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The effect of tooth structure loss on the outcome of root canal retreatments: Experimental and clinical studies

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The effect of tooth structure loss on the outcome of root canal retreatments: Experimental and clinical studies

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A thesis submitted for the degree of

Doctor of Philosophy

Department of Conservative Dentistry

Dental Institute

King's College London

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Abstract

Objectives: The main objective of this research was to determine whether the volume of residual sound coronal tooth structure has an effect on the outcome of root canal retreatments assessed using cone beam computed tomography (CBCT). This research also aims to provide an estimate of the proportion of successful outcomes of primary and secondary root canal treatments (retreatments) determined by CBCT. The effect of the reduction of radiation dose on the detection of apical radiolucencies using CBCT and the accuracy of intraoral digital scanner to determine the volume of remaining coronal tooth structure were investigated *ex vivo* and *in vivo*, respectively.

Materials and methods: Reducing CBCT radiation dose was attempted by using a built-in dose reduction (DR) mode in an Accuitomo CBCT machine at 360° and 180° rotations for detecting simulated apical radiolucencies in a human dry mandible model. Volumetric measurements of the intraoral digital scanner were validated against micro-computed tomography. The differences in volume measurements and three-dimensional (3D) deviations between the two scanners were analysed using specialised surface metrology software (Geomagic Control). One-hundred and thirty-seven posterior teeth in 121 patients requiring root canal retreatment were assessed in a prospective clinical trial. All teeth were examined clinically and radiologically using periapical radiography and CBCT at baseline and 1 year after endodontic retreatment. A clinical impression was obtained for each tooth after completion of root canal retreatment, and following cast restoration placement to produce two casts. All casts were scanned using an intraoral digital scanner, and the 3D volume of remaining coronal tooth structure was calculated. In the pooled study, the one-year results for 354 teeth, including 123 primary treatments and 231 retreatments, were analysed.

Results: With regard to the experimental studies, there were no significant differences in the overall accuracy between CBCT 360°DR and 180°DR when compared to the

control standard dose scans, while reducing the radiation dose by more than 50%. Small volumetric differences (0.68%-1.36%) were observed between the intraoral digital scanner and μCT measurements. At one-year, overall percentage of favourable results was 88.3% using periapical radiographs, and 81.8% for CBCT (*P*=0.035). Teeth retaining less than 30% of their original coronal tooth structure volume had a significantly higher proportion of unfavourable treatment outcomes (*P*=0.040). In the pooled study, the percentage of favourable results for primary treatments (84.7%) with CBCT was not statistically different (*P*=0.316) from that of retreatments (77.9%). Molar teeth were significantly less successful (*P*=0.001) than anterior and premolar teeth pooled together.

Conclusions: The radiation dose to the patients can be significantly reduced by using CBCT DR mode, while maintaining good diagnostic accuracy in detecting small periapical radiolucencies. Intraoral digital scanning accurately quantifies the residual coronal tooth structure. Root canal retreated teeth with less than 30% volume of sound remaining coronal tooth structure had a significantly higher endodontic failure rate than teeth with a remaining tooth structure volume more than 30%. The proportions of favourable results of primary root canal treatment and retreatment are comparable. CBCT detected more failures in molar teeth than anterior teeth and premolars compared with periapical radiographs.

Table of Contents

Abstract **2**

Table of Contents **4**

List of Figures **10**

List of Tables **13**

List of Abbreviations **16**

Acknowledgements **18**

Introduction 20

Overview 20

Research aims 21

Structure of the thesis 23

Chapter 1 Literature Review **25**

1.1 Root canal treatment 25

1.1.1 Reasons for failure of initial root canal treatment 25

1.2 Root canal retreatment 27

1.3 Endodontic treatment outcome 28

1.3.1 Success and failure definition 28

1.3.2 Retreatments success rate 33

1.3.3 Periapical index (PAI) 39

1.4 Limitations of conventional radiography for the diagnosis of outcome of endodontic treatments 40

1.4.1 Compression of three-dimensional anatomy....40

1.4.2 Geometric distortion 41

1.4.3 Anatomical noise....42

1.5 Adjunct and alternative radiographic techniques for the assessment of the outcome of endodontic treatments....43

1.5.1 Cone beam computed tomography....44

1.6 Relationship between the outcome of endodontically treated teeth and residual coronal tooth structure....55

1.6.1 Estimation of remaining coronal tooth structure....55

1.6.2 Effect of remaining tooth structure on fracture resistance: *in vitro* studies....67

1.6.3 Remaining tooth structure and outcome of restorations of endodontically treated teeth 71

1.7 The effect of coronal restoration on endodontic treatment outcome 75

1.7.1 Restoration type 75

1.7.2 Restoration quality 76

1.8 Summary 82

Chapter 2 The detection of simulated periapical lesions in human dry mandibles using cone beam computed tomography – a dose reduction study....83

2.1 Introduction....83

2.2 Materials and methods 86

2.2.1 Subject material preparation 86

2.2.2 Radiographic technique 91

2.2.3 Radiological assessment 93

2.2.4 Statistical analysis 95

2.3 Results 95

2.4 Discussion 98

2.5 Conclusion 105

Chapter 3 Assessment of residual coronal tooth structure post-endodontic cavity preparation using digital dental impressions and micro-computed tomography 106

3.1 Introduction 106

3.2 Materials and methods 109

3.2.1 Tooth preparation 109

3.2.2 Data acquisition and segmentation 110

3.2.3 Alignment of datasets 114

3.2.4 Data evaluation and 3D comparisons 115

3.2.5 Statistical analysis 117

3.3 Results 117

3.4 Discussion 120

3.5 Conclusions 125

Chapter 4 The outcome of endodontic retreatment in teeth with varying degrees of coronal tooth structure loss: a prospective clinical study 126

4.1 Introduction 126

4.2 Materials and methods 129

4.2.1 Study design and ethical approval 129

4.2.2 Sample size and recruitment 130

4.2.3 Inclusion and exclusion criteria 131

4.2.4 Pre-operative assessment 132

4.2.5 Clinical intervention 133

4.2.6 Remaining tooth structure measurements 136

4.2.7 Patient recall 139

4.2.8 Clinical and radiological evaluation at follow-up 140

4.2.9 Quality of coronal restoration assessment 141

4.2.10 Radiological assessment of the endodontic outcome 142

4.2.11 Statistical analysis 145

4.3 Results 147

4.4 Discussion 157

4.5 Conclusions 166

Chapter 5 Pooled analysis of one-year recall data from three endodontic treatment outcome studies undertaken using cone beam computed tomography 167

5.1 Introduction 167

5.2 Materials and methods 168

5.2.1 Selection criteria 168

5.2.2 Inclusion and exclusion criteria 168

5.2.3 Radiographic technique 169

5.2.4 Clinical intervention 169

5.2.5 Outcome assessment 170

5.2.6 Data analysis 171

5.3 Results 171

5.4 Discussion 179

5.5 Conclusion 185

Chapter 6 Summary and suggestions for future work 186

6.1 Summary 186

6.2 Suggestions for future work 189

Appendices 190

Appendix I: Publications 190

List of publications in international peer-reviewed journal 190

List of abstracts submitted to national and international conferences 190

Appendix II: Receiver operating characteristics curves for detection of simulated periapical lesions 204

Appendix III: Research Ethics Committee approval letter 208

Appendix IV: Research and Development approval letter 212

Appendix V: Clinical trial participant's information sheet 214

Appendix VI: Clinical trial consent form 218

Appendix VII: Clinical trial case report form 219

Appendix VIII: Structured step by step form for operators 226

References 227

List of Figures

Figure i-1 Flowchart representing the structure of the PhD project 24

Figure 2-1 Diagram illustrating the variation in CBCT tube current (mA) intensity during dose reduction (DR) mode scanning. 85

Figure 2-2 (a) Dry mandible with lower right first molar sectioned in a bucco-lingual direction through furcation 87

Figure 2-3 (a) Parallel and (b, c) parallax digital periapical radiographs, (d, e) sagittal and coronal reconstructed 180° CBCT images with standard full dose, and (f, g) with dose reduction mode, (h, i) sagittal and coronal reconstructed 360° CBCT images with standard full dose and (j, k) with dose reduction mode following the creation of a small simulated periapical lesion 89

Figure 2-4 (a) Parallel and (b, c) parallax digital periapical radiographs, (d, e) sagittal and coronal reconstructed 180° CBCT images with standard full dose, and (f, g) with dose reduction mode, (h, i) sagittal and coronal reconstructed 360° CBCT images with standard full dose and (j, k) with dose reduction mode following the creation of a large simulated periapical lesion 90

Figure 2-5 Jig used to position mandibles during periapical radiographs taking. 92

Figure 2-6 Jig used to position mandibles during CBCT scanning. 93

Figure 3-1 Measurement process for determining the accuracy of the intraoral digital scanner 111

Figure 3-2 Example scans of (a) the profilometric calibrated model (upper right first molar [highlighted by red circle]) used to assess the precision (repeatability and reproducibility) of measurements by intraoral digital scanner 112

Figure 3-3 Representative samples for the teeth, intraoral digital scanner and μCT models 115

Figure 3-4 Colour-coded difference images presenting for positive and negative deviations analysis between intraoral digital model and (a) μCT1 model, (b) μCT2 model 116

Figure 4-1 Representative stone casts showing the lower right first molar (a) before core placement, (b) and after crown cementation 136

Figure 4-2 Examples of three-dimensional digital models of the right mandibular posterior teeth generated by the 3M True Definition digital scanner 137

Figure 4-3 Examples of three-dimensional digital models of the lower right first molar in Geomagic software 138

Figure 4-4 Examples of three-dimensional digital model representations of the remaining coronal dentine walls following the completion of root canal retreatment 139

Figure 4-5 Intraoral periapical radiographs show examples of inadequate coronal restorations (yellow arrows) 141

Figure 4-6 (a,b) Pre-operative and 1 year post-operative periapical radiographs of the lower left first molar where both examiners confirmed complete healing of the periapical lesion associated with the mesial (yellow arrows) and distal roots (red arrows). (c-d) Pre-operative and 1 year post-operative reconstructed images of the lower left first molar mesial and distal roots in axial, coronal and sagittal planes reveal complete healing of the distal root, (e-f) and reduction in the lesion size of the mesial root 143

Figure 4-7 Flowchart of the trial showing the process of patient recruitment, exclusion and follow-up 148

Figure 4-8 Frequency distribution of teeth according to tooth type 149

Figure 4-9 Frequency distribution of favourable and unfavourable outcomes associated with the volume (%) of remaining coronal tooth structure 150

Figure 4-10 Three-dimensional digital model representations of teeth with different percentages of remaining coronal tooth structure before core build-up and after crown cementation 151

Figure 5-1 Teeth distribution according to the tooth type 174

List of Tables

Table 1-1 Pre-operative, intra-operative, and post-operative prognostic factors affecting the outcome of root canal retreatment (Ng *et al.* 2011)..... 37

Table 1-2 Selected published effective doses in micro Sieverts (μSv) for standard or default exposures for various field of view (FOV) CBCT devices..... 48

Table 1-3 Tooth restorability index (TRI) (Bandlish *et al.* 2006)..... 58

Table 1-4 Classification used to assess the amount of remaining tooth structure in three aspects (vertical, horizontal, and flaring of canal orifice)..... 59

Table 1-5 Classification used to assess the restorability of teeth (Samet & Jotkowitz 2009) 61

Table 1-6 Operating principles and technical data of the currently available market-leading intraoral scanning systems (Masri & Driscoll 2015)..... 64

Table 1-7 Clinical and radiographic criteria for evaluation the quality of coronal restorations (Hommez *et al.* 2002) 78

Table 2-1 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting small periapical lesions..... 96

Table 2-2 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting large periapical lesions 96

Table 2-3 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting all periapical lesions..... 97

Table 2-4 Kappa values for intra- and inter-examiner agreement in reading periapical radiographs and CBCT..... 98

Table 3-1 Accuracy, repeatability, and reproducibility values of the test digital intraoral scanner and the surface metrology software (Geomagic Control) 118

Table 3-2 Comparison of means ±SD (mm^3) and volume differences (%) between the intraoral scanner and µCT scans 119

Table 3-3 Mean and maximum 3D deviations resulting from the superimposition of intraoral scanner (TEST) datasets with both µCT datasets..... 119

Table 4-1 Inclusion and exclusion criteria 131

Table 4-2 Reasons for further exclusions after recruitment 131

Table 4-3 The outcome categories for root canal retreatment (Patel *et al.* 2012b).... 145

Table 4-4 Reasons for patients' non-attendance at the review appointments 147

Table 4-5 Frequency distribution of outcome of treatment for each tooth assessed using periapical radiographs (PA) and CBCT (n=132)..... 152

Table 4-6 Percentage of favourable and unfavourable outcomes based on clinical symptoms and radiological examination with periapical radiographs (PA) and CBCT (n=137) 153

Table 4-7 Kappa values for agreement between and within examiners on outcome diagnosis using periapical radiographs (PA) and CBCT, and on quality of coronal restorations..... 155

Table 4-8 Frequencies and percentages of unfavourable outcomes among groups within different coronal walls remaining 155

Table 4-9 Quality of coronal restoration in relation to root canal retreatment outcome (n=132) (teeth which failed before the one-year recall were excluded)..... 156

Table 5-1 Univariate distribution of pre-operative and post-operative variables 173

Table 5-2 Recall rates for teeth and patients in the included studies 174

Table 5-3 Frequency distribution of outcome of treatment for each tooth in primary root canal treatment, retreatment, and pooled samples (n=346) assessed using periapical radiographs (PA) and CBCT (radiological assessment only) 175

Table 5-4 Percentage of success rates based on clinical symptoms and radiological examination with periapical radiographs (PA) and CBCT for each tooth type in the pooled sample (n=354) 176

Table 5-5 The outcome of root canal treatments according to pre-operative variables as determined by periapical radiography (PA) and CBCT 178

Table 5-6 Kappa values for intra-consensus panel agreement and inter-examiner agreement on outcome diagnosis using periapical radiography (PA) and CBCT 179

List of Abbreviations

Abbreviation	Meaning
AAE	American association of endodontists
ALARA	As low as reasonably achievable
AUC	Area under the curve
CBCT	Cone beam computed tomography
CEJ	Cemento-enamel junction
CI	Confidence interval
CT	Computed tomography
DICOM	Digital imagining and communication in medicine
DO	Distal-occlusal
DR	Dose reduction
ESE	European society of endodontology
FOV	Field of view
GCP	Good clinical practice
GIC	Glass ionomer cement
ICC	Intraclass correlations
ICRP	International commission on radiological protection
IRM	Intermediate restorative material
μCT	Micro-computed tomography
μSv	Micro Sievert
MO	Mesial-occlusal
MOD	Mesial-occlusal-distal
MTA	Mineral trioxide aggregate
NaOCl	Sodium hypochlorite

Abbreviation	Meaning
NPV	Negative predictive value
NRES	National research ethics service
OR	Odds ratio
PA	Periapical
PAI	Periapical index
PPV	Positive predictive value
R&D	Research and development
REC	Research ethics committee
ROC	Receiver operating characteristic
STL	STereo-Lithography format
TIFF	Tagged image file format
TRI	Tooth restorability index
χ^2	Chi-square test

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I dedicate this work to the soul of my deceased **father** who died one week after I joined the PhD programme... I miss you, dad; your memory will be eternal.

Introduction

Overview

The goal of root canal treatment is to prevent or facilitate the healing of apical periodontitis and maintain the function of root canal treated teeth (Ørstavik & Pitt Ford 2008). Root canal treatment sometimes may fail, even when the treatment is carried out to the highest standard. Persistent apical periodontitis after root canal treatment could be the result of intraradicular or extraradicular infection, foreign body reaction, accumulation of endogenous cholesterol crystals, true cystic lesions or scar tissue healing (Nair 2006). Root canal retreatment is often considered the treatment of choice for cases with failed primary root canal treatment (Wenteler *et al.* 2015, Torabinejad *et al.* 2016). The successful outcome of root canal retreatment has been reported to range from 62% to 90% based on 'strict' (complete resolution of periapical radiolucency) criteria, and from 28% to 93% based on 'loose' (reduction in size of periapical radiolucency) radiographic criteria for success (Ng *et al.* 2008), which is comparable to the success rate of primary root canal treatment (Ng *et al.* 2011).

Endodontic treatment currently benefits from the introduction of cone beam computed tomography (CBCT) imaging, which has been proven to overcome most of the limitations of conventional periapical radiography, and to more accurately assess the outcome of root canal treatment (Patel *et al.* 2015). Results from clinical outcomes studies have shown a lower success rate of endodontic treatment when assessed with CBCT compared with periapical radiography (Patel *et al.* 2012b, Davies *et al.* 2016). However, the routine use of CBCT for identification of periapical pathosis has not been recommended yet, primarily due to the concern about the high radiation dose to the patients compared with standard two-dimensional imaging techniques (European Society of Endodontology 2014). Thus, the use of CBCT should be considered when the benefits outweigh the risk, and the clinicians should always adjust the radiation dose to

be as low as reasonably achievable (ALARA) (ICRP 2007). Several studies have attempted to reduce the radiation dose to the patients by adjusting the field of view, voxel size, and the degree of arc of rotation while maintaining an adequate diagnostic image (Lennon *et al.* 2011, Ludlow & Walker 2013).

Several factors have been found to affect the outcome of root canal retreatment; these include the absence of pre-operative periapical lesion and perforation, the quality of root filling and the presence of satisfactory coronal restoration (de Chevigny *et al.* 2008b, Ng *et al.* 2011). Analysis of the remaining coronal sound tooth structure is one of the most important parameters for clinical decision-making, leading to the selection of proper treatment options. The available data on the effect of the remaining coronal tooth structure on the outcome of root canal treatments, on the survival of endodontically treated teeth, and on the prognosis of the restorations of root canal treated teeth are limited, and based on non-reproducible and inaccurate qualitative methods used to estimate the amount of remaining coronal tooth structure.

Research aims

Experimental studies

1. The aim of the first experimental (*ex vivo*) study was to investigate the diagnostic accuracy of periapical radiography and CBCT on the detection of simulated periapical lesions in human dry mandibles, and to investigate the effect of CBCT dose reduction on the ability to detect simulated periapical lesions.

2. The aim of the second experimental (*in vitro*) study was to assess the use of intraoral digital scanning for quantification of the volume of residual coronal tooth structure after access cavity preparation, using micro-computed tomography as a gold standard.

Clinical investigations

1. The aim of the clinical trial was to prospectively evaluate the effect of the volume of residual coronal tooth structure, measured with an intraoral scanner, on the outcome of root canal retreatments on posterior teeth using periapical radiography and CBCT.

2. The aim of the pooled study was to compare the outcomes of teeth following primary root canal treatments and retreatments using periapical radiography and CBCT.

Structure of the thesis

There are six chapters in this thesis. Chapter 1 is a review of the literature with regard to the reasons for the failure of primary root canal treatments, the outcome of root canal retreatments, the limitations of conventional periapical radiography, the advantages and disadvantages of CBCT as an adjunct imaging technique for the assessment of endodontic outcome, the relationship between the outcome of endodontically treated teeth and residual coronal tooth structure, the methods used to estimate the remaining coronal tooth structure with a focus on the use of intraoral digital scanners, and the effect of the quality of coronal restorations on the periapical health of endodontically treated teeth.

Chapter 2 investigates the effect of a CBCT dose reduction mode on the ability to detect simulated periapical lesions in an attempt to reduce the radiation dose to the patients.

Chapter 3 evaluates the volumetric scanning accuracy of digital impressions for the three-dimensional measurement of residual coronal tooth structure.

Chapter 4 describes the clinical trial, investigating prospectively the outcome of endodontic retreatments in teeth with varying degrees of coronal tooth structure loss.

Chapter 5 is a pooled study analysing the 1-year recall data from three endodontic treatment and retreatment outcome studies.

Chapter 6 describes the main findings of the four studies, along with future work that could be carried out on this research topic.

Figure i-1 summarises the workflow of the research accomplished in this project.

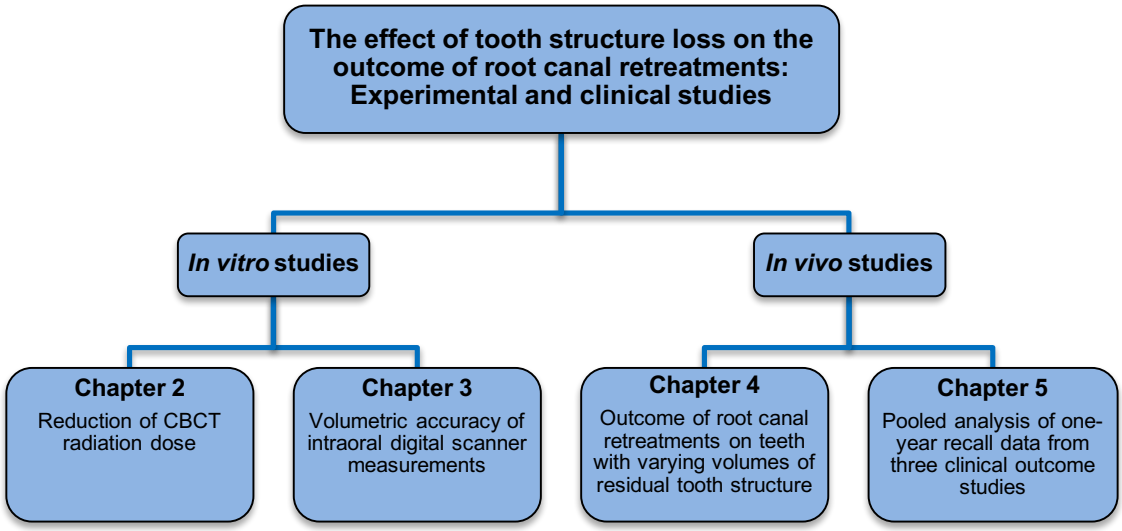

Figure i-1 Flowchart representing the structure of the PhD project

Chapter 1 Literature Review

1.1 Root canal treatment

According to the European Society of Endodontology (ESE) "*Endodontology is concerned with the study of the form, function and health of, injuries to and diseases of the dental pulp and periradicular region, their prevention and treatment; the principle of disease being apical periodontitis, caused by infection*" (European Society of Endodontology 2006). The aim of root canal treatment is to preserve or restore periradicular tissues back to health (European Society of Endodontology 2006) by means of cleaning, shaping, disinfection of contaminated root canals followed by three-dimensional obturation of the root canal system to create a hermetic apical seal (Torabinejad *et al.* 2005).

Instrumentation of the root canal is an important phase of root canal treatment (Schilder 1974) that involves the removal of pathologic pulp (vital and necrotic tissues) from the root canal system, creation of a space for the irrigants and medicaments to disinfect the contaminated root canals, and the creation of root canal shape that allows the obturation of the root canal system in three dimensions (Peters 2004). After this, a permanent coronal restoration can be placed to restore function and aesthetic. The creation of a coronal and apical hermetic seal through adequate root filling and coronal restoration should result in prevention of future reinfection (Ray & Trope 1995, Hulsmann *et al.* 2005).

1.1.1 Reasons for failure of initial root canal treatment

Apical periodontitis is a chronic inflammation in the apical periodontium that develops as a response to the persistence of microbial infection within the root canal system (Sundqvist 1976). Even when adhering to the highest standards during initial root canal treatment and despite the development of new technologies and materials, periapical

healing may not always be achievable in teeth following primary endodontic treatment; and the patient's signs and symptoms might persist or new disease emerge some time following treatment (Sundqvist *et al.* 1998, Salehrabi & Rotstein 2004). Therefore, further clinical intervention is indicated to achieve successful results. It is well acknowledged that the primary reason for post-treatment diseases associated with root filled teeth is recurrent or persistent microbial infection possibly associated with the complex non-accessible areas of root canal system (i.e. accessory canals and/or dentinal tubules) (Davis *et al.* 1972, Stropko 1999, Peters *et al.* 2004, Nair 2006).

Furthermore, debridement and obturation techniques have several inherent limitations that may restrict proper eradication of bacteria from the root canal systems, such as the intricate root canal anatomy, which may prevent a complete removal of bacterial biofilms from the pulp space (Peters 2004). Bacteria remaining in the root canal system at the time of root canal filling or penetrating after filling as a result of coronal restoration leakage may perpetuate periradicular inflammation (Siqueira 2001).

Less frequently, endodontic failures could be extraradicular in origin, attributed to periapical actinomycosis (Tronstad *et al.* 1990), foreign body reactions initiated by periapical over extrusion of root canal materials or other exogenous materials (Nair *et al.* 1990a, Koppang *et al.* 1992), accumulation of endogenous cholesterol crystals in apical periodontitis lesions (Nair *et al.* 1998, Nair 1999), and presence of true cystic lesions (Nair 1999).

Furthermore, it is possible that post-endodontic factors such as lack of adequate coronal seal and/or secondary caries could lead to recontamination of the root canal system and subsequently a persistent apical periodontitis (Ray & Trope 1995, Siqueira 2001, Aquilino & Caplan 2002).

1.2 Root canal retreatment

When the initial root canal treatment has failed, a comprehensive case evaluation should be performed before choosing one of the several treatment options available, including non-surgical root canal retreatment, endodontic surgery, intentional replantation, auto-transplantation or extraction and replacement by fixed dental prosthesis or single-tooth implant (Torabinejad & White 2016). Choosing the optimal treatment option for the management of a patient with persistent apical periodontitis is more complex than the management for a patient with apical periodontitis affecting non-vital teeth (Friedman 2002a).

Non-surgical root canal retreatment is the treatment of choice when the initial root canal treatment has failed, unless the potential risks associated with the root canal retreatment of the individual tooth appears to outweigh those of apical surgery, while endodontic surgery is to be considered prior to tooth extraction and replacement by single-tooth implant (Friedman 2002a, Torabinejad & White 2016). Risk factors associated with retreatments such as the presence of post-and-core restorations, full coverage restorations (crowns, bridges) and root canal obstacles, and with apical surgery such as proximity to inferior alveolar nerve, maxillary sinus, and accessibility are all influencing the decision to undertake either orthograde retreatment or apical surgery in the management of post-treatment disease (Danin *et al.* 1996, Friedman 2002a).

Root canal retreatment is a non-surgical approach indicated to manage teeth that have an inadequate existing root canal filling, which may be associated with radiographic evidence of newly developed or persisting apical periodontitis with or without clinical symptoms (European Society of Endodontology 2006). The goal of root canal retreatment is the management of any pathologic or iatrogenic defects that cause apical periodontitis to re-establish healthy periapical tissues (Ruddle 2002).

When root canal retreatment is performed to high standards, it often results in resolution of apical periodontitis, and reduces the risk of apical surgery or extraction in a considerable number of failed cases (Friedman 2008). Furthermore, non-surgical root canal retreatment is advisable and cost-effective in comparison with extraction and replacement with a bridge, denture or implant (Pennington *et al.* 2009).

1.3 Endodontic treatment outcome

1.3.1 Success and failure definition

Traditionally, clinical, radiographic and histologic characteristics can contribute to analysing the root canal success (Estrela *et al.* 2014). Histologically, endodontic success is defined by the complete repair of the periapical tissues without the presence of inflammatory cells (Abbott 1991). Few studies have used histopathological examination as the reference standard to assess the diagnostic ability of periapical radiographs and cone beam computed tomography (CBCT) (de Paula-Silva *et al.* 2009, Kanagasingam *et al.* 2016b). However, it is unethical to get human tissue from live patients. Thus, clinical and radiological examinations are the most commonly used methods to evaluate endodontic success.

Because patients' symptoms are very subjective and most endodontically treated teeth remain asymptomatic even if apical periodontitis is persisting or developing (Friedman 2002a, Yu *et al.* 2012), the assessment of the outcome of root canal treatment is largely based on the radiographic changes in the size of the periapical lesion as a reflection of the improvement or deterioration of the periapical health, and whether the ultimate goal of endodontics has been reached or not. The current success definition is based on either 'stringent/strict' or 'lenient/loose' criteria (Friedman 2002b). In some studies, the 'stringent/strict' criterion was used which is based on the presence of combined clinical and radiographic normality (complete resolution of the periapical radiolucency) (Strindberg 1956, Bystrom & Sundqvist 1981, Molven & Halse 1988, Sjögren *et al.* 1990,

Friedman *et al.* 1995, Ng *et al.* 2011). While in other studies, the 'lenient /loose' criterion was used, which is primarily based on the absence of clinical signs and symptoms, with radiological evidence of complete resolution or reduction in the size of the periapical radiolucency (Matsumoto *et al.* 1987, Pettiette *et al.* 2001, Ng *et al.* 2011). Clearly, the use of less stringent criteria in assessing the outcome of root canal treatment increases the anticipated success rates. In addition to that, some other studies used the radiological findings as the only outcome measure (Molven & Halse 1988, Murphy *et al.* 1991, Ørstavik & Hörsted-Bindslev 1993, Ørstavik 1996, Trope *et al.* 1999, Pettiette *et al.* 2001).

The earliest study which assessed the outcome of endodontic treatment was published by Strindberg (1956). In this study, a total of 254 patients with 529 endodontically treated teeth were followed for 2-10 years, and assessed on the basis of clinical and radiographic measures. Based on Strindberg's classification, which is designed to detect changes in radiographic appearance, teeth demonstrating an absence of clinical symptoms with normal radiographic contour, width and structure of the periodontal margin or widened periodontal contours mainly around the excess root filling material were classified as a 'success'. On the other hand, the presence of clinical symptoms and/or radiographic signs of a newly emerged lesion or reduced, unchanged, increased in the initial lesion size was considered as a 'failure'. Roots were categorised as 'uncertain' if the radiographs were ambiguous or technically unsatisfactory to assess the periapical health status and could not for some reason be repeated, or when the tooth was extracted before the 3-year recall visit due to an unrelated reason to the root of interest (Strindberg 1956).

According to Bender's outcome criteria, endodontic success involves the absence of pain or swelling, no loss of function, no evidence of tissue destruction, the disappearance of sinuses, and radiological evidence of an eliminated or arrested area of radiolucencies 6 months to 2 years post-endodontic treatment (Bender *et al.* 1966).

In a study by Gorni and Gagliani (2004), the healing process of root canal retreated teeth was evaluated after an observation period of 24 months according to different terms. The term ‘complete healing’ was used for all teeth with a normal/intact periodontal ligament space around the root with the absence of any associated clinical signs and symptoms; the term ‘incomplete healing’ was used only for teeth with pre-operative periapical lesion that show a notable resolution of the periapical lesion with no clinical signs and symptoms during the recall visit. The cases that had no pre-operative periapical radiolucency but have pre-operative clinical signs and symptoms would be considered as ‘unsatisfactory healing’ or ‘failure’ if the signs and symptoms persist at the end of treatment or if a new periapical lesion emerges. Additionally, the cases that have a pre-operative periapical lesion would be considered as a ‘failure’ if the lesion persists, and is not changed or enlarged in size (Gorni & Gagliani 2004).

The ESE (2006) suggests that root canal treatment should be assessed both clinically and radiologically at least 1 year post-treatment and subsequently for up to 4 years before a case is judged as a ‘failure’ (European Society of Endodontology 2006). According to ESE guidelines (1994), root canal treatment is considered as a ‘success’ if there is an absence of pain, swelling and other symptoms, no sinus tract and no loss of function, and radiological evidence of a normal periodontal ligament space surrounding the entire root contour. The treatment is ‘not considered a success’ when periapical radiographs reveal that a lesion has the same size or has just reduced in size; while the treatment is considered as a ‘failure’ if a new lesion developed subsequent to root canal treatment, if a pre-existing lesion has increased in size, remained unchanged or only diminished in size on the 4-year recall radiograph, and if signs of continuing root resorption or hypercementosis are present (European Society of Endodontology 1994). In 2006, the ESE replaced the terms ‘success’, ‘not a success’ and ‘failure’ used to assess the outcome of root canal treatment by the terms ‘favourable’, ‘uncertain’, and ‘unfavourable’ outcomes (European Society of Endodontology 2006).

In the Toronto study (de Chevigny *et al.* 2008a, de Chevigny *et al.* 2008b), the 4-6 years outcomes of 510 initial treatments and 229 retreatments were assessed based on combined clinical and radiographic measures, and were classified as 'healed' when no radiological evidence of apical periodontitis, no signs and symptoms apart from tenderness to percussion were present; 'diseased' when apical periodontitis, signs and symptoms were present; and 'functional' when teeth show absence of any signs and symptoms regardless of the periapical index (PAI) score.

In a 10-year retrospective cohort study by Fonzar *et al.* (2009), the long-term outcomes used were 'complete success' for asymptomatic teeth showing no radiographic appearance of periapical or lateral radiolucency; 'partial success' for asymptomatic teeth with radiological evidence of periapical improvement; 'partial failure' for asymptomatic teeth having no periapical improvement or even worsening; 'complete failure' for all extracted teeth (Fonzar *et al.* 2009).

In a prospective study investigating the factors influencing the periapical health in non-surgical root canal treatments (Ng *et al.* 2011), the treatment success was judged based on both 'strict' and 'loose' criteria. In 'strict' criteria, success was defined as the absence of pain, inflammation or swelling accompanied by radiological evidence of complete healing with normal periodontal ligament space, while in 'loose' criteria, success was defined as the absence of pain, inflammation or swelling with radiographic signs of complete (normal periodontal ligament space) or incomplete healing (reduction in the size of the periapical lesion). Failure was considered if the tooth had been extracted due to endodontic problems.

Wu *et al.* (2011b) suggested the use of 'effective' and 'ineffective' terms in place of 'success' and 'failure' terms in assessing the 1-year outcome following root canal treatment. The term 'effective' treatment is used when no clinical symptoms are present with a partial or complete resolution of the pre-operative periapical lesion or when no

new periapical lesion will emerge 1 year post-operatively. This term would involve both 'healed' and 'healing' categories proposed by Friedman and Mor (2004), and would not require further clinical intervention, while the term 'ineffective' treatment is used when a new periapical lesion developed or a pre-existing lesion enlarged and/or there was emergence or persistence of clinical signs and symptoms that would require further intervention. The authors suggested that using the proposed new terms will have some advantages over the terms 'success' and 'failure'. Firstly, shortening the recall period into one year instead of four, thus improving the recall rate and lessening the required appointments and radiographs; secondly, to avoid unnecessary retreatments demonstrated by adhering to previous definitions (Figdor 2002); thirdly, the terms 'effective' and 'ineffective' specify if further clinical intervention is indicated which will offer easier and more reproducible clinical decisions (Wu *et al.* 2011).

In a recent study (Azim *et al.* 2016), the root canal treatment outcome was evaluated after a mean follow-up period of 2 years using 'healed' (complete healing), 'healing' (incomplete healing) and 'not healing' outcome measures. The main distinction that recognises the outcome measures used in this study from other studies' classification is the 'not healing' outcome. The 'not healing' outcome is considered for teeth showing no change in size, an increase in size, new periapical lesion development, and having clinical signs and symptoms present. This outcome is further divided into 'uncertain healing' if no change in the size of periapical lesion is noticed, with an absence of signs and symptoms, or into 'unsatisfactory healing' if a new periapical lesion developed, increased in size, or there are clinical signs and symptoms present. 'Favourable outcome' was generally used to describe teeth that present with complete and incomplete healing, while 'unfavourable outcome' was used to describe teeth that present with 'uncertain' or 'unsatisfactory' healing.

1.3.2 Retreatments success rate

The potential for success or failure of primary root canal treatments and secondary non-surgical root canal treatments can be gleaned from numerous retrospective and prospective studies based on clinical examination and radiological evaluation (Strindberg 1956, Sjögren *et al.* 1990, Paik *et al.* 2004, Imura *et al.* 2007, Ng *et al.* 2008, de Chevigny *et al.* 2008b, Torabinejad *et al.* 2009, Ng *et al.* 2010, Salehrabi & Rotstein 2010, Ng *et al.* 2011, Patel *et al.* 2012b, Davies *et al.* 2016). Technical and therapeutic challenges during root canal retreatment are often different from those encountered during primary treatment (Ng *et al.* 2008). Iatrogenic factors and microbial flora are the most common causes that potentially contribute to a poor prognosis of endodontic retreatment (Nair *et al.* 1990b, Hepworth & Friedman 1997, Sundqvist *et al.* 1998, Gorni & Gagliani 2004).

As far back as 1956, Strindberg reported that the 10-year follow-up success rate of 187 orthograde retreatments without and with apical periodontitis were 95% and 84%, respectively, which were as successful as those of initial treatments (93% and 80%, respectively) (Strindberg 1956).

One of the most comprehensive studies investigating success rates of endodontic treatment was accomplished by Sjögren *et al. (*1990). Sjögren *et al.* followed Strindberg's (1956) criteria to judge the success of root canal treatment. The results showed that the pre-operative status of the pulp and periapical tissues significantly affected the outcome of treatment. The success rate for 173 retreated teeth without pre-operative periapical lesion was 98% after 8 to 10 years, whereas a 62% success rate was reported for retreatment cases with periapical pathosis (Sjögren *et al.* 1990).

Friedman *et al.* (1995) followed up patients after 6 to 18 months, and reported a 70.3% success rate in 128 retreated teeth, regardless of the pre-operative periapical condition. In this study, the reduction in or unchanging size of a pre-operative periapical lesion was considered as 'incomplete healing' and 'failure', respectively. The success rate was very

high (100%) (42 teeth) when no pre-operative periapical lesions were present, while the success rate was markedly lower at 55.8% (86 teeth) if periapical lesions were present before the retreatment (Friedman *et al.* 1995).

In a retrospective study to compare the outcome of root canal treated and retreated teeth using two different treatment protocols, Hoskinson *et al.* (2002) found that the overall combined success rate of 200 root canal treated teeth was 77%. Treatment protocols used in this study were different regarding instrumentation technique, apical size, degree of taper, irrigant, and obturation technique. The authors found no significant differences in treatment outcome between the two protocols (Hoskinson *et al.* 2002). This study had a high percentage of patients lost to follow-up (42%).

Friedman and Mor (2004) reviewed selected follow-up studies on the outcome of endodontic orthograde retreatment from 1956 till 2004. They reported that teeth present without apical periodontitis have healed rates ranging from 93% till 98% up to 10 years after retreatment, whereas the chance of teeth present with apical periodontitis to completely heal ranged from 74% to 86% (Friedman & Mor 2004).

Gorni and Gagliani (2004) related different clinical situations to the outcome of 452 endodontically retreated teeth from 451 patients monitored during a 24-month period. Teeth with calcification, apical blockage, broken instrument or under-filled canal with gutta-percha or cement were assigned into the ‘root canal morphology respected’ group, while teeth with internal or external transportation, perforation, stripping or internal resorption were assigned into the ‘root canal morphology altered’ group. The observed success rate was 86.8% in teeth with ‘respected root canal morphology’, whereas the success rate was 47% in teeth with ‘altered root canal morphology’. The overall success rate was 69.03% (Gorni & Gagliani 2004).

In a long follow-up study to identify the periapical changes in non-surgically retreated teeth 20-27-year post-endodontic treatment, Fristad *et al.* (2004) noticed a potential for late periapical healing, and an increased number of successful cases recorded when the observation time was extended for another 10 years. The radiographic success rate was 95.5% for retreated teeth recalled 20–27 years post-operatively (Fristad *et al.* 2004), while the success rate was 85.7% at the 10-17-year follow-up (Molven & Halse 1988). However, the retreated teeth included in this 20-27-year follow-up study represents only 53% of the original retreatments available at the 10-17-year follow-up. Moreover, the sample size was limited to 112 roots in 70 patients.

Çalışkan (2005) evaluated the outcome of 75 endodontically retreated teeth and 11 surgically treated teeth with persistent periapical lesions (2-11 mm in diameter). The sample included a combination of single-, 2- and 3-rooted teeth, which were followed for a period of 2 to 8 years. The overall complete healing of retreatment was 61.6%, and the incomplete healing was 14%. The size of the pre-operative periapical lesion negatively affected the healing rate of root canal retreated teeth. The reported complete healing rate for retreated teeth with periapical lesions <5 mm diameter was 64% and the incomplete healing was 13.3%. While the complete and incomplete healing rates for retreated teeth with lesions >5 mm diameter was 58.8% and 14.7%, respectively. For surgically treated teeth, the complete healing was 45.5%, and the incomplete healing was 18.2% (Çalışkan 2005). However, the author did not mention the healing rates recorded in regard to each tooth type.

In a retrospective study of 1376 teeth with initial endodontic treatments and 624 teeth with non-surgical retreatments, Imura *et al.* (2007) reported that the success rate for initial endodontic treatment (94%) was significantly higher than for non-surgical retreatments (85.9%) when reviewed at 18 months or longer. Pre-operative radiolucency, age, and tooth type were found to have a significant influence on the success rate of root canal retreated teeth (Imura *et al.* 2007). However, treatment

aspects used in this study were not standardised as the treatments were performed during a 30-year period, which can interfere with the treatment outcome recorded.

In a systematic review of the literature, Ng *et al. (*2008) assessed 17 studies published between 1961 and 2005 to investigate the success of secondary root canal treatment and the association of 18 clinical factors. After combining the data from these studies, the pooled success rate judged by 'complete healing' was 76.7% (95% confidence interval [CI]: 73.6%, 89.6%) and that by 'incomplete healing' was 77.2% (95% CI: 61.1%, 88.1%). The presence of a pre-operative periapical lesion, apical extent of root filling and quality of coronal restoration have the potential to affect success rates (Ng *et al.* 2008).

In the prospective Toronto study (phases 1-4), the pre-operative root filling quality, presence of a perforation, and apical periodontitis proved to be significant outcome predictors. The pooled success rates of 510 teeth with initial treatment and 229 teeth with retreatment followed 4-6 years post-retreatment were 86% and 82%, respectively (de Chevigny *et al.* 2008a, de Chevigny *et al.* 2008b). One drawback of the Toronto study is the low recall rate (32%-41%). This low recall rate may result in a biased outcome.

Torabinejad *et al.* published a systematic review in 2009 to compare the clinical and radiological outcomes of non-surgical retreatment with those of endodontic surgery. Higher success rate has been reported for endodontic surgery (77.8%) compared with non-surgical retreatment (70.9%) at 2-4 years. Conversely, the success rate was higher for the retreatments (83%) than for the endodontic surgery (71.8%) in the 4-6 years follow-up (Torabinejad *et al.* 2009).

In a 10-year retrospective cohort study of 411 patients (1175 teeth) treated and retreated in a private practice, 84.1% of teeth were considered a 'complete success', 3.9% a 'partial success', 4.4% a 'partial failure' and 5.8% a 'complete failure' (Fonzar *et al.* 2009).

Ng *et al.* (2011b) performed a prospective study to compare clinical and radiological outcomes of 750 root canal retreated teeth in 559 patients for 2-4 years. They reported a periapical healing rate of 80% based on the absence of apical periodontitis (strict criteria). Eleven pre-operative, intra-operative and post-operative prognostic factors were identified (Ng *et al.* 2011) (Table 1-1).

In their study, and in other studies (Liang *et al.* 2012, Huumonen & Ørstavik 2013), the success rate of the more technically challenging molar teeth (82.2%-82.5%) was found to be higher than that of incisors/canines (72.3%-75.4%). Other studies (Liang *et al.* 2011, Fernández *et al.* 2013) found that the tooth type (anterior, premolars, and molars) was not a significant predictor influencing the outcome of root canal treatment. This might be associated with the difficulty in detecting periapical lesions limited to the cancellous bone in the molar regions using periapical radiographs (Patel *et al.* 2009b, Cheung *et al.* 2013).

Table 1-1 Pre-operative, intra-operative, and post-operative prognostic factors affecting the outcome of root canal retreatment (Ng *et al.* 2011)

	Significant prognostic factors
Pre-operative factors	Presence of periapical lesion
	Size of the pre-operative lesion
	Presence of a sinus tract
	Presence of root perforation
Intra-operative factors	Patency at canal terminus
	Apical extent of canal instrumentation
	Additional use of EDTA as irrigant
	Absence of tooth/root perforation
	Absence of inter-appointment flare-up
	Absence of root-filling extrusion
Post-operative factors	Presence of satisfactory coronal restoration

In a recent meta-analysis, Kang *et al.* (2015) evaluated and compared the clinical and radiological outcomes of 7 non-surgical endodontic retreatment studies and 11 endodontic microsurgery studies. The pooled success rates for endodontic retreatment and endodontic microsurgery were 80% and 92%, respectively, assessed by the absence of clinical symptoms with radiographic signs of complete or partial reduction in the apical radiolucency size or with a PAI score ≤2 (Kang *et al.* 2015). However, in this study, the sample size was very low.

Azim *et al.* (2016) assessed retrospectively the treatment outcome and healing time of 422 roots in 291 non-surgical root canal treated and retreated teeth with a mean follow-up period of 2 years. They stated that 68.3% of retreated roots showed 'complete healing', 4.9% showed 'incomplete healing', while 7.3% of retreated roots presented with 'uncertain healing' and 19.5% had 'unsatisfactory healing'. The overall recorded 'favourable outcome' was 81.7%, and the 'unfavourable outcome' was 18.3%. The treatment outcome was significantly impacted by pre-operative pulp condition, procedural errors during treatment, apical extension and density of root fillings (Azim *et al.* 2016). However, in this study, a limited number (41 roots) of retreated roots was assessed compared to the number of vital (180 roots) and non-vital (201 roots) teeth involved.

It is important to realise that most of the reports on the outcome of root canal treatment have been based on clinical studies performed in dental schools or specialist clinics, in which strict operating protocols are enforced (Strindberg 1956, Sjögren *et al.* 1990, Imura *et al.* 2007, Ng *et al.* 2011, Fernández *et al.* 2013, Azim *et al.* 2016). Regardless of whether the 'strict' or 'loose' criteria were used, Ng *et al. (*2007) found in a literature review that initial root canal treatment performed by specialists (84.8%-87.6%) and postgraduate students (77.2%-93.1%) were associated with higher weighted pooled estimate of success than those treated by general dental practitioner (65.7%-86.2%) or undergraduate students (74.8%-83.3%) (Ng *et al.* 2007).

Burry *et al.* (2016) found significant differences in the 5-year survival rate of molars and the 10-year survival rate of all tooth types when the treatments have been performed by endodontists and non-endodontists (Burry *et al.* 2016). Therefore, the reported success rates in these higher standard studies do not necessarily reflect the realistic favoured outcome found within the average dental practices.

1.3.3 Periapical index (PAI)

Because of the frequent absence of clinical symptoms accompanying chronic apical periodontitis, the assessment of treatment outcome becomes mainly based on radiographs. Brynolf (1967) found that histologic changes of the periapical status in human autopsy material from 142 individuals could be differentiated and classified radiographically (Brynolf 1967). In an attempt to overcome the limitations of subjective radiographic criteria in the evaluation of treatment outcome, Ørstavik *et al.* (1986), based on Brynolf's (1967) findings, developed the Periapical Index (PAI), an ordinal scoring scale to radiologically analyse periapical periodontitis (Ørstavik *et al.* 1986). The PAI is based upon a set of five images that represent an ordinal scale of 5 scores ranging from healthy periapical bone (score 1) to severe apical periodontitis with exacerbating features (score 5) depending on the increasing extent and severity. This method was based on radiological and histological findings in the periapical region of maxillary incisors, thus, applying this index to all teeth, which have different thickness of overlying cortical bone and different positions of root tips in association with the cortex, might be questionable (Wu *et al.* 2009, Esposito *et al.* 2011).

The PAI was initially designed and applied to report radiographic changes on periapical radiographs for the factors under investigation in clinical trials (Ørstavik & Hörsted-Bindslev 1993, Trope *et al.* 1999, Delano *et al.* 2001), epidemiological studies (Eriksen *et al.* 1988) and in retrospective analyses of treatment results in endodontics (Ørstavik *et al.* 1986). It can also be adapted to success and failure criteria by dichotomising the

PAI scores into 'healthy' (PAI 1 or 2) or 'diseased' (PAI 3–5) categories (Huumonen & Ørstavik 2002). Furthermore, some epidemiological studies have utilised PAI to evaluate panoramic radiographs (Marques *et al.* 1998, De Moor *et al.* 2000, Lupi-Pegurier *et al.* 2002), or a combination of periapical and panoramic radiographs (Eriksen *et al.* 1988, Dugas *et al.* 2003), while some recent studies (Estrela *et al.* 2008a, Pope *et al.* 2014) modified the PAI based on CBCT (CBCT-PAI) and applied it to CBCT treatment outcome studies.

1.4 Limitations of conventional radiography for the diagnosis of outcome of endodontic treatments

The diagnostic value of radiographs is influenced by many factors such as beam angulation, morphological variations, anatomical structures superimpositions, and surrounding bone density (Shearer *et al.* 1991, Huumonen & Ørstavik 2002).

1.4.1 Compression of three-dimensional anatomy

Conventional radiography compresses all structures in the anatomical three-dimensional space into a two-dimensional image, therefore, certain clinical and biologic features might not be represented adequately (Huumonen *et al.* 2006, Estrela *et al.* 2008a). The compression of three-dimensional anatomy associated with conventional radiography greatly limits the diagnostic performance (Webber & Messura 1999, Cohenca *et al.* 2007, Patel *et al.* 2007). Data about the tooth and its surrounding tissues are obtained in the mesio-distal (proximal) plane only, while structures in the third (bucco-lingual) dimension cannot be fully appreciated (Patel *et al.* 2009b).

Conventional radiographs cannot often precisely assess the spatial relationship of the tooth's roots to their surrounding anatomical structures and any associated periradicular lesions (Cotti *et al.* 1999, Cotti & Campisi 2004). Furthermore, using conventional radiography to determine the actual location, nature and shape of anatomical diseases

affecting the dental hard tissues, such as resorption, is challenging (Cohenca *et al.* 2007, Patel *et al.* 2007, Durack *et al.* 2011).

In some cases, when clinical signs and symptoms are present but the radiographs are not showing any relevant information, taking additional radiographs with 10-15 degree changes in horizontal angulation (parallax technique) may be considered to overcome some of the limitations of conventional radiology (Patel & Pitt Ford 2007, Whaites & Drage 2013, Davies *et al.* 2015, Kanagasingam *et al.* 2016a). However, other studies found no significant difference in identification accuracy of periapical pathosis with different horizontal angulations (Folk *et al.* 2005, Soğur *et al.* 2012).

1.4.2 Geometric distortion

Conventional radiography does not replicate the three-dimensional complex anatomy of the teeth and surrounding tissues under assessment due to the complexity of the maxillo-facial skeleton and the characteristics of the radiation geometry (Gröndahl & Huumonen 2004). The paralleling technique is frequently recommended to take radiographs instead of the bisecting technique as it often provides images with a minimum of geometric distortion (Vande Voorde & Bjorndahl 1969, Forsberg 1987, Gröndahl & Huumonen 2004), but with some enlargement of structures (Nair 2006). However, it is not always feasible to locate the radiographic film parallel to the long axis of the tooth under investigation, such as in cases when the patients have a shallow palatal vault or gag reflex (Patel *et al.* 2010).

Over-angulation or under-angulation of the central beam during X-ray exposure may produce a foreshortened or elongated tooth, respectively (White & Pharaoh 2009, Whaites & Drage 2013), and decrease or increase the size of the radiolucent area or even result in the disappearance of periapical lesions (Bender & Seltzer 1961a, Scarfe *et al.* 1999, Huumonen & Ørstavik 2002).

1.4.3 Anatomical noise

Anatomical structures masking the areas of interest during radiographic imaging may render the interpretation of the two-dimensional radiograph difficult, referred to as anatomical noise (Revesz *et al.* 1974, Kundel & Revesz 1976, Gröndahl & Huumonen 2004). This often occurs where radiopaque anatomical features, such as zygomatic buttress or radiolucent anatomical features, such as maxillary sinus and incisive foramen, overlap over roots of teeth during radiographic imaging (Patel *et al.* 2009b). The more complex the anatomical noise, the greater the influence on the contrast of a radiographic image, and therefore the more difficulty in interpreting the radiographic images (Morgan 1965, Revesz *et al.* 1974, Kundel & Revesz 1976).

Periapical lesions are easily visible on radiographs if a demineralisation of 30% to 50% of the bone has occurred (Bender & Seltzer 1961a, Bender & Seltzer 1961b). Cortical plate involvement as a prerequisite for the radiographic detectability of periapical radiolucency is a subject of controversy. Some authors (Bender & Seltzer 1961a, Bender & Seltzer 1961b, Schwartz & Foster 1971, Bender 1997) demonstrated that periapical radiographs would not detect the periapical lesion unless it internally erodes the surrounding cortical bone or the cortical bone has been extensively eroded or destroyed from the outside. Bender and Seltzer (1961a,b) examined the detection of periapical lesions solely in the mandible, while Schwartz and Foster (1971) recorded lesions of both the maxilla and mandible. Using only five mandibles of human cadavers and based on 20 observations of different thicknesses and variations in depths cut in cortical bone, Bender (1982) reported that 12.5% cortical bone loss with 7.1% mineral bone loss in cortical bone is essential to produce radiographic visualisation (Bender 1982).

On the contrary, in a study that investigated the correlation between histology and radiological examination in adult dogs, Pitt Ford (1984) found no evidence that erosion of cortical plates is a prerequisite for radiographic lesion detection (Pitt Ford 1984).

Similarly, other studies revealed that in areas where the cortical bone was not too bulky, and the anatomical noise was minimal, cortical bone involvement was not necessary for radiographic identification of periapical lesion (Shoha *et al.* 1974, Lee & Messer 1986). Lee and Messer (1986) argued that anatomical structure such as the mandibular canal, as well as extraction socket, could be readily seen on radiographs, at least in many instances. However, in this study, only 20 molar teeth in 17 mandibles were examined, and no soft tissue simulation was used.

Radiographic visualisation is further affected by the lesion location inside the bone (Huumonen & Ørstavik 2002). Although experimentally induced periapical lesions of a certain size can be detected in regions covered by a thin cortex, lesions of the same size might be undetectable in a region covered by thicker cortex (Estrela *et al.* 2008b). The density of the surrounding anatomical structures also accounts for some over- or under-estimation of periapical lesion size due to the observable gray-level difference in radiographic images (Gröndahl & Huumonen 2004).

1.5 Adjunct and alternative radiographic techniques for the assessment of the outcome of endodontic treatments

Several imaging modalities have been demonstrated as viable diagnostic and treatment planning tools in endodontics to overcome the conventional radiographs limitations, namely digital subtraction radiology (DSR), digital radiography, tuned aperture computed tomography (TACT), ultrasound (US), magnetic resonance imaging (MRI), computed tomography (CT) and CBCT (Huumonen & Ørstavik 2002, Nair & Nair 2007, Patel *et al.* 2009b, Peters & Peters 2012). However, CBCT techology is fast gaining popularity in the speciality of endodontics.

1.5.1 Cone beam computed tomography

Cone beam computed tomography (CBCT) is a diagnostic imaging system introduced in the late 1990s particularly to generate three-dimensional images of the maxillofacial skeleton at a significantly lower radiation dose than traditional CT (Mozzo *et al.* 1998, Arai *et al.* 1999, Patel 2009).

1.5.1.1 Background

Unlike conventional computed tomography, CBCT captures a three-dimensional volume of data in a single rotation of the X-ray source and the detector, which rotate synchronously between 180° and 360° around the patient's head depending on the scanner used and/or the exposure parameters selected. A divergent pyramidal or cone-shaped X-ray beam is directed through the centre of the region of interest to capture a cylindrical or spherical volume of data called the field of view (FOV). Throughout the exposure sequence, hundreds of two-dimensional sequential planar projection images are obtained for the field of view. The two-dimensional projection images are then reconstructed to produce a three-dimensional volume of data (Patel 2009).

The generation of three-dimensional images allows a comprehensive three-dimensional evaluation of the entire tooth and its surrounding anatomy, allowing the clinician to choose any slice of volumetric data and view it in three orthogonal (axial, sagittal and coronal) planes simultaneously (Patel 2009, Durack & Patel 2012). This procedure differs from the current medical CT, which acquires individual image slices of the FOV by the use of a fan-shaped X-ray beam in a helical progression, and then these slices are stacked up to produce a three-dimensional representation. A separate scan and separate two-dimensional reconstruction are needed for each slice (Scarfe & Farman 2008).

The use of CBCT in dental practices is progressively increasing worldwide. Currently, a wide range of CBCT machines are available on the market with considerable differences in the FOV, number of projections (rotation angle), beam quality (tube voltage and filtration) and X-ray exposure settings (Pauwels *et al.* 2012). Many of the available CBCT machines offer a choice of certain parameters to be adjusted by the operator, such as FOV, degree of rotation, and exposure settings to be appropriate for a variety of dental applications, while other parameters, like beam quality and filtration, are mostly unique to each specific machine (Ludlow *et al.* 2006, Pauwels *et al.* 2012).

Depending on the type of CBCT device, the size of the FOV can vary substantially between devices. Large FOV (as in i-CAT® [Imaging Sciences International, Hatfield, PA, USA], and NewTom 3G® [Quantitative Radiology, Verona, Italy]) with a height ranging from 15-23 cm can capture the entire craniofacial skeleton. It is most commonly used in orthodontic diagnosis and treatment planning, evaluation of maxillofacial trauma, temporomandibular joint (TMJ) analysis and pathologies of the jaws. Medium FOV (as in Galileos® [Sirona, Bensheim, Germany], and 3D Accuitomo® 170 [J. Morita, Kyoto, Japan]) ranging from 10-15 cm can capture the maxillofacial skeleton, and are typically used for pre-implant planning and pathological conditions. Small FOV or limited FOV (as in Orthophos XG 3D® from Sirona, and the Veraviewepocs 3D® and 3D Accuitomo® from J. Morita) is less than 10 cm in size, which are useful for dento-alveolar imaging. The FOV can be as small as 4 cm high x 4 cm width, which is most popular for endodontic applications (Tyndall & Kohltfarber 2012).

The size of the FOV is determined by the size and shape of the detector, beam projection geometry, and beam collimation (Scarfe & Farman 2008). Generally, smaller FOV CBCT units are usually associated with smaller voxel size, shorter reconstruction time, lower effective doses, and higher resolution images compared to large FOV scans (Dawood *et al.* 2009, Scarfe *et al.* 2009, Maret *et al.* 2012, Tyndall & Kohltfarber 2012).

The three-dimensional volumetric data of a single CBCT scan comprises of millions of small cuboid structures, known as voxels. A voxel is a three-dimensional pixel (Cotton *et al.* 2007, Patel *et al.* 2007). In CBCT, voxels are usually isotropic (equal in all three dimensions) in shape. The voxels size is of significant importance, affecting image quality (resolution), and scanning and reconstruction times of CBCT images. The spatial resolution is found to be higher with smaller voxel sizes (Kamburoğlu *et al.* 2015). The voxel size commonly ranges from 0.4 mm^3 to as small as 0.075 mm^3 (Scarfe & Farman 2008, Patel *et al.* 2009b).

Disruption of the continuity of the lamina dura and widening of the periodontal ligament space in the apical region have long been considered an early indication of periapical pathology (Andreasen & Rud 1972, Lee & Messer 1986). Therefore, it was suggested that selecting a CBCT imaging system to be used in endodontics should ideally have a resolution that does not exceed the average width of the periodontal ligament space (200 *μ*m) (Scarfe & Farman 2008). For endodontic purposes, it is important to always choose a CBCT scanner with the smallest possible FOV (SEDENTEXCT 2012, European Society of Endodontology 2014, American Association of Endodontists 2016), offering higher resolution images and less radiation dose than large FOV options (Pauwels *et al.* 2012, Tyndall & Kohltfarber 2012). In addition to that, using a CBCT machine with a small FOV may allow the operator to exclude areas of high susceptibility to beam hardening from the region of interest, such as metallic restorations and dental implants, that otherwise would reduce image quality if included (Scarfe *et al.* 2009).

1.5.1.2 CBCT effective dose

The radiation emitted during a CBCT scan is basically dependent on the nature of the X-ray beam (continuous versus pulsatile), beam filtration, degree of rotation (180 versus 360), size of the FOV, and the exposure parameters (kilovoltage [kV], milliampere [mA]) utilised (Durack & Patel 2012). Many dosimetric studies have extensively reported on the patient dose for dental CBCT (Ludlow *et al.* 2003, Ludlow *et al.* 2006, Pauwels *et al.* 2012, Ludlow & Walker 2013).

While recent CBCT devices with a limited FOV are able to reach a relatively low dose of only 5 micro Sievert (μSV) (Ludlow *et al.* 2015), the reported effective dose associated with different CBCT machines is variable (Table 1-2) and ranges broadly from 5-652 μSV for small FOV, to 46-1073 μSV for large FOV (Ludlow *et al.* 2015). This is higher than the effective dose produced by intraoral periapical radiograph (1-5 μSV) (Gijbels *et al.* 2002), and as close as to the lower effective dose of panoramic imaging (3-24 μSv) (Ludlow *et al.* 2008, Loubele *et al.* 2009).

Table 1-2 Selected published effective doses in micro Sieverts (μSv) for standard or default exposures for various field of view (FOV) CBCT devices adapted from Ludlow *et al*. (2015)

Examination	CBCT unit name	Manufacturer	FOV size (cm)	Effective dose (μSv)
Large FOV CBCT (>15 cm height/diameter)	DCT PRO	VATECH (Seoul, Korea)	19 x 20	254
	CB MercuRay	Hitachi (Tokyo, Japan)	19 x 19	569, 1073, 916, 256, 466, 683, 932
	NewTom 3G	Cefla Dental Group (Imola, Italy)	19 x 19	68
	NewTom 9000	Cefla Dental Group	19 x 19	95
	Iluma	Imtec (Ardmore, OK)	19 x 19	94, 98, 157, 498
	CS 9500	Carestream Dental (Atlanta, GA)	18 x 20	136, 93, 163, 260, 151
	3D eXam	Imaging Sciences (Hatfield, PA)	17 x 23	72, 156
	i-CAT FLX	Imaging Sciences	17 x 23	69, 136
	i-CAT Next Generation	Imaging Sciences	17 x 23	67, 129, 74, 78, 182
	Skyview 3D	Cefla Dental Group	17 x 17	87
	Accuitomo 170	J. Morita	17 x 12	216, 282
	ProMax Mid-stiched	Planmeca Oy (Helsinki, Finland)	16 x 16	95, 112, 128, 223, 283, 339
Medium FOV CBCT (>10 cm and ≤15 cm height/diameter)	Galileos Comfort	Sirona Dental Systems (Bensheim, Germany)	15 x 15	70, 128, 84, 51, 95,
	3D eXam	Imaging Sciences	13 x 16	83
	3D Accuitomo 170	J. Morita	12 x 17	154, 260, 325, 532, 216
	iCAT Next Generation	Imaging Sciences	13 x 16	87, 40, 66, 83
			11 x 16	36, 58
			10 x 16	32, 53
	iCAT FLX	Imaging Sciences	11 x 16	9/43, 79, 159
	NewTom VG	QR (Verona, Italy)	11 x 15	81
	CS 9300	Carestream Dental	11 x 17	101, 204

Examination	CBCT unit name	Manufacturer	FOV size (cm)	Effective dose (µSv)
Small FOV CBCT (≤ 10 cm height/diameter)	CS 9300	Carestream Dental	10 x 10	76
	3D Accuitomo 170	J. Morita	10 x 14	138, 242, 269, 473, 188
			10 x 10	132, 232, 257, 453
	CB Mercuray	Hitachi	10 x 10	407, 148, 261, 421
	Galileos Comfort Plus	Sirona Dental	8.5 x 15	27, 34, 41
	Scanora 3D	Soredex (Helsinki, Finland)	7.5 x 10	46
	iCAT FLX	Imaging Sciences	6 x 16	4/20, 32, 65
	iCAT Next Generation	Imaging Sciences	6 x 16	32, 60, 22, 35, 37, 68, 33, 29, 47
	Pan eXam Plus 3D	Kavo (Bieberach, Germany)	6 x 8	79, 125
	Newtom VGi	QR	6 x 6	140, 131
	PaX-Uni3D	VATECH	5 x 5	44
	CS 9300	Carestream Dental	5 x 5	35, 59, 48, 80
	CS 9000	Carestream Dental	4 x 5	5,10, 19, 24
	ProMax 3D	Planmeca Oy	4 x 5	10
	3D eXam	Kavo	4 x 16	33, 68
	Veraviewepocs 3D	J. Morita	4 x 4	21
	3D Accuitomo 170	J. Morita	6 x 6	104, 107
			5 x 17	240
			5 x 14	70,123, 136, 214, 70
			5 x 10	54, 58, 102, 113, 198
			4 x 4	32

1.5.1.3 Dose reduction

Different CBCT machines provide different imaging protocols, which result in different radiation doses for the patients. It is important to carefully select appropriate exposure parameters and FOV depending on the diagnostic requirements to produce the optimal level of image quality that achieves the diagnostic task while adhering to the generally applied ALARA (As Low As Reasonably Achievable) principle of radiation exposure (Farman 2005, ICRP 2007, Ludlow 2011).

Because the risks of ionisation radiation are cumulative over time (Ludlow *et al.* 2015), and to ensure patient safety, several strategies have been considered to reduce radiation dose to the patients. The size of the FOV has a direct effect on patient dose if other factors would hold constant (Ludlow 2011). The smaller the size of the FOV, the lower the radiation dose (Ludlow *et al.* 2006, Roberts *et al.* 2009).

During CBCT examination, an operator may reduce patient exposure by the appropriate selection of the FOV to match the area of interest specific to accomplish the diagnostic aim of a particular examination. Typically, using the smallest FOV that is appropriate to cover the area of interest would reduce the effective dose (Qu *et al.* 2010) and enhance the image quality by reducing degradation by scattered radiation (White & Mallya 2012).

Another option that can reduce radiation dose during CBCT examination is lowering the image resolution settings. General voxel size and FOV are associated in many CBCT units. Increasing image resolution by selecting smaller voxel sizes with smaller FOVs can actually increase the radiation dose that is needed to achieve an adequate contrast-to-noise ratio (Ludlow & Walker 2013, Patel *et al.* 2015). Qu *et al.* (2010) found that using low-dose resolution protocol of ProMax 3D CBCT scanner can reduce the effective dose to about 10% of that with normal-dose resolution protocol (Qu *et al.* 2010). Thus, for tasks where higher resolution images are not required, reducing voxel size should be avoided to minimise the risk of unnecessary radiation exposure (Patel *et al.* 2015).

Another potential means to reduce patient exposure is to decrease the rotation angle from 360° to 180°, which reduces the number of basic projection images produced. Using 180° rotation (half arc) rather than 360° rotation (full arc) provides images of appropriate diagnostic quality for the desired task while significantly lowering radiation doses to the patients by half (Durack *et al.* 2011, Lennon *et al.* 2011, Güldner *et al.* 2013).

Selecting the exposure factors (kV, mA) for a CBCT scan is ideally based on the image quality needed to achieve the diagnostic task (Ludlow 2011). Ludlow (2011) reported that increasing kV and beam filtration had reduced the number of low-energy photons in the X-ray beam, which resulted in significant patient dose reduction (43%). X-ray tube current (mA) and exposure time are directly proportional to patient dose when other factors remain constant (Ludlow *et al.* 2015). Thus, it is suggested that the mA and exposure time have to be reduced whenever it is possible (SEDENTEXCT 2012).

Because to some extent image quality is proportional to radiation dose, capturing high-quality images would result in high radiation dose to the patient. Such high-resolution images may not be needed for all clinical applications of CBCT, and there is an obvious risk of unnecessary radiation exposure (Horner *et al.* 2009). Therefore, optimisation of exposure parameters (kV, mA) and filtration for diagnostic tasks that theoretically demand lower contrast-to-noise ratios or lower spatial resolution can significantly reduce radiation dose to the patient (Qu *et al.* 2010, Ludlow & Walker 2013).

1.5.1.4 Advantages of CBCT

CBCT has the potential to overcome most of the limitations of conventional two-dimensional radiography by generating geometrically accurate, three-dimensional images of the region under investigation, making it ideal as an adjunct imaging system in endodontics (Durack & Patel 2012). Moreover, slices can be viewed in all three orthogonal planes, therefore, adjacent anatomical noise can be easily eliminated (Scarfe & Farman 2008, Patel 2009).

CBCT is superior to periapical radiography in detecting abnormalities, and can improve diagnosis, decision-making and management of complex endodontic problems (Cotton *et al.* 2007, Patel *et al.* 2007, Estrela *et al.* 2008b, Patel 2009).

In comparison with conventional medical CT, CBCT produces three-dimensional information on the facial skeleton at higher image quality (Patel 2009, Scarfe *et al.* 2009), lower exposure to ionising radiation (Mozzo *et al.* 1998, Arai *et al.* 1999), shorter scanning time (Patel 2009), less artefacts, and lower cost (Scarfe & Farman 2008, Tyndall & Rathore 2008).

The CBCT scan times are typically between 10-40 seconds and the actual exposure time is significantly less (2-5 seconds). The short scan time compared to medical CT has the advantage of reducing the possibility of patient movement during the scan that can adversely affect the sharpness of the final image (Patel 2009, Scarfe *et al.* 2009).

1.5.1.5 Limitations of CBCT

X-ray beam artefacts, such as cupping artefacts (i.e. distortion of metallic structure), and the manifestation of streaks and dark bands between two dense structures (Scarfe & Farman 2008), arising when X-ray beam of CBCT strikes a very high-density object, such as enamel or metallic posts and crowns (Mora *et al.* 2007), are major problems that considerably downgrade image quality and diagnostic accuracy of CBCT (Lofthag-Hansen *et al.* 2007, Estrela *et al.* 2008b) and may lead to inappropriate CBCT-based decision-making and treatment planning (Peters & Peters 2012).

Another drawback of CBCT is the inferior spatial resolution (two line pairs per mm) compared to conventional (10-15 line pairs per mm) and digital (7-25 line pairs per mm) dental radiography (Farman & Farman 2005, Patel *et al.* 2007). This low spatial resolution may result in inconsistent detection of small objects such as a fractured

endodontic file, or challenging endodontic problems such as incomplete vertical root fractures (D'Addazio *et al.* 2011, Patel *et al.* 2013).

CBCT should only be used for specific clinical indications when conventional periapical radiography has not provided highly reliable diagnostic information regarding root canal morphology; pre-surgical status; periapical pathosis; dentoalveolar trauma; and root resorption (European Society of Endodontology 2014, American Association of Endodontists 2016). Thus, it is the clinician's responsibility to justify that the diagnostic benefits of CBCT to the management of the patient's endodontic problem outweigh the risk of ionising radiation exposure (ICRP 2007).

1.5.1.6 Assessment of endodontic treatment outcome

There is a considerable body of evidence highlighting CBCT as a tool more sensitive than periapical radiographs for the detection of radiolucent endodontic lesions (Patel 2009, Patel *et al.* 2010). Tyndall and Kohltfarber (2012) indicated a 34% increase in the prevalence of periapical radiolucencies detected by CBCT (Tyndall & Kohltfarber 2012).

More recently, Kanagasingam *et al.* (2016b) proved with histopathology that periapical lesions detected by CBCT are true effective inflammatory lesions. Digital periapical radiographs (central and parallax views) and CBCT scans were used for imaging 67 teeth (86 roots) in fresh, unpreserved human cadavers. CBCT had a higher sensitivity (0.89) than central view (0.27) and parallax view (0.38) digital periapical radiography (Kanagasingam *et al.* 2016b).

The majority of root canal treatment outcome studies in the literature are actually based on interpretation of periapical radiography. Few clinical studies have used CBCT. Generally, these studies indicated that the outcome of endodontic treatment monitored by CBCT was significantly less favourable than that observed with conventional

periapical radiographs (Liang *et al.* 2011, Patel *et al.* 2012b, Cheung *et al.* 2013, Fernández *et al.* 2013, Davies *et al.* 2016).

In two retrospective cohort studies, Liang *et al.* (2012) compared the endodontic outcome predictors 2 years after treatment using both periapical radiography and CBCT. In 115 teeth (143 roots) with vital pulps, periapical radiography detected no periapical defect in 87.4% of roots while CBCT detected no lesion in 74.1% of roots (Liang *et al.* 2011). In 234 teeth (268 roots) with pre-operative periapical radiolucency, the complete absence of periapical lesions was observed in 74% of roots on periapical radiography and 61% of roots on CBCT scans (Liang *et al.* 2012). However, in these studies, no pre-treatment CBCTs were taken. The pre-operative existence of apical periodontitis was determined with periapical radiographs only.

Patel *et al.* (2012b) assessed the outcome of endodontic treatment using digital periapical radiographs and CBCT one year following root canal treatment. The results revealed that when the teeth were assessed with digital periapical radiographs, the healed (absence of periapical radiolucency) and healing (reduced size of periapical radiolucency) rates for root canal treatment were found to be higher (87% and 95.1%, respectively) than CBCT (62.5% and 84.7%, respectively) (Patel *et al.* 2012b).

Fernández *et al.* (2013) assessed the impact of using three different radiographic techniques on the outcome of endodontic treatment after 5 years in teeth with vital pulps and without periapical lesions. The results indicated that CBCT showed a lower success outcome (81.3%) compared to periapical film radiograph (94.3%) and digital periapical radiograph (92.3%) (Fernández *et al.* 2013). One limitation of this study is that the pre-operative absence of periapical lesion was confirmed by radiological evaluation with digital periapical radiographs. No CBCT was taken at baseline.

Cheung *et al.* (2013) examined the agreement between periapical radiographs and CBCT obtained at review clinic in assessing the number of canals per tooth, number and coronal-apical dimensions of lesions per tooth, and the presence of 'J'-shaped lesions. The findings showed substantial disagreements between periapical radiographs and CBCT in assessing the periapical status of 60 root filled maxillary and mandibular molars (Cheung *et al.* 2013).

In a 1-year post-treatment follow-up, Davies *et al.* (2016) compared the 1-year outcome of root canal retreatment in 98 teeth (84 patients) using pre-operative and post-operative periapical radiographs and CBCT. The favourable outcome was 93% when the cases were assessed with periapical radiographs, and 77% when assessed with CBCT (Davies *et al.* 2016). Therefore, a decrease of 16% in the percentage of favourable outcome was observed using CBCT.

1.6 Relationship between the outcome of endodontically treated teeth and residual coronal tooth structure

1.6.1 Estimation of remaining coronal tooth structure

In order to judge the amount of remaining coronal tooth structure, different estimation criteria have been proposed. A classification to quantify the remaining tooth structure of endodontically treated teeth was presented by Chalifoux (1998) and adopted by Malferrari *et al.* (2003). According to this classification, the percentage of remaining coronal tooth structure was defined as 'complete' when a range of 66% to 100% of the coronal tooth structure remains; 'partial' when 33% to 65% of the tooth remains; or 'absent' when 0% to 32% of the tooth remains. Based on observation, experience, and estimation, the author measured the percentages of both the coronal height and the smallest horizontal cross-section at the gingival level. The least of these two percentages represents the percentage of coronal tooth structure following endodontic treatment and

restoration preparation (Chalifoux 1998). Although Malferrari *et al.* (2003) reported that remaining tooth structure is relevant to the success of post-and-core restoration (Malferrari *et al.* 2003), they did not mention to what extent the remaining tooth structure affects the success of coronal restorations. The authors did not explain the criteria they used to estimate the percentage of remaining coronal tooth structure. This classification is therefore not reproducible and not clinically applicable.

Edelhoff and Sorensen (2002) used the gravimetric (weight-based) analysis to quantify and compare the amount of coronal tooth structure removed following various tooth preparation designs on artificial resin anterior teeth (Edelhoff & Sorensen 2002). However, this method cannot be applied clinically to measure tooth structure removal.

Because of the difficulty in estimating the extent of dental tissue destruction, Peroz *et al.* (2005) described the amount of remaining coronal tooth structure depending on the number of residual axial cavity walls, and assigned an adequate treatment for each case. Where 'Class I' represents access preparation with four axial walls remaining; 'Class II' represents three axial walls remaining (i.e. mesial-occlusal [MO] or distal-occlusal [DO] cavity); 'Class III' describes two remaining cavity walls (i.e. mesial-occlusal-distal [MOD] cavity); 'Class IV' represents only one cavity wall remaining, and 'Class V' represents a tooth with no cavity walls left (i.e. decoronated tooth) (Peroz *et al.* 2005). In this classification, a minimal thickness of 1 mm and a minimal height of 2 mm were required for an axial cavity wall to be considered existent.

Similarly, many studies have classified the teeth with varying degrees of hard tissue loss according to the number of remaining coronal dentine walls left (n=1-4) (Ferrari *et al.* 2007, Cagidiaco *et al.* 2008, Bitter *et al.* 2009, Signore *et al.* 2011, Ferrari *et al.* 2012, Naumann *et al.* 2012, Sterzenbach *et al.* 2012). However, these studies did not take into consideration the variation in height and thickness of the included walls, and did not explain how and where in the coronal walls the height and thickness was measured.

Nagasiri and Chitmongkolsuk (2005) defined three types of remaining coronal tooth structure in order to be able to judge the long-term survival of endodontically treated molars without crown coverage. Type I represents 'maximum coronal tooth structure' when the amount of residual coronal tooth structure is approximately matches that of class I cavity preparation with at least 2 mm of surrounding wall thickness. Type II represents 'moderate remaining tooth structure' when the amount of residual coronal tooth structure is approximately close to that of Class II cavity preparation with no less than 2 walls of at least 2 mm thickness. Type III represents 'minimum remaining tooth structure' when the remaining coronal tooth structure has less than two walls with at least 2 mm thickness (Nagasiri & Chitmongkolsuk 2005). In this study, the authors did not mention how they measured the thickness of the walls and how this classification can apply to teeth with different heights and thicknesses of remaining coronal walls.

Bandlish *et al.* (2006) developed a method to produce a cast of the remaining coronal dentine in root treated teeth after crown preparation by using a series of interlocking special trays and impressions. The authors scanned this cast with a laser profilometer, and the volume of remaining dentine was measured. A tooth restorability index (TRI) for root treated teeth was also developed to assess the structural contribution of each sextant of remaining coronal tooth structure to the crown retention and resistance form, also to predict the restorability of a tooth. Each tooth was divided into six sextants, then for each sextant, a four-grade scoring system was used in which '0' means no axial wall of dentine; '1' means inadequate dentine; '2' means questionable; and '3' means adequate dentine, based on the height and thickness of the coronal dentine walls remained (Table 1-3). Therefore, each sextant could have a maximum numerical score of 3, and each tooth could have a maximum score of 18 (Bandlish *et al.* 2006).

According to a review by Bitter and Kielbassa (2007), the classification and recommendations proposed by Bandlish *et al.* (2006) would be imprecise if applied without taking into consideration the other significant factors affecting the long-term

outcome of restorations of root canal treated teeth (Bitter & Kielbassa 2007) such as tooth type, type of restoration, stress loads, proximal contacts and alveolar bone loss (Naumann *et al.* 2005b, Naumann *et al.* 2006c). Furthermore, this index has never been adopted by the studies that investigated the survival of restorations and endodontically treated teeth.

Table 1-3 Tooth restorability index (TRI) (Bandlish *et al.* 2006)

Index	Clinical description
0- None	Two-thirds or more of the tooth sextant have no axial wall of dentine, or any dentine present above the finishing line that is unable to contribute to retention and resistance of the core and final restoration
1- Inadequate	Coronal dentine is present in the tooth sextant Dentine walls are less than 1.5 mm thick or more than twice as high as their thinnest part. Height, thickness and distribution of coronal dentine are insufficient to contribute to retention and resistance of the core and final restoration.
2- Questionable	More dentine than in score 1 and less than in score 3. May or may not contribute to retention and resistance.
3- Adequate	Sufficient height, thickness and distribution of coronal dentine to contribute fully to retention and resistance.

In an *in vivo* study, Murphy *et al.* (2009) measured the amount of remaining coronal tooth structure in root treated teeth prepared for complete and partial coverage restorations using a laser scanning profilometer and TRI. Two sectional impressions were taken for 18 human molar teeth *in vivo*: one to record the remaining coronal tooth structure before the placement of the core restoration and a second impression to record the coronal tooth structure after crown preparation. The impressions were poured to produce dies of the remaining coronal tooth structure before and after tooth preparation. A correlation was reported between the volume of remaining coronal tooth structure and the mean total TRI (Murphy *et al.* 2009). However, preparing the tooth for partial and complete coverage restoration while the core restoration is not in place is not clinically applicable in cases when only thin or no coronal dentine wall remained. A drawback of using a laser

profilometer in scanning the remaining tooth structure casts is that the laser scanner was not able to record undercuts areas (Bandlish *et al.* 2006, Murphy *et al.* 2009). Therefore, in these studies, the undercuts areas were blocked out with light body impression material. Subsequently, the impression material was weighted out to determine its volume and added to the total tooth volume.

A newly developed approach was proposed by Naumann *et al.* (2006a) to define the extent of tooth destruction of endodontically treated teeth using three parameters (vertical and horizontal remaining tooth structure, and access cavity orifice size [mm]) (Table 1-4).

Table 1-4 Classification used to assess the amount of remaining tooth structure in three aspects (vertical, horizontal, and flaring of canal orifice) (Naumann *et al.* 2006a)

Parameter	Tool	Category	Description
Remaining crown height	Bucco-lingual view	Level A	Original crown height intact
		Level B	> Half of original crown height present
		Level C	< Half of original crown height present
		Level D	Complete loss of original crown height
Remaining wall thickness	PCP UNC 15 probe*	TOT-ob	The total extension of the tooth in bucco-lingual dimension
		SUM-ob	The sum of the remaining oral and buccal cavity wall thicknesses
		TOT-md	The total extension of the tooth in mesio-distal dimension
		SUM-md	The sum of the remaining mesial and distal cavity wall thicknesses
Size and flare of the canal orifice	Straight plugger with mm scale**		Size of the orifice in the bucco-lingual dimension regarded occlusally
			Size of the orifice in the mesio-distal dimension regarded occlusally
			Measurement of penetration depth of the 1.6 mm probe into the root canal

* Hu-Friedy, Leimen, Germany, ** Aesculap, Tuttlingen, Germany

The authors demonstrated that classifying the remaining tooth structure in one final value including all three aspects (vertical, horizontal, and flaring) would be more desirable to sort out each tooth into a specific treatment procedure or to predict tooth prognosis (Naumann *et al.* 2006a). However, the thickness may not be the same in the entire tooth wall, thus expressing each wall thickness as one overall value might not reflect the clinical condition accurately. Likewise, Murphy *et al.* (2009) claimed that the application of this method is relatively complicated when compared with TRI (Murphy *et al.* 2009).

In order to clinically access the survival of post-and-cores restorations, Creugers *et al.* (2005b) and Fokkinga *et al.* (2007) categorised all teeth according to the expected dentine height after tooth preparation into 'substantial dentine height' or 'minimal dentine height'. 'Substantial dentine height' was assigned to teeth when more than 75% of the circumferential dentine wall has a minimal thickness of 1 mm and a minimal height of 1 mm above the gingival level or when less than 25% of the circumferential dentine has less than 1 mm of dentine above the gingival level, however, a ferrule of 1-2 mm could be achieved. While 'minimal dentine height' was assigned to teeth when less than 75% of the circumferential dentine wall has a height of at least 1 mm above the gingiva, when more than 25% of the circumferential dentine has less than 1 mm of height above the gingiva, or when no ferrule of 1-2 mm could be prepared (Creugers *et al.* 2005b, Fokkinga *et al.* 2007). However, the authors did not mention how they predicted the minimal (1 mm) thickness and height of circumferential dentine walls.

Samet and Jotkowitz (2009) proposed a new classification system that evaluates individual teeth from periodontal, restorative, endodontic, and occlusal plane perspectives, and subsequently allocating each tooth to a relative prognostic value. The presented classification includes five classes (A, B, C, D and X). Regarding the restorative aspect, the authors evaluated the restorability of individual teeth based on the percentage of remaining sound coronal tooth structure (Samet & Jotkowitz 2009) (Table 1-5). However, the authors did not define how this percentage is measured, and

this classification has not been adopted by any clinical outcome studies.

Table 1-5 Classification used to assess the restorability of teeth (Samet & Jotkowitz 2009)

Class	Remaining tooth structure	Prognosis
A	80% to 100% remaining sound coronal tooth structure. Can be easily restored.	Good
B	50% to 80% remaining sound coronal tooth structure. Involved restorative procedures result in no infringement of biologic width, adequate ferrule, or good crown-root ratio and would minimally affect adjacent structures (if at all).	Fair
C	30% to 50% remaining sound coronal tooth structure. Or a tooth with so little tooth structure that achieving adequate ferrule would result in compromising the crown-root ratio to some extent, and/or may affect adjacent structures.	Questionable
D	A tooth with <30% sound tooth structure, or one in which the extent of the lost tooth structure does not enable a good ferrule to be achieved without totally compromising the support of the adjacent tooth structures or crown-root ratio.	Compromised
X	No remaining supra-gingival sound coronal tooth structure. Loss of tooth structure deep into the root dentine/canals	Non-salvageable

Davis *et al.* (2012) developed an *ex vivo* method for measuring local dentine thickness after tooth preparation for metal ceramic crowns. Sixteen extracted anterior teeth were scanned using X-ray micro-tomography before and after crown preparation. Local dentine thickness was defined for every voxel within the three-dimensional tooth image. Three-dimensional colour-coded maps of dentine thickness were generated, and the distributions of dentine thickness throughout the teeth were analysed. The method also allows the thickness of material removed to be quantified (Davis *et al.* 2012). However, this method can only be used as a research tool and cannot be applied directly in clinical procedures.

Another classification system was proposed by Murgueitio and Avila-Ortiz (2012) to evaluate and analyse the remaining tooth structure of endodontically treated anterior teeth. The remaining tooth structure was classified into four types based on crown or abutment-related factors like wall thickness (a minimum of 1 mm), height of crown or abutment (a minimum of 1.5 mm), and circumferential integrity (50%, ≥ 50%, and 100%),

and on root-related factors like canal diameter (narrow, medium, and large), canal shape (tapered and parallel), and depth of the preparation (short, medium, and long) (Murgueitio & Avila-Ortiz 2012). Yet, assessing the agreement between observers using this classification has never been performed.

In a recent study, in order to investigate the influence of remaining coronal tooth structure on the 4-year survival of endodontically treated teeth, Juloski *et al.* (2014) classified the residual coronal dentine after abutment build-up and final preparation into more than 50%, or equal to or less than 50% of coronal residual structure (Juloski *et al.* 2014). However, the authors do not mention how the residual coronal tooth structure volume was measured.

1.6.1.1 Intraoral digital scanners

1.6.1.1.1 Background

Impression materials, such as polyether, vinyl polyether silicone, and vinyl polysiloxane, show limits in terms of accuracy of the information they provide due to imprecise recording of surface details after disinfection (Nassar & Chow 2015), dimensional changes of impression materials before pouring (Johnson & Craig 1985), expansion of dental stone (Millstein 1992, Christensen 2008), separation of the impression material from the tray (Christensen 2008), limited working time, storage, and risk of physical damage during transport (Akyalcin *et al.* 2013, Taneva *et al.* 2015). In addition, conventional impression taking may cause the patient discomfort and trigger the gag reflex (Christensen 2008, Christensen 2009, Kravitz *et al.* 2014).

To eliminate some of the potential shortcomings associated with traditional impression taking and cast production (Schneider *et al.* 2001, Heckmann *et al.* 2004), the concept of chairside digital impressions was originally introduced by Dr Francois Duret in his thesis presented at the Université Claude Bernard, Faculté d'Odontologie, in Lyon,

France in 1973, entitled “Empreinte Optique” (Optical Impression). He developed and patented a computer-assisted design (CAD)/computer-assisted manufacturing (CAM) device in 1984 as an alternative to the use of conventional impression materials in a claim to improve the predictability of treatment outcomes and fit of restorations (Duret & Termoz 1987).

Through improvements in the scanning technologies, new intraoral scanning systems have made their way into clinical practices. Digital intraoral scanners allow dentists to record the intraoral condition, creating a three-dimensional digital representation of the dentition and soft tissue, and sending the virtual models to laboratories to fabricate restorations and prostheses without the need for conventional impressions.

All the existing chairside intraoral systems are based on various non-contact optical principles and technologies to capture scanned objects such as confocal microscopy, optical coherence tomography, active and passive stereovision and triangulation, interferometry and phase shift principles (Logozzo *et al.* 2014). A number of intraoral scanning systems with various working principles to capture scanned objects currently available in the dental market is summarised in Table 1-6.

The most commonly used intraoral digital systems are Cerec AC (Sirona, Behnheim, Germany) based on stripe-light projection and active triangulation, Lava Chairside Oral Scanner (Lava COS, 3M ESPE, St Paul, Minnesota, USA) based on active wavefront sampling, E4D Dentist (D4D Technologies, LLC, Richardson, Texas, USA) based on the principle of optical coherence tomography and confocal microscopy, and iTero (Cadent, Carlstadt, New Jersey, USA) based on the principle of parallel confocal imaging (Giménez *et al.* 2015).

Table 1-6 Operating principles and technical data of the currently available market-leading intraoral scanning systems (Masri & Driscoll 2015)

Intraoral Scanner	CEREC AC Bluecam	CEREC Omnicam	True Definition Scanner	iTero	E4D PlanScan	Trios
Company	Sirona Dental System	Sirona Dental System	3M ESPE	Cadet	D4D Technologies	3Shape
Working Optical Principles	Active Triangulation and Confocal Microscopy	Active Optical Triangulation	3D-in-motion video technology	Parallel Confocal Microscopy	Parallel Confocal Microscopy	Confocal Microscopy
Light Source	Visible Blue Light	White LED, unpolarised, visible spectral range	Pulsating blue light	Red Laser	Blue Laser	Not Disclosed
Imaging Type	Still Images	Continuous Images	3D Video	Still Images	Still Images	Still Images
Weight of Wand	~ 280 g	~ 313 g	~ 200 g	~ 1.5 kg	~ 337 g	~ 1 kg
Wand Tip Dimensions	22 mm × 17 mm	16 mm × 16 mm	14.4 mm × 16.2 mm	25 mm × 25 mm	30 mm × 23 mm (with stand off)	-
Necessity of Surface Powder	Heavy powdering required for antireflective coating	Not Required	Light powdering required to facilitate image stitching	Not Required	Not Required	Not Required

Indirect restorations have been reported to exhibit higher accuracy when fabricated from intraoral digital impressions than from conventional impressions (Syrek *et al.* 2010, Seelbach *et al.* 2013). The workflow with digital impressions is more time-effective compared with the conventional impressions (Patzelt *et al.* 2014b) as it eliminates several working steps at dental practice and lab (Ting-shu & Jian 2015). Additionally, the patient's comfort is also improved by direct data capturing, and real-time on-screen visualisation, as well as potentially reduced treatment time (Jones 2008, Flügge *et al.* 2013, Yuzbasioglu *et al.* 2014). The development of digital models and elimination of traditional impressions also has the advantage of facilitating treatment simulations and enhancing the communication between the dentist and the dental technician as well as between professionals and patients (Kravitz *et al.* 2014, Yang *et al.* 2015). Nonetheless,

intraoral digital scanners are still optical devices that can only record visible surfaces. The presence of blood, saliva, and surface debris in combination with subgingival finishing line may markedly affect the quality of the scan data (Boeddinghaus *et al.* 2015, Kurz *et al.* 2015).

1.6.1.1.2 Accuracy

Several factors do influence the accuracy of intraoral digital impressions, including hardware (i.e. scanner type) and software factors, environmental factors such as scan body visibility, illumination of the scan field, room temperature, and patient-related factors such as patient movement, limited mouth opening, intraoral humidity and saliva flow, which in turn impact on the resulting output (Flügge *et al.* 2013, Patzelt *et al.* 2014a, Giménez *et al.* 2015, Goracci *et al.* 2015). In addition to the aforementioned factors, operator factors (i.e. experience) were found to affect the accuracy of digital impressions (Giménez *et al.* 2015).

The performance of intraoral scanners is usually measured in terms of 'accuracy' and 'precision' (Ender & Mehl 2011). 'Accuracy' refers to the closeness of the impression compared to the reference object (true value). Because of that, it is sometimes termed as 'trueness', while 'precision' refers to the consistency between multiple repeated scans under unchanged (repeatability) or changed (reproducibility) conditions and demonstrating the same results, and is usually expressed in terms of standard deviations (Leach 2010).

Local and full arch accuracy of intraoral scanners to capture single crowns, full arch and implant has been previously determined and compared with conventional impressions in several laboratory investigations (Ender & Mehl 2011, Ender & Mehl 2013, Seelbach *et al.* 2013, Patzelt *et al.* 2014a, Boeddinghaus *et al.* 2015), however, the results of these studies were varied and controversial. It is a fact that the data in these studies cannot be directly compared, owing to the wide ranges of different digital scanning systems used

which would have a significant influence on the diagnostic ability. However, there is a general agreement that local scanning has superior accuracy to full arch scanning. This difference in accuracy may be attributed to the fact that digital impression for long spans inevitably requires more meshed individual images to be sequentially recorded compared to short spans scanning, then the software program stitches the images together into a larger three-dimensional virtual model. Therefore, the chance of a misalignment error occurring increases with each individual stitch during the full arch scanning (Giménez *et al.* 2015).

For full arch scan, the accuracy of CEREC AC Bluecam (Sirona), Lava COS (3M ESPE) and iTero (Cadent) was reported to be 58.6 µm (Ender & Mehl 2013), 38-44.9 µm and 32.4-49 µm (Ender & Mehl 2011, Patzelt *et al.* 2014a), and the precision to be 32.4 µm (Ender & Mehl 2013), 37.9-63 µm and 36.4-40.4 µm (Ender & Mehl 2011, Patzelt *et al.* 2014a). For single tooth scan, the accuracy of CEREC AC Bluecam (Sirona) and CEREC 3D (Sirona) was reported to be 19 µm (Mehl *et al.* 2009) and 27.9 µm (Luthardt *et al.* 2005), respectively, while the precision values were 10.8 ± 1.8 µm (Mehl *et al.* 2009).

1.6.1.1.3 Integration with other technologies

Visualisation of coronal hard structures using CBCT imaging is not accurate due to the impact of scatter and beam hardening caused by dental restorations and orthodontic metal appliances (Mora *et al.* 2007, Soğur *et al.* 2007). Therefore, the integration of digital 3D models from the intraoral scanner with CBCT imaging technology allows creating a 3D virtual planning environment for the crowns, roots and bone, which can be applied in orthodontics, implant surgery, and endodontics. The combination of CBCT DICOM (digital imagining and communication in medicine) files, intraoral scan STL (stereo-lithography format) files and computer-aided design technologies allow three-dimensional guided placement of the custom-designed dental implant with a relative accuracy (Anssari Moin *et al.* 2016).

In a study that presented a novel method for guided access cavity preparation and root canal location, 'Guided Endodontics' through virtual planning of access cavities, sleeves and templates for guidance allowed an accurate and minimal invasive access cavity preparation with full accessibility to all root canals, especially for teeth with radiographic signs of severe root canal calcifications (Zehnder *et al.* 2016).

Similarly, van der Meer *et al.* (2016) described a method of digital designing and prototyping of endodontic guides for anterior teeth with obliterated root canal systems based on CBCT scans and intraoral digital scans of the dentition. Digital planning allows pre-operative visualisation of root canals location and plotting the navigation in detail. A surgical guide was digitally designed with the aid of a specific computer software and fabricated using a 3D printer (van der Meer *et al.* 2016).

1.6.2 Effect of remaining tooth structure on fracture resistance: *in vitro* studies

Root canal treated teeth have an extensive loss of tooth structure as a result of caries or eventual fractures and traumas, and often from repeated restorative procedures, however, a minimal amount of tooth structure should be removed during access cavity preparation, instrumentation, post-space preparation (Tang *et al.* 2010). Conservation of coronal dentine during access cavity preparation could result in increased fracture resistance in maxillary molars and premolars, although it may be associated with the risk of compromising canal instrumentation (Krishan *et al.* 2014).

The strain values and fracture resistance of remaining tooth structure of endodontically treated incisors are directly affected by tooth structure removal (Valdivia *et al.* 2012). An *in vitro* study using strain gauges bonded to cusps of extracted premolars demonstrated that endodontic procedures have a minimal effect on the tooth stiffness compared to occlusal cavity preparation and loss of marginal integrity. Tooth stiffness was reduced by 5% during an endodontic procedure, while the loss of stiffness was 20%, and 63%,

respectively, after occlusal cavity preparation and MOD cavity preparation. Tooth stability is affected by the loss of marginal ridge (Reeh *et al.* 1989).

In a photoelastic study, retaining coronal dentine resulted in a more favourable stress distribution to the root, and reduced stress concentration at the shoulder (Henry 1977).

Sorensen and Engelman (1990) reported that the fracture resistance of endodontically treated teeth was considerably increased when 1 mm of coronal dentine was maintained above the crown margin (Sorensen & Engelman 1990).

In a review, Fernandes and Dessai (2001) evaluated the factors that affect the resistance to fracture of post-core reconstructed teeth. This review indicates that preservation of the residual coronal tooth structure is of utmost importance (Fernandes & Dessai 2001).

On the same hand, Arunpraditkul *et al.* (2009) found that the fracture resistance of endodontically treated teeth with 3 coronal dentine walls remaining and restored with dowel-core-crown was significantly lower than teeth with 4 walls remaining, whereas the location of the missing wall had no influence on the fracture resistance of these teeth (Arunpraditkul *et al.* 2009).

Similar findings were reported by an *in vitro* study that investigated the influence of both the number of residual coronal walls (0-3 walls) and post placement on the fracture resistance of endodontically treated crowned premolars. The number of residual coronal dentine walls and placement of fibre post had a significant impact on the fracture resistance (Mangold & Kern 2011).

A number of studies have investigated the effect of different heights of retained buccal coronal tooth structure on the fracture resistance of teeth restored with a cast-post and partial core restoration (Al-Wahadni & Gutteridge 2002, Creugers *et al.* 2005b, Al-Omiri & Al-Wahadni 2006, Fokkinga *et al.* 2007, ElAyouti *et al.* 2011).

Al-Wahadni and Gutteridge (2002) demonstrated a statistically significant improvement in the fracture resistance of teeth with retained buccal coronal dentine of 3 mm and restored with dowel and partial cores when compared to teeth without retained coronal dentine. However, increasing the heights of retained buccal coronal dentine over 3 mm did not significantly improve the teeth resistance to fracture. Al-Omiri and Al-Wahadni (2006), investigated the effect of three different types of pre-fabricated post systems with different heights of buccally and lingually remaining coronal dentine on the fracture resistance and fracture patterns of teeth restored with composite cores. The fracture resistance of teeth restored with prefabricated metal and fibre reinforced resin posts was improved by the presence of remaining coronal dentine in comparison to teeth with no retained coronal dentine. However, in these two *in vitro* studies, the root canals were not filled before testing and teeth have no cuspal coverage, therefore, this is considered as limitations to simulate the clinical condition of a crown with a ferrule.

In cases with absence of complete circumferential tooth structure between the core and preparation finish line, Ng *et al.* (2006) reported that retaining an axial wall height of 2 mm extending to one-half the circumference of the crown preparation could enhance fracture resistance of restored endodontically treated anterior teeth. The location of the retained coronal tooth structure may affect their fracture resistance as well (Ng *et al.* 2006).

Samran *et al.* (2013) reported that the fracture resistance of endodontically treated premolar teeth restored with a prefabricated post and cast crown would be significantly increased by increasing the number of residual walls and the ferrule height (Samran *et al.* 2013).

In addition to the remaining wall height and number, the remaining coronal wall thickness represents another considerably variable parameter that may be used for clinical evaluation of the amount of remaining tooth structure. The required thickness of dentine

to optimise clinical outcome is not known, therefore, the evaluation of residual wall thickness in endodontically treated teeth could provide relevant information regarding the fatigue resistance, and consequently might influence the proper selection of tooth restoration (Scotti *et al.* 2013).

There are contradictory results in the literature regarding the influence of remaining wall thickness on fracture resistance of endodontically treated teeth. Some data reported that the residual wall thickness, type of adhesive restoration, and fibre post placement have a significant influence on the fracture resistance of endodontically treated maxillary premolar teeth (Scotti *et al.* 2013). Conversely, another study showed that decreasing the cuspal thickness below 3 mm did not decrease the fracture resistance of composite restored premolars, suggesting that the thickness of remaining dentine walls is not relevant to fracture resistance (ElAyouti *et al.* 2011).

Although the majority of clinical and laboratory studies have recommended maintaining the maximum amount of coronal tooth structure to improve retention and stress distribution, some reports have presented contradictory findings regarding the influence of remaining tooth structure on teeth fracture resistance. Patel and Gutteridge (1996) investigated the influence of retained coronal dentine as well as its location on the fracture resistance of teeth restored with post and partial core restorations under direct loading. The authors reported that buccal and lingual or lingual retained coronal dentine did not significantly enhance the strength of a tooth restored with a cast dowel and partial core in comparison to control teeth with post and full core restorations. Furthermore, a significant lower fracture resistance was reported for teeth with buccally placed remaining dentine core when compared to control teeth without coronal dentine (Patel & Gutteridge 1996).

On the same hand, Saupe *et al.* (1996) reported that the presence of a ferrule in anterior teeth having structurally weakened roots and restored with bonded resin reinforcement and dowel cementation did not significantly improve the retention and fracture resistance (Saupe *et al.* 1996).

Melo *et al.* (2005) reported that the presence of remaining coronal structure has no influence on the fracture resistance of endodontically treated teeth (Melo *et al.* 2005). However, in this study, the coronal structure was reduced to a flat plane 3 mm incisal to the cement-enamel junction (CEJ), which did not simulate the most frequent clinical scenarios.

In conclusion, recommendations of *in vitro* studies vary substantially due to the variability in the study designs. Such recommendations should be taken with caution due to the limitations of these studies in simulating the elasticity of the periodontal ligament, bone and tooth structure, and the functional forces generated within the clinical environment.

1.6.3 Remaining tooth structure and outcome of restorations of endodontically treated teeth

The prognosis of endodontically treated restored teeth depends on several baseline factors. Preservation of tooth structure, presence of a ferrule effect, and the type of definitive restoration are among the critical factors influencing long-term survival of endodontically treated teeth and success of the restorations (Sorensen 1988, Nagasiri & Chitmongkolsuk 2005, Naumann *et al.* 2005b, Kishen 2006, Ferrari *et al.* 2012). Several studies have indicated that the degree of coronal hard tissue loss may be considered important for the clinical success of the restorations of endodontically treated teeth (Naumann *et al.* 2005a, Naumann *et al.* 2005b, Naumann *et al.* 2008, Bitter *et al.* 2009, Naumann *et al.* 2012).

The influence of the number of remaining coronal walls and placement of a prefabricated or customised fibre post on the 3-year survival of endodontically treated premolars was examined by Cagidiaco *et al.* (2008). The follow-up period was extended by Ferrari *et al.* (2012) to assess the 6-year clinical survival. The overall results showed that the extent of coronal tissue loss and the presence of a post significantly affected the 3- to 6-year failure risk of endodontically treated premolars.

Similarly, Ferrari *et al.* (2007) reported that, over a two-year observational period, the restoration failure risk of pulpless restored premolars was significantly increased for teeth with no coronal dentine walls retained regardless of the presence or absence of a ferrule (Ferrari *et al.* 2007). This finding is consistent with (Signore *et al.* 2011). The authors found that the survival of post-and-core restorations was significantly higher (P=0.0006) for premolars that had maintained one to four coronal walls.

In a retrospective cohort study, the authors assessed the survival of 220 endodontically treated molar teeth without crown coverage, and evaluated several variable factors including the amount of remaining tooth structure and type of restorative material. The patients were recalled at 1, 2, and 5 years, and the overall survival estimates of root canal treated teeth were 96%, 88%, and 36%, respectively. A tendency of failure to occur in molar teeth with maximum and minimum tooth structure remaining was reported to be 78% and 18%, respectively, at 5-year follow-up. The amount of remaining coronal tooth structure and the types of restorative material (composite, amalgam, intermediate restorative material [IRM]) were the two potential factors that significantly influenced the longevity of endodontically treated molars without crown coverage (Nagasiri & Chitmongkolsuk 2005). However, in this study, the numbers of teeth in each group of the study variables were not mentioned.

Naumann *et al.* (2005b) investigated, in a prospective cohort study, several factors associated with the survival of two different types of glass fibre-reinforced endodontic

post-core restorations in anterior and posterior teeth with varying cavity configurations. Among these factors is the number of surfaces providing adhesion for core build-up (i.e. the number of remaining cavity walls [1-2 walls compared with >2 walls]). The findings showed that the amount of tooth structure loss, defined by the residual surfaces for adhesion, could be a significant predictor of failure risk of glass fibre-reinforced endodontic post-core restorations (Naumann *et al.* 2005b). However, in this study, the sample size was relatively small (105 restorations in 83 patient), and the height of the remaining cavity walls was not measured.

Similarly, Naumann *et al.* (2008) reported that the survival of glass fibre post restorations in anterior and posterior teeth over 5 years was negatively affected by missing proximal contacts (hazard regression [HR]: 2.4; 95% CI: 0.8-7.1), and missing remaining cavity walls (HR: 1.5; 95% CI: 0.6-3.8). However, no statistical significance correlations were recorded (Naumann *et al.* 2008).

In a clinical study by Cagidiaco *et al.* (2007), the 2-year outcome of post-and-core restorative procedures in endodontically treated teeth, as well as the effect of baseline factors such as tooth type, number of remaining coronal walls, and type of definitive restoration on restoration failure, were assessed. Teeth with a high degree of tooth structure loss showed a higher tendency to failure, however, no statistically significant influence was reported (Cagidiaco *et al.* 2007). In this study, both anterior and posterior teeth were included. However, the distribution of treated teeth according to tooth type was not reported.

Three clinical studies have investigated the effect of ‘substantial’ and ‘minimal dentine height’ after tooth preparation on the long-term survival of post-and-core restorations (Creugers *et al.* 2005a, Creugers *et al.* 2005b, Fokkinga *et al.* 2007). A 5-year follow-up prospective clinical study suggested that the remaining dentine height has a significant influence on the survival of post-and-core restorations. The survival of post-and-core

restorations in teeth with ‘substantial dentine height’ was 98% ± 2%, and in teeth with ‘minimal dentine height’ was 93% ± 3% (Creugers *et al.* 2005b).

A similar finding was reported by Fokkinga *et al.* (2007) in an up to 17-year follow-up of two clinical trials (Creugers *et al.* 2005a, Creugers *et al.* 2005b) on the survival of different types of core restorations. With ‘minimal dentine height’, the survival at restoration level was 71%, and at tooth level was 83%, while with ‘substantial dentine height’, the survival at restoration level and tooth level was 80% and 92%, respectively (Fokkinga *et al.* 2007). However, the authors clinically examined only 18% of all teeth, while information on the performance of the rest of restorations was obtained exclusively from the patients’ records. Therefore, there was no standardisation on the criteria to evaluate the performance of the restorations. The recall rate was 28% at 17-year follow-up. The distribution of teeth involved in this retrospective study was not mentioned.

In a randomised controlled trial, the effect of fibre post placement and the amount of residual coronal dentine on time to failure of endodontically treated anterior and posterior teeth were investigated after a mean observation period of 32.4 (±13.7) months (Bitter *et al.* 2009). The results showed that the survival of post-endodontic restorations was dependent on the number of remaining cavity walls, although no significant influence was detected in the multivariate analyses. When teeth with 2 or more coronal walls are left, no failure was reported compared to teeth with no coronal walls. Posts placement had no effect on the failure rate of teeth with one or more coronal walls left. However, drawbacks of this study were the inclusion of various coronal single-unit restorations with and without cusp coverage, unequal distribution of the various tooth types, and a short observation period.

Most recently, Afrashtehfar *et al.* (2016) performed a systematic review to investigate the failure rates of conventional single-unit restorations in root filled posterior teeth. The failure rates of the restorations of root filled teeth were associated with the type of

treatment (post-retained crowns, post-free crowns, and intra-coronal restorations) and remaining coronal tooth structure. Teeth that retained a higher amount of remaining tooth structure showed a better treatment outcome, and post-retained crowns were superior to other treatments in root filled teeth with two or less remaining coronal walls (Afrashtehfar *et al.* 2016). However, the authors reported that the data were retrieved from studies with high risk of bias.

1.7 The effect of coronal restoration on endodontic treatment outcome

Severe loss of tooth structure is typical of root canal retreated teeth due to the removal of existing coronal restorations, which is necessary to gain direct access to the root canal system. It has been suggested that the presence of well-executed coronal restoration serves as a barrier to prevent post-operative coronal leakage from the oral environment and reinfection of the root canal system (Ray & Trope 1995).

Recontamination of the root canals from the oral cavity may occur in certain circumstances such as coronal leakage through the temporary or permanent restoration; fracture of tooth structure; recurrent decay exposing the root canal filling material; or delay in the placement of permanent restorations (Siqueira *et al.* 1999). Long-term studies have shown controversial results regarding the correlation between restoration type and restoration quality with the outcome of endodontically treated teeth.

1.7.1 Restoration type

When restoring endodontically treated teeth, the selection of an appropriate restoration type depends mainly on the amount of remaining coronal tooth structure, which can positively influence the long-term prognosis of teeth following root canal treatment. A systematic review of the literature, which pooled data from four studies (Allen *et al.* 1989, Sjögren *et al.* 1990, Friedman *et al.* 1995, Farzaneh *et al.* 2004), analysed the influence

of type of coronal restoration (crown vs. plastic restorations, permanent vs. temporary restorations, and restored vs. unrestored teeth) on the outcome of secondary root canal treatment (Ng *et al.* 2008). The presence of permanent coronal restoration has been shown to increase the success rate (Allen *et al.* 1989, Friedman *et al.* 1995, Farzaneh *et al.* 2004). In addition to these data, Kayahan *et al.* (2008) found in a cross-sectional study that the type of restoration (posts vs. without posts) can be a contributing factor in the treatment outcome (Kayahan *et al.* 2008).

Unlike previous studies (Allen *et al.* 1989, Friedman *et al.* 1995, Farzaneh *et al.* 2004), a prospective study by Ng *et al.* in 2011 showed that the type of permanent coronal restorations (glass ionomer cement/composite, amalgam, cast restoration) has no significant contribution to the success of endodontic treatment after adjusting the results for other parameters including the quality of coronal restoration (Ng *et al.* 2011).

1.7.2 Restoration quality

There is a general perception that the technical quality of root canal filling is the primary contributing factor for the clinical outcome of root canal treatment, whereas the quality of coronal restoration has a lesser impact. However, when quality of coronal restoration is inadequate, there is an increased risk of leakage, which may often establish an additional pathway for bacterial or microbial endotoxins ingress into the root canal system and apical reinfection (Torabinejad *et al.* 1990, Khayat *et al.* 1993, Saunders & Saunders 1994, Siqueira 2001, Siqueira *et al.* 2005).

In a laboratory study that exposed the obturated root canal to fluids for 19 days or 42 days, Torabinejad *et al.* (1990) found that when the canal and root filling are not properly sealed with a coronal restoration, 50% of single root filled teeth have shown consistent coronal leakage along the whole length of the root (Torabinejad *et al.* 1990). In this study, no coronal restorations were used to seal the coronal portions of the root canals, which were left exposed to only two bacterial species (*Staphylococcus epidermidis* and *Proteus*

vulgaris) for up to 42 days. This situation does not simulate the intraoral clinical conditions, and the finding is questionable since the success rate reported by many outcome studies is considerably high (Molven *et al.* 2002, Imura *et al.* 2007, Ng *et al.* 2011).

In many studies, the criteria used to assess the quality of the coronal restoration were based on an evaluation of periapical radiographs. The radiographic quality of coronal restoration was considered to be 'good' when any permanent restoration appeared radiographically intact and sealed, while it was considered to be 'poor' if there are radiographic signs of overhangs, recurrent decay or open margins (Ray & Trope 1995, Tronstad *et al.* 2000, Siqueira *et al.* 2005).

Hommez *et al.* (2002), evaluated the impact of the technical quality of coronal restorations scored on a clinical and radiographic basis on periapical health (Hommez *et al.* 2002). The clinical scoring was done according to modified Ryge's criteria for marginal adaptation (Ryge 1980), and the radiographic scoring was based on the presence of signs of marginal leakage or decay (Table 1-7).

According to Hoskinson *et al.* (2002), the quality of the coronal restoration is defined as 'satisfactory' when the restorations show no clinical and radiological evidence of marginal discrepancy, recurrent caries at the restoration margins, discoloration, or with no history of decementation (Hoskinson *et al.* 2002).

Table 1-7 Clinical and radiographic criteria for evaluation the quality of coronal restorations (Hommez *et al.* 2002)

Parameter	Outcome	Score
Clinical coronal status	Good margin	Acceptable
	Catching of the explorer, no visible crevice	Acceptable
	Crevice limited to the enamel	Acceptable
	Crevice penetrating the dentine	Unacceptable
	Fracture of restoration	Unacceptable
	Detached restoration	Unacceptable
	Lost restoration	Unacceptable
	Marginal decay	
	Crown or filling	
Radiographic coronal status	Intact restoration	Acceptable
	Restoration with open margin	Unacceptable
	Restoration with recurrent decay	Unacceptable
	Presence or absence of a base under the restoration	
	Amalgam or composite	
	Presence of a post in the root canal	

The criteria proposed by Hoskinson *et al.* (2002) to define satisfactory restoration was not adequate to define coronal leakage when the inner core was still intact (Ng & Gulabivala 2011, Ng *et al.* 2011). Therefore, a modified definition for unsatisfactory restorations was adopted by Ng *et al.* (2011) in order to discriminate between obvious and potential coronal leakage more efficiently. According to the modified definition, the quality of restorations was judged as 'unsatisfactory' when there were either obvious visual signs of root filling exposure or a potential leakage indicated by marginal defects and history of decementation (Ng *et al.* 2011). Ng *et al.* (2011) reported that the adoption of the modified criteria for assessing the quality of coronal restoration in their study may perhaps contribute to the much larger overall adjusted effect of the quality of restoration

(odds ratio [OR]= 10.73; 95% CI: 3.65, 31.54) on the treatment outcome compared to the results reported in a meta-analysis for root canal retreatment (OR= 3.31; 95% CI: 1.07, 10.30) (Ng *et al.* 2008).

Three clinical studies involved the evaluation of the association between periapical status and quality of the coronal restorations both clinically and radiologically reported that assessing the quality of coronal restoration using either a clinical or radiological approach alone yields weak correlation and inconsistent results (Hommez *et al.* 2002, Dugas *et al.* 2003, Craveiro *et al.* 2015). Therefore, Hommez *et al.* (2002) and Craveiro *et al.* (2015) suggested that both clinical and radiological assessments should be performed in order to investigate the influence of coronal restorations quality on the periapical status of endodontically treated teeth.

With slight modifications to the criteria used by Tronstad *et al.* (2000), Craveiro *et al.* (2015) described criteria to assess the quality of coronal restoration both clinically and radiologically. According to this criterion, teeth are judged as having 'adequate' coronal restoration if permanent, intact restoration, with a good marginal fit, no fractures, cracks, or recurrent caries present. While 'inadequate' coronal restoration is assigned to any permanent restoration showing detectable signs of overhangs, fractures, cracks, poor marginal fit, or recurrent caries, or else the presence of a temporary restoration (Craveiro *et al.* 2015). However, relying on two-dimensional radiographs to assess the quality of coronal restorations is still questionable.

In recent years, the correlation of the quality of coronal restoration with the periapical health of endodontically treated teeth has been assessed (Ray & Trope 1995, Tronstad *et al.* 2000, Hommez *et al.* 2002, Tavares *et al.* 2009, Gillen *et al.* 2011, Craveiro *et al.* 2015). However, contradictory results have been reported when it comes to the level of influence of coronal restoration on the outcome of the endodontic treatment.

In a cross-sectional study of 1010 root filled teeth, Ray and Trope (1995) came to the conclusion that the technical quality of the coronal restoration, scored only on radiographs, had a relatively greater clinical importance than the quality of the root canal filling on the periapical health (Ray & Trope 1995). The limitations of this study included, the quality of endodontic obturation and coronal restorations was assessed based on retrospective two-dimensional radiographic data that was taken at some time point more than 1 year prior to the study. No information was available, either for the pre-operative periapical status nor for the time elapsed between the treatment completion and radiological evaluation. In addition to that, the type of teeth and type of restorations involved in this study were not mentioned.

The importance of a good restoration for the periapical health of root filled teeth was also confirmed in other studies (Kirkevang *et al.* 2000, Hommez *et al.* 2002, Song *et al.* 2014), although not as pronounced as reported by Ray and Trope (1995). They suggested that the quality of the root canal filling and coronal restoration were of equal importance on treatment success rate. In addition to these data, other studies (Siqueira *et al.* 2005, Craveiro *et al.* 2015) also found a less pronounced influence of coronal restoration quality on endodontic treatment outcome when combined with adequate endodontic treatment. In the Craveiro *et al.* (2015) retrospective study, a low recall rate (23%) was recorded.

On the other hand, Tronstad *et al.* (2000) found that in cases with inadequate endodontic treatment, the quality of the coronal restoration was of no significance on the outcome of endodontic treatment. The only statistically significant impact of the restoration on the periapical health of root filled teeth was observed in cases where the endodontic treatment appeared satisfactory (Tronstad *et al.* 2000). Similar results were supported by Dugas *et al.* (2003). However, Hoskinson *et al.* (2002) and Ricucci *et al.* (2011) found that the quality of the final coronal restoration had no significant influence on the treatment outcome (Hoskinson *et al.* 2002, Ricucci *et al.* 2011). In Hoskinson *et al.* (2002) retrospective study, the sample size is considered relatively small (200 teeth) in relation

to the objectives under investigation. In Ricucci *et al.* (2011) study, the recall rate was 60.3% at the 5-year evaluation.

Treatment success of adequately treated canals was significantly reduced when no coronal restoration was in place, allowing bacterial penetration along the root canal system (Siqueira *et al.* 2005). More understandable was the observation that the highest odds for healing of apical periodontitis was observed when the quality of the coronal restoration and the quality of the endodontic treatment are adequate (Kirkevang *et al.* 2000, Segura-Egea *et al.* 2004, Siqueira *et al.* 2005, Tavares *et al.* 2009, Moreno *et al.* 2013, Song *et al.* 2014, Craveiro *et al.* 2015).

It is far from clear if the above-mentioned studies have measured the correct relationship between both the quality of endodontic treatment and the quality of coronal restoration, and analysed its impact on periapical health. It is confirmed that cases with over- or under-extended root canal filling are associated with higher failure rates, therefore, it is doubtful if the failure in such cases is in any way associated with coronal leakage (Bergenholtz & Spångberg 2004). In addition, it is important to mention that cross-sectional studies investigating the influence of the quality of coronal restorations on periapical health have certain limitations. Examinations were essentially based on periapical radiographs taken at one point in time with no knowledge of the exact time elapsed between root canal treatment and radiological evaluation. For instance, some of the radiolucencies associated with root canal treated teeth might be mistakenly considered as a failure, while they might actually represent healing lesions. Therefore, more frequent failures in the assessment of endodontic treatment may have been detected in these studies.

In conclusion, an inadequate coronal restoration might be conducive to a poor prognosis, therefore, the need for an adequate root filling with a sufficient and tight coronal restoration is an essential aspect to improve the clinical outcome associated with

endodontically treated teeth.

1.8 Summary

Several studies have attempted to investigate the correlation between the remaining coronal tooth structure and both the survival of endodontically treated teeth and the success of restorations. However, all these studies have used inaccurate methods to estimate the amount of remaining coronal tooth structure. In addition, many of these studies were limited to only endodontically treated premolars restored with and without posts. The literature review clearly highlights the need to develop a reliable and reproducible method to measure the remaining volume of coronal tooth structure, and investigate in a prospective study the impact of the remaining volume of coronal tooth structure primarily on the survival and secondarily on the endodontic success of root canal treated teeth.

Chapter 2 The detection of simulated periapical lesions in human dry mandibles using cone beam computed tomography – a dose reduction study

2.1 Introduction

Periapical radiographs have invariably been used as the principal technique in the endodontic diagnosis, treatment planning, and assessment of the healing outcome of root canal treated teeth (Gröndahl & Huumonen 2004, Patel *et al.* 2009b). As described in Chapter 1, the inherent limitations of periapical radiography associated with the compression of the complex three-dimensional anatomy onto a two-dimensional image, geometric distortion and anatomical noise, reduce the diagnostic information gained and hinder their ability to initially detect a large number of radiolucencies (Patel *et al.* 2009b).

CBCT has been shown to diagnose periapical lesions that periapical radiographs were unable to detect (Lofthag-Hansen *et al.* 2007, Liang *et al.* 2012, Patel *et al.* 2012a). It generates a typically lower effective dose when compared to medical CT (Ludlow *et al.* 2003, Suomalainen *et al.* 2009, Pauwels *et al.* 2012). However, the patient is still exposed to higher effective doses compared to conventional intraoral periapical imaging (Ludlow *et al.* 2006, Roberts *et al.* 2009) which greatly limits the routine use of CBCT in endodontics. Based on that, the general guidelines confirmed that the use of CBCT imaging should be considered only when the lower-dose conventional dental radiography fails to provide adequate diagnostic information, or for diagnosis in patients with contradictory clinical signs and symptoms (SEDENTEXCT 2012, European Society of Endodontology 2014, American Association of Endodontists 2016).

As described in Chapter 1, several different CBCT scanners are available on the market, and they differ in respect to tube current/voltage, exposure time, field of view, and degree of rotation of the gantry around the patient's head. Some of these exposure parameters

can be modified depending on the CBCT system. Adjustment of these settings can significantly reduce the radiation doses, however, the image quality might be degraded (White & Mallya 2012).

Current CBCT scanners, including the Morita 3D Accuitomo (J. Morita, Osaka, Japan), can generate a three-dimensional volume of data by half (180°) or full (360°) rotation of the X-ray gantry around the patient's head (Patel 2009). Although both CBCT rotations have the same voxel resolution (0.080 mm^3 or 0.125 mm^3), they generate different numbers of basic projections required to reconstruct three-dimensional images. During the 360° rotation of the gantry, 586 basic projection images are usually generated in the 17.5 second scan time, while the 180° rotation reduces the number of projections to only 329 slices in 9 seconds.

Recent studies have demonstrated that reducing the arc of rotation of the scanner from 360° to 180° provided images with similar diagnostic accuracy to 360° scans in the detection of artificial bone lesions (Lennon *et al.* 2011) and external root resorption (Durack *et al.* 2011), and sufficient to make accurate clinical measurements (Hashem *et al.* 2013). This adjustment from 360° to 180° arc of rotation effectively reduces the radiation dose to patients by approximately 50% (Güldner *et al.* 2013).

While scanning, most CBCT devices maintain a constant tube current (mA) throughout the rotation angles. The 3D Accuitomo (J. Morita) CBCT scanner has the ability to apply a dose reduction (DR) feature during the 180° and 360° rotation resulting in reduced radiation dose for the same number of basic projections. According to the manufacturer (J. Morita), the DR mode is a pre-programmed profile of tube current (mA) adjustment that reduces the effective dosage by up to 40% in comparison to the standard-dose programme. During the standard dose mode, the intensity of the tube current (mA) is fixed during the whole gantry rotation, whereas the intensity of mA during the DR mode fluctuates according to the position of the X-ray gantry in relation to the patient's head.

Therefore, as the X-ray beam is passing from the patient's left to right side (0° angle), where bone and soft tissue thicknesses are the lowest, the tube current is at the minimum value. As the rotation angle of the gantry increases to 90°, the X-ray beam passes from patient's posterior to anterior side, where bone and soft tissues thicknesses are the highest, the tube current increases to the maximum value selected previously on the control panel. The mA value then reduces and increases again as the rotation angle approaches 180° and 270°, respectively (Figure 2-1).

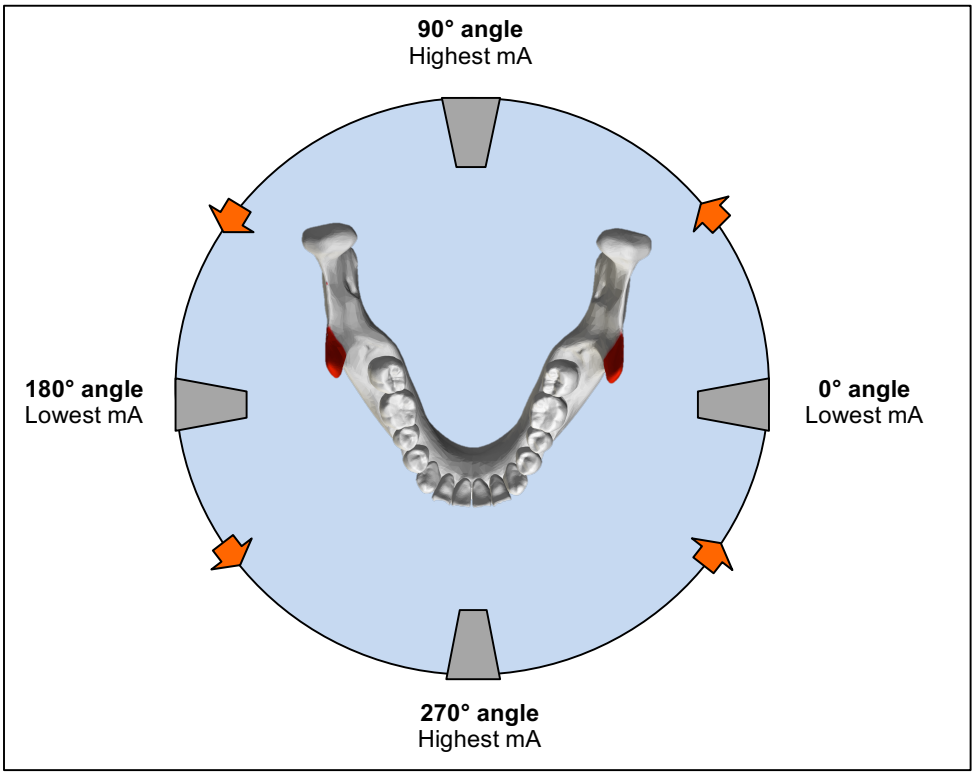

Figure 2-1 Diagram illustrating the variation in CBCT tube current (mA) intensity during dose reduction (DR) mode scanning. The tube current is at its minimum value when the X-ray beam is passing from the patient's left to right side, and at its maximum value when the X-ray beam is passing from the patient's posterior to anterior side

The risks associated with the use of ionisation radiation are cumulative over time (Ludlow *et al.* 2015). Therefore, it is essential to reduce or eliminate unnecessary radiation to the patients during diagnostic imaging (ALARA) (Farman 2005, ICRP 2007).

The aim of this study was to investigate, in an *ex vivo* model, the diagnostic accuracy of periapical radiography and CBCT on the detection of simulated periapical lesions in human dry mandibles, and to investigate the influence of CBCT dose reduction mode on the detection ability. The null hypothesis was that periapical radiographs and both CBCT dose modes would show no difference in the detection of simulated periapical lesions.

2.2 Materials and methods

2.2.1 Subject material preparation

Fourteen unrestored mandibular first and second molars from 10 dry human mandibles provided by the Department of Anatomy and Human Sciences (King's College London Dental Institute, London, UK) were used. Screening periapical radiographs and CBCT scans were taken to confirm that there were no existing periapical lesions associated with the assessed teeth.

Prior to tooth extraction and radiographic imaging, each mandible was rehydrated with soapy water (Fairy Liquid Original, Procter and Gamble, Weybridge, UK) for 90 min to decrease the surface tension, increase resilience, and reduce the possibility of root fracture during tooth extraction (Patel *et al.* 2009a). The crowns of the molar teeth were sectioned through the furcation, using a tapered 557-diamond bur (Dentsply, Addlestone, UK), in a high-speed hand-piece (W&H, St Albans, UK). Following crown sectioning, the distal roots of the molar teeth were carefully extracted with a forceps (Henry Schein, Langen, Germany) (Figure 2-2).

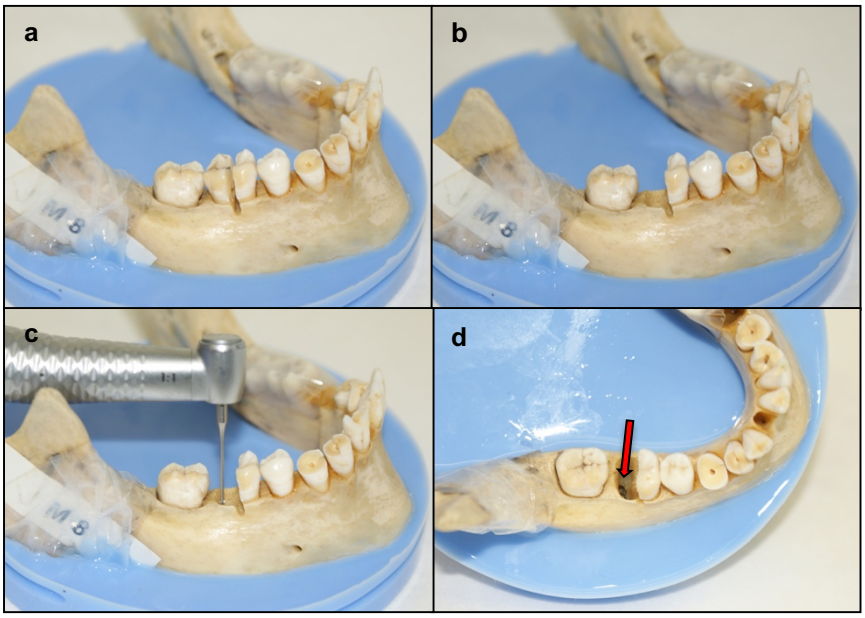

Figure 2-2 (a) Dry mandible with lower right first molar sectioned in a bucco-lingual direction through furcation, (b) distal root has been atraumatically extracted, (c) pulp chamber bur inserted into the socket to prepare a periapical lesion in the cancellous bone, (d) periapical lesion prepared at the base of the socket (red arrow)

A dental operating microscope (3 step entrée Dental Microscope, Global, St. Louis, Missouri, USA) was used to confirm that the underlying cancellous bone was intact. The roots were then replanted, and control radiographs and CBCT scans were acquired before the creation of the lesions. Simulated periapical lesions were prepared into the cancellous bone at the base of the socket of the distal root of the molars using 100 and 160-191R pulp chamber burs (Meissenger, Häger & Meissenger, Neuss, Germany) with a diameter of 0.85 mm and 1.5 mm, respectively, in a slow-speed hand-piece (W&H) to the depth of its head as previously described by Patel *et al.* (2009a). The dimensions of the simulated lesions used in this study were designed according to the findings of a recent *ex vivo* study (Tsai *et al.* 2012).

To calculate the depth of the tooth socket, the pulp chamber bur was oriented along the longitudinal axis of the tooth into the full depth of the socket then the bur's shank was marked at the crestal level of bone. The length of the bur head was measured by using a measuring microscope (EZ measurement system, Starett Kinemetric, Laguna Hill,

California, USA) at 7x magnification and added to the length of the tooth socket obtained previously. The bur's shank was remarked with the new settings prior to cavity drilling. The bur was adjusted within the long axis of the root, and drilling stopped as soon as the bur marking matched with the crestal bone level. A dental operating microscope (Global) was used during lesions preparation to ensure accurate depth of the cavities.

'Small' lesions (0.85 mm in diameter and 1.0 mm in width) were created, the roots were then relocated into the extraction sockets, and the mandibles were rehydrated. Periapical radiographs and CBCT scans of mandibular teeth were repeated (Figure 2-3). The teeth were then removed from their sockets, and the 160-191R bur (Meissenger) was used to create the 'large' lesions (1.5 mm in diameter and 1.5 mm in depth) by enlarging the existing lesion dimensions; the scans were repeated as described previously (Figure 2-4). Three mandibular molars in three dry mandibles were damaged during lesion preparation and were discarded.

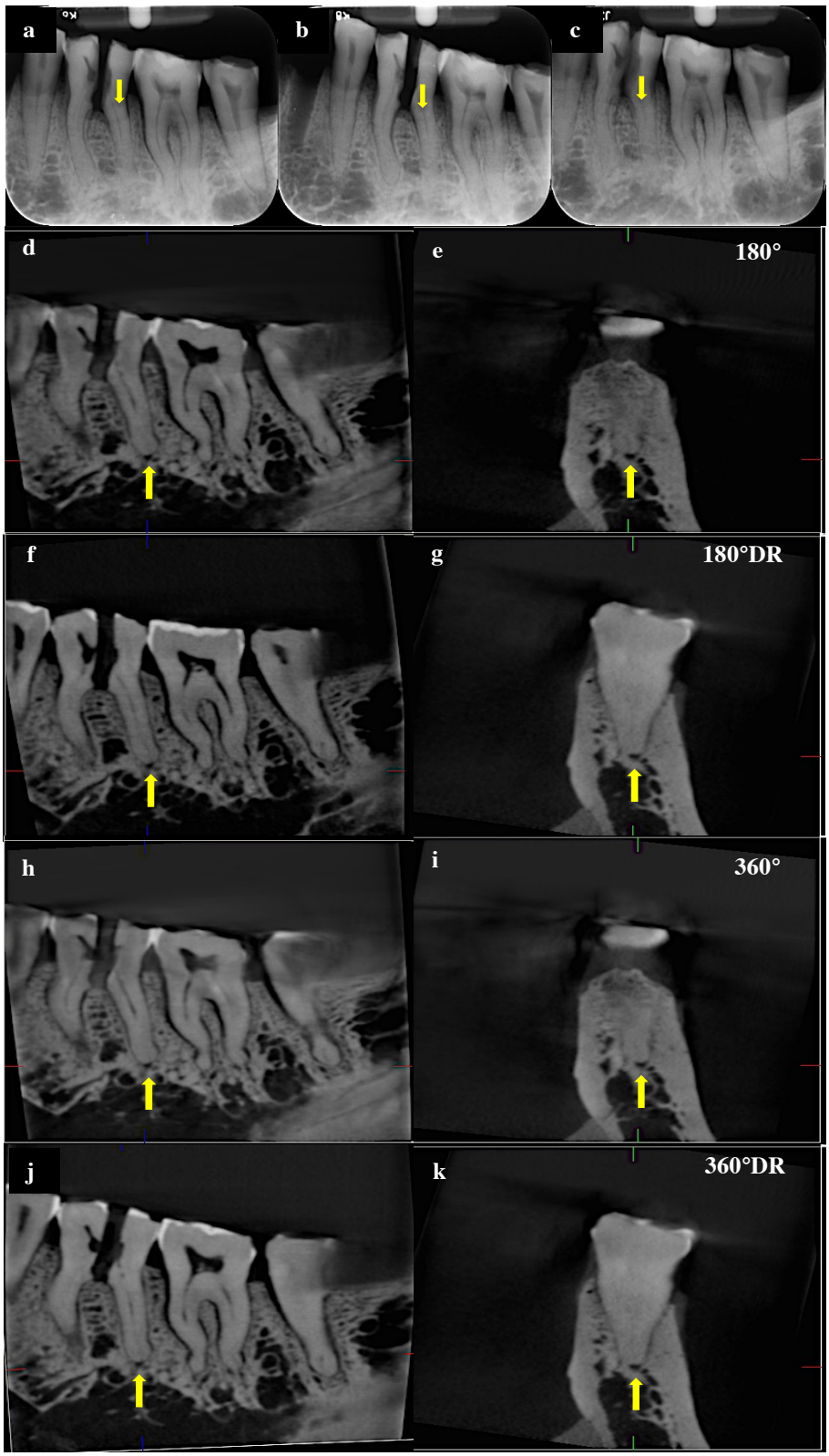

Figure 2-3 (a) Parallel and (b, c) parallax digital periapical radiographs, (d, e) sagittal and coronal reconstructed 180° CBCT images with standard full dose, and (f, g) with dose reduction mode, (h, i) sagittal and coronal reconstructed 360° CBCT images with standard full dose and (j, k) with dose reduction mode following the creation of a small simulated periapical lesion on the distal root of lower left molar tooth. The simulated lesion (indicated by yellow arrows) cannot be detected on the (a-c) radiographs while it can be clearly detected on all (d-k) CBCT images

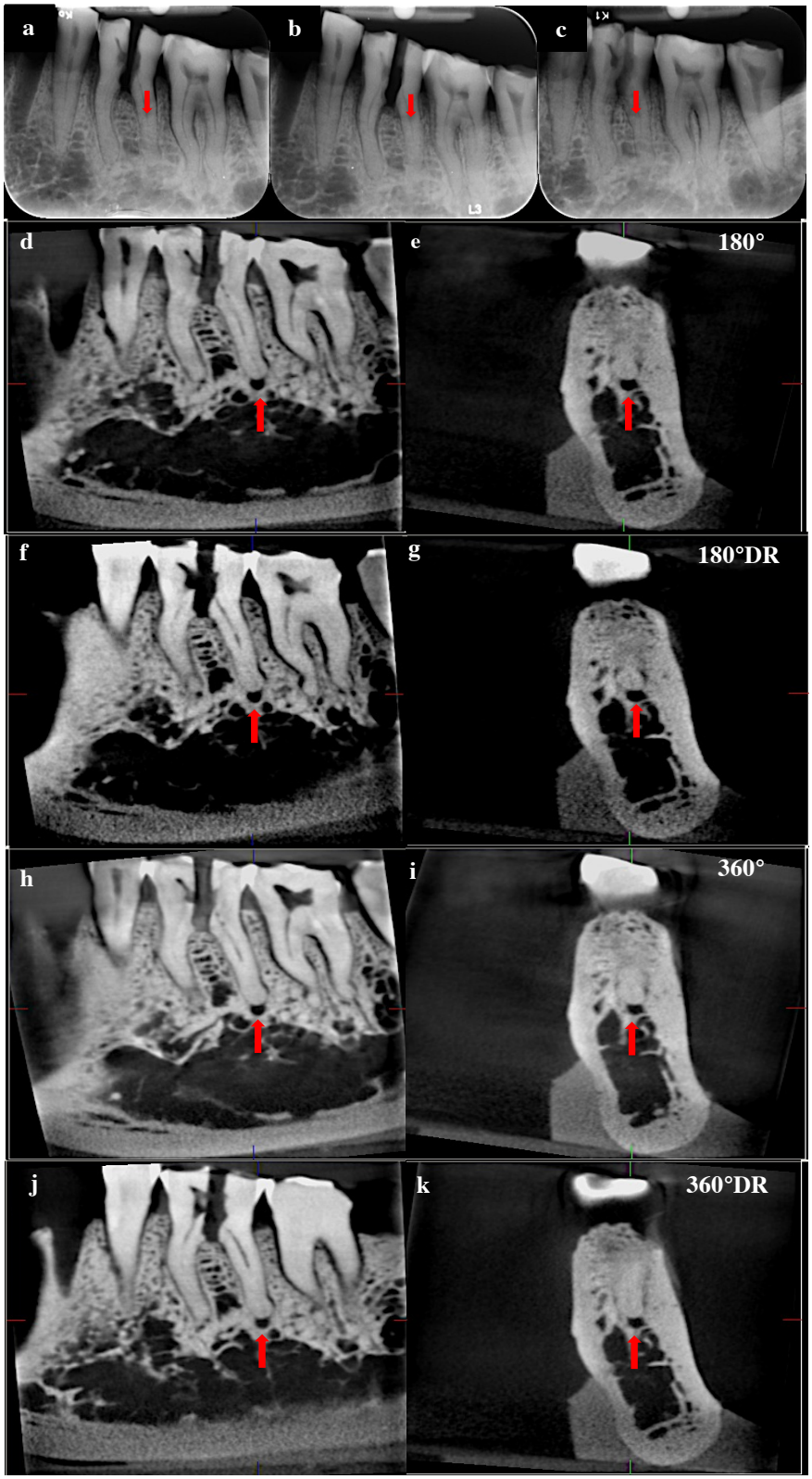

Figure 2-4 (a) Parallel and (b, c) parallax digital periapical radiographs, (d, e) sagittal and coronal reconstructed 180° CBCT images with standard full dose, and (f, g) with dose reduction mode, (h, i) sagittal and coronal reconstructed 360° CBCT images with standard full dose and (j, k) with dose reduction mode following the creation of a large simulated periapical lesion on the distal root of lower left molar tooth. The simulated lesion (indicated by red arrows) cannot be detected on the (a-c) radiographs while it can be clearly detected on all (d-k) CBCT images

2.2.2 Radiographic technique

Two custom-designed jigs were made for each mandible to allow standardised re-seating of the mandibles during each stage of the imaging (radiographs and CBCT). The jig designed for periapical radiographs enabled the teeth within the mandible to be situated at a fixed distance of 35 cm from the X-ray source. Customised silicone templates were created by entirely positioning the inferior margin of the mandible within a polyvinyl-siloxane material (Aquasil, Dentsply DeTrey, GmbH, Konstanz, Germany) mounted onto a plastic rotating base to ensure reproducible and precise repositioning of each mandible into its own putty template during every stage of radiographic scanning (Figure 2-5).

A digital phosphor plate system (Digora® Optime, Soredex, Tuusula, Finland) was used in conjunction with a beam aiming device (Dentsply Rinn, Elgin, Illinois, USA) and a dental X-ray unit (Heliodent, Sirona, Bensheim, Germany) operating at 65 kV, 7 mA and 0.16 seconds. Parallel and parallax radiographs (10° mesial and 10° distal angulations) were taken. The parallax radiographs were taken with the aid of a protractor attached to the rotating base. A 10 mm thick acrylic sheet (Plexiglas®, Evonik Industries AG, Essen, Germany) was used to mimic the attenuation of the X-ray beam by soft tissue encountered clinically (Noujeim *et al.* 2009, Durack *et al.* 2011).

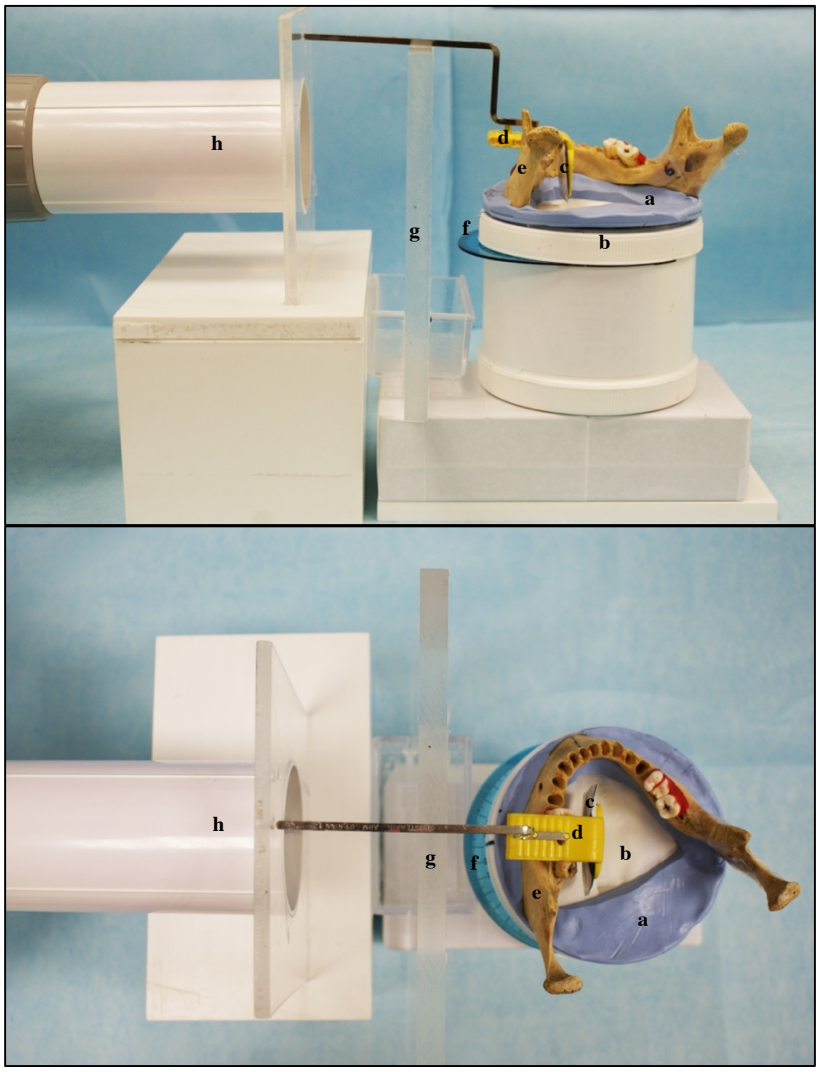

Figure 2-5 Jig used to position mandibles during periapical radiographs taking. (a) Putty silicone template, (b) rotating plastic base, (c) phosphor plate, (d) standard posterior film holder, (e) mandible specimen, (f) mathematical protractor, (g) acrylic soft tissue equivalent, (h) X-ray tube

A small volume CBCT scanner (3D Accuitomo® 80, J. Morita) with a 4 x 4 cm field of view (FOV) and 0.125 mm of voxel size were used to obtain CBCT images. Manufacturer's standard exposure protocol for mandibular posterior teeth (tube voltage of 90 kV, and a tube current of 4 mA) was used while scanning. All CBCT data were reconstructed with 0.16 mm slice intervals and 1.2 mm slice thickness. During 360° and 180° rotations, the mandibles were scanned using standard dose mode and dose reduction (DR) mode.

A second jig was used to allow the mandibles to be seated correctly during the CBCT scans. The jig consisted of an individual silicone template placed over a plastic platform of 8 cm in diameter with a metal dowel rod of 2 cm in length secured to the centre of its lower surface. The jig was positioned instead of the scanner's chin rest by means of the dowel attachment (Figure 2-6).

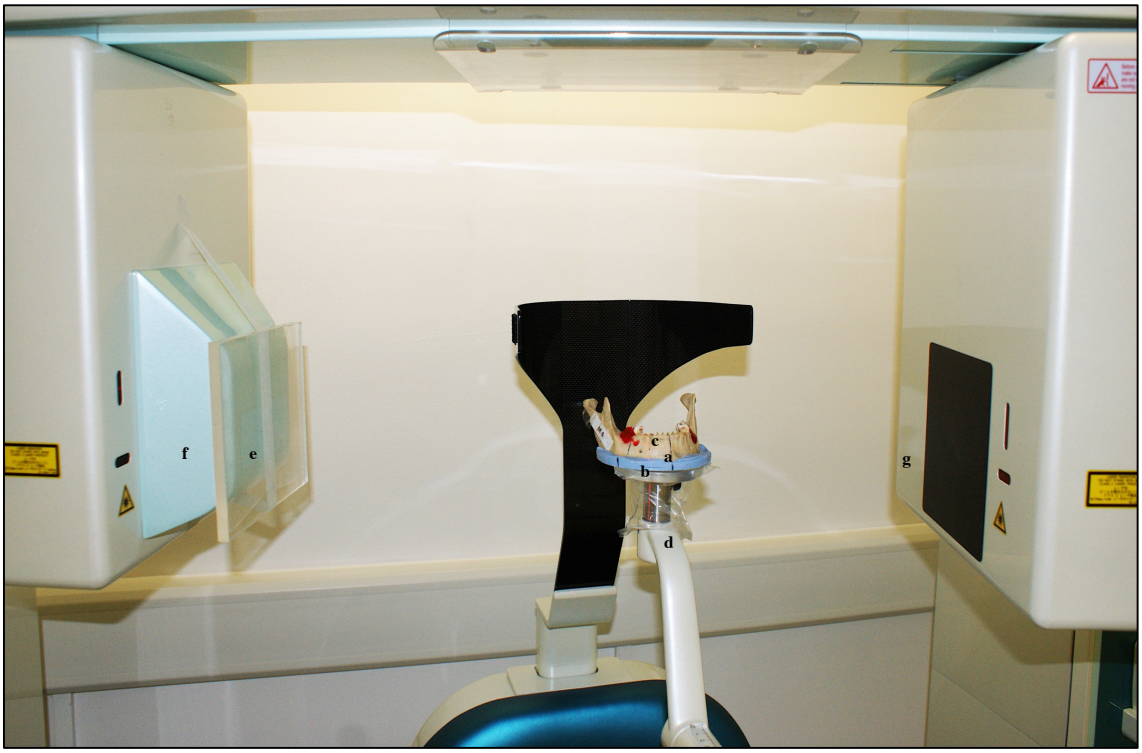

Figure 2-6 Jig used to position mandibles during CBCT scanning. (a) Putty silicone template, (b) plastic platform, (c) mandible specimen, (d) chin rest arm, (e) acrylic soft tissue equivalent, (f) CBCT X-ray source, (g) panel detector

2.2.3 Radiological assessment

For the CBCT scans, the slices that showed the widest diameter of the periapical lesion in sagittal and coronal planes were identified by an endodontist, who was experienced in using CBCT imaging. The slices were aligned vertically to the axis of the apical third of the root, and the brightness and contrast of the slice were optimised using the Accuitomo viewing software (i-Dixel® images, J. Morita) for best visualisation by the examiners. After optimisation, the data was exported as BMP format files.

For the data to be viewed by the examiners, the images were randomly ordered in each session by using computer-specialised software and presented as a PowerPoint (Microsoft PowerPoint 2011, Microsoft®, Redmond, Washington, USA) presentation on a laptop computer (MacBook Pro®, Apple, Cupertino, California, USA) with a screen pixel resolution of 1280 x 800. Raw CBCT data was accessible to the examiners when they intended to examine the orthogonal scans to assist in lesion detection. Six examiners (two endodontists, one radiologist, and three senior endodontic postgraduate students) individually assessed a total of 99 periapical radiographs and 132 CBCT scans in four sessions: 1- all radiographs and 66 CBCT 360° scans examination (both exposure modes); 2- 66 CBCT 180° scans examination (both exposure modes); 3- repeat all radiographs and all 360° scans; 4- repeat all CBCT 180° scans. Sessions 3 and 4 were carried out after 2 weeks to assess intra-examiner agreement.

The examiners were asked to score the presence or absence of simulated periapical lesions by using a 5-point confidence scale to score the appearance of the lesions (Patel *et al.* 2009a): 1: definitely absent; 2: probably absent; 3: uncertain; 4: probably present; 5: definitely present. The examiners were blinded as to whether or not a lesion was present and whether the scans were obtained with standard dose mode or DR mode. All examination sessions were carried out in a quiet, dark room and no time limit has been set for the examiners.

All examiners had considerable experience in interpreting CBCT images, and were calibrated using examples of radiographs and CBCT images for some of the excluded mandibles with and without the presence of periapical lesions prior to the assessment of the study specimens.

2.2.4 Statistical analysis

SPSS software (SPSS version 22, IBM, New York, USA) was used to analyse the raw data. The diagnostic accuracy of each imaging modality for detecting the presence or absence of a periapical lesion was analysed to determine their sensitivity, specificity, receiver operating characteristic (ROC) area under the curve, positive and negative predictive values (PPV, NPV) by using paired sample *t*-tests. Cut-off points were 1-3 for the absence of a lesion and 4-5 for the presence of a lesion. Inter-examiner and intra-examiner agreement were analysed using kappa statistics on the basis of two repeats for 100% of the radiographs and CBCT scans.

2.3 Results

Seven mandibles containing 11 first and/or second molars were finally used in this study. Mean sensitivity and specificity for radiographs and CBCT for detecting small, large, and both lesions pooled together are presented in Table 2-1, Table 2-2, and Table 2-3, respectively. Regardless of simulated periapical lesion size, the overall sensitivity of periapical radiography (0.37) was significantly lower (P<0.001) compared to 360° (0.96), 360° with DR mode (0.96) scans, 180° (0.93) and 180° with DR mode (0.95) scans.

The specificity of periapical radiography, 360° scans with standard dose and dose reduction, and 180° scans with standard dose and dose reduction was 0.848, 0.909, 0.928, 0.955 and 0.985, respectively. There was no significant difference in the sensitivity and specificity between the standard-dose scans and DR scans for both CBCT rotations (P>0.05).

Table 2-1 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting small periapical lesions

	Sensitivity	**Specificity**	**PPV**	**NPV**	**ROC**
PA	0.27*(0.20)	0.86 (0.18)	0.75 (0.29)	0.55*(0.05)	0.56* (0.08)
360°	0.91 (0.06)	0.91 (0.08)	0.91 (0.08)	0.91 (0.06)	0.92 (0.05)
360°DR	0.92 (0.11)	0.92 (0.07)	0.93 (0.07)	0.93 (0.09)	0.92 (0.07)
180°	0.88 (0.18)	0.96 (0.08)	0.96 (0.07)	0.91 (0.13)	0.92 (0.08)
180°DR	0.91 (0.10)	0.99 (0.04)	0.99 (0.04)	0.92 (0.08)	0.95 (0.05)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic; PA, periapical radiograph; DR, dose reduction
* Significantly different from 360° and 180° CBCT (P<0.001)

Positive predictive value and negative predictive value for radiographs and CBCT for detecting small and large lesions are presented in Table 2-1 and Table 2-2. No significant differences were detected in the PPV, NPV between both standard dose and DR scans for both 360° and 180° scans (P>0.05). The overall NPV value of periapical radiography was significantly lower compared to CBCT (180°/360°) NPV values (P<0.001) (Table 2-3).

Table 2-2 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting large periapical lesions

	Sensitivity	**Specificity**	**PPV**	**NPV**	**ROC**
PA	0.47* (0.17)	0.86 (0.18)	0.83 (0.20)	0.62*(0.07)	0.66**(0.10)
360°	1.00 (0.00)	0.91 (0.08)	0.92 (0.07)	1.00 (0.00)	0.95 (0.05)
360°DR	1.00 (0.00)	0.92 (0.07)	0.93 (0.06)	1.00 (0.00)	0.96 (0.04)
180°	0.99 (0.04)	0.96 (0.08)	0.96 (0.07)	0.99 (0.03)	0.97 (0.04)
180°DR	0.99 (0.04)	0.99 (0.04)	0.99 (0.03)	0.99 (0.03)	0.99 (0.02)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic; PA, periapical radiograph; DR, dose reduction
* Significantly different from 360° and 180° CBCT (P<0.01)
** Significantly different from 360° and 180° CBCT (P<0.001)

The ROC analysis revealed that there was no significant difference in the diagnostic accuracy of 360° full-dose and 360° with DR in detecting small (*P*=0.616) and large (*P*=0.606) simulated periapical lesions. Similarly, between 180° full-dose and 180° with DR, there was no significant difference in the accuracy of detecting small (*P*=0.234) and large (*P*=0.360) simulated periapical lesions, whilst CBCT accuracy was significantly different when compared with that of periapical radiography (*P*<0.001) Table 2-1 and Table 2-2. The ROC curves can be found in Appendix II.

Table 2-3 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for periapical radiographs and CBCT for detecting all periapical lesions (small and large lesions pooled together)

	Sensitivity	**Specificity**	**PPV**	**NPV**	**ROC**
PA	0.37*(0.15)	0.85 (0.17)	0.85 (0.12)	0.41*(0.04)	0.62*(0.07)
360°	0.96 (0.03)	0.91 (0.08)	0.96 (0.04)	0.91 (0.06)	0.94 (0.05)
360°DR	0.96 (0.05)	0.93 (0.68)	0.96 (0.03)	0.93 (0.09)	0.95 (0.05)
180°	0.93 (0.09)	0.96 (0.08)	0.98 (0.04)	0.90 (0.13)	0.95 (0.05)
180°DR	0.95 (0.07)	0.99 (0.08)	0.99 (0.02)	0.91 (0.10)	0.97 (0.04)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic: PA, periapical radiograph; DR, dose reduction
* Significantly different from 360° and 180° CBCT (*P*<0.001)

The kappa values for the inter-examiner agreement were 0.15 for periapical radiography, 0.71 and 0.77 for 360° scans with standard and DR modes, respectively; the values for 180° scans with standard and DR modes were 0.80 and 0.88, respectively (*P*<0.01). The mean intra-examiner agreement value was 0.434 for periapical radiography, and 0.85, 0.89, 0.88, 0.93 for 360° scans with standard and DR modes and 180° scans with standard and DR modes, respectively (*P*<0.01) (Table 2-4).

Table 2-4 Kappa values for intra- and inter-examiner agreement in reading periapical radiographs and CBCT

Examiner	Intra-examiner kappa score				
	Radiographs	CBCT 360°		CBCT 180°	
		No DR	DR	No DR	DR
1	0.10	0.76	0.94	0.94	0.94
2	0.84	0.88	0.94	0.94	0.88
3	0.40	0.82	0.81	0.79	0.94
4	0.30	0.81	0.93	0.82	1.00
5	0.38	0.81	0.70	0.77	0.82
6	0.60	1.00	1.00	0.94	1.00
Mean (SD)	0.43* (0.26)	0.85 (0.09)	0.89 (0.11)	0.88 (0.10)	0.93 (0.07)
Inter-examiner kappa score	0.15*	0.71	0.77	0.80	0.88

SD, standard deviation; DR, dose reduction

* Significantly different from 360° and 180° CBCT (P<0.01)

2.4 Discussion

In the present study, the effect of the built-in DR mode in 3D Accuitomo CBCT machines on the diagnostic accuracy of both 360° and 180° scans for the detection of small and large simulated periapical lesions created in human dry mandibles was determined.

A previous study demonstrated that CBCT devices had good accuracy in detecting lesions between 0.8 mm and 1.4 mm in diameter while the accuracy was poor when detecting simulated lesions smaller than 0.8 mm in diameter (Tsai *et al.* 2012). It is therefore clinically relevant to assess the effect of applying the dose reduction protocol on the diagnostic accuracy to detect the smallest lesion that the CBCT can readily visualise with fair to good quality. Thus, two simulated periapical lesions were used in the present study, small (0.85 mm diameter and 1.0 mm depth) and large (1.5 mm diameter and 1.5 mm depth).

One advantage of using simulated periapical lesions is that it gives a reference standard; that is, the periapical status is known beforehand, to which all CBCT scan modalities can be compared. Chemically induced periapical lesions demonstrate diffuse borders radiographically that more closely resemble naturally occurring periapical lesions (Koenig *et al.* 2004, Soğur *et al.* 2009). However, it would be difficult to have small size standardised lesions by using the chemical technique. Simulated lesions prepared using a bur do not mimic the diffuse border of naturally occurring lesions (Petersson *et al.* 2012) and the density between the surrounding bone and the outer border of the lesion is quite distinguishable (Lee & Messer 1986), which would improve the detectability of simulated lesions in comparison to naturally occurring lesions (Lee & Messer 1986, Soğur *et al.* 2009, Liang *et al.* 2014). However, creating lesions with a bur permitted accurate control of the dimensions of the bony cavity, allowing good standardisation, which is desirable when assessing the accuracy of two different X-ray modalities (Patel *et al.* 2009a, Tsai *et al.* 2012).

In actual clinical settings, the presence of radiographic artefacts related to the X-ray beam influences the observer performance and limits the diagnostic yield of the final reconstructed images. Scattering, beam hardening (Mora *et al.* 2007, Soğur *et al.* 2007) and motion artefacts (Schulze *et al.* 2015) are significant artefacts, which can influence the image quality and diagnostic accuracy of the CBCT image. Scattering and beam hardening are caused by differential absorption of the X-ray beam by very high-density structures, such as enamel, metallic restorations and dental implants (Scarfe & Farman 2008). A patient motion such as shaking or patient's breathing during the scan can reduce the spatial resolution, resulting in deterioration of the 3D volume data that may cause incorrect interpretation (Hanzelka *et al.* 2013, Spin-Neto *et al.* 2013). Reproducing these artefacts was not relevant to the main aim of this *ex vivo* study.

In order to simulate the clinical situation, all mandibles were hydrated in water before scanning (Patel *et al.* 2009a) and a 10 mm thick acrylic plate (Evonik) was placed in front of the X-ray source to absorb and scatter radiation in a similar way to the presence of oral hard and soft tissues, as successfully used by earlier studies (Noujeim *et al.* 2009, Kamburoğlu *et al.* 2010, Durack *et al.* 2011). Although using dry mandibles might be considered as a limitation compared to the actual patient mandible, a pilot study revealed that the images generated using standard exposure settings together with a 10 mm thick tissue equivalent acrylic plate were comparable to corresponding clinical images from patients.

Choosing among different imaging modalities is attributed to the increasing concern about high radiation dose to the patients. In the present study, comparison of the standard CBCT exposure and DR mode demonstrated no significant differences in the overall sensitivity, specificity, positive predictive value, negative predictive value and ROC value for both lesion sizes, whereas the sensitivity, NPV and ROC value of the periapical radiography were significantly lower compared to both CBCT scan modalities. Sensitivity and specificity of 360° (0.96, 0.93) and 180° (0.95, 0.99) scans with DR mode to diagnose both small and large lesions were higher than 360° (0.96, 0.91) and 180° (0.93, 0.96) scan with standard dose mode, respectively.

In this study, dose reduction scans had an accurate diagnostic quality to detect apical radiolucencies due to the fact that the intensity of the X-ray during the DR mode is optimised according to the bone thickness and the position of the X-ray tube in relation to the skull. This minimises overexposure for easily penetrated tissue, resulting in more optimised image quality with fewer artefacts compared to standard exposure scans.

The results of the present study are in agreement with other studies (Stavropoulos & Wenzel 2007, de Paula-Silva *et al.* 2009, Patel *et al.* 2009a, Soğur *et al.* 2009), which indicate that periapical radiography had a lower sensitivity (0.37) in detecting periapical

lesions regardless of the lesion size, while the specificity was 0.85. Stavropoulos and Wenzel (2007) reported that the sensitivity of CBCT (NewTom 3G) to detect mechanically created periapical defects in pig jaws was twice as high as that for periapical radiographs.

Petersson *et al.* (2012) evaluated in a systematic review the diagnostic accuracy of different radiographic methods in the detection of the presence/absence and changes over time of periapical bone lesions. The authors reported that the mean sensitivity and specificity values for periapical radiographs for all groups of teeth reached 0.55 and 0.98, respectively (Petersson *et al.* 2012). Regardless of the type of radiographic system used, larger lesions are more readily detected than smaller lesions (Sullivan Jr *et al.* 2000). None of the studies included in Petersson's *et al.* (2012) study has investigated the detection of artificially created bone lesions smaller than 1 mm in size.

In the current study, the lower overall sensitivity value for radiographs (0.37) probably reflects the difficulty in detecting a very small artificial lesion size (0.85 mm depth X 1.00 mm width). However, the periapical radiograph sensitivity reported in the present study for diagnosing the presence of large simulated periapical lesions (0.47) favourably compare with the findings of Petersson *et al.* (2012). Furthermore, the mean sensitivity and specificity index values demonstrated by Petersson *et al.* (2012) represented 19 different studies, with each having its own methodology, different mandibles, anatomic region examined (cortical/trabecular bone), bone lesion sizes, different scanners, and perhaps different examiner experience between the countries where these studies were done.

Tsai *et al.* (2012) investigated the diagnostic accuracy of two CBCT machines and periapical radiography to detect artificially created apical lesions smaller than 1 mm and reported that the specificity for periapical radiography was 0.75 and the overall ROC value was 0.58, which are comparable to the findings of the present study.

Regardless of the exposure settings selected, the sensitivity for CBCT scans was in accordance with the findings of previous investigations (de Paula-Silva *et al.* 2009, Patel *et al.* 2009a, Liang *et al.* 2014). Patel *et al.* (2009a) and Liang *et al.* (2014) reported that CBCT scans are 100% accurate in diagnosing the presence of small and large simulated periapical lesions in human dry mandibles, while the sensitivity of intraoral radiography was 0.24 and 0.67, respectively. de Paula-Silva *et al.* (2009) investigated the sensitivity and specificity of CBCT in detecting apical lesions on teeth in dogs, while using the histopathological examination as a reference standard. The authors reported a sensitivity of 0.91 and 0.77 for CBCT and periapical radiography, respectively.

In the present study, the accuracy of the CBCT to confirm the absence of artificial bony cavities was less than 100% as the detection of small periapical radiolucencies was probably affected by the sparse trabeculation of cancellous bone (false-negatives). However, the specificity of CBCT was higher (P>0.05) than the specificity of periapical radiography.

The overall PPV for both 360° and 180° CBCT scans compare favourably with the values demonstrated by an *ex vivo* study (Lennon *et al.* 2011) investigating the influence of using half-scan mode (180°) on the diagnostic accuracy to detect small artificially created apical lesions. The authors reported PPV of 89.1% and 93.2% for the 360° and 180° scans, respectively. de Paula-Silva *et al*. (2009) reported a PPV value of 1.0 when they evaluated the accuracy of CBCT against periapical radiography in diagnosing apical periodontitis. The high PPV values noticed in CBCT evaluations confirmed the greater accuracy to discriminate cases with simulated periapical lesion from no lesion cases (low risk of false-positive results).

Regarding the NPV values which define the ability of a test to distinguish control cases from those with simulated periapical lesions (risk of false-negative), the NPV for the 360° and 180° dose reduction scans were 0.931 and 0.913, respectively, which compare

favourably with the values (1.0) demonstrated by Patel *et al.* (2009a) and Liang *et al.* (2014). However, the present study values were considerably higher than those of Lennon *et al.* (2011), which reported NPV for the 360° and 180° scans of 76% and 74.3%, respectively.

The ROC curve and area under the curve (AUC) give an overall summary of diagnostic accuracy based on a combination of both sensitivity and specificity values. The higher the ROC value (AUC=1.0), the perfect the diagnostic accuracy of a test (Zou *et al.* 2007). Regardless of the lesion size, the ROC values for both CBCT rotations with DR mode were higher than the CBCT with standard dose mode confirming the high diagnostic accuracy of the scans with DR feature. The ROC curve finding confirmed the PPV and NPV results. The overall ROC values for all CBCT scans modalities were equivalent to the findings of similar studies (Patel *et al.* 2009a, Tsai *et al.* 2012).

The intra-examiner agreement was higher for DR (0.89-0.93) scans compared to that of standard dose (0.85-0.88) scans. Similarly, the inter-examiner agreement for DR scans (0.77-0.88) scans was higher than that of standard dose (0.71-0.80) scans. This better level of performance in assessing CBCT DR scans was due to minimising the over-exposure of easily penetrated tissues that resulted in sharper images of soft tissue with fewer artefacts.

Brown *et al*. (2009) reported that reducing the number of image projections to construct 3D images did not lead to reduced dimensional accuracy of 3D measurements, while potentially reducing the radiation dose to the patient (Brown *et al.* 2009). Dawood *et al*. (2012) examined the possibility of reducing radiation dose using variable exposure parameters, including the 180° rotation, while evaluating patients implant sites. They demonstrated that the level of confidence in the diagnostic yield of the images was only marginally affected by the lower dose protocols, whereas the patient dose was potentially reduced during implant site evaluation (Dawood *et al.* 2012).

In an *in vitro* study, Bechara *et al.* (2013) found that the accuracy and sensitivity of CBCT scans acquired with 180° rotation to detect root fracture in endodontically treated teeth did not vary significantly compared to those scans acquired with 360° rotation, but 180° rotation scans had a significantly lower specificity (Bechara *et al.* 2013). Whereas, Hassan *et al.* (2012) reported that using a lower number of basis projection (180°) had significantly influenced the visibility of the root canal space with CBCT (Hassan *et al.* 2012).

A better outcome of root canal treatment is anticipated when the treatment is performed before apical periodontitis become radiographically evident (Friedman 2002a). The ability of CBCT to diagnose early signs of periapical disease that have never been visible on radiographs could result in more effective management of periapical disease (Patel *et al.* 2015).

In scenarios where patients have poorly localised symptoms associated with teeth with suspected endodontic disease, and the clinical and periapical radiological examination show no evidence of disease, CBCT may be indicated to confirm the presence of previously undiagnosed pathosis (Patel *et al.* 2015). CBCT may also be indicated to help confirm the absence of an odontogenic aetiology of pain when managing non-odontogenic causes of pain (Patel 2009, European Society of Endodontology 2014).

The effective radiation dose from CBCT scan is higher compared to conventional digital radiography; hence it is essential to choose the smallest field of view (FOV) and optimal exposure (ALARA). Future investigations are needed to assess the influence of using DR mode on other applications of CBCT in dentistry such as detecting internal and external resorption, and horizontal tooth fractures.

2.5 Conclusion

The null hypothesis stating that periapical radiographs and CBCT would show no difference in the detection of simulated periapical lesions was rejected. The null hypothesis stating that there is no difference in the detection of simulated periapical lesions using CBCT standard dose and dose reduction modes was accepted.

Periapical radiographs demonstrated poor diagnostic accuracy in the detection of small simulated periapical lesions compared with CBCT. There was no difference in the overall accuracy between 360°DR and 180°DR when compared to the control standard dose scans.

The DR CBCT scans maintained good diagnostic accuracy while reducing the radiation dose by 54% during the full-arc rotation (360°) and by 51% during the half arc rotation (180°). The radiation dose was reduced by up to 74% between 360° standard dose and 180° DR mode.

Further studies could potentially confirm the present results clinically, which may provide greater weight to the benefits of using dose reduction protocols on patients.

Chapter 3 Assessment of residual coronal tooth structure post-endodontic cavity preparation using digital dental impressions and micro-computed tomography

3.1 Introduction

There is increasing evidence that one of the key prognostic indicators for the survival of endodontically treated teeth and the prognosis of the restorations of root canal treated teeth is the amount of remaining coronal tooth structure post-endodontic and restorative tooth preparation (Nagasiri & Chitmongkolsuk 2005, Bitter *et al.* 2009, Naumann *et al.* 2012). However, as described in Chapter 1, this evidence is limited due to relying on *in vitro* studies as a precise measurement of the amount and location of remaining coronal dentine has historically required *ex vivo* measurement (Al-Omiri & Al-Wahadni 2006, Ibrahim *et al.* 2016). Therefore, there is a need to precisely measure residual coronal tooth tissue and assess endodontic anatomy *in vivo* in order to plan and design the most minimally invasive endodontic and restorative preparations, prior to embarking on therapy.

In vivo clinical studies investigating the restorability of teeth were limited to subjective indices and examination of 2D imaging (McDonald & Setchell 2004). However, recent developments in 3D imaging and intraoral digital scanning allow precise quantitative assessment of the amount of residual coronal tooth structure which may be used to influence therapeutic decision-making and aid in future treatment planning.

Currently, the scientific basis for a clinical measure to define the optimal amount of coronal tooth substance required prior to final restoration is lacking (Goodacre *et al.*

2001). Therefore, it is challenging for clinicians to reliably advise patients on how long root canal treated teeth are likely to survive.

As described in Chapter 1, several studies have attempted to compare the probability of the survival of the restorations of endodonically treated teeth with different amounts of residual coronal tooth structure (Creugers *et al.* 2005a, Ferrari *et al.* 2012, Naumann *et al.* 2012). Naumann *et al.* (2006a) proposed a novel approach to identify the extent of loss in tooth structure before restoration placement. The authors measured the remaining tooth structure in vertical and horizontal dimensions using a colour-coded PCP probe, and the size and flare of the access orifice using a straight plugger with millimetre scale (Naumann *et al.* 2006a).

Other authors defined the remaining tooth structure according to the number of coronal walls left with no consideration to dentine wall height and thickness (Cagidiaco *et al.* 2007, Ferrari *et al.* 2012, Sterzenbach *et al.* 2012). These qualitative methods do not allow for precise quantification of the amount of the residual coronal tooth structure for endodontically treated teeth and therefore, prior to conducting prospective clinical studies investigating the influence of volume of residual tooth structure on tooth survival, it is essential to establish a reliable method to enable clinicians to accurately quantify the amount of remaining coronal hard tooth tissue, ideally using non-ionising radiation imaging.

Three-dimensional radiographic imaging techniques are being progressively utilised for enhanced diagnostics in dentistry and more recently developments in digital impressions technology are opening digital diagnostic opportunities based on non-ionising optical principles (Masri & Driscoll 2015). Micro-computed tomography (μCT) produces high-resolution images for 3D evaluation of root canal system anatomy *in vitro* (Peters *et al.* 2000) and provides a widely accepted ‘gold standard’ measurement for dental volumetric reference comparisons.

The combination of 3D radiography datasets with digital impressions of surface data is providing novel approaches and replacing conventional impressions for the construction of conventional fixed dental restorations (Ender & Mehl 2011, Flügge *et al.* 2013, Güth *et al.* 2013). Moreover, the generation of anatomical 3D data can be utilised for digital diagnostic applications, including 3D volumetric analysis of dental hard tissues before, during and after endodontic therapy.

As described in Chapter 1, the range of available digital impression devices has varying operative principles which influence the resulting resolution, local and full arch accuracy and also the precision of the acquired 3D data (Nedelcu & Persson 2014, Masri & Driscoll 2015). The 3M™ True Definition scanner was introduced in October 2012 and superseded the Lava Chairside Oral Scanner (Lava COS), which was the first continuous video capture scanner using visible blue light to be introduced to the market in 2008 (Rohaly 2006).

In order to reproduce the intraoral 3D situation, three tiny sensors at the lens capture images for the surfaces to be scanned from three diverse angles at the same time. Three-dimensional surface patches are generated using in-focus and out-of-focus data by means of proprietary image-processing algorithms (ESPE 2009). The video capture rate (flash rate) is twenty captures per second (60 images/second), therefore almost 2400 datasets are captured for obtaining an accurate arch scan (Syrek *et al.* 2010). The 3M True Definition scanner has been reported to have very good local and full arch accuracy and precision (Güth *et al.* 2013, Patzelt *et al.* 2014a) and has been used in a variety of dental perspectives.

The accuracy and precision of intraoral digital scanning has been reported in a variety of dental studies, in relation to the fabrication of single crowns (Syrek *et al.* 2010, Seelbach *et al.* 2013, Pradíes *et al.* 2015) or single tooth restorations (Boeddinghaus *et al.* 2015), reference scanning (Nedelcu & Persson 2014), full arch scanning (Patzelt *et al.* 2014a),

obtaining digital models (Güth *et al.* 2013), and for digital implant impression (Giménez *et al.* 2015). However, no published studies have so far assessed the performance of intraoral scanners in the measurements of the volume of coronal tooth structure before or after endodontic access cavity preparation, in comparison with 3D radiography.

It was thus the aim of this study to use the intraoral digital scanning for the quantification of the volume of residual tooth structure after endodontic access cavity preparation, using micro-computed tomography as a reference standard. The null hypothesis was that there is no difference between the 3D measurements of residual coronal tooth structure obtained with intraoral digital scanning and micro-computed tomography.

3.2 Materials and methods

3.2.1 Tooth preparation

Thirty-four intact human extracted maxillary and mandibular molars with no caries were collected from the Department of Oral Surgery at Guy's Hospital (King's College London Dental Institute) and included in this study. Ethical approval was granted by the Research Ethics Committee in London (Reference number 10/H0804/056), and verbal and written consent was obtained prior to teeth extraction.

Initial preparation of the teeth involved the removal of calculus, if any, using a conventional ultrasonic scaler (EMS, Nyon, Geneva, Switzerland). In accordance with the tooth anatomy and clinical root canal preparation principles, endodontic access cavities were cut in all teeth by a skilled operator using a high-speed hand-piece (W&H) and diamond burs (REF 878–2800 Henry Schein, Gillingham, UK) under constant water cooling.

During access cavity preparation, teeth were mounted on a phantom head in order to simulate the clinical situation, and a dental operating microscope (3 step entrée Dental Microscope, Global) was used in order to achieve the most conservative access opening, which allowed testing the performance of the digital scanner to scan these cavities. The roof of the pulp chamber was removed, and a thin layer of flowable composite (Synergy Flow, Coltène/Whaledent AG, Genf, Switzerland) was placed to seal the canals orifices and fill the pulp chamber floor to the level of the cemento-enamel junction (CEJ) subsequent to completion of access cavity preparation.

3.2.2 Data acquisition and segmentation

3.2.2.1 Accuracy and precision of the test measurement system (True Definition scanner and Geomagic Control software)

The accuracy and precision of the test intraoral scanning device (3M™ True Definition scanner, 3M ESPE, St Paul, Minnesota, USA) and the surface metrology software (Geomagic® Control™ 2014.3, 3D Systems, Cary, North Carolina, USA) were quantified following dimensional metrology good practice guidelines (Bell 2010). Geomagic Control is a three-dimensional inspection and surface metrology software, which enables accurate graphical comparisons between digital reference models.

The accuracy (trueness) describes the deviation of the tested model from the original model geometry (Leach 2010). To ascertain the accuracy of measurement, calibrated steel gauge block (Mitutoyo®, Mitutoyo Corporation, Japan) with 0.5 mm step height was sequentially scanned 30 times using the digital scanner and the accuracy (µm) was expressed as the mean difference between the resulting data and the truly known dimensions of the gauge block (Figure 3-1).

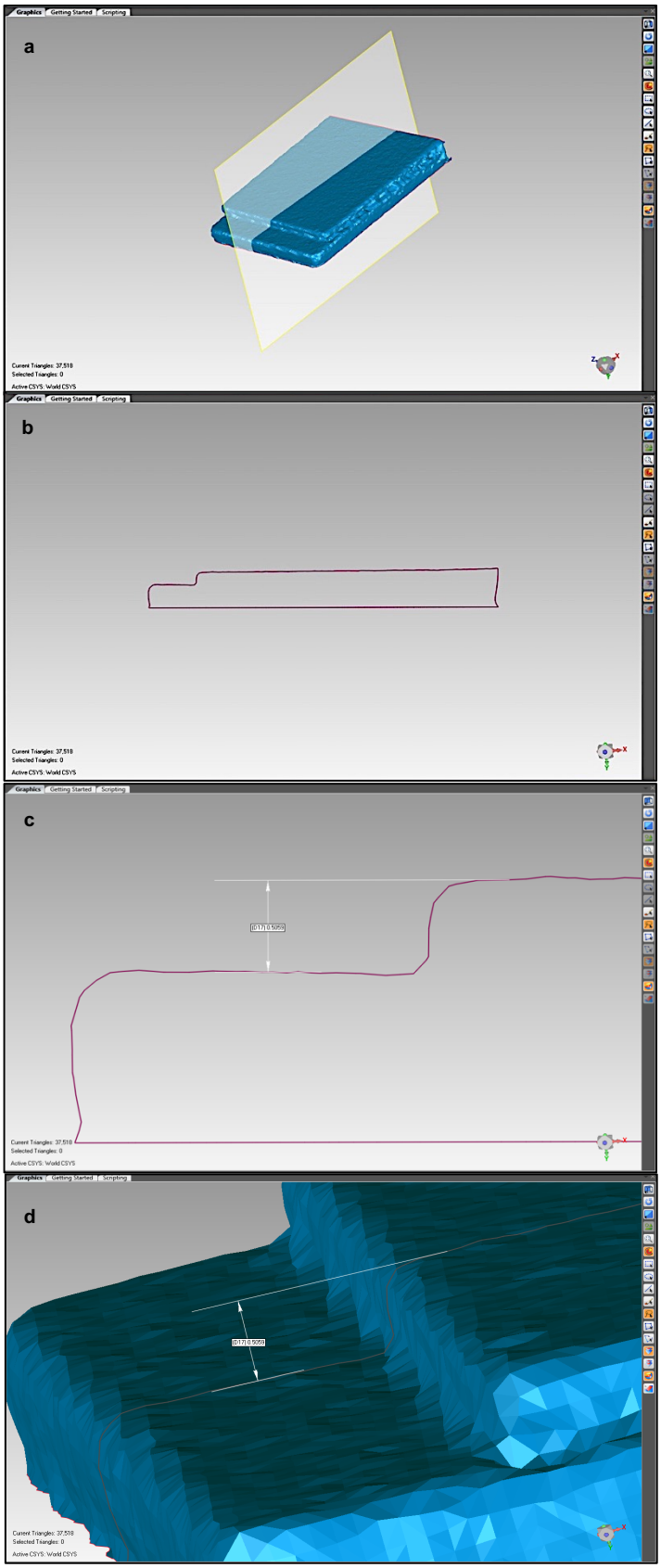

Figure 3-1 Measurement process for determining the accuracy of the intraoral digital scanner (a) surface mesh of the gauge block, (b) 2D cross-section is taken from the central area of the gauge block, (c, d) measurements of the distance between two parallel sections

While a precision refers to the closeness of agreement between replicated measurements under unchanged (repeatability) or changed (reproducibility) conditions (Leach 2010). To ascertain the precision (repeatability and reproducibility) of measurements, a profilometric calibration dental model (upper right first molar) was used following previously published protocols (Rodriguez *et al.* 2012) (Figure 3-2).

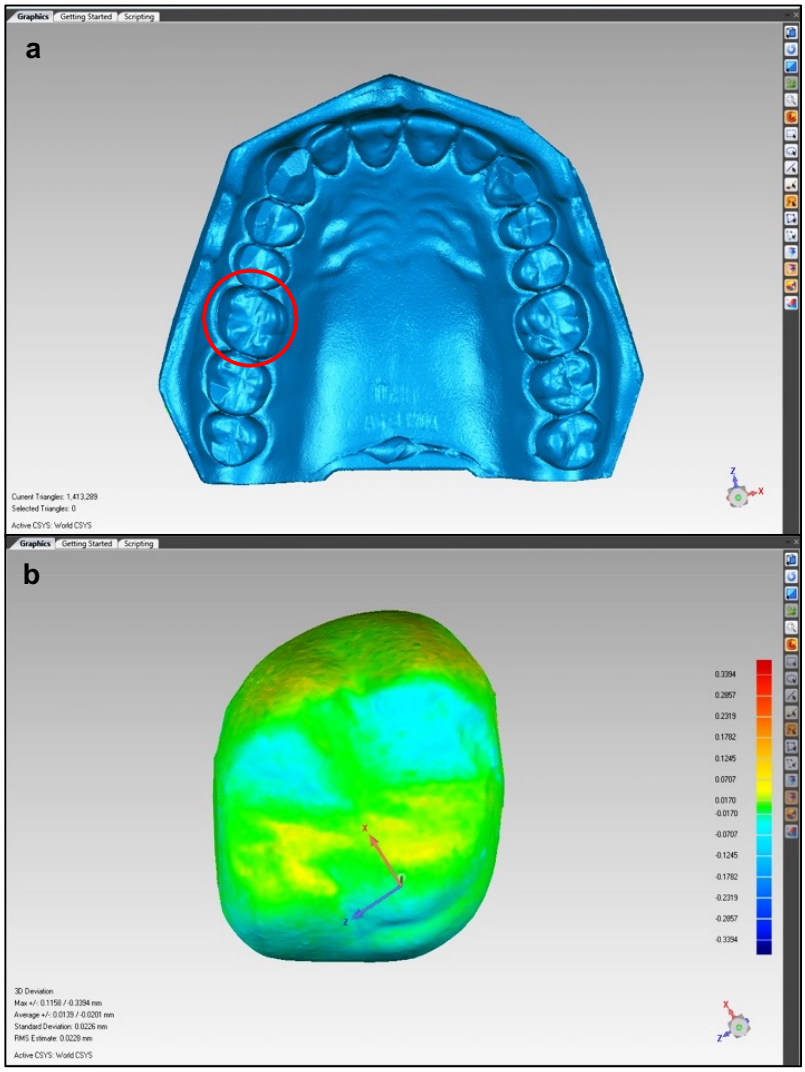

Figure 3-2 Example scans of (a) the profilometric calibrated model (upper right first molar [highlighted by red circle]) used to assess the precision (repeatability and reproducibility) of measurements by intraoral digital scanner, and (b) a superimposition using best-fit alignment (Geomagic software) showing 3D comparison of upper right first molar tooth scans

For the repeatability assessment, 10 immediately repeated scans were obtained using unchanged measurement conditions (i.e. same laboratory, same operator and same equipment), however for reproducibility, before and after each measurement the model was cleaned off, re-dusted with Lava Powder (3M ESPE), repositioned and there was a time delay of 24 hours between scans.

The scans were imported into the surface metrology (Geomagic Control) software then repeatedly superimposed for 3D comparison analysis of the calibration model using the same technique as was to be applied for the volumetric analysis of the crown structure in the current study. The repeatability and reproducibility were expressed as the average of root mean square (RMS) differences in the *x*-, *y*- and *z*-axis (μm) of the superimposed scans.

3.2.2.2 Digital impression device scanning protocol

All samples were subsequently scanned with the intraoral digital scanner following the manufacturer's instructions using a zigzag scanning pathway. Prior to scanning, teeth surfaces to be scanned were lightly dusted with titanium-oxide scanning powder spray (3M high-resolution scanning spray, 3M ESPE).

3.2.2.3 Micro-computed tomography scanning protocol

All teeth were fixated on a wax base for immobilisation purposes during the scanning process. Each sample was scanned with a micro-computed tomography scanner (Locus SP μCT scanner, GE Medical Systems, London, Ontario, Canada) using constant parameters (tube voltage, 80 kV; tube current, 79 mA; voxel size resolution 28 μm; aluminium filter 0.04 mm) to obtain the reference data. After scanning, the sliced data images generated by the μCT machine were exported as VFF data format, following which they were reconstructed using 3D Reconstruction Utility software (GE Healthcare, London, Ontario, Canada).

All teeth were segmented semi-automatically using MicroView software (version 2.5.0, Parallax Innovations, Ilderton, Ontario, Canada) and 3D surface meshes were generated. An independent observer repeated the segmentation twice. The grey-scale threshold value used for segmentation was identified using the automatic threshold tool with the histogram plot to distinguish the mid-point between the tooth tissue and air for each μCT scan.

Two 3D surface mesh datasets were created for each sample by adjusting the surface quality and decimation factor intensities. The first surface mesh (μCT1) had 100% surface quality and 0% decimation factor, which showed the highest quality and the maximum number of triangles (i.e. highest resolution). The second (μCT2) had 100% surface quality and 80% decimation factor, which showed the minimum number of triangles (i.e. lowest resolution).

3.2.3 Alignment of datasets

All intraoral scanner and μCT datasets were saved and exported as STereo-Lithography (STL) format files (Figure 3-3) and were imported into surface metrology (Geomagic Control) software for data analysis. STL data are composed of small triangles, which function as a surface geometry of a three-dimensional polygonal model. Data that were out of the field of interest were eliminated using the Geomagic software to ensure an accurate virtual superimposition.

Alignment was made by superimposing the intraoral digital scanner dataset, defined as the TEST value, on the μCT datasets, designated as μCT1 and μCT2. The first superimposition was performed between the intraoral digital scanner and μCT1 datasets, while the second superimposition was performed between the intraoral digital scanner and μCT2 datasets using the best-fit alignment method of the Geomagic software. The best fit-alignment system was set to match 15,000 common points between the test (intraoral scanner) and reference (μCT) datasets. All superimposed datasets were

trimmed to the level of a reference line (CEJ). Thus the measurements were of the coronal tooth structure only, and the CEJ of the teeth was used as a datum plane to ensure precise standardised measurements.

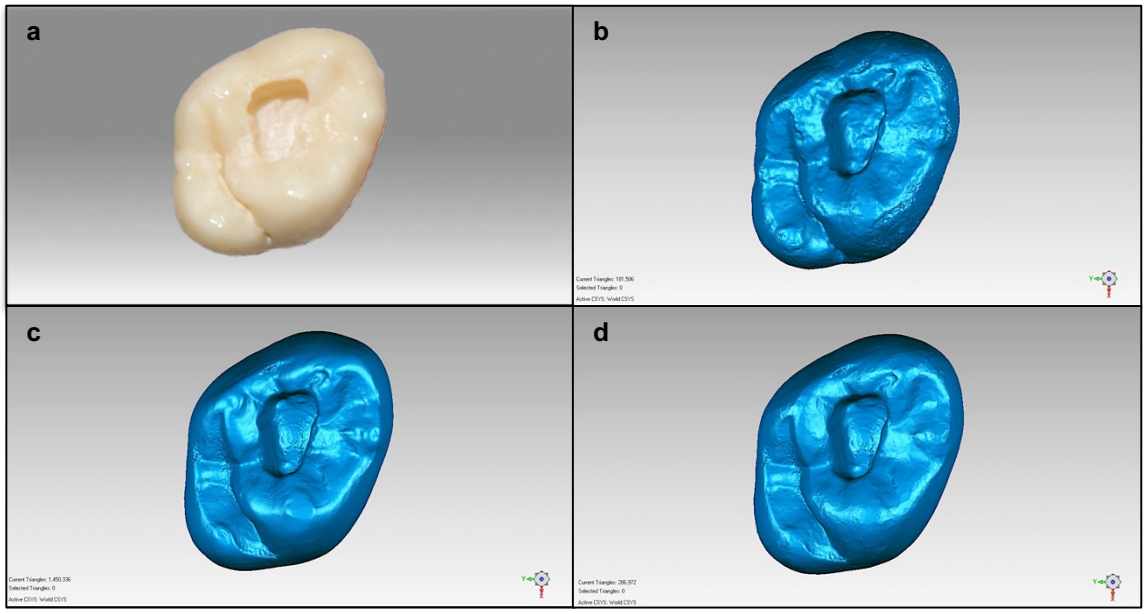

Figure 3-3 Representative samples for the teeth, intraoral digital scanner and µCT models before 3D superimposition (a) tooth's occlusal surface after access preparation, (b) intraoral digital model (181,506 triangles), (c) µCT1 model (1,450,336 triangles), (d) µCT2 model (296,972 triangles)

3.2.4 Data evaluation and 3D comparisons

After superimposition, the corresponding volume measurements of the residual coronal tooth structure following access cavity preparation were performed separately and recorded for each scan modality. Subsequently, the obtained intraoral scanner volume measurements were compared with their µCT counterparts. In order to test the intra-examiner reproducibility, the same operator repeated the segmentation process and volumetric measurements for 50% of the samples one week later.

The 3D deviations distribution in the *x*-, *y*- and *z*-axis between the intraoral scanner and µCT datasets superimpositions were analysed and displayed in a colour-coded image using the metrology software (Figure 3-4). The 3D compare analysis provided data including the standard deviations and mean positive/negative (+/-) and maximum positive/negative (+/-) deviations. Fifteen colour segments were used to describe the analysis histogram spectrum.

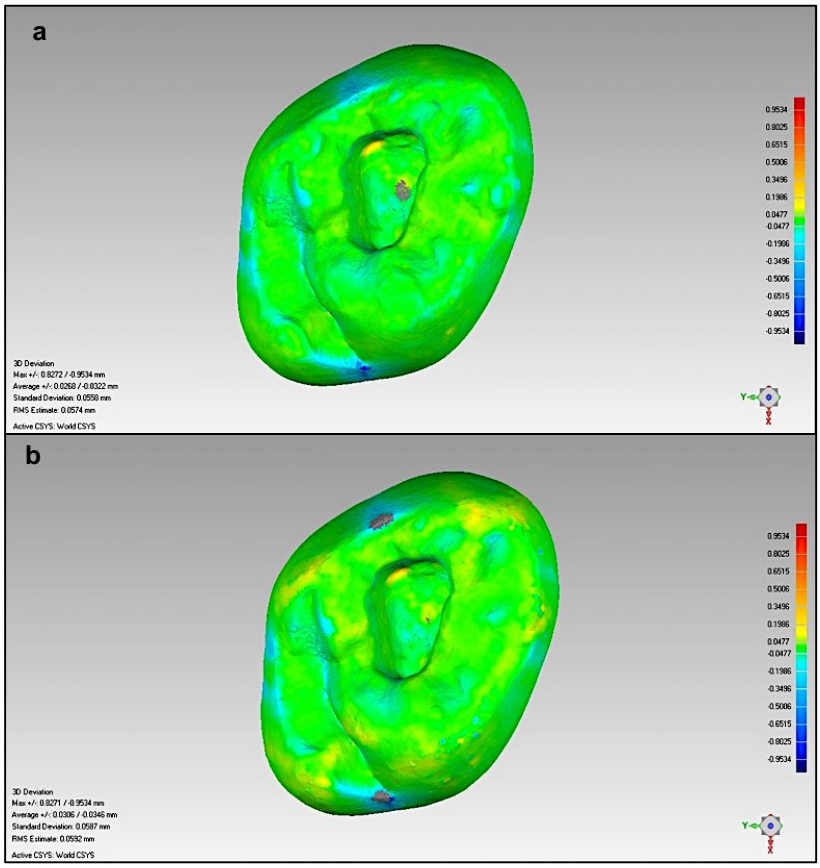

Figure 3-4 Colour-coded difference images presenting for positive and negative deviations analysis between intraoral digital model and (a) µCT1 model, (b) µCT2 model

3.2.5 Statistical analysis

The statistical analysis was carried out with SPSS software (SPSS version 22, IBM). A power analysis was performed by a specific software (G-Power, version 3.1.9 for Mac OS, Heinrich Heine University, Dusseldorf, Germany) to estimate the sample size needed.

A sample of 24 was required to achieve an effect size of 0.3 and 80% power to detect the true difference at 5% level. However, an additional 10 samples were added to improve the statistical power. Kolmogorov-Smirnov and Shapiro-Wilk tests (P<0.05) were carried out to test the normality distribution of the data. One-way repeated measures analysis of variance (ANOVA) in combination with Bonferroni post hoc test was conducted to compare the differences in volume measurements between scanning methods.

Differences in mean and maximum 3D deviations between the intraoral scanner and µCT datasets were evaluated using paired sample *t*-test. For all two tests, statistical significance was set at α=0.05. The intraclass correlation coefficient (ICC) was performed to determine the level of intra-observer reliability of the measurements of each scanning method. The Pearson correlation coefficient was used to measure whether there was a linear relationship between the three different measurements.

3.3 Results

Following the assessment of measurement quality of the intraoral digital scanner and metrology software, as described above, the accuracy was 2 µm, and the repeatability and reproducibility were 14.4 µm and 16.6 µm, respectively (Table 3-1).

Table 3-1 Accuracy, repeatability, and reproducibility values of the test digital intraoral scanner and the surface metrology software (Geomagic Control)

Measurement quality observation (number)		Minimum value (μm)	Maximum value (μm)	Mean (SD) (μm)	Overall result (μm)
Accuracy (n=30)		457	560	502 (15.32)	2
Precision (n=10)	**Repeatability**	11.0	18.9	14.4 (3.3)	14.4
	Reproducibility	10.7	48.8	16.6 (11.4)	16.6

SD, standard deviation

The intraclass correlation coefficient for measurements for both intraoral scanner and μCT indicated high intra-observer reproducibility (ICC=1) with a strong correlation between the volume measurements (r=1) of both scanners. The Kolmogorov-Smirnov and Shapiro-Wilk normality distribution tests revealed a normal distribution of data (P>0.05).

Regarding the volume measurements, the intraoral digital scanner revealed smaller volume measurement by 1.36% and 0.68% compared to μCT1 and μCT2, respectively. Figure 3-3 shows representative examples of the images generated by the intraoral scanner and the μCT. These images demonstrate the increase in textural features that become clearer with increased resolution: Figure 3-3c (μCT1) shows the highest resolution with 1.45 million triangles followed by Figure 3-3d (μCT2) comprising 296,972 triangles and finally Figure 3-3b (intraoral scanner) comprising of 181,506 triangles.

Repeated measures ANOVA determined that volume measurements differed significantly between scanners (F(1.3,43.3)= 310.5, P<0.001). Post hoc Bonferroni tests also indicated significant differences among the 3 volume measurements (P<0.001). The mean values and standard deviations (SD) of the crown volume measurements of the digital scanner and μCT scan were calculated and displayed in Table 3-2.

Table 3-2 Comparison of means ±SD (mm^3) and volume differences (%) between the intraoral scanner and µCT scans

	Intraoral scanner	µCT	
		µCT1	µCT2
Mean ± SD (mm^3)	435.491 ± 69.03	441.397 ± 69.71	438.440 ± 69.41
Volume difference		+ 1.36%	+ 0.68%

SD, standard deviation

Table 3-3 gives the calculated mean and maximum 3D deviations between the intraoral scanner and µCT after superimposition of all 34 datasets. Mean positive and negative deviations revealed that the digital scanner datasets showed +16 µm/-32 µm and +27 µm/-33 µm 3D deviations compared to µCT1 and µCT2, respectively. Regarding maximum positive and negative deviations, digital scanner datasets showed +278 µm/-445 µm and +399 µm/-434 µm deviations compared to µCT1 and µCT2, respectively. Data analysis yielded statistically significant differences for the mean and maximum positive 3D deviations between the intraoral digital scanner and the two reference datasets (P<0.001).

Table 3-3 Mean and maximum 3D deviations resulting from the superimposition of intraoral scanner (TEST) datasets with both µCT datasets

System		Max. +ve dev. (µm)	Max. –ve dev. (µm)	Mean +ve dev. (µm)	Mean –ve dev. (µm)
TEST vs µCT1	**Mean**	+278*	-445	+16*	-32
	SD	134	109	5	6
TEST vs µCT2	**Mean**	+399*	-434	+27*	-33
	SD	143	106	6	6

SD, standard deviation
* Significantly different (P<0.001)

3.4 Discussion

The main finding of this study was that the intraoral digital scanner was reliably able to measure the volume of remaining coronal tooth structure in a minimally accessed tooth, showing small volume differences (0.68%-1.36%) compared to the reference standard.

This study investigated the accuracy of an intraoral digital scanner in comparison to micro-computed tomography for measurement of the volume of residual sound tooth structure, in order to validate the method for later application to clinical studies utilising intraoral scanning and cone beam computed tomography to investigate the relationship between remaining coronal tooth substance and the prognosis of root canal treated teeth.

Intraoral digital scanners generate 3D surface data, without the limitations associated with 3D radiography, namely artefacts created by metal scattering and patient movement, not to mention potential harm from ionising radiation.

Considering that access cavity preparation is dependent on tooth morphology, human extracted teeth were used instead of using geometrically shaped models. Furthermore, extracted tooth produces an exact light refraction close to the clinical situation. Based on a minimally invasive concept, and also to examine the performance of the intraoral digital scanner, the access openings were cut to the smallest size possible.

Micro-computed tomography (µCT) is an accurate, reproducible and non-invasive technique which can be used to measure the internal and external tooth structure (Rhodes *et al.* 1999, Kim *et al.* 2007), to evaluate the surface area and volume changes within hard tissues (Nielsen *et al.* 1995, Bergmans *et al.* 2001, Neves *et al.* 2010), and to evaluate the root canal anatomy (Peters *et al.* 2000, Gluskin *et al.* 2001). However, µCT generates high radiation doses, which are not compatible with living organisms, therefore, µCT is not clinically applicable and its use was limited to *in vitro* studies

(Kamburoglu *et al.* 2011). Other limitations of μCT relate to the choice of the values of segmentation threshold, which may affect the appearance of objects of interest (Peters *et al.* 2000).

Micro-computed tomography offers the opportunity to assess the accuracy of the recently available intraoral scanners. In this study, we used μCT to obtain a highly accurate reference dataset to assess the volumetric measurements of the intraoral digital scanner. μCT has been used as the reference in several previous volumetric accuracy studies (Wang *et al.* 2011, Maret *et al.* 2012, Yang *et al.* 2015) and dimensional stability study (Steinhäuser-Andresen *et al.* 2011).

Basically, no standard procedure is available for tooth segmentation. Segmentation of the consecutive 2D slices depends in large part on imaging thresholding. Imaging thresholding in μCT depends on grey-scale value (16-bit grey-scale) and not on Hounsfield unit. Teeth densities are not the same among different individuals; therefore, using one fixed threshold for all teeth could lead to data loss of teeth tissues in some samples. In this study, the grey-scale threshold value was selected individually for each single tooth using the automatic threshold tool of MicroView software.

A pilot study confirmed that the appearance of the μCT image is affected by choice of segmentation threshold values (i.e. surface quality and decimation factor settings) selected during the segmentation. In turn, these factors affect the number of triangles produced per image and affect the volume measurement of the sample itself.

Intraoral scanner datasets have a fewer number of triangles compared to that of μCT datasets. Therefore, to minimise the difference between the scanners triangles number and in order to match up the number of the μCT triangles to that of the corresponding digital scans, two different segmentation settings were used to create two μCT datasets. The first mesh (μCT1) has the maximum number of triangles, and the other one (μCT2) has the minimum number of triangles.

For 3D dataset comparison, superimposition was performed by employing a best-fit alignment process to the closest 15,000 common points between the test and reference datasets. This approach was applied by several previous studies (Güth *et al.* 2013, Ender & Mehl 2015, Yang *et al.* 2015).

The intra-observer agreement was excellent, confirming a reliable reproducibility of the segmentation process and volumetric measurements. A pilot study confirmed that the volumetric measurements of metrology software were similar to the measurements obtained by MicroView software.

Despite the growing popularity of intraoral digital scanners, a question remains regarding its ability to measure the volume of remaining coronal tooth structure in minimally invasive accessed tooth. In the present study, the intraoral scanner datasets have a lower resolution (approximately 62 µm in high-resolution areas) compared to that of µCT datasets (28 µm), and as shown in Figure 3-3, even the lower resolution µCT2 dataset had a greater number of triangles to the intraoral scanner (296,972 vs. 181,506). However, despite its lower resolution, the intraoral digital scanner was reliably able to measure the volume of remaining coronal tooth structure (in a minimally accessed tooth), showing small volume difference (0.68%-1.36%) compared to the reference standard; this could be regarded as clinically insignificant. The higher the µCT resolution, the more the volume discrepancy between µCT and intraoral digital scanner scans. The difference in volume measurements between the two scanning techniques is relatively small and is likely to be clinically irrelevant, especially considering the superior local accuracy (2 µm) and precision (~15 µm) of the intraoral digital scanner in the present study, in comparison to studies measuring the full arch accuracy of digital dental impressions (Ender & Mehl 2011, Nedelcu & Persson 2014, Patzelt *et al.* 2014a). Moreover, the correlation between measurements was strong for both scanners, suggesting a good potential for the use of intraoral digital scanning in prospective clinical trials evaluating endodontic outcome prediction and treatment planning.

The 3D deviations of each test dataset in relation to the reference dataset were interpreted from the calculated mean positive and negative values of the volumetric deviations. Displaying the positive and negative deviation in colour-coded images permitted qualitative visualisation of the deviations. The average volumetric deviations were greater between intraoral digital scanner and μCT2, and smaller between intraoral digital scanner and μCT1. The inferior accuracy between intraoral digital scanner and μCT2 may be explained by a fewer number of triangles produced per μCT2 image during segmentation that in turn reduced the scan quality in comparison to the μCT1. Yet, the deviation results remain minimal and can be considered within acceptable limits.

The accuracy of digital impressions is directly proportional to the number of sampling images captured during the scan, since an increased number of sampling images results in higher accuracy of the 3D surface model (Frigerio 2006). The inaccuracy of digital impressions, represented by 3D deviations, might be related to technology-related errors, like software processing errors (Ender & Mehl 2013), or to operator-related errors, such as inappropriate scan workflows or sample surface preparation (Mada *et al.* 2003) leading to uncertain measurements and 3D image distortion. Güth *et al.* (2013) reported that the precision of the single datasets captured could be affected by the scanning software mechanisms that may intend to filter out possible outliers, and results in smoothening of the surfaces of the constructed datasets (Güth *et al.* 2013).

The intraoral digital scanner used in this present study requires a light dusting of titanium dioxide powder with average particle size of 1.6 μm in order to enhance scanning accuracy and speed by creating reference points on the tooth surfaces, which facilitates alignment (‘stitching’) of individual images (Kravitz *et al.* 2014). There is no evidence that the coating contributes to inaccuracies, even when excessive (Nedelcu & Persson 2014), and there is increasing data to suggest that the scanning powder improves scanning speed and full-arch accuracy (van der Meer *et al.* 2016), in comparison to non-powder-based scanners.

The level of resolution of CBCT is reduced by artefacts which limit the ability to make fine reconstructions of the occlusal aspect of the molar teeth, especially in the presence of metal-based restorations (Mora *et al.* 2007, Soğur *et al.* 2007), which complicates the use of CBCT for designing precise access cavity. To overcome this, superimposition of the digital impressions from intraoral scanner onto the CBCT imaging with virtual endodontic access planning will improve the ability to access the root canal space precisely.

One of the limitations of the present study was that various clinical oral parameters, which may affect the digital scanning processes, were not reproduced. In a clinical situation, saliva, sulcular fluid and oral biofilm, as well as patient-related factors including limited scanning space, oral humidity, patient and operator movement artifacts, tongue blocking and ambient light condition, especially in the molar regions, could have an effect on the accuracy of the 3D scanner intraorally, causing high 3D deviations in intraoral scans in the molar regions (Flügge *et al.* 2013, Patzelt *et al.* 2014a). As in many *in vitro* studies, the results of this study might not relate directly to a clinical situation. Therefore, further *in vivo* studies will be needed to confirm the accuracy of intraoral digital scanner considering normal clinical parameters.

The volume difference was small and appeared to be clinically insignificant. Clearly, further research is required to assess the capability of the digital scanner to scan the intra-coronal features of the endodontic access preparations with greater axial undercuts, as observed in the primary endodontic treatment of teeth with limited pre-operative loss of tooth structure. Furthermore, intraoral digital scanners can open up possibilities in dental research to compare, by superimposition, and analyse the progression of several dental and oral situations recorded at different time points. Such difference analyses can be used to assess gingival swelling and recession, tooth wear, and quantifying the amount of tooth structure removed during different restorative

techniques, giving a chance to point out the most conservative preparation, leading to improvements in clinical procedures.

3.5 Conclusions

The null hypothesis stating there is no difference between the 3D measurements of residual coronal tooth structure obtained with intraoral digital scanning and micro-computed tomography was rejected.

Within the limitations of this study, the intraoral digital (3M™ True Definition) scanner was able to adequately quantify and analyse the amount of residual coronal tooth structure following minimally invasive endodontic access cavity preparation. The intraoral digital scanner accurately scanned the entire intra- and extra-coronal residual tooth structure, with strong correlation to the μCT measurements.

Combining intraoral scanning of the extra- and intra-coronal aspect of the endodontically accessed tooth with volumetric CBCT scanning may ultimately improve assessment of the likely residual coronal tooth structure following combined endodontic and restorative treatment. This may in turn contribute to clinical decision making through more precise clinical assessment of the quality and quantity of remaining tooth structure, leading to improvements in the treatment planning and prognostication process prior to endodontic and restorative treatment. Moreover, in contrast to a conventional impression, digital impressions can be acquired while a rubber dam is applied, therefore opening possibilities for enhanced applications and quality for endodontic-related digital diagnostics.

Chapter 4 The outcome of endodontic retreatment in teeth with varying degrees of coronal tooth structure loss: a prospective clinical study

4.1 Introduction

The outcome of root canal treatment is based on analysing the clinical and radiological findings to detect signs and symptoms of periapical healing within a specific period (Ng *et al.* 2010). Teeth with apical periodontitis are usually asymptomatic (Nair 2004), therefore, the diagnosis of apical periodontitis is primarily based on radiological examination.

As described in Chapter 1, determining the outcome of root canal treatment using periapical radiographs is questionable. CBCT has been successfully used in assessing the outcome of root canal treatment and retreatment (Patel *et al.* 2012b, Liang *et al.* 2013, Davies *et al.* 2016). In a prospective clinical study, the healing rate (reduced size of periapical radiolucency) of 123 teeth in 99 patients was 95.1% using periapical radiographs and 84.7% using CBCT ($P<0.002$) 1 year after primary root canal treatment. This result suggests that an approximately 10% overestimation of healing rate can likely be expected when radiographs are used to diagnose post-treatment apical periodontitis (Patel *et al.* 2012b). Davies *et al.* (2016) assessed the diagnostic outcome of root canal retreatment after 1 year using pre-operative and post-operative periapical radiographs and CBCT. The favourable outcome was 16% lower when teeth were assessed with CBCT compared with periapical radiographs (Davies *et al.* 2016).

Endodontically treated teeth are generally associated with a shorter survival compared with vital pulp teeth. By far the most prevalent cause of extraction of root canal treated teeth is linked to their restorability (Fuss *et al.* 1999, Chen *et al.* 2007, Zadik *et al.* 2008). In an epidemiologic study evaluating the reasons for tooth extraction after root canal

treatment during a 5-year follow-up period, Chen *et al.* (2008) reported that endodontically related diseases accounted for only 10.7% of teeth extraction, periodontal diseases for 26.8%, and tooth fracture for 32.1%, whereas extensively decayed or unrestorable teeth dominated, and representing 46.4% (Chen *et al.* 2008).

The amount of remaining hard tooth structure is one of the most important parameters in the planning of the restoration of endodontically treated teeth (Tait *et al.* 2005, Mannocci & Cowie 2014).

While recommendations based on clinical experience have been suggested, there is little evidence in the literature on the impact of remaining coronal tooth structure on the outcome of endodontic retreatment and the survival of teeth that have undergone root canal retreatment.

In order to investigate the advantage of retaining sound tooth structure on the outcome of endodontically treated teeth, a reliable measure should be used to quantify the amount of remaining coronal tooth structure. There have been several suggestions on how to classify the amount of remaining sound coronal tooth structure in endodontically treated teeth. Some authors refer to the percentage of residual tooth structure without defining how this percentage is measured (Samet & Jotkowitz 2009, Juloski *et al.* 2014, Aurelio *et al.* 2016), while others use more generic terms such as 'substantial' or 'minimal dentine height' remaining (Creugers *et al.* 2005b, Fokkinga *et al.* 2007), limited loss of coronal tooth structure in teeth with mesial or distal decay with cusp preservation (Mannocci *et al.* 2002).

Numerous *in vivo* studies have associated the medium- to long-term survival of endodontically treated teeth and their restorations with the number of remaining cavity walls, presence of a ferrule (Monticelli *et al.* 2003, Ferrari *et al.* 2012, Naumann *et al.* 2012, Sterzenbach *et al.* 2012) and height of coronal dentine remaining (Creugers *et al.* 2005b, Fokkinga *et al.* 2007) prior to core build-up and crown preparation. As described

in Chapter 1, none of these methods quantifies in a reproducible fashion the amount of residual coronal tooth structure.

While recommendations on the acceptable minimum number of coronal dentine walls (Ferrari *et al.* 2012), height of remaining coronal tooth structure (Sorensen & Engelman 1990, Al-Wahadni & Gutteridge 2002, Ng *et al.* 2006), coronal dentine thickness (Peroz *et al.* 2005, Scotti *et al.* 2013) and length of ferrules (Tan *et al.* 2005, Naumann *et al.* 2006b) have been emphasised, the results in the literature are controversial.

The outcome of root canal treatment also depends on the quality of coronal restoration (Ray & Trope 1995, Hommez *et al.* 2002, Liang *et al.* 2012, Craveiro *et al.* 2015). In the long-term, an inadequate coronal restoration may be a source of micro-leakage responsible for a bacterial reinfection of the root canal system, and ultimately failure of the endodontic and restorative treatment (Saunders & Saunders 1994, Siqueira *et al.* 1999).

Evidence on the influence of the quality of coronal restorations on the periradicular status of root canal treated teeth is contradictory. The reports showed that the quality of coronal restoration had either a greater (Ray & Trope 1995), equal (Kirkevang *et al.* 2000, Hommez *et al.* 2002, Song *et al.* 2014), or less (Tronstad *et al.* 2000, Siqueira *et al.* 2005, Craveiro *et al.* 2015) impact on the periradicular status than the quality of the endodontic treatment.

Recent developments in digital dentistry allow the creation of high-resolution 3D virtual models of the patient's dentition and soft tissues. Digital impressions are becoming increasingly common in dentistry (Seelbach *et al.* 2013, Lin *et al.* 2015, Martin *et al.* 2015). The accuracy of linear measurements on digital models obtained from intraoral scanner has been demonstrated in a recent study (Wiranto *et al.* 2013).

Providing relevant knowledge on the clinical outcome and prognosis of root canal retreatment in teeth with different extent of coronal tooth structure loss may assist clinicians in a rational evidence-based case selection and decision-making process regarding the tooth in question, whether to preserve the tooth with root canal retreatment, endodontic surgery, or even selecting other alternative treatment plans like tooth extraction and potential replacement.

When considering root canal treatment, the clinician should verify whether the tooth would have a long-term prognosis. There is no evidence in the endodontic literature on the correlation between the volume of remaining coronal tooth structure and the outcome of endodontic retreatment.

Therefore, the aim of this prospective CBCT study was to evaluate the effect of the volume of residual coronal tooth structure, measured with an intraoral scanner, on the outcome of root canal retreatments on posterior teeth. Data on overall survival are insufficiently mature to present. The null hypothesis was that the volume of residual coronal tooth structure would have no influence on the outcome of root canal retreated teeth 1 year post-operatively.

4.2 Materials and methods

4.2.1 Study design and ethical approval

This prospective cohort study investigated the outcome of root canal retreated posterior teeth with varying degrees of coronal tooth structure loss. The research project was reviewed and approved by the NRES West-London Research Ethics Committee (REC reference 13/LO/1171) and the Guy's and St Thomas' NHS Foundation Trust R&D office (RJ113/N237) (Appendix III-IV). The study was carried out in compliance with the principles of the Declaration of Helsinki 2013 and good clinical practice (GCP).

Patient information sheets that contained a detailed explanation of the purpose of the study, treatment protocol, follow-up examinations, and the total radiation dose anticipated during the study, were provided to all patients before their participation in the study (Appendix V). Patients were clearly informed that participation was entirely voluntary and if they did not take part in the study or if they wished to withdraw at any point, they were not required to give a reason, and this would not adversely affect the standard of treatment they were receiving in any way. Patients were also reassured that treatment protocol would not adversely affect the outcome of treatment and that all information collected during the course of the research would be kept strictly confidential and accessed only by authorised people. Informed written consent was obtained from all patients prior to embarking on the study (Appendix VI).

4.2.2 Sample size and recruitment

A power analysis was performed at the beginning of the present study. This study was designed to have 80% power to detect a difference in success ratio between two groups at 5% level of significance using a two-tailed Z-test for comparing two independent proportions. Considering a success rate of 50% and 80% for group 1 and group 2, respectively, the study required a total sample of 97 teeth (24 teeth in group 1 and 73 teeth in group 2) with an allocation ratio of 1:3. Adjusting for an expected drop-out rate of 25% one year after the completion of root canal retreatment, the study required a total sample of 129 teeth (32 teeth in group 1 and 97 teeth in group 2).

The sample included in this study consisted of patients recruited from the postgraduate endodontic unit at Guy's Hospital (King's College London Dental Institute). The patients were referred from general dental practices or other clinical units of the dental hospital for management of failed initial endodontic treatments.

4.2.3 Inclusion and exclusion criteria

Patients included in this study had at least one posterior root treated tooth diagnosed with signs and symptoms of post-treatment endodontic disease, based on clinical and radiological findings, which required root canal retreatment. The criteria for inclusion and exclusion are presented in Table 4-1.

Table 4-1 Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
1	Patients (male or female) over the age of 16 (who can consent for themselves) in a good generic health.	Pregnant women, in view of requirements for radiographic scans
2	Teeth with endodontic problems that require root canal retreatment.	Immunosuppressed patients.
3	Teeth must be restorable.	Teeth with probing periodontal depths >3 mm.
4	The selected teeth need to be in occlusal function with a natural opposing tooth.	No opposing teeth.

A total of 204 posterior teeth from 182 patients with varying degrees of remaining coronal tooth structure were initially enrolled for the study between November 2013 and April 2015. Of the 204 teeth included, 48 teeth (42 patients) did not complete the root canal retreatment procedure for various reasons, presented in Table 4-2, and therefore were excluded (Figure 4-7).

Table 4-2 Reasons for further exclusions after recruitment

Reason of exclusion	Number of excluded teeth
Withdrawal of consent	10
Loss of contact with patient	6
Non-restorable teeth	31
Patient passed away	1
Total	48

4.2.4 Pre-operative assessment

All included patients were assessed clinically and radiologically at baseline (T0), and at recall (T12). The clinical examination included routine medical and dental history taking, pre-operative pain history evaluation, teeth assessment and soft tissues assessment. Teeth were assessed for response to percussion, mobility, increased periodontal probing depth, quality of the previous treatment, and the type and integrity of the existing coronal restoration. Soft tissues were assessed for tenderness to palpation, swelling, and sinus tract presence. Other pre-operative information such as relevant demographic data, tooth number, periapical status, the number of roots and root canals, the presence of root perforation or fractured instruments, and time interval since primary root canal treatment performed was recorded (Appendix VII). The data were anonymised and transferred into electronic datasheets (Microsoft Excel 2011, Microsoft®).

The radiological examination at T0 and T12 included exposure to both digital periapical radiography and CBCT scans to evaluate radiographic healing. Periapical radiographs (PA) using the paralleling technique were obtained with a size 2 digital phosphor plate system (Digora® Optime, Soredex) used in conjunction with a beam positioning film holder (Dentsply Rinn). All PA images were exposed using a dental X-ray machine (Heliodent, Sirona) operating at 65 kV, 7 mA and an exposure time of 0.16-0.25 seconds. The exposed phosphor plates were immediately scanned after exposure with Digora Optime scanner. The selected scanning resolution was 400 dpi. The raw data images were processed with Digora default software.

A small volume CBCT scanner (3D Accuitomo® 80, J. Morita) with a 4 x 4 cm FOV and 0.125 mm of voxel size were used to obtain CBCT images for the area of interest. The exposure parameters were set at 90 kV, 4 mA, and 17.5 seconds. For each tooth, the degree of beam angulation was set according to the manufacturer's instructions, and the tooth under investigation was positioned in the centre of the FOV.

All CBCT data were reconstructed using the system's proprietary software (i-Dixel® images, J. Morita) with 0.16 mm slice intervals and 1.2 mm slice thickness. The exposure parameters of each patient were standardised, and a thyroid collar was used.

4.2.5 Clinical intervention

Root canal retreatments and subsequent restoration with a cuspal coverage restoration were carried out by 20 endodontic postgraduate students supervised by qualified endodontic staff. Prior to the initiation of the study, the operators were trained and calibrated to follow a structured treatment protocol provided to them, which is consistent with the ESE guidelines (European Society of Endodontology 2006). A structured step-by-step form was prepared for operators to uniformly record all the pre-operative and intra-operative information including the patency of canals and working lengths achieved, and the occurrence of procedural complications such as a ledge, perforation, and instrument breakage to make sure the treatment was performed according to the planned protocol (Appendix VIII).

Root canal retreatment was carried out in two treatment sessions. The entire retreatment procedures were performed under local anaesthesia and aseptic conditions with rubber dam isolation. The CBCT scans were accessible to the operators prior to and during the root canal retreatment procedure. The operators used dental operating microscopes (3 step entrée Dental Microscope, Global) during all procedures. In cases when teeth had previous full coverage restorations, the crowns were cut in half and discarded. Provisional crowns were fabricated chairside to protect teeth within the treatment sessions. If needed, coronal reconstruction with conventional glass-ionomer cement (GIC) (Fuji IX, GC Corporation, Tokyo, Japan) was performed to enhance isolation with a rubber dam. After isolation, diamond burs mounted on high-speed hand-piece (W&H) were used to completely remove the existing restorations and any caries present

underneath. At this stage, the restorability of teeth was assessed by an experienced restorative dentist.

After existing restorations were removed, coronal gutta-percha was removed using Gates-Glidden drills (Dentsply Maillefer) sizes 2 or 3 in a low-speed hand-piece (W&H). If required, the root canal orifice was flooded with a little amount of chloroform for 30s to soften the existing gutta-percha. Hedström files and K-flexofiles (Dentsply Maillefer) were used to remove the existing gutta-percha from the middle and apical third of the canal, respectively. A hand instrument K-flexofile (Dentsply Maillefer) size 6 to size 10 was used to negotiate each canal until full working length confirmed by both electronic apex locator (Root ZX, J. Morita) and digital periapical radiograph. Re-instrumentation was performed in a crown-down manner using ProTaper Universal rotary instruments (Dentsply Maillefer) to the full working length, using size S1 to a minimum of F2. The final size used for canal enlargement was strictly dependent upon the canal morphology and when no evidence of old gutta-percha was detected on the instrument or inside the root canals. In compliance with the manufacturer's instructions, the instruments were used with an electric motor (X-Smart™, Dentsply Maillefer) at a constant speed of 300 rpm. The canals were frequently irrigated with a copious amount of 1% sodium hypochlorite (Adams Healthcare, Leeds, UK) delivered using a syringe and a 27-guage needle at each file change. Calcium hydroxide dressing (Hypocal®, Ellman International, Oceanside, New York, USA) was applied into the root canals as a standard inter-appointment medicament and a dry cotton pellet placed over the canal orifices. The access cavity was provisionally restored with intermediate restorative material (IRM) (Dentsply Maillefer) in between treatment sessions.

In the final visit and once root canal instrumentation was completed, the dressing was removed and passive ultrasonic irrigation with 2 mL of 1% sodium hypochlorite (Adams Healthcare) and a penultimate irrigation with 17% EDTA (Ethylene Diamine Tetraacetic Acid, Pulpdent, Watertown, Massachusetts, USA) was performed in all canals for 3

minutes for smear layer removal. The root canals were irrigated again with 1% sodium hypochlorite then gently dried with sterile absorbent paper points (Dentsply Maillefer). All canals were filled with gutta-percha (Dentsply Maillefer) and Pulp Canal Sealer (Kerr-Sybron, Romulus, Michigan, USA) using a warm vertical condensation technique. This technique consisted of vertical compaction of gutta-percha with heat carriers (System B, Analytic Technologies, Redmond, Washington, USA) then backpacking was performed with the Obtura (Obtura Spartan, Foothill Ranch, California, USA) syringe.

Upon completion of root canal retreatment, the canal orifices were filled with a thin layer of either flowable composite resin (X-Flow, Dentsply Maillefer) or conventional GIC cement (Fuji IX, GC Corporation). Subsequently, all enamel and dentine surfaces of the cavities were etched (De Trey Conditioner 36, Dentsply DeTrey), and prime bonded (Scotchbond Universal System, 3M ESPE) as per manufacturers' instructions. Finally, the tooth was restored incrementally with permanent composite resin (Ceram X Duo, Dentsply Maillefer) with light-polymerisation for 40 seconds for each increment. A final radiograph was taken after placement of the restoration. Only one maxillary and one mandibular premolar tooth received a fibre post. All root retreated teeth received a cuspal coverage restoration (single-unit metal-ceramic crown) no more than one month after root canal retreatment completion. Self-adhesive resin cement (RelyX Unicem, 3M ESPE) was used for crown cementation.

In the event of perforation, mineral trioxide aggregate (MTA) (ProRoot MTA, Dentsply, Weybridge, UK) or IRM was used to seal the perforation area. Separated instruments were primarily bypassed with hand instruments or retrieved by ultrasonic vibration. If bypassing was unsuccessful, using specialised extractor devices was considered. Posts, when present, were carefully removed using ultrasonic vibration or removed by using burs.

4.2.6 Remaining tooth structure measurements

4.2.6.1 Volume measurements

Once root canal retreatment had been completed and prior to core placement, a single-phase consistency impression (impression a) was taken using polyvinylsiloxane impression material (Aquasil Monophase, Dentsply Caulk, Milford, Delaware, USA) in a sectional impression tray. A second sectional impression (impression b) was taken after the tooth had been restored with a crown. For cases with an insufficient amount of remaining coronal tooth structure, crown-lengthening procedures were performed. Impressions were taken 2 weeks post-surgery and before definitive cores were placed.

The impressions were poured using Moonstone™ dental stone (Bracon, Etchingham, UK). Patients' casts were stored in boxes with unique identification numbers to be used later in analysing the amount and percentage of remaining coronal tooth structure (Figure 4-1).

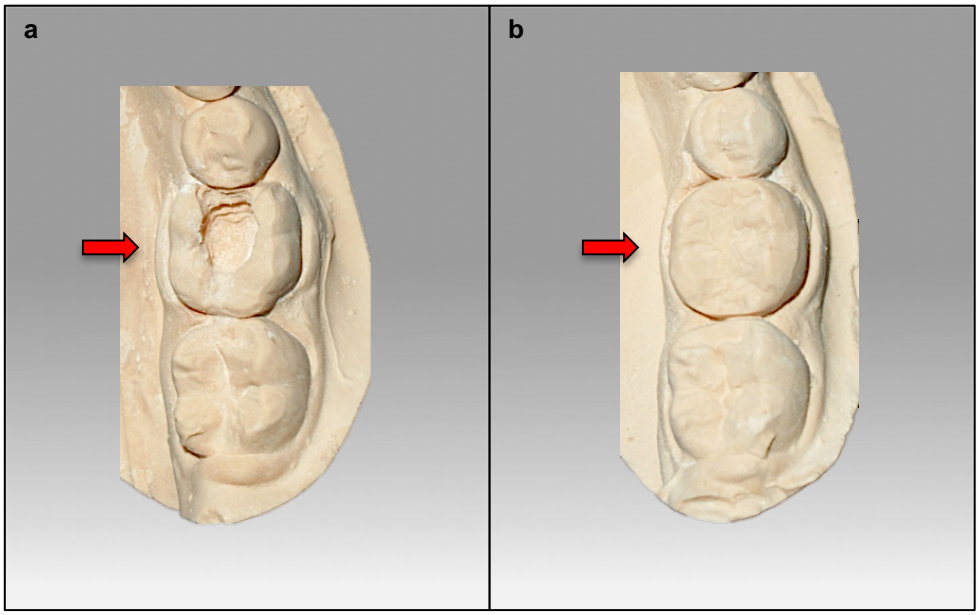

Figure 4-1 Representative stone casts showing the lower right first molar (a) before core placement, (b) and after crown cementation

All casts were digitised using a 3M™ True Definition scanner (3M ESPE) to generate 3D datasets. These 3D datasets were imported into surface metrology software (Geomagic Control) for superimposition. For superimposing the 3D datasets, 25,000 common points were used. Once the superimposition was performed, the coronal tooth structure was isolated from the surrounding gingiva and adjacent teeth by using Geomagic software. The differences in the volume of remaining coronal tooth structure between these two datasets were computed in order to obtain the percentage of remaining coronal tooth structure. Three-dimensional images of a tooth as scanned by the intraoral digital scanner showing the remaining coronal tooth structure prior to core placement and subsequent to crown placement are shown in Figure 4-2.

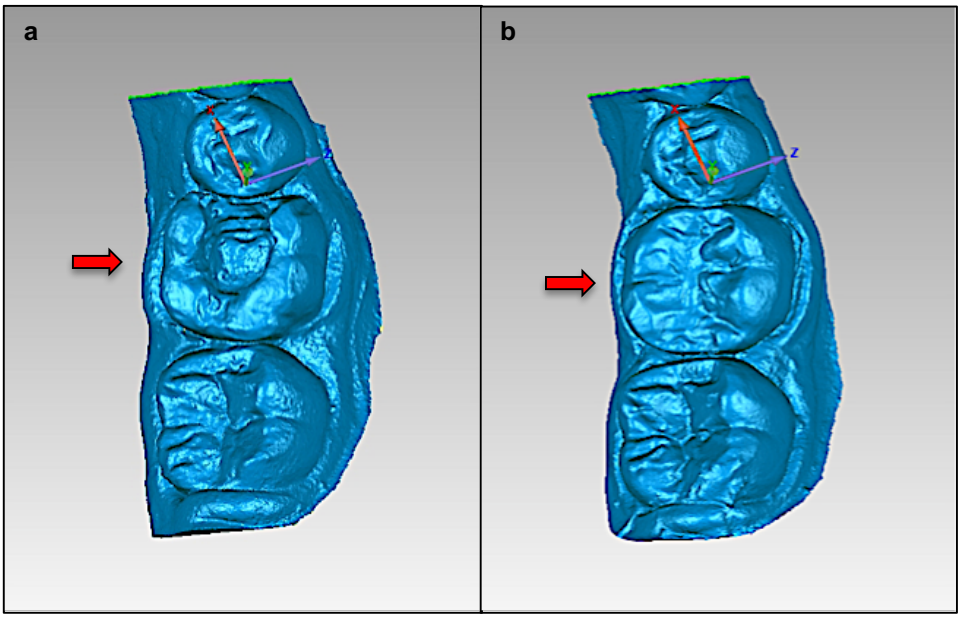

Figure 4-2 Examples of three-dimensional digital models of the right mandibular posterior teeth generated by the 3M True Definition digital scanner. (a) before core build-up of the lower right first molar, and (b) after crown placement

The percentage (*P*) of remaining coronal tooth volume was calculated per tooth according to the following equation:

$$P = \frac{V0}{V1} \times 100$$

Where *V*0, the volume of remaining coronal tooth structure before core placement, and *V*1, the volume of coronal tooth structure after crown placement (Figure 4-3).

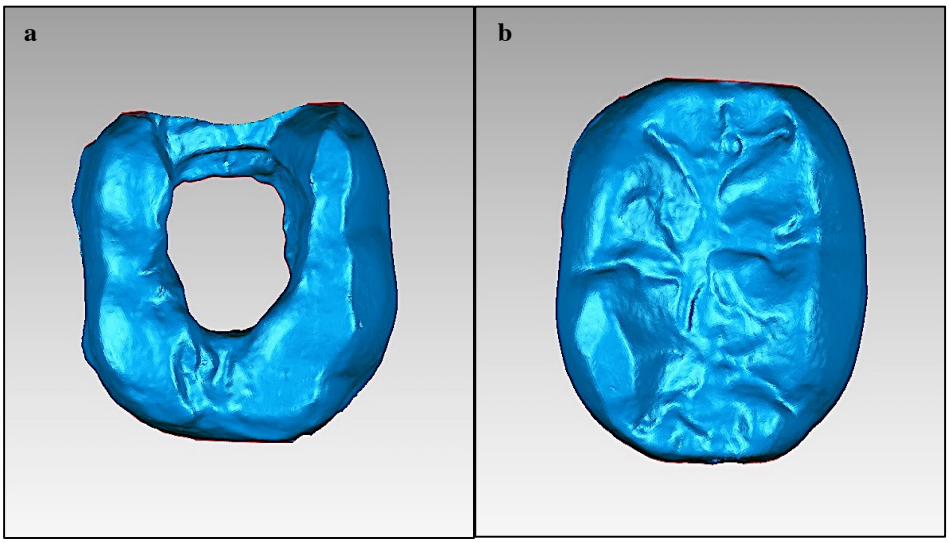

Figure 4-3 Examples of three-dimensional digital models of the lower right first molar in Geomagic software. (a) remaining coronal tooth structure prior to core placement, and (b) tooth structure after crown placement

4.2.6.2 Number of residual dentine walls

For teeth with no pre-operative crowns, all cavity walls, which exceeded a minimum height of 3 mm, a minimum thickness of 1 mm, and extended at least 3 mm in length, were included. The height of the walls was measured from the gingival margin to the tip of the residual dentine wall in a vertical direction, and the thickness of the walls was measured from the inner to the outer surface of the residual dentine wall in a horizontal direction. Height, thickness, and length of walls were measured using the distance tool

in Geomagic Software. All teeth retained at least one coronal wall. Representations of the remaining cavity walls are shown in Figure 4-4.

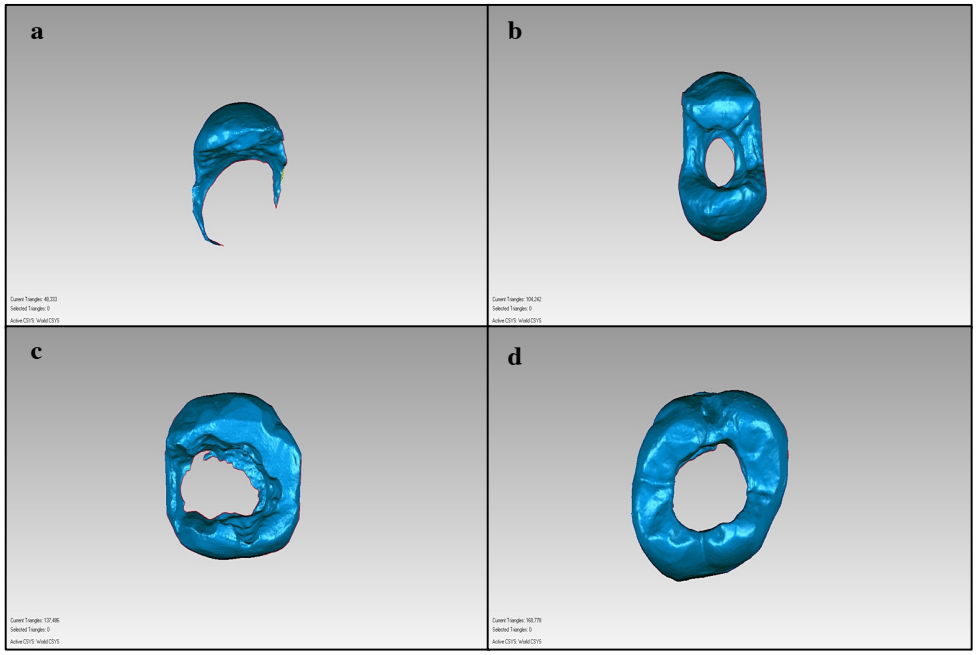

Figure 4-4 Examples of three-dimensional digital model representations of the remaining coronal dentine walls following the completion of root canal retreatment. (a) only one wall remained, (b) two walls remained, (c) three walls remained, and (d) four walls present

4.2.7 Patient recall

Root canal retreatment completion was considered as the baseline for the analyses of the present study. Follow-up appointments were scheduled to be 12 months (±4 weeks) post-endodontic retreatment to assess the clinical and radiographic signs of healing. Initially, all patients were contacted by phone one month in advance of the T12 follow-up appointment to confirm their attendance. Non-responding patients were given at least two additional attempts by phone before a letter was mailed. The letter explains the importance of the follow-up and to encourage them to attend follow-up appointments, a free of charge dental check-up was offered. An additional letter was sent to patients who had not reacted to the first letter. The reasons for not appearing at recalls were recorded (Table 4-4). The main three reasons for patients not attending the recalls were either

loss of contact, not having spare time to attend the recall visit or withdrawal of consent. Two of the responding patients could not arrange to come due to relocation; another patient had no complaints about the treated tooth, but she could not attend the recall appointment due to serious physical illness.

4.2.8 Clinical and radiological evaluation at follow-up

Postgraduate students, under the direct supervision of one of the endodontic specialist staff, carried out the follow-up examinations at T12 for healing assessment. The primary endpoint was the failure of root canal retreatment defined by no change or increase in the size of the pre-existing periapical lesion, or the development of new lesion along with the presence of signs and symptoms. The treatment was considered successful when there was no new periapical radiolucency or a reduction in size or complete resolution of a periapical radiolucency accompanied by the absence of clinical signs and symptoms.

A clinical and radiological assessment was carried out, including parallel periapical radiographs and CBCT scans with the same exposure settings used for the pre-operative scans. The following post-operative information was recorded for each tooth: pain, tenderness to percussion, soft tissues tenderness to palpation, periodontal probing, mobility, swelling, as well as the integrity of the existing coronal restoration. Again, all information was recorded into the patient's case report form and then transferred to a computerised database.

In cases when the radiographic scan was not possible to achieve, such as in pregnancy, the scan was delayed until after delivery. Patients who had taken antibiotic medication for any reason during the period starting from the day of root canal retreatment completion were recorded. If the tooth had been extracted, the date and reason for extraction were recorded.

4.2.9 Quality of coronal restoration assessment

The quality of coronal restoration at T12 was assessed clinically and radiologically. Two experienced, trained and calibrated examiners assessed the clinical and radiographic quality of restorations according to criteria modified from those described by Craveiro *et al.* (2015). The two examiners had not been involved in the operative procedures. For clinical evaluation, a dental mirror and a dental probe were used under ample lighting to evaluate the quality of coronal restoration. Clinically, coronal restoration quality was considered to be 'adequate' when it showed good marginal fit with no recurrent caries or when, despite superficial ceramic fractures, the tooth was still intact, while restorations with detectable evidence of any marginal discrepancy, overhangs, open contact with recurrent caries, or debonded restoration were considered as 'inadequate' (Figure 4-5).

For radiological evaluation, all periapical radiographs were displayed on a PowerPoint (Microsoft®) presentation and evaluated by two examiners jointly. Any restoration was judged as 'adequate' if it appeared intact on periapical radiographs and considered as 'inadequate' if there were radiographic signs of restoration with open margins, overhangs, or recurrent caries. After follow-up, all inadequate restorations were replaced.

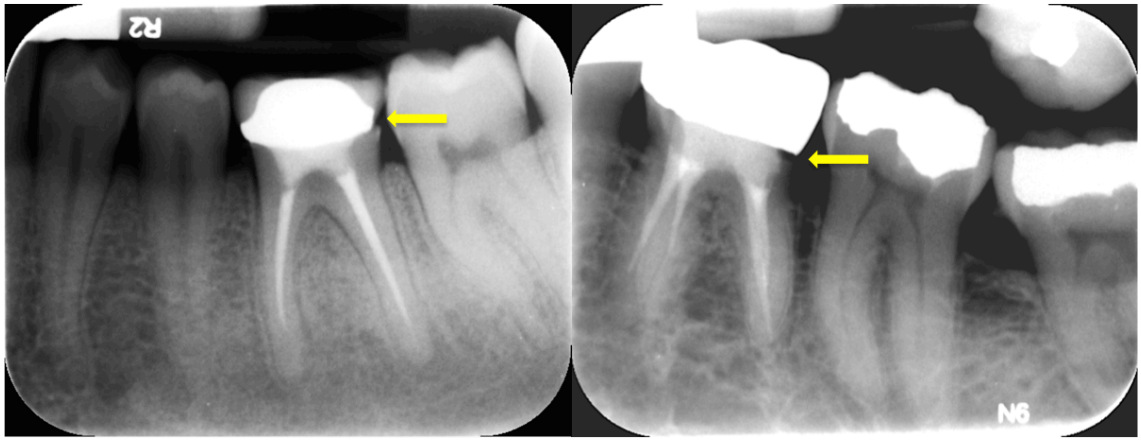

Figure 4-5 Intraoral periapical radiographs show examples of inadequate coronal restorations (yellow arrows)

4.2.10 Radiological assessment of the endodontic outcome

For each tooth, an endodontist, who was not part of the radiological assessment and experienced in using CBCT in endodontic therapy was responsible for identifying the relevant sagittal, coronal, and axial slices that best confirmed the presence/absence of periapical radiolucency or showed the largest periapical radiolucency. The apical-third of each root was vertically aligned and optimised in contrast and brightness using Accuitomo software (One Volume Viewer®, J. Morita) to improve the visualisation. Screenshots for these slices were taken and exported in TIFF format. All identifying patient information was removed.

The periapical radiographs at T0 and T12 were displayed together as PowerPoint (Microsoft®) presentations using two 13-inch laptop computers (MacBook Pro®, Apple) with a resolution of 1680 x 1050 pixel to allow the examiners to determine the healing status of each root. A similar approach was followed when the CBCT images were assessed. All slides in the presentations were randomly ordered, and each slide included 1 periapical radiograph or 3 CBCT spatial planes (sagittal, coronal and axial) for each root of the tooth under examination (Figure 4-6). The raw CBCT data were also accessible for the examiners whenever additional information was needed. The examiners were allowed to measure the maximum diameter of the periapical lesion when they thought this was appropriate. The radiological interpretation was conducted in a quiet, dimly lit room.

A consensus panel of two pre-calibrated experienced endodontists were asked to identify the presence/absence or change (increase/decrease) in the size of an existing periapical radiolucency associated with the apical portion of the roots. The examiners were endodontists who are experienced in interpreting CBCT images, and they were not blinded to whether the images were taken pre-operatively or 1 year post-operatively. The examiners were not involved in carrying out the endodontic treatment.

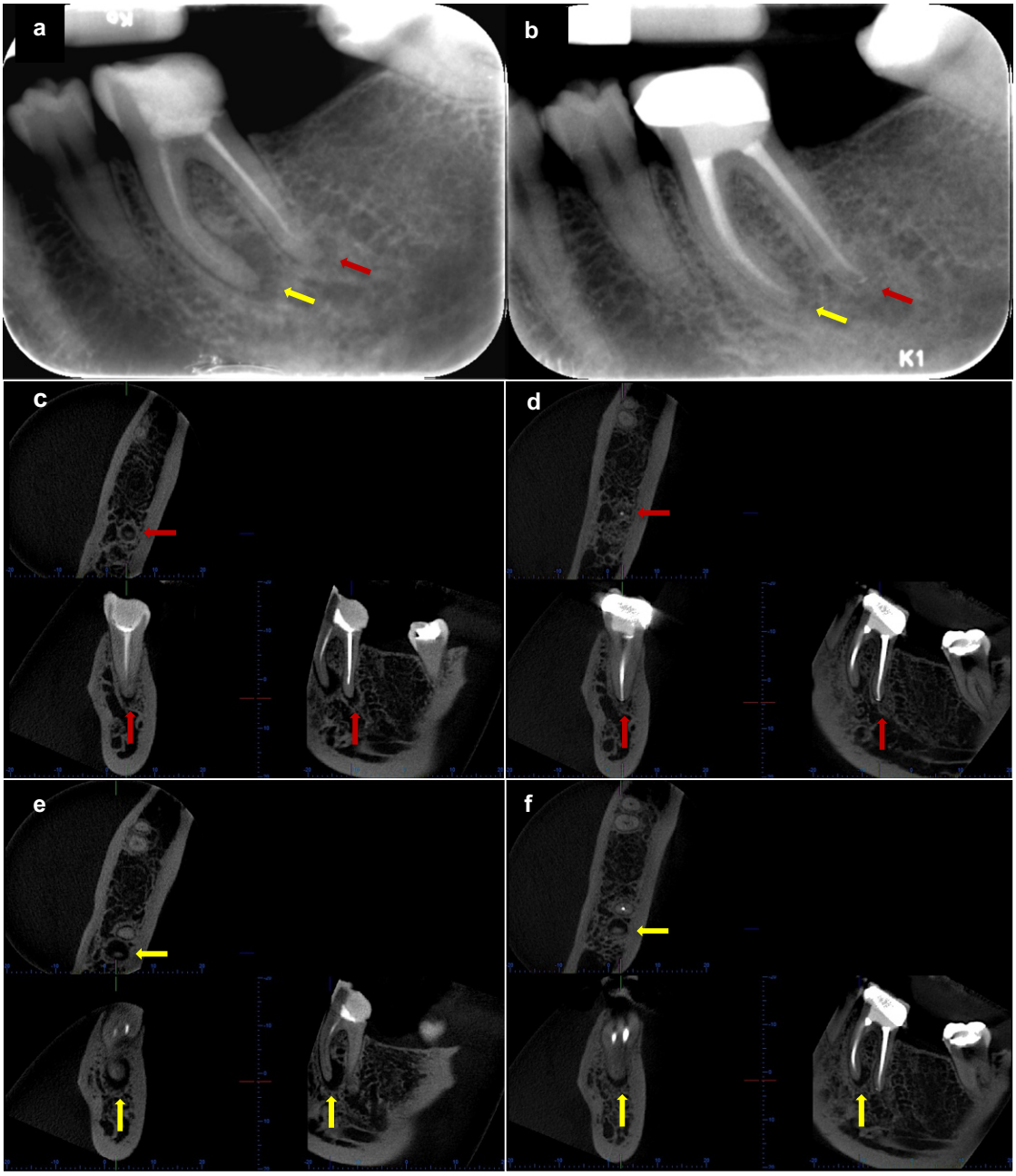

Figure 4-6 (a,b) Pre-operative and 1 year post-operative periapical radiographs of the lower left first molar where both examiners confirmed complete healing of the periapical lesion associated with the mesial (yellow arrows) and distal roots (red arrows). (c-d) Pre-operative and 1 year post-operative reconstructed images of the lower left first molar mesial and distal roots in axial, coronal and sagittal planes reveal complete healing of the distal root, (e-f) and reduction in the lesion size of the mesial root

To achieve unbiased assessment, the examiners were pre-calibrated. For calibration, the examiners were asked to assess the healing status in 50 examples of 1-year follow-up periapical radiographs and CBCT images of endodontically treated teeth that did not belong to the present experimental material. Furthermore, each examiner was asked individually to assess 50 pairs of the periapical radiographs and CBCT images a second time after 4 weeks in order to determine the inter-examiner reliability.

The assessment of radiographic images was performed in two viewing sessions, with at least a one-week interval in between, using the same computers under standardised lighting and viewing conditions. Separate viewings were conducted per session to minimise the probability of examiner fatigue. No time restriction was set out for viewing. During each session, the consensus panel was asked to assess 50% of the periapical radiographs (n=68/137) and 50% of CBCT scans (n=160/320). Disagreements were resolved by discussion. The consensus panel reliability was determined by jointly re-assessing 100 pairs of the pre-operative and 1 year post-operative radiographic images following a two-week interval.

In multi-rooted teeth, each individual root was numbered, and the presence/absence or change in the size of an existing periapical radiolucency on each identifiable root was reported. This allowed a direct comparison of like-pairs of specific roots using radiographs and CBCT images as described by Patel *et al.* (2012b). In this study and irrespective of the numbers of treated roots, the tooth as a whole was considered as the unit of evaluation. In the case of multi-rooted teeth, the outcome of the tooth was assessed according to the root that had the worst treatment outcome. A Microsoft Excel (Microsoft®) spreadsheet was produced to record all the collected data.

A periapical lesion was diagnosed as a periapical radiolucency associated with the radiographic apex of the root which was at least twice the width of the periodontal ligament space (Low *et al.* 2008, Bornstein *et al.* 2011). Based on the radiographic

changes between T0 and T12 images, the examiners were asked to allocate each root to an outcome category (Table 4-3).

Table 4-3 The outcome categories for root canal retreatment (Patel *et al.* 2012b)

Score	Description	Outcome
1	New periapical radiolucency	Unfavourable outcome
2	Enlarged periapical radiolucency	
3	Unchanged periapical radiolucency	
4	Reduced periapical radiolucency	Favourable outcome
5	Resolved periapical radiolucency	
6	Unchanged healthy periapical status (no radiolucency before and after retreatment)	

In the present study, teeth with healing lesions (outcome 4), healed lesions (outcome 5) or unchanged healthy periapex (outcome 6) were considered to have a 'favourable outcome', whereas teeth that developed a new lesion (outcome 1), teeth with an increase in the size of existing lesion (outcome 2), no change in the existing lesion size (outcome 3), and teeth with symptoms and/or clinical signs of failure, irrespective of the radiographic outcome, were considered to have an 'unfavourable outcome'.

Post-operative root filling length was assessed radiologically using periapical radiographs and was dichotomised as 'adequate' (0-2 mm short of the root end) and 'inadequate' (short [>2 mm short of the radiographic apex] or long).

4.2.11 Statistical analysis

Data analysis was carried out using IBM SPSS software (SPSS version 23, IBM). All study data were first analysed descriptively. A Fleiss's kappa coefficient was used to assess the intra-consensus panel agreement and inter-examiner agreement for radiological assessments of periapical health, also to evaluate the intra-consensus panel agreement for restorations quality. A Cohen's kappa correlation was calculated to determine the correlation between clinical and radiological assessments of the quality of

coronal restorations. The outcome of root canal retreatment was dichotomised into 'favourable' versus 'unfavourable', whereas the apical extension of the root filling and the quality of coronal restoration were dichotomised into 'adequate' versus 'inadequate'.

In order to determine the association between the volume of remaining coronal tooth structure and the outcome of root canal retreatment, the raw volume was analysed by means of a receiver operating characteristic *(*ROC*)* curve and Youden's index (sensitivity+ specificity-1) to identify the optimal cut-off point for volume dichotomisation.

Chi-square tests were used to determine the association between the outcome and the other variables (volume of remaining coronal tooth structure, the number of dentine walls remaining, the apical extension of root canal filling and the quality of coronal restoration). If the chi-square test showed that any of these variables was significant, then the joint association of these variables with the treatment outcome was tested using a logistic regression model. The significance level was set at α=0.05.

A Wilcoxon signed-rank test was performed to determine whether there was any difference in diagnostic outcomes when assessed by periapical radiography and CBCT. A McNemar's test was used to determine if there were any significant differences in favourable and unfavourable outcomes of retreatment when assessed by periapical radiographs and CBCT. A Fisher's exact test was used to determine whether there was any significant association between the pre-operative periapical status and the outcome of the treatment.

4.3 Results

One-hundred and fifty-six teeth (140 patients) completed the root canal retreatment procedure (Figure 4-7). Nineteen (13.6%) patients dropped out of the trial. Of those patients, 10 were not able to attend the review appointment, but they confirmed that the tooth was asymptomatic and in good function. Reasons for drop-out are described in Table 4-4.

At the T12 review, 137 (121 patients) of the original 156 teeth were available for evaluation. The recall rate was 87.8% for the teeth, and 86.4% for the patients. Among 137 teeth, 5 teeth (4 molars, 1 premolar) in 5 patients experienced complications (apical perforation [n=1], root resorption [n=1], ledged [n=2] and blocked canals [n=1]) and did not reach the endpoint of follow-up as further treatment was required. These patients had persistent clinical symptoms prior to and post-retreatment. These five teeth underwent periapical microsurgery, and they were asymptomatic 1 year post-surgery. This group of teeth was included in the analysis of the outcome of root canal retreatment and excluded from the analysis of the quality of coronal restorations assessment.

Table 4-4 Reasons for patients' non-attendance at the review appointments

Reasons for drop-out	**Number of patients**
Withdrawal of consent	3
Loss of contact with patient	7
Patient passed away	2
Work commitments	3
Pregnancy at review time	1
Health issues	1
Relocation to another country	2
Total	19

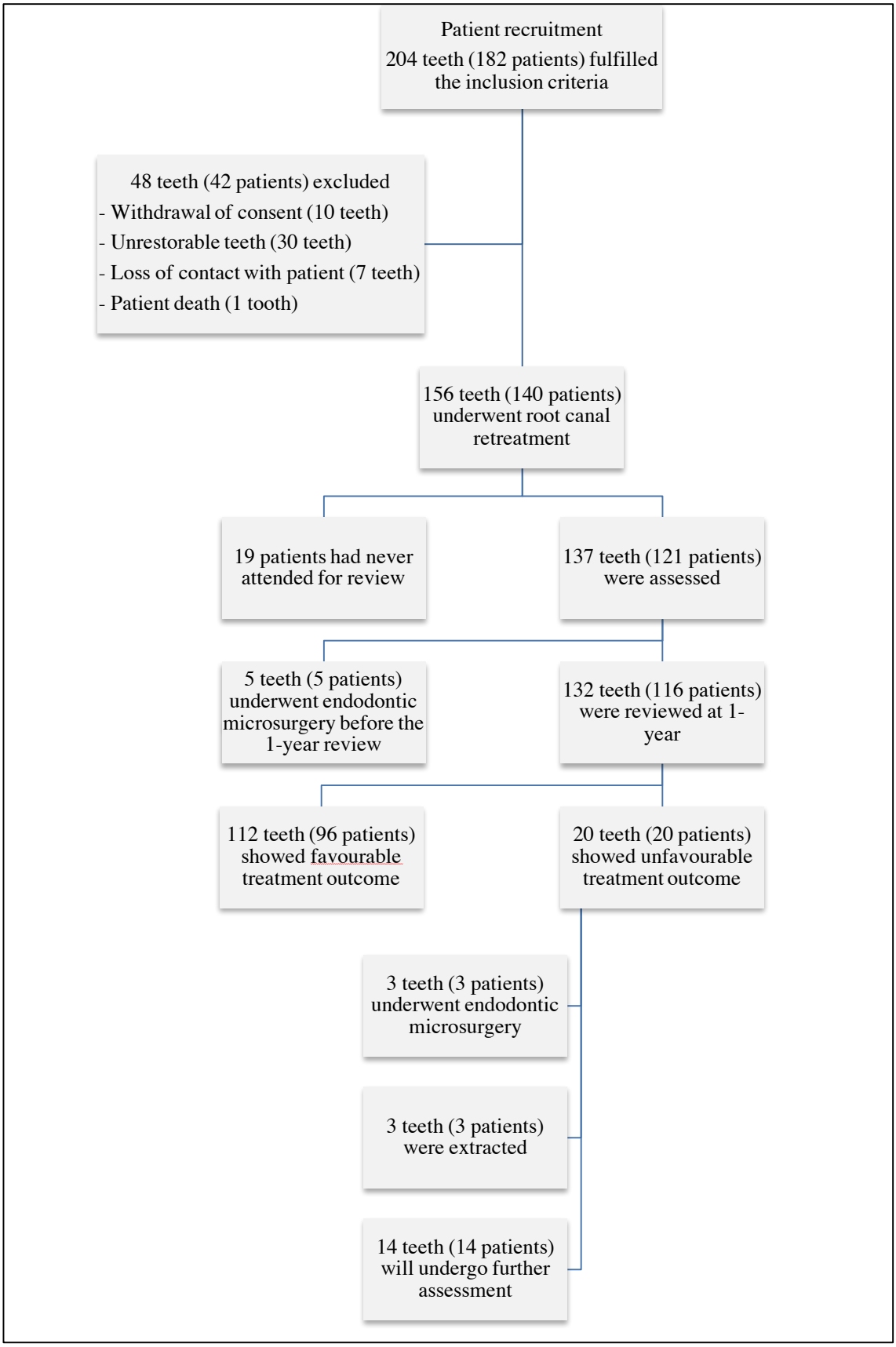

Figure 4-7 Flowchart of the trial showing the process of patient recruitment, exclusion and follow-up

The average age was 43 years; 84 patients were female (69.4%) and 37 male (30.6%). The frequency distribution of endodontically retreated teeth according to the tooth type is presented in Figure 4-8.

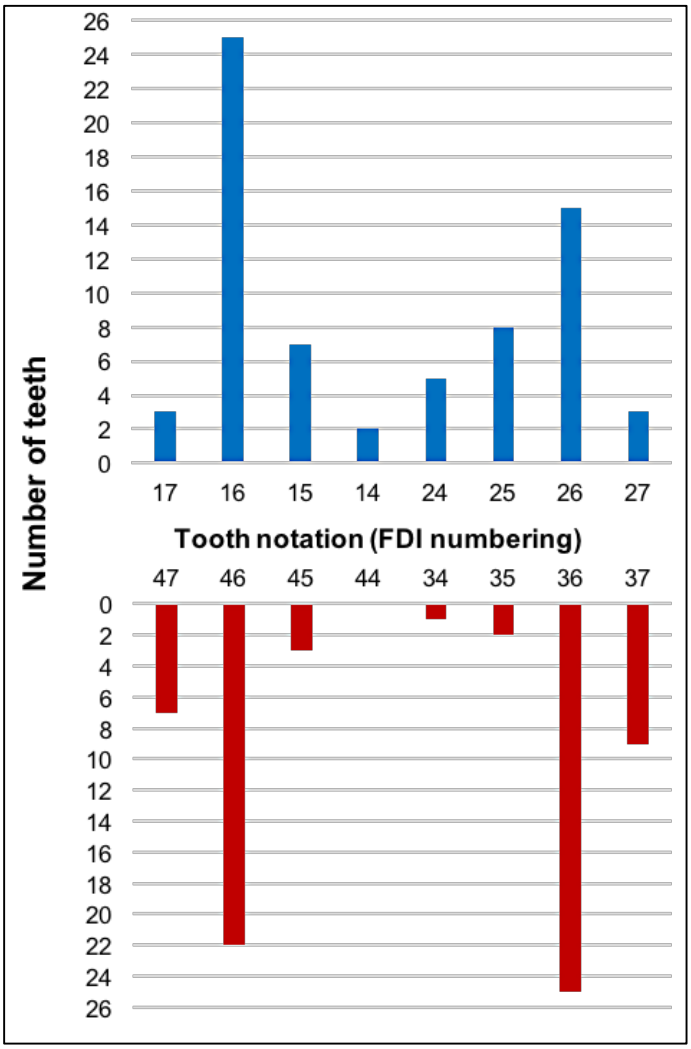

Figure 4-8 Frequency distribution of teeth according to tooth type

Of the 137 teeth, 101 (74%) were symptomatic (tender to percussion [32%], palpation [9%] or both [33%]) during initial examination. The percentage of teeth with healthy pre-operative periapical status was 36.5% (50 teeth) when assessed by periapical radiography, and 13.9% (19 teeth) when assessed by CBCT. Forty-eight teeth of 137 had full coverage restorations at baseline.

More failures were recorded in mandibular molars (44%) compared to maxillary premolars (16%) and maxillary molars (40%). There was no significant difference between treatment outcomes in maxillary versus mandibular teeth (*P*=0.484).

Based on Youden's index associated with ROC curve, the optimal cut-off point (highest sensitivity and specificity values) of remaining tooth volume was 29.5%. Accordingly, the residual coronal tooth structure volume was dichotomised into less than 30% (n=33) and more than 30% (n=104). The percentages of unfavourable outcomes associated with teeth presented with different volumes (<30%, >30%) of remaining coronal tooth structure are shown in Figure 4-9. Three-dimensional digital model representations of teeth with different percentages of remaining coronal tooth structure are shown in Figure 4-10.

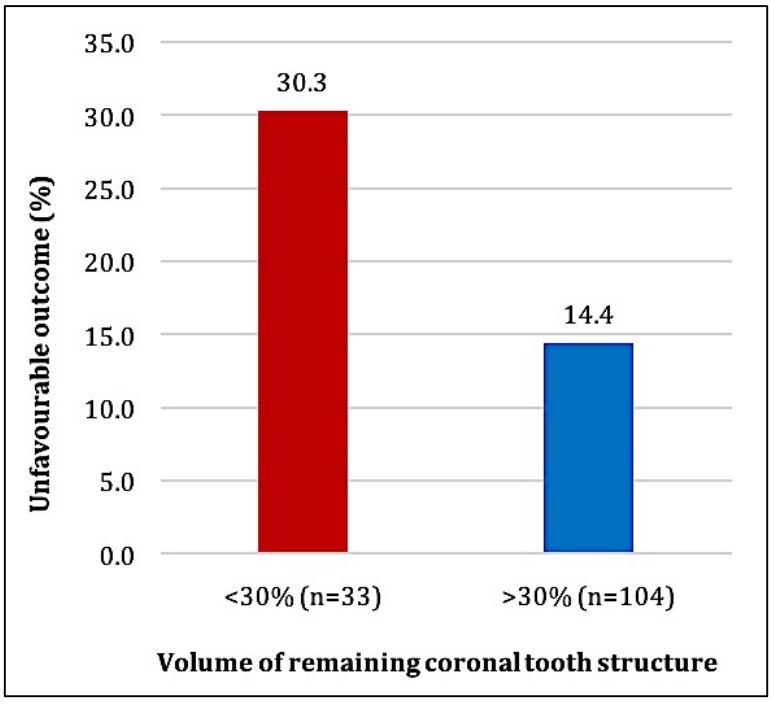

Figure 4-9 Frequency distribution of favourable and unfavourable outcomes associated with the volume (%) of remaining coronal tooth structure

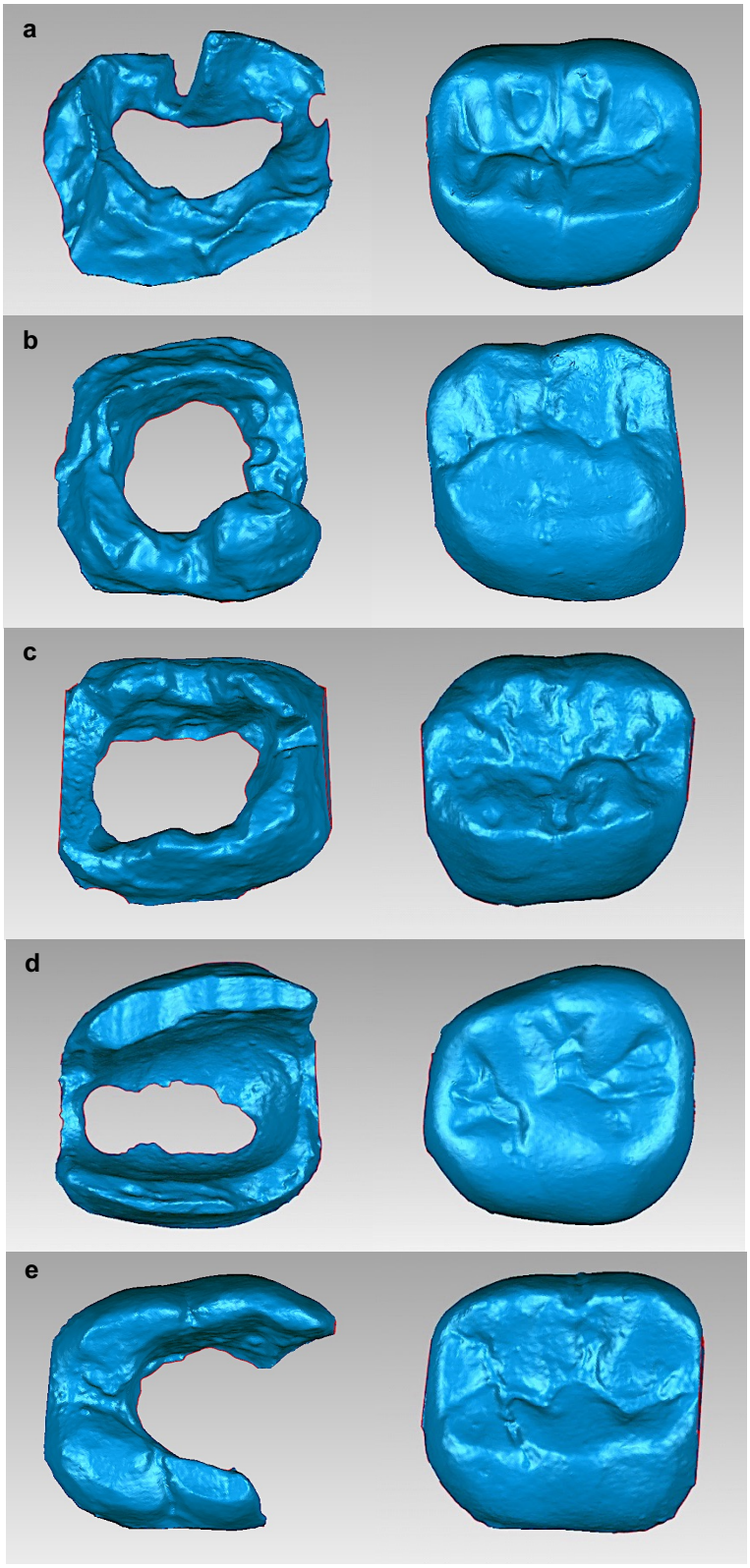

Figure 4-10 Three-dimensional digital model representations of teeth with different percentages of remaining coronal tooth structure before core build-up and after crown cementation. (a) less than 20%, (b) less than 30%, (c) less than 40%, (d) less than 50%, (e) less than 60%

Chi-square test revealed that the volume of remaining coronal tooth structure (<30%, >30%) was a significant predictor of treatment failure as demonstrated by CBCT, with teeth with less than 30% remaining coronal tooth structure having a significantly higher number of unfavourable outcomes (χ^2=4.235, OR=2.58; 95% CI: 1.026, 6.487, *P*=0.040).

At the T12 recall assessment, periapical radiographs revealed that the healing (outcome 4) and healed rates (outcomes 5 & 6) were 18.2% (24 teeth) and 74.2% (98 teeth), respectively. With CBCT scanning, the healing and healed rates were 34.1% (45 teeth) and 50.8% (67 teeth), respectively (Table 4-5). A significant difference in outcome diagnosis of teeth (Z=-5.891, *P*<0.0001) was observed when comparing periapical radiographs with CBCT.

Table 4-5 Frequency distribution of outcome of treatment for each tooth assessed using periapical radiographs (PA) and CBCT (n=132)

Outcome category	**Maxillary premolar**		**Maxillary molar**		**Mandibular premolar**		**Mandibular molar**		**% (all cases)**	
	PA	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**
1- new lesion	0	0	0	0	0	0	0	0	0 (0)	0 (0)
2- enlarged lesion	0	1	3	4	0	0	1	4	3 (4)	6.8 (9)
3- unchanged lesion	1	2	3	3	0	0	2	6	4.5 (6)	8.3 (11)
4- reduced lesion	2	4	4	12	2	3	16	26	18.2 (24)	34.1 (45)
5- resolved lesion	6	10	9	15	1	1	32	22	36.4 (48)	36.4 (48)
6- no lesion before/after retreatment	12	4	24	9	3	2	11	4	37.9 (50)	14.4 (19)

The overall percentage of favourable results was 88.3% using periapical radiographs, and 81.8% using CBCT (Table 4-6). There was a significant difference in the favourable and unfavourable outcomes of teeth when assessed by periapical radiography and CBCT (*P*=0.035). Of all the teeth with the unfavourable outcome, 4 were maxillary premolars and the others were all molars. There was also a significant difference in the outcome identified between radiographs and CBCT for mandibular molars (*P*=0.031); however, the differences were not significant for maxillary premolars and maxillary molars (*P*>0.05). Table 4-6 displays the favourable and unfavourable outcomes based on clinical and radiological examinations, including the five teeth that underwent surgical intervention before the 1-year recall.

There was one tooth that demonstrated a complete healing with radiographs but had a tenderness to percussion and palpation with periapical radiolucency present on CBCT, therefore, its outcome was classified as unfavourable.

Table 4-6 Percentage of favourable and unfavourable outcomes based on clinical symptoms and radiological examination with periapical radiographs (PA) and CBCT (n=137)

Outcome category	**Maxillary premolar**		**Maxillary molar**		**Mandibular premolar**		**Mandibular molar**		**All cases**	
	PA	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**
Unfavourable (1,2,3)	9.1	18.2	19.6	21.7	0	0	7.9	17.5	11.7	18.2
Healing (4)	9.1	18.2	8.7	26.1	33.3	50	25.4	41.3	17.5	32.8
Healed (5,6)	81.8	63.6	71.7	52.2	66.7	50	66.7	41.3	70.8	48.9
Favourable (4,5,6)	90.9	81.8	80.4	78.3	100	100	92.1	82.5	88.3	81.8

All patients who presented with clinical symptoms had radiological evidence of periapical radiolucency detected by CBCT. Of the 25 teeth with CBCT unfavourable outcome, 11 teeth had signs and symptoms. Of these, 3 teeth were extracted, and periapical microsurgeries were carried out for 8 teeth and reviewed 1 year post-operatively. They all were asymptomatic with radiological evidence of periapical healing at the follow-up appointment, while 14 teeth were asymptomatic, and it was advised to assess further the lesions at 2-year recall before further treatment is undertaken.

Pre-operative perforations were detected in 12 teeth, of which 11 had favourable outcomes. Eleven teeth were treated with mineral trioxide aggregate (MTA) and one tooth with intermediate restorative material (IRM).

The apical extension of root filling had no significant impact on periapical health (χ^2=0.300, OR=0.756; 95% CI: 0.277, 2.063; *P*=0.584). Six out of the 25 teeth with unfavourable outcome had inadequate (short or overfilled) root filling length. Of the 112 teeth with favourable outcome, 33 (30%) had not been filled to an adequate length (short [19%] or overfilled [11%]). Pre-operative periapical radiolucencies were found in 12 of 13 teeth (92%) with long root filling and in 17 of 26 teeth (65%) with short root filling. Eight of the 33 teeth with <30% volume of remaining coronal tooth structure had inadequate root filling length, of which 1 tooth had unfavourable outcome and 7 teeth had favourable outcome.

CBCT showed that the favourable outcome for teeth that presented without and those with pre-operative periapical radiolucency was 100% and 78.8%, respectively. The Fisher's exact test revealed a significant association between the treatment outcome and the pre-operative apical status (*P*=0.024).

The intra-consensus panel agreement and the inter-examiner agreement for assessing the treatment outcome and the quality of coronal restorations ranged between 0.71 and 0.76 (Table 4-7).

Table 4-7 Kappa values for agreement between and within examiners on outcome diagnosis using periapical radiographs (PA) and CBCT, and on quality of coronal restorations

	PA	CBCT
Inter-examiner agreement for treatment outcome	0.72	0.71
Consensus agreement for treatment outcome	0.71	0.71
Consensus agreement for coronal restorations quality	0.76	-

Eighty-nine teeth (67 molars, 22 premolars) with no pre-operative full cuspal coverage were included in the analysis to assess the influence of the number of remaining dentine walls on the outcome of root canal retreatment. Because of the very small sample size (3 teeth) in the 1-wall group, these teeth were added to the 2-wall group for statistical analysis considerations. The chi-square test showed no significant association between the number of coronal walls remaining and the outcome of the treatment (χ^2=0.719, OR=2.44; 95% CI: 0.291, 20.517; *P*=0.698). Frequencies and percentages of the unfavourable treatment outcomes among the four tested groups are reported in Table 4-8.

Table 4-8 Frequencies and percentages of unfavourable outcomes among groups within different coronal walls remaining (teeth with pre-existing crowns were excluded)

Remaining coronal walls	No of samples	No of unfavourable outcome	% Unfavourable outcome
One wall	3	0	0
Two walls	19	4	21.1%
Three walls	55	10	18.2%
Four walls	12	1	8.3%
Total	89	15	16.9%

A total of 132 teeth (116 patients) were assessed clinically and radiologically. The clinical evaluation of the quality of coronal restoration identified six (4.5%) restorations with marginal discrepancy; these restorations were replaced. No caries, crowns decementation or root fractures were recorded. Radiologically, seven (5.3%) of the coronal restorations were unacceptable, including six restorations with open margins and one restoration with overhang margins. Comparing clinical to radiographic scoring, the percentage of agreement was 91.7% and the kappa score was 0.11. When the clinical and radiological evaluations were combined, unfavourable treatment outcomes were detected in 15% of teeth with acceptable restorations and 16.7% of teeth with unacceptable restorations. No correlations were observed between treatment outcome and restoration quality when the clinical and radiographic criteria for the coronal restorations were combined (χ^2=0.024, OR=1.133; 95% CI: 0.229-5.606; *P*=0.878). Table 4-9 shows data on the quality of coronal restoration and its relation to the outcome of root canal retreatment.

Table 4-9 Quality of coronal restoration in relation to root canal retreatment outcome (n=132) (teeth which failed before the one-year recall were excluded)

Coronal restoration quality assessment	**Score**	**No.**	**Total (%)**	**Retreatment outcome**		
				Favourable	**Unfavourable**	**% Unfavourable**
Clinically	Acceptable	126	95.5	106	20	15.9
	Unacceptable	6	4.5	6	0	0
Radiologically	Acceptable	125	94.7	107	18	14.4
	Unacceptable	7	5.3	5	2	28.6
Combined (clinically and radiologically)	Acceptable	120	90.9	102	18	15
	Unacceptable	12	9.1	10	2	16.7

4.4 Discussion

The most significant finding of this prospective study was that root canal retreated teeth with <30% volume of sound remaining coronal tooth structure had a significantly higher endodontic failure rate than teeth with a residual tooth structure volume >30% (*P*=0.040). Teeth maintaining less than 30% of their original tooth volume had a 2.58-fold (95% CI: 1.026, 6.487) greater chance of unfavourable treatment outcome (apical periodontitis) than those which maintained more than 30% volume at the 1-year follow-up period. These results were independent of the pre-operative presence of procedural mistakes. A combination of variables, such as undetected tooth cracks, the difficulty to achieve ideal isolation, the increased exposure time to oral bacteria, and the difficulty in achieving a perfect coronal seal may affect more severely the outcome of root canal retreatment of teeth with increased loss of coronal tooth structure.

To our knowledge, this is the first clinical study investigating this particular aspect of root canal retreatment. In this research, 137 of the 156 teeth, which had received root canal retreatment during the 2013–2015 period, were re-examined one year later for treatment outcome. The number of teeth reviewed in this study (n=137) is higher than the number of teeth (n=123) in the study by Patel *et al.* (2012b) and the number (n=98) in the study by Davies *et al.* (2016), where CBCT imaging was used for assessing the outcome of root canal treatment and retreatment, respectively.

Patients were reviewed 1 year post-treatment as per ESE guidelines (European Society of Endodontology 2006). Several studies have shown that healing of apical periodontitis occurred in most cases during the first year (Ørstavik 1996, Huumonen & Ørstavik 2013, Zhang *et al.* 2015, Azim *et al.* 2016).

The recall rate in the current study was 87.8% for teeth and 86.4% for patients. This recall rate is similar to the 12-month recall rate for patients (83%) reported by Davies *et al.* (2016). Both studies were based in the same hospital. This high recall rate would

allow the conclusion that the present outcome will not be adversely affected by the outcome of the relatively low dropouts. The recall rate could not be improved further because of the mobile nature of the population in large cities like the city where this clinical trial was conducted. The difficulties of running clinical studies in the mobile population are well documented (Sprague *et al.* 2003, Ng *et al.* 2007, Ross *et al.* 2009).

The success and failure of endodontic treatment should not be judged depending on radiological evidence alone, due to the fact that cancellous bony defects may not be adequately demonstrated by radiographic images (Bender & Seltzer 1961a). This is also consistent with Nair *et al.* (1999), who reported that patients exhibiting unresolved periapical radiolucencies after conventional root canal treatment may sometimes be due to healing by a scar tissue and this should therefore not be mistakenly considered as a sign of root canal treatment failure (Nair *et al.* 1999).

The tooth was used as a unit of measure in this study as the use of root as a unit of measure would overestimate the success rate, especially in studies with a large proportion of multi-rooted teeth (Friedman 2002b). The tooth was judged according to the root with the worst scenario.

The examiners were asked to use the 6-point classification, which had been used successfully by Patel *et al.* (2012b), Metska *et al.* 2013, and Davies *et al.* (2016), to record their level of confidence with regard to the status of the periapical health. The examiners were experienced in interpreting CBCT data and were calibrated to obtain a consistent and reliable assessment of the treatment outcome. Viewing sessions were kept as short as possible to minimise the chance of examiner fatigue. The use of a consensus panel was in accordance with several previous studies to minimise inter-examiner variation (Patel *et al.* 2012b, Hashem *et al.* 2015, Davies *et al.* 2016). A good level of consensus panel agreement and inter-examiner agreement (0.71-0.76) was found for periapical radiographs and CBCT assessment of treatment outcome, and for

radiological assessment of coronal restoration quality. The examiners were blinded to the volume of remaining tooth structure corresponding to the teeth assessed.

Before commencing treatment, an accurate assessment of the remaining coronal tooth structure, the available treatment options, and prognosis evaluation are important to make a good treatment plan. Tzimpoulas *et al.* (2012) reported that a significant loss of dentine was the main reason for the extraction of endodontically treated teeth referred to endodontists (Tzimpoulas *et al.* 2012). In a review of the literature, Tang *et al.* (2010) concluded that although the causes of potential tooth fracture are multifactorial, the loss of tooth structure and the stresses generated during endodontic and restorative procedures were possible causes of post-endodontic tooth fractures (Tang *et al.* 2010).

There is evidence to suggest a direct correlation between the remaining coronal tooth structure, and the survival of root canal treated teeth and long-term success of the restorations (Monticelli *et al.* 2003, Nagasiri & Chitmongkolsuk 2005, Cagidiaco *et al.* 2007, Ferrari *et al.* 2012). In these studies, the qualitative means used to estimate the amount of remaining tooth structure may have led to overestimation or underestimation of the amount of dentine that is actually remaining at the coronal level. Moreover, many of these studies (Monticelli *et al.* 2003, Cagidiaco *et al.* 2007, Ferrari *et al.* 2012) were limited to assess endodontically treated premolars with and without posts, and thus the findings may not be applicable to molar teeth.

Murphy *et al.* (2009) attempted to assess both thickness to height ratio and volume of remaining coronal tooth structure using a laser profilometer scanner and a tooth restorability index (TRI). In that study, the authors blocked the dentine wall undercuts with a siloxane impression material to overcome the inability of a laser profilometer to scan these undercuts. However, some imprecise measurements might be anticipated by introducing another variable (impression material) into the laser profilometer

measurements. This measurement method is, therefore, inaccurate, and its ability to predict tooth survival or endodontic outcome has not been proven in a clinical trial.

Currently, there is no standardised method to quantify the amount of remaining coronal tooth structure. In the present study, the intraoral digital scanning provides a reliable and accurate measurement of tooth volume, as described earlier in Chapter 3.

More than half (58%) of the included teeth in this study had less than 50% of their coronal tooth structure remaining. However, only 6% of the teeth presented with less than 20% of remaining coronal tooth structure. This was within expectations because teeth with less remaining tooth structure were more likely to be judged as non-restorable.

The percentage of remaining coronal tooth volume was expressed as the difference between the volume of coronal tooth structure before core build-up and after crown cementation, which we assumed to be comparable to that of the original tooth before any loss of coronal tooth structure occurred. This was the only option available to get a reliable estimation of the volume of original tooth structure, which would be consistently applicable to all teeth involved.

Concerning the role of residual coronal dentine based on the number of dentine walls remaining (1-4 walls), several previously published clinical studies (Ferrari *et al.* 2007, Cagidiaco *et al.* 2008, Ng *et al.* 2011, Ferrari *et al.* 2012) have examined the influence of post placement and residual coronal dentine (i.e. number of dentine walls remaining) on the survival of endodontically treated premolars. However, root canal treatments and restorations of premolars represent a small proportion of restorations of root canal treated teeth, and an even smaller proportion of root canal retreated teeth. For example, most outcome studies on root canal treatment (Ng *et al.* 2011, Patel *et al.* 2012b, Davies *et al.* 2016) included a very small number of premolars and a much larger number of molars. Therefore, this classification was included in the present study to examine if the findings on premolars are valid to all posterior teeth.

The present study was not statistically powered to assess the effect of the number of remaining dentine walls on the outcome of root canal retreatments, however, in 2-, 3- and 4-walls groups, the percentage of unfavourable outcomes was 18.2%, 18.2%, and 8.3% respectively. Teeth with 2 and 3 walls remaining had a 2.44-fold (95% CI: 0.291, 20.517) greater chance of unfavourable outcome than teeth with 4 walls remaining, however, this difference did not reach statistical significance (*P*=0.698). A similar but statistically significant trend was revealed in previous studies assessing the survival of endodontically treated premolars restored with and without fibre posts (Ferrari *et al.* 2007, Cagidiaco *et al.* 2008, Ferrari *et al.* 2012).

The use of CBCT for the detection of apical radiolucencies has been recently validated in a histological human cadavers study (Kanagasingam *et al.* 2016b). CBCT has been successfully used recently for healing assessment after root canal treatment, retreatment and indirect pulp capping procedures (Patel *et al.* 2012b, Hashem *et al.* 2015, Davies *et al.* 2016). Clinically, complete or partial resolution of apical periodontitis together with the absence of clinical signs and symptoms is an indication of endodontic success (Ng *et al.* 2007, Wu *et al.* 2011). In this study, the healed (complete absence of periapical radiolucency) and healing (reduction in the size of periapical radiolucency) outcomes were combined with the absence of clinical signs and symptoms and considered as a 'favourable' outcome, whilst teeth were considered to have 'unfavourable' outcome when a new lesion emerged, or pre-existing lesion enlarged or never changed in size, and when teeth had symptoms and/or clinical signs of failure, irrespective of the radiographic outcome. This was a common approach used by previous studies (Azim *et al.* 2016, Davies *et al.* 2016).

Irrespective of the clinical signs and symptoms, CBCT imaging revealed lower healing outcome rates (84.8%) for root canal retreatment compared with periapical radiographs (92.4%) when the outcome was assessed at T12 (*P*=0.021).

The favourable outcome observed in the present clinical trial, as assessed by periapical radiographs, concurs with the findings of previous studies (Imura *et al.* 2007, Ng *et al.* 2011), which also reported a success rate (loose criteria) for root canal retreatments comparable to the 88.3% value recorded in this research. In a systematic review of 17 retrospective and prospective studies, complete healing (strict criteria) of periapical radiolucency, as determined by periapical radiographs, was observed in 76.7% of root canal retreated teeth (Ng *et al.* 2008), compared to 70.8% observed in the current study. Of the 98 cases that appeared to have no periapical radiolucency on periapical radiograph at recall, 10 appeared as enlarged or maintained the same lesion size when imaged using CBCT.

The favourable outcome percentages recorded in this study are similar to a previous prospective retreatment study (Davies *et al.* 2016), where favourable periapical radiographs and CBCT percentages were 93% and 77%, respectively. In contrast, in a study by Metska *et al.* (2013), the percentage of retreated teeth with complete absence or reduced volume of periapical radiolucencies assessed by CBCT was 63%, which was lower than the finding of the present study. However, in the study of Metska *et al*. (2013) the sample size was limited to 35 teeth, and using the volumetric changes in periapical lesion size instead of the visual interpretation of the images could explain the low percentage of healed cases 1 year after retreatment.

Pre-operative periapical radiolucencies were detected in 86.1% of cases with CBCT and in 63.5% of cases with periapical radiographs. Thus, CBCT detected 22.6% more pre-operative periapical radiolucencies than periapical radiographs. This finding has been documented in several previous clinical studies (Estrela *et al.* 2008b, Patel *et al.* 2012a, Weissman *et al.* 2015). The results of this study showed a significant association between the pre-operative apical status and the treatment outcome (P=0.024). The favourable outcome for teeth without and with pre-operative periapical radiolucency was

100% and 78.8%, respectively, which is in agreement with other studies (Imura *et al.* 2007, Ng *et al.* 2011, Azim *et al.* 2016).

Moreover, of the 12 teeth that presented with a pre-operative perforation in the present study, 11 had favourable outcomes, indicating that the perforation was effectively sealed with MTA at the time of retreatment. It has been emphasised that the use of MTA in perforation repair is associated with a more considerably favourable response (Pitt Ford *et al.* 1995, Holland *et al.* 2001).

It should be questioned if the unfavourable outcomes were due to the loss of coronal tooth structure, inadequate root canal filling, or other factors. In the current study, over- or under-filling of the root canal had limited impact on periapical health even with the presence of pre-operative periapical radiolucencies (OR=0.756; 95% CI: 0.277, 2.063; *P*=0.585). These results agree with the findings of previous studies (Sjögren *et al.* 1990, Lin *et al.* 1992) but contradicted others (de Chevigny *et al.* 2008b, Ng *et al.* 2011, Liang *et al.* 2012, Azim *et al.* 2016) which confirmed the necessity to achieve adequate filling of the root canal system. Sjögren *et al.* (1990) and Lin *et al.* (1992) found no significant correlation between the outcome of endodontically retreated teeth and the apical extent of root canal fillings.

In this study, CBCT identified 20 teeth with unfavourable outcomes where the periapical lesions had remained the same size (11 teeth) or had increased in size (9 teeth) during the 1-year assessment period. Three teeth required extraction, 14 teeth will be reviewed at 2-year recall before further treatment is undertaken, while periapical microsurgeries were carried out for 3 teeth and were reviewed 1 year post-operatively. All teeth were asymptomatic and showed a radiological evidence of healing at the follow-up appointment.

Many studies have attempted to investigate the influence of the quality of coronal restorations on the periapical health. Most of these studies (Ray & Trope 1995, Kirkevang *et al.* 2000, Tronstad *et al.* 2000, Siqueira *et al.* 2005, Tavares *et al.* 2009) examined the correlation between quality of coronal restorations and periapical health based entirely on radiological examinations. However, most of these studies were retrospective in design, therefore, it was not certain whether the detected periapical radiolucencies were healing or expanding lesions. It is acknowledged that using periapical radiographs alone to assess the quality of coronal restoration has limitations. Periapical radiographs provide incomplete diagnostic value, as leaky occlusal margins, cracks and perforations in restorations might not be visible (Hommez *et al.* 2002, Craveiro *et al.* 2015), and can be influenced by a variety of factors, including changes in beam angulation (Goldman *et al.* 1972). Only periapical radiographs were used for this evaluation because beam hardening associated with metal crowns renders the CBCT scan inappropriate for such observation (Mora *et al.* 2007, Soğur *et al.* 2007).

In the present study, the inadequate coronal restorations observed were due to the presence of open margins or overhang restorations; no debonding was recorded. The presence of large marginal discrepancies can expose the luting material to the oral environment (Jacobs & Windeler 1991). Recontamination of the root canal system by coronal leakage has been emphasised (Siqueira *et al.* 1999, Siqueira 2001). Ray and Trope (1995) found in a retrospective study that the quality of coronal restorations, scored only on radiographs, had a higher significant impact on the periapical health than the quality of root canal filling (Ray & Trope 1995). However, no information was available regarding the pre-operative diagnosis of the teeth, and the time elapsed between root canal completion and placement of the coronal restoration. To a lesser degree, Tronstad *et al.* (2000) found that the influence of the quality of coronal restoration was statistically significant only when combined with a good quality root canal filling (Tronstad *et al.* 2000).

Adequate coronal restorations were observed in 125 (95%) of the 132 teeth based on radiological examinations alone. However, when coronal restorations were scored both clinically and radiologically, 120 (91%) of restorations were found to be acceptable. In accordance with Hommez *et al.* (2002) and Craveiro *et al.* (2015), poor correlation (kappa value=0.11) was found between clinical and radiological assessments of coronal restoration quality. A combined clinical and radiographic scoring was used in this study to evaluate the influence of coronal restoration quality on the treatment outcome.

The unfavourable outcome in teeth assessed both clinically and radiologically as having adequate restoration was 15%, compared to 16.7% in endodontically treated teeth with inadequate restorations. Based on these data, the interaction between the quality of coronal restoration, assessed clinically and radiologically, and the outcome of root canal retreatment teeth in the present study was not statistically significant (P=0.878), however, this study was not statistically powered to demonstrate such differences and the follow-up was only 12 months.

When comparing the results of this prospective study and other studies, it is noteworthy to appreciate the variability in terms of tooth type (anterior, premolar, molar), operators (specialist, generalists, undergraduate or postgraduate students), restoration type (crown, amalgam-or composite-restored), and observation period. In the current study, postgraduate students under supervision of experienced educators in endodontics carried out all the endodontic treatments and definitive coronal restorations; also, anterior teeth were not included in the current study. All coronal restorations were metal ceramic crowns. This allowed the exclusion of variables such as different tooth types, different operator skills and different restoration types which may had the potential to affect the outcome of the root canal retreatments.

Despite the high recall rate in this study, one limitation is the unknown outcome of the patients who did not respond to our calls and letters, which may result in overestimated or underestimated success rate. The difference in experiences between the postgraduate students, who performed the endodontic and restorative treatments in the current study, cannot be completely excluded. However, a standardised protocol for endodontic treatment and crown preparation was applied to potentially reduce the effect of different operators on the treatment outcome.

Further investigation, along with a longer observation period (2-5 years), is currently ongoing to assess the success and survival of the teeth included in the present study.

4.5 Conclusions

The null hypothesis stating there is no difference in the treatment outcome with varying degrees of coronal tooth structure loss was not confirmed.

At 1-year follow-up, the unfavourable outcome of root canal retreated teeth was significantly higher when less than 30% of the original tooth tissue structure was preserved.

Chapter 5 Pooled analysis of one-year recall data from three endodontic treatment outcome studies undertaken using cone beam computed tomography

5.1 Introduction

As described earlier in Chapter 2, periapical radiography has limited value in diagnosing apical periodontitis. Several clinical studies have revealed a higher prevalence of apical periodontitis with 3D CBCT imaging compared to periapical radiography (Abella *et al.* 2012, Patel *et al.* 2012a, Cheung *et al.* 2013, Chapter 4). Outcomes studies using pre-operative and post-operative CBCT have shown a lower success rate of endodontic treatment at follow-up when assessed with CBCT (Patel *et al.* 2012b, Liang *et al.* 2013, Metska *et al.* 2013, van der Borden *et al.* 2013, Davies *et al.* 2016, Chapter 4). Successful outcomes derived from previous periapical radiograph-based outcome studies may not necessarily guarantee the true resolution or reduction of apical periodontitis (Patel *et al.* 2011).

A retrospective pooled analysis was performed using the data obtained from three prospective clinical trials (including the clinical trial study in Chapter 4) undertaken at King's College London Dental Institute. The aim was to provide a broader dataset to estimate the proportion of successful outcomes of root canal treatment and retreatment when assessed by CBCT, and also to investigate the degree of success according to the tooth type.

The null hypotheses investigated were:

1. There is no difference in the accuracy of PA and CBCT in assessing the outcome of root canal treatment and retreatment at 1-year recall.

2. There is no difference in the proportion of successful outcomes between root canal treatments and retreatments.

3. There is no difference in the degree of success between different tooth types.

5.2 Materials and methods

5.2.1 Selection criteria

Data collected from three previous prospective clinical outcome studies were pooled together, including one study on primary root canal treatments (Patel *et al.* 2012b) and two retreatment studies (Davies *et al.* 2016, Chapter 4). All teeth in the primary root canal treatment sample were treated by a single operator in a specialist endodontic practice between October 2008 and April 2009. All teeth in the root canal retreatment sample were treated by endodontic postgraduate students at the postgraduate endodontic unit at Guy's Hospital (King's College London Dental Institute) supervised by qualified endodontic staff between July 2012 and April 2015.

Ethical approvals for the three studies were granted by the Guy's Research Ethics Committee, Guy's and St Thomas' Hospital National Health Service Trust (National Research Ethics Service, England), the NRES London Bridge and Dulwich Research Ethics Committees, and the NRES West-London Research Committee. Patient information sheets were provided, and informed verbal and written consent was obtained from all patients enrolled in these studies prior to their treatment (Appendix III-IV).

5.2.2 Inclusion and exclusion criteria

All patients were examined clinically and radiologically before inclusion. Individual subjects were included in the primary treatment study (Patel *et al.* 2012b) if they had symptoms and/or signs of endodontic disease, while subjects diagnosed with symptoms and/or signs of post-treatment endodontic disease were considered for inclusion in

retreatment studies (Davies *et al.* 2016, Chapter 4). Common exclusion criteria were pregnant women, immunosuppressed patients, teeth with periodontal probing depth more than 3 mm and unrestorable teeth.

Data from 123 teeth (99 patients) with primary root canal treatment and 238 teeth (208 patients) with root canal retreatment were available. In the retreatment sample, 7 teeth (6 patients) were included in both retreatment studies, therefore, those teeth were included only once in the pooled analysis. Finally, the pooled cohort consisted of 354 teeth in 301 patients. Eight patients in the retreatment sample had clinical complications and underwent endodontic surgery (n=7) and extraction (n=1) before the 1-year recall. Those patients were excluded from the radiological outcome assessment because no post-operative CBCT scans were taken, but they were classified as clinical failures.

5.2.3 Radiographic technique

Digital intraoral periapical radiographs and CBCT scans for all cases were taken pre-operatively (T0) and at approximately twelve months after treatment (T12). In Patel *et al.* (2012b) study, the intraoral PA were obtained with a digital CCD (Schick Technologies, New York, USA) using a parallel technique and a dental X-ray machine (Planmeca Prostyle Intra, Helsinki, Finland) operating at 66 kV, 7.5 mA with an exposure time of 0.10 seconds. CBCT images of the patients were obtained with a 3D Accuitomo CBCT scanner (J. Morita) with 4 X 4 cm field of view and exposure parameters of 90 kV, 5.0 mA and 17.5 seconds. The radiographic technique used in the retreatment studies has already been described in Chapter 4.

5.2.4 Clinical intervention

All primary root canal treatments were completed in a single session; the root canal retreatments were completed in two treatment sessions with an inter-appointment calcium hydroxide medication for a minimum of 2 weeks. All treatment was carried out using a standardised protocol. Root canal treatment and retreatment procedures were

described previously (Patel *et al.* 2012b, Davies *et al.* 2016, Chapter 4). All procedures were performed under rubber dam isolation with the aid of a dental operating microscope (3 step entrée Dental Microscope, Global).

Briefly, stainless steel K-flexofiles (Dentsply Maillefer) were used to negotiate the canals to its provisional working length. In root canal retreatment cases, Gates-Glidden burs and hand files (Hedström and K-flexofiles, Dentsply Maillefer) were used to remove the existing gutta-percha, and chloroform was used as a solvent when required. A crown-down technique with ProTaper Universal nickel-titanium rotary instruments (Dentsply Maillefer) at 300 rpm was used to prepare the root canals. The apical enlargement was completed to a minimum of ProTaper F2 according to the root canal morphology.

The canals were continuously irrigated with 1% or 2% sodium hypochlorite during the procedure, and the irrigant was replenished every 3-4 min. A penultimate irrigation with 15% or 17% EDTA was undertaken followed by a final irrigation with sodium hypochlorite. The irrigant was energised for one minute. All the canals were obturated with gutta-percha (Dentsply Maillefer) using a warm vertical condensation technique.

Permanent glass-ionomer (Fuji IX GIC, GC Corporation) or composite resin (Herculite Ultra, Kerr Corporation, Orange, California, USA), (Ceram X Duo, Dentsply) was then used to restore the teeth immediately. Where indicated, teeth were restored with cuspal coverage restorations as soon as feasibly possible after root (re)treatment had been completed.

5.2.5 Outcome assessment

Patients were reviewed 12 months after the completion of the treatment (T12). The treatment outcome was determined by clinical findings and radiological examinations as described previously by Patel *et al.* (2012b), Davies *et al.* (2016), and in Chapter 4. At T12, the presence/absence of pain, swelling, tenderness to percussion or palpation were

recorded. The radiological assessment was carried out by a consensus panel consisting of two pre-calibrated experienced endodontists. The consensus panel assessed the images of the two radiographic methods using a six-points classification, as described in Chapter 4, to record the outcome of the treatment.

As in Chapter 4, the outcomes were classified as healed, healing (favourable), and failed (unfavourable). The whole tooth was used as a unit of evaluation. Multi-rooted teeth were assessed according to the root with the worst diagnostic outcome.

5.2.6 Data analysis

Univariate analysis was used to analyse the study data descriptively using percentage frequencies. The McNemar's test was used to compare the treatment outcomes determined by PA and CBCT imaging. A Pearson chi-square (χ^2) test was used to compare the outcome according to the treatment modality (primary root canal treatment and retreatment). The difference in treatment outcomes between anterior, premolar, and molar teeth was analysed using a chi-square test/Fisher's exact test. The proportion of favourable outcome in maxillary and mandibular molars was compared using a Z test for proportions. SPSS statistical software (SPSS version 23, IBM) was used to perform all statistical analyses. The level of significance was set at α=0.05.

5.3 Results

The teeth were classified according to the pre-operative and post-operative variables as shown in Table 5-1. In total, 354 teeth (301 patients) were included in this pooled study, of which 123 teeth (99 patients) were primary treatments and 231 teeth (202 patients) were retreatments. This sample included 45 anteriors (13%), 64 premolars (18%), and 245 molars (69%). More teeth were located in the maxillae (56%) than in the mandible (44%). The distribution of teeth according to the tooth type is shown in Figure 5-1.

Eight out of the 354 teeth were classified as clinical failures due to the development of clinical symptoms between T0 and T12. After 12 months (T12), 346 teeth in 293 patients (65% female and 35% male) were reviewed clinically and radiologically. The overall recall rate was 85% for teeth and 82% for patients (Table 5-2). The average age of patients was 42 years. Three-hundred and twelve teeth had received full cuspal coverage restorations within 1-2 months of completion of the root canal (re)treatment, and 21 teeth had been restored with plastic restorations.

Table 5-1 Univariate distribution of pre-operative and post-operative variables

Variables	Primary treatment (1)	Retreatment (2)	Retreatment (3)	Pooled sample
Pre-operative				
Number of patients reviewed	99	87	115	301
Mean age	44.5	39	43	42
Gender				
Male	42	29	34	105 (35%)
Female	57	58	81	196 (65%)
Tooth type				
Anterior	30	15	-	45 (13%)
Premolars	18	18	28	64 (18%)
Molars	75	68	102	245 (69%)
Tooth location				
Maxilla	67	65	66	198 (56%)
Mandible	56	36	64	156 (44%)
Pre-operative radiolucency (PA)				
Absent	75	35	48	158 (45%)
Presence	48	66	82	196 (55%)
Pre-operative radiolucency (CBCT)				
Absent	51	12	19	82 (23%)
Presence	72	89	111	272 (77%)
Post-operative				
Clinical signs and symptoms of apical periodontitis				
Absent	123	90	124	337 (95%)
present	0	11	6	17 (5%)

(1) Patel *et al*. (2012b); (2) Davies *et al.* (2016); (3) Chapter 4

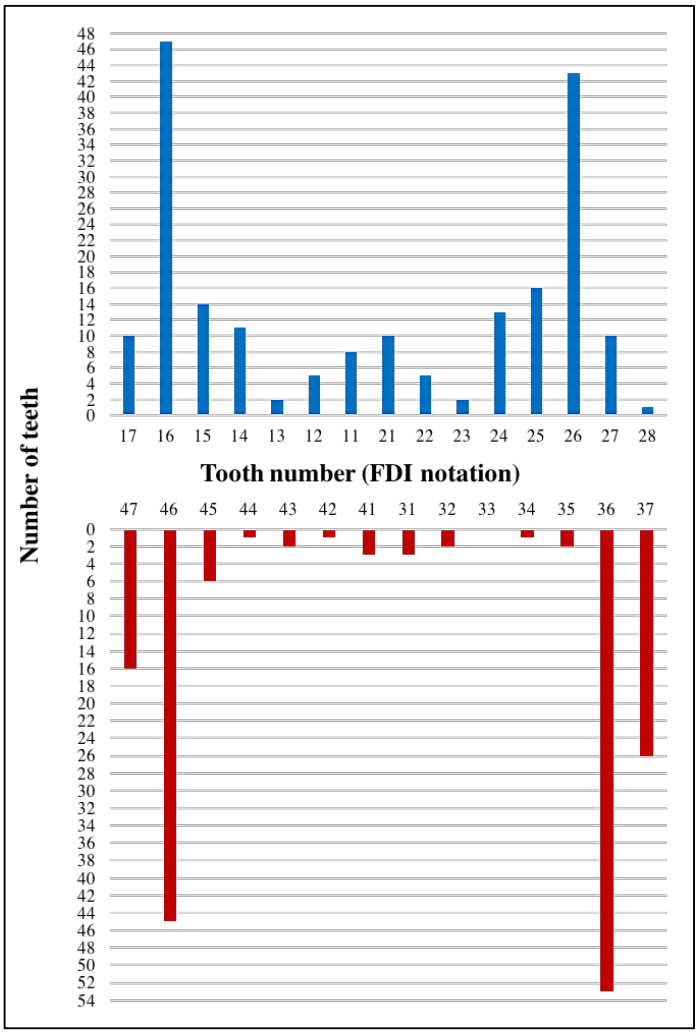

Figure 5-1 Teeth distribution according to the tooth type

Table 5-2 Recall rates for teeth and patients in the included studies

	Recruited		Treated		Reviewed		Recall rate %	
	Teeth	**Patients**	**Teeth**	**Patients**	**Teeth**	**Patients**	**Teeth**	**Patients**
Patel *et al.* (2012b)	151	132	151	132	123	99	82%	75%
Davies *et al.* (2016)	148	135	114	101	98	84	86%	83%
Chapter 4	204	182	156	140	137	121	88%	86%
Pooled sample	503	449	421	373	358	304	85%	82%

Table 5-3 shows the distribution of outcome diagnosis based on the radiological assessment. At T12 recall, all teeth with primary root canal treatment were asymptomatic, while 17 teeth in the retreatment sample had clinical signs and/or symptoms of apical periodontitis.

Table 5-3 Frequency distribution of outcome of treatment for each tooth in primary root canal treatment, retreatment, and pooled samples (n=346) assessed using periapical radiographs (PA) and CBCT (radiological assessment only)

Outcome category	**Primary treatment sample**		**Retreatment sample**		**Pooled sample**	
	PA	**CBCT**	**PA**	**CBCT**	**PA**	**CBCT**
1- New lesion	1	9	0	2	1	11
2- Enlarged lesion	1	5	6	17	7	22
3- Unchanged lesion	4	5	11	24	15	29
4- Reduced lesion	10	27	37	54	47	81
5- Resolved lesion	33	35	86	97	119	132
6- No lesion before/after treatment	74	42	83	29	157	71
Total	123	123	231	231	346	346

The overall percentage of favourable outcomes was 91% and 80.2% as assessed by PA and CBCT, respectively (McNemar's test, $P<0.001$). Table 5-4 lists the percentages of favourable, unfavourable and healed outcomes, including the eight teeth that required further intervention prior to the 1-year recall.

For the primary root canal treatment sample, the favourable outcome percentages were 95.1% and 84.7% as assessed by PA and CBCT, respectively (McNemar's test, P<0.001). In the retreatment sample, the favourable outcomes were 88.7% and 77.9% as assessed by PA and CBCT, respectively (McNemar's test, P<0.001). With CBCT, there was no significant difference (χ^2=2.224, P=0.136) between the favourable outcome percentages after primary treatments and retreatments, with an odds ratio of 0.645 (95% CI: 0.361, 1.151).

Table 5-4 Percentage of success rates based on clinical symptoms and radiological examination with periapical radiographs (PA) and CBCT for each tooth type in the pooled sample (n=354)

Outcome category	Incisor/canine		Premolar		Molar		All cases	
	PA	CBCT	PA	CBCT	PA	CBCT	PA	CBCT
Unfavourable (1,2,3)	8.9	8.9	6.3	9.4	9.8	24.5	9.0	19.8
Favourable (4,5,6)	91.1	91.1	93.7	90.6	90.2	75.5	91.0	80.2
Healed (5,6)	82.2	80.0	79.7	59.4	76.3	52.7	78.8	57.3

With pre-operative CBCT scans, apical radiolucencies were observed in 58.5% of the teeth in the root canal treatment sample, and in 86.6% of the teeth in the retreatments sample compared to 39% and 64.1% on PA, respectively. In the primary treatment sample, CBCT showed that the favourable outcome for teeth that presented without and those with pre-operative periapical radiolucency was similar (82.4% and 86.1%, respectively, χ^2=0.323, P=0.570) with an odds ratio of 0.75 (95% CI: 0.282, 2.010).

In the retreatment sample, the favourable outcomes of CBCT determined in teeth with absence of pre-operative radiolucency (93.5%) were significantly more numerous than those of teeth with pre-operative radiolucency (75.5%) (Fisher's exact test, P=0.021) with an odds ratio of 4.7 (95% CI: 1.083, 20.438). In the pooled sample, the chi-square test revealed no significant association between the treatment outcome and the pre-

operative apical status (χ^2 = 2.721, *P*=0.099) with an odds ratio of 1.788 (95% CI: 0.890, 3.591). The outcomes of teeth presenting with and without pre-operative periapical radiolucency are shown in Table 5-5.

With periapical radiography, there was a lower favourable outcome in molar teeth (90.2%) compared with anterior and premolar teeth (92.7%), however, the difference was not statistically significant (χ^2=0.554, *P*=0.453). With CBCT, molar teeth showed an overall favourable result of 75.5% (76% for primary treatments, and 75.3% for retreatments) and were less successful than anterior and premolar teeth, which had a favourable result in 91.1% (*P*=0.019) and 90.6% (*P*=0.009), respectively. Within the pooled sample, molar teeth (75.5%) were less successful than anterior teeth and premolars (90.8%) pooled together (χ^2=11.154, *P*=0.001). There was no significant difference in the outcome between maxillary and mandibular molar teeth (Z score= -1.213, *P*=0.226). All failures in premolars occurred in the retreatment sample. The favourable and unfavourable outcomes according to tooth type are presented in Table 5-5.

Table 5-5 The outcome of root canal treatments according to pre-operative variables as determined by periapical radiography (PA) and CBCT

Variables	PA		CBCT	
	Favourable outcome	Unfavourable outcome	Favourable outcome	Unfavourable outcome
Preoperative apical periodontitis				
Primary treatment sample				
Absence	98.7% (74)	1.3% (1)	82.4% (42)	17.6% (9)
Present	89.6% (43)	10.4% (5)	86.1% (62)	13.9% (10)
Retreatment sample				
Absence	98.8% (82)	1.2% (1)	93.5% (29)	6.5% (2)
Present	83.1% (123)	16.9% (25)	75.5% (151)	22.5% (49)
Pooled sample				
Absence	98.7% (156)	1.3% (2)	86.6% (71)	13.4% (11)
Present	84.7% (166)	15.3% (30)	78.3% (213)	21.7% (59)
Tooth type				
Primary treatment sample				
Anterior	96.7% (29)	3.3% (1)	96.7% (29)	3.3% (1)
Premolar	100% (18)	0 (0)	100% (18)	0 (0)
Molar	93.3% (70)	6.7% (5)	76% (57)	24% (18)
Retreatment sample				
Anterior	80% (12)	20% (3)	80% (12)	20% (3)
Premolar	91.3% (42)	8.7% (4)	87% (40)	13% (6)
Molar	88.8% (151)	11.2% (19)	75.3% (128)	24.7% (42)
Pooled sample				
Anterior	91.1% (41)	8.9% (4)	91.1% (41)	8.9% (4)
Premolar	93.8% (60)	6.2% (4)	90.6% (58)	9.4% (6)
Molar	90.2% (221)	9.8% (24)	75.5% (185)	24.5% (60)

For the three pooled studies, the Cohen kappa values for intra-consensus panel agreements reported on outcome diagnosis ranged between 0.61 to 0.78 using periapical radiography and from 0.66 to 0.92 using CBCT, indicating substantial to almost perfect agreement (Landis & Koch 1977). The inter-examiner agreement between all the examiners of the pooled studies ranged from 0.44 to 0.84 using periapical radiography and from 0.71 to 1 using CBCT (Table 5-6).

Table 5-6 Kappa values for intra-consensus panel agreement and inter-examiner agreement on outcome diagnosis using periapical radiography (PA) and CBCT

	Intra-consensus panel agreement		**Inter-examiner agreement**	
	PA	**CBCT**	**PA**	**CBCT**
Primary treatment sample	0.74-0.78	0.86-0.92	0.44-0.84	0.73-1
Retreatment sample	0.61-0.71	0.66-0.71	0.53-0.72	0.71-0.72

0.40-0.60 moderate agreement, 0.60-0.70 substantial agreement, 0.80-01.00 almost total agreement

5.4 Discussion

The results of the analysis of the pooled data of 354 teeth showed that molar teeth had an overall percentage of favourable results of 75.5% (76% for primary treatments, and 75.3% for retreatments) and were less successful than anterior teeth (91.1%) and premolars (90.6%) when assessed with CBCT. The percentage of healed and healing molars were respectively 24% and 15% less when assessed with CBCT compared with periapicals.

The three studies in this pooled analysis were under the management of the same research team. They used similar treatment protocols and recall times and adopted the same radiological assessment criteria. Pre-operative and post-operative scans were taken using an Accuitomo CBCT scanner (3D Accuitomo, J. Morita). However, a potential for clinical heterogeneity due to variation in study characteristics such as

experience of operators (specialists, postgraduate students), individuals in the studies (age, sex, baseline severity of disease), intervention (primary treatment, retreatment), and location of the study (private clinic, University hospital) may be considerable; in particular the primary treatments were all undertaken by a single specialist endodontist, while the retreatments were undertaken by a large pool of endodontic postgraduate students.

The overall recall rate was above 80% (85% for the teeth, and 82% for the patients), which is required to achieve a high level of evidence (MUHSC 1981, Sackett *et al.* 1991). This recall rate is similar to the 10-19 months recall rate (82%) reported by Liang *et al.* (2013), but higher than the 1-year recall rate (78% for teeth, and 73% for patients) reported by Metska *et al.* (2013). The outcomes of the dropouts were unknown, which may relatively overestimate or underestimate the overall outcome.

With the recognition of the dynamic nature of healing of periapical pathology that may extend up to 4 years (Ørstavik 1996), it has been emphasised that a short follow-up may underestimate the proportion of teeth with a complete absence of periapical radiolucencies (Ng *et al.* 2007). However, Zhang *et al.* (2015) reported that 22% of the periapical lesions present at 1 year post-treatment on CBCT scans had completely resolved at 2 years. Similarly, 63% of the radiolucencies were significantly reduced in volume at 2 years. This means that the majority of lesions which are healing at the 1-year recall will be noticeably progressing towards a complete healing during the second year or later. Indeed, this finding supports the use of 1-year healing data as a source of information for the outcome of root canal treatments.

Knowledge about the actual success rate of molar teeth, which is clearly overestimated when assessed by PA, may provide important information that contributes to clinical decision-making. CBCT showed a significantly lower favourable outcome in molars (75.5%) compared with anterior and premolar teeth (90.8%) pooled together. The higher

failure rate in molar teeth compared to other tooth types agrees with studies (Fernández *et al.* 2013, Gomes *et al.* 2015) that have also used CBCT imaging at recall but not at baseline.

Studies which have used periapicals to compare success rates for different tooth type show a higher success rate for molars compared with premolars (Hoskinson *et al.* 2002), and incisors and canines (Liang *et al.* 2011, Ng *et al.* 2011). The differing results of these studies could be attributed to the limitations of periapicals to diagnose apical periodontitis in the posterior maxillary region due to superimposition of roots with each other and other structures, such as the maxillary sinus and the zygomatic arch (Low *et al.* 2008, Ørstavik & Larheim 2008, Shahbazian *et al.* 2015). In the posterior mandibular region, the thick overlying cortical plate of the mandible may also cause anatomic noise and obscure the area of interest (Patel *et al.* 2009b, Patel *et al.* 2015).

Cheung *et al.* (2013) found a substantial disagreement between PA and CBCT for assessing the presence/absence and size of periapical lesions of molar teeth, and highlighted the increased possibility of underestimating the number of lesions if periapical radiographs was the only means to evaluate the outcome of root canal treatment (Cheung *et al.* 2013). In a recent retrospective study, CBCT imaging showed a significantly higher detection rate of periapical lesions than PA in maxillary incisors/canines and maxillary molars (Uraba *et al.* 2016).

Lower success rates can be explained by the complex root canal anatomy of molar teeth compared to single-rooted teeth (Cleghorn *et al.* 2006, de Pablo *et al.* 2010) that presented a greater challenge to disinfect and obturate.

Based on PA results, the favourable outcome of the present pooled study (91%) compares favourably to that obtained (93.9%) by Friedman *et al.* (1995), including both treatment and retreatments cases that were followed-up for 6-18 months (Friedman *et al.* 1995).

The pooled favourable outcome observed by CBCT (80.2%) was significantly lower compared with that observed by periapical radiography (91%) (P<0.001). Overall, CBCT detected 21.1% more post-treatment periapical lesions than PA which is broadly in agreement with the findings of other studies that also used pre-operative and post-operative CBCT scans to assess the outcome of treatment (Liang *et al.* 2013, van der Borden *et al.* 2013).

van der Borden *et al.* (2013) used the changes in size (area and 3D volumetric measurements) of periapical radiolucencies as revealed by periapical radiography and CBCT imaging to assess the outcome of the root canal treatment in 71 roots (50 teeth including anterior teeth, premolars, and molars) after 1-37 months. It was found that the absence of lesions was demonstrated in 45.1% of roots on PA and in 15.5% of roots on CBCT (P<0.001), whereas the reported absence or reduction in the size of periapical lesions was 88.7% on PA and 77.5% on CBCT (P=0.073) (van der Borden *et al.* 2013). Likewise, Liang *et al.* (2013) compared the area and volume of the periapical lesions at the first visit and at recall (10-19 months) in 86 single-rooted anterior and premolar teeth. They found that the post-treatment apical periodontitis detected by CBCT (81%) was significantly greater than that detected by periapical radiography (67.9%) (P=0.038). However, there was no significant difference in the percentages of absence and reduction of the radiolucency together as observed by PA and CBCT (P=0.383) (Liang *et al.* 2013). This study was entirely based on the assessment of single-rooted teeth that explains why there was no significant difference between PA and CBCT.

The discrepancy between the observations made by PA and CBCT could be attributed to the more accurate detection of apical periodontitis on CBCT images. Considering the above findings, the complete absence of a periapical lesion on PA does not guarantee that the lesion is not present, which could lead to overestimation of the successful outcome of the treatment. In contrast, CBCT may provide a more accurate radiological assessment of the outcome of root canal treatment and, therefore, re-evaluation of the

success of root canal treatment with long-term follow-up studies using CBCT is needed (Wu *et al.* 2009, Kanagasingam *et al.* 2016b).

Root canal retreatment procedures are frequently complicated by technical difficulties to remove previous posts, silver points, gutta-percha, and broken instruments, and to overcome procedural errors (ledges, blocks, transportations and perforations) and aberrant anatomy before effective cleaning and shaping of the root canal system can be achieved (Ruddle 2004). Another challenge is the microbial flora which is an important factor in endodontic failure (Sundqvist *et al.* 1998).

Based on CBCT imaging, the percentage of favourable results for primary treatments (84.7%) was not statistically different (P=0.136) from that of retreatments (77.9%), which agrees with other studies (de Chevigny *et al.* 2008a, de Chevigny *et al.* 2008b, Ng *et al.* 2011). In a well-controlled prospective study, Ng *et al.* (2011) reported comparable success rates between initial root canal treatment and retreatment using 'strict' criteria (83% vs. 80%) or 'loose' criteria (89% vs. 86%), respectively (Ng *et al.* 2011). Similarly, in the Toronto study, the pooled outcome of primary (de Chevigny *et al.* 2008a) and orthograde retreatment (de Chevigny *et al.* 2008b) was investigated. After 4 to 6 years, 86% of teeth with primary root canal treatment and 83% of teeth with orthograde retreatment were healed.

In this study, the interaction between the pre-operative periapical status and treatment outcome has a different effect on primary treatment and retreatment. In the primary treatment, the prevalence of failure of molar teeth with no pre-operative apical radiolucencies assessed with CBCT (17.6%) was higher compared with those with existing periapical radiolucency (13.9%). The difference was not statistically significant (OR=0.75, P=0.570). This result is consistent with Sjögren *et al.* (1990) who reported that the success rate of primary treatment with previous apical periodontitis was as good as that without apical periodontitis (Sjögren *et al.* 1990). However, this finding contrasts

with that of other studies (Chugal *et al.* 2001, Imura *et al.* 2007, Liang *et al.* 2012) where the presence of pre-operative apical periodontitis determined with PA was a significant predictor of treatment outcome.

Unlike in primary treatment, the impact of the periapical status at the start of retreatments was more pronounced (P=0.021). The favourable outcome of 93.5% for teeth retreated without pre-operative apical periodontitis, determined by CBCT, was 18% (OR=4.7) higher than in those with pre-operative apical periodontitis present (75.5%). This result is in line with the findings reported by previous studies (Gorni & Gagliani 2004, Azim *et al.* 2016). The negative influence of periapical status on retreatments may be explained by the ability of bacteria in teeth with persistent apical lesions, in particular, *Enterococcus faecalis,* to resist eradication by conventional endodontic treatment (Nair *et al.* 1990a, Molander *et al.* 1998, Sundqvist *et al.* 1998). Furthermore, bacteria present in inaccessible areas within the root canal system may be occasionally unaffected by conventional instrumentation procedures and disinfecting agents (Siqueira *et al.* 1996, Nair *et al.* 2005). In addition to the intraradicular microbes, it should be noted that, in some cases, persistent lesions associated with root treated teeth may occasionally be caused by extraradicular infection, which can be a factor of root canal treatment failure (Siqueira 2001).

Primary treatments included in the present pooled data investigation were completed in one visit, while retreatments were carried out in two visits, and calcium hydroxide was used in between visits. Studies in the literature had shown good results when calcium hydroxide was applied as an interim medicament in root canals of teeth with periapical lesions (Byström *et al.* 1985, Sjögren *et al.* 1991, Trope *et al.* 1999). The use of inter-appointment dressing such as calcium hydroxide between appointments has been proved to assist in the reduction or elimination of surviving bacteria in the root canal system, and therefore favouring the periapical healing process (Byström *et al.* 1985, Chong & Pitt Ford 1992).

5.5 Conclusion

The null hypothesis stating there is no difference in the accuracy of PA and CBCT in assessing the outcome of root canal treatment and retreatment at 1-year recall was rejected. The null hypothesis stating there is no difference in the proportion of successful outcomes between root canal treatment and retreatment was accepted. The null hypothesis stating there is no difference in the degree of success between different tooth types was rejected.

In the present study, the percentage of favourable results of primary root canal treatments and retreatments assessed with CBCT was lower than those historically reported by periapical radiograph-based outcome studies. The proportion of favourable results of primary treatment and retreatment are comparable. CBCT demonstrated more failures in molar teeth than anterior teeth and premolars.

Future outcome studies exploring the effect of new materials and techniques on the outcome of root canal treatments should be based on pre-operative and post-operative CBCT images and focus on the healing rate of molar teeth.

Chapter 6 Summary and suggestions for future work

6.1 Summary

The aim of this PhD was to test a method of measuring the volume of residual coronal tooth structure following root canal retreatment, and use this information to predict the probability of endodontic failure and the survival of endodontically treated teeth.

Dental radiography is an integral part of the diagnosis, treatment planning and long-term assessment of healing outcomes in endodontics. Cone beam computed tomography is more sensitive and specific than conventional two-dimensional imaging methods in detecting apical radiolucencies and has been successfully used for healing assessment after root canal treatment and retreatment.

Minimising the dose of ionising radiation administered to patients is paramount, taking into consideration the widespread use of CBCT in several diagnostic tasks in dentistry.

To reduce the patient dose to the greatest possible extent, an *ex vivo* study using human dry mandibles was conducted, which demonstrated that the use of a built-in dose reduction mode did not affect the accuracy of the Accuitomo CBCT machine in detecting small simulated periapical lesions, which resulted in significant patient dose reductions (54% during the full-arc rotation [360°] and 51% during the half-arc rotation [180°]).

In the current dental literature, there is a lack of accepted standardised tools for the quantification of the residual coronal tooth structure following root canal treatment. Digital intraoral impression devices are used to capture high-resolution three-dimensional virtual models, offering a consistent alternative to traditional impression materials for several clinical applications.

An *in vitro* study was conducted prior to the start of the clinical trial which proved that the measurements of the volume of residual coronal tooth structure, obtained with an intra-oral scanner following endodontic access cavity preparation, differed only by 0.68%-1.36% from those obtained using the gold standard measurement tool (micro-computed tomography).

It has been widely documented that the amount of intact coronal and radicular tooth structure plays a central role in the restoration of endodontically treated teeth. However, there was no direct evidence on the association of the remaining coronal tooth structure volume with the outcome of endodontic treatment and the survival of endodontically treated teeth.

In the clinical trial, we evaluated the association of the volume of residual sound coronal tooth structure, measured with an intraoral scanner, with the 1-year outcome of endodontic retreatments of posterior teeth assessed using CBCT.

The percentage of remaining coronal tooth structure was obtained by measuring the difference between the volume of coronal sound tooth structure before core build-up and the volume of the tooth crown after cast restoration placement.

CBCT detected more unfavourable treatment outcomes in teeth with less than 30% of remaining coronal tooth structure than in those with more than 30% of residual tooth volume.

CBCT detected 23.5% more post-treatment periapical radiolucencies than periapical radiography, confirming the superior diagnostic capabilities of CBCT compared with the two-dimensional radiographs.

Furthermore, to provide a broader estimate of the successful outcomes of root canal treatments and retreatments determined by CBCT, a pooled analysis was performed

using data extracted from three prospective clinical trials, including the current one, undertaken at King's College London Dental Institute.

The proportions of favourable results of primary root canal treatments and retreatments assessed with CBCT were found to be significantly lower than those previously reported by periapical radiograph-based clinical outcome studies. Primary treatments and retreatments had a comparable proportion of favourable results.

Similarly, CBCT demonstrated that endodontic treatments are less successful in molar teeth than in anterior and premolar teeth. This observation contradicts those of historic periapical radiograph-based outcome studies in endodontics, which in general, failed to detect any significant difference in outcome between single rooted teeth and molars; this could be attributed to the limitations of periapicals to diagnose apical periodontitis in the posterior regions due to superimposition of roots with each other and other structures, such as the maxillary sinus, the zygomatic arch and the thick posterior cortical plate of the mandible.

In conclusion, the results of this thesis may allow clinicians to predict the prognosis of root canal retreated teeth with various amounts of remaining coronal tooth structure, and help the patient in making the correct decision as to whether to retain or extract root canal treated teeth presenting with endodontic failures.

6.2 Suggestions for future work

1. The clinical trial is still ongoing, and longer-term follow-ups are currently being undertaken. This involves:

    a. Assessment of the association of the volume of residual coronal tooth structure with the success and survival of root canal retreated teeth 2 and 5 years post-treatment.

    b. Assessing the influence of remaining coronal tooth structure location on the survival of root canal retreated teeth 2 to 5 years after root canal retreatment.

    c. Further assessing if the volume of contra-lateral tooth can be used as a clinical reference to assess the restorability of the tooth in question in comparison to the results found in this thesis.

2. Further studies should also include:

    a. The design of a software that automatically computes the percentage of residual coronal tooth structure, possibly subtracting the existing pre-core build-up tooth volume from a digital mock-up of the restored tooth.

    b. An *ex vivo* study to assess the influence of dose reduction mode on other diagnostic applications of CBCT in dentistry, such as detection of internal and external root resorption, and horizontal tooth fractures.

Appendices

Appendix I: Publications

List of publications in international peer-reviewed journal

1. Al-Nuaimi N, Patel S, Foschi F, Mannocci F (2016) **The detection of simulated periapical lesions in human dry mandibles with cone-beam computed tomography: a dose reduction study**. *International Endodontic Journal* **49**, 1095-104.

2. Al-Nuaimi N, Patel S, Austin R, Mannocci F (2017) **A prospective study assessing the effect of coronal tooth structure loss on the outcome of root canal retreatment**. *International Endodontic Journal* doi:10.1111/iej.12760.

3. Al-Nuaimi N, Patel S, Davies A, Foschi F, Mannocci F **Pooled analysis of 1-year recall data from three endodontic treatment outcome studies undertaken using cone beam computed tomography.** Submitted to the International Endodontic Journal.

4. Al-Nuaimi N, Patel S, Foschi F, Mannocci F, Austin R (2017) **Assessment of residual coronal tooth structure post-endodontic cavity preparation using digital dental impressions and micro-computed tomography**. International Journal of Computerized Dentistry (in press).

List of abstracts submitted to national and international conferences

1. Al-Nuaimi N, Patel S, Foschi F, Mannocci F (oral presentation), '**Micro-computed tomography in-vitro evaluation of coronal tooth tissue volume changes following primary and secondary root canal treatment'** Annual Postgraduate Research Day at King's College London Dental Institute (2014).

2. Al-Nuaimi N, Patel S, Foschi F, Mannocci F (oral presentation), '**Dose reduction and cone beam computed tomography accuracy**' Annual Postgraduate Research Day at King's College London Dental Institute (2015).

3. Al-Nuaimi N, Patel S, Foschi F, Mannocci F (oral presentation), '**Dose reduction and cone beam computed tomography accuracy**' European Society of Endodontology, ESE Biennial Congress, Barcelona, Spain, 17th-19th September (2015).

4. Al-Nuaimi N, Patel S, Foschi F, Mannocci F (poster presentation), '**The detection of simulated periapical lesions in human dry mandibles with cone-beam computed tomography: a dose reduction study**' European Society of Endodontology, ESE Biennial Congress, Barcelona, Spain, 17th-19th September (2015). [Abstract] published in International Endodontic Journal, 0 (Suppl. 0), 1–90, 2015.

5. Al-Nuaimi N, Patel S, Foschi F, Mannocci F, Austin R S (poster presentation), '**Assessment of residual coronal tooth structure post-endodontic cavity preparation using digital dental impressions and high-resolution micro-computed tomography'** Dimensional X-ray Computed Tomography Conference, National Physical Laboratory, Teddington, UK, 10th May (2016). [Abstract] published in National Physical Laboratory (NPL) website.

6. Al-Nuaimi N, Patel S, Austin R S, Mannocci F (oral presentation), '**A prospective study assessing the effect of coronal tooth structure loss on the success, and survival of root canal re-treated teeth – part 1: periapical health**' American Association of Endodontist, AAE Annual Session, New Orleans, USA, 26th-29th April (2017).

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The detection of simulated periapical lesions in human dry mandibles with cone-beam computed tomography: a dose reduction study

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Abstract

Al-Nuaimi N, Patel S, Foschi F, Mannocci F. The detection of simulated periapical lesions in human dry mandibles with cone-beam computed tomography: a dose reduction study. *International Endodontic Journal*, **49**, 1095–1104, 2016.

Aim To assess in an *ex vivo* model the accuracy of detection of simulated periapical lesions using two cone-beam computed tomography (CBCT) dose modes and periapical radiography.

Methodology Small and large artificial periapical lesions were created with burs at the base of the socket of eleven mandibular molars, in seven human dry mandibles. Digital periapical radiographs, 360° and 180° rotations CBCT scans with standard dose and dose reduction (DR) modes were obtained before and after periapical lesions were prepared. Six blinded examiners scored the presence/absence of lesions. Inter- and intra-examiner reliability were determined. Sensitivity, specificity, positive predictive values and negative predictive values and receiver operating characteristic (ROC) area under the curve (overall accuracy) were determined for each modality.

Results The mean sensitivity and specificity of both CBCT rotations with dose reduction mode were higher compared to that of standard dose CBCT scans. The ROC Az mean values for periapical radiographs, 360° scan with standard dose and dose reduction and 180° scans with standard dose and dose reduction were 0.62, 0.94, 0.95, 0.95 and 0.97, respectively. No significant difference in the diagnostic accuracy of CBCT scans taken with standard and dose reduction modes, whilst their accuracy was significantly higher than periapical radiographs.

Conclusions Using dose reduction with 360° and 180° CBCT scans demonstrated good diagnostic accuracy in the detection of simulated periapical lesions whilst reducing the radiation dose by 54% and 51%, respectively, compared to conventional settings. Clinical evaluation is now needed to determine whether this is applicable to patients.

Keywords: cone-beam computed tomography, dose reduction, human dry mandibles, periapical lesions, receiver operating characteristic curve.

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Introduction

Intraoral radiography is the radiographic imaging system of choice for diagnosis and management of endodontic problems (Durack & Patel 2012). It is well established that intraoral radiography has several limitations for diagnosing periapical radiolucencies (Bender & Seltzer 1961, Bender 1997). The two-dimensional nature of the image produced affects radiographic interpretation (Estrela *et al.* 2008). Superimposition of anatomical structures impairs the assessment of periapical tissues (Patel *et al.* 2009a). Therefore, periapical lesions confined to the cancellous bone and masked by the overlying cortical plate are not readily detected by periapical radiographs (Bender & Seltzer 1961, Patel *et al.* 2009b, Tsai *et al.* 2012).

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Cone-beam computed tomography (CBCT) was introduced in the late 1990s specifically to generate a reconstructed 3-dimensional image of the maxillofacial skeleton (Mozzo *et al.* 1998, Arai *et al.* 2001) and since then it has been used in several areas of dentistry (Liang *et al.* 2014). CBCT been shown to diagnose periapical lesions that periapical radiographs were unable to detect (Lofthag-Hansen *et al.* 2007, Tyndall & Rathore 2008, Durack *et al.* 2011, Liang *et al.* 2012, Patel *et al.* 2012).

It is the clinician's responsibility to justify each radiographical exposure on an individual needs basis; the potential benefits should outweigh the risks (ICRP 2007). In addition, the radiation exposure should be 'as low as reasonably achievable' (ALARA) (Farman 2005, ICRP 2007). CBCT generates a typically lower effective dose when compared to medical CT (Ludlow *et al.* 2003, Suomalainen *et al.* 2009, Pauwels *et al.* 2012). However, the patient is still exposed to higher effective doses compared to intraoral periapical imaging.

Several different CBCT scanners are available on the market, and they differ in respect to tube current/voltage, exposure time, field of view and degree of rotation of the gantry around the patient's head. The radiation dose and image quality are dependent to a great extent on these factors (Durack & Patel 2012). CBCT manufacturers often recommend exposure protocols that ensure having high quality images with little noise, despite the fact that such protocols are associated with higher exposure radiation (Neves *et al.* 2014). Some of these exposure parameters can be modified depending on the CBCT system. Adjustment of these settings can significantly reduce the exposed radiation doses; however, the image quality might be degraded (White & Mallya 2012).

Current CBCT scanners including the Morita 3D Accuitomo (J Morita Corporation, Osaka, Japan) can generate 3D volume of data by half (180°) or full (360°) rotation of the X-ray gantry around the patient's head (Patel 2009). Although both CBCT rotations have the same voxel resolution (0.125 mm), they generate different numbers of basic projections required to reconstruct three dimensional images. During the 360° rotation of the gantry, 586 basic projections images are usually generated in the 17.5-s scan time whilst the 180° rotation reduces the number of projections to only 329 slice and the exposure time to 9 s, therefore reducing the exposed radiation dose by approximately half.

Recent studies have demonstrated that reducing the arc of rotation of the scanner from 360° to 180° provided images with similar diagnostic accuracy to 360° scans in the detection of artificial bone lesions (Lennon *et al.* 2011) and external root resorption (Durack *et al.* 2011). This adjustment from 360° to 180° arc of rotation effectively reduces the radiation dose by 50% (European Commission 2012).

Whilst scanning most CBCT devices maintain constant tube current (mA) throughout the rotation angles. The 3D Accuitomo (J Morita) CBCT scanner has the ability to apply a dose reduction (DR) feature during the 180° and 360° rotation resulting in reduced radiation dose for the same number of basic projections. According to the manufacturer (J Morita), the DR mode is a pre-programmed profile of tube current (mA) adjustment that reduces the effective dosage by up to 40% in comparison with the standard dose programme. During the standard dose mode, the intensity of the tube current (mA) is fixed during the whole gantry rotation, whereas the intensity of mA during the DR mode fluctuates according to the position of the X-ray gantry in relation to the patient's head. Therefore, as the X-ray beam is passing from the patient's left to right side (0° angle), where bone and soft tissues thicknesses are the lowest, the tube current is at the minimum value. As the rotation angle of the gantry increases to 90°, the X-ray beam passes from patient's anterior to posterior side, where bone and soft tissues thicknesses are the highest, the tube current increases to the maximum value selected previously on the control panel. The mA value then reduces again as the rotation angle approaches 180°.

The aim of this study was to investigate, in an *ex vivo* model, the diagnostic accuracy of periapical radiography and CBCT on the detection of simulated periapical lesions in human dry mandibles and to investigate the influence of using CBCT dose reduction mode on the detection ability. The null hypothesis was that periapical radiographs and both CBCT dose modes would show no difference in the detection of simulated periapical lesions.

Materials and methods

Subject material preparation

Fourteen unrestored mandibular first and second molars belonging to 10 dry human mandibles provided by the Department of Anatomy and Human

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Sciences (King's College, London, UK) were used. Screening radiographs and CBCT scans were taken to confirm that there were no existing periapical lesions associated with the assessed teeth.

Prior to tooth extraction and radiological imaging, each mandible was rehydrated with soapy water (Fairy Liquid Original, Procter and Gamble, Weybridge, UK) for 90 min to decrease the surface tension, increase the resilience and reduce the possibility of root fracture during tooth extraction (Patel *et al.* 2009a). The crowns of the molars teeth were sectioned through the furcation, using a tapered 557-diamond bur (Dentsply, Addlestone, UK), in a high-speed hand-piece (W&H, St Albans, UK). Following crown sectioning, the distal roots of the molars teeth were carefully extracted with a forceps (Henry Schein, Langen, Germany).

A dental operating microscope (G9 Global Surgical, St. Louis, MO, USA) was used to detect apical pathosis at the base of the socket or any defects that might have been caused by the extraction procedure. Three mandibles containing three teeth with detectable defects were discarded. The roots were then replanted, and control radiographs and CBCT scans were acquired before the creation of the lesions.

Simulated periapical lesions were prepared into the cancellous bone at the base of the socket of the distal root of the molars using 100 and 160–191R pulp chamber burs (Meissenger, Häger & Meissenger, Neuss, Germany) with a diameter of 0.85 mm and 1.5 mm, respectively, in a slow hand-piece (W&H) to the depth of its head. The dimensions of the simulated lesions used in this study were designed according to the findings of a recent *ex vivo* study (Tsai *et al.* 2012).

To calculate the depth of the tooth socket, the pulp chamber bur was oriented along the longitudinal axis of the tooth into the full depth of the socket; then, the bur shank was marked at the crestal level of bone. The length of the bur head was measured using a measuring microscope (EZ measurement system; Starett Kinemetric, Laguna Hill, CA, USA) at 7× magnification and added to the length of the tooth socket obtained previously. The bur shank was remarked with the new settings prior to cavity drilling.

The bur was adjusted within the long axis of the root and drilling stopped as soon as the bur marking matched with the crestal bone level. A dental operating microscope (Global Surgical) was used during lesions preparation to ensure accurate depth of the cavities. 'Small' lesions (0.85 mm in diameter and 1.0 mm in width) were created, the roots were then relocated into the extraction sockets, and the mandibles were rehydrated. Periapical radiographs and CBCT scans of mandibular teeth were repeated (Figs 1–3). The teeth were then removed from their sockets, and the 160–191R bur (Meissenger) was used to create the 'large' lesions (1.5 mm in diameter and 1.5 mm in depth) by enlarging the existing lesion dimensions, and the scans were repeated as described previously. Three mandibular molars in three dry mandibles were damaged during lesion preparation and were discarded.

Radiographic technique

Two custom designed jigs were made for each mandible to allow standardized reseating of the mandibles during each stage of the imaging. The jig designed for periapical radiographs enabled the teeth within the mandible to be situated at a fixed distance of 35 cm from the X-ray source. Customized silicone templates were created by entirely positioning the inferior margin of the mandible within a polyvinyl siloxane material (Aquasil, Dentsply DeTrey, Konstanz, Germany) mounted onto a plastic rotating disc to ensure reproducible and precise repositioning of each mandible into its own putty template during every stage of radiographic scanning.

A digital phosphor plate system (Digora® Optime; Soredex, Tuusula, Finland) was used in conjunction with a beam aiming device (Dentsply Rinn, Elgin, IL, USA) and a dental X-ray unit (Heliodent; Sirona, Bensheim, Germany) operating at 65 kV, 7 mA and 0.16 s. Parallel and parallax radiographs (10° mesial and 10° distal angulations) were taken. The parallax radiographs were taken with the aid of a protractor attached to the rotating disc. A 10-mm-thick acrylic sheet (Plexiglas®; Evonik Industries AG, Essen, Germany) was used to mimic the attenuation of X-ray beam by soft tissue encountered clinically (Noujeim *et al.* 2009, Durack *et al.* 2011).

A small volume CBCT scanner (3D Accuitomo, J. Morita) with a 4 × 4 cm field of view (FOV) and 0.125 mm of voxel size were used to obtain CBCT images. Manufacturer's standard exposure protocol for mandibular posterior teeth (tube voltage of 90 kV, and a tube current of 4 mA) was used whilst scanning. All CBCT data were reconstructed with 0.16-mm slice intervals and 1.2-mm slice thickness. During 360° and 180° rotations, the mandibles were scanned using standard dose mode and dose reduction (DR) mode.

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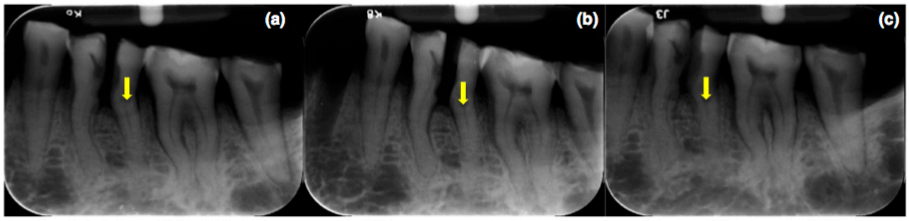

Figure 1 Parallel (a) and parallax (b, c) digital periapical radiographs following the creation of the small simulated periapical lesion on the distal root indicated with arrows.

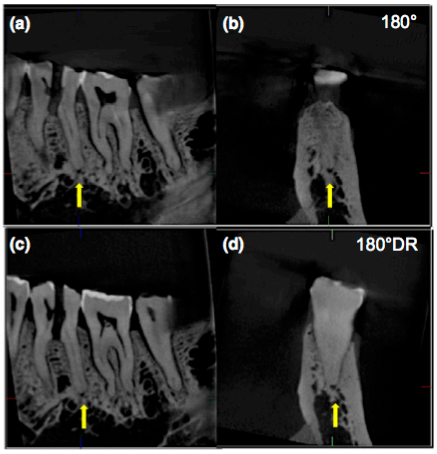

Figure 2 Sagittal and coronal reconstructed 180° CBCT image with dose reduction mode (a, b) and standard full dose showing small simulated periapical lesions (c, d).

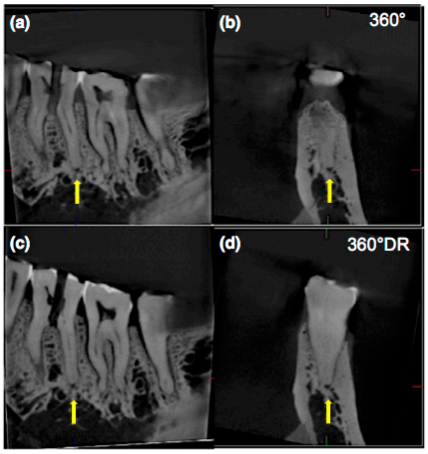

Figure 3 Sagittal and coronal reconstructed 360° CBCT image with dose reduction mode (a, b) and standard full dose showing small simulated periapical lesions (c, d).

A special jig was used to allow the mandibles to be seated correctly during the CBCT scans. The jig consisted of individual silicone template placed over a plastic platform of 8 cm in diameter with a metal dowel rod of 2 cm in length was secured to the centre of its lower surface. The jig was positioned instead of the scanners chin rest by means of the dowel attachment.

Radiographic assessment

Six examiners (2 endodontists, 1 radiologist and 3 senior endodontic postgraduate students) individually assessed a total of 99 periapical radiographs and 132 CBCT scans in four sessions: (i) all radiographs and 66 CBCT 360° scans examination (both exposure modes); (ii) 66 CBCT 180° scans examination (both exposure modes); (iii) repeat all radiographs and all 360° scans; and (iv) repeat all CBCT 180° scans. Sessions 3 and 4 were carried out after 2 weeks to assess intra-examiner agreement.

For the CBCT scans, the brightness and contrast of the slice that showed the widest diameter of the periapical lesion in sagittal and coronal planes were optimized using the Accuitomo viewing software (i-Dixel images, J. Morita) for best visualization by the examiners. After optimization, the data were exported as bmp format files. For the data to be viewed by the examiners, the images were randomly ordered in each session using a computer-specialized software and presented as a PowerPoint® presentation (Microsoft®,

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Redmond, WA, USA) on a laptop computer (MacBook Pro®; Apple, Cupertino, CA, USA) with a screen pixel resolution of 1280 × 800. Raw CBCT data were accessible to the examiners when they intended to examine the orthogonal scans to assist in lesion detection. The examiners were blinded to whether or not a lesion was present and to whether the scans were obtained with standard dose mode or DR mode. All examination sessions were carried out in a quiet, dark room, and no time limit has been set for the examiners.

All examiners had considerable experience in interpreting CBCT images and were calibrated using examples of radiographs and CBCT images for some of the excluded mandibles with and without the presence of periapical lesions prior to embarking the assessment. The examiners were asked to score the presence or absence of simulated periapical lesions using a 5-point confidence scale to score the appearance of the lesions: 1: definitely absent; 2: probably absent; 3: uncertain, 4: probably present; 5: definitely present.

Statistical methodology

SPSS software (SPSS version 22; IBM, New York, NY, USA) was used to analyse the raw data. The diagnostic accuracy of each imaging modality for detecting the presence or absence of a periapical lesion was analysed to determine their sensitivity, specificity, receiver operating characteristic (ROC) area under the curve, positive and negative predictive values (PPV, NPV) using paired *t*-tests. Inter-examiner and intra-examiner agreement were analysed using kappa statistics on the basis of two repeats for 100% of the radiographs and CBCT scans.

Results

Seven mandibles containing 11 first and/or second molars were finally used in this study. Mean sensitivity and specificity for radiographs and CBCT for detecting small and large lesions are presented in Tables 1–3. Regardless of simulated periapical lesion size, the overall sensitivity of periapical radiography (0.37) was significantly lower ($P < 0.001$) compared to 360° (0.96), 360° with DR mode (0.96) scans, 180° (0.93) and 180° with DR mode (0.95) scans. There was no significant difference in the sensitivity and specificity between the standard dose scans and DR scans for both CBCT rotations.

Positive predictive value and negative predictive value for radiographs and CBCT for detecting small and large lesions are presented in Tables 1–3. No significant differences were detected in the PPV, NPV between both standard dose and DR scans for both 360° and 180° scans. The ROC analysis (Tables 1–3) revealed that there was no significant difference in the diagnostic accuracy of 360° full dose and 360° with DR in detecting small ($P = 0.616$) and large ($P = 0.606$) simulated periapical lesions. Similarly, between 180° full dose and 180° with DR, there was no significant difference in the accuracy of detecting small ($P = 0.234$) and large ($P = 0.360$) simulated periapical lesions, whilst CBCT accuracy was significantly different when compared with that of intraoral radiography.

The kappa values for inter-examiner agreement were 0.15 for periapical radiography, 0.71 and 0.77 for 360° scan with standard and DR modes, respectively; the values for 180° scans with standard and DR modes were 0.80 and 0.88, respectively ($P < 0.01$). The mean intra-examiner agreement value was 0.434 for periapical radiography and 0.85,

Table 1 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for radiographs and CBCT for detecting periapical lesions (small and large lesions pooled together)

	Sensitivity	Specificity	PPV	NPV	ROC
PA	0.37* (0.15)	0.85 (0.17)	0.85 (0.12)	0.41* (0.04)	0.62* (0.07)
360°	0.96 (0.03)	0.91 (0.08)	0.96 (0.04)	0.91 (0.06)	0.94 (0.05)
360° DR	0.96 (0.05)	0.93 (0.68)	0.96 (0.03)	0.93 (0.09)	0.95 (0.05)
180°	0.93 (0.09)	0.96 (0.08)	0.98 (0.04)	0.90 (0.13)	0.95 (0.05)
180° DR	0.95 (0.07)	0.99 (0.08)	0.99 (0.02)	0.91 (0.10)	0.97 (0.04)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic: PA, periapical radiograph; DR, dose reduction.
*Significantly different from 360° and 180° CBCT ($P < 0.001$).

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Table 2 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for radiographs and CBCT for detecting small periapical lesions

	Sensitivity	Specificity	PPV	NPV	ROC
PA	0.27* (0.20)	0.86 (0.18)	0.75 (0.29)	0.55* (0.05)	0.56* (0.08)
360°	0.91 (0.06)	0.91 (0.08)	0.91 (0.08)	0.91 (0.06)	0.92 (0.05)
360° DR	0.92 (0.11)	0.92 (0.07)	0.93 (0.07)	0.93 (0.09)	0.92 (0.07)
180°	0.88 (0.18)	0.96 (0.08)	0.96 (0.07)	0.91 (0.13)	0.92 (0.08)
180° DR	0.91 (0.10)	0.99 (0.04)	0.99 (0.04)	0.92 (0.08)	0.95 (0.05)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic; PA, periapical radiograph; DR, dose reduction.
*Significantly different from 360° and 180° CBCT ($P < 0.001$).

Table 3 Mean (SD) values of sensitivity, specificity, PPV, NPV and ROC for radiographs and CBCT for detecting large periapical lesions

	Sensitivity	Specificity	PPV	NPV	ROC
PA	0.47* (0.17)	0.86 (0.18)	0.83 (0.20)	0.62* (0.07)	0.66** (0.10)
360°	1.00 (0.00)	0.91 (0.08)	0.92 (0.07)	1.00 (0.00)	0.95 (0.05)
360° DR	1.00 (0.00)	0.92 (0.07)	0.93 (0.06)	1.00 (0.00)	0.96 (0.04)
180°	0.99 (0.04)	0.96 (0.08)	0.96 (0.07)	0.99 (0.03)	0.97 (0.04)
180° DR	0.99 (0.04)	0.99 (0.04)	0.99 (0.03)	0.99 (0.03)	0.99 (0.02)

SD, standard deviation; PPV, positive predictive value; NPV, negative predictive value; ROC, receiver operator characteristic; PA, periapical radiograph; DR, dose reduction.
*Significantly different from 360° and 180° CBCT ($P < 0.01$).
**Significantly different from 360° and 180° CBCT ($P < 0.001$).

Table 4 Kappa values for intra- and inter-examiner agreement in reading radiographs and CBCT four modalities images

		Intra-examiner Kappa score			
		CBCT 360°		CBCT 180°	
Examiner	Radiographs	No DR	DR	No DR	DR
1	0.10	0.76	0.94	0.94	0.94
2	0.84	0.88	0.94	0.94	0.88
3	0.40	0.82	0.81	0.79	0.94
4	0.30	0.81	0.93	0.82	1.00
5	0.38	0.81	0.70	0.77	0.82
6	0.60	1.00	1.00	0.94	1.00
Mean (SD)	0.43* (0.26)	0.85 (0.09)	0.89 (0.11)	0.88 (0.10)	0.93 (0.07)
Inter-examiner kappa score	0.15*	0.71	0.77	0.80	0.88

SD, standard deviation; DR, dose reduction.
*Significantly different from 360° and 180° CBCT ($P < 0.01$).

0.89, 0.88 and 0.93 for 360° scan with standard and DR modes and 180° scan with standard and DR modes, respectively ($P < 0.01$) (Table 4).

Discussion

In the present study, the effect of built-in DR mode in 3D Accuitomo (J Morita) CBCT machines on the diagnostic accuracy of both 360° and 180° scans for the detection of small and large simulated periapical lesions created in human dry mandibles was determined.

A previous study demonstrated that CBCT devices had good accuracy in detecting lesions between 0.8 mm and 1.4 mm in diameter whilst the accuracy was poor when detecting simulated lesions smaller than 0.8 mm in diameter (Tsai *et al.* 2012). It is therefore clinically relevant to assess the effect of applying the dose reduction protocol on the diagnostic accuracy to detect the smallest lesion that the CBCT

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can readily visualize with fair to good quality. Thus, two simulated periapical lesion were used in the present study, small (0.85 mm diameter and 1.0 mm depth) and large (1.5 mm diameter and 1.5 mm depth).

Although the use of human cadavers model would be more representative of the clinical situation, it was not possible to use human cadavers in this study due to the restrictions under the United Kingdom Human Tissue Act (2004); therefore, human dry mandibles were used instead. Chemically induced periapical lesions demonstrate diffuse borders radiographically that more closely resemble naturally occurring periapical lesions (Koenig *et al.* 2004, Soğur *et al.* 2009). However, it would be difficult to have small size standardized lesions using the chemical technique. Simulated lesions prepared using a bur do not mimic the diffuse border of naturally occurring lesions (Petersson *et al.* 2012), and the density between the surrounding bone and the outer border of the lesion is quite distinguishable (Lee & Messer 1986), which would improve the detectability of simulated lesions in comparison with naturally occurring lesions (Lee & Messer 1986, Soğur *et al.* 2009, Liang *et al.* 2014). However, creating lesions with a bur permitted accurate control of the dimensions of the bony cavity, allowing good standardization, which is desirable when assessing the accuracy of two different X-ray modalities (Patel *et al.* 2009a, Tsai *et al.* 2012).

In the clinical settings, the presence of radiographical artefacts related to the X-ray beam affect the diagnostic yield of the final reconstructed images. Scattering, beam hardening (Mora *et al.* 2007, Soğur *et al.* 2007) and motion artefacts (Schulze *et al.* 2015) are significant artefacts, which can influence the image quality and diagnostic accuracy of CBCT image. Scattering and beam hardening caused by differential absorption of X-ray beam by very high-density structures, such as enamel, metallic restorations and dental implants (Scarfe & Farman 2008). Patient motion such as shaking or patient's breathing during the scan can reduce the spatial resolution 'motion blur' resulting in deterioration of the 3D volume data that may cause incorrect interpretation (Hanzelka *et al.* 2013, Spin-Neto *et al.* 2013). However, reproducing these artefacts was not relevant to the main aim of this *ex vivo* study.

To simulate the clinical situation, all mandibles were hydrated in water before scanning (Patel *et al.* 2009a) and a 10-mm-thick acrylic plate (Evonik) was placed in front of the X-ray source to absorb and scatter radiation in a similar way to the presence of oral hard and soft tissues, as successfully used by earlier studies (Noujeim *et al.* 2009, Kamburoğlu *et al.* 2010, Durack *et al.* 2011). Although using dry mandibles might be considered as a limitation compared to actual patient mandible, a pilot study revealed that the images generated using standard exposure settings together with a 10-mm-thick tissue-equivalent acrylic plate were comparable to corresponding clinical images from patients.

In the present study, comparison of the standard CBCT exposure and DR mode demonstrated no significant differences in the overall sensitivity, specificity, PPV, NPV and ROC value for both lesion sizes, whereas the sensitivity, NPV and ROC values of the periapical radiography were significantly lower compared to both CBCT scan modalities.

Sensitivity and specificity of 360° (0.96, 0.93) and 180° (0.95, 0.99) scans with DR mode to diagnose both small and large lesions were higher than 360° (0.96, 0.91) and 180° (0.93, 0.96) scan with standard dose mode, respectively. In this study, dose reduction scans had an accurate diagnostic quality to detect apical periodontitis due to the fact that the intensity of the X-rays during the DR mode is optimized according to the bone thickness and the position of the X-ray tube in relation to the skull. This minimizes overexposure for easily penetrated tissue resulting in more optimized image quality with fewer artefacts compared to standard exposure scans.

The results of the present study are in agreement with other studies (Stavropoulos & Wenzel 2007, Patel *et al.* 2009a, de Paula-Silva *et al.* 2009, Soğur *et al.* 2009), which indicate that intraoral radiography had a lower sensitivity 0.37 in detecting periapical lesions regardless of the lesion size whilst the specificity was 0.85. Stavropoulos & Wenzel (2007) reported that the sensitivity of CBCT (NewTom 3G) to detect mechanically created periapical defects in pig jaws was twice as high as that for intraoral radiographs. Petersson *et al.* (2012) evaluated in a systematic review the diagnostic accuracy of different radiographic methods in the detection of the presence/absence and changes over time of periapical bone lesions. The authors reported that the mean sensitivity and specificity values for periapical radiographs for all groups of teeth reached 0.55 and 0.98, respectively. In the current study, the lower overall sensitivity value for PA (0.37) probably reflects the difficulty in detecting a very small artificial lesion size

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(0.85 mm depth × 1.00 mm width). However, the periapical radiographs sensitivity reported in the present study for diagnosing the presence of large simulated periapical lesions (0.47) favourably compare with the findings of Petersson *et al.* (2012). Furthermore, the mean sensitivity and specificity values demonstrated by Petersson *et al.* (2012) represented 19 different studies, with each having its own methodology, different mandibles, body part, lesions size, different scanners, perhaps different examiner experience between the countries where these studies were performed (Petersson *et al.* 2012). None of these studies has investigated the detection of artificially created bone lesions smaller than 1 mm in size. Tsai *et al.* (2012) investigated the diagnostic accuracy of two CBCT machines and periapical radiography to detect artificially created apical lesion smaller than 1 mm and reported that the specificity for periapical radiography was 0.75 and the overall ROC value was 0.58, which are comparable to the findings of the present study (Tsai *et al.* 2012).

Regardless of the exposure settings selected, the sensitivity for CBCT scans was in accordance with the findings of previous investigations (Patel *et al.* 2009a, de Paula-Silva *et al.* 2009, Liang *et al.* 2014). Patel *et al.* (2009a) and Liang *et al.* (2014) reported that CBCT scans are 100% accurate in diagnosing the presence of small and large simulated periapical lesions in dry mandibles, whilst the sensitivity of intraoral radiography was 0.24 and 0.67, respectively. de Paula-Silva *et al.* (2009) investigated the sensitivity and specificity of CBCT in detecting apical lesions on teeth in dog whilst using the histopathological examination as a reference standard. The authors reported a sensitivity of 0.91 and 0.77 for CBCT and intraoral radiography, respectively.

In the present study, the accuracy of the CBCT to confirm the absence of artificial bony cavities was less than 100% as the detection of small periapical radiolucencies was probably affected by the sparse trabeculation of cancellous bone. However, the specificity of CBCT was higher ($P > 0.05$) than the specificity of periapical radiography. Hedeşiu *et al.* (2012) demonstrated that the specificity ranged from 60% to 77% whilst they assessed the diagnostic accuracy of three different CBCTs with different FOV in detecting simulated periapical lesions (Hedeşiu *et al.* 2012). The authors believed that the reason behind this poor specificity might be related to the presence of more anatomical bone spaces and varied periapical anatomy compared to human dry mandibles.

The overall PPV for both 360° and 180° CBCT scans compare favourably with the values demonstrated by an *ex vivo* study (Lennon *et al.* 2011) investigating the influence of using half-scan mode (180°) on the diagnostic accuracy to detect small artificially created apical lesions. The authors reported a PPV of 89.1% and 93.2% for the 360° and 180° scans, respectively. de Paula-Silva *et al.* (2009) reported a PPV value of 1.0 when they evaluated the accuracy of CBCT against periapical radiography in diagnosing apical periodontitis. Whilst the NPV for the 360° and 180° dose reduction scans were 0.931 and 0.913, respectively, which compare favourably with the values (1.0) demonstrated by (Patel *et al.* 2009a, Liang *et al.* 2014). However, the present study values were considerably higher than those of Lennon *et al.* (2011), which reported NPV for the 360° and 180° scans of 76% and 74.3%, respectively.

Regardless of the lesion size, the ROC values for both CBCT rotations with DR mode were higher than the CBCT with standard dose mode confirming the high diagnostic accuracy of the scans with DR feature. The overall ROC values for all CBCT scans modalities were equivalent to the findings of a similar study (Patel *et al.* 2009a, Tsai *et al.* 2012). The intra-examiner agreement was higher for DR (0.89–0.93) scans compared to that of standard dose (0.85–0.88) scans. Similarly, the inter-examiner agreement for DR scans (0.77–0.88) was higher than that of standard dose (0.71–0.80) scans. This better level of performance in assessing CBCT DR scans was due to minimizing the overexposure of easily penetrated tissues that resulted in sharper images of soft tissue with fewer artefacts.

Brown *et al.* (2009) reported that reducing the number of image projections to construct 3D images did not lead to reduced dimensional accuracy of 3D measurements whilst potentially reducing the radiation dose to the patient (Brown *et al.* 2009). Dawood *et al.* (2012) examined the possibility of reducing radiation dose using variable exposure parameters, including the 180° rotation, whilst evaluating patient's implant site. They demonstrated that the level of confidence in the diagnostic yield of the images was only marginally affected by the lower dose protocols whereas the patient dose was potentially reduced during implant site evaluation (Dawood *et al.* 2012).

In scenarios where patients have poorly localized symptoms associated with teeth with suspected endodontic disease and clinical and periapical

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radiographic examination show no evidence of disease, CBCT may be indicated to confirm the presence of previously undiagnosed pathosis (Patel *et al.* 2015). CBCT may also be indicated to help confirm the absence of an odontogenic aetiology of pain when managing nonodontogenic causes of pain (Patel 2009, Patel *et al.* 2014). The effective radiation dose from CBCT scan is higher compared to conventional digital radiography; hence, it is essential to choose smallest FOV and optimal exposure ALARA.

Conclusion

There was no difference in the overall accuracy between 360° DR and 180° DR when compared to the control standard dose scans. The CBCT scans with DR feature maintained good diagnostic accuracy and image quality for detecting the presence of small simulated periapical lesions whilst markedly reducing the radiation dose by 54% during the full-arc rotation (360°) and by 51% during the half arc rotation (180°). Therefore, the radiation dose reduced by up to 74% between 360° standard dose and 180° DR mode. Further studies could potentially confirm the present results clinically, which may provide greater weight to the benefits of using dose reduction protocol on patients.

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The authors deny any conflict of interest related to this study.

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A prospective study assessing the effect of coronal tooth structure loss on the outcome of root canal retreatment

N. Al-Nuaimi[1,3], S. Patel[1,4], R.S. Austin[2,5], F. Mannocci[1]

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Running Title: Retreatment outcome and remaining coronal tooth structure

Keywords: Remaining coronal tooth structure, outcome of root canal retreatment, cone beam computed tomography, periapical lesions

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Accepted Article

International Endodontic Journal
The Official Journal of the British Endodontic Society and the European Society of Endodontology

Pooled analysis of 1-year recall data from three endodontic treatment outcome studies undertaken using cone beam computed tomography

Journal:	*International Endodontic Journal*
Manuscript ID	IEJ-16-00730
Manuscript Type:	Original Scientific Article
Keywords:	Primary root canal treatment, root canal retreatment, treatment outcome, cone beam computed tomography, periapical lesions

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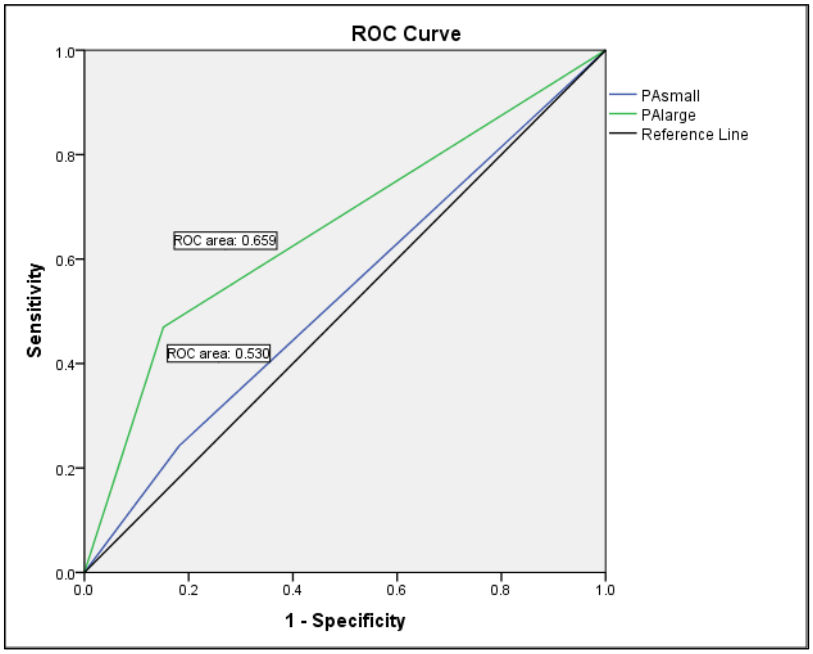
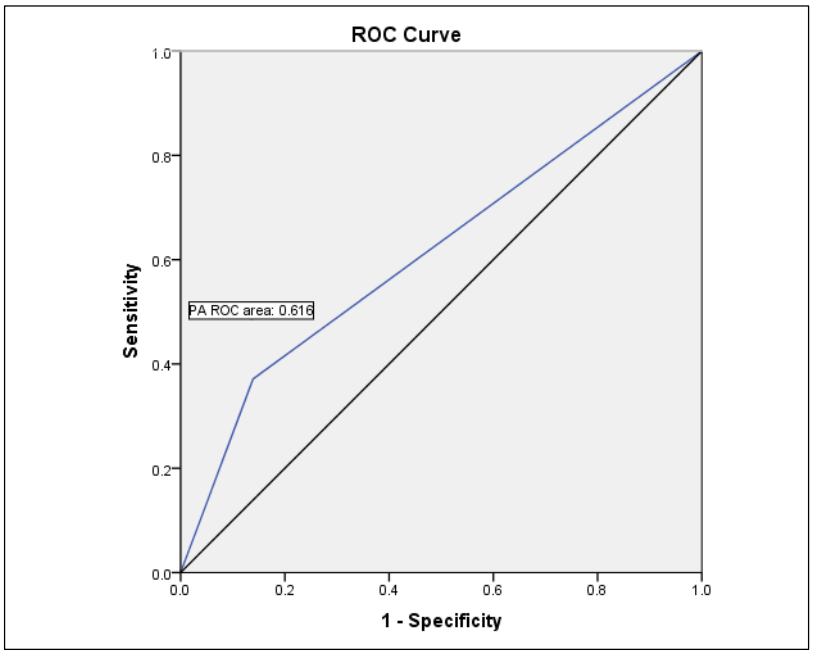
For Review

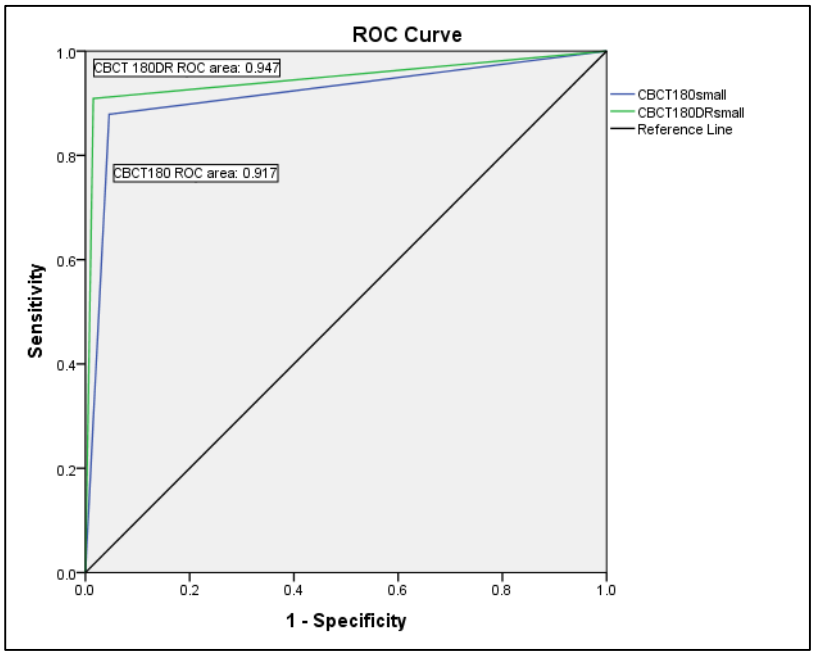
Appendix II: Receiver operating characteristics curves for detection of simulated periapical lesions



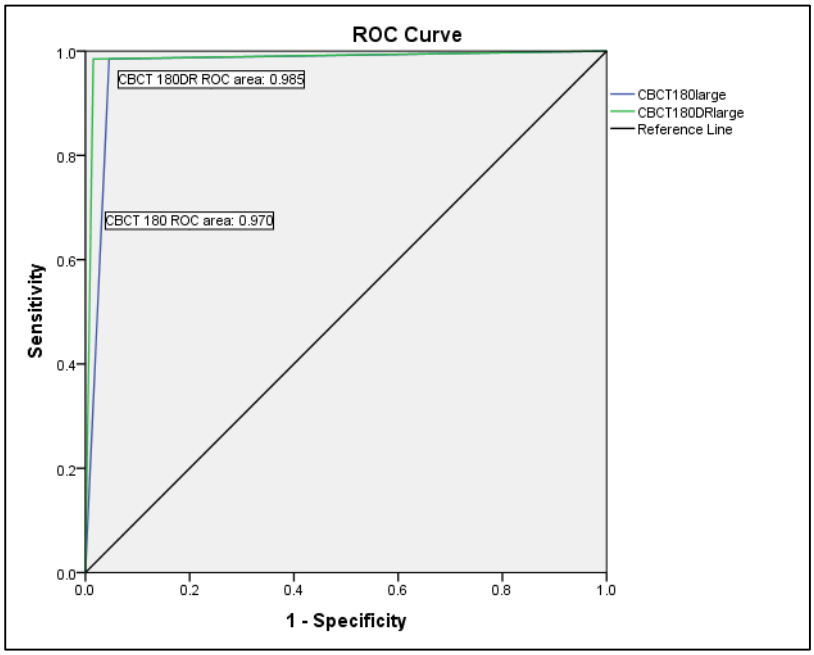
Receiver operating characteristics (ROC) curves for detection of both small (0.85 mm) and large (1.5 mm) periapical lesions with periapical radiographs (PA).



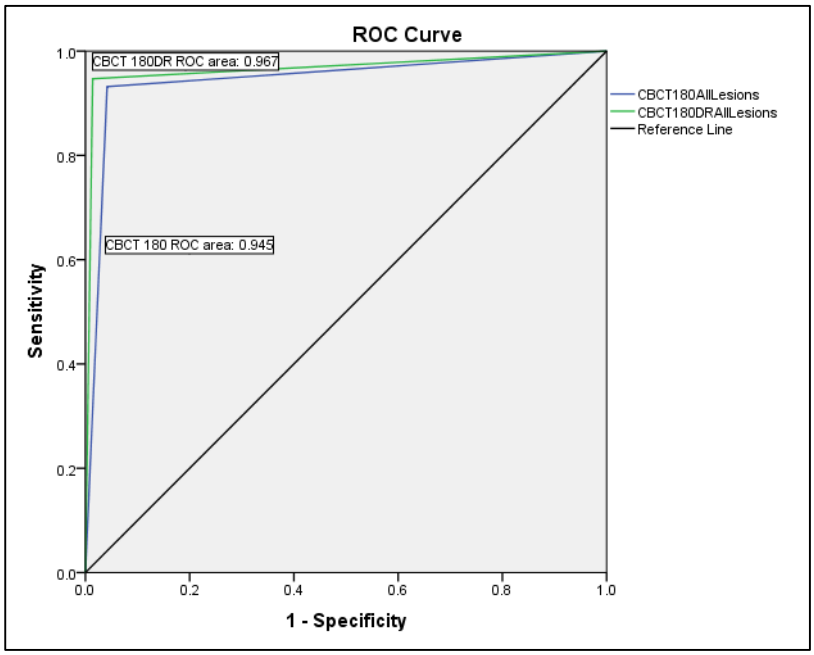
Receiver operating characteristics (ROC) curves for detection of small and large periapical lesions pooled together with periapical radiographs (PA).



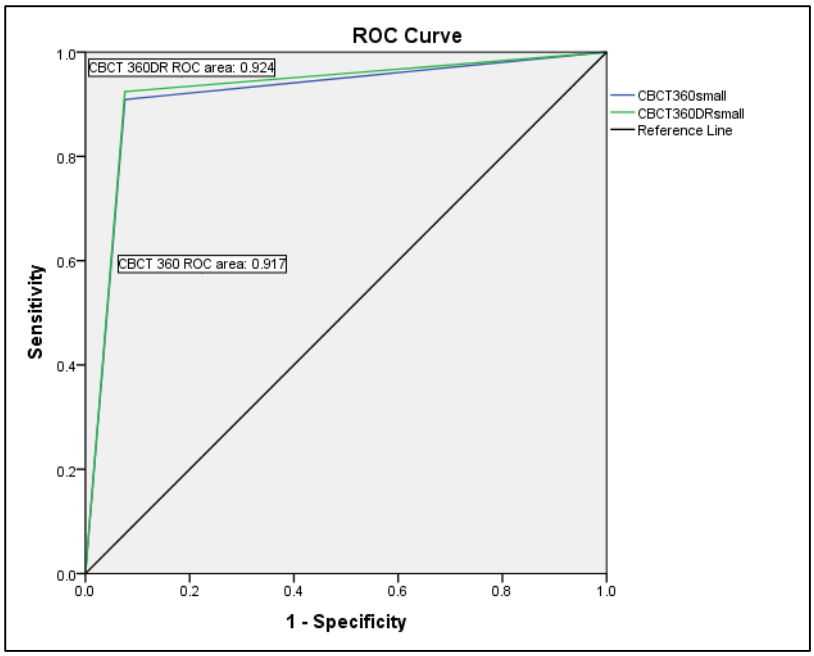
Receiver operating characteristics (ROC) curves for detection of small periapical lesions with CBCT 180° (full dose and dose reduction [DR]).



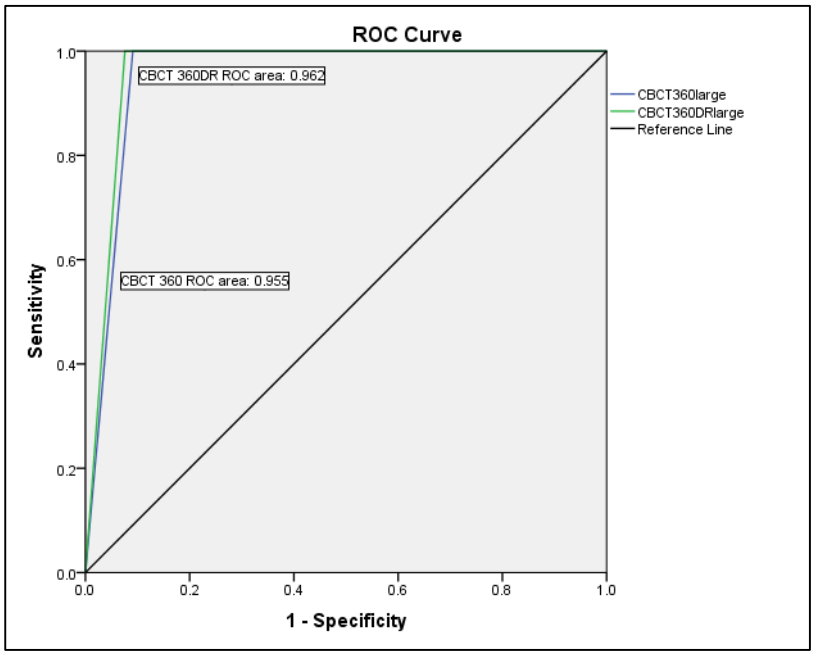
Receiver operating characteristics (ROC) curves for detection of large periapical lesions with CBCT 180° (full dose and dose reduction [DR]).



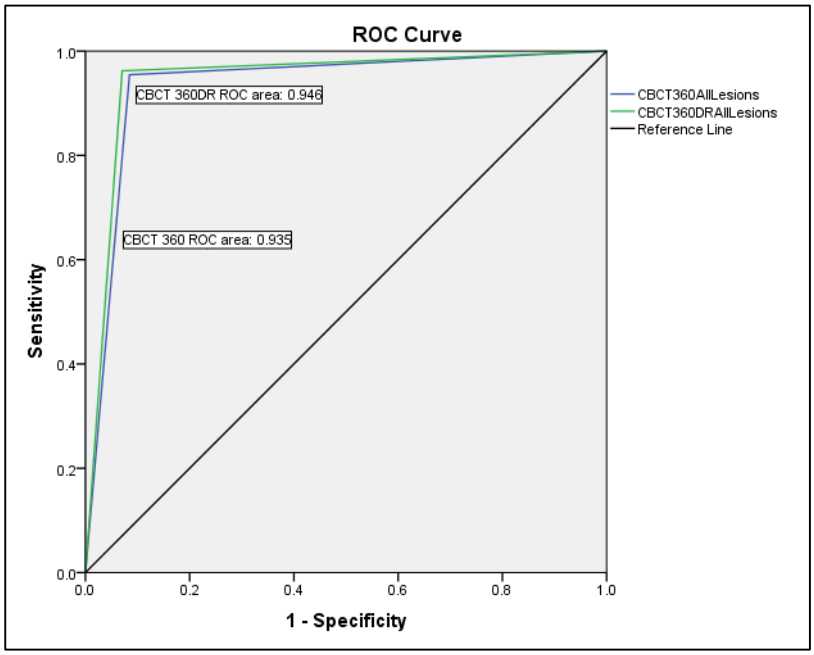
Receiver operating characteristics (ROC) curves for detection of small and large periapical lesions pooled together with CBCT 180° (full dose and dose reduction [DR]).



Receiver operating characteristics (ROC) curves for detection of small periapical lesions with CBCT 360° (full dose and dose reduction [DR]).



Receiver operating characteristics (ROC) curves for detection of large periapical lesions with CBCT 360° (full dose and dose reduction [DR]).



Receiver operating characteristics (ROC) curves for detection of small and large periapical lesions pooled together with CBCT 360° (full dose and dose reduction [DR]).

Appendix III: Research Ethics Committee approval letter

NHS
Health Research Authority

NRES Committee London - West London & GTAC
Nottingham REC Centre
The Old Chapel
Royal Standard Place
NG1 6FS

Telephone: 0115 8839311
Facsimile: 0115 8839294

23 August 2013

Mr. Nassr Al-Nuaimi
King's College London Dental Institute
Biomaterial Department, Guy's Hospital
Floor 17, Tower Wing
SE1 9RT

Dear Mr. Al-Nuaimi

Study title:	**The survival of teeth following root canal re-treatment with varying degrees of tooth structure loss.**
REC reference:	**13/LO/1171**
Protocol number:	**N/A**
IRAS project ID:	**127295**

The Research Ethics Committee reviewed the above application at the meeting held on 14 August 2013. Thank you for attending to discuss the application with Professor Mannocci .

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the Co-ordinator Miss Andrea Graham, nrescommittee.london-westlondon@nhs.net.

The Committee has considered and reviewed the project as research and given the ethical opinion detailed below. However, we are of the view that the project would be more appropriately classified as service evaluation rather than research. We suggest that you discuss the matter with the sponsor and lead R&D office, and following that discussion advise the REC how it is intended to manage the project. If the sponsor and R&D office advise that the project can now be considered not to be research the application should be withdrawn. If it will continue to be managed as research, the opinion given below will remain in place.

Ethical opinion

- The Chair introduced herself to the Researchers, thanked them for their submission and asked them to introduce themselves to the Committee.
- The Committee explained the Study was relatively straightforward.
- The Committee asked the Researcher whether they would be carrying out the dental work anyway. The Researchers explained they would be but these Participants would be

having more scans.

- The Committee asked the Researchers whether there would be any additional visits. The Researchers confirmed there would not be.
- The Researchers were asked who would take consent and when. The Researchers explained the Study would be explained at the appointment when the diagnosis is made and consent would be signed at the next appointment.
- The Committee asked the Researchers why they are not using interpreters. The Researchers explained it was to speed things up. The Committee explained they would expect the study where possible to reflect as wider population as possible. The Researchers explained it is rare in their clinic that a Patient would need an interpreter. However the Researchers agreed they would provide an interpreter if needed.
- The Committee discussed with the Researcher whether this is more Service Evaluation than Research. The Researchers explained they will spot failures with the CT which they would not otherwise have spotted. The Committee explained that it was common to evaluate their procedures but could not see the Research element to their Study

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering Letter		19 July 2013
Evidence of insurance or indemnity	Gallagher Heath	01 August 2012
Investigator CV	Nassr Al-Nuaimi	12 July 2013
Letter from Statistician		10 July 2013
Other: Synopsis and flowchart of Protocol	1.0	12 July 2013
Other: CV - Professor Francesco Mannocci		12 June 2013
Other: CV - Federico Foschi		10 May 2013
Other: Medical Physics Department - Patient Radiation Dose Assessment		09 July 2013
Other: Case Report Form	1.0	12 July 2013
Participant Consent Form	1.1	12 July 2013
Participant Information Sheet	1.0	12 July 2013
Protocol	1.1	26 July 2013
REC application	127295/479093/1/480	22 July 2013

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

13/LO/1171	**Please quote this number on all correspondence**

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

With the Committee's best wishes for the success of this project.

Yours sincerely

Dr Catherine Urch
Chair

Email: nrescommittee.london-westlondon@nhs.net

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
"After ethical review – guidance for researchers"

Copy to: *Mr. Keith Brennan*
Ms Karen Igantian, Guy's & St Thomas' Foundation NHS Trust

Appendix IV: Research and Development approval letter

Guy's and St Thomas' NHS
NHS Foundation Trust

Research & Development
16th Floor Tower Wing
Guy's Hospital
Great Maze Pond
London SE1 9RT
Tel: 020 7188 7188

Mr Nassr Al-Nuaimi
KCL Dental Institute
Biomaterial Department
Floor 17, Tower Wing
Guy's Hospital
London SE1 9RT

20/09/2013

Dear Mr Al-Nuaimi

Title: The survival of teeth following root canal re-treatment with varying degrees of tooth structure loss.

In accordance with the Department of Health's Research Governance Framework for Health and Social Care, all research projects taking place within the Trust must receive a favourable opinion from an ethics committee and approval from the Department of Research and Development (R&D) prior to commencement.

- **Ethics Number:** 13/LO/1171
- **Sponsor:** KCL
- **Funder:** None
- **End Date:** 01/08/2016
- **Protocol:** Version 1.1 – 26/07/2013
- **Site:** Guy's & St. Thomas NHS Foundation Trust
- **R&D Approval Date:** 20/09/2013
- **Chief Investigator:** Mr Nassr Al-Nuaimi

NHS permission for the above research has been granted on the basis described in the application form, protocol and supporting documentation as listed in the ethics letter of favourable opinion letter dated **23/08/2013**. I am pleased to inform you that we are approving the work to proceed within Guy's and St Thomas' NHS Foundation Trust and that the study has been allocated the Trust R&D registration number **RJ113/N237**. I can confirm that from the SSI application form you have agreed to recruit **120 participants** within 3 years.

Whilst the Trust takes on non funded research without charge for sponsorship, research management and governance or research costs we encourage all research to be funded and particularly encourage UKCRN portfolio eligible research. Prior to your next research proposal please contact the R&D department about portfolio eligibility and how to gain funding for research so as to ensure that the study can gain appropriate funding prior to your research application.

Conditions of Approval:

- The principal investigator must ensure that the recruitment figures are reported.
- The principal investigator must notify R&D of the actual end date of the project.
- R&D must be notified of any changes to the protocol prior to implementation.

- The project must follow the agreed protocol and be conducted in accordance with all Trust Policies and Procedures especially those relating to research and data management.
- Members of the research team must have appropriate substantive or honorary contracts with the Trust prior to the study commencing. Any additional researchers who join the study at a later stage must also hold a suitable contract.

Data Protection:
Please ensure that you are aware of your responsibilities in relation to The Data Protection Act 1998, NHS Confidentiality Code of Practice, NHS Caldicott Report and Caldicott Guardians, the Human Tissue Act 2004, Good Clinical Practice, the NHS Research Governance Framework for Health and Social Care, Second Edition April 2005 and any further legislation released during the time of this study.

The Principal Investigator is responsible for ensuring that Data Protection procedures are observed throughout the course of the project.

Amendments:
Please ensure that you submit a copy of any amendments made to this study to the R&D Department.

ISRCTN registration:
If appropriate it is recommended that you register with the Current Controlled Trials website http://isrctn.org/. Find out more about registering for an International Standard Randomised Controlled Trial Number (ISRCTN) as part of the Portfolio application process. Non-commercial studies with an interventional component that are eligible for NIHR CRN support can register for an ISRCTN for free via the Portfolio Database.

Annual Progress Report:
It is obligatory that an annual report is submitted by the Chief Investigator to the research ethics committee, and we ask that a copy is sent to the R&D Department. The yearly period commences from the date of receiving a favourable opinion from the ethics committee.

Please submit a copy of the progress report on the anniversary of the Ethics favourable opinion **(23 August)**

Should you require any further information please do not hesitate to contact us.

In line with the Research Governance Framework, your project may be randomly selected for monitoring for compliance against the standards set out in the Framework. For information, the Trust's process for the monitoring of projects and the associated guidance is available from the Trust's intranet or on request from the R&D Department. You will be notified by the R&D Department if and when your project has been selected as part of the monitoring process. No action is needed until that time.

Thank you for registering your research project.

Yours sincerely

Jessey Bonsu
R&D Governance Coordinator

cc: Professor Francesco Mannocci

Appendix V: Clinical trial participant's information sheet

Guy's and St Thomas' NHS
NHS Foundation Trust

KING'S College LONDON

Guy's Hospital
Great Maze Pond
London SE1 9RT

PARTICIPANT INFORMATION SHEET

1. **Study title**

"The survival of teeth following root canal re-treatment with varying degrees of tooth structure loss"

2. **Invitation paragraph**

You are being invited to take part in a research study. Before you decide whether or not to do so, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information.
Take time to decide whether or not you wish to take part. *Thank you for reading this.*

3. **What is the purpose of the study?**

Dental radiographs (X-rays) are usually taken immediately after completion of treatment and on a periodic basis (review appointments), usually 1 and 2 years after treatment has been completed to assess how successful treatment has been. The amount of information gained from conventional dental radiographs is limited as the images produced are only 2 dimensional (like a photograph).
This study aims to assess the success and survival rate of teeth following root canal re-treatment procedure. Before we carry out with root canal re-treatment and at your review appointments in addition to the conventional radiograph we would also like to take an additional specialised 3-dimensional scan of the tooth. This 3-dimensional scan is called 'Cone Beam Computed Tomography (CBCT) scan' which is the latest technology for imaging teeth. It allows us to assess your tooth in 3-dimensions and therefore generates potentially more precise information about your tooth including the degree of healing. This specialised CBCT scan may give us a better understanding of the anatomy of your tooth and detect signs of periapical healing earlier than conventional radiographs, this may influence treatment planning. Review appointments will also be arranged 1 and 2 years after the completion of your root canal re-treatment. The additional scan will be taken straight after the conventional radiograph, and therefore will only add another 5-10 minutes to your appointment. The additional radiation dose from this second scan is minimal and is very similar to the conventional radiograph.
To measure the volume of tooth structure lost following endodontic re-treatment procedure, an impression of your tooth will be made. The impression will be taken straight after the completion of the endodontic re-treatment procedure and after the placement of the final restorative filling and therefore will only add another 5-10

minutes to your appointment. This study is being carried out as the researcher's partial fulfilment of the requirements for the degree of Doctor of Philosophy (PhD).

4. **Why have I been invited?**

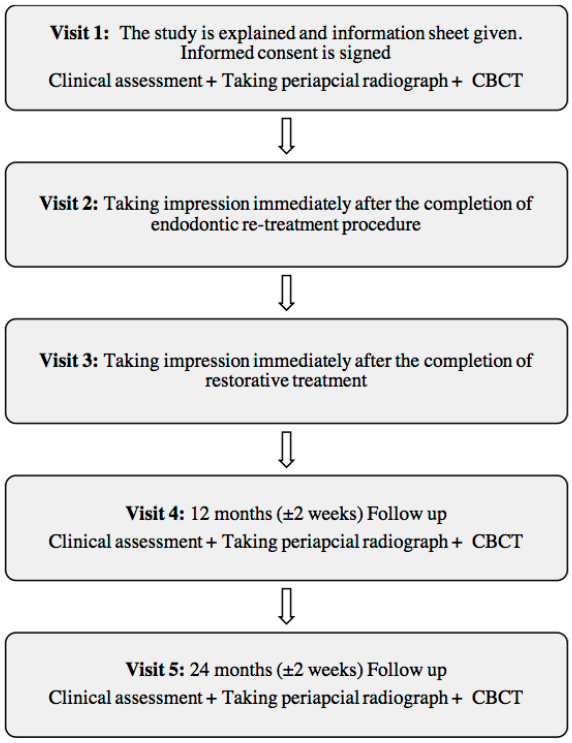
We are inviting you to take part in this study because you have a failed endodontic treatment and an endodontic re-treatment procedure is indicated in your case. This makes you suitable for this study. We hope to recruit 120 volunteers.

5. **Do I have to take part?**

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. If you do not take part in the study you will not be required to give a reason and there will be no detriment. This will not affect the standard of treatment you receive in any way.

6. **What will happen to me if I take part?**

If you decide to take part in this research your dental care will proceed as normal. The following flow chart will help you understand what will happen:



7. **What do I have to do?**

Patients who agree to take part in this study will be required to attend his/her routine dental visits to Guy's Hospital for follow-up of the endodontically treated tooth during a 24-month period as shown in the flow chart.

8. **What is the drug or procedure that is being tested?**

We are not testing any new procedure or drug under development. We are trying to compare the success and survival rate of teeth with varying degrees of tooth structure loss following endodontic re-treatment procedure. CBCT has been proved by previous research studies to detect the presence of bony disease around the tooth roots earlier than conventional X-rays. This can help improve our diagnosis and treatment plan for future patients.

9. **What are the side effects of taking part?**

There are no side effects of taking part in this study other than those expected from routine dental care.

10. **What are the possible disadvantages and risks of taking part?**

There are no disadvantages and risks of taking part in this study other than those expected from routine dental care
Every exposure to ionising radiation (X-rays) carries a risk. However, due to the low doses of radiation from dental X-rays including CBCT, this risk is negligible. Periapical X-rays are normally taken for routine dental treatment and the effective dose from this conventional X-ray is equal to 0.19% of annual background radiation. While the additional dose comes from the CBCT scan is equal to 2.43% annual background radiation. The total radiation dose corresponds to approximately 28 days equivalent natural background radiation.

11. **What are the possible benefits of taking part?**

There are no advantages to you personally from taking part. The CBCT scans could allow us to accurately and objectively assess how successful your treatment has been. And the information we get from this study may influence future treatment planning decisions.

12. **What if something goes wrong?**

If taking part in this research project harms you, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaint mechanisms may be available to you.

13. **Will my taking part in this study be kept confidential?**

Each patient will be given a unique identification number, which will be used throughout the study. All information that is collected about you during the course of the research will be kept strictly confidential and accessed only by authorised people.

14. **What will happen to the results of the research study?**

Results of this research will be published in appropriate dental and scientific journals. No personal information or other information that could be identified as relating to you will be published. You will be informed of the results of the study.

15. **Who is organising and funding the research?**

King's College London.

16. **Who has reviewed the study?**

This study will be reviewed by West London Research Ethics Committee.

17. **Summary**

You are invited to participate in this study because you have failing endodontic treated tooth that needs endodontic re-treatment procedure. After completion of endodontic re-treatment, clinical and radiographical assessment will be carried out. During the follow-up visits at 12-month and 24-month post treatment, your tooth will be examined and CBCT scans will be taken and evaluated. Also, an impression of your tooth will be taken to measure the volume of tooth structure lost following endodontic re-treatment procedure.

18. **Contact for Further Information**

For further information please contact:
Nassr Al-Nuaimi
King's College London Dental Institute
Biomaterials research group
Floor 17 Guy's Tower
SE1 9RT
Tel: 07563347311
E-mail: nassr.al-nuaimi@kcl.ac.uk

Appendix VI: Clinical trial consent form

Guy's and St Thomas' NHS
NHS Foundation Trust

KING'S College LONDON

Study Number: **13/LO/1171**
Patient Identification Number for this trial:

CONSENT FORM FOR RESEARCH STUDY
(Version 1.1/ 12-07-2013)

Title of Project: "The survival of teeth following root canal re-treatment with varying degrees of tooth structure loss**"**
Name of Researcher: Nassr Al-Nuaimi

Please write your initials to confirm

- I confirm that I have read and understood the information sheet dated **12-07-2013** (version **1.0**) for the above study. ☐
- I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
- I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
- I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from Guy's Hospital, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
- I agree to take part in the above research study. ☐

Name of Patient	Date	Signature
Name of Person taking consent (if different from researcher)	Date	Signature
Researcher	Date	Signature

1 copy for patient: 1 copy for researcher site file: 1 (original) to be kept in medical notes.

Appendix VII: Clinical trial case report form

Guy's and St Thomas' NHS
NHS Foundation Trust

KING'S College LONDON

Case Report Form

Visit One

Patient Identification Number/Code:

Date:

Demographics:

Gender	Male (0) ☐ Female (1) ☐
Date of Birth	☐☐ ☐☐ ☐☐☐☐ Day Month Year
Age	
Ethnicity	British ☐ Black ☐ Asian ☐ Hispanic ☐ Other ☐ Caucasian ☐
Occupation	
Smoking Status	Smoker ☐ Non-Smoker ☐
Alcohol Consumption	

Medical History:

Are there any medical conditions to report? Yes* ☐ No ☐ Diabetes ☐ Systemic steroid uptake ☐ *If "Yes" please describe below:

Dental History:

Presenting Complaint	
History of Presenting Complaint	Commencement: Location: Type of pain: Incidence: Duration: Initiating/Relieving factors:
Past Dental History	Previous dental treatment: How regularly do you visit your dentist? Preventive protocols do you follow?
Social History	Availability for appointments:
Habits	OH procedures/frequency: Diet: Parafunctional habits:

Full Clinical Oral Examination

Extra-Oral Examination			
	Present	Absent	Comment
Normal Facial Symmetry	☐	☐	
Normal Temporomandibular Joint	☐	☐	
Normal Lips	☐	☐	
Normal Upper Cervical Lymph Nodes	☐	☐	
Normal Submandibular Triangle	☐	☐	
Normal Salivary Glands	☐	☐	
Other, (specify)	☐	☐	

Intra-Oral Examination			
	Present	Absent	Comment
Normal Mucosa	☐	☐	
Normal Outer and Inner lips	☐	☐	
Normal Gingiva	☐	☐	
Normal Tongue	☐	☐	
Normal Floor of the Mouth	☐	☐	
Normal Hard Palate	☐	☐	
Normal Soft Palate	☐	☐	
Normal Oropharynx	☐	☐	

Clinical Examination:

Clinical Examination of the involved tooth	
Involved Tooth number (FDI tooth notation system)	
Number of Tooth Surfaces Left	1 ☐ 2 ☐ 3 ☐ 4 ☐
Percussion Test	TTP ☐ Not TTP ☐
Palpation Test	Normal ☐ Abnormal ☐
Sinus Tract, Fistula, Swelling, Abscess	Present ☐ Absent ☐
Mobility	0 ☐ 1 ☐ 2 ☐ 3 ☐
Probing Depth (mm)	Buccal ☐ Lingual ☐ Mesial ☐ Distal ☐
Time Interval between Primary and Secondary Endodontic Treatment	≤ 1 year ☐ >1 year ☐
Quality of the Existing Coronal Restoration	Satisfactory ☐ Unsatisfactory ☐

Radiographic Examination:

		Periapical Date taken:	CBCT Date taken:
Periapical Lesion and Size		Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐	Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐
Pre-operative Root Filling Quality	Root Filling Length	Adequate ☐ Short ☐ Long ☐ Unfilled ☐	Adequate ☐ Short ☐ Long ☐ Unfilled ☐
	Root Filling Voids	Absent ☐ Present ☐	Absent ☐ Present ☐
Widening of Apical Periodontal Ligaments		Absent ☐ Present ☐	Absent ☐ Present ☐
Root Fracture		Absent ☐ Present ☐	Absent ☐ Present ☐
Post		Absent ☐	Present ☐
Root Perforation		Absent ☐	Present ☐
Number of Roots		1 ☐ ≥2 ☐	
Number of Root Canals		1 ☐ 2 ☐ 3 ☐ 4 ☐	
Fractured Instruments		Absent ☐ Present ☐	

Restoration

Restoration Type	
Crown Type	

Visit 4:

Clinical Examination:

Clinical Examination of the involved tooth	
Involved tooth number (FDI tooth notation system)	
Signs & Symptoms	Absent ☐ Present ☐
Percussion Test	TTP ☐ Not TTP ☐
Palpation Test	Normal ☐ Abnormal ☐
Sinus Tract, Fistula, Swelling, Abscess	Present ☐ Absent ☐
Mobility	0 ☐ 1 ☐ 2 ☐ 3 ☐
Probing Depth (mm)	Buccal ☐ Lingual ☐ Mesial ☐ Distal ☐
Quality of the Coronal Restoration	Satisfactory ☐ Marginal discrepancy ☐ Discolouration ☐ Recurent caries ☐ Post debonding ☐ Post fracutre ☐

Radiographic Examination:

		Periapical Date taken:	**CBCT** Date taken:
Periapical Lesion and Size		Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐	Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐
Root Filling Quality	Root Filling Length	Adequate ☐ Short ☐ Long ☐	Adequate ☐ Short ☐ Long ☐
	Root Filling Voids	Absent ☐ Present ☐	Absent ☐ Present ☐
Widening of Apical Periodontal Ligaments		Absent ☐ Present ☐	Absent ☐ Present ☐
Root Fracture		Absent ☐ Present ☐	Absent ☐ Present ☐

Visit Five:

Clinical Examination:

Clinical Examination of the involved tooth	
Involved Tooth number (FDI tooth notation system)	
Signs & Symptoms	Absent ☐ Present ☐
Percussion Test	TTP ☐ Not TTP ☐
Palpation Test	Normal ☐ Abnormal ☐
Sinus Tract, Fistula, Swelling, Abscess	Present ☐ Absent ☐
Mobility	0 ☐ 1 ☐ 2 ☐ 3 ☐
Probing Depth (mm)	Buccal ☐ Lingual ☐ Mesial ☐ Distal ☐
Quality of the Coronal Restoration	Satisfactory ☐ Marginal discrepancy ☐ Discolouration ☐ Recurent caries ☐ Post debonding ☐ Post fracutre ☐

Radiographic Examination:

		Periapical Date taken:	**CBCT** Date taken:
Periapical Lesion and Size		Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐	Absent ☐ < 2mm ☐ 2-5mm ☐ >5mm ☐
Root Filling Quality	Root Filling Length	Adequate ☐ Short ☐ Long ☐	Adequate ☐ Short ☐ Long ☐
	Root Filling Voids	Absent ☐ Present ☐	Absent ☐ Present ☐
Widening of Apical Periodontal Ligaments		Absent ☐ Present ☐	Absent ☐ Present ☐
Root Fracture		Absent ☐ Present ☐	Absent ☐ Present ☐

Study Conclusion:

Did the subject complete the entire study? ☐ Yes ☐ No*

*If "No" is marked, please indicate the primary reason below. Please mark only one.

Lost to follow-up ☐

Protocol deviation ☐

Withdrawal of Consent ☐ Please specify:

Adverse Event ☐ Please specify:

Other ☐ Please specify:

Was there contact with the subject after the final visit? ☐ Yes ☐ No

If there was contact in relation to this study, please complete the following.

Method of contact: ☐ Telephone ☐ Letter

☐ Other Please specify:

Date of last contact:

Investigator's Signature:

I confirm that I have reviewed all the data collected in this Case Report Form and take responsibility that the information is accurate and complete.

Principle Investigator's Signature: _____ Date: _____

Appendix VIII: Structured step by step form for operators

Data Sheet for the Outcome of Root Canal Re-treatment Study

Patient Demographics		
Patient identification number		
Patient phone number 1		
Patient phone number 2		
Patient age		
Patient sex		
Smoking status		
Preoperative Tooth Factors		
Tooth number		
Number of tooth surfaces left		
Quality of the existing coronal restoration (caries/fracture lines)		
Quality of preoperative root filling		
Presence of periapical lesion		
Presence of root perforation, ledge, and instrument breakage		
Presence of root fracture		
Presence of sinus tract		
Operative Factors and Standardised Procedure		
Dental operating microscope was used	YES	NO
Rubber dam was used	YES	NO
All restorations and caries were removed prior to root treatment	YES	NO
Tooth was build up as in interim with GIC if required for isolation	YES	NO
An apex locater was used	YES	NO
Working length was 0.5mm short of the 0 reading for each canal	YES	NO
Canals prepared with flexofiles to a minimum of size 20	YES	NO
Rotary ProTaper used for shaping the canals	YES	NO
Irrigation with NaOCL and EDTA	YES	NO
$CaOH_2$ placed in the canals with a syringe in between appointments	YES	NO
Treatment was carried out over at least 2 visits	YES	NO
Final flush of the canals with EDTA followed by NaOCL	YES	NO
Obturation with warm vertical condensation using GP & Tubiseal	YES	NO
Procedural complications (i.e. ledge, perforation, instrument breakage)	YES	NO
Definitive Composite core placed	YES	NO
Type of final restoration		
Margins of the restoration are subgingivally extended	YES	NO
Impression taken before & after final restoration placement	YES	NO
Postoperative Complications		
Was patency achieved in all canals		
Were there any ledges that had to be negotiated? If so, which root?		
Were there any other complications? If so describe below:		

Recall

Date when treatment completed	
Date of 12-month review	

Treatment Outcome	PA	CBCT
Healing category of tooth at 12-month review		

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