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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.

Johnathan Grove

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Johnathan L.E. Grove
Dedication

To my mum Lynn and dad Don, for all your love, patience, and encouragement over the years. Without you I would not be where I am today. Thank you for always being only a phone call away!

To my beautiful Adriana, for all your love and support. You always manage to bring a smile to my face. Thank you for sharing this journey with me!

To all my friends and family, thank you for simply understanding!

“All men by nature desire to know”

(Aristotle)

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Abbreviations

2D Two dimensional
3D Three dimensional
AAC Acellular afibrillar cementum
AEFC Acellular extrinsic fibre cementum
AIFC Acellular intrinsic fibre cementum
BMP Bitmap
cAMP Cyclic adenosine monophosphate
CIFC Cellular intrinsic fibre cementum
CEJ Cemento-enamel junction
CMSC Cellular mixed stratified cementum
FEM Finite element model
GIC Glass ionomer cement
HERS Hertwig’s epithelial root sheath
Hz Hertz
IL-1 Interleukin-1
IL-1b Interleukin-1beta
Micro-CT Micro computed tomography
MM Millimeters
NSAID Non-steroidal anti-inflammatory drug
OIIIRR Orthodontically induced inflammatory root resorption
OPG Osteoprotegrin
OTM Orthodontic tooth movement
PA Periapical radiograph
PDL Periodontal ligament
PEMF Pulsed electromagnetic field
PTH Parathyroid hormone
RANK Receptor activator of nuclear factor kappa beta
RANKL Receptor activator of nuclear factor kappa beta ligand
SEM Scanning electron microscopy
TEM Transmission electron microscopy
TIFF Tagged image file format
TMA Beta-titanium molybdenum alloy
TNF Tumour necrosis factor
TNFRSF11A Tumour necrosis factor receptor super-family 11alpha
TRAP Tartrate resistant acid phosphotase
µE Micro strain
WBV Whole body vibration
XMT X-ray microtomography
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1 Introduction

Orthodontic tooth movement (OTM) occurs as a result of the mechanical stimulus, produced by a force applied to the crown of a tooth, and the biological response of the periodontium\(^1\). There are three fundamental biologic responses associated with application of orthodontic force, including bone apposition, bone resorption, and root resorption.

The occurrence of root resorption was first mentioned in 1856\(^2\), and has been described as a physiological or pathological process that involves the active breakdown and destruction of formed tooth structure\(^3\), specifically mineralised and non-mineralised cementum and mineralised dentine\(^4\)\(^-\)\(^5\). Physiological resorption occurs naturally and can be seen in the deciduous dentition during the process of tooth eruption. Pathological resorption involves either internal resorption within the canal, or external resorption of the root surface.

Although the link between root resorption and orthodontic force was first suggested by Ottolengui\(^6\) in 1914, the relationship is still not well understood. It appears external root resorption occurs during orthodontic tooth movement in association with the removal of hyalinised tissue resulting from local injury to the periodontal ligament (PDL)\(^4\) i.e. orthodontic force. Brezniak and Wasserstein\(^7\) suggested the application of an orthodontic force induces an inflammatory reaction within the PDL which is essential to tooth movement and is also fundamental to root resorption. They described this orthodontic force induced root resorption as Orthodontically Induced Inflammatory Root Resorption (OIIRR), and concluded it is an undesirable and unavoidable consequence of orthodontic treatment\(^7\)\(^-\)\(^10\).
The incidence of OIIRR varies within the literature ranging from a greater than 90% occurrence of root resorption in histological studies\textsuperscript{11-13} to incidences of 0% - 100% in radiographic studies\textsuperscript{14-20}. More recently, the incidence of root resorption in adults has been reported as 25% - 76% after at least 12 months of treatment\textsuperscript{21-25}, while in adolescents the incidence has been reported as 5% - 18\%\textsuperscript{16, 22, 26, 27}. Root resorption has also been reported in untreated teeth increasing in conjunction with age, suggesting some degree of loss of root structure can be considered normal\textsuperscript{11, 28}.

The aetiology of root resorption appears to be remarkably multifactorial and remains largely unknown. Many studies have investigated and attempted to isolate causative factors related to OIIRR, and have identified numerous risk factors\textsuperscript{29, 30}. These can be broadly grouped into biological, dental, and mechanical factors. Examples of biological factors include genetic factors such as individual susceptibility\textsuperscript{31-34} and ethnicity\textsuperscript{24}, as well as environmental factors such as allergies\textsuperscript{35, 36} and medications\textsuperscript{37-40}. Previous history of resorption and trauma\textsuperscript{15, 26, 41, 42}, tooth morphology\textsuperscript{24, 43, 44}, and bone density\textsuperscript{39, 45}, are examples of dental factors. Lastly, treatment duration\textsuperscript{27, 46-48}, force magnitude\textsuperscript{12, 49-52}, and type of tooth movement\textsuperscript{53-57} are examples of mechanical factors implicated in OIIRR. These mechanical factors are of particular interest to the clinician as they may be controlled and modified in an attempt to reduce their influence upon root resorption.

In terms of clinical and practical significance, the degree of root resorption in most cases will be inconsequential and will not affect the long term survival or functionality of the afflicted teeth or dentition\textsuperscript{10, 48}. However, in some cases the decreased crown to root ratio resulting from severe resorption can significantly affect the prognosis, especially in the presence of periodontal disease or trauma\textsuperscript{58}. Fortunately the risk of severe root resorption
is rare occurring in less than 5% of treated patients\textsuperscript{21, 23, 59}, and a number of strategies have been suggested to help minimise the process including:

\textbf{I.} pre-treatment assessment of medical and family history\textsuperscript{24, 28, 31, 34},

\textbf{II.} radiographic assessment at 6 months into treatment (or at 3 months in high risk individuals)\textsuperscript{46, 60},

\textbf{III.} reducing treatment duration\textsuperscript{13, 27, 46, 61},

\textbf{IV.} reducing force magnitude\textsuperscript{9, 12, 13, 62}, and

\textbf{V.} halting treatment for periods of up to 3 months if resorption is detected\textsuperscript{33, 61, 63}.

The resorption process usually ceases once the orthodontic force is removed\textsuperscript{10, 64}, with repair beginning once the force has decreased below a certain level\textsuperscript{62, 65} and tending to increase with time\textsuperscript{66-68}.

Recently, the use of mechanical vibration concurrently with orthodontic treatment has been suggested as a possible means of reducing treatment duration as well as root resorption; however there is limited research in this area. Mechanical modulation of bone architecture has been found to have beneficial effects on fracture healing\textsuperscript{69, 70}, disuse atrophy\textsuperscript{71-73}, and musculoskeletal degeneration\textsuperscript{74, 75} including osteoporosis\textsuperscript{76-78}, as well as enhancing mechanical signalling within bone\textsuperscript{79-81}. Cyclical mechanical loading in animal models has also been shown to increase bone remodelling\textsuperscript{82-84}, and vibration of rat molars at 60 Hz has demonstrated significantly increased tooth movement and a suggested trend towards decreased root resorption\textsuperscript{85}. Vibration produced as a result of a pulsed electromagnetic field has also demonstrated evidence for faster tooth movement\textsuperscript{86}. Furthermore,
vibratory stimulation has been reported as a method to significantly reduce pain after orthodontic appliance adjustment\textsuperscript{87, 88}.

Previous studies have used a wide range of methods to investigate root resorption, ranging from two dimensional (2D) radiographs\textsuperscript{17, 31, 35, 60, 89-93}, and light microscopy\textsuperscript{9, 49, 66, 90, 94-100}, to scanning electron microscopy (SEM)\textsuperscript{12, 32, 67, 101}, and transmission electron microscopy (TEM)\textsuperscript{102}. However, three dimensional (3D) methods, including stereo SEM imaging\textsuperscript{55, 103}, and X-ray microtomography (XMT)\textsuperscript{52, 64, 104-106} have been shown to be more accurate and more reliable for quantitative measurements of root resorption\textsuperscript{52, 107, 108}.

The aim of this study was to investigate the effect of mechanical vibration, applied over 4 weeks to maxillary first premolars, on the volume of root resorption craters associated with application of a buccally directed controlled orthodontic force (150g), using Micro-computed tomography for qualitative and quantitative volumetric analysis. This study is a continuation of the root resorption research conducted by the Orthodontics Department in the Faculty of Dentistry at the University of Sydney.
2  Review of the Literature

2.1  Cementum

The periodontium is a complex structural and functional component of the dental apparatus. It is defined as those tissues supporting and investing the tooth, and consists of cementum, periodontal ligament (PDL), alveolar bone, and gingiva\textsuperscript{109-112}. Cementum is a major component of the tooth root and it plays a very central role in the process of orthodontically induce inflammatory root resorption. As a result of its significance in root resorption, this section of the review will focus principally upon cementum and its characteristics.

2.1.1  Definition & Role of Cementum

Human cementum was first described in 1853, and has since been described as the thin layer of non-uniform calcified connective tissue secreted by cementoblasts onto the root dentine\textsuperscript{111, 113}. Cementum is continuous with the underlying root dentine and the overlying PDL, forming an interface between the two\textsuperscript{111}. Its slow formation throughout life allows for continual adaptation and reattachment of the PDL fibres.

Developmentally, cementum appears to be derived from the investing layer of the dental follicle, and it is similar in composition and physical properties to bone except it is avascular, and lacks innervation\textsuperscript{114}. It is also less readily resorbed than bone, which is important for orthodontic tooth movement. The reason for this feature is unknown but it may be related to\textsuperscript{111}:

- Physicochemical or biological differences between bone and cementum.
- Inherent properties of the pre-cementum layer.
- The increased density of Sharpey’s fibres (particularly in acellular cementum).
- The proximity of epithelial cell rests to the root surface.

The prime and vital function of cementum is to provide an interface on the root surface for attachment of the principle collagen fibres of the PDL\textsuperscript{109, 110, 115}. It is a highly responsive mineralised tissue that maintains the integrity of the root, helps to maintain the tooth in its functional position via adaptation of fibre attachment, and is involved in tooth repair, regeneration and pulp protection\textsuperscript{109, 111, 115, 116}.

2.1.2 Classification & Types of Cementum

Previous studies have identified several different types of cementum, which vary according to a number of factors including formation, location, function, structure, composition, and degree of mineralisation\textsuperscript{109, 111, 114}. Based on these characteristics, cementum can be classified as follows\textsuperscript{111, 112, 117, 118}:

1. **Primary or Secondary cementum.**
   
   This classification is related to the timing of development. Primary cementum is formed during root formation, whilst secondary cementum is formed when the tooth is in occlusion and then on throughout life.

2. **Cellular or Acellular cementum.**
   
   This classification is related to the presence or absence of cells within the matrix. Acellular cementum covers the root adjacent to the dentine, while cellular cementum is usually found mainly in the apical regions or overlying the acellular cementum layer.
3. **Extrinsic or Intrinsic fibre cementum.**

   This classification is related to the origin of the collagenous fibres in the matrix. Intrinsic fibres originate from secretion by cementoblasts, and extrinsic fibres are PDL fibres incorporated into the matrix.

   Seven different types of cementum have been illustrated in the literature\(^1\)\(^1\), \(^1\)\(^2\), \(^1\)\(^8\), however Bosshardt\(^1\)\(^9\) describes 3 fundamentally different varieties of human cementum and these can vary from tooth to tooth and/or region to region on the same tooth. These are:

   1. **Acellular extrinsic fibre cementum (AEFC).**

      This type of cementum corresponds with primary acellular cementum and is the first cementum variety deposited on the developing root, and therefore is mostly found on the cervical and middle thirds of the root, although it may extend further apically in anterior teeth\(^1\)\(^7\). AEFC formation begins shortly after crown formation concludes, and is completed prior to the tooth reaching occlusion, at which point cellular intrinsic fibre cementum formation begins\(^1\)\(^9\). AEFC formation is slow and differentiation of the cementoblasts involved occurs in close proximity to the advancing root edge. As the name indicates, this type of cementum is cell free; however it is densely packed with collagen fibres known as Sharpey’s fibres\(^1\)\(^2\) which are derived from the principle fibres of the PDL\(^1\)\(^1\). This high density of fibre insertions reflects its vital role in anchoring PDL attachment and tooth support during function\(^1\)\(^2\)\(^1\). AEFC has the ability to adapt according to functional demands and physiological movements, altering the orientation of the Sharpey’s fibres as required\(^1\)\(^2\)\(^0\).
2. **Cellular intrinsic fibre cementum (CIFC).**

This third variety of cementum in humans generally corresponds with secondary cellular cementum and is usually found in the apical third or furcation regions where no AEFC has been laid down\(^{111, 118}\). CIFC contains intrinsic fibres which run parallel to the root surface in a circular fashion, and cementoblasts which have become trapped in the ECM during its rapid deposition\(^{109}\). Acellular intrinsic fibre cementum (AIFC) may result when the formation occurs more slowly and cells are not incorporated. The lack of Sharpey's fibres means CIFC doesn’t have a direct role in tooth attachment\(^{120}\), however its adaptive behaviour allows it to maintain the tooth in its proper position\(^{112, 117, 118}\) and its rapid formation gives it a reparative role. As a result, it tends to be the main type of cementum found in areas of resorption repair. Towards the root apex, and in furcation areas, AEFC and the CIFC may commonly be present in alternating layers described as cellular mixed stratified cementum (CMSC)\(^{109, 111, 118}\). CMSC serves to reshape the root surface to compensate for physiological drift and non-physiological shifting of teeth within their sockets\(^{110}\).

3. **Acellular afibrillar cementum (AAC).**

This type of cementum is found either at or just above the cemento-enamel junction (CEJ) covering minor areas of cervical enamel\(^{110}\). AAC formation is believed to begin at the end of enamel maturation\(^{109}\), and it is usually thinly distributed, acellular with a mineralised ground structure, and is the only type of cementum containing no collagen fibres. Due to the lack of collagen fibrils and absence of cells within the matrix, its precise function is unknown\(^{109}\).
2.1.3 Development of Cementum

Although cementum formation occurs along the entire length of the root, cementogenesis and root dentine formation are intimately related in that cementogenesis initiation is limited to the advancing root edge during root development\textsuperscript{111, 117, 118}. At this site, Hertwig’s epithelial root sheath (HERS) is believed to send an inductive message to the ectomesenchymal pulp cells, stimulating them to differentiate into odontoblasts and deposit a layer of pre-dentine\textsuperscript{111, 112}. Soon after odontoblast differentiation, HERS becomes interrupted and detaches from the dentine surface allowing ectomesenchymal cells from the dental follicle to come into contact with the pre-dentine surface\textsuperscript{109-111, 117, 118}. The next series of events leads to differentiation of cementoblasts and subsequent deposition of cementum on the root surface, however the specific cells involved and the exact sequence of events is still unresolved\textsuperscript{111}. The classical theory suggests the cementoblasts are derived from the mesenchymal cells of the dental follicle\textsuperscript{109, 110, 113, 114}, whereas others have suggested the cementoblasts are derived from the epithelial cells of HERS\textsuperscript{120, 122-124}. The evidence seems to favour the classical theory\textsuperscript{109}.

When root development is about two thirds completed and the tooth is about to enter its functional stage, AEFC formation gives way to CIFC formation (although CIFC may be produced earlier, on furcation surfaces in multi-rooted teeth)\textsuperscript{109, 125-127}. The conditions and factors responsible for this transition are unknown. When root formation is complete, the whole surface is covered by cementum, with cervical AEFC layers having attained a thickness of \(-15\) pm and apical CIFC layers exceeding this value. In addition, CMSC starts its development on the apical root portion\textsuperscript{109, 110, 118}. 
The formation of cementum can also be divided into 2 distinct developmental stages, the pre-functional stage, and the functional stage. The pre-functional stage consists of cementum formation (primary cementum) prior to occlusal loading, and also determines the distribution of the cementum varieties along the root surface. The formation during this stage is slow, resulting in the acellular cementum varieties. The functional stage consists of cementum formation (secondary cementum) just prior to occlusal loading, which then continues through life. The formation during this stage is mainly rapid, resulting in cellular cementum varieties\textsuperscript{117}.

2.1.4 Composition & Components

As mentioned previously, the composition of cementum is very similar to bone\textsuperscript{128}, containing on a wet-weight basis 65% inorganic material, 23% organic material and 12% water. By volume, the composition comprises approximately 45% inorganic material, 33% organic material, and 22% water\textsuperscript{111, 129}. These values may vary however from sample to sample, and within the different types of cementum\textsuperscript{109} as the degree of mineralisation varies in different parts of the tissue; some acellular zones may be more highly calcified than dentine.

The organic matrix on the other hand is primarily collagen (principally type I collagen), in addition to concentrations of non-collagenous proteins that appear to be similar to those found in bone\textsuperscript{109, 111, 115}. Among these proteins are bone sialoprotein, osteopontin and other cementum specific elements that are involved in periodontal reattachment and/or remineralisation.
The principal inorganic component is found in the form of hydroxyapatite crystals, although other forms of calcium are also present at higher levels than in enamel and dentine. As with enamel, the concentration of trace elements including fluoride tends to be higher at the external surface. Fluoride levels are also found to be higher in acellular cementum.

2.1.4.1 Organic matrix

The cemental organic matrix is primarily derived from the extrinsic fibres of the PDL (Sharpey’s fibres), and from the intrinsic fibres produced by local cementoblasts. Type I collagen constitutes approximately 90% of this matrix, while type III collagen constitutes 5% and is found in high concentrations during development and repair of mineralised tissues. The collagen plays an important structural and morphogenic role, as well as providing a scaffold for mineralisation.

As mentioned, the organic matrix also comprises a number of non-collagenous proteins including primarily bone sialoprotein and osteopontin, as well as other examples such as fibronectin, dentine matrix protein, proteoglycans, glycosaminoglycans, and several growth factors. Overall, the function of the non-collagenous proteins within the organic matrix includes stimulation of cell migration, attachment, proliferation, protein synthesis, and mineralisation during root formation.

2.1.4.2 Mineral component

The mineral content of cementum tends to vary according to the type of cementum present, with AEFC being more highly mineralised than CIFC and CMSC. It is made up in the most part by hydroxyapatite crystals which are thin and plate-like and similar to those found in bone, as well as small concentrations of amorphous calcium phosphate. These
hydroxyapatite crystals are on average 55 nm wide and 8 nm thick, which is much smaller than the crystals within enamel. As a result of this, the cemental surface has a greater capacity for absorption of other trace elements such as Fluoride, but is also more susceptible to decalcification in the presence of acid conditions\textsuperscript{111, 128, 133}.

   It has been proposed in the literature that the mineral content or components of cementum may influence its resistance to root resorption\textsuperscript{11, 134}. Fluoride has been shown to have a relatively high concentration of 0.9\% in cementum, which is related to the fluoride exposure of the individual, and also generally increases with age\textsuperscript{109, 130}. Rex and co-workers found fluoride tended to accumulate in the surface layers of the cementum where it reacted with the hydroxyapatite, showing limited diffusion into deeper layers\textsuperscript{135}.

\section*{2.2 Root Resorption & Orthodontically Induced Inflammatory Root Resorption}

\textbf{Root Resorption}

The term “root resorption” is a general term that can be used to describe either the physiological or pathological process that results in loss of tooth structure.

Physiological root resorption occurs naturally and primarily refers to the resorption of the roots of the deciduous dentition during the process of tooth eruption. It can also be seen in the permanent dentition to a lesser extent as a result of physiological changes occurring over time\textsuperscript{111}.

Pathological root resorption on the other-hand is not as benign. It usually results from trauma, disease, or iatrogenic causes\textsuperscript{65}, and involves either internal resorption within the canal or external resorption of the root surface. Internal pathological resorption affects
the dentine and pulpal walls within the root canal and is initiated within the pulp. External pathological resorption affects the outer dentine and cementum surfaces and is initiated within the periodontium\textsuperscript{111}.

2.2.1 Definition

Root resorption has had several descriptions and definitions as the process has been studied and further understood. It was initially defined as the destruction of formed tooth structure\textsuperscript{3} but more recently it has been described as a physiological or pathological process that involves the active removal of tooth structure\textsuperscript{5}, specifically mineralised and non-mineralised cementum and mineralised dentine, in association with the PDL remodelling process\textsuperscript{136}.

Pathological external root resorption occurring as a result of the inflammatory reaction within the PDL induced by orthodontic force and tooth movement, has been defined separately by Brezniak and Wasserstein\textsuperscript{7} as Orthodontic Induced Inflammatory Root Resorption (OIIRR). This inflammatory process is fundamental to tooth movement as well as root resorption and as such is present to some degree in all orthodontic patients\textsuperscript{7-10}.

2.2.2 History

Root resorption has been studied extensively over the last century. The occurrence of root resorption in permanent teeth was first documented and discussed by Bates in 1856\textsuperscript{2}, who referred to the process as “absorption” resulting from trauma to the periodontal membrane. The link between root resorption and orthodontic tooth movement wasn’t made until 1914 when Ottolengui identified resorption that resulted specifically from orthodontic treatment\textsuperscript{6}.
In 1927, Ketcham radiographically investigated apical root resorption and suggested root shortening could result from an anatomical variation, impaction, or orthodontic treatment. He found 21% of his sample showed some degree of resorption of the anterior teeth with the maxillary teeth being more affected than the mandibular teeth. In a later study, he found root resorption was present in approximately 1% of non-orthodontic patients and concluded that hormonal or dietary factors may also play a role in the aetiology of root resorption.

During this period, both of the terms “absorption” and “resorption” were used interchangeably in the literature to describe the process of root resorption. The term “resorption” was proposed as being the most appropriate to describe the process in 1932, and this terminology remains in use today.

Since then, the process of root resorption has been further defined and described culminating in its contemporary definition as stated above.

### 2.2.3 Incidence & Prevalence

The incidence of OIIRR in the general population is unpredictable and varies within the literature as a result of the different techniques used to assess and measure the presence and volume of resorption ‘craters’.

Previous histological studies of orthodontically treated teeth have reported a greater than 90% occurrence of root resorption, while radiographic studies have suggested incidences ranging from 0% - 100%. More recently, the incidence of root resorption in adults has been shown to increase from 15% pre-treatment, to 25% - 76% after at least 12 months of treatment. In adolescents the incidence has been reported between 5% -
18%\textsuperscript{16, 22, 26, 27}, while Kurol used combined histological and radiographic techniques and found an incidence of 93%\textsuperscript{90}.

The incidence of root resorption in untreated teeth has also been reported in many of the same studies, similarly suggesting incidences ranging from 0%\textsuperscript{89} - 100%\textsuperscript{15, 28}. A histological study by Henry and Weimann\textsuperscript{11} found 90.5% of non-orthodontically treated teeth displayed evidence of resorption. The most commonly affected area was the root apex, followed by the mesial, buccal, distal, and lingual surfaces. They also found resorption increased with age, and concluded from their study that some degree of root resorption can be considered normal and is associated with the remodelling of bone and tissue that accompanies physiological tooth movement throughout life\textsuperscript{11, 28}.

When assessed using panoramic or peri-apical radiographs, the average OIIRR is usually found to be less than 2.5mm\textsuperscript{16, 22, 93, 137, 138}, or varying from 6% - 13% for different teeth\textsuperscript{58}. When graded scales are used\textsuperscript{26}, OIIRR is primarily found to be minor or moderate in most patients\textsuperscript{27, 35, 139, 140}. Fortunately, severe root resorption, defined as exceeding 4mm or one third of the original root length, is rare and seen in only 1% – 5% of teeth\textsuperscript{16, 21, 23, 27, 60, 139}.

### Incidence of Moderate Resorption

<table>
<thead>
<tr>
<th>Definition</th>
<th>Incidence</th>
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<tbody>
<tr>
<td>&gt; 2mm resorption</td>
<td>25%\textsuperscript{24}</td>
</tr>
<tr>
<td>&gt; 3mm resorption</td>
<td>30%\textsuperscript{31}</td>
</tr>
<tr>
<td>&gt; 2mm to 1/3\textsuperscript{rd} of root length</td>
<td>10% - 20%\textsuperscript{27, 141}</td>
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<td></td>
<td>12% - 17%\textsuperscript{137}</td>
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### Incidence of Severe Resorption

<table>
<thead>
<tr>
<th>Definition</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 5 mm resorption</td>
<td>5%\textsuperscript{21}</td>
</tr>
<tr>
<td>&gt; ¼ of root length</td>
<td>3%\textsuperscript{59}</td>
</tr>
<tr>
<td>&gt; 1/3\textsuperscript{rd} of root length</td>
<td>&lt; 1% - 3%\textsuperscript{16, 23}</td>
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</table>
Maxillary teeth, especially the lateral incisors, tend to be at greater risk of root resorption\textsuperscript{17, 24, 31, 137, 142}, followed by mandibular incisors and first molars. This appears to be related to the transfer and concentration of forces at the root apex\textsuperscript{143}.

### 2.2.4 Classification

Pathological external root resorption has a variety of appearances and has been classified accordingly by several authors within the literature including Andreasen\textsuperscript{144}, Tronstad\textsuperscript{145}, and Brezniak and Wasserstein\textsuperscript{29}. These classifications include:

1. **Surface resorption** – Tends to involve brief resorption of small areas of cementum followed by spontaneous repair. It is a self limiting process followed by repair and not usually detected radiographically.

2. **Replacement resorption** – Occurs where the PDL is absent or suffered extensive necrosis, and bone replaces the resorbed surface. This process results in ankylosis and is often seen after traumatic dental injuries.

3. **Inflammatory resorption** – Occurs where resorption reaches the dentinal tubules of a tooth with an infected, necrotic pulp. Inflammatory mediators and phagocytic cells colonise the resorbed and denuded cementum surface, and later invade the tubules and pulpal tissue. Under normal circumstances, the root is protected from resorption via cementum externally and pre-dentine internally; however, inflammatory resorption occurs when the pre-dentine or cementum become mineralised. Tronstad further classified inflammatory resorption into 2 categories:

   i. **Transient inflammatory resorption** – Occurs where root damage is minimal and the resorptive stimulation is brief, and is frequently seen in traumatised, or orthodontically or periodontally treated teeth. It usually lasts only 2-3
weeks followed by repair with cementum-like tissue, and is usually undetected radiographically.

II. **Progressive inflammatory resorption** – Occurs where the resorptive stimulus remains for a longer duration, as in orthodontic treatment. Once the pressure in the PDL is released, the resorption is halted. It is usually visible radiographically.

Root resorption associated with orthodontic treatment is most commonly surface resorption or transient inflammatory resorption\(^{29}\), and rarely results in replacement resorption (ankylosis)\(^7\). In 2001, Brezniak and Wasserstein classified OIIRR into 3 types based upon severity; which is determined by the extent to which the root surface is involved\(^7,146\). These types are:

1. **Cemental or surface resorption with remodelling** – Affects the outer cemental layers which are resorbed and then subsequently fully regenerated or remodelled once the etiologic factor has been removed.

2. **Dentinal resorption with repair (Deep resorption)** – Affects both the cementum and outer layers of dentine which are resorbed and the defect is usually repaired with cementum. The subsequent root shape after this resorption and repair may not be identical to the original form.

3. **Circumferential apical root resorption** – Involves significant resorption of the hard tissue components of the root apex, and results in root shortening. Repair only occurs within the cemental layers, so resorption is irreversible once apical root tissue loss occurs beneath the cementum. Sharp edges may remodel however.

2.2.5 Grading

Several subjective scoring systems have also been proposed for grading the severity of the OIIRR\textsuperscript{15, 147}. The grading system still commonly utilised today was proposed by Malmgren et al\textsuperscript{26}, and classifies apical root resorption into 4 categories (Appendix 6.1).

<table>
<thead>
<tr>
<th>Root Resorption Index</th>
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<tbody>
<tr>
<td>Grade 1</td>
</tr>
<tr>
<td>Grade 2 (minor)</td>
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<tr>
<td>Grade 3 (severe)</td>
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<tr>
<td>Grade 4 (extreme)</td>
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2.2.6 Aetiology

As mentioned previously, root resorption occurs as a physiological process, primarily in the deciduous dentition but also in the permanent dentition. It can also occur as a pathological process, with potentially significant resorption, as a result of a number of factors including impaction of adjacent teeth, peri-apical or periodontal inflammation, occlusal trauma, tumours or cysts, metabolic or systemic disturbances, orthodontic treatment, and idiopathic resorption\textsuperscript{148}.

The aetiology of root resorption associated with orthodontic treatment however, remains largely unknown, and appears to be remarkably multifactorial. Many studies have investigated and attempted to isolate causative factors related to OIIRR, and have identified numerous risk factors\textsuperscript{29, 30} associated with increased resorption. These can be broadly grouped into biological, dental, and mechanical factors and it is the mechanical factors which are of particular interest to the clinician as they may be potentially controlled and modified in an attempt to influence and reduce root resorption.
The exact contribution of patient versus treatment factors to the aetiology of OIIRR is still elusive in the literature, and the existence of large individual variation in responses appears to be the only consistent finding_149_.

### 2.2.6.1 Biological Risk Factors

The biological risk factors associated with OIIRR include those factors which are directly related to the patient and cannot be altered or controlled by the clinician. Some of these factors may be within the control of the patient suggesting a genetic or environmental origin.

#### 2.2.6.1.1 Genetic factors

1. *Individual susceptibility & genetics*

   Individual susceptibility is considered to be one of the major factors in determining root resorption potential with or without treatment, highlighted by the fact that resorption can occur in both cases_11, 47, 150_, as well as varying between individuals and within the same individual at different times_29, 62_. Root resorption is related to the individual’s own tissue response and metabolic activity so, metabolic signals such as hormones, body type and metabolic rate may play a crucial role affecting the relationship between osteoblastic and osteoclastic activity which modifies cell metabolism and individual response to disease and trauma_62_.

   The genetic influence on susceptibility to OIIRR remains somewhat controversial mainly due to the difficulty in separating the contribution of genetic factors from environmental factors such as orthodontic treatment_34_. Newman was the first to formally propose a genetic component to OIIRR_31_ and a number of recent studies also support the idea of a genetic influence_34, 150, 151_. Harris et al, investigated the incidence of OIIRR in
sibling pairs and reported a heritability of 70% for resorption of the maxillary incisor roots and the mesial and distal roots of the mandibular first molars\textsuperscript{151}. Ngan et al, investigated OIIRR using a twins model and found the quantitative concordance estimate was 49.2% for monozygotic twins and 28.3% for dizygotic twins\textsuperscript{34}. Both studies confirm the presence of a genetic component. Other studies have also reported familial clustering of OIIRR, however the pattern of inheritance was unclear\textsuperscript{31, 152}.

Interleukin-1 (IL-1) and tumour necrosis factor (TNF) are pro-inflammatory cytokines known to induce the synthesis of a variety of proteins that in turn elicit acute or chronic inflammation. IL-1b has been implicated in bone resorption accompanying orthodontic tooth movement, and increased levels have been found in the gingival crevicular fluid of patients undergoing orthodontic treatment. Tumour necrosis factor receptor super-family 11alpha (TNFRSF11A) is another candidate gene which encodes for receptor activator of nuclear factor kappa beta (RANK)\textsuperscript{153}. RANK together with its ligand (RANKL) is an essential signalling molecule for osteoclast formation and activation. Polymorphism can influence the activity of these molecules; Al-Qawasmi and colleagues identified the roles of gene polymorphism of IL-1b and TNFRSF11A in OIIRR. They found patients homozygous for IL-1b allele 1 (known to decrease production of IL-1) had a 5.6 fold increased risk of resorption\textsuperscript{154}.

2. **Ethnicity**

Ethnicity has also been implicated in influencing susceptibility. Sameshima and Sinclair\textsuperscript{24} investigated the prevalence of resorption in several populations, and found Caucasians and Hispanics were more prone to OIIRR than patients of Asian descent. However, Smale and colleagues did not report any association between race and extent of OIIRR\textsuperscript{155}. 

By Johnathan Grove
3. **Gender**

The incidence of OIIRR, or its severity during treatment, does not appear to be associated with gender. While several studies have reported a higher incidence in females \(^{14, 31, 156}\), and others have reported a higher incidence in males \(^{48, 157}\), most investigators have concluded there is no correlation between OIIRR and gender \(^{24, 33, 58, 151, 158-160}\).

4. **Age**

Historically it was believed the incidence of resorption increased with age in conjunction with the aging changes experienced by the periodontium such as increased cemental thickness, increased bony density and concurrent decreased vascularity, and decreased PDL plasticity and vascularity \(^9, 16\). As a result, tooth movement is associated with the generation of more areas of hyalinisation \(^{30}\). However, almost all recent studies suggest age at the start of treatment is poorly correlated with the incidence of OIIRR \(^{41, 48, 63, 66, 160-165}\).

Some investigations have found the risk of OIIRR is lower in patients treated before the age of 11 years, reporting roots with incomplete development before treatment reached a significantly greater length than those that were fully developed \(^{137, 166}\).

2.2.6.1.2 **Environmental factors**

1. **Asthma & allergy**

Several studies have implicated both asthma and allergy as aetiological risk factors in OIIRR.

Increased incidence of resorption has been found in patients suffering from chronic asthma regardless of whether the condition was medicated or not \(^{35, 96, 167}\). McNab and co-workers described a higher incidence of root resorption, especially blunting of the maxillary molars, in chronic asthmatic patients compared to healthy controls. Davidovitch et al found
The effect of mechanical vibration (113 Hz applied to maxillary first premolars) on root resorption associated with orthodontic force: A micro-CT study.

By Johnathan Grove

Elevated levels of alveolar bone osteoclasts in areas of PDL compression in guinea pigs with induced allergic asthma, suggesting that chemical mediators produced in the asthmatic state may influence cell populations and enhance the resorption process. It has been proposed that the incidence of resorption of posterior teeth may be related to changes in the immune system in asthmatic patients resulting from proximity of the upper molar roots to the inflamed maxillary sinus, and/or the presence of inflammatory mediators in these patients. These inflammatory mediators may enter the periodontal ligament and act synergistically to increase susceptibility to resorption. However, the increased incidence of root resorption appeared to be confined to an increase in root blunting, and therefore asthma may only represent a minimal risk that may not affect the function or longevity of the posterior teeth.

Allergies also appear to increase the likelihood of developing OIiRR. Nishioka et al, investigated the correlation between excessive root resorption and several immune system factors, and found the incidence of allergy, asthma, and root blunting were increased in root resorption patients. Other studies have also demonstrated an association between asthma and allergies, and increased occurrence of root resorption.

2. Endocrine & hormone imbalance

The endocrine system is closely tied to bone activity and metabolism so disorders affecting calcium metabolism such as hypothyroidism, hyperparathyroidism, Paget’s disease, and other diseases, have been associated with altered resistance to root resorption. Linge and Linge suggest the hormonal imbalance doesn’t cause resorption it only influences the process.
The risk of resorption has been shown to be higher in subjects with a decreased bone turnover rate, such as in patients with hypothyroidism\(^{39, 171}\); and lower in subjects with increased bone turnover, such as with hyperparathyroidism.

3. **Nutrition**

A number of authors have concluded that malnutrition or nutritional imbalance is not a major aetiological factor in root resorption\(^{16, 45}\), however calcium and vitamin D deficiency in rats has been associated with increased parathyroid hormone (PTH) and osteoclast levels, greater and more rapid bone resorption, and more severe OIIRR\(^{3, 171}\).

4. **Drugs & medications**

The role of certain drugs and medications in the pathogenesis of root resorption has also been investigated in the literature, including non-steroidal anti-inflammatory drugs (NSAIDS)\(^{37, 38, 172-174}\), corticosteroids\(^{22, 175-179}\), L-thyroxine\(^{180-182}\), and most recently bisphosphonates\(^{39, 40, 134, 183}\).

NSAIDS inhibit cyclo-oxygenase and subsequent prostaglandin production, and are commonly taken for treatment of pain and inflammation. The effect of NSAIDS on tooth movement and root resorption has been controversial in the literature but recent research has shown some NSAIDS produce a reduction in root resorption\(^{37, 38, 184}\) without affecting tooth movement\(^{37}\).

Corticosteroids are commonly used to treat allergies and asthma as well as a variety of other conditions. A recent study reported reduced root resorption in an experimental group receiving long term corticosteroids which they suggested may be due to faster remodelling of bone, reduced hyalinisation, and reduced remodelling of root tissue\(^{178}\).
However, the effect of corticosteroids on resorption is still unclear and appears to be dependent upon the dose and the animal model\textsuperscript{175, 177}.

Potent bone resorption inhibitors like bisphosphonates have become a popular treatment option for patients suffering from osteoporosis. They inhibit resorption by directly or indirectly inducing apoptosis in osteoclasts, and have been found to cause a dose-dependent inhibition of root resorption in rats as well as decreased osteoclast numbers and tooth movement\textsuperscript{39, 40, 185, 186}. On the other hand, it has also been demonstrated that these drugs can actually increase vulnerability to the resorptive process\textsuperscript{134, 183} by producing alterations in the cemental surface of the root via inhibition of acellular cementum formation.

Administration of L-thyroxine in rats has been demonstrated to increase the resistance of cementum and dentine to osteoclastic activity\textsuperscript{181} and reduce the extent of root resorption\textsuperscript{182}.

5. \textit{Alcohol consumption}

Chronic alcoholics are at increased risk of developing severe root resorption during orthodontic treatment as a result of altered calcium homeostasis which stimulates PTH production that in turn enhances resorption of mineralised tissues\textsuperscript{167, 187}.

6. \textit{Habits}

Habits such as nail biting\textsuperscript{15, 31, 188}, finger sucking beyond the age of seven\textsuperscript{137}, and tongue thrust\textsuperscript{31, 162} have historically been associated with the development of resorption. Conversely, more recent reviews have suggested habits do not play any significant role\textsuperscript{16, 161}. 
Orthodontic elastic wear during treatment for anterior open bite (AOB), resulting from long term tongue thrust, may promote root resorption rather than the habit itself\textsuperscript{41}.

\subsection*{2.2.6.2 Dental Risk Factors}
A number of local dental risk factors have also been proposed as potential aetiological agents in the pathogenesis of OIIRR.

\subsubsection*{2.2.6.2.1 Pre-existing resorption}
Pre-existing root resorption has been shown to be an important risk factor for the development of severe OIIRR with treatment\textsuperscript{26, 30, 31, 41}. Studies such as Massler and Malone\textsuperscript{15} have shown there is a high correlation between the amount and the severity of root resorption present before treatment and the root resorption discovered after orthodontic treatment.

\subsubsection*{2.2.6.2.2 History of trauma}
Teeth which have been previously traumatized may experience external root resorption even in the absence of orthodontic treatment, the extent of which is related to the severity of the trauma\textsuperscript{42}. For example, mild to moderate injuries such as subluxations can cause resorption in less than 1\% of injured teeth while more severe injuries such as avulsion and re-implantation can cause resorption in 74\% - 96\% of affected teeth\textsuperscript{42}.

OTM of traumatised teeth may increase the risk of OIIRR\textsuperscript{16, 137, 189}, though once again this may be dependent upon the severity. Malmgren et al\textsuperscript{26} found that traumatized teeth with no sign of resorption are no more resorbed than non-traumatized teeth while Kjaer\textsuperscript{156} found teeth with minor to moderate injuries are at no greater risk of OIIRR than uninjured teeth.
A recent study found no statistically significant difference in the incidence of OIIRR between patients with traumatized and non-traumatized teeth\textsuperscript{140}, yet if a previously traumatized tooth exhibits resorption before treatment, then there is a greater chance that OTM will enhance the resorptive process\textsuperscript{29, 150}.

2.2.6.2.3 Dental morphology, anomalies, and agenesis

A number of mostly observational studies have reported abnormal root shape, such as pipette shaped or narrow roots and dilacerations, as well as other dental anomalies including taurodontia, agenesis, and ectopic or transplanted teeth, are risk factors for OIIRR\textsuperscript{24, 27, 31, 60, 155, 156, 162, 190}. Oyama and colleagues\textsuperscript{43} suggested abnormal root morphology may increase the risk of root resorption due to the greater loading of the roots during orthodontic treatment.

Conversely, other investigators have found no significant correlations between dental anomalies\textsuperscript{140, 191}, peg-shaped roots or microdontia of lateral incisors\textsuperscript{142}, and OIIRR.

Short roots are also commonly believed to undergo more resorption\textsuperscript{31, 158}, although a more recent study supports the opposite view that the tendency for resorption increases with increasing tooth length\textsuperscript{44}. This is possibly because longer teeth need stronger forces to be moved meaning the actual displacement of the root apex will be greater during torquing movements\textsuperscript{24, 44, 143}.

Agenesis of multiple teeth (4 or more missing teeth) is also associated with increased risk of root resorption\textsuperscript{22}. This is probably due to orthodontic forces being distributed over fewer teeth as well as the requirement for more extensive and longer treatment in such cases\textsuperscript{60}. 

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2.2.6.2.4  **Endodontic treatment**

The effect of previous endodontic treatment on the incidence of resorption during OTM has always been of concern however the link between endodontic treatment and OIIRR is still not clearly established.

A higher frequency and severity of resorption in endodontically treated teeth during orthodontic treatment has been reported. On the other hand, recent authors have found teeth with previous root canal treatment exhibit a lesser propensity for apical root resorption and have suggested these teeth are more resistant to resorption because of increased dentine hardness and density. Recent work by Esteves and colleagues demonstrated no significant difference between endodontically treated teeth compared to vital teeth in terms of OIIRR, suggesting endodontically treated teeth can be moved orthodontically as readily as vital teeth.

OTM itself creates an inflammatory response which may exacerbate an existing resorptive process but, if the tooth has been successfully treated endodontically with healthy periodontium, it should be no more susceptible to resorption than a normal tooth.

2.2.6.2.5  **Periodontal status**

Owman-Moll and Kurol concluded from their study that periodontal disease, as well as habits like nail-biting and lip/tongue dysfunction, increases the risk of external root resorption during orthodontic treatment.

Hypo-functional periodontium has also been documented as an aetiological factor. Hypo-functional periodontium exhibits progressive atrophic changes in all functional
periodontal structures, and it may accelerate resorption as a result of decreased ability to
distribute the mechanical stress of orthodontic forces\textsuperscript{194,195}.

\textbf{2.2.6.2.6 Specific tooth type vulnerability}

According to the literature, maxillary teeth have the highest risk and incidence of
root resorption\textsuperscript{15,92,138}, exhibiting more resorption than mandibular teeth\textsuperscript{10,17,31,58,149}.
According to severity, the most frequently affected teeth have been listed (from highest to
lowest) as the maxillary laterals, maxillary centrals, mandibular incisors, distal root of
mandibular first molars, mandibular second molars and maxillary second premolars\textsuperscript{24,29,30,140,142,149,158,196}.

The maxillary incisors, especially the lateral incisors, are generally the most affected
since they tend to undergo the most movement during orthodontic treatment.
Furthermore, their root form, and relationship to the surrounding periodontium, means
most of the forces tend to be transferred to the apex\textsuperscript{24}.

Beck and Harris\textsuperscript{160} have explained that the use of archwire anchorage bends, mesial
to the first molars, causes compression of the distal roots within the socket and subsequent
initiation of resorption.

\textbf{2.2.6.2.7 Severity & type of malocclusion}

A positive association between malocclusion and OIIRR has been made within the
literature\textsuperscript{41,93,137,140,149,151}, however the relationship seems to be more related to the
amount and type of tooth movement required, and the duration of treatment, rather than
the malocclusion itself\textsuperscript{151,160}. I.e. the extent of apical resorption is associated with the
amount of tooth movement\textsuperscript{33, 44, 47, 150, 197} which in turn is a function of the severity of the malocclusion.

Kaley and Phillips found Class I patients with acceptable overjet were significantly less likely to show OIIRR compared to Class II or III patients\textsuperscript{59}. Similarly, Taner et al\textsuperscript{198} found Class II division 1 patients experienced significantly more resorption than Class I patients undergoing orthodontic treatment with first premolar extraction, although no significant differences were found between the amount of OIIRR and tooth inclination or duration of active treatment.

Significant associations between resorption and the magnitude of overbite\textsuperscript{139} or overjet reduction during treatment have also been found by some\textsuperscript{24, 48, 140, 150}, but not all, investigators\textsuperscript{16}. Patients undergoing extractions during treatment had greater root resorption which may be related to longer treatment duration and an increased amount of tooth movement\textsuperscript{149}.

From the literature, it can be concluded that root resorption can be associated with all types of malocclusion when combined with orthodontic treatment\textsuperscript{7, 161}.

\textbf{2.2.6.2.8 Alveolar bone density & turnover rate}

The density of the alveolar bone may also affect the incidence of root resorption. It has been postulated that OTM in dense bone requires greater or longer force application, consequently resulting in increased OIIRR\textsuperscript{9, 62, 65}. Goldie and King\textsuperscript{45} hypothesised there are more marrow spaces in less dense alveolar bone which facilitate and improve the action of active resorptive cells resulting in reduced OIIRR\textsuperscript{45}. Conversely, when the rate of bone turnover is decreased the risk of OIIRR increases\textsuperscript{39}.
In a human study, Otis and co-workers\textsuperscript{199} measured the amount of alveolar bone around the root including the thickness of cortical bone and density of the trabecular network, and found no significant correlation with the extent of the OIIRR.

### 2.2.6.2.9 Dental age & stage of root development

Several studies have suggested that teeth with open apices may be more resistant to OIIRR than teeth with closed apices (i.e. completed root development)\textsuperscript{19, 137, 200}, although others have disagreed, suggesting instead that these teeth do not achieve normal root length\textsuperscript{164}.

Dilaceration and root stunting may be the final result of deflection of Hertwig’s epithelial root sheath caused by orthodontic tooth movement. The incidence of dilaceration has been shown to increase with treatment from 25% - 33%\textsuperscript{200}.

### 2.2.6.3 Mechanical Risk Factors

Finally, there are also a number of mechanical factors which have been linked to root resorption. These mechanical factors are directly related to the mechanics or orthodontic therapy itself and are of particular interest to the clinician as they may be controlled or modified in an attempt to reduce their influence upon root resorption.

### 2.2.6.3.1 Treatment duration

The majority of studies in the literature agree that the severity of root resorption is directly related to treatment duration\textsuperscript{7, 9, 16, 27-30, 46, 65, 101, 137, 140, 149, 155, 158, 160, 196, 198, 201}.

Considering that orthodontic force induces an inflammatory reaction that is fundamental to both tooth movement and root resorption\textsuperscript{7}, it makes sense that the longer a tooth is exposed to the inflammatory process the more likely and more severe the resorption may be. Samehshima and Sinclair\textsuperscript{149} described a significant correlation between duration of

treatment and root resorption on maxillary central incisors, and in their study evaluating the extent of OIIRR following 4, 8, and 12 weeks of light (25g) and heavy (225g) buccally directed forces on maxillary and mandibular premolars Paetyangkul et al concluded that the extent of resorption increased significantly with treatment duration.\(^{106}\)

Artun and co-workers concluded that the risk of one or more teeth with more than 1mm of resorption from T2 to T3 (6months to 12 months after bracket placement respectively) was 3.8 times higher than from T1 to T2.\(^{46}\) Similarly, Levander and Malmgren reported 34% of the teeth examined in their study showed root resorption after 6-9 months of treatment and this number increased to 56% at the end of treatment (19 months).\(^{27}\)

The duration of treatment is often related to factors such as the severity of the case and also patient co-operation. As the difficulty of the case increases often larger movements are required resulting in increased treatment time. Similarly, poor patient attendance will also result in prolonged treatment. Levander and colleagues investigated the effect of a pause in active treatment, on teeth that had experienced root resorption during the initial 6-months of treatment, and showed that the amount of resorption was significantly more in those patients treated with continuous forces without a pause.\(^{61}\)

2.2.6.3.2 Type & extent of tooth movement

The type, direction, and extent of tooth movement have a considerable role in OIIRR. The greatest damage is observed with intrusion and torque as these movements produce a higher force per unit area and thus cause more tissue necrosis and root resorption.\(^{33, 52, 54, 59, 67, 102, 160, 202}\) Han et al, found intrusion of teeth causes 4 times more root resorption than extrusion mainly because the root shape concentrates the pressure at the conical apex.\(^{54}\) Another study reported maxillary incisors are 4.5 times more likely to have severe root...
resorption if they undergo root torque\textsuperscript{59}. It has been proposed that a combination of intrusion and root torque has the highest risk for OIIRR\textsuperscript{33, 63}.

In contrast, bodily tooth movement has been associated with decreased risk of root resorption compared to tipping due to the differences in stress distribution along the root surface\textsuperscript{33, 53, 65}. In their finite element model (FEM) study, Rudolph and colleagues\textsuperscript{203} found tipping movements resulted in stress concentration at the alveolar crest and root apex, while bodily movement resulted in a more even distribution across the root surface. Purely intrusive, extrusive, and rotation movements resulted in stress concentration at the apex. Extrusive tooth movement is considered to induce the least root resorption when compared to other types of tooth movement\textsuperscript{54}.

As mentioned previously, teeth that are moved further have extended exposure to the resorptive process\textsuperscript{47, 197} and not surprisingly, the extent of tooth movement has been linked to the degree of root resorption\textsuperscript{89, 141, 149, 196}. The maxillary incisors are at the highest risk of OIIRR since they are commonly moved the greatest distance especially in extraction cases\textsuperscript{141, 149, 196, 204-207}.

2.2.6.3.3 Force magnitude & duration

Many animal\textsuperscript{208-210} and human studies\textsuperscript{12, 50, 102, 211, 212} have demonstrated that the severity of OIIRR is directly proportional to the magnitude of the applied orthodontic force. As discussed previously, heavy forces exceeding the PDL capillary blood pressure\textsuperscript{9, 213} induces excessive hyalinisation\textsuperscript{161} and interferes with the repair process of resorption craters\textsuperscript{12, 13, 62, 209}. This has been confirmed by recent SEM, TEM, and Micro-CT studies on human premolars which have found an increased amount of root resorption associated with increased force levels\textsuperscript{12, 52, 102, 107, 214}. It has been suggested that the distribution of
resorption lacunae is related to the amount of stress on the root surface, and that the rate of lacunae development is more rapid with increasingly larger applied forces\textsuperscript{12, 50, 51, 56, 102}.

In contrast, several studies have suggested there is weak\textsuperscript{9} or no correlation between the amount of root resorption and force magnitude\textsuperscript{49, 98}. From their histological studies, Owman-Moll and co-workers found that root resorption was not particularly force-sensitive but there was a large individual variation\textsuperscript{49, 98}.

In terms of duration of applied force, the results within the literature are conflicting. It has been proposed that a potential difference may exist between the tissue responses to continuous or discontinuous forces\textsuperscript{32}. I.e. an intermittent force prevents formation of hyalinised zones and when inactive, allows reorganization of tissues and restoration of blood flow in the compressed areas\textsuperscript{53, 65}, while a continuous force on the other hand does not allow adequate restoration or repair of the damaged cells and tissues. Several studies have supported this demonstrating that a pause in force application or intermittent force application results in lesser root resorption compared to continuous force application\textsuperscript{32, 61, 102, 215-217}. Conversely, others have found no difference between teeth that were moved with either a continuous or an interrupted force\textsuperscript{89, 97}. It must be noted that intermittent forces produce less tooth movement than continuous forces over the same period\textsuperscript{97, 216, 218} and may be a confounding factor when comparing continuous versus intermittent forces.

There is weak evidence suggesting jiggling forces have a role in increasing root resorption and as a result removable appliances and inter-maxillary elastics should be used sparingly\textsuperscript{16, 161}. 

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By Johnathan Grove
2.2.6.3.4 Appliances & treatment techniques

A number of studies within the literature have compared the extent of resorption following treatment with different types of orthodontic appliances in an attempt to identify an appliance or technique that causes less OIIRR. Some authors have found one or another technique to be more advantageous over another\(^{33, 138, 139, 204, 206, 219-221}\), for example McNab et al found more external root resorption in patients treated with Begg appliances compared to those treated with Edgewise appliances\(^ {220}\). Conversely, others have found no significant difference when comparing appliance or technique\(^ {26, 33, 58, 160, 222}\), for example Blake and co-workers\(^ {58}\) found no statistically significant difference in resorption between Speed appliances & Edgewise appliances. The clear advantage of one system over the others has yet to be demonstrated within the literature and it may also be argued that the differences between techniques is due more to their respective differences in treatment time and mechanics employed rather than the appliances themselves.

In terms of conventional edgewise systems compared to various active and passive self-ligating appliances no statistically significant differences in resorption has been found\(^ {58, 223, 224}\). Similarly, Alexander\(^ {225}\) reported the same amount of root resorption associated with both continuous arch and sectional arch mechanics, and concluded that individual variability has greater influence than so called “round tripping” of teeth.

With regard to fixed versus removable appliances, one group has found significantly greater resorption associated with fixed appliances\(^ {16, 137}\). Along the same lines, Barbagallo and colleagues\(^ {214}\) compared fixed appliances and removable sequential thermoplastic appliances but found light forces produced by fixed appliances and thermoplastic aligners affect root resorption in a similar way.
Magnets have been suggested by some to produce a more favourable physiological tissues response thus decreasing the risk of OIIRR$^{226, 227}$, although further research in this area is required.

2.2.6.3.5 Extraction versus non-extraction

This topic is controversial in the literature and both techniques have the potential to induce soft and hard tissue damage. McNab and co-workers stated the incidence of root resorption after extraction treatment was 3.72 times higher than non-extraction treatment$^{35}$. Similarly, Sameshima and Sinclair also reported extractions to be a significant factor in root resorption$^{149}$. In contrast, McFadden et al$^{158}$ reported no difference in the extent of root resorption in patients treated with or without extractions.

2.2.6.3.6 Transplanted teeth

Transplantation of teeth is particularly technique sensitive and success is predominantly determined by the care taken to avoid injury to the PDL and cemental surfaces during the procedure. Successfully transplanted and fully assimilated teeth will react to orthodontic force in a similar way to normal teeth$^{228}$ and will be subject to the same influencing factors.

2.2.7 Diagnosis of Root Resorption

Clinically, radiographs are the only method for diagnosing OIIRR and the most commonly used are periapical radiographs and panoramic radiographs such as the orthopantomogram, and to a lesser extent lateral cephalograms.

The orthopantomogram is often indicated during orthodontic treatment for a number of reasons and has a number of advantages including providing an overall view of
the dentition, lower radiation dose for the patient than a full mouth series\textsuperscript{91}, and are fairly simple and fast to obtain. However, the quality of the image is dependent on correct patient positioning, the closeness of the desired anatomical structures to the focal trough as objects outside the trough will be out of focus, and the amount of magnification\textsuperscript{108} which is relatively constant in the vertical dimension but horizontal measurements are less reliable\textsuperscript{229}. According to Sameshima and Asgarifar\textsuperscript{93}, if initial and final orthopantomograms are used for root resorption assessment, the results may be exaggerated by 20% due to magnification. The lower incisor area is the most likely to be distorted.

In comparison, periapical radiographs are often considered superior to orthopantomograms and are recommended instead\textsuperscript{60} as they result in less radiation exposure, and are subject to less distortion and fewer superimposition errors\textsuperscript{93, 230}. Paralleling techniques can also be used which allow for geometrically accurate images which can then be standardised at different time points. The lateral cephalogram has been shown to provide an accurate and reproducible view of the length of the upper incisor, but overlapping results in an obscured image making diagnosis difficult\textsuperscript{91}.

When comparing digital and conventional radiographs, there appears to be little difference in terms of diagnostic sensitivity\textsuperscript{231}. The only advantages of a digital system are that it can allow earlier quantification of small changes in root length\textsuperscript{60, 222}, and provides similar diagnostic sensitivity with lower radiation doses. On the other hand, computed tomographic scanning offers a significant advantage in terms of detection and quantification\textsuperscript{232-234}, but is also more costly and associated with higher levels of radiation which limits its clinical application\textsuperscript{93}. 
2.2.7.1 Location of OIIRR

The distribution of resorptive areas on the root surface varies in association with the pressure zones generated by different types of tooth movement. Non-orthodontically induced root resorption appears to distribute equally over the marginal and apical regions of the root\textsuperscript{13} unlike OIIRR, which tends to occur preferentially in the apical region because the fulcrum of most tooth movement usually lies occlusal to the apical half of the root\textsuperscript{159}. The apical region is also more susceptible to OIIRR as a result of the different orientation of the apical PDL fibres, which increase the stresses in this region\textsuperscript{11}, as well as the presence of the more friable acellular cementum\textsuperscript{48,159}.

2.2.8 Pathogenesis & Mechanisms of Root Resorption

The development and pathogenesis of OIIRR can be summarised simply into the following 7 steps:

<table>
<thead>
<tr>
<th>Development and Pathogenesis of OIIRR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Application of orthodontic force</td>
</tr>
<tr>
<td>2. Over compression of PDL</td>
</tr>
<tr>
<td>3. Initiation of local inflammatory reaction</td>
</tr>
<tr>
<td>4. Resorption of hyalinised tissue begins</td>
</tr>
<tr>
<td>5. Formation of resorption lacunae</td>
</tr>
<tr>
<td>6. Resorption continues until hyalinised zone is removed, or force level decreases</td>
</tr>
<tr>
<td>7. Repair begins when PDL is de-compressed</td>
</tr>
</tbody>
</table>

As mentioned, OIIRR is associated with local compression of the periodontal membrane during orthodontic tooth movement. Historically, Schwartz\textsuperscript{213} hypothesised forces exceeding the capillary blood pressure would lead to over-compression of the PDL, cutting of the blood supply, and resulting in an aseptic coagulation necrosis process, i.e. hyalinisation. These hyalinised areas must then be removed to facilitate tooth
A series of studies by Brudvik and Rygh in rats and mice have confirmed root resorption is part of the cellular activity involved in eliminating these hyalised zones.\textsuperscript{4, 100, 136, 237-239}

The pathogenesis of OIIRR occurs in two phases:\textsuperscript{146}

1. Injury to the external root surface, yielding denuded mineralized tissue.
2. Extended stimulation of multinucleated cells.

Multinucleated cells colonise the denuded mineralized tissue, initiating the resorption process. Without continued stimulation by those cells involved in the resorption process, spontaneous repair will occur with cementum-like material within 2-3 weeks (surface resorption). With continued stimulation, the inflammatory process in the presence of the denuded root will persist, and may involve the underlying dentine which is usually non-reversible and detected radiographically\textsuperscript{7, 29, 136, 240}.

In orthodontic-induced resorption, the initial injury results from the pressure applied to the root during tooth movement. The pressure subsequently produces the areas of ischemic necrosis and hyalinisation in the PDL\textsuperscript{7, 146}, which then initiate the inflammatory response.

The initial elimination process takes place at the periphery of the hyaline zone, where blood supply to the periodontal ligament exists or is even increased\textsuperscript{116}. During removal of the hyaline zone, the nearby root surface consisting of the cementoblast layer covering the cementoid can be damaged\textsuperscript{241}, exposing the underlying mineralized cementum to the resorptive process\textsuperscript{136, 237}. In severe cases the orthodontic pressure itself may directly damage the outer root surface\textsuperscript{7}.
The first cells to be involved in the resorption process are macrophage-like cells, scavenger cells from the hematopoietic lineage, most probably activated by the signals coming from the sterile necrotic tissue\(^7\).

The root surface under the main hyaline zone is resorbed several days later when the repair process in the periphery is already taking place\(^49, 66, 90, 94-98\). The resorption process continues until no hyaline tissue is present and/or the force level decreases\(^7\). Resorption lacunae expand the root surfaces and indirectly decrease the pressure exerted through force application. This decompression of the PDL allows the resorption process to reverse and the cementum to be repaired, and as a result these resorbing areas may show signs of concurrent active resorption and repair\(^13, 67\).

2.2.8.1 **Histopathology**

Brudvik and Rygh’s extensive rodent research has provided illumination of the histological sequence of the resorption and repair process. They found that periodontal cellular activity varies with time and location\(^4, 100, 136\); describing three sequences of events occurring in two locations, the peripheral and main hyalinised zones.

1. Tartrate resistance acid phosphotase (TRAP)-negative macrophage-like cells from the PDL, with no ruffled borders, initiate resorption in the peripheral zone. These cells remove necrotic tissue as well as the surface layers of un-mineralised and mineralised cementum.

2. TRAP-positive multinucleated or mononucleated cells initiate resorption of the main hyalinised zone and continue resorbing the damaged and un-damaged mineralised cementum. These cells are derived from the adjacent marrow spaces and PDL, and
have similar origins, cytological characteristics, and functional characteristics, to osteoclasts\textsuperscript{136, 237, 242}.

3. The reparative process occurs while active resorption is still taking place in the central zone. It begins in the periphery and extends to the central zone.

2.2.8.2 Biochemistry

As mentioned, the mechanical stimulation of the PDL cells results in initiation of a local inflammatory reaction which is characterized by synthesis of Prostaglandin E2 and increased Cyclic adenosine monophosphate (cAMP)\textsuperscript{243}. The process is regulated by hormones, neurotransmitters, and cytokines including IL-1a, IL-1b, and TNF\textsuperscript{243-247}.

Recent research has investigated the role of osteoprotegrin (OPG) and RANKL in osteoclastogenesis\textsuperscript{248}, and hence it’s possible role in resorption\textsuperscript{249}. RANKL is a TNF related ligand expressed by osteoblasts, and acts by binding to the RANK receptor on the osteoclast lineage cells, which then stimulates rapid differentiation of osteoclast pre-cursors into mature osteoclasts\textsuperscript{250}. OPG is a decoy receptor produced by osteoblastic cells which competes for RANKL binding. Wise and colleagues\textsuperscript{251} in rats, as well as Yasuda et al\textsuperscript{252, 253} have identified this role of cytokines as well as RANKL & OPG, demonstrating increased RANKL and decreased OPG expression in physiological root resorption associated with tooth eruption. Low et al induced root resorption in rats and found increased levels of RANKL in sites adjacent to resorption zones\textsuperscript{242}. Compressive forces have also been found to be associated with increased production of RANKL & decreased production of OPG\textsuperscript{254}. More recently, Nishimura et al investigated vibration in rats and noted enhanced RANKL expression in PDL fibroblasts and osteoclasts on the compression side after 3 days, and increased numbers of PDL osteoclasts after 8 days\textsuperscript{85}. 
2.2.8.3  **Resorptive Resistance**

Cementum appears to be more resistant to resorption than alveolar bone\(^{109}\), however the precise mechanism of this resistance is still poorly understood. When this resistance is compromised\(^7\), severe OIIRR although rare, can occur. A number of explanations exist within the literature attempting to explain this resorptive resistance, and most agree that the root’s outer layers including the cementoblasts, and pre-cementum and cementoid layers, provide an overall protective function\(^7,238\).

It has been hypothesised that odontoclasts are unable to resorb the mature collagen of the un-mineralised pre-cementum and cementoid layers\(^9\), and that these layers may also inherently synthesise potent anti-collagenases which are no longer produced when the root surface is damaged or the PDL is compressed\(^7,62,255\). It has also been suggested that a physical breach in these layers will allow mineralised tissue to come into contact with the PDL matrix providing a chemotactic stimulus for resorbing cells\(^145,255\).

Andreasen postulated cemental resistance was mainly due to the cells within the PDL such as cementoblasts, fibroblasts, osteoblasts, endothelial, and peri-vascular cells, which repair areas of resorption by generating new cementum and PDL fibre attachments\(^144\).

A recent clinical study revealed that exposure of roots to two sequential periods of orthodontic treatment actually decreased the extent of OIIRR\(^22\), suggesting remodelled cementum may contribute some additional protective effect.
2.2.8.4 Repair

The process of repair of resorption craters begins when the orthodontic force is removed or reduced below a certain level\textsuperscript{62, 65}. \textsuperscript{213}Schwarz\textsuperscript{213} suggested this level is equivalent to the capillary blood pressure of 20-26g/cm\textsuperscript{2}, however this is still uncertain. Regardless, the result is repair via deposition of cementum and establishment of new PDL\textsuperscript{9, 67, 68, 256, 257}.

The repair process has been described as a migration of cementoblasts over the resorbed surface, which then compete for available surface space and progressively exclude the osteoclasts and cementoclasts\textsuperscript{258}. The initial repair material is acellular cementum which is laid down and then gradually replaced by cellular cementum as repair continues\textsuperscript{66, 95, 188, 259-261}. The location and direction of the initial repair is controversial, and has been described as beginning from the periphery, the bottom, or from all directions\textsuperscript{67, 102, 238, 239}.

A number of studies have discussed the timing of onset of repair, with considerable variation, and have found that the reparative process may occur even in the presence of active resorption\textsuperscript{12, 67}. Repair has been reported to occur as little as one week into retention\textsuperscript{66}, while other studies have found repair between 2 and 3 weeks\textsuperscript{260}, and even up to 35 to 70 days after force removal\textsuperscript{9, 12, 13}.

The amount of repair is not constant and appears to increase with time\textsuperscript{66-68} especially during the first 4 weeks. By the 5th to 6th week the process slows down and reaches a steady state\textsuperscript{98}.

Vardimon and colleagues described the repair process as occurring in 4 phases\textsuperscript{261}:
1. The Lag phase - which occurs between the end of resorption and the beginning of repair. This phase is largely explained by the dissipation of residual forces, and the differentiation of cementoblasts\textsuperscript{9,13}.

2. The Incipient phase – which occurs 14 days later, and is a transitional phase between no apposition and active deposition.

3. The Peak phase – follows between 14 to 28 days later, and involves a spurt in matrix formation and incorporation of extrinsic fibres into the intrinsic cementum matrix.

4. The Steady deposit phase – which occurs between 42 to 56 days, and involves a steady deposition of mixed fibrillar cementum.

2.2.9 Prognosis, Prevention, & Management of OIIRR

As mentioned previously, the extent of root resorption in most cases is minor and is inconsequential to the long term survival or functionality of the afflicted teeth or dentition\textsuperscript{10,48}. However, in some cases the decreased crown to root ratio resulting from severe resorption can significantly affect the prognosis, especially in the presence of periodontal disease or trauma\textsuperscript{58}.

Loss of apical root length due to resorption appears to be less detrimental than an equivalent loss of periodontal attachment at the alveolar crest, especially in cases with less than 3mm of external root resorption\textsuperscript{23}. Apical root length loss of up to 3mm is equivalent to only 1mm of crestal bone loss and clinically has a similar effect\textsuperscript{262}. In an average sized normally shaped maxillary central incisor, with no alveolar bone loss during orthodontic treatment, a root shortened by 5mm will still have 75% of its periodontal attachment remaining (95% of patients). No adverse physiological or pathological effects have been reported with loss of root length of up to 20\%\textsuperscript{48}.
However, increased mobility has been reported when 9mm or more of the root length has been lost to resorption\(^{263, 264}\), and the reduction in root length can result in an unfavourable crown to root ratio of the affected teeth affecting their suitability for prosthetic anchorage and abutments\(^{58}\).

\subsection*{2.2.9.1 Prevention}

Fortunately the risk of severe root resorption is rare, occurring in less than 5% of treated patients\(^{21, 23, 59}\). A number of prevention strategies have been proposed in the literature\(^{28}\) to help minimise the risk and extent of OIIRR and many are targeted at factors implicated as aetiological risk agents. These strategies include:

\begin{enumerate}
  \item A thorough assessment of the patients medical and family history prior to treatment to identify potential risk factors\(^{24, 28, 31, 34}\),
  \item Resolution of habits such as nail biting and tongue thrusting\(^{162, 188}\),
  \item Treatment at an earlier age as younger patients and developing teeth have been found to have a reduced incidence of root resorption\(^9\).
  \item Reduction of treatment duration\(^{13, 27, 46, 61}\),
  \item Reduction of force magnitude\(^{9, 12, 13, 62}\) and use of intermittent forces\(^{28, 32, 216}\),
  \item Increasing the interval between appointments to reduce the frequency of force activation.
  \item Radiographic assessment at 6 months into treatment (or at 3 months in high risk individuals)\(^{46, 60}\), and
  \item Halting treatment for periods of up to 3 months if resorption is detected\(^{33, 61, 63}\).
\end{enumerate}

Once the orthodontic force has been removed research has shown the resorption process usually ceases\(^{10, 64}\), and repair begins. The repair process has been found to begin
once the orthodontic force has decreased below a certain level\textsuperscript{62, 65} and tends to increase with time\textsuperscript{66-68}. When post treatment root resorption does occur, it is usually associated with factors such as traumatic occlusion and active force-delivering retainers\textsuperscript{265}.

\textbf{2.2.9.2 Management}

The potential risk of OIIRR as a consequence of orthodontic treatment must be discussed with the patient and parents during the initial consultation\textsuperscript{266}. If root resorption is detected during active treatment, the decision to continue, modify, or discontinue treatment must be made. A number of management techniques or procedures have been outlined within the literature including:

\textit{I.} Halting treatment and placing passive arch wires for 2-3 months\textsuperscript{61}.

\textit{II.} Cease force application for 4-6 months or in extreme cases terminate treatment\textsuperscript{149}.

\textit{III.} Reassess treatment goals to reduce further damage. Either terminate treatment or consider a compromise. For example, compromise options may include prosthodontic restoration instead of closing spaces, surgery to minimise further tooth movement, and inter-proximal reduction rather than extractions\textsuperscript{161}.

\textit{IV.} Continued radiographic examination until resorption has ceased\textsuperscript{161}.

\textit{V.} Appropriate counselling and regular review\textsuperscript{149}.

As mentioned previously, active resorption usually ceases after appliance removal but if this does not occur, subsequent root canal therapy with calcium hydroxide may be required\textsuperscript{267}. Fixed retaining appliances should be placed with caution as occlusal trauma to the fixed teeth or segments may lead to further extreme resorption\textsuperscript{161}.
2.3 Research Methodologies for Evaluation of OIIRR

Historically, OIIRR has been studied utilising histological or radiographic methodologies however these are not always the most accurate means of assessment or measurement, hence the variability in root resorption incidence in the existing data. Radiographs provide only a 2D representation of a 3D process, meaning resorption in certain areas such as the buccal and lingual root surfaces may not be detected\textsuperscript{268}. Histological examination is more accurate than radiographic assessment however this can only be performed on extracted teeth.

More recently, 3D volumetric quantitative evaluation of resorption craters using SEM or XMT technology has been shown to be a feasible alternative with a high level of accuracy and repeatability\textsuperscript{107, 108, 211}. A mathematical computer based reconstruction of pre- and post treatment dental images has also been shown to be a reliable technique for measuring root resorption\textsuperscript{222}.

2.3.1 Radiography

Radiographic detection is an important tool in identifying root resorption and has been used in a number of studies\textsuperscript{17, 31, 35, 60, 89-93}; however it is less useful in quantifying the extent of the resorption present. Due to their 2D nature, radiographs can help detect root shortening before, during, or after treatment, but surface resorption can only be detected if it occurs mesio-distally at direct right angles to the focal beam of the X-rays or if resorption has progressed to an advanced stage\textsuperscript{108}. Varying degrees of magnification also affect the quantitative value of radiographs.
Panoramic radiographs are widely considered to be a valuable tool for identifying resorption as they provide a low radiation overall view of the entire dentition\textsuperscript{269}, however they have been found to overestimate the amount of root loss by 20% or more when compared with periapical radiographs (PA’s)\textsuperscript{24}. Furthermore, superimposition of other anatomical structures over the teeth may show up as real or actual shadows, or the roots of proclined teeth may appear shortened or even lie outside the focal trough, thus reducing the quality of the final image\textsuperscript{91, 219, 270}.

Periapical radiographs have been used as an alternative, and have been found to provide less distortion and finer detail in comparison to panoramic radiographs\textsuperscript{60, 61, 93}. The quality and accuracy of PA’s may be affected by a number of factors including film orientation and x-ray tube position\textsuperscript{91}, and they also have an inherent magnification factor however this is usually less than 5%\textsuperscript{271}. The paralleling technique with PA’s has been described as the technique of choice for detecting root shortening although it has also been shown to be geometrically inaccurate\textsuperscript{272}.

The lateral cephalogram has been shown to yield an accurate and reproducible view, however its use is limited to the upper incisors, and it is also affected by a magnification factor of 5-12% as a result of the radiographic set up\textsuperscript{91}. Furthermore, overlapping of the right and left side make the individual images unclear\textsuperscript{108} and difficult to assess.

While radiography is a valuable diagnostic tool in detecting OIIRR, quantitative measurements are relatively poor and it is limited to the clinical situation\textsuperscript{108}. It may also be argued that routine use of radiographs during orthodontic treatment may introduce a source of bias into the assessment of incidence by facilitating detection\textsuperscript{28}. 
2.3.2 **Serial Sectioning & Light Microscopy**

Serial sectioning and light microscopy has also been used in a number of publications investigating the extent and repair of OIIRR in various clinical scenarios. This method involves progressive sectioning of the tooth, with the resulting slices stained and examined under light microscope. Using this technique, less detail is missed and the measurements are more accurate than light microscopy alone.

The limitations of this method relate to the fact that craters may be missed or overlooked, and the difficulty of the technique may introduce some bias. Root resorption craters vary in size and shape and thus irregularly shaped or small craters could be partially or totally overlooked as a result of the 2D nature of the sections. Additionally, tooth shape is hardly uniform making it difficult to accurately section a tooth along its long axis, potentially resulting in apical or some mid-root craters being missed.

2.3.3 **Scanning Electron Microscopy**

As mentioned, a number of studies have also utilised SEM in order to investigate OIIRR. The SEM technique allows enhanced visual and perspective assessment of the root surface and resorption craters, with minimal specimen and tissue preparation. Despite providing detailed information regarding the resorption lacunae as well as the mineralised structure of cementum, this method is very time consuming and difficult to perform on larger samples as the specimen must be prepared and the desired image view chosen before an image is created. Another limitation relates to parallax errors resulting from the difficulty in obtaining an absolute straight on view of the curved resorption lacunae, which can subsequently lead to significant measurement errors.
Stereo SEM imaging was subsequently devised to overcome the inherent difficulty in obtaining an accurate 3D quantitative measurement of irregularly shaped craters on a curved root surface\(^{107}\). This method involves taking 2 images, offset by 6°, of each crater producing a stereo pair of each crater. These stereo images are then converted into an 8-bit greyscale depth map allowing 3D mapping and volumetric analysis of each crater. This method has been shown to be highly accurate and reproducible\(^{107, 108}\), although relatively time consuming and technique sensitive.

### 2.3.4 X-ray Micro-Tomography

Micro-computed tomography (Micro-CT) is a variant of a medical computed tomography scan system that allows non-destructive high spatial-resolution imaging of the interior micro-structure of a material\(^{274, 275}\). With this technique, a series of x-ray projections are made and recorded through each 2D slice of the object at various angles around an axis which is perpendicular to the slice plane. Each 2D x-ray ‘absorption’ map is then combined to produce a 3D map using digital computing\(^{276}\). The slices can be recreated in any plane, and the data is reproducible in all 3 dimensions. The 3D dataset makes identification of the resorption lacunae easier\(^{273}\) and can be used to qualify and quantify the resorption craters on the root surface\(^{52, 104}\).

In 2-dimensional digital images the unit of measurement is a pixel, which is a 2D representation of the smallest unit of colour value or shade of grey within the image. In computed tomography, the pixel is assigned an x and y-axis value. The number of pixels per unit surface area is related to the resolution of the image in that increasing the number of pixels per unit area increases the resolution of the image\(^{275}\). In 3-dimensional imaging, the
The basic unit of measurement is a voxel. The voxel is has an added z-axis value which indicates depth, and thus allows the voxel to be used to measure volume.

The use of this technology for patient applications is limited by radiation dose and duration of exposure. The radiation dosage must be kept to a minimum ‘safe’ level, and the duration reduced to avoid unwanted distortion as a result of involuntary patient movement. These limitations are not applicable to inanimate objects, where higher radiation dosage and longer scan times can be used to improve image quality.

Micro-CT relies on a density difference between the structure of interest and the surrounding material. Porous materials such as minerals, ceramics, or polymers, are particularly suited to this method. Other suitable materials include bone, teeth, lung tissue, archaeological and paleontological specimens, coral and wood.

2.3.4.1 SkyScan 1172 Desktop X-ray Micro-Tomograph

The SkyScan 1172 Desktop X-ray Micro-tomograph (SkyScan, Aartselaar, Belgium, Appendix 6.4), is a fourth generation computed tomography scanner which, as the name suggests, is a compact desktop system utilised for microscopy and micro-tomography. Its components include an X-ray shadow microscopic system combined with a computer with tomographic reconstruction software.

The SkyScan 1172 unit utilises a cone beam X-ray source and is able to achieve a maximum spatial resolution of 2 - 5 µm. The system obtains multiple x-ray shadow transmission images of the object from different angular views, as the object rotates on a high-precision stage. The X-ray detector consists of a high-resolution charged coupled device, and the images received from these detectors are stored as 16 bit Tagged Image File

Format (TIFF) picture files with a resolution of 1024x1024 pixels. Once image acquisition is complete, software utilising a modified Feldkamp cone-beam algorithm\textsuperscript{277} (NRecon, Version 1.4.2; Skyscan, Aartselaar, Belgium) produces slice-by-slice axial reconstruction. The resultant axial 2D images are generated as 1024x1024 pixel bitmap (BMP) image stacks with an 8-bit greyscale dynamic range.

The cross-sectional datasets can be used with a variety of image analysis and 3D volume rendering software packages such as VG StudioMax (Version 1.2, Volume Graphics, GmbH, Heidelberg, Germany), for 2D or 3D morphometrical analysis or to produce 3D images and animations.

2.3.4.2 Previous Dental Research Using Micro-CT Technology

Micro-CT technology has been utilised in a number of studies investigating a variety of subjects ranging from material science and mineral analysis, to the study of calcified tissues including teeth and bone\textsuperscript{278}. While some have attempted in-vivo studies, this technology has been mostly limited to in-vitro or inanimate specimens\textsuperscript{279, 280}.

In terms of dental research, Micro-CT has been used to investigate the mineral content of human enamel, dentine\textsuperscript{281-283} and carious dentine\textsuperscript{284}; study the internal anatomy of teeth and root canals\textsuperscript{285-288}; analyse oral implants and their stability in bone\textsuperscript{289-291}; and examine the effects of lasers and phosphoric acid etching on enamel\textsuperscript{278, 292}.

Only recently has Micro CT technology been utilised to investigate and examine OIIR. Harris and co-workers\textsuperscript{52} investigated the volume of root resorption associated with no force versus light force (25g) and heavy force (225g), finding a significant 2-fold and 4-fold increase in the light- and heavy-force groups respectively\textsuperscript{51, 106}. In their study comparing the

effect of continuous and intermittent forces on OIIRR, Ballard et al\textsuperscript{217} found intermittent forces induce significantly less resorption. When looking at the repair of resorption craters after continuous light and heavy forces, Cheng and co-workers\textsuperscript{64} found no significant difference in the amounts of repair at 4 or 8 weeks after 4 weeks of continuous force, although the resorptive activity was more pronounced with heavy forces; furthermore crater volume was positively correlated with tooth movement and negatively correlated with chronologic age. In other studies, the maxillary first premolars were shown to be more likely to suffer from OIIR than mandibular first premolars\textsuperscript{106}, and certain types of tooth movement (torque and rotation etc) were shown to induce more resorption than other types\textsuperscript{202, 293}.

Clear sequential thermoplastic appliances are a popular alternative to traditional orthodontic appliances in some cases. Barbagallo and co-workers\textsuperscript{214} used Micro CT to quantify the effect of these thermoplastic appliances on OIIRR craters, concluding that sequential thermoplastic appliances produced similar effects to light orthodontic forces with traditional fixed appliances on root cementum.

Fluoride has been reported to be beneficial in preventing root resorption in cases of dental trauma, however Foo et al\textsuperscript{104} found that while systemic fluoride reduced the size of resorption craters it was variable and statistically insignificant.

Finally, Deane and co-workers utilised XMT technology to investigate the incidence of physiological root resorption associated with unerupted third molars\textsuperscript{105}. They compared physiological root resorption found in unerupted non-impacted maxillary third molars with premolar teeth from previous studies which had undergone light and heavy orthodontic...
forces. From their study, they found unerupted third molars had similar cube-root resorption volumes to first premolars subjected to light buccal and intrusive forces, and concluded that resorption might occur as part of hard tissue remodelling and turnover.

### 2.4 Vibration

Mechanical vibration can be described as a mechanical stimulus characterised by an oscillatory motion and its intensity is determined by certain variables which include:

I. **Frequency**: The frequency of vibration is determined by the number of cycles in 1 second and is measured in Hertz (Hz).

II. **Amplitude**: The amplitude is determined by the extent of the oscillatory motion and is measured in millimeters (mm).

III. **Magnitude**: Vibration can also be described as having a magnitude which is expressed as a function of Earth’s gravitational field (9.8ms$^2 = 1g$) and is measured in grams (g).

In the biological setting, it is undisputed that external mechanical signals or stimuli are in general vital in maintaining the skeletal structure and integrity, with bone remodelling continually being influenced by the magnitude and distribution of the functional strains within the bone. I.e. decreases in functional loading induce elevation of osteoclastic activity resulting in a net loss of bone, whereas increases in loading (such as exercise) stimulate osteoblastic activity resulting in net improvements in both bone quantity and quality.

Associations between bone morphology and mechanical load stimuli were made as early as Galileo who supported the theory that bony trabeculae are arranged in
particular morphological patterns induced by function in order to optimise resistance to loading. Wolff in 1892 attempted to explain this relationship between bone morphology and function, and was the first to publish the concept of “form follows function” more commonly known as “Wolff’s Law”, however Wolff’s law is unable to fully explain functional bone adaptation as it fails to identify the specific parameters of the osteogenic mechanical stimulus.

Early human observational studies have also made the link between weight bearing/mechanical loading activity and bone mineral density. Human exercise studies show that high impact activity such as gymnastics have a higher osteogenic potential than low impact activity such as swimming or rowing. Similarly, exercises involving unilateral activity such as tennis show greater bone mass in the loads bearing limb. In contrast, disuse from immobilisation or space travel induces catabolic effects in the bone.

Following on from these initial observations, it was the investigation into possible treatment modalities for osteoporosis that formed the impetus for further research into dynamic mechanical stimuli in the biological and medical setting. In recent years, a number of therapeutic uses for mechanical modulation of bone structure and density have been identified including:

1. Improving the rate of fracture healing,
2. Reversing the decrease in bone mass and density associated with disuse atrophy,
3. Enhancing muscle and bone mass in cases of musculoskeletal degeneration and osteoporosis.
IV. Enhancing mechanical signalling within bone\textsuperscript{79-81}.

2.4.1 Whole Body Vibration

Whole body vibration (WBV) as apparent from its name, involves exposure of the entire body to vibration, as opposed to local vibration where stimulation is applied to an isolated region. WBV is produced with the use of a vibrating platform through which vibrations generated by motors underneath the platform are transmitted to the person\textsuperscript{295}.

WBV has been examined for its potential as a means of reducing the loss of bone density associated with extended periods in space\textsuperscript{314, 316}, or patients with disabling conditions\textsuperscript{71, 72, 74}. The fitness industry has also introduced and used WBV\textsuperscript{294, 317}, while more recently it has found applications in the areas of physical therapy and rehabilitation\textsuperscript{318}, and professional sports\textsuperscript{294}. There are currently many whole body vibration devices available commercially for use in both the fitness and health care areas\textsuperscript{294, 295, 319}. These devices all vary in terms of the frequency of vibration, which can range from a few Hz up to 50 Hz, and the amplitude which can range from a few micrometres to several millimetres\textsuperscript{295}. The attractive advantages of vibration therapy are that it is non invasive, and can be applied in a low impact manner which is critical in elderly or diseased individuals\textsuperscript{319}.

In their review, Prisby and co workers\textsuperscript{319} noted that although the scientific knowledge base behind the use of vibration devices is increasing steadily, an optimal operating threshold is as yet undetermined and it is unknown whether such a threshold would be applicable to all tissues of the body. The vibratory protocols (i.e. frequency, duration, and amplitude) utilised in the literature to date lack standardisation and vary considerably, making it difficult to formulate appropriate conclusions regarding the most
effective protocol(s)\textsuperscript{319, 320}. They suggest that future research is required to determine and develop an optimal vibration protocol which will most likely vary depending on the population using the vibration (e.g. young vs. elderly) as a result of differences in bone quality, remodelling patterns, and responsiveness\textsuperscript{319}.

2.4.2 Vibration & Dentistry

In more recent times, the use of mechanical vibration concurrently with orthodontic treatment has been suggested as a possible means of not only reducing treatment duration but also root resorption and pain perception. To date however there is limited research in this area.

2.4.2.1 Rate of Tooth Movement

As has been discussed previously, duration of treatment is one of the more important mechanical risk factors involved in the aetiology of OIIRR\textsuperscript{16, 27, 28, 149, 161, 167} and has also been associated with an increased risk of caries\textsuperscript{321} and periodontal sequelae\textsuperscript{322}.

Treatment duration is directly influenced by the rate of tooth movement which is limited by the physiological processes involved in remodelling the paradental tissues i.e. bone and PDL remodelling\textsuperscript{1, 243, 323-326}. In their study, Roberts et al described the maximum rate of molar translation in the maxilla as approximately 2mm/month in a rapidly growing child or 1mm/month in a non growing adult\textsuperscript{327}. Numerous attempts have been made to increase this rate of movement ranging from reducing appliance friction\textsuperscript{328} and using adjunctive pharmacological or hormonal therapies\textsuperscript{329-331}, to the more recent introduction of surgical corticotomy and distraction techniques\textsuperscript{332-337}, however these techniques are often
invasive or further complicate treatment. Several studies more recently, have investigated
the efficacy of mechanical vibration in relation to increasing the rate of OTM\textsuperscript{85,86}.

In their rat study, Darendeliler and co-workers\textsuperscript{86} explored the effect of high
frequency low magnitude vibration induced by pulsed electromagnetic fields (PEMF) on the
rate of tooth movement. They compared the effect of vibration alone; vibration versus
vibration and coil spring; PEMF alone versus PEMF and coil spring; and finally vibration and
coil spring versus PEMF and coil spring. Their results showed:

i. The coil spring with sham or active magnets moved the teeth more than the magnets
   with or without vibration,

ii. The coil spring moved the teeth more than coil-magnet combination under the
   PEMF,

iii. The magnets moved the teeth more than the sham magnets under the PEMF,

iv. There was no significant difference in tooth movement between the coil spring and
    magnet combinations without the PEMF, and

v. There was no difference between magnets and sham magnets without the PEMF.

From these results, the authors concluded that OTM with coil and magnets may be
enhanced by vibration induced by PEMFs.

Nishimura et al\textsuperscript{85} also conducted an animal study investigating the effects of
vibratory stimulation on rate of tooth movement and root resorption in rats. As part of the
study, they also examined the cellular and molecular mechanisms underlying the
acceleration of tooth movement. A buccal force was applied to the rat molar and in the
experimental group a vibratory protocol of 60Hz, 1g was also applied for a period of 8
minutes on days 0, 7 and 14. The results obtained demonstrated tooth movement in the experimental group was significantly greater than the control group, as seen by enhanced RANKL expression of fibroblasts and osteoclasts in the PDL of the vibration group. No significant difference in root resorption between the two groups was found, although a trend towards reduced resorption was noted in the vibration group. From these results, the authors concluded that adjunctive mechanical vibration might increase the rate of orthodontic tooth movement via enhanced expression of RANKL in the PDL without additional damage to the tissues, such as root resorption.

2.4.2.1.1 Acceledent Device

A new oral vibrating device, the Acceledent device (OrthoAccel technologies Inc, USA), has recently become commercially available and is intended for adjunctive use during orthodontic treatment. OrthoAccel technologies Inc, claims the Acceledent device enhances conventional fixed appliances or aligners and moves teeth faster via accelerated bone remodelling achieved using pulsing forces.

The device concept was developed by Dr Jeremy Mao, who investigated the effects of cyclical forces on sutural growth\textsuperscript{82-84, 338}. Mao and colleagues based this research upon the experimental suture model designed by Meikle and co-workers which mimics the forces that the PDL and other sutures of the cranium are exposed to during OTM\textsuperscript{339}. From this research, Mao and co-workers found cyclical forces between 1 Hz and 8 Hz, with forces ranging from 0.3N to 5N, increased bone remodelling\textsuperscript{82-84, 338} commonly by an order of up to 2.5 times the non-vibration rate.

According to OrthoAccel technologies Inc, the vibratory protocol of the Acceledent device is based upon on the whole body vibration studies conducted by Rubin and

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The device produces an operating frequency of 30Hz with amplitude of 20g, and patients are instructed to utilise the device for 20 mins per day during the course of their orthodontic treatment. OrthoAccel technologies Inc, claims the results of a prospective randomised control trial conducted on 45 patients at the University of Texas Health Science Centre, San Antonio, confirms an accelerated tooth movement both during initial alignment (2.06 times or 106% faster) and space closure (1.38 times or 38% faster) phases of orthodontic treatment.

2.4.2.2 Pain Control

Pain is a complex experience which often accompanies orthodontic appointments and is one of the most cited negative effects of orthodontic treatment. It is of concern to patients as it is listed as one of the key reasons for avoiding orthodontic therapy, and to clinicians as it is one of the main reasons for poor compliance and oral hygiene. The perception of orthodontic pain is part of the inflammatory reaction generated by the application of orthodontic forces and is evoked by the release of pro-inflammatory mediators such as substance P, histamine, and prostaglandins induced by the changes in PDL blood flow. Traditionally, analgesics and NSAIDs have been used for control of pain during orthodontic treatment however the major concern with NSAIDs is their anti-inflammatory action which may interfere with the process of tooth movement. Several other methods of pain control have been proposed ranging from anaesthetic gels and bite wafers or chewing gum, to using lower force levels although pain is still experienced by most patients. More recently, low level laser therapy, transcutaneous electrical nerve stimulation have been shown to be effective in dental and orthodontic pain control.
Vibratory stimulation also appears to be a potential method of pain control\textsuperscript{88, 341}. It is thought that vibratory stimulation may interfere with the pain pathways\textsuperscript{350} and also act to intercept the ischemic response by re-establishing the blood supply\textsuperscript{88}. Nanitsos et al\textsuperscript{87} found local anaesthetic injections given with concurrent vibration elicited a lower pain rating and less pain descriptors on a visual analogue scale than. They concluded that vibration can be used to decrease the pain associated with dental local anaesthesia. In the orthodontic setting, Marie and colleagues\textsuperscript{88} investigated the effect of a small battery operated vibrating motor with a soft detachable mouthpiece on post orthodontic adjustment pain. They found the appliance was effective at reducing pain but only if used prior to the onset of pain. If applied after the onset of pain, most patients were unable to tolerate the vibration.
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4.1 Abstract

Introduction: Recent research has suggested vibratory stimulation may enhance bone turnover, increase rate of tooth movement, and reduce root resorption. However to date there is little research investigating the influence of vibration on orthodontically induced inflammatory root resorption. This study was undertaken to examine the effect of mechanical vibration on the extent of root resorption craters associated with the application of a controlled orthodontic force.

Method: 14 patients (11 females and 3 males) aged 12.1 to 15.5 years, requiring premolar extraction as part of their orthodontic treatment, were used for this study. A controlled buccal tipping force of 150 grams was applied bilaterally to the maxillary first premolars of each patient for an experimental period of 4 weeks (28 days). Using a split-mouth procedure, each patient was randomly assigned a “vibration” and “non-vibration” side. Buccally directed vibration of 113Hz, using an Oral B HummingBird unit with a modified tip, was applied to the maxillary first premolar on the “vibration” side for 10mins/day for the experimental period. At the end of the experimental period, the maxillary first premolar teeth were extracted according to a strict protocol to avoid damage to the cementum and root surface. Each sample was imaged using a Micro-CT scan x-ray system (SkyScan 1172, SkyScan, Aartselaar, Belgium), and then analysed with specially designed software to determine the volumetric measurements of the resorption craters.

Results: Overall, there was a significant difference in the total root resorption volume between the vibration and non-vibration sides (p=0.003), with vibration reducing the amount of resorption by 33% on average. Except for the buccal surface, all other tooth
surfaces and vertical thirds studied exhibited a reduction in root resorption volume with vibration, however only the palatal surface was significant (p=0.006) while the mesial surface and apical third were marginally significant (p=0.018, & p=0.019 respectively). Regression analyses of all regions studied showed the amount of reduction in resorption volume associated with vibration was correlated with the amount of resorption experienced by the control teeth. This was evident especially on the mesial and palatal surfaces (p<0.001 & p=0.006 respectively).

Conclusions: Mechanical vibration as applied in this study shows the potential of its use in preventing or reducing orthodontic root resorption. However the clinical significance of such application should be evaluated on a sample undergoing a complete course of orthodontic treatment.

Key words: Root resorption, vibration, orthodontic force, micro-computed tomography, 3D analysis, volumetric measurements.

4.2 Introduction & Literature Review

Root resorption is an undesirable and unavoidable consequence of orthodontic treatment\(^1\,\text{--}\,^4\). Brezniak and Wasserstein\(^4\) suggested the application of an orthodontic force induces an inflammatory reaction within the PDL which is essential to tooth movement and is also fundamental to root resorption. They described this orthodontic force induced root resorption as Orthodontic Induced Inflammatory Root Resorption (OIIRR).

The aetiology of root resorption appears to be remarkably multifactorial and remains largely unknown. Many studies have investigated and attempted to isolate causative factors related to OIIRR, and have identified numerous risk factors\(^5\,\text{--}\,^6\). These can be broadly
grouped into biological, dental, and mechanical factors. Examples of biological factors include genetic factors such as individual susceptibility\textsuperscript{7-10} and ethnicity\textsuperscript{11}, as well as environmental factors such as allergies\textsuperscript{12, 13} and medications\textsuperscript{14-17}. Previous history of resorption and trauma\textsuperscript{18-21}, tooth morphology\textsuperscript{11, 22, 23}, and bone density\textsuperscript{16, 24}, are examples of dental factors. Lastly, treatment duration\textsuperscript{25-28}, force magnitude\textsuperscript{29-33}, and type of tooth movement\textsuperscript{34-38} are examples of mechanical factors implicated in OIIRR. These mechanical factors are of particular interest to the clinician as they may be controlled and modified in an attempt to reduce their influence upon root resorption.

In terms of clinical and practical significance, the degree of root resorption in most cases will be inconsequential and will not affect the long term survival or functionality of the afflicted teeth or dentition\textsuperscript{3, 28}. However, in some cases the decreased crown to root ratio resulting from severe resorption can significantly affect the prognosis, especially in the presence of periodontal disease or trauma\textsuperscript{39}. Fortunately the risk of severe root resorption is rare, occurring in less than 5\% of treated patients\textsuperscript{40-42}, and a number of strategies have been suggested to help minimise the process including 1) pre-treatment assessment of medical and family history\textsuperscript{7, 10, 11, 43}, 2) radiographic assessment at 6 months into treatment (or at 3 months in high risk individuals)\textsuperscript{26, 44}, 3) reducing treatment duration\textsuperscript{25, 26, 45, 46}, 4) reducing force magnitude\textsuperscript{2, 29, 46, 47}, and 5) halting treatment for periods of up to 3 months if resorption is detected\textsuperscript{9, 45, 48}. The resorption process usually ceases once the orthodontic force is removed\textsuperscript{3, 49}, with repair beginning once the force has decreased below a certain level\textsuperscript{47, 50} and tending to increase with time\textsuperscript{51-53}.

Recently, the use of mechanical vibration concurrently with orthodontic treatment has been suggested as a possible means of reducing treatment duration as well as root

resorption; however there is limited research in this area. Mechanical modulation of bone architecture has been found to have beneficial effects on fracture healing\(^54\),\(^55\), disuse atrophy\(^56\)-\(^58\), and musculoskeletal degeneration\(^59\),\(^60\) including osteoporosis\(^61\)-\(^63\); as well as enhancing mechanical signalling within bone\(^64\)-\(^66\). Cyclical mechanical loading in animal models has also been shown to increase bone remodelling\(^67\)-\(^69\), and vibration of rat molars at 60 Hz has demonstrated significantly increased tooth movement and a suggested trend towards decreased root resorption\(^70\). Vibration produced as a result of a pulsed electromagnetic field has also demonstrated evidence for faster tooth movement\(^71\). Furthermore, vibratory stimulation has been reported as a method to significantly reduce pain after orthodontic appliance adjustment\(^72\),\(^73\).

The aim of this study was to investigate the effect of mechanical vibration applied over 4 weeks to maxillary first premolars, on the volume of root resorption craters associated with application of a buccally directed controlled orthodontic force (150g) using Micro-computed tomography for qualitative and quantitative volumetric analysis.

### 4.3 Material and Methods

#### 4.3.1 Sample

The sample consisted of 28 maxillary first premolar teeth obtained from 14 patients (11 females and 3 males) who required extraction of these teeth as part of their orthodontic treatment at Ondokuz Mayis University, Turkey. Written informed consent was obtained from all subjects and parents or guardians, and ethics approval was obtained from the University of Ondokuz Mayis Medical Research Ethics Committee (Decree No: OMU-TAEK

2010/135) and the South Western Sydney Local Health Network Ethics Review Committee (Protocol No x11-0016 & HREC/11/RPAH/19).

All subjects were aged between 12.1 to 15.5 years, with a mean age of 13.6 years, and were recruited according to strict selection criteria:

1. Need bilateral maxillary first premolar extractions and fixed appliance orthodontic treatment.

2. Permanent Dentition.

3. Similar degree of minimal crowding on each side of the maxillary arch.

4. No previous orthodontic or orthopaedic treatment.

5. No previous dental treatment of the maxillary canines (reported or observed).

6. No history of trauma, bruxism or parafunction.

7. No past or present signs or symptoms of periodontal disease.

8. No craniofacial anomalies.

9. No significant medical history or medication that would adversely affect the development or structure of the teeth and jaws and any subsequent tooth movement.

150 grams of controlled buccally directed force was applied to the left and right first maxillary premolar of each subject. Using a split-mouth design, each subject was randomly assigned a “Vibration” and “Non-vibration” side. The maxillary first premolars were then extracted after the experimental period of 4 weeks (28 days).
The experimental period, appliance design, and force level used in this study were chosen to comply with the resorption protocols previously carried out in the Department of Orthodontics at the University of Sydney. 

4.3.2 Appliance design

0.022” x 0.028” slot SPEED Orthodontic brackets (Strite Industries Cambridge, Ontario, Canada) were bonded to the maxillary first permanent molar and first premolar teeth. Bilateral 0.017” x 0.025” Beta-titanium molybdenum alloy (TMA) springs were used to apply 150 grams of buccally directed force to the first premolars for the experimental 28 days. The force magnitude of the spring was measured using a strain gauge (Dentaurum, Germany). A layer of multi-cure Glass ionomer cement (GIC) (3M Unitek, USA) was bonded onto the occlusal surfaces of the lower first molar teeth to minimise occlusal trauma & interferences during the experimental period.

Using a split-mouth study design, each subject was randomly assigned a “Vibration” and “Non-vibration” side. Buccally directed vibration using a Hummingbird (Oral B, USA) with a modified tip was applied to the maxillary first premolar on the “Vibration” side for 10 mins per day for 28 days. According to the operating specifications the HummingBird operates at approximately 8000 RPM, which corresponds to 133 Hz. Pre-study testing using an optical tacheometer, found the average frequency was 6800 RPM or 113Hz. The batteries in the device were changed every 2 weeks to ensure maximal consistent output.

Each subject was monitored on a daily basis by one of the authors (SE) to ensure compliance with the vibration protocol.
4.3.3 **Specimen collection**

At the end of the 4 week experimental period, the maxillary first premolars were extracted with necessary care taken to avoid surgical trauma to the root cementum during the extraction procedure. Upon removal, each tooth was separately stored in a container of sterilized de-ionized water (Milli-Q®, Millipor, Bedford, Mass) which has been tested previously as an appropriate storage media. The teeth were then sent to the Orthodontic Department at the University of Sydney for analysis.

Each tooth was placed in an ultrasonic bath for a period of ten minutes and then cleaned with a damp gauze swab in a rubbing motion to remove all traces of residual PDL and soft tissue fragments. Care was taken to avoid damage to the cementum. Each tooth was then disinfected in 70% alcohol for 30 minutes and left to bench dry.

4.3.4 **Sample Analysis**

Each sample was scanned using the SkyScan 1172 desktop x-ray micro-tomograph system (SkyScan, Aartselaar, Belgium), which allows non-destructive three-dimensional reconstruction of an object’s inner structure from two-dimensional x-ray shadow projections. The system obtains multiple x-ray shadow transmission images of the object from different angular views as it rotates on a high-precision stage. From these shadow images, cross-sectional images of the object are reconstructed by a modified Feldkamp cone-beam algorithm creating a complete 3D representation of internal microstructure and density over a selected range of heights in the transmission image.

Each tooth was scanned individually from just below the cemento-enamel junction (CEJ) to just above the apex, rotating 360 degrees around the vertical axis with a rotation
step of 0.23 degrees. The x-ray tube was set at a voltage of 60kV and current of 167µA, and each sample was scanned without filters at a resolution of 17.2µm.

Three dimensional (3D) data sets were obtained for each sample from Skyscan’s volumetric reconstruction software NRecon (Version 1.4.2; Skyscan, Aartselaar, Belgium), which uses a modified Feldkamp algorithm to reconstruct the acquired angular two dimensional (2D) projections. The three dimensional data sets were then rendered as 3D visualisations using VG StudioMax software (Version 1.2; Volume Graphics GmbH, Heidelberg, Germany). From these 3D visualisations, the resorption craters were located, recorded with reproducible X, Y, and Z coordinates, and then exported for volumetric analysis. The craters were grouped 1) according to their location on the root surface e.g. buccal, palatal, mesial or distal; and 2) according to their location in the vertical plane e.g. apical, middle or cervical. The vertical location was determined by measuring the total length of the root from the CEJ to the apex and dividing it into equal thirds.

Quantitative volumetric analysis was achieved using Convex Hull Software (CHull2D) developed by the Australian Centre for Microscopy and Microanalysis at the University of Sydney. This program applies 2D convex hull algorithms to each 2D slice of the 3D data set, allowing the volume to be measured in each slice and then compiled to give an overall volume per crater in Voxels.

All measurements were carried out by one operator (JG) to eliminate inter-operator variability.
4.3.5 **Statistical Analysis**

Statistical analysis was performed using IBM SPSS Statistics, Version 19 (IBM Corporation, USA). Paired t-tests were performed to determine the significance of vibration versus non-vibration in relation to the total resorption volume per tooth, per root surface (buccal, palatal, mesial, and distal), and per vertical third (cervical, middle, and apical). Regression analyses were also performed to determine the relationship between the amount of root resorption and the improvement due to vibration, in the various regions studied. Repeat measurements were carried out to determine the error of measurement.

To allow for multiple comparisons, a “P” value of ≤ 0.01 (rather than P ≤ 0.05) was considered significant.

4.4 **Results**

The compliance rate during the experimental period was 100%, with all subjects monitored each day by one of the authors (SE) for the duration of the vibration application.

The sum of the volume of resorption craters for each tooth was calculated (Table I), as well as the overall total volume, mean, and standard deviation, in the vibration and non-vibration groups. The mean total volume in the vibration group was 0.261mm$^3$ whereas the mean total volume in the non-vibration group was 0.389mm$^3$ (Table II). All but 2 of the subjects experienced a decrease in the volume of root resorption in the vibrated teeth (Figure 3), and a paired t-Test showed a statistically significant difference in the total root resorption volume per tooth on the vibration side when compared to the non-vibration side (p=0.003) (Table V). On average, vibration reduced the amount of resorption by 0.128mm$^3$ (or 33%).
When the sample was analysed in terms of the different tooth surfaces, the distal, palatal, and mesial surfaces experienced a decrease in total root resorption volume in the vibration sample (Figure 4), however only the palatal surface showed a statistically significant difference \((p=0.006)\) while the mesial surface showed marginal significance \((p=0.018)\) (Table V). Interestingly, the buccal surface showed more resorption in the vibration sample compared to the non-vibration sample, however this was not statistically significant \((p=0.311)\) (Table V). The mean volume and standard deviation for each surface is shown in Table III.

When the sample was evaluated by vertical thirds, all three regions exhibited a decrease in total resorption volume with vibration (Figure 5), however only the apical third showed marginal significance \((p=0.019)\) (Table V). The mean volume and standard deviation for each third is shown in Table IV.

A regression analysis (Table VI) was performed comparing the amount of root resorption experienced by the non vibration teeth and the reduction/improvement \((\text{non-vibration volume} – \text{vibration volume})\) in root resorption as a result of vibration. This analysis revealed a marginally significant relationship \((p=0.082)\) between the amount of reduction in resorption volume, and the amount of resorption experienced by the associated non-vibration side. Similar regression analyses (Tables VII & VIII) performed on the various tooth surfaces and vertical thirds found similar significant relationships associated with the mesial and palatal surfaces \((p=0.000, \text{ and } p=0.006, \text{ respectively})\), and marginal significance associated with the cervical and apical thirds \((p=0.019 \text{ respectively})\). The remaining regions did not show a significant relationship.
When analysed graphically (Figures 6b, 7, & 8), these regression analyses revealed a consistent positive trend between the improvement (reduction in resorption volume) associated with vibration, and the amount of resorption associated with non-vibration, in all the aspects studied.

Repeat measurements were carried out to determine the overall standard error of measurement (SEMeas=0.012mm$^3$) and the coefficient of variance (CV=6.8%).

### 4.5 Discussion

This prospective clinical trial examined the effect of mechanical vibration on the volume of root resorption craters to determine if the application of vibration would reduce or exacerbate the resorption resulting from a controlled orthodontic force of 150grams. Despite its multi-factorial nature, root resorption severity has been closely linked to a number of mechanical factors including force magnitude and duration. These factors are fundamentally associated with stress distribution and concentration within the PDL and alveolar bone, development of areas of hyalinisation, and subsequent bony remodelling and root resorption$^{12, 13, 21, 80, 81}$. Recent research has shown that mechanical vibration can enhance bone remodelling and turnover$^{54, 57, 62, 67, 68, 82-84}$, and thus could potentially reduce root resorption by reducing the stress concentration and duration within the PDL.

In this investigation a force of 150grams was chosen to represent a more clinically relevant force, intermediate between the relatively light and heavy forces used in previous root resorption studies$^{32, 33, 37, 75, 76, 85-88}$. The study duration of 4 weeks (28 days) is consistent with previous studies, conducted at the orthodontics department at the
University of Sydney\textsuperscript{32, 37, 49, 76, 85, 86, 88-91}, and while others have employed longer experimental duration\textsuperscript{22, 23} resorption craters were still evident.

The vibration protocol utilised in this study was 113Hz applied for only 10 minutes a day. This protocol would have produced a force characteristic closest to intermittent forces which have been shown to allow cementum to heal and prevent further resorption\textsuperscript{8, 92, 93}, as well as increasing RANKL expression in PDL cells with less cell damage\textsuperscript{94}. This protocol is in contrast to the Acceledent device, which is able to produce vibration of 30Hz with a force of 20 grams and is meant to be applied for 20mins per day. The Acceledent protocol is similar to that used by the Juvent 1000 vibration plate which produces 0.2 - 0.3G (force of gravity) at 30-45 Hz and is designed for use in strengthening the musculoskeletal system.

The frequency of 113Hz was chosen as there is little agreement in the literature regarding an optimal vibration protocol, and it was also practical to modify a device (Humming Bird Dental Floss Device) which is approved for intra-oral use. The majority of studies investigating vibration to date have utilised a large range of frequencies, durations, and applied force. Prisby and co-workers have summarised most of this data in their review of the effect of whole body vibration in humans and animals\textsuperscript{95}. They conclude that the vibratory protocols (i.e., waveform, frequency, duration, and amplitude) reported in the literature vary considerably, making definitive conclusions regarding the most effective protocol extremely difficult, and in addition they suggest the most appropriate protocols will most likely depend upon the subject population as protocols developed for young individuals may be inappropriate for the elderly.
This study found a significant difference in resorption volume between vibration and non-vibration, showing a decrease in resorption in all but 2 of the subjects. In their study, Nishimura and co-workers\textsuperscript{70}, applied 60 Hz, 1.0 m/s\textsuperscript{2} to the first molars of rats by using a loading vibration system for 8 minutes on days 0, 7, and 14 during orthodontic tooth movement. They reported no significant difference between vibration and non-vibration in terms of root resorption after 21 days; however they did note a trend towards decreased resorption in the vibration group. They suggested this trend may have been the result of vibration preventing blood flow obstruction and the development of areas of hyalinization.

In their review, Prisby et al proposed that vibration has the potential to alter tissue perfusion, however the magnitude of this effect is tissue specific and depends on the vibration regimen\textsuperscript{95}.

In our study, the resorption in the buccal-cervical & palatal-apical regions corresponded with the areas of expected pressure within the PDL, and was consistent with the resorption associated with a buccal tipping movement as shown in previous studies\textsuperscript{49, 75, 77, 96, 97}. The presence of resorption on the mesial and distal surfaces is not consistent with a buccal tipping movement suggesting a rotational or torquing component to the tooth movement\textsuperscript{96}, which is highly probable considering the simple design of the force delivery appliance that was a compromise between simulating the real clinical scenario and reducing complexity and patient discomfort. This may have affected the locations and amounts of the resorption craters measured. Future studies ideally should attempt to completely isolate individual tooth movements.

Interestingly, the buccal surface showed more resorption in the vibration group compared to the non-vibration group although this was not statistically significant. This
finding could potentially indicate a concentration of vibration in this region which may be detrimental by interfering with the vascularity or bone turnover. Studies looking into the effect of vibration on tissue perfusion have found differing results, with one study finding reduced tissue perfusion with 5mins vibration at 31.5Hz and 125Hz\(^98\), while another found increased perfusion with 3 bouts of 60s vibration at 30Hz\(^99\). However, the ability of vibration to alter tissue perfusion and modify the vascular network appears to be tissue specific and dependent upon the vibration regimen\(^95\).

In terms of vertical thirds, the pattern of resorption in the non-vibration group was consistent once again with the expected areas of stress concentration within the PDL. All 3 regions experienced a decrease in resorption in the vibration group however the apical region experienced a much greater decrease compared to the cervical region. This may be due to a greater susceptibility to resorption in the apical region\(^100\), and differing cementum composition with apical cementum being softer with less Sharpey’s fibres\(^49,101\).

The results of the regression analyses comparing the volume of resorption on the non-vibration teeth with the resorption difference showed a consistent trend of increasing resorption reduction with vibration that was associated with increasing resorption volume with non-vibration. Individual susceptibility is considered to be one of the major factors in determining root resorption potential with or without treatment, highlighted by the fact that resorption can occur in both cases\(^27,100,102\), as well as varying between individuals and within the same individual at different times\(^5,47\). This trend suggests that the beneficial effect of vibration is dependent upon the individual susceptibility of the patient to root resorption, i.e. the more susceptible the patient, the greater the potential benefit of vibration.
The results of this study are promising, suggesting a potentially distinct benefit from the use of vibration in conjunction with orthodontic treatment, although the sample size of this study is small and limits the extent and strength of the data obtained. The results suggest vibration frequencies higher than 30Hz may very well be applicable to the dental environment; however, the most appropriate frequencies, durations, and amplitudes of vibration necessary for a beneficial response are still unknown. Subsequent research is required to further elucidate the potential benefits and effects of vibration in the dental arena.

4.6 Conclusions

Based on the results obtained in this study regarding the effect of 113Hz mechanical vibration applied for 10mins per day for 4 weeks in conjunction with 150g buccal tipping forces, the following conclusions can be drawn:

1. Mechanical vibration seems promising in preventing or reducing orthodontic root resorption.

2. There is a consistent trend toward increased benefit from vibration in those patients who experience higher amounts of root resorption.

3. Vibration in orthodontics is a new field and shows potential based on this study. However, the clinical significance of such application and potential optimal protocol(s) should be evaluated on a sample undergoing a complete course of orthodontic treatment to ensure efficacy and safety.
4.7 Acknowledgement

This study was supported by the Australian Society of Orthodontics Foundation for Research and Education Inc., and the Australian Dental Research Foundation.

We wish to thank Leanne Batley, NSW Oral B representative, and Oral B for providing the HummingBird units for use in this study.
4.8 References


4.9 List of Figures

Figure 1: Intra-oral views, and schematic design, of the 0.017” x 0.025” TMA spring.

Figure 2: Oral B HummingBird unit with modified tip
**The Effect Of Mechanical Vibration (113 Hz Applied to Maxillary First Premolars) On Root Resorption Associated With Orthodontic Force: A Micro-CT Study.**

**Figure 3: Total resorption volume per tooth**

![Total resorption volume per tooth](image)

**Figure 4: Overall resorption volume per surface**

![Overall resorption volume per surface](image)

Figure 5: Overall resorption volume per vertical thirds

![Graph showing overall resorption volume per vertical thirds](image)

Figure 6: a) Graph of resorption volume per subject (vibration versus non-vibration), with line of best fit (dotted line = equal amounts of resorption, vib & non-vib). b) Regression graph with line of best fit showing the relationship between the effect of vibration and the amount of resorption experienced on the non-vibration side per subject.

![Graphs showing resorption volume](image)
Figure 7: Regression graphs, with lines of best fit, showing the relationship per subject between the effect of vibration (Improvement) and the amount of resorption experienced on the a) Buccal, b) Mesial, c) Palatal, and d) Distal, aspects.
Figure 8: Regression graphs, with lines of best fit, showing the relationship per subject between the effect of vibration (Improvement) and the amount of resorption experienced on the a) Cervical, b) Middle, and c) Apical, aspects.
4.10 List of Tables

Table I: Total volume of root resorption per tooth

<table>
<thead>
<tr>
<th>Subject</th>
<th>Vibration (mm³)</th>
<th>Non-vibration (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.078</td>
<td>0.084</td>
</tr>
<tr>
<td>2</td>
<td>0.569</td>
<td>0.674</td>
</tr>
<tr>
<td>3</td>
<td>0.238</td>
<td>0.263</td>
</tr>
<tr>
<td>4</td>
<td>0.271</td>
<td>0.555</td>
</tr>
<tr>
<td>5</td>
<td>0.372</td>
<td>0.576</td>
</tr>
<tr>
<td>6</td>
<td>0.678</td>
<td>0.622</td>
</tr>
<tr>
<td>7</td>
<td>0.145</td>
<td>0.299</td>
</tr>
<tr>
<td>8</td>
<td>0.121</td>
<td>0.219</td>
</tr>
<tr>
<td>9</td>
<td>0.206</td>
<td>0.170</td>
</tr>
<tr>
<td>10</td>
<td>0.280</td>
<td>0.453</td>
</tr>
<tr>
<td>11</td>
<td>0.232</td>
<td>0.293</td>
</tr>
<tr>
<td>12</td>
<td>0.121</td>
<td>0.196</td>
</tr>
<tr>
<td>13</td>
<td>0.157</td>
<td>0.524</td>
</tr>
<tr>
<td>14</td>
<td>0.186</td>
<td>0.521</td>
</tr>
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</table>

Table II: Total volume of root resorption per experimental group

<table>
<thead>
<tr>
<th>Group</th>
<th>Total (mm³)</th>
<th>Mean (mm³)</th>
<th>SD (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibration</td>
<td>3.654</td>
<td>0.261</td>
<td>0.173</td>
</tr>
<tr>
<td>Non-vibration</td>
<td>5.450</td>
<td>0.389</td>
<td>0.192</td>
</tr>
</tbody>
</table>

Table III: Total volume of root resorption per tooth surface

<table>
<thead>
<tr>
<th>Tooth surface</th>
<th>Vibration (mm³)</th>
<th>Mean (mm³)</th>
<th>SD (mm³)</th>
<th>Non-vibration (mm³)</th>
<th>Mean (mm³)</th>
<th>SD (mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal</td>
<td>1.382</td>
<td>0.099</td>
<td>0.077</td>
<td>1.115</td>
<td>0.080</td>
<td>0.057</td>
</tr>
<tr>
<td>Mesial</td>
<td>0.593</td>
<td>0.042</td>
<td>0.054</td>
<td>1.547</td>
<td>0.110</td>
<td>0.103</td>
</tr>
<tr>
<td>Palatal</td>
<td>1.008</td>
<td>0.072</td>
<td>0.073</td>
<td>1.662</td>
<td>0.119</td>
<td>0.098</td>
</tr>
<tr>
<td>Distal</td>
<td>0.672</td>
<td>0.048</td>
<td>0.083</td>
<td>1.127</td>
<td>0.081</td>
<td>0.065</td>
</tr>
<tr>
<td>Total</td>
<td>3.654</td>
<td>5.450</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table IV: Total volume of root resorption per vertical third**

<table>
<thead>
<tr>
<th>Tooth thirds</th>
<th>Vibration</th>
<th>Mean</th>
<th>SD</th>
<th>Non-vibration</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>1.880</td>
<td>0.134</td>
<td>0.069</td>
<td>2.324</td>
<td>0.166</td>
<td>0.080</td>
</tr>
<tr>
<td>Middle</td>
<td>0.438</td>
<td>0.031</td>
<td>0.076</td>
<td>0.896</td>
<td>0.064</td>
<td>0.068</td>
</tr>
<tr>
<td>Apical</td>
<td>1.336</td>
<td>0.095</td>
<td>0.088</td>
<td>2.230</td>
<td>0.159</td>
<td>0.108</td>
</tr>
<tr>
<td>Total</td>
<td>3.654</td>
<td></td>
<td></td>
<td>5.450</td>
<td></td>
<td></td>
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**Table V: Paired Differences**

<table>
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<tr>
<th></th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>95% Confidence Interval of the Difference</th>
<th>t</th>
<th>df</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibration - Non-vibration</td>
<td>-0.128</td>
<td>0.132</td>
<td>0.035</td>
<td>-0.205 - 0.052</td>
<td>-3.624</td>
<td>13</td>
<td>.003</td>
</tr>
<tr>
<td>Buccal(V) - Buccal(NV)</td>
<td>0.019</td>
<td>0.067</td>
<td>0.018</td>
<td>-0.020 - 0.058</td>
<td>1.053</td>
<td>13</td>
<td>.311</td>
</tr>
<tr>
<td>Mesial(V) - Mesial(NV)</td>
<td>-0.068</td>
<td>0.094</td>
<td>0.025</td>
<td>-0.122 - 0.014</td>
<td>-2.705</td>
<td>13</td>
<td>.018</td>
</tr>
<tr>
<td>Palatal(V) - Palatal(NV)</td>
<td>-0.047</td>
<td>0.053</td>
<td>0.014</td>
<td>-0.077 - 0.016</td>
<td>-3.309</td>
<td>13</td>
<td>.006</td>
</tr>
<tr>
<td>Distal(V) - Distal(NV)</td>
<td>-0.033</td>
<td>0.078</td>
<td>0.021</td>
<td>-0.077 - 0.012</td>
<td>-1.576</td>
<td>13</td>
<td>.139</td>
</tr>
<tr>
<td>Cervical(V) - Cervical(NV)</td>
<td>-0.032</td>
<td>0.075</td>
<td>0.020</td>
<td>-0.075 - 0.012</td>
<td>-1.573</td>
<td>13</td>
<td>.140</td>
</tr>
<tr>
<td>Middle(V) - Middle(NV)</td>
<td>-0.033</td>
<td>0.070</td>
<td>0.019</td>
<td>-0.073 - 0.008</td>
<td>-1.747</td>
<td>13</td>
<td>.104</td>
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<tr>
<td>Apical(V) - Apical(NV)</td>
<td>-0.064</td>
<td>0.089</td>
<td>0.024</td>
<td>-0.115 - 0.013</td>
<td>-2.689</td>
<td>13</td>
<td>.019</td>
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### Table VI: Regression analysis – Comparing overall non-vibration & overall improvement with vibration

<table>
<thead>
<tr>
<th>Model</th>
<th>Un-standardised Coefficients</th>
<th>Standardised Coefficients</th>
<th>t</th>
<th>Sig.</th>
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</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonvibration</td>
<td>-.001</td>
<td>.075</td>
<td>-.013</td>
<td>.990</td>
</tr>
<tr>
<td></td>
<td>.332</td>
<td>.175</td>
<td>1.900</td>
<td>.082</td>
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</table>

*a.* Dependent Variable: Impr

### Table VII: Regression analyses per tooth surface – Comparing non-vibration & the improvement with vibration.

<table>
<thead>
<tr>
<th>Model</th>
<th>Un-standardised Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Sig.</th>
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</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BuccalNV</td>
<td>-.042</td>
<td>.032</td>
<td>-1.316</td>
<td>.213</td>
</tr>
<tr>
<td></td>
<td>.286</td>
<td>.327</td>
<td>.877</td>
<td>.398</td>
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*a.* Dependent Variable: BuccImp

<table>
<thead>
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<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MesialNV</td>
<td>-.018</td>
<td>.020</td>
<td>-.902</td>
<td>.385</td>
</tr>
<tr>
<td></td>
<td>.783</td>
<td>.138</td>
<td>5.692</td>
<td>.000</td>
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*a.* Dependent Variable: MesImp

<table>
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<th>t</th>
<th>Sig.</th>
</tr>
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<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PalatalNV</td>
<td>.003</td>
<td>.017</td>
<td>.154</td>
<td>.880</td>
</tr>
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<td></td>
<td>.371</td>
<td>.112</td>
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*a.* Dependent Variable: PalImp

<table>
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<tr>
<th>Model</th>
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<th>Standardised Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DistalNV</td>
<td>.001</td>
<td>.033</td>
<td>.018</td>
<td>.986</td>
</tr>
<tr>
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<td>.398</td>
<td>.327</td>
<td>1.217</td>
<td>.247</td>
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*a.* Dependent Variable: DisImp
Table VIII: Regression analyses per vertical third – Comparing non-vibration & the improvement with vibration

<table>
<thead>
<tr>
<th>Model</th>
<th>B</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
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<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CervicalNV</td>
<td>-.064</td>
<td>.039</td>
<td></td>
<td>-1.639</td>
<td>.127</td>
</tr>
<tr>
<td></td>
<td>.579</td>
<td>.215</td>
<td>.614</td>
<td>2.698</td>
<td>.019</td>
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</table>

(a. Dependent Variable: CerImp)

<table>
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<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MiddleNV</td>
<td>.006</td>
<td>.025</td>
<td></td>
<td>.255</td>
<td>.803</td>
</tr>
<tr>
<td></td>
<td>.413</td>
<td>.277</td>
<td>.395</td>
<td>1.491</td>
<td>.162</td>
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</tbody>
</table>

(a. Dependent Variable: MidImp)

<table>
<thead>
<tr>
<th>Model</th>
<th>B</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ApicalNV</td>
<td>-.017</td>
<td>.036</td>
<td></td>
<td>-.468</td>
<td>.648</td>
</tr>
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<td></td>
<td>.505</td>
<td>.186</td>
<td>.616</td>
<td>2.710</td>
<td>.019</td>
</tr>
</tbody>
</table>

(a. Dependent Variable: ApImp)
5 Future Directions

The benefits of mechanical vibration therapy have been studied increasingly in the medical field for a wide range of uses including improving bone mass and density, improving balance and mobility, and preventing or improving muscle strength and performance etc. In contrast, the utilisation of vibration protocols is relatively new in the realms of dentistry, and very little is known about the potential benefits for the orthodontist. What little research exists, investigating the effect of vibration on orthodontic tooth movement, pain sensation, and craniofacial structures, is mainly limited to animal studies.

This study was based upon the methodology of previous root resorption studies conducted at the Department of Orthodontics, Faculty of Dentistry University of Sydney. Certain limitations of this methodology include short duration and small sample size. A number of the results obtained in this study showed a distinct trend however were not statistically significant, which could be the result of the short duration or small sample size. Further research should utilise longer study durations and larger sample sizes to circumvent these limitations.

As previously discussed, little consensus exists in the literature regarding optimal vibration protocols to enhance benefit and ensure minimal detriment. This study demonstrated positive results utilising a frequency of 113Hz. Future studies should investigate the effect of different vibration protocols (comparing different frequencies, magnitudes, and durations) and different vibration devices or methods of application. These future investigations should attempt to determine the optimal vibration protocol(s) for the oral environment. Furthermore, the influence of age and sex need to be assessed, as
different protocols may be required depending upon age and sex to achieve maximum beneficial results.

The Acceledent device has been advertised to work with all orthodontic appliances including lingual fixed appliances, labial fixed appliances and removable thermoplastic appliances. The efficacy of mechanical vibration protocols in conjunction with different orthodontic appliances needs further investigation.

In accordance with the methodology of previous studies, the maxillary first premolars were used in this study as these teeth were to be extracted as part of the orthodontic treatment plan. As discussed previously however, the maxillary incisor teeth are the most effected by root resorption and as such further investigations need to assess the effect of vibration protocols on different teeth.

This study focused solely upon the effect of mechanical vibration on the incidence and amount of root resorption. For mechanical vibration to become a true adjunctive treatment in the orthodontic field, future research should examine the effect of vibration protocols on the rate of orthodontic tooth movement, orthodontic pain perception, and rate of repair of resorption. Furthermore, Nishimura and co-workers suggested the application of mechanical vibration may induce alterations in blood flow in the adjacent periodontal ligament. To examine this possibility, further biomolecular and biochemical research is required.

Further research is required to investigate the potential correlation bwn individual susceptibility and the benefit of vibration. Analysis of the results of this study suggested a
distinct correlation between increased benefit of vibration and those patients who experienced more root resorption. This research may possibly involve genetic testing.

FEM analysis offers a unique opportunity to model and observe the distribution and propagation of vibration through the dental, paradental, and craniofacial structures; as well as the effect of vibration on areas of compression & tension within the PDL after application of various types and magnitudes of orthodontic force. In future studies, different vibration protocols should be modelled, as well as the effect of vibration in conjunction with different types of orthodontic appliances including sequential thermoplastic aligners.

Adjunctive vibration protocols in orthodontics are new and their effects and benefits are still relatively unknown. The results of initial investigations have been positive, and the introduction of the AcceleDent device has opened the door for potentially widespread mainstream use of vibration in the orthodontic arena. Further studies both clinical and laboratory will be needed to expand our knowledge in this burgeoning field.
6 Appendices

6.1 Appendix: Index for Qualitative Assessment of Root Resorption


![Root Resorption Index](image-url)
6.2 Appendix: Sample distribution and split-mouth study design

14 Subjects

Randomly assigned "Side A" (No-Vibration).

Application of 150g orthodontic force.

No vibration applied.

Sample collected for analysis.

Randomly assigned "Side B" (Vibration).

Application of 150g orthodontic force.

Vibration protocol applied 10 mins/day.

Sample collected for analysis.

6.3 Appendix: Specimen collection procedure

Extraction of 1st PM

Stored in de-ionized water (Milli Q)

Ultrasonic bath for 10 min.

Mechanical cleaning with a rubbing motion

Disinfection with 70% alcohol for 30 min.

Bench dry at ambient temperature
6.4 **Appendix: SkyScan 1172 desktop x-ray micro-tomograph**

(SkyScan, Aartselaar, Belgium)

6.5 **Appendix: Images from VGStudio Max**

(Volume Graphics GmbH, Heidelberg, Germany)
6.6 **Appendix: Data – Total resorption per tooth**

<table>
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<th>Subject</th>
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<th>Non-vibration</th>
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### 6.7 Appendix: Data – Total resorption per tooth surface

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<th>Buccal-NV</th>
<th>Mesial-V</th>
<th>Mesial-NV</th>
<th>Palatal-V</th>
<th>Palatal-NV</th>
<th>Distal-V</th>
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<td><strong>0.119</strong></td>
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<td><strong>0.081</strong></td>
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### Appendix: Data – Total resorption per vertical third

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<th>Middle Vibration</th>
<th>Middle Non-vibration</th>
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<td>0.064</td>
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<td>0.159</td>
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<td>SD</td>
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