparent exploration of the data. It is also important to acknowledge that the database searches were completed in the

early stages of this thesis, with the last search conducted on 31 March 2023. Given the rapidly evolving nature of the literature, a considerable amount of time has since passed, increasing the likelihood that the review may now be outdated. Additional studies have been published since, some of which are referenced in Chapter 3.

6.2 Tooth volume loss following dynamic navigation and freehand endodontic access in calcified maxillary molars: An in vitro analysis

In this in vitro study, two operators with different levels of experience in endodontics performed DN and FH endodontic access on 3D-printed maxillary molars with simulated calcified canals. The study aimed to evaluate the differences in tooth volume loss and the influence of operator experience. To date, no studies had been published comparing DN and FH endodontic access for multiple canals in posterior teeth. This study established any potential clinical benefits of using DN for access in posterior teeth.

6.2.1 Discussion of results

6.2.1.1 Total 3D volume loss

The current study found no significant difference in total volume loss between DN and FH. Therefore, the null hypothesis that there is no difference in tooth volume loss between DN and FH endodontic access in anatomically accurate 3D printed maxillary molars with simulated calcified canals was accepted. This finding was contrary to the existing evidence base on the location of single canals, where previously published studies have found that DN significantly reduces tooth volume loss when compared to FH (Dianat et al. 2020; Jain et al. 2020b; Connert et al. 2021a; Huth et al. 2024). One possible explanation could be the software-related issues discussed in section 5.6.1.2. where software limitations required modifications to the initial access design. Briefly, the primary purpose of the software is for planning and guidance of implant placement, so overlap of guide paths cannot be coincident. So, for endodontic access planning, while the entry points on the occlusal surface were in close proximity to each other, they could not significantly overlap, leading to greater volume loss than may otherwise have been necessary.

Nonetheless, the current study did show that DN had a lower interquartile range, indicating greater consistency and reliability in access cavity preparation for this technique, which aligns with a recent study (Huth et al. 2024). Figure 5-33 and Figure 5-34 demonstrate the typical access cavity designs performed using DN and FH. Dynamic navigation produced an access cavity that closely resembles ConsAC, while in the FH group, the operator modified their access to reduce tooth volume loss, resembling TrussAC as defined in section 1.3.1. It is worth noting that the FH group's access cavity design does not reflect the typical clinical approach used by the operators, but it was important for the operators to perform an access with the smallest possible volume loss to act as a suitable comparator for the DN group.

When evaluating the impact of operator experience on tooth volume loss within the DN group, operator 1 (the specialty trainee) performed significantly better than operator 2 (the specialist endodontist), suggesting that the DNS is not dependent on prior endodontic experience. Contrary to findings in the existing literature, the specialist endodontist did not appear to gain a benefit from using DN (Connert et al. 2021b). The specialty trainee achieved reduced volume loss and greater consistency with DN compared to FH, indicating that MIE access cavities can be reliably performed by less experienced operators, achieving outcomes comparable to those of a specialist endodontist performing FH access.

6.2.1.2 Incidence of successful canal location

The FH group demonstrated a 100% canal location success rate, a result not previously reported in existing studies (Dianat et al. 2020; Jain et al. 2020c; Connert et al. 2021a; Huth et al. 2024). One possible explanation for this outcome could be the use of identical molars in the current study, whereas earlier studies utilised a variety of tooth types. Although measures were taken to prevent the operators from learning the location of the canals by limiting the number of teeth accessed per session and spacing out the sessions, it remains possible that the operators became familiar with the canal locations over time.

There were four unlocated canals within the DN group. A visual analysis of the post-operative CBCT of tooth 29 (subgroup A) revealed that the DB and P canal access paths followed the pre-planned trajectories but terminated 1mm short of

the actual canals. A review of the navigation footage confirmed that both access paths adhered to the protocol and reached the planned canal depths. This discrepancy suggests "anatomical" variation, potentially due to an undetected increase in simulated canal calcification due to variability in manufacture of the teeth. For tooth 17 (subgroup B), the post-operative CBCT revealed a complete shift of the access cavity towards the DB aspect of the tooth (Figure 6-1). Trace registration was successfully performed and verified without complications. However, the DB and P access paths showed a greater deviation from the planned access compared to MB1 and MB2. This DB shift in the access cavity was also observed in the post-operative STL file (Figure 6-2). One explanation may be inadequate stabilisation of the tooth within the jaw model allowing movement during the procedure, suggesting a deviation from the study protocol rather than a limitation of the DNS.

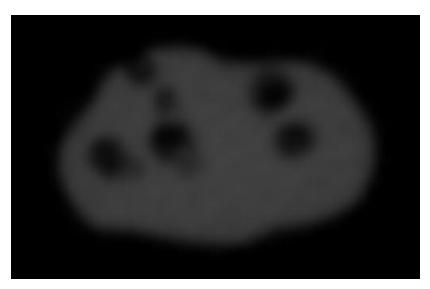


Figure 6-1 - Post-operative axial CBCT view of tooth 17 (DN; subgroup B)

Demonstrates a shift in the access cavity towards the DB aspect of the tooth and unlocated DB and P canals.

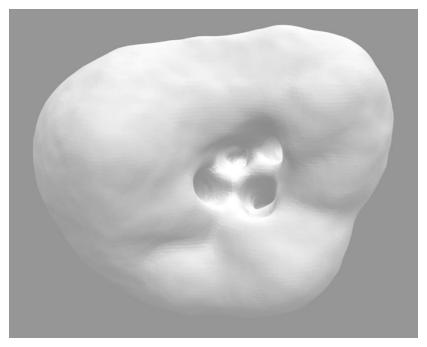


Figure 6-2 - STL file of tooth 17 (DN; subgroup B) access cavity Demonstrates DB shift of the access cavity in tooth 17.

6.2.1.3 Incidence of perforation

The current study did not find that DN reduced the incidence of perforation, contrary to some findings in the existing literature (Connert et al. 2021a; Huth et al. 2024). The incidence of perforations was low, with a single perforation in the DB aspect of the DB root, which was not recognised until completion of access. Evaluation of the navigation footage revealed a horizontal deviation of 0.1-0.5mm within the apical 5mm of the preparation. Considering that the root canal wall was at least 1.5mm thick at the point of perforation, this degree of deviation alone would not have been sufficient to cause the perforation. Instead, the perforation appeared to result from a shift in the access cavity, as described in the previous section (6.2.1.2), due to a deviation from the study protocol. Therefore, in a clinical environment the perforation is likely not to have occurred.

No perforations were observed in the FH group, despite an absence of internal anatomical landmarks to aid the operators in canal location within the 3D printed teeth. This contrasts with all previously published studies, which have reported one or more perforations (Dianat et al. 2020; Connert et al. 2021a; Huth et al. 2024). Providing an explanation for this is challenging, as the operators' level of experience was comparable to that in previous studies, and

neither operator had prior practice performing FH on this specific tooth before the study.

6.2.1.4 Time

This was the first study to report registration and calibration times in addition to access preparation time. Despite including these additional steps, DN proved to be significantly quicker and more consistent than FH access, supporting findings from previous studies and demonstrating it to be an efficient technique in molars (Dianat et al. 2020; Jain et al. 2020b). This is an important clinical consideration, as it can reduce the length and number of appointments required, enhancing patient and operator experience. Dynamic navigation reduced the total time required for both operators, highlighting its benefits for operators of all levels of experience, consistent with the findings from Dianat et al. (Dianat et al. 2020). In addition, the current study found no significant difference between the specialty trainee and the specialist endodontist, reinforcing the consistency of DN and its independence from experience level. In contrast, the times for FH access were highly variable.

The current study was the first study to report the time required to access multiple canals. Although the median total time was higher than reported in previous studies, this can be explained by the inclusion of access to four canals (Dianat et al. 2020; Jain et al. 2020a; Jain et al. 2020b; Connert et al. 2021a; Torres et al. 2021; Huth et al. 2024). The median total time for DN in this study was 412s, which falls within the range of average access times reported in earlier studies when considering time per canal. Additionally, it may be faster when considering access time alone (Jain et al. 2020a; Huth et al. 2024). It is important to note that DN requires extensive training to develop the necessary hand-eye coordination, especially considering the operator must adapt to looking away from the patient during the procedure. In this study, the operators practiced on 20 teeth to achieve proficiency. This is supported by existing literature on the use of DN in implant dentistry in both clinical and laboratory settings, indicating that efficiency improves significantly after 12 procedures and proficiency is typically achieved after 20 (Block et al. 2017; Wang et al. 2022). Following completion of this in vitro study, new research has been published evaluating the learning curve associated with DN for canal location in

teeth with PCO. In this study, an endodontist with no prior DN experience performed DN access on 45 maxillary anterior teeth with PCO in adult patients (Sharma et al. 2024). The study concluded that proficiency was generally reached between 18 and 28 cases. However, it is important to note that the operator participated in a two-day training course, including hands on experience, and the exact number of practices prior to the study was not specified. In addition, these studies were conducted with a limited number of operators and the learning curve may vary between individuals. The high efficiency observed in this study, compared to others like Huth et al., where only five practice teeth were used and DN was found to be less efficient than FH, may be attributed to the more intensive training (Huth et al. 2024). Notably, in the current study, four canals were accessed in a comparable time to that required for a single canal in the study by Huth et al. (Huth et al. 2024). With adequate training, DN appears to be an efficient method for canal location in molars with calcified canals.

6.2.2 Limitations

As with any in vitro study, inherent limitations in study design may impact the clinical applicability of the results.

Firstly, there were several limitations associated with the use of 3D-printed teeth, despite them being the standard for in vitro studies. While the use of 3D-printed teeth allowed standardisation and comparability between the groups, the monochromatic nature of the resin removed all internal anatomical landmarks ordinarily used to aid canal location, as described by Krasner and Rankow detailed in section 1.2 (Krasner and Rankow 2004). This does not accurately reflect a clinical scenario and could have inadvertently increased tooth volume loss and decreased operator efficiency within the FH group. Additionally, the tactile sensation of resin teeth differs from that of natural dentine. Existing literature suggests that the most notable difference between resin and natural teeth is material hardness, with natural dentine being significantly harder (Reymus et al. 2019; Reymus et al. 2020; Kolling et al. 2022). However, while the absolute values for volume loss and time may differ to natural teeth, the overall trends should remain consistent, as both groups used identical teeth. Another concern is the printing accuracy of the root canal

anatomy in 3D-printed teeth. However, a limited number of studies, including Cui et al., have found no significant difference when comparing internal and external surfaces of 3D-printed teeth to their natural tooth counterparts using CBCT (Cui et al. 2018). Despite this, 3D-printing still has a margin of error, which could be significant when the small diameter of calcified canals in considered. Therefore, the study required canals of larger diameter beyond the initial simulated calcification of the pulp chamber and root canal orifices. Nonetheless, the current study still identified variation among the 3D-printed teeth, as evidenced by the significant number excluded after clinical and CBCT examination during the tooth-by-tooth suitability assessment. Furthermore, it was deduced that two canals were not located in the DN group due to an increase in simulated canal calcification due to retained resin during the 3D printing process. Finally, the use of identical molars raises the possibility that the operators were able to learn the location of the canals, as previously discussed in section 6.2.1.2. While it would be advantageous to have included a range of 3D-printed teeth, developing the custom tooth was time-intensive, and optimising multiple teeth would have been impractical in this study. In addition, the 'plan' and 'scan' stages of the Navident protocol would need to be duplicated for each tooth type.

Errors may be introduced at any stage of the four stages during the Navident protocol (scan, plan, register and treat). System factors, including hardware and software issues are discussed here. Firstly, errors introduced during the 'scan' stage should be considered. The quality of the CBCT depends upon several factors, including the FOV and voxel size. While FOV and voxel size have not been shown to significantly impact the accuracy of DN, CBCT has been shown to cause measurement shrinkage compared to actual values (Komuro et al. 2021; Wang et al. 2023; Martinho et al. 2024a). The degree of shrinkage that occurs in capturing the CBCT differs to that of the model scanners, leading to a discrepancy, potentially impacting the accuracy of the trace registration when using surface-based registration. During the 'treat' stage, minor challenges were encountered, including difficulty securing the tooth and unintended movement within the jaw model during the experiment. This led to two undetected canals and a perforation in the DN group that would likely not have occurred in a clinical setting. This highlights that tooth mobility is a strict contraindication for

DN. Additionally, the operators also experienced challenges with drill axis calibration, likely due to wear on the calibration tool pin after extensive use. System-related issues lead to two teeth within each subgroup (subgroup A and B) requiring repeat calibration, unnecessarily increasing the total time.

6.3 Implications for future research

The systematic review highlighted the need for clinical studies, research using molar teeth with PCO and comparison to SN. While the in vitro study addressed the inclusion of molar teeth, it identified the need for further research using a broader range of multi-rooted teeth. This would help eliminate the risk of operator bias due to familiarity with canal position and support validation of the study's findings. Once DN has been validated across various multi-rooted teeth, clinical studies will be necessary to evaluate its clinical application and address the limitations described in both in vitro and ex vivo studies.

The steep learning curve and extensive training required for DN, explained by the need for the operator to adapt to looking away from the patient during the procedure, needs to be addressed. Augmented reality techniques offer a promising solution by superimposing the navigation target view onto the tooth using a head-mounted device (Martinho et al. 2024b). This technology allows the operator to maintain full visibility of the operative field, enhancing familiarity and simplifying the procedure. Furthermore, superimposition of the target view within the DOM would further enhance operator familiarity.

Additionally, robotic-assisted implant surgery has been shown in a recent systematic review to improve the accuracy of dental implant placement, making the potential application of robotics in endodontics an interesting area for further exploration (Yang and Li 2024). While research has demonstrated improved accuracy and efficiency in peri-radicular surgery using robotics compared to DN, the application of robotics for locating root canals in cases of PCO has yet to be explored (Chen et al. 2024; Liu et al. 2024).

6.4 Conclusions

The systematic review demonstrated that DN may increase the accuracy of canal location in teeth with PCO when compared to FH access in an in vitro setting. However, these findings should be interpreted with caution due to the limited number of included studies.

In the present in vitro study, no significant difference was observed in the total volume loss between DN and FH endodontic access in 3D-printed maxillary molars with simulated calcified canals, although DN demonstrated greater consistency. Importantly, DN enabled a less experienced operator to efficiently and reliably perform a MIE access cavity comparable to an experienced specialist endodontist. Although DN did not significantly improve the success of canal location or reduce the incidence of perforation, it offered superior efficiency and consistency compared to FH access for operators of all levels of experience.

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