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THE EXTENT OF ORTHODONTICALLY INDUCED INFLAMMATORY ROOT RESORPTION FOLLOWING TRANSVERSE AND VERTICAL JIGGLING MOVEMENT WITH HEAVY FORCES FOR 12 WEEKS: A MICRO-CT STUDY

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Australia

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Clinical Dentistry (Orthodontics)

September 2014
DECLARATION

CANDIDATE CERTIFICATION

This is to certify that the candidate carried out the work in this thesis,

in the Orthodontic Department, University of Sydney,

and it has not been submitted to

any other University or Institution for a higher degree.

Carolyn Lian Tst Ng
DEDICATION

To my loving husband Andrew

For all your patience, love and support on this journey with me,

To my parents Gloria and Ming

For all your inspiration, encouragement and guidance,

To Selena and Jonathan

For all your insight and companionship,

To all my dearest family and friends

For all your thoughts and prayers,

“With God all things are possible”

Matthew 19:26
ACKNOWLEDGEMENTS

“I can do everything through Him who gives me strength.” Philippians 4:13

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<td>NSAID</td>
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<td>Orthodontically Induced Inflammatory Root Resorption</td>
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<td>PGE₂</td>
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<td>RANK</td>
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<td>Beta-Titanium Molybdenum Alloy</td>
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<td>TNF</td>
<td>Tumour Necrosis Factor</td>
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<td>TNFRSF11A</td>
<td>Tumour Necrosis Factor Receptor Super-Family 11 Alpha</td>
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<td>TRAP</td>
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INTRODUCTION

Orthodontically induced inflammatory root resorption (OIIRR) is the term given to the unavoidable pathologic loss of root structure that occurs as a consequence of orthodontic tooth movement. In 2014, the localised aseptic inflammation produced by orthodontic force application has been considered under a new term, Orthodontitis, which also encompasses the various types of OIIRR within the groups of Instrumental-Orthodontitis (IO) and Instrumental-Detrimental Orthodontitis (IDO).

The incidence of OIIRR in adults has been reported at 25-76% after at least 12 months of treatment, while in adolescents it has been reported at 5-18%. When graded scales are used, OIIRR is usually classified as minor or moderate in most orthodontic patients. Severe resorption, exceeding 4mm or one-third of the original root length is reported to be seen in 1% to 5% of teeth.

A reduced root length subsequent to OIIRR could potentially compromise the longevity of affected teeth by complicating restorative treatment planning, and placing affected teeth at greater risk of loss secondary to periodontal disease or trauma. Fortunately, in the majority of cases, the extent of root loss is mild and inconsequential to the long term survival and functionality of the affected teeth or dentition.

Since the relationship between root resorption and orthodontic treatment was proposed in 1914, OIIRR has been studied extensively, both radiographically and histologically. As a result of these studies, OIIRR is recognized as having a multifactorial aetiology, and risk factors for OIIRR are classified as either biologic or mechanical in origin. Biologic factors include both genetic and environmental factors, which may be further divided into either systemic or localised factors. Mechanical factors pertain mainly to various characteristics of orthodontic force application.
Alternating patterns of orthodontic force application or “jiggling forces” have long been implicated in OIIRR. This study follows on from a forthcoming prospective x-ray microtomography study investigating the effect of light (25g) and heavy (225g) jiggling forces in comparison with unidirectional light and heavy forces on human premolars. To supplement this investigation, this study aims to compare the effect of controlled heavy (225g) jiggling forces occurring in 4 weekly cycles in the transverse and vertical plane over a 12 week period utilising x-ray micro-tomography for qualitative and quantitative volumetric analysis. In doing so, this study aims to elucidate the effect of this pattern of force application in the process of OIIRR; in continuance of root resorption research conducted by the Orthodontic Department in the Faculty of Dentistry at The University of Sydney.
LITERATURE REVIEW

2.1 Cementum

The principal tissue of the tooth that is concerned with orthodontically induced inflammatory root resorption is cementum. Together with the periodontal ligament, alveolar bone and gingiva, cementum forms a structural and functional unit, which surrounds and supports the teeth, collectively known as the periodontium. The primary function of cementum is to anchor the principal collagen fibres of the periodontal ligament to the root surface. It is described as a specialised, complex, and responsive tissue that is slowly formed throughout life, allows for continual reattachment of the periodontal ligament fibres and is capable of repair, regeneration and pulpal protection following damage to the root surface. These dynamic features of cementum are critically involved in orthodontic tooth movement as well as orthodontically induced inflammatory root resorption, and as such, an overview of its characteristics, development, structure and function provides a contextual background for root resorption studies.

2.1.1 Characteristics of Cementum

Cementum is pale yellow in appearance with a dull surface. When compared with dentine, cementum is softer and more permeable with a lower elastic modulus, which, together with hardness, is reported to decrease from the cervical to the apical area when measured on premolar teeth. On a respective wet-weight or volume basis, cementum is composed of 65% or 45% inorganic hydroxyapatite crystals and amorphous calcium phosphate, 23% or 33% organic Type I collagen (90%) and Type III collagen (5%) and non-collagenous proteins (bone sialoprotein and osteopontin), proteoglycans and glycosaminoglycans, and 12% or 22% water. The hydroxyapatite crystals are thin and plate-like, approximately 55nm wide and 8nm thick, with an increased capacity for absorption of trace elements. Fluoride has been found in relatively high concentrations (0.9%) in cementum, which increased with age, in association with exposure, and was predominantly localized in the surface layers with limited diffusion. As with the physical properties, the structure...
and degree of mineralisation of cementum is not uniform throughout the tissue. Although, cementum has many chemical properties similar to bone; it is avascular, lacks innervation, does not undergo physiologic resorption or remodelling, and is also less readily resorbed. Possible reasons for the reduced susceptibility to resorption when compared with bone may be attributed to: differences in the properties between bone and cementum, protective features of pre-cementum, an increased density of Sharpey’s fibres and the presence of the epithelial cell rests of Malassez (ERM) on the root surface.

2.1.2 Development, Structure and Function of Cementum

During the late bell stage of tooth development, when the enamel organ is at its final size and dentine formation reaches the cervix of the tooth, the internal and external enamel epithelia converge and proliferate together as a double layered sheet, known as Hertwig’s Epithelial Root Sheath (HERS), to map out the shape of the tooth root/s. The formation of cementum is temporally and spatially related to root dentine formation as it is restricted to a narrow band encircling the forming root, 200-300nm coronal to the advancing root edge, and continues apically as the root elongates. Due to a process of reciprocal epithelial-mesenchymal interactions, HERS induces the peripheral cells of the dental papilla to differentiate and begin formation of radicular mantle dentine. Before mineralization of this pre-dentine matrix reaches the lining of the inner epithelial cells, HERS disintegrates into isolated bundles of cells surrounded by a basement membrane, known as epithelial cell rests of Malassez (ERM), and allows fibroblast-like cells of the adjacent dental follicle to contact the unmineralised pre-dentine matrix. These follicular ectomesenchymal cells receive a reciprocal inductive signal from the dentine and/or the surrounding HERS cells and differentiate into cementoblasts. HERS cells have also been implicated in contributing to the differentiation of cementoblasts. Following differentiation, cementoblasts produce a cementum matrix, and implant collagen fibrils (1-2um in diameter) into the predentine, enabling an intimate interdigitation of collagen fibrils at the dentinocemental junction (DCJ). Once the cementum matrix is established on
the root surface, a mineralising front, originating in the root dentine, reaches or just surpasses the fibrillar DCJ, resulting in mineralisation of the cementum matrix. In this way, mineralisation of the cementum matrix is not controlled by the cementoblasts but rather the presence of hydroxyapatite crystals in the adjacent dentine, and possibly as well as the adjacent periodontal fibroblasts that are rich in alkaline phosphatase. Mineralisation proceeds in a slow linear fashion and calcospherites are not observed in cementum. This initial zone of cementum formation has been described as a primary acellular intrinsic fibre cementum (AIFC), which is formed slowly with incremental lines in close proximity, and attains a thickness of approximately 10um. Eventually, with increasing thickness, collagen fibres of Sharpey from the periodontal ligament become attached to the surface of the cementum layer and a zone of primary acellular extrinsic fibre cementum (AEFC) is formed. These Sharpey’s fibre bundles are round or ovoid and are approximately 5-7um in diameter. This cementum increases slowly and evenly in thickness at rates of 2-2.5um per year, attains a thickness of approximately 15um, and covers the cervical two-thirds of the root. This period of cementogenesis has been termed the pre-functional stage as this cementum is formed prior to occlusal loading, and is characterized by the slow rate of formation and an acellular structure. Sharpey’s fibres in AEFC fulfil the function of providing attachment of the tooth to the surrounding bone.

Upon eruption of the tooth, and following formation of primary cementum in the cervical portion of the root, secondary cellular cementum appears in the apical region of the root as well as in furcation areas of multi-rooted teeth. It is also found to be present in resorption lacunae. This type of cementum is associated with an increased rate of cementum formation. Large basophilic cells rich in rough endoplasmic reticulum differentiate from cells in the adjacent dental follicle, and secrete ground substance and collagen, which forms the intrinsic fibres (1-2um) of cellular intrinsic fibre cementum (CIFC). These fibres are oriented parallel to the root surface. As with bone, a multipolar mode of matrix secretion by cementoblasts results in a thin (5um thick) layer of unmineralised cementum at the surface; and cementoblasts become incorporated into the forming matrix, as cementocytes, which necessitates the generation of new cementoblasts from stem cells within the
PDL. Mineralisation of the deep layers of precementum occurs in a linear manner, however, this cellular cementum is overall less mineralised than primary cementum. CIPC has an adaptive and reparative function with no role in tooth attachment.22

In some regions of the root AEFC and CIPC may be present in alternating layers, resulting in variations in the amount of PDL attachment to the tooth. This type of cementum has been termed cellular mixed stratified cementum (CMSC). In some cases, regions of AIFC may also be found in these areas of CMSC.39 This type of cementum has been implicated in adaptation and repair.

A type of afibrillar acellular cementum (AAC) that is sparsely distributed and consists of well mineralised ground substance may be seen on cervical enamel or intervening between fibrillar cementum and dentine. This type of cementum usually forms when the reduced enamel epithelium overlying the enamel on an unerupted tooth is damaged or lost, allowing adjacent connective tissue cells of the dental follicle to contact the enamel surface and become induced into differentiating into cementoblasts.24 27
The complex structure of cementum is summarised in table 1, which demonstrates the variable nature in fibre origin, distribution and function.

<table>
<thead>
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<th>CHARACTERISTICS OF CEMENTUM</th>
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<tr>
<td><strong>Type</strong></td>
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<tr>
<td>Acellular (Primary) AIFC</td>
</tr>
<tr>
<td>Acellular (Primary) AEFC</td>
</tr>
<tr>
<td>Cellular (Secondary) CIFC (+ AIFC)</td>
</tr>
<tr>
<td>Mixed (Alternating AEFC + CIFC/AIFC)</td>
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<td>Acellular Afibrillar AAC</td>
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**Table 1: Characteristics of Cementum.**

25, 27
2.2 Orthodontically Induced Inflammatory Root Resorption

2.2.1 History & Definition

Root resorption may be classified as either physiological or pathological. In the permanent dentition, physiologic root resorption is usually a result of physiological changes that occur over time, whereas, pathological root resorption usually results from trauma, disease or iatrogenic causes. Reports on pathologic root resorption of permanent teeth began in 1856 by Bates, and its association with orthodontic treatment was established in 1914 by Ottolengui, with major concerns reported in a radiographic investigation in 1927 by Ketcham. In a literature review by Becks and Marshall in 1932, it was concluded that the destruction and uptake of formed tissues by the blood or lymph system in medical or dental literature should be termed resorption, as opposed to absorption, which by its derivation, means to “absorb again.”

The term Orthodontically Induced Inflammatory Root Resorption was introduced in 2002 by Brezniak and Wasserstein to describe a transient inflammatory external surface resorption, which is an iatrogenic and unavoidable pathological consequence of orthodontic tooth movement. More recently, a new classification has been proposed that encompasses the term Orthodontically Induced Inflammatory Root Resorption under the title of Orthodontitis, which describes an aseptic local inflammation in the PDL produced by orthodontic forces.
2.2.3 Incidence & Prevalence

As explained by Harris,49 the reported frequency of OIIRR is variable in the literature and largely results from the diverse and poorly defined criteria used to identify resorption. This subsequently results in an unreliable prediction of the prevalence of OIIRR when the findings are applied to a general population. However, a recent systematic review by Weltman50 summarises that the incidence of OIIRR reported histologically is greater than 90% in orthodontically treated teeth,51, 52 while radiographically it has been reported as 15% before treatment and 73% after treatment.6 The average amount of OIIRR detected radiographically is less than 2.5mm,5, 8, 53–55 varying from 6% to 13% for different teeth.56 When graded scales are used, OIIRR is usually classified as minor or moderate in most orthodontic patients.10–13 Severe resorption, exceeding 4mm or a third of the original root length is reported to be seen in 1% to 5% of teeth.5, 8, 10–12, 14–16

2.2.4 Classification, Grading and Diagnosis

Histologically, there are three degrees of severity of OIIRR as defined by Brezniak and Wasserstein:1

1. Cemental or surface resorption with remodelling: outer cemental layers are resorbed and are fully regenerated or remodelled, a process resembling trabecular bone remodelling.

2. Dentinal resorption with repair (deep resorption): Cementum and the outer layers of dentine are resorbed and repaired with cementum material. The final shape of the root may or may not be identical to the original form.

3. Circumferential apical root resorption. Full irreversible resorption of the hard tissue components of the root apex with root shortening. Repair occurs only within the cemental layers.
Radiographically, Malmgren\textsuperscript{9} compared pre- and post- orthodontic treatment radiographs and registered root resorption lesions with index scores based on a four point scale as shown in Figure 1. Using this index teeth with root resorption may be classified in levels ranging from 1 to 4.

\textbf{Figure 1: Root resorption index for quantitative assessment of root resorption.}\textsuperscript{9}

- **Grade 1**: Irregular root contour
- **Grade 2**: Less than 2mm of apical root resorption
- **Grade 3**: Root resorption amounting to from 2mm to one third of the original root length
- **Grade 4**: Root resorption exceeding one third of the original root length
A clinical diagnosis of OIIRR is currently achieved with radiographs. It is often desirable to screen for root resorption from routine orthodontic radiographic records (orthopantomogram and lateral cephalogram) and supplement findings with periapical films of selected teeth. The advantages and disadvantages of various radiographic methods for diagnosis of OIIRR are explained in table 2.

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopantomogram (OPG)</td>
<td>Low radiation dose when compared to full mouth PA series.</td>
<td>Magnification and improper patient positioning within the focal trough may result in exaggeration by 20% when pre and post OPG are used. Maxillary anterior teeth outside the focal trough are likely to appear short.</td>
</tr>
<tr>
<td>Peri-apical Films (PA)</td>
<td>Lowest radiation exposure when used selectively. Less distortion and superimposition errors particularly when parallel techniques are used.</td>
<td></td>
</tr>
<tr>
<td>Lateral Cephalogram (LC)</td>
<td>Useful for upper incisors.</td>
<td>Overlapping roots obscures diagnosis Risk of 5-12° enlargement factor.</td>
</tr>
<tr>
<td>Cone Beam Computed Tomography (CBCT)</td>
<td>High detection and quantification.</td>
<td>More costly and higher levels of radiation when used routinely.</td>
</tr>
</tbody>
</table>

Table 2: Clinical Methods for Diagnosis of OIIRR.
The recent classification of Orthodontitis has the following categories which are used to describe OIIRR:\textsuperscript{2}

**Instrumental Orthodontitis (IO):** This category describes controlled bone modelling as well as bone and reversible cemental remodelling which occurs during orthodontic tooth movement.

**Instrumental and Detrimental Orthodontitis Grade 1 (IDO1):** This category describes the changes in the effect on cementum from a remodeling process to a modeling process, whereby resorption progresses into the dentine with irreversible minor to moderate root shortening and scattered lacunae on the root surfaces.

**Instrumental and Detrimental Orthodontitis Grade 2 (IDO2):** This category describes the progression of OIIRR resulting in tooth mobility, sensitivity and severe root shortening in radiographs. The consequences of IDO2 require treatment, which depends on the stage of identification and severity. Treatment may vary from fixed retention/splinting affected teeth with unaffected teeth, to extractions and implant replacement, in extremely rare cases.

### 2.2.5 Biochemical Assays

Recent research has focussed on identifying biologic markers in saliva, gingival crevicular fluid, blood serum and urine, and relating these factors to the risk of OIIRR. If successful, these techniques could be easily implemented in identifying at risk patients prior or during orthodontic treatment and allow treatment to be modified accordingly.

#### 2.2.5.1 Saliva

In saliva, an increase in the cytokines: interleukin-7, interleukin-10, interleukin-12p70 and interferon gamma, as well as a decrease in interleukin-4 has been identified in patients with moderate to severe OIIRR.\textsuperscript{64}
2.2.5.2 Gingival Crevicular Fluid

Elevated levels of dentine phosphoproteins has been reported in the gingival crevicular fluid of exfoliating primary teeth and teeth undergoing orthodontic treatment when compared with the GCF of untreated permanent teeth. An increase in dentine phosphophoryn and dentine sialoprotein concentration has also be identified in the GCF of severe root resorption patients, which promotes the use of dentine phosphophoryn and dentine sialoprotein as biologic markers for identifying at risk patients, and monitoring root resorption during orthodontic treatment.

Matrix proteins and cytokines have also been confirmed in GCF of patients with OIIRR, along with an increased receptor activator of nuclear factor kappa B ligand (RANKL) to osteoprotegerin (OPG) ratio, reflecting an increase in bone resorption activity. Studies are currently being undertaken to investigate changes in the cytokine profile of GCF after application of heavy orthodontic forces and compare the cytokine profile between patients showing high and low volumes of OIIRR. Preliminary results indicate that higher levels of anti-resorptive cytokines IL-4 and GM-CSF in low root resorption cases may indicate a role in reducing the level of OIIRR.

2.2.5.3 Urinary Excretion Products

Currently, research is being undertaken to profile the protein composition (proteome) of root dentine in search for useful biomarkers for OIIRR. Dentine proteins are resolved by gel electrophoresis and bands of interest identified by mass spectrometry. From this, several dentine-specific proteins have been proposed as biomarkers for OIIRR (e.g. dentine phosphoprotein and related breakdown products), which are currently being investigated for excretion in urine during physiologic root loss during the transitional dentition, in the eventual hope of identifying real time OIIRR in susceptible patients.

2.2.5.4 Serum

Elevated levels of salivary sIgA in serum before treatment have been associated with more severe root resorption after 6 months of treatment. Several studies have demonstrated the role of
osteoprotegerin and receptor activator of nuclear factor kappa B ligand in osteoclastogenesis,72, 73 while other studies have explored the possibility of their role in OIIRR.74, 75 Subsequently, several authors are investigating the levels of RANKL and OPG in serum and GCF to determine a possible link between the relative concentrations of these biomarkers and OIIRR.76, 77

2.2.6 Aetiology

The precise aetiology of OIIRR is unknown and at this stage, appears to be multifactorial. The literature has identified multiple risk factors that can be grouped into biological or mechanical factors. Mechanical factors are of particular interest to clinicians as they may be controlled to reduce the risk of OIIRR.

2.2.6.1 Biologic Risk Factors

Biologic risk factors associated with OIIRR are directly related to the patient and are not associated with mechanical aspects of orthodontic treatment. They may be further divided into a genetic or environmental origin.

2.2.6.1.1 Genetic Factors

Individual susceptibility, heritable genetic factors and ethnicity are the main intrinsic genetic factors that have been linked with OIIRR. Both gender,5, 56, 78, 81 and age at the start of treatment18, 45, 81, 88 have generally been found to have little correlation with OIIRR.

Individual susceptibility to root resorption is an important factor in determining the risk of root resorption.80 During compression of the PDL, within the microenvironment of the periodontal ligament, an individual’s tendency for root resorption may be a result of individual disturbances or peculiarities in the complex relationship between an individual’s hormones, body type and metabolic rate, which modifies an individual’s cellular metabolism and hence an individual’s reaction to disease, trauma or aging.80 OIIRR varies among individuals and within the same individual at various times, 22
with some individuals demonstrating severe resorption even in the absence of orthodontic treatment.88,89

Identification of familial or genetic predispositions to OIIRR may enable clinicians to accurately counsel patients about their individual risk and manage those at risk by altering their treatment as needed. Since Newman in 1975, many studies have attempted to identify genetic causes of OIIRR.92–98 In a study of 103 sibling pairs, the reported heritability for resorption of maxillary incisor roots and mandibular first molars was 70%.95 In a sample of 16 monozygotic and 10 dizygotic twin pairs, a concordance estimate for OIIRR was found to be 49.2% in monozygotic twins and 28.3% in dizygotic twins.93 More recently, studies have investigated the following two pathways by which genetic factors may influence OIIRR: 1) Activation control of osteoclasts through the ATP/P2XR7/IL-1B inflammation modulation pathway and 2) RANK/RANKL/OPG osteoclast activation control pathway.98 The TNFRSF11A gene, which encodes for receptor activator of nuclear factor-kappa B (RANK) and allele 1 at the IL-1B gene, which decreases production of cytokine IL-1 in-vivo, have been identified to play a role in increasing the risk of OIIRR.94,96

In the United States, patients of Asian descent have been reported to exhibit less root resorption than patients of Caucasian or Hispanic descent,5 while no differences in resorption were detected between patients from the Netherlands, United States or Kuwait.99

2.2.6.1.2 Environmental Factors

2.2.6.1.2.1 Systemic

Systemic environmental factors considered in the risk of OIIRR include: asthma and allergies, endocrine and hormonal imbalances, nutrition, medications and alcohol consumption.

A higher incidence of OIIRR in maxillary molars has been reported in both patients11 and animals100 with asthma and allergies.101–103 It has been proposed that the increased presence of inflammatory mediators in the maxillary sinus penetrate the periodontal ligament of adjacent teeth
and act synergistically to increase the OIIRR process, resulting in root blunting of maxillary molars.44

Endocrine and hormonal imbalances found in hypothyroidism, hyperparathyroidism, Paget’s disease and other metabolic disorders have been associated with altered resistance to root resorption.8, 104-106 Some animal studies report that OIIRR appears to be increased in conditions with increased bone turnover rate, e.g. hyperparathyroidism106 and osteoporosis.107 Conversely, in an alternate rat model the risk of OIIRR has also been suggested to increase in subjects with decreased bone turnover rate, e.g. hypothyroidism.108

There are conflicting reports in the literature regarding nutritional deficiencies and the risk of OIIRR. Some authors have reported that calcium and vitamin D deficiency in rats has been associated with increased parathyroid hormone and osteoclast levels and more severe OIIRR, 42, 106 while other authors have reported that secondary hyperparathyroidism was correlated with increased bone turnover and less OIIRR, 109 and the marked variation in resorption levels in teeth of the same individual throws doubt on the role of diet or hormone balance as a primary cause of OIIRR.8

The effect of a number of pharmacologic agents on OIIRR have been investigated in the literature. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)110-112 and supplementation with hormone L-thyroxin in rats113 and humans114 has been associated with reduced OIIRR. Conversely, corticosteroids have been associated with an increased risk of OIIRR5 particularly with short term use, and careful monitoring of patients undergoing acute corticosterone treatment, particularly in the management of asthma or allergies, has been suggested.115 Bisphosphonates have also been found to increase the vulnerability of the root surface to OIIRR,116, 117 while chronic alcohol consumption during treatment has been found to increase root resorption through vitamin D hydroxylation in the liver and altered calcium homeostasis.106, 118
2.2.6.1.2.2  Local

The following localised factors have been investigated as possible aetiological factors for OIIRR: habits, pre-existing resorption, previous trauma, dental morphologies/anomalies or agenesis, endodontic treatment, periodontal status, alveolar bone density and turnover rate, dental age and developmental stage and malocclusion.

Nail biting habits\textsuperscript{91, 92, 119}, finger sucking habits beyond the age of seven years\textsuperscript{53} and tongue thrust\textsuperscript{82, 82} have been associated with an increased risk of OIIRR. When treatment was delayed until after adverse habits were discontinued, no increased OIIRR was found during treatment.\textsuperscript{8}

Pre-existing resorption has been reported as a clear indicator of increased risk of severe OIIRR during treatment.\textsuperscript{9, 86, 91, 92}

Previous trauma may be a predictive of an increased risk of OIIRR.\textsuperscript{8, 53, 120} It has been reported that the distribution of root resorption in patients with only a history of trauma was 6.7%, while those with a history of orthodontic treatment was 7.8%, and those with orthodontic treatment and a history of trauma was almost four times higher, at 27.8%.\textsuperscript{121} Traumatized teeth that exhibit signs of resorption prior to treatment tend to undergo more resorption during orthodontic treatment than teeth without such signs,\textsuperscript{9} and the extent of external root resorption following trauma is related to the severity of the injury.\textsuperscript{122} Damage to the periodontal ligament or cementum during traumatic injuries may be responsible for the increased risk of OIIRR.\textsuperscript{9, 46}

Abnormal root morphology and length, dental anomalies, agenesis and ectopia have been reported to be associated with increased OIIRR.\textsuperscript{5, 10, 54, 92, 99, 123-126} Features of abnormal root morphology include pipette-shape, thin, pointed, dilacerated, blunt or bottle-shaped, while features of dental anomalies include invagination of incisors, peg shaped lateral incisors or taurodontism. The increased risk of OIIRR may be associated with greater forces being applied to the roots during orthodontic treatment.\textsuperscript{10, 127} Interestingly, these findings of increased OIIRR are not consistent throughout the literature.\textsuperscript{13, 128, 129}
Endodontic treatment has been reported to be both a preventive factor for OIIRR as well as a causative factor for OIIRR, although this finding may be confounded by a history of trauma that was found in the majority of cases analysed. It has been proposed that an increased density and hardness of the dentine in endodontically treated teeth is responsible for resistance against OIIRR.

Both periodontal disease and a hypofunctional periodontium have been associated with increased risk of OIIRR. Concomitant inflammation in a diseased periodontium is expected to reinforce the inflammatory process associated with OIIRR during tooth movement. In the absence of occlusal function, the periodontium exhibits progressive atrophic changes in all functional structures, such as the functional arrangement of Sharpey’s Fibres, fibroblastic proliferation, vascularity, and distribution of Ruffini’s nerve endings and proteoglycans. Accelerated root destruction has been proposed to result from the narrow periodontal space and derangement of the functional fibres providing an inadequate cushioning effect and stress distribution, resulting in increased concentration of compression zones. Interestingly, a study in rats found that although root size and PDL structure may be reduced due to disuse atrophy resulting from defective occlusal function, they may be recovered following re-establishment of occlusal stimuli.

It has been reported that increased bone turnover and decreased bone density may allow faster remodelling of bone and less remodelling of root tissue and consequently less OIIRR. It has been suggested that in patients where decreased bone turnover rates are expected, reactivation of appliance forces should be performed less frequently and the risk of OIIRR carefully evaluated. However, the radiographic bone density and morphology of the dentoalveolar complex have been reported to have little correlation to OIIRR.

Teeth with incomplete root formation at the onset of orthodontic treatment have been reported to have a higher protection or resistance against OIIRR when compared to teeth with completed root formation, a finding which favours early orthodontic treatment. However,
application of these findings should be tempered by the incidence of root dilaceration caused by orthodontic treatment, reported at 8%. 139

Although no malocclusion is immune to OIIRR\(^1\) certain types of malocclusion have been reported to have a higher prevalence of root resorption. Class III patients were found to have a higher prevalence of root resorption, which may be related to forward tipping of maxillary incisors with root apices against the lingual cortical plate during dentoalveolar compensation of a Class III jaw relationship. 140 Class II Division 1 patients were found to have increased OIIRR when compared to Class I patients, however it was unrelated to the degree of tooth movement or treatment time. 141 Malocclusions that require extractions have also been found to have greater resorption than those that do not require extractions. 5 Open-bite cases have recently been reported to have more teeth with abnormal root shape and OIIRR when compared to normal overbite cases. 134 Deep bite cases were reported to have greater incisor and maxillary first molar distal root OIIRR. 81 Importantly, the amount of OIIRR is positively associated with the amount of orthodontic tooth movement, which is a function of the severity of the malocclusion. 86, 96, 142

2.2.6.2 Mechanical Risk Factors

Orthodontic tooth movement has been reported to account for approximately 10 to 30% of the total variation in OIIRR.

2.2.6.2.1 Force Magnitude

The severity of OIIRR is directionally proportional to the magnitude of the applied force. 48, 52, 143-148 Numerous three-dimensional quantitative studies on human maxillary first premolars have demonstrated an increased amount of OIIRR with increased force levels, 149-152 and in a rigorous systematic review of the literature, Weltman in 2010 concluded that heavy force application produced significantly more OIIRR than light force application or control groups. 50 Heavy forces that induce excessive hyalinisation interferes with the repair of root resorption craters, resulting in an increased prevalence of OIIRR. 48, 51, 90, 136, 144 Two histologic studies have failed to detect a significant
difference in the frequency or severity of OIIRR between light and heavy forces, however these findings were attributed to large individual variations in the subject sample and may hence be related to the employed methodology. 60, 153, 154

2.2.6.2.2 Treatment Duration

The severity of OIIRR is directly related to treatment duration, thus the longer the force application the more severe the OIIRR. 22, 46, 48, 155 Paetyangkul et al152 reported a statistically significant increase in the amount of OIIRR in heavy force groups (225g) between 4, 8 and 12 weeks and, as well as in light force groups (25g) at 12 weeks when compared to 4 and 8 weeks of force application. Artun et al156 reported the risk of one or more teeth undergoing more than 1.0mm of OIIRR from 6 to 12months of treatment is 3.8 times higher than that in the first 6months of treatment. At 3-9months after initiation of fixed appliance treatment, Smale et al99 reported approximately 4% of patients had an average OIIRR of ≥1.5mm in maxillary incisors and 15.5% had more than one maxillary incisor with OIIRR ≥2mm. Levander and Malmgren10 reported 35% of teeth showed OIIRR after 6-9months of treatment, which later increased to 56% at 19months of treatment. In the management of Class II malocclusions, Brin et al13 reported a greater proportion of incisors with moderate-severe OIIRR in one-phase treatment when compared with two-phase treatment.

2.2.6.2.3 Appliances and Treatment Philosophy

Some studies have reported differences in OIIRR between different orthodontic appliances. The Begg appliance has been reported to have more OIIRR than edgewise appliances, which may be attributed to excessive palatal root uprighting in stage three of the Begg technique. 157 Bioefficient therapy, utilizing heat activated and superelastic wires, a different bracket design and smaller rectangular stainless steel wires during incisor retraction and finishing, has been reported to have less OIIRR when compared with standard and straight-wire edgewise systems. 11 When serial panoramic radiographs were used to compare the effects of a preadjusted edgewise appliance, the Speed appliance and the Tip-Edge appliance in 114 extraction and non-extraction cases, statistically
significant OIIRR was detected on the following teeth treated with: the preadjusted appliance: 12, 11, 21 and 26 (0.76-1.68mm); the Speed appliance: 26, 31, 41, 42 (1.11-2.35mm); and the Tip-Edge appliance: 31 (1.12mm). However, many studies have also found no statistical difference among various orthodontic appliances and bracket systems (Tweed, Begg, edgewise and self-ligating, sectional and continuous mechanics), which may be attributed to individual variation and difficulties in applying split-mouth study designs as malocclusions are often asymmetrical.

Removable appliances are generally considered less detrimental than fixed appliances in causing OIIRR due to the intermittent pattern of force application. Barbagallo et al found the degree of OIIRR from clear sequential thermoplastic aligners was comparable to light buccally directed forces of 25g, however heavy 225g forces induced twice as much OIIRR.

Some authors have reported greater OIIRR in extraction treatment, with up to 3.72 times increased incidence of OIIRR. These findings should be applied with caution as emphasis should be placed on the amount of tooth displacement required rather than the decision to extract. Extractions to resolve an increased overjet may require more maxillary incisor displacement than extractions to resolve severe crowding, resulting in increased treatment duration and increased OIIRR.

The effect of ultrasound and vibration on OIIRR has been investigated. Low Intensity Pulsed Ultrasound (LIPUS) has been reported to enhance repair of OIIRR lesions associated with continuous orthodontic force resulting in lower resorption areas and craters. A buccally directed vibration of 113Hz applied for 10min per day has been found to result in 33% less OIIRR volumes, which may play a role in prevention or repair of OIIRR.

Rapid maxillary expansion appliances have been associated with increased OIIRR on anchor teeth, studied by scanning electron microscopy after extraction, particularly on the buccal surfaces. However, no differences are detectable in periapical films when rapid and slow expansion appliances are compared.
2.2.6.2.4 Distance, Type and Direction of Tooth Movement

The distance, type and direction of tooth movement are important mechanical factors affecting the incidence and distribution of OIIRR.

The severity of OIIRR has been shown to be positively related to the distance of tooth movement, with maxillary incisors, having the highest risk of OIIRR, moving the greatest distance. 155, 161, 162, 169, 170

Teeth may be moved by rotation, tipping of the crown, torqueing of the root or bodily translation through the bone. Heavy rotational forces produce predictably more OIIRR than light rotational forces, with concentration of lesions at the buccodistal and linguomesial surfaces171 or regions corresponding to prominent zones of the roots.172 A greater angle of crown tipping (15°) produces more OIIRR than a smaller angle of crown tip (2.5°)173 with a greater concentration of lesions at the buccal-cervical region and lingual apical region when a buccally directed force is applied. 152, 160, 174 When buccal root torque was applied to maxillary first premolars, there was no difference detected in the total root resorption volumes between a small angle (2.5°) and a large angle (15°), while concentration of the lesions occurred at the buccoapical, mid-buccal and palatocervical regions.176 Labial root torque on a maxillary incisor root apex has been reported to produce 12.7% apical OIIRR annually.176 Bodily tooth movement has been reported to have no discernible influence on OIIRR.142 A recent rat study reported that OIIRR was more pronounced in teeth undergoing tipping movements as opposed to bodily tooth movement, and although the amount of tooth movement decreased when extremely heavy forces were applied, OIIRR increased in both tipping and bodily tooth movement groups.177

The direction of tooth movement may be either intrusive or extrusive in nature. Intrusive forces have been reported to elicit an increased incidence of OIIRR, with light (25g) and heavy (225g) force groups producing approximately 11 and 68 times greater OIIRR volumes than control groups
(0g) respectively, and a significant concentration of lesions at the mesio-apical and distoapical regions. Clinically, utility arches have been reported to result in 1.84mm of root shortening for maxillary incisors and 0.61mm for mandibular incisors with no significant correlation between resorption and the amount of intrusion. Following marginal bone loss, the amount of OIIRR after intrusion has been reported to vary between 1 to 3mm. Conversely, heavy extrusive forces have been reported to produce greater OIIRR than light extrusive forces with the distal surfaces of the roots more affected than other surfaces. However, extrusive forces have also been reported to produce less OIIRR than intrusive forces.

Jiggling forces have generally been accepted to be responsible for OIIRR. Jiggling was first described by Oppenheim and defined as “small intermittent movements along the tooth axis originating from biting forces when antagonizing teeth oppose extrusive forces,” or a tooth oscillating along a line of movement. Jiggling forces are thought to be produced during orthodontic treatment when there are occlusal interferences, when deformation of light archwires occurs during function with concomitant use of intermaxillary elastics, and following dental relapse that occurs after removal of palatal expanders. Restorative build-ups on first premolars, used to increase the vertical dimension by 2 mm for 4 weeks, have been found to have increased OIIRR during the active bite-increase period, which may be due to the premature contacts that transmit excessive uncontrolled vertical forces. Two animal studies have investigated the effects of jiggling on OIIRR. Kim and Son (1994) found no histological or radiographic difference in the pattern of OIIRR in a feline model when alternating mesial and distal forces were applied in 3 day cycles over 6, 12, 18 and 24 days when compared to unidirectional mesial forces; while Matsuda et al found that weekly cycles of alternating buccal and lingual jiggling forces produced more OIIRR in Wistar rats than two or four weekly cycles, which continued to increase as the duration of applied jiggling forces lengthened. Interestingly, Baumrind (1996) also advised, “resorption in the absence of overt root displacement seems... consistent with the purported role of “jiggling” during orthodontic treatment.”
More importantly, the literature shows the distribution of OIIRR lesions reflects the location of pressure zones on the periodontium. Rudolph et al.\textsuperscript{185} demonstrated in a finite element study that when tipping movements occur, stress concentrations exist at the alveolar crest and root apex, whereas when bodily tooth movements occur, there is more even distribution along the root surface. Purely intrusive, extrusive and rotational movements were found to result in stress concentration at the apex. Furthermore, OIIRR occurs preferentially at the apical region because the variable orientation of periodontal fibres in this region enables increased stress concentration,\textsuperscript{186} the acellular cementum covering the apical third of the root is more friable and prone to injury,\textsuperscript{18, 80, 186} and the perpetual challenge of aligning forces through the centre of resistance of a tooth in all three planes to achieve a true bodily translation, results in undesirable stress concentrations in the apical third of the tooth.\textsuperscript{80}

2.2.6.2.5 Pattern of Force Application

The pattern of force application may be either continuous or intermittent. The effect of applying forces continuously or intermittently on OIIRR in the literature is unclear. One view is that an intermittent pattern of force application allows resorbed cementum to repair with less resultant OIIRR.\textsuperscript{48, 124, 187-193} The alternate view is that there is no difference in the amount of OIIRR between intermittent and continuous force applications.\textsuperscript{194} More importantly, even though continuous forces cause more OIIRR, they are more efficient at orthodontic tooth movement than intermittent forces. In the case where intermittent forces are beneficial, various studies have attempted to determine an appropriate length of pause between force applications,\textsuperscript{192, 193} with a regime of 18 days-on and 3 days-off scheme producing significantly less OIIRR when compared with a 3-week continuous force application, albeit with a slower mean tooth movement rate.\textsuperscript{192}
2.2.7 Pathogenesis

2.2.7.1 Mechanism of resorption: histopathology and biochemical mediators

The process of OIIRR is characterised by the following features:

1. Application of orthodontic force to the tooth,
2. In areas of high stress concentration, exceeding the capillary blood pressure (20-25g/cm²), overcompression of the periodontium occurs with collapse of the local blood supply,
3. Formation of aseptic necrosis occurs in the periodontal membrane and bone, which has a glass-like hyalinised histologic appearance,
4. An inflammatory process is initiated at the periphery of the hyalinised zone, in adjacent vital parts of the PDL. The following hormones are involved in orchestrating this initial inflammatory process via synthesis of signalling molecule prostaglandin E2 (PGE₂) and an intracellular “second messenger” cyclic adenosine monophosphate (cAMP): IL-1α, IL-1β and TNF,
5. At the periphery, viable resident macrophages and fibroblast-like cells begin phagocytosis of cellular and connective tissue remnants of the periodontal membrane and precementum, while mono-nucleated tartrate resistant acid phosphatase (TRAP) - negative fibroblast-like cells continue to remove the necrotic hyaline tissue and surface layers of precementum and mineralised acellular cementum,
6. The cementoblast lining and cementoid on the root surface becomes damaged during resorption of the hyaline zone or as a result of orthodontic pressure, and the underlying mineralized cementum becomes exposed,
7. Blood-borne TRAP-positive multi-nucleated giant cells (MNGC) infiltrate and remove the main part of the necrotic tissue and upon reaching the contaminated and damaged root surface, continue resorption of the cementum surface. Although these MNGCs lack ruffled borders and have many morphological traits similar to odontoclasts and osteoclasts, and are assumed to be derived from the mono-nucleated phagocytic system.
8. It has been suggested that, in areas where the cementum has been partly or fully removed, new odontoclasts differentiate, appearing as multi-nucleated TRAP-positive cells with ruffled borders and clear zones, as they are found only within root resorption lacunae in contact with resorbed dentine surfaces. The following osteoblast-derived factors are involved in the differentiation and activation of osteoclasts: receptor activator of nuclear factor kappa B ligand promotes osteoclast formation, while osteoprotegerin (OPG) down-regulates osteoclastogenesis, and may similarly be involved in the regulation of odontoclast activity. An increased production of RANKL, decreased production of OPG and a stimulated osteoclast formation has been detected in the compressed PDL cells obtained from patients with severe apical root resorption, while increased levels of RANKL and OPG have been detected in rats in the environment of root resorption following the application of heavy forces.

9. The inflammatory resorptive process continues until no necrotic tissue is present and/or when there is relief of compression. Resorption of the alveolar bone wall as well as resorption lacunae on the root surface, expanding the amount of root surface under compression, contributes to decompression of the periodontal membrane. As the local stress concentration abates, stimulation of the inflammatory process is reduced and spontaneous repair of resorption lacunae in cementum is permitted.

2.2.7.2 Resistance and Repair

The precementum and cementoblast lining of the root surface have been recognized as providing a protective barrier against root resorption which may be attributed to potent anti-collagenases that inhibit the extracellular removal of the cementoid lining and prevent access and stimulation of clastic cells by the underlying mineralised tooth structure. Some authors have explored the role of remodelled cementum in providing additional protective effects when reporting on findings of patients having less OIIRR following orthodontic retreatment. However, it should be
noted that patients seeking retreatment in general need less tooth movement to correct the malocclusion, and these findings of less OIIRR should be evaluated with care. 4

Once the necrotic tissue is cleared and as the local stress concentration reduces, repair of OIIRR lesions commences. During this process, cementoblasts rich in rough endoplasmic reticulum and dense bodies indicating synthesis of fibrillar collagen material, migrate into the lesions and begin deposition of acellular cementum which is later replaced by cellular cementum, and a new periodontal ligament is established. This new PDL is comparable to that found in control specimens. Thus the risk of tooth loss due to OIIRR is not high. Some authors have reported that repair is initiated from the periphery, while others have reported repair initiating from the central zone. 

Repair of OIIRR lesions has been described in four phases:

I. Lag Phase: End of resorption and beginning of repair: With dissipation of residual forces differentiation of cementoblasts occurs.
II. Incipient Phase: 14 days later: a transitional phase between no apposition and active deposition.
III. Peak phase: 14-28 days later: Short spurt in matrix formation and incorporation of extrinsic fibres into the intrinsic cementum matrix.
IV. Steady Deposit phase: 42-56 days: steady deposition of mixed fibrillar cementum.

Repair of OIIRR lesions has been reported to occur during the application of light forces and simultaneously with OIIRR continuing in a different zone of a lesion. The onset of repair has been reported in histological studies of human premolars, to occur as early as the first week of retention, and the amount of repair increases with increased time in retention. After 5-6 weeks, the process slows down and reaches a steady phase with up to 75-82% of the resorptive areas
undergoing repair at 6-8 weeks of retention, with great individual variation in healing potential reported. 88, 207

After analysing the repair process in a rat model, OIIRR at the end of treatment has been proposed to result from a series of repetitive resorption and healing cycles throughout the treatment period, and hence the time span between each orthodontic adjustment may allow healing to occur. 213 Consequently, it has been suggested that frequent reactivation of orthodontic appliances as well as re-establishing new or additional mechanical loading before the repair process overcomes the resorption process, may result in severe root resorption. Longer time intervals between orthodontic reactivations may enable more healing to take place. For these reasons, when heavy orthodontic forces are applied, more than 12 weeks between each force application have been recommended.

In terms of the level of force application, Cheng et al 214 evaluated cementum repair at 4 and 8 weeks of retention after 4 weeks of continuous light and heavy orthodontic forces and reported that light orthodontic forces had the least OIIRR crater volume following passive retention.

2.2.8 Prognosis and Prevention, Management

There are no reports of iatrogenic tooth loss as a result of severe OIIRR. 215 A reduced root length subsequent to OIIRR could potentially compromise the longevity of affected teeth by complicating restorative treatment planning and placing them at greater risk of loss secondary to periodontal disease or trauma. Fortunately, in the majority of cases, the extent of root loss is mild and inconsequential to the long term survival and functionality of the affected teeth or dentition. 17, 18 Furthermore, OIIRR does not progress after appliance removal. 8, 17, 215, 216, 217

The most adverse outcome from OIIRR reported in the literature is hypermobility. 215 At a mean follow-up examination of 14 years, only 1% of teeth examined exhibited apical root resorption of more than one third the root length and 2% of patients reported hypermobility. 17 At long term
follow-up 5-15 years after active treatment, maxillary incisors with severe OIIRR and remaining root lengths less than or equal to 9mm are at increased risk of tooth mobility; the risk is less if the remaining length is >9mm. Increasing mobility can be expected with age in teeth with extremely resorbed roots, while teeth with root length ≥10mm and a healthy periodontium have been reported to remain stable. Root shortening of 0-3mm has been reported to equate to 0-1mm of crestal bone loss, with 4mm of apical root loss translating to 20% loss of total attachment. Consequently, patients that are susceptible to marginal periodontal breakdown may be at higher risk of losing severely resorbed teeth prematurely. Despite these findings, it is encouraging to note that OIIRR levels over 50% of the root length has not been found to be adequate reason for extraction and prosthetic replacement.
The following recommendations have been made for clinically reducing the risk of OIIRR: 58

✓ Identify risk factors with a thorough medical and family history, 5, 21

✓ Habit cessation, 82, 119

✓ Commencement of treatment when incisors have open apices, 85, 136

✓ Efficient treatment planning and mechanics to minimise treatment duration, 10, 51, 124, 156

✓ Light forces: especially for intrusion, maxillary incisor palatal torque and premolar de-rotation, 51, 52, 90, 136

✓ Intermittent forces to allow periods of rest and repair, 181, 187, 191

✓ Increased intervals between appointments (repair), 136

✓ Avoid sustained jiggling: e.g. intermaxillary elastics, 53

✓ Radiographic assessment at 6 months into treatment (or 3 months in high risk individuals) 145

  109 and

✓ Enable repair by pausing treatment for up to 3 months if resorption is detected, 142

There has been recent interest in the role of fluoride and the prevention of OIIRR. Foo et al found that fluoride reduces the average volume of root resorption craters in rats. 221 Gonzales et al found that fluoride reduces the depth and roughness of resorption craters in rats exposed to fluoride in drinking water from birth, suggesting an increased resistance to demineralisation. 222 Karadeniz et al reported patients residing in regions of high fluoride concentration in public water supplies (>2ppm) have been found to have significantly reduced volume of OIIRR craters when heavy buccal tipping forces are applied. 223 This effect was not significant with light forces. This study indicated that fluoride may reduce the acidic effect of clastic activity and decreased cementum solubility.
Interestingly, another study by the same group found that high fluoride intake from public water supplies did not have a beneficial effect on the severity of OIIRR after 4-weeks orthodontic force application and 12 weeks of passive retention.\textsuperscript{224}

The following guidelines has been recommended for managing OIIRR clinically:\textsuperscript{48}

- Pause treatment with passive arch wires for 2-3 months, cease force application for 4-6 months or in extreme cases terminate treatment\textsuperscript{124, 155}

- Reassess treatment objectives to reduce further damage: compromise or terminate early,

- Continue radiographic examination until resorption has ceased,\textsuperscript{44} especially in severe OIIRR cases. If OIIRR continues to worsen, sequential root canal therapy with calcium hydroxide may be considered.\textsuperscript{225}

- Appropriate counselling and regular review,\textsuperscript{155}

- Ensure that final radiographs at take at the time of fixed appliance removal,\textsuperscript{44}

- Retention of teeth with severely resorbed roots should be carefully considered to avoid adverse occlusal trauma that may exacerbate the root resorption.\textsuperscript{44}

2.3 Research Methods for Investigation and Evaluation of OIIRR

2.3.1 Radiography (2D)

Various radiographic techniques have been employed to document the incidence, prevalence and severity of OIIRR following orthodontic treatment.\textsuperscript{14, 41, 57, 58, 92, 180, 226, 227} Radiographic techniques employed include: periapical bisecting or paralleling angle, orthopantomogram, cephalogram and laminogram films. While these films are useful in recording the amount of root shortening, there are several limitations, explored previously, relating to: the two dimensional nature of the analysis, distortion and variable magnification factors.\textsuperscript{57, 60} Periapical paralleling techniques provide the least
distortion and superimposition errors when compared with orthopantomograms and lateral cephalograms. Due to these limitations alternate forms of investigation have been employed.

2.3.2 Histologic Analysis (2D)

Histological analysis, by way of hard tissue sectioning, staining and analysis by light microscopy, are conducted for research purposes where all stages of resorption can be observed. This analysis provides only a two-dimensional analysis and is limited by the ability to ensure that all craters are accurately identified, isolated, processed and analysed. Issues relating to variable tooth morphology further complicate preparation of the samples and accurate isolation of the lesions. Furthermore, samples are destroyed by this process and no further records of the original structure are maintained for subsequent analysis.

2.3.3 Scanning Electron Microscopy (2D)

In an effort to improve the identification and evaluation of OIIRR lesions, scanning electron microscopy has been employed, which utilises minimal specimen preparation to provide enhanced visual assessment of the root surface. Despite providing detailed information about resorption lacunae and the mineralised structure, SEM has been described as a difficult method of examining root resorption because sputtering of specimens with a carbon coating is necessary, and the desired image view must be chosen before an image is created; furthermore, parallax errors due to convexity in the tooth surface may manifest, resulting in errors in measurement.

To enable 3-dimensional mapping and volumetric analysis of the craters, stereo SEM imaging was developed. This method involves collection of two SEM images of a lesion to create a stereopair with a 6-degree difference in perspective, which is then converted to an 8-bit greyscale depth map to enable volumetric analysis of the lesion. Although highly accurate and reproducible, this technique is still relatively time consuming and technique sensitive.
2.3.4 X-ray Micro-Computed Tomography (3D)

Computed axial tomography uses computer-processed x-rays to produce tomographic slices of a scanned object. X-ray micro-computed tomography (XMT) is a high resolution version of computerized axial tomography enabling analysis in the order of micrometres. Digital geometry processing is then used to combine a series of tomographic images taken around a single axis of rotation to generate a three-dimensional reconstruction of the scanned object.

The resolution of medical computed axial tomography can only be obtained to a fraction of a millimetre, owing to limitations in radiation exposure. In order to obtain a higher resolution, the exposure must be increased 10,000-fold in order to achieve a tenfold improvement in resolution. With smaller specimen sizes, lower x-ray energies are required, enabling only 1000-fold increases in exposure for a tenfold improvement in resolution. Consequently, in order to obtain imaging on a micrometre scale, XMT is best suited to small inanimate specimens, and can only be considered a non-destructive technique, rather than a non-invasive technique, as only biopsy specimens are suited for analysis.237

XMT has been employed in several aspects of dentistry and include: measurement of enamel thickness and tooth measurement,238-243 analysis of root canal morphology,244-256 evaluation of root canal preparation,257-268 evaluation of craniofacial skeletal structure and development,269-273 micro finite element modelling,274-279 dental tissue engineering,280-282 mineral density of dental hard tissues283-293 and applications in dental implantology.294-303

The SkyScan 1172 high resolution commercial laboratory (absorption) XMT system (SkyScan, Aartselaar, Belgium) is a cone beam system that is suited to specimen sizes with a diameter up to 16mm and enables reconstruction sizes of <1um, 2um, 5 or 8um.304 Following scanning, SkyScan Nrecon package (Version 1.4.2; SkyScan, Aartselaar, Belgium) is used to reconstruct cross-section images from tomography projection images utilizing the Feldkamp algorithm.305
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The reconstructed cross-section images may then be imported into a variety of 3D reconstruction and visualisation software packages for volumetric analysis and imaging. The following findings have been reported from human studies utilizing XMT with the SkyScan 1172 system to investigate OIIRR:

1. The mean volumes of OIIRR craters in light (25g) and heavy (225g) force groups were approximately 11 and 68 times greater than in control groups respectively and the mesial and distal surfaces had the greatest resorption volumes.150

2. OIIRR sites were significantly increased in groups receiving orthodontic tooth movement, and fluoride has been found to reduce the size of resorption craters, although the effect is variable and not statistically significant.221

3. Clear removable thermoplastic aligners have similar effects on root cementum as light (25g) orthodontic force with fixed appliances.160

4. The volume of OIIRR craters on maxillary and mandibular first premolars induced by buccally directed forces for 12 weeks was directly proportional to the magnitude of the force, with maxillary premolars more susceptible to OIIRR than mandibular premolars.152

5. Intermittent forces of 226cN produced less OIIRR than continuous forces of 226cN over an 8 week period, with the buccal-cervical region having the most lesions.193

6. Unerupted and nonimpacted maxillary third molars exhibited the greatest OIIRR on the mesial root surface adjacent to erupted second molars. They also exhibited slightly greater cube-root volumes of resorption per tooth when compared with erupted first premolars not subjected to orthodontic forces, and similar cube-root volumes of resorption per tooth as first premolars subjected to light (25g) buccal and intrusive orthodontic forces. These findings suggested that OIIRR may occur as part of hard tissue remodelling and turnover, eruption or transmission of masticatory forces through the dentition to the alveolar bone.306

7. When used in combination with light microscopy, XMT has been reported to improve the efficiency and accuracy of histologic techniques.212
8. The amount of OIIRR in the left and right sides of both jaws was similar when heavy buccal forces are applied. Thus, it is expected that a split mouth technique may be used with teeth from one side of the jaw serving as controls.  

9. When comparing 2.5° and 15° of buccal root torque, higher magnitudes of torque can cause more OIIRR, particularly in the apical region, which is clinical significant because it can adversely affect the crown-to-root ratio.  

10. With high fluoride intake and heavy force application (225g) less OIIRR was found in all root surfaces and root thirds.  

11. A 15° distal root tip bend causes more OIIRR than a 2.5° distal root tip bend. Greater OIIRR can be found in areas under pressure compared with areas under tension.  

12. Heavy rotational forces cause more OIIRR than light rotation forces. Compression areas (buccal – distal and lingual mesial surfaces in this study) showed significantly higher OIIRR than other areas at all levels of the root.  

13. Greater OIIRR volumes were observed after heavy (225g) extrusive forces when compared with light (25g) forces. The distal surfaces of the root were significantly more affected than other root surfaces and may be influenced by root morphology and initial angulation of the tooth. There was no significant difference in the amount of OIIRR in the vertical thirds of the root for either force groups.  

14. Intermittent forces result in less tooth movement and OIIRR than continuous forces. With intermittent forces, when a pause is given, OIIRR decreases irrespective of the timing of reactivation. With continuous forces, 2 weekly reactivations produced faster tooth movement with similar OIIRR when compared with intermittent forces.  

15. In split-mouth study of 30 maxillary first premolar teeth, there was no statistical difference between control teeth and teeth exposed to vibration of 30Hz or 20grams with AcceleDent in terms of OIIRR volume and distribution, when 150g buccal directed forces are applied. Furthermore, a regression analysis revealed that patients with a higher level of individual
susceptibility to OIIRR may potentially benefit more from the use of vibration than those less susceptible.\textsuperscript{308}

16. In another split-mouth study of 28 maxillary first premolar teeth, exposure to vibration with 113 Hz and produced 33% less OIIRR than control teeth when exposed to 150g buccally directed forces.\textsuperscript{167}

17. High fluoride intake from public water supplies did not have a statistically beneficial effect on the severity of OIIRR after application of 4 weeks orthodontic forces and 12 weeks of passive retention.\textsuperscript{224}

18. Restorative build-ups, used to increase the vertical dimension by 2mm over a 4 week period, caused OIIRR along the sides of the teeth during the active bite increase period. No significant differences existed in the amount of OIIRR among the different surfaces or regions and there was no correlation between age, sex, volume of OIIRR and pain.\textsuperscript{182}
REFERENCES


68. Chiu, J., Ahuja, R., Khan, A., Dalci, O. and Darendeliler, M.A., *A preliminary investigation of cytokine expression in gingival crevicular fluid following orthodontic forces and associated...


MANUSCRIPT

THE EXTENT OF ORTHODONTICALLY INDUCED INFLAMMATORY ROOT
RESORPTION FOLLOWING TRANSVERSE AND VERTICAL JIGGLING MOVEMENT
WITH HEAVY FORCES FOR 12 WEEKS: A MICRO-CT STUDY

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4.1 Abstract

**Introduction:** Jiggling tooth movements may be responsible for root resorption in the absence of overt root displacement. This study aims to quantify and compare the effects of controlled heavy transverse buccal and palatal, and vertical extrusive and intrusive jiggling forces applied over a 12 week period on root resorption, and to localize the sites of prevalence in premolars.

**Method:** Ten patients who required bilateral maxillary first premolar extractions as part of their orthodontic treatment participated in this study. The total sample consisted of 20 maxillary first premolars. Heavy (225g) forces were applied to the right or left first premolar with the direction of force alternating along either the transverse or vertical plane every 4 weeks over a 12 week period. After the experimental period, the teeth were extracted without root damage and analysed with micro computed tomography. Each specimen was studied in 3 dimensions with specifically designed software to measure the volume of each crater.

**Results:** Heavy vertical forces produced marginally more root resorption than heavy transverse forces with median total crater volumes of 1.51mm\(^3\) and 0.92mm\(^3\), respectively (p=0.032). There was also a significant difference in the total root resorption on each root surface caused by heavy vertical and transverse forces (p<0.001) with greater resorption on the distal root surface of premolars undergoing heavy vertical jiggling forces. The cervical, middle or apical thirds of the root for both heavy vertical and transverse jiggling forces did not show any significant difference in root resorption.

**Conclusion:** Heavy vertical jiggling forces produced more root resorption than heavy transverse jiggling forces. Clinicians should especially avoid mechanics that apply vertical jiggling forces as these maybe more detrimental.
Key Words: Root resorption, jiggling, heavy forces, transverse, vertical, micro-computed tomography, volumetric analysis.

4.2 Introduction

Jiggling forces have generally been accepted to be responsible for Orthodontically Induced Inflammatory Root Resorption (OIRR). Jiggling was first described by Oppenheim and defined as “small intermittent movements along the tooth axis originating from biting forces when antagonizing teeth oppose extrusive forces,” or a tooth oscillating along a line of movement. Jiggling forces are thought to be produced during orthodontic treatment when there are occlusal interferences; when deformation of light archwires occurs during function with concomitant use of intermaxillary elastics; and following dental relapse that occurs after removal of palatal expanders. Restorative build-ups on first premolars, used to increase the vertical dimension by 2mm for 4 weeks, have been found to have increased OIRR during the active bite-increase period, which may be due to the premature contacts that transmit excessive uncontrolled vertical forces. Two animal studies have investigated the effects of jiggling on OIRR. Kim and Son (1994) found no histological or radiographic difference in the pattern of OIRR in a feline model when alternating mesial and distal forces were applied in 3 day cycles over 6, 12, 18 and 24 days when compared to unidirectional mesial forces; while Matsuda et al found that weekly cycles of alternating buccal and lingual jiggling forces produced more OIRR in Wistar rats than two or four weekly cycles, which continued to increase as the duration of applied jiggling forces lengthened. However, Baumrind in 1996 also advised, “resorption in the absence of overt root displacement seems entirely consistent with the purported role of “jiggling” during orthodontic treatment...”

The severity of OIRR is directionally proportional to the magnitude of the applied force. Numerous three-dimensional quantitative studies on human maxillary first premolars have demonstrated an increased amount of OIRR with increased force levels and in a rigorous systematic review of the literature, Weltman in 2010 concluded that heavy force application...
produced significantly more OIIRR than light force application or control groups. Heavy forces that induce excessive hyalinisation interferes with the repair of root resorption craters, resulting in an increased prevalence of OIIRR.

There are several x-ray microcomputed tomography (XMT) studies analysing the effect of heavy and light forces on OIIRR on human premolars. The volume of root resorption produced over a 12 week period by heavy buccal forces has been found to be 2.25 times greater than light forces. Over a 4 week period, the volume of root resorption produced by heavy intrusive and extrusive forces have been found to be approximately 6 and 3 times greater than light forces, respectively.

This study aims to quantify and compare the effects of controlled heavy transverse buccal and palatal, and vertical extrusive and intrusive jiggling forces applied over a 12 week period on root resorption, and to localise the sites of prevalence in premolars. It was hypothesized that: heavy vertical jiggling forces would result in greater root resorption volumes than transverse forces; the pattern of root resorption, in terms of the root surfaces and vertical third regions between the transverse and vertical jiggling force groups, would differ based on the location of force concentration; and heavy jiggling forces would result in clinically significant or severe root shortening in both the transverse and vertical groups.

4.3 Material and Methods

4.3.1 Sample

The sample consisted of 20 maxillary first premolars extracted from 10 orthodontic patients (7 girls, 3 boys), requiring removal of these teeth as part of their orthodontic treatment at Ondokuz Mayis University, Turkey. The mean age of these patients was 14 years and 7 months, (11 years and 9 months to 17 years and 7 months). Patients were selected according to a strict selection criteria described previously, with sufficient room for the proposed tooth movements to be carried out.
Ethics approvals were obtained from Zonguldak Karaelmas University (now known as University of Bulent Ecevit) Clinical Research Ethics Committee in Turkey (2012/06) and the University of Sydney Human Research Ethics Committee (2013/1095). Written and verbal informed consent was obtained from the participants and their parents or guardians. This study was also registered in the Australian and New Zealand Clinical Trials Registry.

Heavy (225g) forces, measured using a strain gauge (Dentaurum, Germany), were applied to a randomly selected right or left first premolar with the direction of force alternating along either the transverse (bucco-palatal) or vertical (intrusive-extrusive) plane every 4 weeks over a 12 week period. In transverse plane, the premolar was moved buccally for four weeks, palatally for four weeks and buccally again for another 4 weeks. In the vertical plane, the premolar was intruded for four weeks, extruded for four weeks and intruded again for another 4 weeks. All patients were treated by the same operator.

4.3.2 Appliance Design

SPEED™ orthodontic brackets with a 0.022 inch slot (Strite Industries, Cambridge, Ontario, Canada) were bonded to the maxillary first molars and premolars. A 0.017 x 0.025 inch Titanium Molybdenum Alloy wire was used to apply transverse and vertical forces. A transpalatal arch connecting the upper first molars was included in the setup with occlusal stops to prevent occlusal interferences (Figure 1).

4.3.3 Specimen Collection

After the experimental period, the teeth were extracted without root damage and placed in individual containers of 10% buffered formalin. Any residual periodontal ligament and soft tissue was removed by placement in an ultrasonic bath for 10 minutes followed by gently rubbing the root with damp gauze. The teeth were then immersed in 70% ethanol for 30min for disinfection and bench dried for at least 24 hours.
4.3.4 Specimen Analysis

A desktop microcomputed tomography x-ray system (SkyScan 1172, Aartselaar, Belgium) was used to produce multiple high resolution tomography projection images of the tooth. The x-ray tube operated at 59kV with a current of 167μA, and without filters. The rotation step of the tooth was at 0.200° and images were saved as 16 bit Tagged Image File Format (TIFF) files. Axial slice-by-slice reconstruction was achieved using Nrecon (version 1.4.2, Aartselaar, Belgium), which is SkyScan's reconstruction software. Avizo Fire Version 8 (FEI Visualisation Sciences Group, Burlington, MA, USA) was used for 3D reconstruction and visualisation of the dataset. Craters were manually isolated, duplicated and volumetrically calculated using a convex hull macro within Fiji, an image processing package comprising of ImageJ 1.47g, Java and Java 3D. This macro was developed by Dr Matthew Foley at the Australian Centre for Microscopy & Microanalysis at the University of Sydney. Once the craters were duplicated, the macro applies a 2D convex hull algorithm to each axial slice and calculates the number of pixels within the isolated crater. The macro then adds the total number of pixels across all slices and multiplies this value by the voxel volume, determined by the resolution (17.6μm), to calculate the total volume of the crater.

Craters were grouped according to their location on the root surface (buccal, lingual, mesial, distal) and according to their location in the vertical regions of the tooth (cervical, middle, apical). The total number of cross-sectional slices from the CEJ to the apex for each tooth was divided into thirds to determine the different vertical regions. Craters were allocated based on which region that corresponded to the majority of slices.

4.3.5 Statistical Analysis

Statistical analysis was performed using commercial software (SPSS for Windows, version 21, SPSS Inc., Chicago Ill). In order to create a model that satisfied the assumptions of the analysis, the scale of measurement was converted from volume (cubic millimetres) to cube-root-volume.
(millimetres). In doing so, the forces were compared to equivalent radii of the craters. This method has been used in similar studies. For statistically significant results, the mean values were transformed back to the volumetric scale, which adjusts for patient and other factors used in the analysis, and effectively translates to the median values for the sample.

The statistical analysis was conducted using a Univariate Analysis of Variance (ANOVA) with a modified Bonferroni adjustment for each of the cube-root volumes as response-variables: patient was assigned as a random factor (which links the two teeth from each person); and force, surface, region and their interactions as fixed factors. Due to the large number of tests examined, a significance level of 0.01 has been used, and p-values between 0.01 and 0.05 were considered marginally significant, in order to have some protection against type 1 errors (falsely rejecting a true null hypothesis).

Craters were measured three times for 15% of the sample, 2 and 3 months after the initial analysis, to determine the overall standard error of measurement.

4.4 Results

Heavy vertical jiggling forces produced more resorption than transverse forces at 1.15mm (1.51mm³) and 0.97mm (0.92mm³), respectively (Figure 2). This difference was marginally significant, \( p = 0.032 \).

The mean cube-root volumes for the different force and region combinations is shown in Table 2 and is depicted in the profile plot in Figure 3. Heavy vertical jiggling forces produced more resorption than transverse jiggling forces, however this difference was not statistically significant \( p = 0.127 \). Cervical regions appeared to have more resorption than middle or apical regions, however these differences were also not statistically significant \( p = 0.06 \). Although the trend of resorption values across the different vertical regions appear to be different for vertical and transverse forces in Figure 3, these differences were not found to be statistically significant \( p=0.438 \).
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The mean cube-root volumes for the different forces and surface combinations is shown in
Table 3 and is depicted in the profile plot in Figure 4. There was no overall difference (p=0.66) in the amount of root resorption between vertical and transverse forces. Irrespective of the type of force applied, the distal surfaces had the highest amount of root resorption (0.755mm or 0.430mm³) followed by the mesial (0.646mm or 0.270mm³), buccal (0.527mm or 0.146mm³) and lingual (0.410mm or 0.069mm³). These differences between surfaces were statistically significant (p<0.001). Vertical jiggling forces produced both the greatest and the least amount of resorption, which were found on the distal and lingual surfaces respectively (p<0.001). The difference in the trends of resorption volumes across the different root surfaces for vertical and transverse forces in Figure 4 is statistically significant (p<0.001).

Overall the statistical analysis revealed both statistically significant and marginally significant differences in root resorption between patients for all analyses conducted. Consequently patients were included as a random factor in the analysis which links the data obtained from the left and right sides of the mouth.

The overall standard error of measurement was found to be 0.0442mm³ and the coefficient of variance was 7.1%.

4.5 Discussion

Jiggling forces have long been implicated in OIIRR. Previous animal and human studies exploring the role of jiggling in OIIRR do not provide 3D quantitative conclusions on the amount of resorption. Additionally, due to the substantive methodological differences between these studies the results are also incomparable. Studies that discuss the effect of jiggling forces on OIIRR in humans have been of a short intermittent duration, caused by either the use of intermaxillary elastics, active removable appliances or occlusal interferences. Furthermore, while these studies report on the effects of jiggling in the transverse and vertical plane, there are no studies to date comparing the amount of OIIRR caused by controlled jiggling forces between the transverse and vertical planes of space.
This study follows up from a forthcoming prospective XMT study investigating the effect of light and heavy jiggling forces in comparison with unidirectional light and heavy forces on human premolars. To supplement this investigation, this study aims to compare the effect of controlled heavy jiggling forces occurring in 4 weekly cycles in the transverse and vertical plane over a 12 week period.

It is expected that vertical jiggling forces would have a higher force per unit area and thus cause more tissue necrosis and OIIRR, a finding that is supported by this study. Vertical jiggling forces produced a significant 65% more resorption than transverse jiggling forces. Clinically, these findings indicate that round tripping with heavy vertical forces should be avoided in patients with pre-existing root resorption, emphasizing the importance of efficient treatment planning.

Although the patient groups in previous root resorption studies analysed by XMT are not comparable, Harris et al found that heavy intrusive orthodontic forces produced a median average resorption volume of 9.41 x 10^{-3} mm^3, while Jimenez Montenegro et al found that heavy extrusive orthodontic forces produced a median resorption average volume of 6.33 x 10^{-3} mm^3; however, the heavy forces in both of these studies were applied for only 4 weeks. These values are much less than the median resorption values found for vertical (1.51mm^3) and transverse (0.92mm^3) forces in this study. Conversely, Paetyangkul et al reported heavy buccal forces applied over a 12 week period resulted in a median average of 17.31mm^3. This volume of OIIRR is 18 times greater than that found in the transverse jiggling group of this study.

In terms of the vertical thirds of the root, although there was no statistical difference in the mean cube-root volume of resorption between horizontal and vertical force groups, and between the different regions, there appears to be a general trend for the heavy vertical force group to exhibit greater resorption in the cervical third. Given that purely intrusive and extrusive forces are difficult to obtain without any mesiodistal tipping using the type of spring design in this study, the finding of greater resorption in the cervical third appears to be concordant with a finite element study.
demonstrating that the principal stress from a tipping force is located at the alveolar crest. The lack of statistical difference between regions is also concordant with results published in other similar XMT studies. 

Apical cementum is characterised by cellular intrinsic fibre cementum which has an adaptive and reparative function, with no role in tooth attachment. Apical cementum also has a reduced hardness and elastic modulus in comparison with cervical cementum, while the deficiency of Sharpey’s fibres in cellular cementum is assumed to make repaired and apical cementum more vulnerable to resorption. Consequently, the lack of statistical significance between the different vertical thirds found in this study and in other similar XMT studies may indicate that the hardness, elastic modulus and composition of cementum is unrelated to the distribution of OIIRR. Alternately, the findings in this study may be confounded by the alternating nature of the applied forces that may have enabled repair of the OIIRR lesions in the apical third, masking the effect of the heavy forces and reducing the discrepancy in OIIRR volumes between the different regions. Furthermore, the chosen sample size may be inadequate to elicit statistical differences in the vertical thirds and factor for variations in individual susceptibility, while the treatment duration of the study may also be inadequate to produce a noticeable difference; Matsuda et al found that the amount of root resorption area caused by jiggling forces in rats increased with increased time lapse of the experiment.

In this study, the distal root surface was found to have statistically more resorption in the heavy vertical jiggling group. This may be due to distal placement of the centre of rotation during extrusive and intrusive movements, caused by the design of the springs, resulting in uncontrolled distal tipping with greater tooth-to-bone contact along the distal surface, facilitating root resorption. This finding is concordant with those reported in similar micro-CT studies of vertical forces. Additional factors that predispose the distal surfaces to greater root resorption include the original
tooth position affecting the axial direction of applied forces\textsuperscript{28} and a distally inclined/dilacerated root morphology\textsuperscript{1, 20, 28, 19}.

Although, a new algorithm was written for this convex hull calculation, as explained by other XMT studies, there continues to be a limitation of underestimated crater volume on convex surfaces and overestimation of crater volumes on concave surfaces, which is mitigated because the crater volume measurement is based on direct imaging of the tooth as a fully three dimensional object\textsuperscript{19}.

In the process of calculating resorption volumes, there are two points in the process whereby voxel data is intentionally removed, which may affect the resultant reading on repeated measurements. When the teeth are scanned by SkyScan 1172 XMT unit, a series of high resolution projections of the tooth are produced with varying degrees of radiopacity. On reconstruction into cross-sectional slices, in SkyScan’s Nrecon software package, the images undergo a process of beam hardening and artefact reduction, and a user-defined greyscale range within the image is selected for the desired reconstruction. Through this process, pixels outside of this greyscale range are omitted from the cross-sectional slices, which is attributed to the extremes of being completely opaque or transparent. Typically this greyscale range should be selected based on the best imaging that can be achieved across the whole sample. Variations in this range may occur due to individual variations in tooth mineralisation and radiopacity. The cross-sectional slices are then compiled as a three-dimensional image of the tooth and is inspected for resorption craters in Avizo Fire. Once the resorption craters have been identified, the collection of cross-sectional slices are imported into Fiji (an image processing package based on Image J) and binarisation of the images in the stack of slices occurs following selection of an appropriate greyscale threshold with black set as background and white set as tooth structure. Once again, this greyscale threshold is selected based on the best imaging threshold that applies across the whole sample. Once a crater is identified and isolated, a range of x, y and z coordinates are then selected that define the location of the crater. Although the coordinates of the crater have been defined; to get to this stage, there have been two time points (at
THE EXTENT OF ORTHODONTICALLY INDUCED INFLAMMATORY ROOT RESORPTION FOLLOWING TRANSVERSE AND VERTICAL JIGGLING MOVEMENT WITH HEAVY FORCES FOR 12 WEEKS: A MICRO-CT STUDY

Carolyn Ng

reconstruction and on binarisation) whereby voxel data is omitted from the final sample from which crater volumes are calculated. Selection of different greyscale ranges and different greyscale thresholds may result in omission of different voxels in the final sample when the process is repeated, which effectively translates as variability in the number of craters and/or total volume of OIIRR.

To measure the reliability of the method, 15% of the sample underwent the process of reconstruction, conversion to binary scale and analysis, three times, 2 and 3 months after the initial analysis, to produce an overall standard error of measurement of 0.0442mm³ and a coefficient of variance of 7.1%. The sample size chosen for repeat analysis follows that used in a previous micro-CT study. The importance of repeating the process from reconstruction to volumetric analysis ensures that discrepancies in greyscale range and threshold selection are factored into the error of measurement. If the teeth do not undergo the whole process from reconstruction to volumetric analysis on repeat measurements, then there is unlikely to be a significant difference in the standard error of measurement as the x, y, z coordinates of a binary image are unlikely to deviate from the initial analysis. The standard error of measurement in this study is similar to that reported in a similar XMT study on OIIRR.

Volumetric root resorption results obtained by different XMT studies are often not comparable because of variations in the scanning environment, x-ray beam properties and the operator involved in establishing image reconstruction and volumetric analysis parameters. The use of a calibrated phantom at the time of scanning each tooth would enable the entire sample to be calibrated and measured according to a defined greyscale range and threshold. When subsequent samples and studies are scanned with the same calibrated block it is expected that there may be greater standardisation and comparability between studies and samples. However, there is a practical issue of space optimisation in the chamber when inadequate space is available for the
sample alone. Furthermore there may be considerations relating to degradation of the calibrated phantom on repeated analysis.

The force characteristics employed by this study were chosen to reflect those used in routine clinical orthodontic treatment. Although the experimental period was short, the transverse force group may have a force pattern similar to that used in alternating rapid maxillary expansion and contraction (ALT-RAMEC) protocols advocated by Liou\textsuperscript{41, 42} for disarticulation of circumaxillary sutures for maxillary protraction in cleft and Class III patients. Alternately, the vertical force group may have a force pattern similar to that used in correction of deep bite Class II division 2 malocclusions, whereby maxillary incisors are intruded to reduce the deep bite and allow Class II correction, extruded during incisor palatal-root torque expression and re-intruded again to re-establish optimal overbite. The findings from this study indicate that the latter form of mechanics, when used with heavy forces, is more damaging than the former, which typically uses heavy forces, and as such, should be avoided in patients with clinical signs of increased risk for OIIRR. Considerations for efficient mechanotherapy with light forces is especially important in management of patients with malocclusions that may result in alternating vertical intermittent forces. Further treatment considerations may include the avoidance of intermaxillary elastics on light archwires and prevention of premature occlusal contacts in the final stages of incisor retraction to avoid occlusal interferences.\textsuperscript{6}

This findings of this study also suggest that combined tooth-borne and bone-borne expansion appliances may be a desirable option to reduce the transverse loading on the teeth during ALT-RAMEC expansion protocols. Vardimon\textsuperscript{5} demonstrated in an animal model that bone-borne direct magnetic expansion resulted in less OIIRR than indirect tooth-borne magnetic expansion, and there was less OIIRR after 4 months retention and 2 months relapse due to repair of the OIIRR lesions.
4.6 Conclusion

Heavy vertical jiggling forces produced greater OIIRR volumes than heavy transverse jiggling forces, neither of which appear to result in severe root shortening. Vertical jiggling forces produced greater OIIRR lesions on the distal surface of the root, which may be related to the type of spring design used. Clinicians should avoid mechanics that apply vertical jiggling forces as these may be more detrimental.

4.7 Acknowledgement

The authors would like to thank the ASO Foundation for Research and Education for their kind financial support and acknowledge the role of the Australian Microscopy and Microanalysis Facility in this research.
4.8 References


4.9 Figures

Figure 2: Experiment protocol........................................................................................................ 77

Figure 3: Mean resorption values for heavy jiggling forces. ...... Error! Bookmark not defined.

Figure 4: Mean resorption values for each vertical third region. ................................................. 78

Figure 5: Mean resorption values for each root surface.......... Error! Bookmark not defined.
A randomly selected right or left first premolar was moved buccally for four weeks, palatally for four weeks and buccally for four weeks, while the contralateral premolar was intruded for four weeks, extruded for four weeks and intruded for four weeks. 225g of heavy force was used on both sides.
Figure 2: Mean resorption values for heavy jiggling forces.
Figure 3: Mean resorption values for each vertical third region.
Figure 4: Mean resorption values for each root surface.
4.10 Tables

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Table 1: Force Direction: Mean Resorption Values (mm)

<table>
<thead>
<tr>
<th>Force Direction</th>
<th>Mean Resorption Values (mm)</th>
<th>SD</th>
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</thead>
<tbody>
<tr>
<td>Transverse</td>
<td>0.972</td>
<td>0.049</td>
</tr>
<tr>
<td>Vertical</td>
<td>1.147</td>
<td>0.049</td>
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</table>

Table 2: Vertical Third Region vs. Force Direction: Mean Resorption Values (mm)

<table>
<thead>
<tr>
<th>Vertical Third Region</th>
<th>Force Direction</th>
<th>Mean Resorption Values (mm)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Transverse</td>
<td>Vertical</td>
<td></td>
</tr>
<tr>
<td>Mesial</td>
<td>0.6</td>
<td>0.665</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.27</td>
<td></td>
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<tr>
<td>Distal</td>
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</tr>
<tr>
<td></td>
<td>0.08</td>
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</table>
**The extent of orthodontically induced inflammatory root resorption following transverse and vertical jiggling movement with heavy forces for 12 weeks: A Micro-CT study**

<table>
<thead>
<tr>
<th></th>
<th>Buccal</th>
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<tbody>
<tr>
<td></td>
<td>0.6</td>
<td>25</td>
<td>.429</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>38</td>
<td>.282</td>
</tr>
</tbody>
</table>

**Buccal**

- Force: 0.6 N
- Distance: 25 mm
- Value: 0.429

**Lingual**

- Force: 0.5 N
- Distance: 38 mm
- Value: 0.282
Table 3: Tooth Surface vs. Force Direction: Mean Resorption Values (mm)

<table>
<thead>
<tr>
<th>Vertical Third Region</th>
<th>Force Direction</th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
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</tr>
<tr>
<td>Mesial</td>
<td>0.6</td>
<td>027</td>
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<td>08</td>
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</tr>
<tr>
<td>Lingual</td>
<td>0.5</td>
<td>38</td>
<td>.282</td>
</tr>
</tbody>
</table>
Future Directions

It is expected that the differences in cementum hardness between the apical and cervical regions and the mosaic nature of cementum composition would result in regional differences in resorption and repair. Consequently, from a methodological perspective, further OIIRR studies that incorporate both hardness testing and XMT analysis may assist with determining possible reasons for the lack of variation in OIIRR for the different vertical thirds. Larger sample sizes that enable greater levels of stratification in terms of the timing of repair may also assist with achieving a greater spectrum of OIIRR volumes across the different vertical thirds. With adequate sample sizes, histologic and XMT studies may be conducted in tandem with hardness testing and XMT studies to further elucidate the role of cementum composition in OIIRR. There are obvious ethical considerations pertaining to extended intervention periods, however with well-planned study designs, larger scale studies may be more easily implemented with the current study protocols.

Unfortunately, due to magnification and corresponding radiation exposure issues relating to XMT in comparison with cone beam computed tomography, scanning with CBCT technology before and after application of orthodontic forces is unlikely to yield adequate data except in cases where severe OIIRR has occurred.
Appendices

6.1 Sample Distribution

10 participants

Randomly assigned first premolar

Transverse Jiggling 225g

Buccal 4 wks
Palatal 4 wks
Buccal 4 weeks

Extraction & Analysis

Vertical Jiggling 225g

Intrusion 4 wks
Extrusion 4 wks
Intrusion 4 wks

Extraction & Analysis
6.2 Specimen Collection Sequence

10% buffered Formalin → 10min Ultrasonic Bath → Gentle removal of PDL with damp gauze → 70% Ethanol disinfection → 24 Hours Bench Dry
6.3 Specimen Analysis Sequence

*SkyScan 1172 scanner* was used to produce multiple high resolution tomography projection images of the tooth. *SkyScan Nrecon* software package was used to reconstruct axial cross-sectional images. *Avizo Fire* was used for the 3D reconstruction of the tooth to allow visualization and identification of craters. Craters were manually isolated, duplicated and volumetrically calculated using a convex hull macro within Fiji, an image processing package comprising of *Image J*. 
### 6.4 Total Volumetric Resorption per Tooth

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<thead>
<tr>
<th>Subject</th>
<th>Transverse (T)</th>
<th>Vertical (V)</th>
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<td>0.024</td>
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<tr>
<td>2</td>
<td>0.075</td>
<td>0.142</td>
</tr>
<tr>
<td>3</td>
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<td>0.070</td>
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<tr>
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<td>0.072</td>
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<tr>
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<td>0.049</td>
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<tr>
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<td>0.166</td>
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### 6.5 Total Volumetric Resorption per Region

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<th>Apical</th>
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<td>V</td>
<td>T</td>
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<tr>
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<td>0.007</td>
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<td>0.024</td>
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T= transverse, V = Vertical
6.6 Total Volumetric Resorption per Surface

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<thead>
<tr>
<th>Subject</th>
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<th>Distal</th>
<th>Lingual</th>
<th>Mesial</th>
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</thead>
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<td>V</td>
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<td>B</td>
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<td>0.005</td>
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</table>

T= transverse, V = Vertical

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