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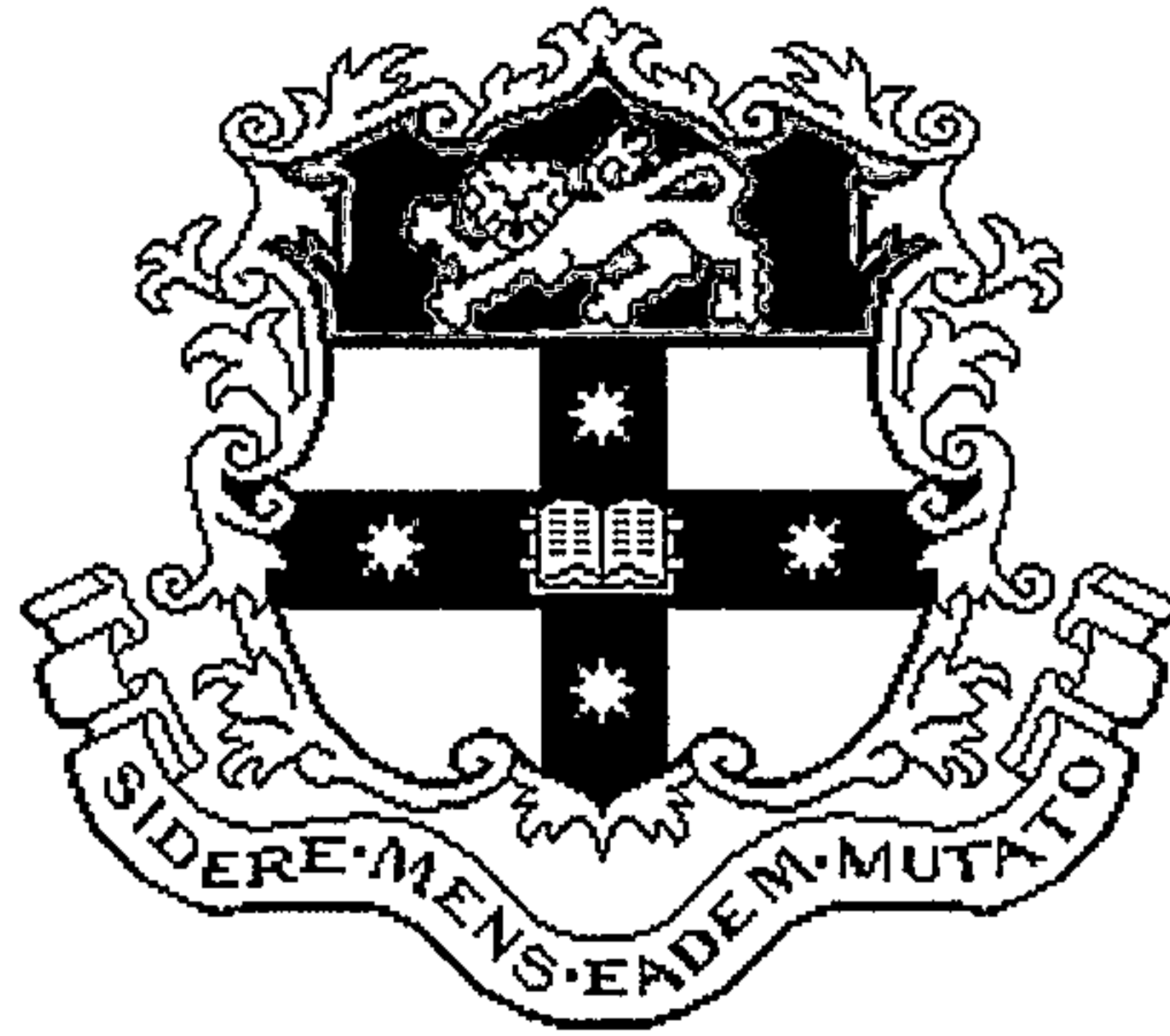
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PROPERTIES OF ROOT CEMENTUM: PART 11
CONTINUOUS VERSUS INTERMITTENT
CONTROLLED ORTHODONTIC FORCES ON ROOT
RESORPTION.
A MICRO-CT STUDY

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A thesis submitted in partial fulfillment of the requirements for the
degree of Master of Dental Science (Orthodontics)

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Australia
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Dedication

To my beautiful wife, Teriko.

Thank you for your patience, tolerance and for being there in my countless times of need. I would not have made it without you.

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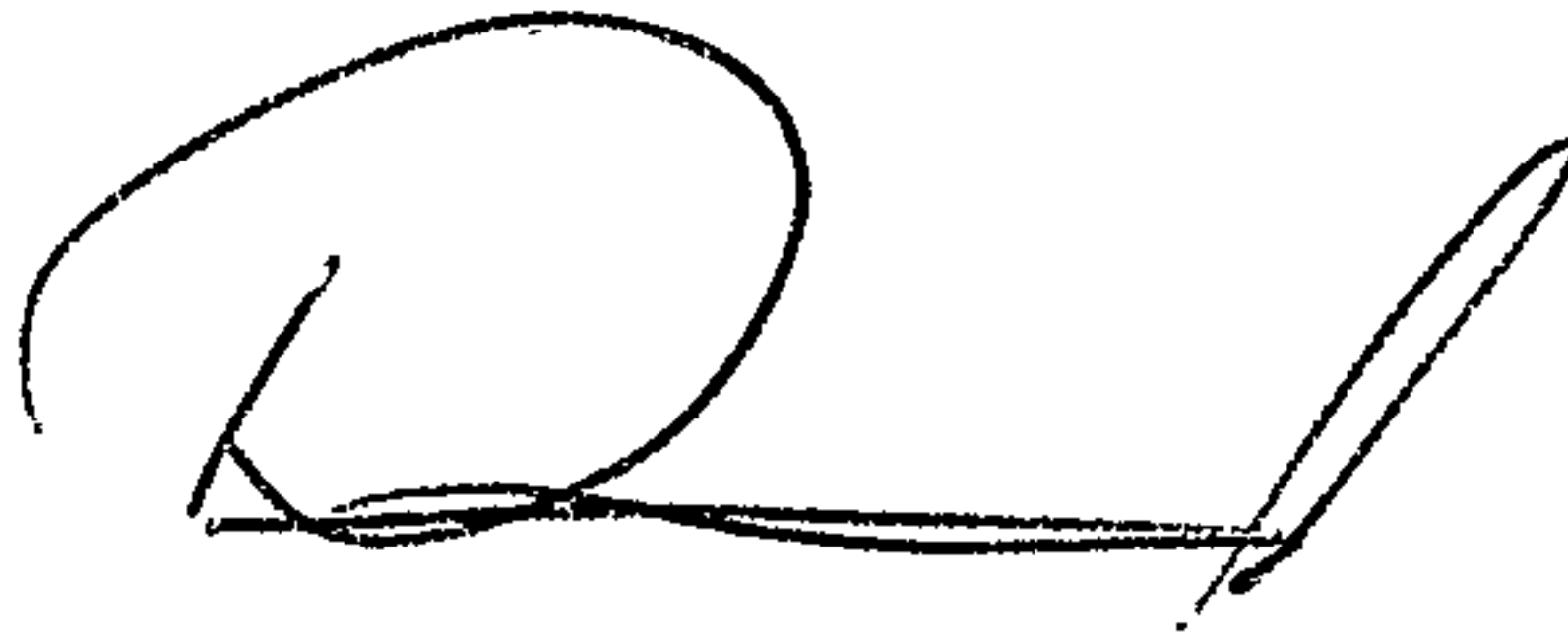
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Declaration

CANDIDATE CERTIFICATE

This is to certify that the candidate carried out the work in this thesis in the Orthodontic Department, University of Sydney and has not been submitted to any other University or Institution for a higher degree.



Darin Ballard

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DEDICATION

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DECLARATION

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ABBREVIATIONS

ANOVA	Analysis Of Variance
CT	Computed Tomography
OIRR	Orthodontically Induced Inflammatory Root Resorption
OPG	Orthopantomogram
PTH	Parathyroid Hormone
PDL	Periodontal Ligament
PVS	Polyvinyl-Siloxane
SEM	Scanning Electron Microscope
TMD	Temporo-Mandibular Dysfunction
UV	Ultraviolet
VIS	Visible
XMT	X-ray Micro-Tomography

1. INTRODUCTION

External surface root resorption may be defined as the active removal of mineralised and non-mineralised cementum and dentine (Brudvik & Rygh, 1993a). The factors that may cause pathological external root resorption can be divided into three groups; traumatic, infection related and tooth movement related (Ghafari, 1994; Reitan, 1985). Although the outcome of the different root resorptive processes is frequently similar, orthodontic root resorption is distinct from the other types of root resorption with the term orthodontically induced inflammatory root resorption (OIIRR) having been suggested (Brezniak & Wasserstein, 2002a).

Extensive OIIRR becomes irreversible when it extends beyond the cementum layer into dentine (Brezniak & Wasserstein, 1993b) and may compromise an otherwise successful orthodontic outcome. It is thus important that more knowledge be sought regarding of the mechanism, risk factors and preventive factors involved in the root resorptive process.

There are studies in the literature investigating the relationship between interrupted or discontinuous forces compared to continuous forces and OIIRR. A pause in tooth movement is believed by many authors to allow the resorbed cementum to heal and thus many conclude that discontinuous force causes less root resorption (Acar et al., 1999; Dougherty, 1968; Levander et al., 1994; Maltha & Dijkman, 1996; Oppenheim, 1930; Oppenheim, 1942; Reitan, 1964; Weiland, 2003). There are a number of

studies with varying durations and frequencies of interruption in the applied forces which have led to varied results. One SEM study involved human premolar teeth in a split-mouth set up (Acar et al., 1999). The authors found that a discontinuous force of 100 cN, 12 hours per day resulted in less OIIRR than the same force applied 24 hours per day. A study involving young adult beagle dogs was conducted to compare continuous (24 hours/day) to discontinuous (16 hours/day) forces (Maltha & Dijkman, 1996). Although there was great variation in the force level (10 to 200 cN) and the treatment duration (4 to 100 days) in this study, histological and histomorphometric evaluation revealed that the discontinuous regime of force application caused significantly less resorption than the continuous force. Another histological study involving human premolar teeth (Owman-Moll et al., 1995a) where one force was not reactivated over three weeks, whilst the other “constant force” was reactivated every week over three week. After an additional week of “recovery”, they were found to have no histological evidence of a significant difference in the amount of OIIRR.

Excessive forces generated from both removable and fixed appliances can provoke OIIRR. It is well accepted that the force pattern for removable appliances is intermittent and is in distinct contrast to that of fixed appliances where continuous force is exerted. One radiographic study established that fixed appliances are more detrimental to the roots of upper incisors than “activators and spring plate” removable appliances (Linge & Linge, 1983). Another radiographic study by the same authors (Linge & Linge, 1991) involved a comparison of patients treated with full fixed

edgewise appliances with Class II elastics and rectangular wires and patients treated with activators, plates with clasps and vertical elastics. The patients treated with fixed appliances, rectangular arch wires and Class II elastics had notable OIIRR. The latter group of patients was found to have no OIIRR.

Until recently, the detection of OIIRR has mainly been achieved through two-dimensional measurement techniques such as radiographs (Ketcham, 1927; Ketcham, 1929), light microscopy (Reitan, 1974) and Scanning Electron Microscopy (SEM) (Jones & Boyde, 1972; Kvam, 1972a; Kvam, 1972b). Whilst two-dimensional radiography remains the most conservative diagnostic tool for the clinical detection of root resorption in patients, three-dimensional techniques such as stereoinaging SEM measurements (Chan & Darendeliler, 2005; Chan & Darendeliler, 2004; Chan et al., 2004) and X-ray microtomography (Micro-CT) (Foo et al., 2005; Harris et al., 2005) may allow more accurate and reliable measurements for researchers. However its high cost and high radiation exposure to the patient limit its clinical use (Ngan et al., 2003).

The aims of this study were to investigate quantitatively, via Micro-CT, the amount of OIIRR induced by intermittent and continuous forces on human premolar teeth and to identify the surfaces where root resorption is more prevalent after controlled orthodontic buccal movement.

2. REVIEW OF THE LITERATURE

2.1 CEMENTUM

2.1.1 Definitions And Functions Of Cementum

Cementum is a non-uniform mineralized tissue covering the dentine of the tooth root. It is a specialized connective tissue that has many physical, chemical and structural features in common with compact bone (Armitage et al., 1980).

Cementum differs from bone in that it contains no neural or vascular tissue, continues to grow in thickness throughout life and does not undergo remodeling or mineral turnover (Ten Cate, 1998).

Cementum is an element of the tooth itself, however functionally it belongs to the dental attachment apparatus known as the periodontium (Bosshardt & Selvig, 1997).

One of the key purposes of cementum is to provide support to the functioning tooth. It attaches the principal collagen fibres of the periodontal ligament to the root surface.

Cementum has essential adaptive and reparative functions. It is responsible for sustaining occlusal relationships and preserving the integrity of the root surface.

At the cemento-enamel junction (CEJ), the cementum layer is relatively thin, generally ranging from 20 to 50 μm thick. At the apex it occurs in a thicker layer of approximately 150 to 200 μm (Ten Cate, 1998).

2.1.2 Classification Of Cementum

Cementum may be classified according to:

Its timing of development: primary or secondary cementum.

The presence or absence of cementocytes within its structure: cellular or acellular cementum.

The origin of the collagenous fibres of the matrix: that is intrinsic fibres which result from cementoblasts activity or extrinsic fibres which result from the incorporation of periodontal ligament (fibroblast formed) fibres (Schroeder, 1986; Schroeder, 1993; Ten Cate, 1998).

Consequently, the following types of cementum have been described (Schroeder, 1986; Ten Cate, 1998):

Acellular Afibrillar Cementum - This type of cementum is deposited in isolated patches over minor areas of enamel just coronal to the CEJ. It plays no role in tooth attachment and is considered to be a developmental anomaly.

Primary Acellular Intrinsic Fibre Cementum - This type of cementum extends 15-20µm at the most cervical region of the root. It has an anchorage function.

Primary Acellular Extrinsic Fibre Cementum – This cementum continues apically from the Primary Acellular Intrinsic Fibre Cementum to cover at least two thirds of the root and often more. Lacking cells, it is composed almost entirely of densely packed bundles of Sharpey's fibres, reflecting its anchorage function. It is the most highly mineralized cementum.

Secondary Cellular Intrinsic Fibre Cementum – This cementum is located at the apical and inter-radicular regions of the root. It is the main reparative tissue in the restoration of root resorption defects (Bosshardt & Selvig, 1997).

Secondary Cellular Mixed Fibre Cementum – This cementum has a highly variable distribution and quantity reflecting its adaptive function.

Cellular Mixed Stratified Cementum – This cementum is found on the apex, the apical third of the root and the furcations. Its thickness varies between 100 and 1000 μm . It has both anchorage and adaptive roles.

Intermediate Cementum – This type of cementum is a form of Secondary Cellular Intrinsic Fibre Cementum and is located only at the apex. It contains entrapped cellular debris either from the root sheath or the odontoblast layer. It is not involved in root attachment and appears to have no function.

2.1.3 Composition Of Cementum

Cementum consists of water, organic matrix and (inorganic) mineral. Volumetrically, its composition is on average 45% inorganic material, 33% organic and 22% water (Berkovitz et al., 1992). The relative amount of the mineral component however varies depending on the cementum type, location and root resorption activity. The inorganic material, like in bone, is calcium and phosphate in the form of hydroxyapatite $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$, with small amounts of amorphous calcium phosphates (Bosshardt & Selvig, 1997). The hydroxyapatite is not chemically pure as it also consists of ions that were taken up from the tissue fluid during the mineralization phase. The amount of these incorporated elements reflects their concentration in the tissue fluid that was present during this process. Following the initial formative process, the concentration of the various ions may change again by further incorporation or replacement with other ions (Bosshardt & Selvig, 1997). Fluoride found in cementum is by far the most concentrated of all mineralized tissues (Ishiguro et al., 1994; Kato et al., 1990).

The organic matrix of cementum consist of approximately 90% type I collagen and 5% type III collagen (Christner et al., 1977). The major roles of collagen are structural and to provide a scaffold for mineralization (Christoffersen & Landis, 1991).

The noncollagenous proteins of cementum are composed of several glycoproteins, enamel-related proteins, proteoglycans and osteocalcin. The glycoproteins in cementum include bone sialoprotein, osteopontin, osteonectin and fibronectin (Ivanovski et al., 2001).

2.1.4 Development And Distribution Of Cementum

Cementum is secreted by cementoblasts onto the surface of root dentine or in some animals onto the crown enamel (Diekwisch, 2001). Its formation begins following the onset of root formation and elongation. Hertwig's epithelial root sheath (HERS) guides the formation of the root. The HERS is a collar of epithelial cells resulting from the apical elongation of the enamel organ (Ten Cate, 1998). Prior to cementogenesis, the HERS disintegrates and dental follicle cells penetrate the epithelial layer to access the root surface. Cementoblasts deposit the cementum and constitute a large number of these invading dental follicle cells (Diekwisch, 2001).

When cementum is formed slowly it is usually acellular (primary cementum). When it is formed rapidly, however, cementoblasts may become trapped in lacunae in the cementum and they are then known as cementocytes. This is similar to how osteocytes are in lacunae in bone. Cementum that contains cementocytes is cellular (secondary cementum). Both types of cementum are formed in layers throughout life in response to the physiological demands on the tooth. The first formed cementum is acellular; it is deposited onto the surface of the dentine and is mostly found near the cemento-enamel junction (CEJ). Acellular cementum may cover the entire root from the CEJ to the apex, but it is often missing in the apical third. Cellular cementum is usually found in the apical region and progressively builds in thickness towards the apex (Ten Cate, 1998).

There are two separate cementoblast inhabitants according to the type of cementum formed. One cementoblast population produces primary (acellular) cementum and the other secondary (cellular) cementum (Ten Cate, 1998). The phenotypes of the cells differ. This may be demonstrated by monoclonal antibody staining. A monoclonal antibody (E11) stains the cementoblasts and cementocytes of secondary cementum. The cementoblasts that cover primary cementum do not stain for this antibody. The cementoblasts differ in developmental origin: The cells of primary cementum arise from the dental follicle, whereas the cells associated with secondary cementum originate from a non-follicular population (Ten Cate, 1998).

The production of cementum continues throughout life unless upset by periodontal pathology (Bosshardt & Selvig, 1997). A linear relationship between the depth of the cementum and the age of the tooth has been found with an average thickness of 0.1mm at age 20 years and 0.2mm at age 55 years (Zander & Hurzeler, 1958).

2.2 ROOT RESORPTION

2.2.1 History Of Root Resorption

Bates first described the root resorption of permanent teeth, a process he referred to as “absorption” (Bates, 1856). Root resorption was first linked to orthodontic treatment in 1914 (Ottolengui, 1914). Ketcham was the first to describe radiographic evidence of root resorption and observed that the phenomenon occurred in all orthodontically treated patients, regardless of the appliance or technique employed (Ketcham, 1927; Ketcham, 1929). Ketcham suggested that hormonal imbalance and dietary deficiencies were possible reasons for its occurrence.

Comprehensive research has been performed into this phenomenon since Ketchams’ investigations; however the process is not completely understood.

2.2.2 Definition Of Root Resorption

Root resorption was defined by Becks and Marshall (1932) as the destruction of formed tooth structure (Becks & Marshall, 1932).

Brudvik and Rygh defined root resorption as the active removal of mineralized and a thin layer of non-mineralized cementum (Brudvik & Rygh, 1994b). They further described the process as the removal of mineralised cementum and dentine associated with the remodeling process of the periodontal ligament, more specifically, during the removal of hyalinized necrotic tissue (Brudvik & Rygh, 1994a).

Although the outcome of the different root resorptive processes is frequently similar, orthodontic root resorption is distinct from the other types of root resorption. Thus the term Orthodontically Induced Inflammatory Root Resorption (OIIRR) has been suggested (Brezniak & Wasserstein, 2002a).

2.2.3 Cementum And Root Resorption

As cementum is continuously formed throughout life, a layer of cementoblasts line the surface of the cementum (Scott & Symons, 1982). Between the layer of cementoblasts and cementum is the uncalcified matrix known as cementoid. It has been found that root cementum is more resistant to resorption than bone. Some authors suspect that this resistance is due to the existence of the cementoid and the protective formative cell layer (Jones & Boyde, 1988; Lindskog & Hammarstrom, 1980; Tronstad, 1988). If there is a breach in these protective components, the mineralized tissue and periodontal matrix will come into contact and osteoclasts will thus have access (Jones & Boyde, 1988; Tronstad, 1988).

The precise method by which resorption is inhibited is poorly understood. There are however a number of theories.

A number of uncalcified mineral tissues have been found to be more resistant to resorption when exposed to orthodontic force. The minerals include precementum (Gold & Hasselgren, 1992), osteoid (Chambers et al., 1984) and predentine (Stenvik & Mjor, 1970).

It has been suggested that the innermost layer of the periodontal ligament (PDL), including cementoblasts, fibroblasts, osteoblasts, endothelial and perivascular cells are associated with cementum's resistance to resorption. The peripheral part of the

PDL, namely Sharpey's fibres, cementum, precementum and epithelial rests of Mallassez may not be related to the resistance (Andreasen, 1988b). However other authors suggest Sharpey's fibres, precementum, predentine and elements of the organic matrix may still have a role in resistance to resorption (Jones & Boyde, 1988).

2.2.4 Classification Of Root Resorption

External root resorption has been classified by a number of authors including Andreasen (Andreasen, 1988b); Tronstad (1988) and (Ghafari, 1994). Their classifications have included the following categories of external resorption:

Surface resorption: This is a self limiting process, involving small surface areas including cementum and possibly dentine. It is a brief process followed by spontaneous repair with cementum from cells in adjacent intact regions of the periodontal ligament. It is not usually detected radiographically (Andreasen, 1988b; Ghafari, 1994).

Inflammatory resorption: This occurs where the initial root resorptive process has reached the dentinal structures of the infected necrotic pulpal tissues or an infected leukocytic zone (Andreasen, 1988b). Inflammatory mediators and phagocytic cells inhabit the mineralised or denuded cementum surfaces and later dentinal tubules or pulpal tissues (Ghafari, 1994). Tronstad (1988) further divided inflammatory resorption into two types:

Transient inflammatory resorption occurs where root damage is minimal and the stimulation for the resorptive process is of a short duration. This form of resorption is usually undetectable radiographically and is repaired by a cementum-like tissue.

Progressive inflammatory resorption occurs where the resorptive stimulus continues for a longer duration, leading to a radiographically discernible change in root structure.

Replacement resorption: This type of resorption occurs where bone replaces the resorbed root structure, eventually leading to ankylosis (Andreasen, 1988b; Tronstad, 1988). This resorption is detectable radiographically (Ghafari, 1994)

Orthodontically Induced Inflammatory Root Resorption (OIIRR) is classified by Brezniak and Wasserstein into three groups depending upon the level of severity (Brezniak & Wasserstein, 2002a):

Cemental or surface resorption with remodeling: the outer cemental layers only are resorbed and are subsequently totally regenerated or remodeled. They liken this to trabecular bone remodeling.

Dentinal resorption with repair (deep resorption): the cementum and outer dentine layers are resorbed and usually repaired with cementum material. The resultant form of the root may or may not be distinguishable to the previous contour.

Circumferential apical root resorption: Full resorption of the hard tissue structure of the root apex takes place and root shortening results. There is a potential for variable

amounts of root length reduction. When the root structure is lost into dentine, no regeneration is possible.

OIRR rarely leads to ankylosis (Brezniak & Wasserstein, 2002a).

2.2.5 Incidence Of Root Resorption

Studies in the literature regarding the prevalence of root resorption are either histological or radiographic. Due to the two-dimensional nature of radiographs, detail regarding the amount resorption may be missed with this methodology. The histological studies involve progressive slices of roots, thus less detail is missed, and the measurements are more accurate. The most accurate methods of quantification of root resorption are three-dimensional methods including SEM and x-ray microtomography (Chan & Darendeliler, 2004). Histological, SEM and microtomography studies may only be performed on extracted teeth. Teeth are not usually extracted at the end of a protracted period of fixed appliance treatment, thus these three types of studies are not useful for assessing populations of patients that have completed orthodontic treatment.

Root resorption has been reported in both orthodontically treated and untreated populations.

2.2.5.1 Untreated Populations

From a histological study of 261 permanent teeth from untreated individuals, 90% of the teeth exhibited histological evidence of root resorption (Henry & Weimann, 1951).

Up to 76.8% of these resorption areas occurred in the apical third of the root, 19.2% in the middle third and 4% in the gingival third. The average size of the resorption areas measured 0.73mm in length, and 0.10mm in depth. The number of resorption areas increased with age. The resorption regions were more numerous on the mesial than on the distal surface, and more numerous on the buccal than on the lingual surfaces. Little difference was noted between the right and left or upper and lower teeth. Repair was evident in 85% of the resorption areas.

Henry and Weimann (1951) came to the following conclusions:

It is normal for a tooth to incur resorption to some degree during its life and age is a contributory factor in the causation of resorption.

Resorption occurred more readily on surfaces facing physiological tooth movement.

Resorptions are usually small, shallow and readily repaired.

The size of the resorption area is a good index of its severity while the number of resorption areas is an index of the number of incidents that caused root resorption.

Acellular cementum, found mainly in the cervical region of the tooth root, is more resistant to root resorption than the more apically positioned cellular cementum.

A certain amount of root resorption may be a normal physiological process, perhaps connected to continuous bone remodeling (Vlaskalic et al., 1998). Numerous studies agree that idiopathic root resorption also occurs in untreated populations; however its incidence is variable amongst these populations. Studies also vary in sample size and methodological protocols, thus making comparisons of reported incidences difficult.

2.2.5.2 Orthodontically Treated Populations

The incidence of OIRR is high; however the incidence of severe resorption is low.

In a ten-year evaluation of 3300 fixed appliance patients at a university department, all were found to have between 1 and 3mm of root resorption (Ahlgren, 1993).

In a study with a sample of 343 consecutively treated adults from four orthodontic practices, 40% of the patients were found to have one or more teeth with 2.5 mm resorption or greater (Mirabella & Artun, 1995a). Standardized periapical radiographs taken before and after treatment were used for this study.

Lupi et al. (1996) reported from their sample of 88 ethnically and racially diverse adults that 15% of them had resorption of their incisors before orthodontic treatment and this increased to 73% after at least 12 months of fixed appliance therapy. A smaller percentage (2%) showed severe resorption beyond one third of the original

root length (Lupi et al., 1996). Resorption was assessed with standardized periapical radiographs taken before and after treatment.

A radiographic and histological study of the premolars of 56 adolescents was performed (Kurol et al., 1996). The teeth studied were orthodontically treatment planned for extraction. The study teeth were moved for between one and seven weeks prior to extraction. Standardized periapical radiographs were taken before and after tooth movement. The extracted teeth were sectioned for histological study and 93% of the teeth moved were found to have root resorption (Kurol et al., 1996).

Moderate to severe apical root resorption ($>2\text{mm}$ to $<1/3$ root length loss) has been found in 12-17% of orthodontically treated patients (Linge & Linge, 1991). Excessive root resorption ($>1/3$ of root length) has been found in 1-5% of a treated population (Davidovitch, 1996; Levander & Malmgren, 1988).

2.2.6 The Mechanism Of Root Resorption

Orthodontic forces applied to the periodontal system exert similar pressures onto bone as to cementum via the periodontal ligament. If there were no differences in the biologic behaviour of these two tissues, both would resorb equally. It was thought that since cementum is more resistant to resorption when compared to the more vulnerable bone, applied forces usually cause bone resorption, which leads to tooth movement. However, resorption of the cementum and dentine may also occur.

The exact mechanism of root resorption is not yet fully known. Resorption of the calcified dental tissues occurs if osteoclast-like cells obtain access to the mineralized tissue by a breach in the formative cell layer covering these tissues (Jones & Boyde, 1988; Tronstad, 1988). Resorption may also occur if the mineral and matrix surfaces contact (Jones & Boyde, 1988), or if the precementum is mechanically damaged or scraped off (Tronstad, 1988). The mineralized or denuded root areas are attractants for colonisation by hard tissue resorbing cells (Tronstad, 1988).

After application of force, it can take between 10 and 35 days for resorbed lacunae to appear (Harry & Sims, 1982; Reitan, 1974; Rygh, 1977; Stenvik & Mjor, 1970). Clinically, this degree of resorption cannot be detected with radiographs, especially when occurring on the buccal and lingual surfaces (Andreasen, 1988b; Wainwright, 1973).

Resorbed lacunae appear mainly on the pressure side (Gaudet, 1970; Reitan, 1964; Reitan, 1974; Reitan, 1985; Rygh, 1977), and rarely on the tension side (Williams, 1984). It has been claimed that root resorption during orthodontic treatment occurs in the same areas where physiologic root resorption originates (Reitan, 1974). These areas may be more sensitive to local changes.

The application of orthodontic force induces a local inflammatory reaction (Bosshardt et al., 1998). This inflammation is essential for tooth movement to occur, and is also induces the root resorption process (Brezniak & Wasserstein, 2002a).

When a prolonged orthodontic force of greater than 20-26 g/cm² (Schwartz, 1932) is applied to a tooth, the loaded region of periodontal ligament will suffer over-compression and undergo hyalinization (also known as sterile coagulation necrosis) (Kvam, 1973; Nakane & Kameyama, 1987; Reitan, 1951; Rygh, 1977; Tanaka et al., 1990). These sterile tissue changes promote an inflammatory reaction in an attempt to remove the necrotic tissue and initiate tissue repair (Hellsing & Hammarstrom, 1996; Rygh, 1974; Rygh, 1983; Vandevska-Radunovic et al., 1994). The inflammatory process involves both bone and cementum resorption as resorbed lacunae associated with hyalinized tissue elimination appear mainly on the pressure side 10 to 35 days after force application (Harry & Sims, 1982; Reitan, 1974; Rygh, 1977). When orthodontic pressure is below the optimal level of 20-26 g/cm², root resorption ceases but tooth movement is still possible (Schwartz, 1932).

The periodontal ligament yields in a two-step process: an initial morphometric change (compression) followed by biochemical changes. The histochemical changes seen in the periodontal ligament include: fibre coalescence; hyalinization (Reitan, 1985); degradation of connective tissue matrices by both an extracellular pathway (matrix metalloproteinases) and an intracellular phagocytic pathway (lysosomal enzymes) (Sodek & Overall, 1988); and demineralisation of Sharpey's fibres (Jones & Boyde, 1988). Odontoclastic activity follows these changes.

Investigations into the histological changes in the tissues surrounding the zone of hyalinization have mainly been conducted on animal samples, particularly rats. During the process of bone remodelling, the surrounding osteoclasts show a high content of Tartrate-Resistant Acid Phosphatase (TRAP) (Hammarstrom & Hasselgren, 1974; Lilja et al., 1983) and it is this content that can be stained positive for cells involved in orthodontic tooth movement and root resorption (Farrell et al., 1990; Farrell et al., 1991; Lilja et al., 1983).

Brudvik and Rygh investigated the processes of orthodontic root resorption and repair in rats and mice and published their results in a series of papers (Brudvik & Rygh, 1993a; Brudvik & Rygh, 1993b; Brudvik & Rygh, 1994a; Brudvik & Rygh, 1994b; Brudvik & Rygh, 1995a). The authors studied the histological changes seen under light microscopy of the molar teeth of animals that had undergone orthodontic tooth movement (Brudvik & Rygh, 1993a; Brudvik & Rygh, 1993b). The stains used in this

study were Tartrate-Resistant Acid Phosphatase (TRAP) and Haematoxylin & Eosin (H&E). They found that the first phase of root resorption involves the reactions of and penetration by adjacent healthy periodontal membrane TRAP-negative cells into unmineralized precementum. This first resorptive attack on the root surface occurred in the over-compressed zone. These invading periodontal cells were originally either stationary or blood borne. Root resorption occurred in the perimeter of the hyalinized tissue after 2 to 3 days in the rat samples. Prior to loss of root structure, mononucleated cells were observed proximal to or contacting the root surface. The authors suggested that it is these cells that start the resorption of the unmineralized cementoid and mineralized acellular cementum. They proposed that some of these cells were macrophages, fibroblasts or cementoblasts; which are all TRAP-negative (Brudvik & Rygh, 1993a).

In another study using transmission electron microscopy, Brudvik and Rygh studied in greater detail the penetration of cells into precementum and mineralized cementum (Brudvik & Rygh, 1994a; Brudvik & Rygh, 1994b). They confirmed that mononucleated non-clast cells were found during the initial removal of precementum and mineralized acellular cementum at the periphery of the hyalinized tissue and also some distance from it. Macrophage-like cells phagocytosed necrotic tissue in the periodontal ligament after 6 hours and near the root surface after 24 hours. Fibroblast-like and cementoblast-like cells were involved in the resorptive process of precementum after 24 hours. Mononucleated cells removed the surface layers of

mineralized cementum after 3 days. Multi-nucleated cells were seen in surrounding tissues but not usually near the mineralized cementum surface during the 5-day test period (Brudvik & Rygh, 1993b).

Brudvik and Rygh investigated further the resorptive processes beneath the main hyalinized zone (Brudvik & Rygh, 1994a; Brudvik & Rygh, 1994b). They found that the majority of cells involved in the removal of the hyalinized tissues and root resorption were multinucleated and TRAP-positive. The root surface adjacent to the hyalinized tissues underwent necrotic degenerative changes. They found that the cells involved in the removal of the main part of the necrotic periodontal membrane, as well as the damaged root surface tissue, differ from those involved during the initial phase. Twelve Wistar rats were studied and the results indicated that multi-nucleated TRAP-positive giant cells with non-ruffled borders were involved in the removal of necrotic tissues as well as damaged root surface. They hypothesized that after removal of damaged cementum the cells continued cementum resorption. Mono-nucleated giant cells with ruffled borders were never observed near the remnants of necrotic tissue, but were found in the resorption lacunae of root and bone surfaces. Cementum fragments were not found inside these cells and they postulated that removal of cementum tissue occurred extra-cellularly. They also suggested that the multi-nucleated cells are derived from monocytes and macrophages that initially invaded the necrotic hyalinized tissues. These observations have since been supported by further publications (Hellsing & Hammarstrom, 1996; Mavragani et al., 2004).

In summary, Brudvik and Rygh concluded that orthodontic root resorption is a part of the hyaline zone elimination process. There are two stages in the removal of the hyaline zone: (1) Initially mononuclear TRAP-negative cells remove necrotic tissue in the periphery of the hyalinized zone as well as the surface layers of unmineralized cementum and mineralized acellular cementum, (2) After four days multinuclear and mononuclear, TRAP-positive cells remove central parts of the hyalinized zone and continues resorbing the damaged and undamaged mineralized cementum.

There are several existing theories explaining the resorption resistance of the dental tissues, especially cementum. After extensive research in this field, mainly with tooth replantation models, Andreasen, related surface resistance to the innermost cellular layer of the periodontal ligament on the root surface (Andreasen, 1988a). He suggests that this layer supplies the protective mechanism to the root, as well as the potential for repair. The cementoblasts, fibroblasts, osteoblasts, endothelial, and perivascular cells are included in the protective layer. Small areas of cell damage in which surface resorption occurs are fully repaired with new cementum and periodontal ligament fibres from the adjacent vital parts of the periodontal ligament. Larger zones of damage are repaired by alveolar bone and bone marrow derived cells, which leads to ankylosis. However, Andreasen disqualified the role of the peripheral part of the periodontal ligament; Sharpey's fibers, cementum, cementoid, and Mallassez epithelial cells with regards to a possible role in the preventive resorption mechanism

of the periodontal ligament (Andreasen, 1988a). This theory has been supported by Jones and Boyde (1988).

It is documented that the uncalcified mineral tissues, osteoid, precementum, and predentine are resistant to resorption and may initially prevent loss of root tissue (Reitan, 1985). However, continuous pressure will eventually lead to resorption of these areas (Reitan, 1985; Tronstad, 1988). It has also been demonstrated that root resorption occurs even in teeth where deposition of mineralised material was prevented (Wesselink & Beersten, 1988).

It has been found that resorption activity by the cells of the periodontal ligament, as a response to mechanical or chemical stimuli, is characterised by synthesising prostaglandin E with an associated increase in cAMP (Ngan et al., 1988b). This process is regulated by hormones including parathyroid hormone (Ngan et al., 1988a; Takahashi et al., 1989) and calcitonin (Takahashi et al., 1989). There is also regulatory contributions from the neurotransmitter, substance P (Nicolay et al., 1988), vasoactive intestinal peptide (Patrone et al., 1989), and calcitonin gene related peptide (Davidovitch et al., 1990), and cytokines or monokines including interleukin- 1 alpha (Davidovitch et al., 1988; Takahashi et al., 1989), interleukin-1 beta (Lynch et al., 1988; Ngan et al., 1988a), interleukin-2 (Davidovitch et al., 1989), tumour necrosis factor (Davidovitch et al., 1989; Takahashi et al., 1989), and interferon-gamma (Ngan et al., 1990).

If orthodontic forces are reactivated during active root resorption, the process will continue (Reitan, 1974). It is believed that if active orthodontic forces are removed, but passive stress remains applied to the periodontal ligament with a retention appliance, root resorption will continue if necrotic tissue is close to the resorptive site (Brudvik & Rygh, 1994b). It is not certain how long the rest period needs to be to allow time for the repair of root resorption cavities prior to the safe reapplication of orthodontic force.

2.2.7 The Aetiology Of All The Types Of Root Resorption

The factors that may cause pathological external root resorption may be divided into three groups; traumatic, related to infection or related to tooth movement (Ghafari, 1994; Reitan, 1985).

Trauma related root resorption: Examples of trauma include acute acceleration-deceleration injuries, bruxism, occlusal interferences, tooth transplantation or reimplantation, adjacent impacted tooth pressure, pressure from tumours or cysts and local functional problems.

Infection related root resorption has causes that include periapical or periodontal ligament inflammation, metabolic and systemic disturbances.

Tooth movement related root resorption includes physiological tooth movement and orthodontic tooth movement (Brezniak & Wasserstein, 1993a; Ghafari, 1994; Reitan, 1985)

2.2.8 The Aetiology Of Orthodontically Induced Inflammatory Root Resorption (OIIRR)

The aetiology of orthodontically induced inflammatory root resorption is multifactorial. The causative factors may be of biological or mechanical origin.

2.2.8.1 Biologic Factors

Biologic factors include those that are not within the control of the clinician, and are directly related to the patient. Some of these factors may be within the control of the patient. Broadly classified they are of environmental or genetic origin.

2.2.8.1.1 Individual Susceptibility, Genetics And Ethnicity

The incidence of root resorption varies between individuals and within the same person at different times (Rygh, 1977). Becks stated that OIIRR is the result of individual susceptibility to endogenous factors (Becks, 1936; Becks, 1939). Studies since Becks' investigations have been able to elucidate the associated factors.

Harris et al., (1997) demonstrated the genetic contribution to external apical root resorption within and amongst siblings. They studied the crown and root lengths on lateral cephalograms and OPGs of a sample of 103 pairs of siblings, all of whom were treated by the one orthodontist with the same treatment technique. Heritability

estimates were high, averaging 70% for three roots. They concluded that siblings experience similar levels of OIIRR from orthodontic treatment and a prior sibling's outcome is a valuable predictor of another siblings' risk of root resorption.

Sameshima and Sinclair analysed the treatment records of 868 patients and found that Hispanic patients were more susceptible to root resorption than Asians or Caucasians (Sameshima & Sinclair, 2001a).

Al Qawasmi et al., analysed the effect of the interleukin IL-1 genes and external apical root resorption, finding that their samples homozygous for the IL-1B allele 1 had a 5.6 fold risk of external apical root resorption of greater than 2mm, as compared to those who were not homozygous (Al-Qawasmi et al., 2003a; Al-Qawasmi et al., 2003b).

One of the difficulties in assessing the genetic contribution to OIIRR is to separate the input from genetic factors from the contribution made from environmental factors such as orthodontic treatment (Ngan et al., 2004). Ngan et al., (2004) investigated the genetic contribution to orthodontic root resorption by retrospectively assessing the pre- and post-treatment records of 16 monozygotic and 10 dizygotic twins. Each twin pair had the same malocclusion and the same type of appliance treatment with the same clinician. Concordance refers to the presence or absence of an observed phenotype. OPG tooth root measurements were used to obtain quantitative and qualitative estimates of concordance for external apical root resorption. The

concordance estimate for root resorption in monozygotic twins was 44.9% for qualitative measurements and 49.2% for quantitative measurements. The concordance estimate for root resorption in dizygotic twins was 24.7% for qualitative measurements and 28.3% for quantitative measurements. The authors thus confirmed that there is a genetic component to OIIR, however, they advised that a larger sample is required before a model of heritability can be used to determine the components contributing to the variance (Ngan et al., 2004).

2.2.8.1.2 Endocrine Imbalance

Endocrine disorders associated with bone metabolism have been found to be related to root resorption. Three hormones primarily control the metabolism of mineralized tissues; 1,25-Dihydroxycholecalciferol, parathyroid hormone (PTH) and calcitonin (Ganong, 1997). 1,25-Dihydroxycholecalciferol is a steroid hormone formed from vitamin D by successive hydroxylation in the liver and kidneys. Its primary function is to increase calcium absorption in the kidney. PTH is secreted by the parathyroid glands and its main action is to mobilise calcium from bone and increase urinary phosphate excretion. Calcitonin is secreted by the thyroid gland and inhibits bone resorption. All three hormones operate jointly to maintain a constant calcium level in body fluids. A fourth hormone, parathyroid hormone related protein (PTHrP), acts on PTH receptors and is important in skeletal development in utero. Other hormones that may play a role in calcium metabolism are phosphate-regulating hormone,

glucocorticoids, growth hormone, oestrogen and various growth factors (Ganong, 1997).

It is not surprising that disorders of endocrine balance related to calcium metabolism are associated with altered resistance to root resorption. These include hyperparathyroidism (Engstrom et al., 1988; Goultschin et al., 1982), Paget's disease (Smith, 1978), hypophosphataemia (Tangney, 1979), hypothyroidism, hypopituitarism and hyperpituitarism (Becks, 1939; Hemley, 1941).

Goultschin et al, in a review article described a patient with hyperparathyroidism who had internal and external root resorption in most of their teeth (Goultschin et al., 1982).

Smith published a case report of a patient who had Monostotic Paget's disease of the mandible with progressive resorption of teeth over a period of seven years (Smith, 1978). Hypercementosis of tooth roots is common in patients with Paget's disease; however Smith suggested that root resorption may precede hypercementosis or accompany it (Smith, 1978).

2.2.8.1.3 Asthma And Allergies

In a radiographic study using OPGs, McNab et al (1999) demonstrated that asthmatics had a higher incidence of apical root resorption, irrespective of

medications compared to non-asthmatics. They suggested that the inflammatory mediators produced in an asthmatic episode may enter the periodontal ligament and enhance root resorption (McNab et al., 1999).

Davidovitch et al (2000) looked at a sample of 102 orthodontically treated patients who were found radiographically to have excessive OIIRR in one or more teeth and compared them with a pair-matched control group of 102 orthodontic patients with no signs of root resorption (Davidovitch et al., 2000). They found that the patients with asthma and allergies had an increased incidence of OIIRR (Davidovitch et al., 2000).

In a histological study, Owman-Moll and Kurol (2000) assessed the amount of OIIRR after orthodontic tooth movement of maxillary premolars in a group of 50 patients. They divided the patients into two groups according to whether they had a high or low risk for root resorption. They did find an association between allergies and the extent of root resorption; however no statistically significant difference between the two groups was established (Owman-Moll & Kurol, 2000).

2.2.8.1.4 Psychological Stress

In the previously mentioned radiographic study of OIIRR patients and their pair-matched controls by Davidovitch et al., (2000), it was found that patients who experienced psychological stress had a higher incidence of excessive root resorption.

2.2.8.1.5 Alcohol Consumption

The presence of ethanol in the circulation inhibits the hydroxylation of vitamin D3 in the liver, thus hindering calcium homeostasis and resulting in a rise in parathyroid hormone (PTH). PTH in turn enhances the resorption of mineralized tissues including tooth roots. It has thus been suggested that chronic alcohol consumption during orthodontic treatment increases the risk of severe OIIR (Davidovitch, 1996).

2.2.8.1.6 Nutrition

It has been proposed that malnutrition may cause root resorption (Marshall, 1929). Root resorption has been demonstrated in animals deprived of dietary calcium and vitamin D (Becks, 1936; Engstrom et al., 1988).

Engstrom et al (1988); in a study involving rats; deprived their diet of calcium and vitamin D. The test group was found to have hypocalcaemia, increased alkaline phosphatase activity and increased circulating PTH compared to the control group which was fed a normal diet. Orthodontic tooth movement produced greater and more rapid bone resorption and more severe OIIR in the test group. They discovered an increased number of osteoclasts in the periodontal ligament of the test group. It has been suggested that this is due to the increased PTH levels (Midgett et al., 1981).

Midgett et al., (1981) studied the effect of a diet deficient in calcium and phosphorus on tooth movement and bone remodeling in beagle dogs. The test group was found to have osteoporosis with a large loss of trabecular bone, while cortical bone was similar to controls. Study of the parathyroid glands of the test dogs revealed that the dogs had a hyper-parathyroid state.

It has been proposed by other authors that poor nutrition is not a major aetiological factor in OIRR (Goldie & King, 1984; Linge & Linge, 1983). Goldie and King (1984) deprived lactating rats of dietary calcium and phosphorus and compared them with a control group on a normal laboratory diet. Despite a greater amount of tooth movement and loss of bone mass in the dietary deficient group, the OIRR craters were actually smaller.

2.2.8.1.7 Chronological Age

The aging process results in changes to the hard and soft tissues of the dentoalveolus including reduced vascularity, plasticity and width of the periodontal ligament, increased density and reduced vascularity of bone and an increase in thickness of cementum. Reitan proposes that these changes are responsible for the increased incidence of root resorption found in adults (Reitan, 1985). Many studies have found adult patients to have an increased susceptibility to root resorption (Dougherty, 1968; Goldin, 1989; Kennedy et al., 1983; Linge & Linge, 1983; Reitan, 1974; Reitan, 1985; Sameshima & Sinclair, 2001a; Thilander et al., 2000; VonderAhe, 1973). Only

a few studies disagree with the suggestion that the susceptibility to OIIRR increases with age (Massler & Malone, 1952; Massler & Malone, 1954).

2.2.8.1.8 Dental Age

Partially formed roots have been found to develop normally during orthodontic treatment and it has been suggested that teeth with open apices may be more resistant to apical root resorption (Linge & Linge, 1983; Rosenberg, 1972; Rudolph, 1940). Contrary to these findings another group of authors found that teeth with incomplete root formation at the onset of orthodontic treatment did not reach “normal tooth length” (Hendrix et al., 1994). The design of this study has been criticized by others as it relies on OPGs with no adjustment for radiographic projection differences between pre-treatment and post-treatment films and it thus has been proposed that this method is inaccurate (Vlaskalic et al., 1998).

2.2.8.1.9 Gender

Many studies have suggested no correlation between gender and the extent of OIIRR (Goldin, 1989; Harris et al., 1997; Kennedy et al., 1983; Massler & Malone, 1954; McFadden et al., 1989; Sameshima & Sinclair, 2001a). Other research groups have however found that females are more susceptible to OIIRR (Baumrind et al., 1996; Dougherty, 1968; Kinsella, 1971; Newman, 1975). Newman (1975) found a ratio of OIIRR susceptibility of 3.7 to 1 for females to males respectively. Dougherty (1968)

suggested that this finding might be due to differences in root maturity between males and females at the age of tooth movement.

2.2.8.1.10 Presence Of Root Resorption Prior To Treatment

Patients with pre-existing evidence of root resorption have been found to have a greatly increased chance of developing further severe OIIRR with treatment (Harris & Butler, 1992; Massler & Malone, 1954).

2.2.8.1.11 Habits

A number of habits have been reported to result in an increased risk of OIIRR. Finger sucking beyond the age of 7 years has been suggested to be a risk factor (Linge & Linge, 1991). Nail-biting (Odenrick & Brattstrom, 1985), forward tongue pressure and tongue thrust (Linge & Linge, 1991; Newman, 1975) are also proposed to be linked.

2.2.8.1.12 History Of Trauma

A history of traumatic injury to the teeth may increase the risk of developing OIIRR (Andreasen, 1988b; Linge & Linge, 1991).

It has been reported that incisors which have been injured and then subjected to orthodontic movement develop more extensive resorption than either incisors that had been traumatized without orthodontic treatment or incisors that had orthodontic treatment without previous trauma (Brin et al., 2000).

Linge and Linge (1983) found that teeth which had previous trauma had an average loss of root structure after orthodontic movement of 1.07mm compared with a loss of 0.64mm for untraumatized teeth.

Trauma as a risk factor has been refuted by authors who carried out a study of orthodontically treated Class II patients (Brin et al., 2003). The study revealed no statistically significant difference in the incidence of OIIRR in teeth that were traumatized before treatment and those which were not.

2.2.8.1.13 History Of Endodontic Treatment

There are opposing opinions regarding the susceptibility of endodontically treated teeth to root resorption. One group has found a greater incidence of OIIRR in endodontically treated teeth (Wickwire et al., 1974). However, many other authors believe that endodontically treated teeth are more resistant to root resorption due to an increase in dentine hardness and density (Mirabella & Artun, 1995b; Reitan, 1985; Remington et al., 1989; Spurrier et al., 1990; Thilander et al., 2000).

The disagreement may be due to the presence or absence of active inflammation related to residual infection during the orthodontic movement. Orthodontic movement itself creates an inflammatory response that may increase an already existing resorptive process. A successful endodontically treated tooth with healthy periodontal support, in the absence of inflammation should not be more susceptible to resorption than a normal tooth.

2.2.8.1.14 Density And Turnover Of Alveolar Bone

It has been suggested that OIIRR is amplified in dense alveolar bone compared to less dense alveolar bone, especially if there is an increased number of resorptive cells associated with small marrow spaces (Reitan, 1974; Reitan, 1985). The author also proposes that a strong continuous force on low density alveolar bone causes an equivalent amount of OIIRR to that of a mild continuous force on high density alveolar bone (Reitan, 1974; Reitan, 1985).

It has been found that there is increased OIIRR of the upper and lower incisors during Stage II of Begg treatment (Goldson & Henrikson, 1975). This may be explained by the proximity of the apices of these teeth with the labial cortical plate (Goldson & Henrikson, 1975).

An animal study whereby a deficiency in bone density was induced, resulted in reduced OIIRR (Goldie & King, 1984). The rats were fed a calcium deficient diet which led to increased PTH levels and subsequently a loss of bone density.

A more recent animal study was made of bone turnover rate and OIIRR (Verna et al., 2003). The subject group consisted of 52 six-month old Wister rats. The resorption in the lower bone turnover group was higher, suggesting that reduced bone turnover results in a greater risk of OIIRR.

2.2.8.1.15 Abnormal Root Morphology

It has been found that aberrant shaped roots have an increased susceptibility to root resorption (Kjaer, 1995; Levander et al., 1998a; Levander & Malmgren, 1988; Mirabella & Artun, 1995b; Newman, 1975; Sameshima & Sinclair, 2001b).

Sameshima and Sinclair (2001a) compared the amount of OIIRR in normal, blunted, pipette-shaped, pointed, dilacerated and incomplete roots after treatment and found that dilacerated roots had the most resorption, followed by pipette-shaped and pointed roots. Blunted roots were found to have the least resorption. They also suggested that lateral incisors are the most likely to experience OIIRR because they are the most common teeth to have root anomalies (Sameshima & Sinclair, 2001a). However, small amounts of resorption in slender rooted teeth may produce a significantly

greater and more readily identifiable effect compared with the same amount of resorption in a thicker root.

It has been suggested that the mechanism causing the atypical root shape may be linked to its increased risk of OIIRR (Mirabella & Artun, 1995b).

More recent studies suggest that OIIRR may have less correlation with irregular root morphology than was previously thought. One study compared 84 patients with at least one dental anomaly and 84 patients with no abnormalities (Lee et al., 1999). The anomalies included agenesis, small or peg-shaped lateral incisors, dens invaginatis, taurodontism, ectopic eruption and short roots. Root lengths on radiographs before and after treatment were compared. They concluded that patients with dental anomalies were not at increased risk of apical root resorption during orthodontic treatment (Lee et al., 1999). A similar study was conducted concentrating on lateral incisors (Kook et al., 2003). Periapical radiographs of 54 small and 60 peg-shaped lateral incisors from before and after treatment were compared. There was found to be no statistically significant difference in OIIRR susceptibility between peg laterals and normal laterals. There was a statistically significant difference between small and normal lateral incisors, but this was clinically insignificant.

2.2.8.1.16 Type Of Malocclusion

A number of studies have found a relationship between OIIRR and malocclusion (Harris & Butler, 1992; Harris et al., 1997; Linge & Linge, 1983; Linge & Linge, 1991; Sameshima & Sinclair, 2001b). The association may be a consequence of the distance the teeth are moved, for example retraction of upper incisors in the treatment of a class II division I malocclusion, or the direction of tooth movement, such as intrusion and torquing movements, rather than the malocclusion itself. In addition, a more severe malocclusion may take longer to correct and thus certain malocclusions may be associated with increased OIIRR because of protracted treatment duration and thus longer exposure to the resorptive process.

One study demonstrated that patients with an increased ANB angle were correlated with OIIRR (Harris et al., 1997).

Other studies have found that both increased overjet and the distance of root movement have a positive association with the magnitude of OIIRR (Brin et al., 2003; Harris & Butler, 1992; Hendrix et al., 1994; Linge & Linge, 1991).

Brin et al., (2003) suggest that early growth modification treatment that reduces the severity of the overjet may reduce the extent of OIIRR during fixed appliance treatment.

Class III malocclusions with roots touching the cortical plates have been found to have significant OIIRR, and Class III surgical cases demonstrated a 1.6% and 20.8%

reduction in maxillary and mandibular incisor lengths respectively (Kaley & Phillips, 1991).

It has been proposed that orthognathic surgery contributes to OIIRR by altering the blood supply to the periodontal ligament (Ghafari, 1994).

2.2.8.1.17 Specific Tooth Vulnerability To Root Resorption

The teeth most frequently affected by OIIRR in reducing order of severity are the upper lateral incisors, the upper central incisors, lower incisors, distal root of the lower first molars, lower second premolars and upper second premolars (Kook et al., 2003; McFadden et al., 1989; Newman, 1975; Phillips, 1955; Sameshima & Sinclair, 2001b; Sharpe et al., 1987; Sjolien & Zachrisson, 1973).

In a large study of patients from six orthodontic offices by Sameshima and Sinclair (2001b), one of the trends identified was that maxillary teeth are more severely affected than mandibular teeth. The most severely affected teeth in reducing order were the upper laterals, upper centrals, upper canines, lower canines, lower central incisors and lower lateral incisors (Sameshima & Sinclair, 2001b). They suggested that lateral incisors are most susceptible to resorption due to the higher incidence of abnormal root shape. This is in contrast to Mirabella and Arun (1995) who found that only upper central incisors with anomalous roots had increased vulnerability to OIIRR.

2.2.8.1.18 Missing Teeth

One group of authors has found that patients with multiple tooth aplasia (four or more missing teeth) were more prone to OIIRR especially teeth with irregular root morphology and protracted treatment with elastics and rectangular arch wires (Levander et al., 1998b). This finding may be a consequence of the increased distance of movement needed in the treatment of such malocclusions.

2.2.8.2 Mechanical Factors

These are factors that are considered contributory to the resorptive process that are non-biological in origin. They include most aspects of orthodontic treatment that are within the control of the clinician or require patient compliance.

2.2.8.2.1 Duration Of Treatment

Most studies agree that the severity of OIIRR is directly related to the duration of orthodontic treatment (Brezniak & Wasserstein, 1993a; Brezniak & Wasserstein, 1993c; Dougherty, 1968; Goldin, 1989; Kvam, 1972b; Levander & Malmgren, 1988; Linge & Linge, 1983; Linge & Linge, 1991; McFadden et al., 1989; Reitan, 1974; Reitan, 1985; Rudolph, 1940; Sameshima & Sinclair, 2001b; Sharpe et al., 1987; Vlaskalic et al., 1998). Only a limited number of studies disagree with this finding (Phillips, 1955; VonderAhe, 1973).

An SEM study of 40 human premolar teeth which were exposed to 50 cN buccal force and durations varying from 5 to 76 days supported the finding that the amount of root resorption increases with time(Kvam, 1972b).

Another SEM study was conducted involving 300 or 600cN continuous torque to 28 human upper first premolars with durations of 1, 2, 3 and 4 weeks (Casa et al., 2001).

It was found that teeth which have been moved for a greater time period had greater OIIRR in width and depth.

Animal studies in rats (Williams, 1984) and monkeys (Vardimon et al., 1991) have demonstrated increased levels of root resorption with extended treatment protocols.

One large study involved 868 patients from six different specialist practitioners with at least 10 years experience (Sameshima & Sinclair, 2001b). Digitized peri-apical radiographs were measured for a change in root length. From the data, a significance correlation between treatment duration and root resorption of the maxillary central incisors was found ($p < 0.05$).

The amount of root loss during treatment is estimated to be 0.9mm per year according to Goldin (1989).

McFadden et al., (1989) stated that treatment duration is the most significant factor contributing to the extent of root shortening after intrusion.

Another group of authors believe that the total treatment time is more significant than the magnitude of force in the occurrence of OIIRR (Thilander et al., 2000).

This direct relationship between duration and severity of resorption is probably due to the roots being exposed to the resorption mechanism for a longer period of time.

2.2.8.2.2 Distance Of Tooth Movement

Teeth that are moved large distances receive extended exposure to the resorptive process. Thus the severity of OIIRR may be regarded to be positively related to the distance the tooth is moved (Dermaut & De Munck, 1986; Hollender et al., 1980; Phillips, 1955; Sameshima & Sinclair, 2001b; Sharpe et al., 1987; VonderAhe, 1973).

The upper incisors are commonly moved the greatest distance and are thus at the most risk of OIIRR (DeShields, 1969; Goldson & Henrikson, 1975; Hollender et al., 1980; Kennedy et al., 1983; Kinsella, 1971; Phillips, 1955; Sameshima & Sinclair, 2001b; Sharpe et al., 1987; Sjolien & Zachrisson, 1973). Sameshima and Sinclair (2001b) found a mean amount of 1mm more OIIRR than the control group when the root apices of the upper incisors were displaced palatally.

2.2.8.2.3 Magnitude Of Applied Force

It has been proposed that if the force which induces orthodontic movement is greater than the partial pressure of the periodontal capillaries (26gram/cm²) (Schwartz, 1932), periodontal ischaemia will occur (Reitan, 1974) which will lead to root resorption (Brudvik & Rygh, 1993b; Brudvik & Rygh, 1994b; Harry & Sims, 1982; Reitan, 1974). Many animal studies (Dellinger, 1967; King & Fischlschweiger, 1982; Vardimon et al., 1991) and human studies (Casa et al., 2001; Darendeliler et al.,

2004; Faltin et al., 1998; Faltin et al., 2001; Harry & Sims, 1982) have agreed that the force magnitude is directly proportional to the severity of OIIRR.

Harry and Sims (1982) in an SEM study assessed 36 human premolar teeth that had been subjected to 50, 100 and 200g of intrusive force over 14, 35 and 70 days. They found that greater forces increased the stress on the root surface and increased the rate of lacunae development, thus increasing the amount of OIIRR. The longer periods of force application also increased the amount of OIIRR.

Another human study was conducted on 12 upper first premolars that had undergone 50 or 100cN intrusion prior to extraction (Faltin et al., 2001). With transmission electron microscopy, the researchers concluded that there was greater OIIRR in the teeth that had undergone the highest intrusive force.

More recent studies on human upper first premolars involved 25 and 225g buccal force in an SEM study (Chan et al., 2004), and 25g and 225g intrusive force in a micro-CT study (Harris et al., 2005). These volumetric studies also found that increased force levels increased the amount of OIIRR.

There are other studies that disagree with the principle that the force level is correlated with the severity of OIIRR.

A human histological study compared the effects of buccal forces of 50 and 100g using sectional appliances on the premolar teeth of 16 patients (Owman-Moll et al., 1996a; Owman-Moll et al., 1996b). The right premolar served as the experimental tooth and the left premolar as the control. All of the patients had a control tooth with no force; there were no patients with a direct comparison between the two force levels. The treatment periods were either four or seven weeks. The depth and extent of OIIRR was measured histologically. There was great inter-individual variation in the size of the resorptive defects across the different groups and no significant difference in OIIRR could be established between the groups exposed to the different force level groups.

Owman-Moll et al., (1996b) conducted another human histological study on 8 patients in which one premolar received 50g of buccal force and the contralateral premolar received 200g of buccal force. The treatment duration was seven weeks. There was again no major difference in the frequency or severity of OIIRR between the different force levels.

Another human study involved 72 premolars that received 25g to 240g of intrusion, extrusion and tipping movements and was conducted over 10 to 47 days (Reitan, 1974). It was concluded that the amount of OIIRR was poorly correlated with the magnitude of force applied.

2.2.8.2.4 Type Of Tooth Movement With Different Appliances And Treatment Techniques

The type and direction of tooth movement has a considerable role in OIIRR. A given force will have less affect on the periodontal ligament if it is dissipated over a large surface area. The different types of orthodontic tooth movement include tipping, torque, rotation, intrusion, extrusion and bodily translation. It is expected that bodily movement, torque, and tipping have a lower force per unit area and thus cause less necrosis and less OIIRR (Linge & Linge, 1983; Reitan, 1974). Some authors have suggested that there is less root resorption associated with bodily movement compared with tipping due to the differing stress distribution (Reitan, 1964; Reitan, 1985; Thilander et al., 2000). In contrast, intrusive movements produce a greater force per unit area and are likely to cause the most OIIRR (McFadden et al., 1989; Parker & Harris, 1998).

Finite element model analysis was used to investigate the types of orthodontic forces that cause excessive stress at the root apex (Rudolph et al., 2001). The authors found that purely intrusive, extrusive and rotational forces produce stresses concentrated at the apex of the root. Tipping movement concentrates stress at the alveolar crest. Bodily movement distributes stress throughout the PDL (Rudolph et al., 2001).

Parker and Harris (1998) examined the orthodontic treatment records of 110 subjects in a mixed longitudinal retrospective analysis to quantify apical and incisal

movements in the vertical and sagittal planes. Stepwise multivariate linear regression analysis was used to determine which tooth movement is most predictive of OIIRR. The subjects were from three solo orthodontic practices which practiced Tweed Standard Edgewise, Begg and Roth Straight Wire. The patients were all adolescents with similar pre-treatment malocclusions (Class I crowding or bimaxillary protrusion) and had the extraction of four first premolars. The movement of the most protrusive upper central incisor was measured from pre-, mid- and post-treatment lateral cephalograms. There were no statistical differences in the average OIIRR between sexes or among techniques. Measures of tooth movement were highly predictive, explaining up to 90% of the variation in OIIRR. Apical and incisal vertical movements and palatal root torque were the strongest predictors of OIIRR for each regression model. Intrusion and palatal root torque produced the greatest OIIRR.

There are several studies that have assessed the correlation between the different types of orthodontic appliances and the extent of OIIRR.

One radiographic study established that fixed appliances are more detrimental to the roots of upper incisors than removable appliances (Linge & Linge, 1983). Eighty one patients who were treated with removable appliances alone ("activators and spring plates") were compared to 638 fixed appliance patients, and a highly significant difference in the changes in root length was found; 0.14mm and 0.82mm decrease respectively. The maximum root shortening values were 0.39mm and 1.46mm respectively.

Another radiographic study by the same authors (Linge & Linge, 1991) involved a comparison of patients treated with full fixed edgewise appliances and patients treated with activators only. The activator group was found to have no OIIRR. They concluded that open activators, plates with clasps and vertical elastics had a very low correlation with root resorption. The patients treated with fixed appliances, rectangular arch wires and Class II elastics had notable OIIRR.

Other studies have found differences between fixed appliances (Armstrong et al., 2002; Kinsella, 1971; Parker & Harris, 1998)). This may be due to the mechanics specific to the appliances that move the teeth. The Begg technique utilizes “light round wires” and “light elastics” to generate tooth movement, tipping teeth initially then torquing the roots in the third stage of treatment. In contrast, Edgewise appliances move teeth in a bodily manner on rectangular wires.

There is disagreement regarding whether there is a difference in the amount of OIIRR that results from treatment with the Begg and Edgewise techniques. One study found less OIIRR was found in the patients treated with the Begg appliance (Kinsella, 1971). However, another study found no difference between the two techniques (Malmgren et al., 1982).

A recent radiographic study found that the Speed appliance causes more root resorption compared to the Tip-Edge and MBT straight wire technique (Armstrong et al., 2002).

These results are in contrast to another study involving the comparison of pre- and post-treatment periapical radiographs of 63 patients treated with the Speed and Edgewise techniques (Blake et al., 1995). No significant difference in the amount of OIIRR between the two groups was found.

In a previously mentioned study involving 110 adolescent patients, the Tweed Standard Edgewise technique, the Begg Light Wire technique and the Roth Straight Wire technique were compared and no significant difference in the average OIIRR could be found (Parker & Harris, 1998).

Treatment with the Standard Edgewise technique has been radiographically compared to treatment with the Straight Wire Edgewise technique (Mavragani et al., 2000). The Standard Edgewise group was found to have significantly more OIIRR. The authors believed the difference was due to a more efficient force control system in the Straight Wire group.

Root resorption from treatment with 0.016 x 0.022" arch wires has been compared to smaller wires in the 0.018" slot (Linge & Linge, 1983). The authors found significantly more resorption using the larger dimension wires. In contrast, another

study found no difference between arch wire types in the severity of OIIRR (Mirabella & Artun, 1995b).

Sameshima and Sinclair (2001b) revealed no difference in the amount of OIIRR when comparing the 0.018" slot and the 0.022" slot or between steel and titanium arch wires (Sameshima & Sinclair, 2001b).

Sectional mechanics have been compared to continuous arch wire mechanics and no significant difference in the amount of OIIRR was found (Alexander, 1996).

It has been suggested by one group of authors that the use of intermaxillary elastics increases the amount of OIIRR due to the existence of jiggling forces (Linge & Linge, 1983), however another group of authors found no correlation (Sameshima & Sinclair, 2001b).

It has been shown that magnets may stimulate a more physiologic tissue response and decrease the potential for root resorption (Blechman & Smiley, 1978; Kawata, 1987).

Rapid maxillary expansion appliances have been found to cause significant OIIRR of the upper first molars and premolars (Barber & Sims, 1981; Odenrick et al., 1991; Thilander et al., 2000; Vardimon et al., 1991). The suggested reason for this is that the heavy buccal forces compress the premolars and molars against the buccal cortical plate (Thilander et al., 2000). In a monkey study, the regions with the most

OIIRR have been found to be the buccal surfaces, furcation areas, and on the mesio-buccal root of multi-rooted teeth (Vardimon et al., 1991). One study however compared rapid, slow and no maxillary expansion and found no difference between the groups (Sameshima & Sinclair, 2001b).

2.2.8.2.5 Duration Of Force Application

There are conflicting reports as to whether continuous or discontinuous force produces a difference in the amount of OIIRR. A pause in tooth movement is believed by many authors to allow the resorbed cementum to heal and thus many conclude that discontinuous force produces less root resorption (Acar et al., 1999; Dougherty, 1968; Levander et al., 1994; Maltha & Dijkman, 1996; Oppenheim, 1930; Oppenheim, 1942; Reitan, 1964; Weiland, 2003). There are a number of studies with varying durations and frequencies of interruption in the applied forces which have led to varied results.

One SEM study involved 22 human premolar teeth from eight patients aged 15 to 23 years (Acar et al., 1999). One premolar was subjected to a continuous tipping force (24 hours/day) of 100g and the contra-lateral premolar received a discontinuous force (12 hours/day) for a total duration of nine weeks. The force application was via vertical elastics extending from each premolar to a stainless steel utility arch wire. The authors found that the discontinuous force resulted in less OIIRR, and they believed that the pause allows the resorbed cementum to heal (Acar et al., 1999). The

study relied on the cooperation of the subjects in the application of the 12 and 24 hour elastics. This approach may be criticized due to the potential for poor patient compliance. In addition, upper and lower premolars were treated as equivalent teeth, despite the existence of evidence that different teeth have differing susceptibilities to OIIRR.

A histological study involved 16 patients and 32 upper first premolar teeth (Owman-Moll et al., 1995a). The patients were divided into two groups (with 8 patients each) for experimental periods of either 4 or 7 weeks. In the 4 week group, one tooth was subjected to a continuous 50g buccal force from a sectional Sentalloy wire and fixed appliances; this force was reactivated every week to 50g. The contra-lateral premolar received an initial 50g buccal force that was left uncontrolled for 3 weeks, after which the wire was made passive for one week. Both premolars were then extracted and quantitatively assessed for OIIRR. In the 7 week group, one tooth was subjected to a continuous 50g buccal force reactivated every week. The contra-lateral premolar received an initial 50 g buccal force left uncontrolled for 3 weeks, made passive for one week, and reactivated once again to 50g and left uncontrolled for another 3 weeks.

In both groups of patients there was no histological evidence of a difference in the amount of OIIRR between the two types of forces (Owman-Moll et al., 1995a).

Recently, a study involving confocal laser scanning microscopy was conducted to compare “constant versus dissipating forces” on human premolar teeth (Weiland, 2003). There were 84 premolars from 27 patients, and the treatment duration was 12 weeks. The set-up was a split mouth design, where the premolar on one side was activated with a stainless-steel 0.016” wire with a buccal offset of 1mm that was reactivated every 4 weeks. The contra-lateral premolar was moved with a super-elastic 0.016” wire with an initial activation of 4.5mm that was not reactivated. Their results showed that the teeth receiving the super-elastic force moved significantly more, and had greater perimeter, area and volume of OIIRR (140% more) than the teeth with the stainless steel wire. The depth of the resorption cavities between the two force types did not differ significantly (Weiland, 2003).

A study involving 10 young adult beagle dogs was conducted to compare continuous (24 hours/day) to discontinuous (16 hours/day) forces (Maltha & Dijkman, 1996). The forces ranged from 10 to 200 cN and the duration of treatment ranged from 4 to 100 days. Histological and histomorphometric evaluation was conducted to quantify the amount of OIIRR. The discontinuous regime of force application was found to cause significantly less extensive resorption than the continuous force. Due to the large individual differences, no conclusions were made regarding the magnitude of the force or total duration of treatment (Maltha & Dijkman, 1996).

One radiographic study evaluated the effect of a two to three month pause in treatment for patients who were found to have OIIRR after 6 months of fixed

appliance therapy (Levander et al., 1994). Forty patients with initial apical resorption in 62 upper incisors were involved in the study. Twenty of the patients continued active treatment whilst the other 20 underwent a two to three month pause prior to resuming therapy. Standardized radiographs with individual film holders were used to quantify OIIRR. The amount of OIIRR was significantly less in the patients who were treated with the pause (Levander et al., 1994).

2.2.8.2.6 Extraction Versus Non-Extraction Treatment Protocols

There are studies which discuss the amount of OIIRR associated with extraction treatment protocols (McFadden et al., 1989; McNab et al., 2000; Sameshima & Sinclair, 2001b). The approach of categorizing an extraction or non-extraction plan as being associated with OIIRR is overly simplistic. Attention should be made to the distance the teeth are moved. Extractions for severe crowding do not have as much impact on the movement of the maxillary incisors as much as the displacement following extractions for overjet reduction.

In the radiological study by Sameshima and Sinclair (2001b) involving 868 patients from 6 fixed edgewise practices, extractions and the extraction pattern were amongst the variables assessed and related to the severity of OIIRR. The authors found that patients who had 4 first premolars extracted had more resorption than those patients who were treated with a nonextraction protocol. In addition, patients with other types of extractions including 4 second premolars, a mandibular incisor and asymmetric

extractions also had more OIIRR than non-extraction patients. It was also found that cases which only involved extraction of the upper first premolars did not have more resorption than the non-extraction cases. They acknowledged that this contradicts their own conclusions that overjet and horizontal distance of movement of root apices (as measured from lateral cephalograms) are significant contributing factors to OIIRR (Sameshima & Sinclair, 2001b).

An investigation has been made into the association between appliance type and tooth extraction with the prevalence of OIIRR in posterior teeth (McNab et al., 2000). The authors found that non-extraction patients treated with the edgewise appliance had less posterior OIIRR than patients treated with extractions or the Begg appliance.

2.2.9 The Repair Of Root Resorption

The repair of resorption cavities has been recorded 35 to 70 days after force application (Harry & Sims, 1982; Stenvik & Mjor, 1970). It has also been found to occur two weeks after the cessation of orthodontic pressure (Sismanidou & Lindskog, 1995) and during the first week of retention (Owman-Moll et al., 1995b). After five to six weeks of retention, the mending of root resorption seems to slow down and reach a steady rate (Owman-Moll et al., 1995b; Vardimon et al., 1993).

The healing process may only begin when the hyaline tissue has been removed and/or the applied orthodontic pressure is discontinued or reduced to below a certain level (Brudvik & Rygh, 1995a; Brudvik & Rygh, 1995b; Reitan, 1974; Reitan, 1985; Rygh, 1977). According to Schwartz, when the orthodontic force has reduced to below the optimal force of $20\text{-}26\text{g/cm}^2$, root resorption stops (Schwartz, 1932).

The lacunae that extend only into cementum are fully anatomically reorganized. The deep cavities which extend into dentine are repaired by a thin layer of cementum, resulting in an irregular root form (Andreasen, 1988a). After the repair of both the cementum and dentine regions, the resulting periodontal ligament width is usually normal.

Repair occurs following migration of cementoblasts over the resorbed surface, these cells compete for available surfaces and exclude the access of osteoblasts and osteoclasts to the root surface (Jones & Boyde, 1988).

The repair material is principally cellular cementum, which always follows an initial layer of acellular cementum (Barber & Sims, 1981; Bosshardt & Schroeder, 1994; Owman-Moll & Kurol, 1998; Owman-Moll et al., 1995b; Sismanidou & Lindskog, 1995; Vardimon et al., 1993). Sismanidou and Lindskog found that within two weeks of force cessation, the healing process involves a preliminary deposition of acellular cementum, followed in the advanced stages by a slow production of cellular cementum (Sismanidou & Lindskog, 1995).

Research focusing on root resorption repair were conducted on adolescent patients who were treatment planned for the extraction of their maxillary first premolars (Owman-Moll & Kurol, 1998; Owman-Moll et al., 1995b). A buccally directed continuous force of 50g was applied to the teeth and reactivated weekly for six weeks. Following this, the appliances were made passive for 2, 3, 6, and 7 weeks. The subjects were divided into two groups of eight individuals for whom the retention periods were either 2 and 6 weeks (Group I), or 3 and 7 weeks (Group II), implying intra-individual differences of 4 weeks. The percentage of root resorption with varying degrees of repair was reported to be 28% after 1 week (Owman-Moll et al., 1995), 35% at 2 weeks (Owman-Moll and Kurol, 1998), 44% at 3 weeks (Owman-Moll and Kurol, 1998), and 82% after 6 and 7 weeks of retention.

In studies of human teeth, the reparative process appears to commence near the centre, at the bottom of the resorption cavity (Owman-Moll and Kurol, 1998; Barber & Sims, 1981).

The following patterns of repair were described by Owman-Moll et al., 1995:

- **No repair**
- **Partial repair:** has occurred when part of the surface of the resorption cavity is covered with reparative cementum.
- **Functional repair:** has taken place when the total surface of the resorption cavity is covered with reparative cementum without re-establishment of the original root contour.
- **Anatomic repair:** This type of repair has happened when the total surface of the resorption cavity is covered with reparative cementum to such an extent that the original root contour is re-established.

There was a great amount of individual variation; however, the results of this study (Owman-Moll et al., 1995) showed that partial repair was the most frequent type of repair during the first 4 weeks of retention (17-31%) and most commonly seen in the cervical third of the root. Functional repair was the most common healing pattern after 5, 6, 7, and 8 weeks of retention (33-40%) and anatomical repair was most often seen in the apical third. Almost every second resorption cavity showed resorption

surfaces with open dentine tubules after 8 weeks of retention. The healing potentials of the cervical, middle and apical thirds of the root showed no great differences (Owman-Moll et al., 1995).

Some authors have proposed that root resorption and repair with secondary cementum may occur concurrently (Barber & Sims, 1981; Harry & Sims, 1982; Stenvik & Mjor, 1970).

2.2.10 The Diagnosis Of Root Resorption

The most widely used method for assessment of root resorption is via radiographic means. The two-dimensional nature of radiography limits its accuracy. Buccal and lingual root defects are not detectable (Brezniak & Wasserstein, 2002b). Digital reconstruction using computer software may increase the precision of the analysis of root resorption (Heo et al., 2001; Reukers et al., 1998).

CT scanning offers a significant advantage over conventional radiography in the detection and quantification of root resorption; however its high cost and high radiation exposure to the patient limit its use to mainly *in vitro* research.

2.2.11 The Clinical Consequences Of OIIRR

Although the majority of orthodontic patients experience OIIRR, it has not been found to increase their future risk of tooth loss (Parker, 1997; Remington et al., 1989; VonderAhe, 1973). Remington et al., (1989) assessed 100 cases of OIIRR and the worst outcome was hypermobility which happened in only two of the cases. VonderAhe (1973) looked at 57 patients who had suffered from mild, moderate and severe amounts of OIIRR, an average of 6.5 years post-retention and found no cases of hypermobility or other detrimental consequences.

In a review article by Vlaskalic et al., (1998) six references were found from between the years 1914 and 1997 that discussed cases of apical root resorption that caused a problem to the patient and the clinician (Chadwick & Carter, 1996; Crane, 1926; Langford & Sims, 1981; Lussier, 1936; Lyndon Carman, 1936; Miller, 1930). There were no reports found with tooth loss from severe apical root resorption after orthodontic treatment unless there was some other form of trauma to the tooth/teeth.

Another study involved a long-term evaluation of upper incisors with severe apical resorption 5 to 15 years following orthodontic treatment (Levander & Malmgren, 2000). A significant correlation was found between tooth mobility, total root length and intra-alveolar root length. They found that there is a significant risk of tooth mobility if an upper incisor has OIIRR resulting in 9mm root length or less. Thus

they recommend regular follow-up assessments of teeth with severe OIRR (Levander & Malmgren, 2000).

A reduction in root length due to apical resorption has been described as less detrimental than an equivalent loss of periodontal attachment at the alveolar crest especially in cases (3mm or less) of early root resorption (Lupi et al., 1996). Computer graphic analysis of the area of periodontal attachment following various amounts of apical root resorption has quantified this phenomenon (Kalkwarf et al., 1986). A central incisor with 1mm of apical loss was determined to be equivalent to a central incisor of the same dimensions with 5% periodontal attachment loss. Similarly, an incisor with 5mm of apical resorption is analogous to an incisor with 25% cervical attachment loss.

Vlaskalic et al., (1998) warns that with the increasing number of adult orthodontic patients, the combined long-term effects of apical root resorption and alveolar bone loss may produce more negative sequelae than has been revealed the studies to date.

2.2.12 The Prevention And Management Of OIIRR

A number of approaches have been suggested in the literature to minimize OIIRR and were summarized by Vlaskalic et al., (1998). The recommendations included short treatment duration (Levander & Malmgren, 1988; Stenvik & Mjor, 1970), the use of light intermittent forces (Harry & Sims, 1982; Reitan, 1974; Rudolph, 1940; Rygh, 1977; Stenvik & Mjor, 1970), habit control (Newman, 1975; Odenrick & Brattstrom, 1985) and a thorough assessment of familial tendency and medical history (Jacobson, 1952; McFadden et al., 1989; Newman, 1975).

Vlaskalic et al., (1998) also suggest that the treatment of moderate to severe malocclusions be commenced when most of the incisors have open apices, which is before the age of 9 years. They recommend this strategy as incomplete root formation has been found to be significantly associated with a lower severity of OIIRR (Linge & Linge, 1983; Rosenberg, 1972; Rudolph, 1940).

The avoidance of intermaxillary elastics which thus reduces jiggling forces has been suggested by Linge and Linge (1991). The limitation of tooth movements that are associated with a high risk of OIIRR (especially intrusion and torque) has been proposed by Parker and Harris (1988).

It is strongly suggested that after 6 months of active orthodontic treatment, periapical radiographs be taken and when OIIRR is diagnosed, a two to three month pause in

treatment with passive arch wires is implemented (Levander et al., 1998a; Levander & Malmgren, 2000; Levander et al., 1994). It has also been recommended that where OIIRR is detected, an additional radiograph be taken 3 months later (Ghafari, 1994). Three-monthly radiographic review of blunt and pipette-shaped apices has been proposed by Levander et al., (1998a).

Where severe resorption is found, the treatment goals should be revised with the patient and a compromised treatment plan may need to be agreed upon (Brezniak & Wasserstein, 2002b).

It is mandatory to take final radiographs at the time of removal of fixed appliances (Brezniak & Wasserstein, 2002b). In the case of teeth with severe OIIRR, follow-up radiographs are recommended until additional root loss is no longer detected (Levander & Malmgren, 2000).

It has been recommended that retention with fixed attachments be applied with caution as occlusal trauma to the fixed teeth may lead to extreme resorption (Roberts, 2000).

2.3 X-RAY MICRO-TOMOGRAPHY

2.3.1 History And Development

The phenomenon known as X-rays were first created and described by Wilhelm Conrad Roentgen. He reported his finding to the Wurzburg Physical-Medical Society on 28 December 1895. The name X-rays was used by Roentgen due to the unknown nature of his discovery (Foundation, 2004).

Irradiation makes it possible to non-invasively see inside objects, both living and non-living. The limitation of conventional radiography is that it produces a two-dimensional projection of the three-dimensional subject. Attempts have been made to reproduce three-dimensional structures from a two-dimensional film, namely laminography or focal plane tomography (Webb, 1990). This involves the translation of the object/subject together with the detection medium in such a way that only one narrow slice parallel to the translation plane is in focus. The contrast from features outside the slice of interest is blurred, reducing its appearance from the image. The attainment of sharp images of the slices is challenging due to the thickness of each slice and the superimposed smearing of the images outside the region of interest (Webb, 1990).

Digital computers have made possible an approach superior to laminography; computed tomography. Cormack, 1963 was the first to demonstrate the ability of x-

rays to produce a projection of a cross-section of an object. In 1973, Hounsfield developed a commercially available computed tomography system for medical imaging (Hounsfield, 1973).

Tomography produces a two-dimensional map of x-ray absorption in a slice of the subject, thus there is no compression of the three-dimensional data into a two-dimensional plane. A series of x-ray projections is made through the slice at various angles around an axis perpendicular to the slice. Digital computing allows the series of projections or two-dimensional absorption maps to be combined into the three-dimensional map (Davis & Wong, 1996).

There are limitations to the use of this technology for patient applications; the doses of x-rays must be kept to a minimum and the duration must be reduced as involuntary movement by the subject will cause image distortion (Stock, 1999b). These constraints are not applicable to the study of inanimate objects, thus longer data collection times and greater x-ray intensities may be used to improve image quality.

There are four generations of computed tomography scanners. The first generation is known as the pencil beam system. It has the simplest arrangement consisting of the x-ray source, a pin-hole collimator and a single detector, as designed by Hounsfield (Hounsfield, 1973). The second generation scanner uses a parallel beam of x-rays and the third generation uses a flat fan distribution of x-rays. The fourth generation of computed tomography scanners uses a cone beam geometry of x-rays, which is a

three- dimensional analogue of the two-dimensional fan beam geometry (Feldkamp et al., 1984). This design is ideal for volumetric computed tomography (Stock, 1999b).

Advances in computed tomography have made possible the analysis of small structures at high resolution; that is computed X-ray micro-tomography (XMT). The demand for improving area detectors for consumer electronics in the 1980s prompted this innovation (Stock, 1999b).

In 1982, Elliot and Dover developed the first XMT machine and produced an image of hard tissue specimens with a resolution of 12 micrometers.

Medical computed tomography scanners are able to achieve a resolution of a fraction of a millimeter. However, even with technological advances in detector design, it is unlikely the resolution can be improved due to X-ray dosage limitations. To improve the resolution by a factor of two, the exposure must be increased by a factor of 16. A ten thousand-fold increase in exposure is required for only a ten-fold improvement in resolution (Davis & Wong, 1996).

The resolution of XMT images is in the order of micrometers (μm), approaching that of optical microscopy.

Two-dimensional digital image dimensions are measured in units of pixels. A pixel is a two-dimensional representation of the smallest unit of colour value within an

image. This colour value may also be a shade of grey. Imaging software for computed tomography usually assigns the dimensions of a pixel to the x and y axis, and it is able to represent a given area. The number of pixels per surface area may be used to describe the resolution of the image. The increasing the number of pixels per unit area improves image quality and increases resolution (Stock, 1999b).

In three-dimensional imaging the unit voxel is used. A voxel is a three-dimensional modification of a pixel with the added dimension of depth. Thus a voxel has a volume and its dimensions have an x, y and z axis (Stock, 1999b).

In addition to the smaller scale, XMT systems have another significant characteristic that is different from medical computed tomography scanners; instead of the X-ray source moving around the subject, the specimen rotates whilst the X-ray source and detector are stationary.

2.3.2 The SkyScan 1172 desktop X-ray micro-tomograph

The SkyScan 1172 X-ray micro-tomograph (SkyScan, Aartselaar, Belgium) is a compact desktop system for microscopy and micro-tomography. Its components include an X-ray shadow microscopic system and a computer with tomographic reconstruction software. Two-dimensional X-ray shadow projections (or “slices”) of the sample are able to be reconstructed into a three-dimensional representation of the sample including its inner structure. The SkyScan is a fifth generation scanner; it has a cone beam X-ray source with a spatial resolution of down to one micrometres. The recommended sample size has a diameter of 1.5 cm and a height of 3 cm. The sample is positioned on a rotating platform, which is programmed to revolve over either 180 degrees if the object contains no highly radio-opaque structures or 360 degrees if it does. Human teeth usually only require a 180 degree rotation. The distance of the platform from the X-ray source determines its the magnification. The X-ray detector consists of a high resolution charged coupled device with a resolution of 1024 x 1024 pixels. The images received are stored as 16 bit Tagged Image File Format (TIFF) picture files with a resolution of 1024 x 1024 pixels. After image acquisition is completed, soft-ware for axial slice-by-slice reconstruction uses the Feldkamp cone-beam algorithm (Cone beam reconstruction 2.13, SkyScan-1072, Belgium) (Feldkamp et al., 1984). The resultant axial two-dimensional images are generated as 1024 x 1024 pixel bitmap (BMP) images having an 8 bit gray-scale dynamic range. The software package, VG StudioMax version 1.2 (Volume Graphics, GmbH,

Heidelberg, Germany) is used to collate the axial two-dimensional slices to form a three-dimensional reconstruction of the images.

In the case of this project, the scanned samples are human teeth. Defects on the cementum surface are easily visualized, including root resorption craters.

2.3.3 X-Ray Micro-Tomography Of Calcified Tissues

The applications of XMT systems are numerous and include fatigue analysis, performance prediction of materials, mineral analysis, and the study of calcified tissues including bone and teeth (Mercer & Anderson, 1996).

Contemporary technology has mostly limited the use of XMT to inanimate and in vitro specimens. However, one in vivo study has been conducted to assess the changes in bone associated with ovariectomy in rats (Kinney et al., 1995) and another in vivo study was performed on living snails (Postnov et al., 2002).

There have been various XMT studies of the mineral concentration of enamel and dentine. One study quantitatively determined the amount of mineral loss from human enamel rods after acid demineralization and how much mineral was regained after remineralisation (Gao et al., 1993). The deciduous incisors of low birth weight children were scanned by XMT to seek abnormalities in the mineral concentration which may be related to developmental defects (Fearne et al., 1994). The enamel mineral concentration distribution of deciduous human molars has also been studied (Wong et al., 2004). An XMT study of the mineral concentration of carious human dentine was of high enough resolution to detect calcified and enlarged tubule spaces in the lesion. The remineralised regions had a very high mineral content suggesting a loss of organic matter (Kinney et al., 1994). A study of rat lower incisors was performed with sequential XMT slices to measure differences in enamel mineral

concentrations progressing from the apex to the incisal edge (Wong et al., 2000). A 500-year old human tooth has also been studied with XMT, investigating features including attrition, cervical root caries, sclerotic dentine and calculus (McErlain et al., 2004).

XMT has been utilized to study the anatomy of root canals (Peters et al., 2000). Some of the studies have involved extracted human teeth which were scanned before and after endodontic treatment and have determined the area and volume changes related to instrumentation and obturation (Dowker et al., 1997; Nielsen et al., 1995). The resultant canal anatomy has also been compared following the use of different instrumentation techniques (Peters et al., 2001a; Peters et al., 2001b).

The effect of lasers on enamel has been studied with XMT technology. One study assessed the effect of the continuous wave carbon-dioxide laser. The changes in mineral density and cracking induced in enamel when lasers are used to cut enamel were investigated (Mercer & Anderson, 1996). The use of a laser and phosphoric acid to etch enamel was compared with laser-only and acid-only etching. The depth of etch and amount of enamel subsurface damage were evaluated for the different etch methods. It was found that laser and acid conditioning resulted in an increased etching depth, but did not induce significant damage in the enamel subsurface (Groth et al., 2001). The XMT has also been used to quantify the progression of growth of enamel and dentine craters that form after sequential application of the Er:YAG laser (Mercer et al., 2003).

There are a number of recent XMT studies involving bone. Comparisons have been made of biopsies from normal and synostosed human coronal sutures (Sherick et al., 2000). Assessments have also been made of normal and osteoarthritic bone structures in knee specimens from human cadavers (Patel et al., 2003). One study has involved finite element analyses of human trabecular bone architecture based on XMT images to obtain information about bone mechanical characteristics (Ulrich et al., 1998). A comparison has been made of different bone graft approaches in rabbit mandibles. It was found that intramembranous bone grafts integrate better than endochondral bone grafts in three-dimensions when they are grafted into membranous bony defects in the mandibles (Lu & Rabie, 2003). One group of authors have described the advantages of synchrotron radiation microtomography in quantifying the degree of mineralization of bone in three dimensions involving human iliac crest bone biopsy samples (Nuzzo et al., 2002). The process of tissue engineered bone growth into polymer scaffolds has been studied with XMT technology at a resolution of 2 micrometres (Jones et al., 2004). Bone structural changes caused by periapical pulpal infections in rats have been analysed (Balto et al., 2000). A study involving rats during a postnatal acceleratory growth period was used to evaluate changes in the calcified tissue of the mandibular condyle from altered function. A maxillary occlusal splint was designed to shift the mandible laterally during closure. The authors found that compared to controls, the experimental animals' mandible and the condyle had a modified shape and size, including alterations in the trabecular bone of the condyle

(Nakano et al., 2004). The process of bone regeneration following amputation of the forelimbs of newts has been assessed via XMT (Stock et al., 2003a).

The micro-structure of bone around retrieved titanium micro-implants from humans has been investigated (Sennerby et al., 2001). Another study to assess the osseointegration of a dental implant in a rabbit tibia has compared the quality of XMT, synchrotron radiation x-ray micro-imaging and conventional dental radiography (Jung et al., 2003).

Sea urchin teeth have been studied with XMT (Stock et al., 2002; Stock et al., 2003b) and so have sea urchin ossicles (Stock et al., 2003c).

There are a limited number of studies in the dental literature investigating root resorption using XMT technology. One study utilized X-ray microfocus-tomographical scanning to assess a case of cervical external root resorption in human teeth (Bergmans et al., 2002). Two studies have been conducted involving the assessment of OIIRR via XMT. A comparison was made of no force (control), light and heavy forces for the intrusion of human premolars that were treatment planned for extraction. It was found that the volume of resorption craters in the light and heavy force groups were two and four times greater than the control group respectively (Harris et al., 2004). Another study which involved rats was undertaken to investigate if fluoride has a beneficial effect in reducing the incidence of OIIRR. It

was concluded that fluoride on average does reduce the size of resorption craters, but the effect was variable and found not to be statistically significant (Foo et al., 2004).

There have been no studies published in the orthodontic literature involving the use of XMT technology to volumetrically quantify OIIRR from intermittent and continuous forces.

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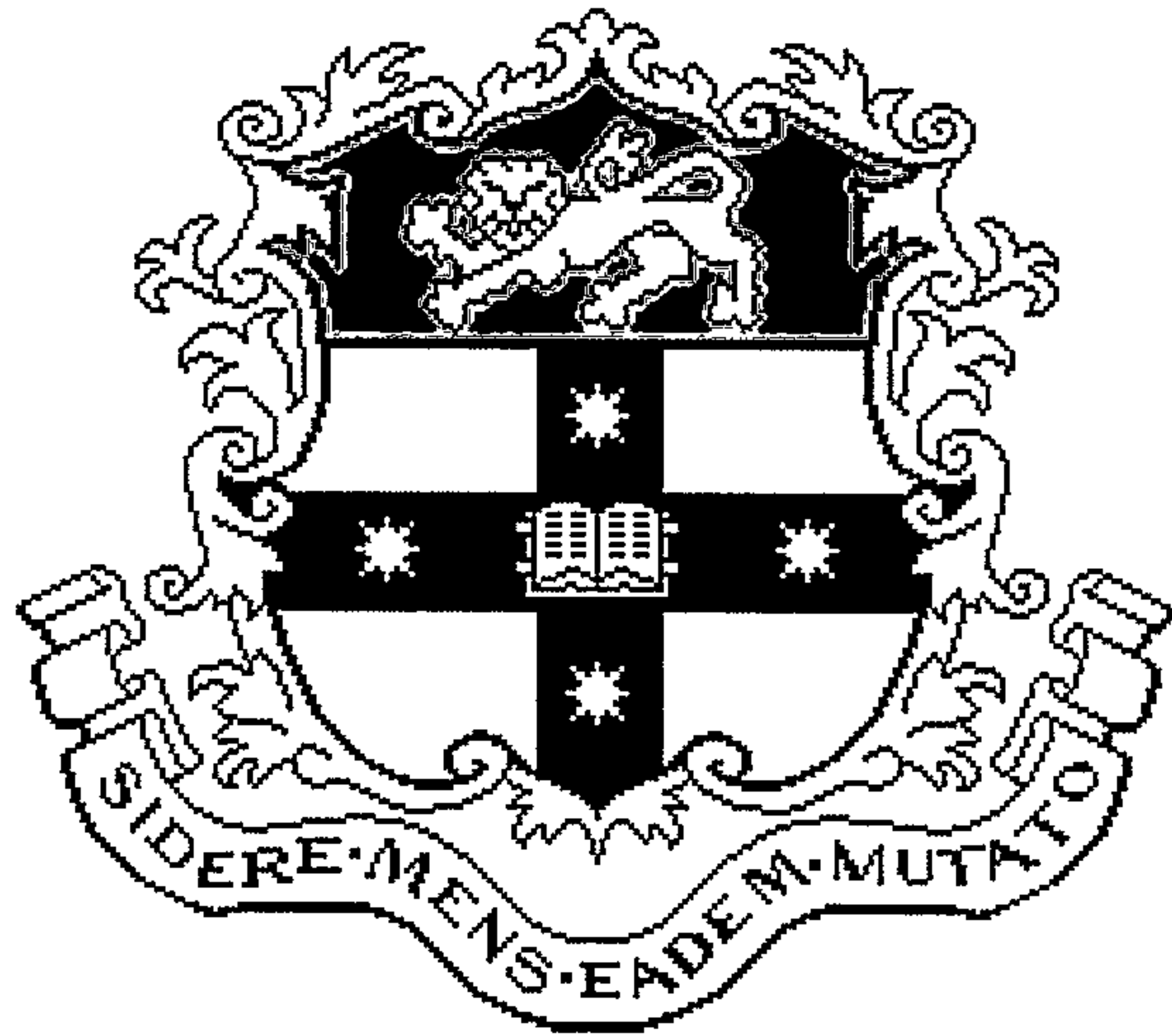
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4. MANUSCRIPT



PROPERTIES OF ROOT CEMENTUM: PART 11. CONTINUOUS VERSUS INTERMITTENT CONTROLLED ORTHODONTIC FORCES ON ROOT RESORPTION-A MICRO-CT STUDY.

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Properties of Root Cementum: Part 11. Continuous versus intermittent controlled orthodontic forces on root resorption-a Micro-CT study.

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4.1 ABSTRACT

Aims: Ambiguity still exists as to whether continuous or intermittent forces produce more root resorption. This prospective randomized clinical trial was designed to compare the root resorption generated by these two force patterns.

Method: The sample consisted of 16 upper first premolar teeth from 8 patients who required the bilateral removal of these teeth as part of their planned orthodontic treatment. In each subject, a fixed experimental appliance was placed on the maxillary teeth on both sides, allowing a buccally directed force. The force was generated by a segmental wire made from β -titanium molybdenum alloy (TMA®). The first premolar on one side received a buccally directed continuous force and the contralateral premolar received intermittent force. The force magnitude for both sides was 225cN. After 14 days initial activation, an operator controlled the intermittent force with three days rest followed by four days activation. At the completion of the experimental period of 8 weeks, the teeth were extracted under strict protocol to avoid root surface damage and analysed using a Micro-CT scan system (SkyScan-1172, Belgium) and specially designed software for direct volumetric measurements (CHULL2D).

Results: It was found that;(1) Intermittent force produced less root resorption than continuous force ($p<0.05$). (2)Analysis by position showed buccal-cervical region to have significantly higher amounts of root resorption than the other positions ($p<0.001$), corresponding to a region of compression generated by a tipping.

Conclusion: Compared to continuous force, intermittent orthodontic activation may be safe to avoid significant root resorption. This regimen of force however, may compromise the efficiency of tooth movement.

Key words: Root resorption, continuous orthodontic forces, intermittent orthodontic forces, X-ray micro tomography (XMT).

4.2 INTRODUCTION

External surface root resorption may be defined as the active removal of mineralised and non-mineralised cementum and dentine (Brudvik & Rygh, 1993a). The factors that may cause pathological external root resorption can be divided into three groups; traumatic, infection related and tooth movement related (Ghafari, 1994; Reitan, 1985). Although the outcome of the different root resorptive processes is similar, orthodontic root resorption is distinct from the other types of root resorption with the term orthodontically induced inflammatory root resorption (OIIRR) having been suggested (Brezniak & Wasserstein, 2002a).

Extensive OIIRR becomes irreversible when it extends beyond the cementum layer into dentine (Brezniak & Wasserstein, 1993b) and may compromise an otherwise successful orthodontic outcome. It is thus important that more knowledge be sought regarding the mechanism, risk factors and preventive factors involved in the root resorptive process.

There are studies in the literature investigating the relationship between interrupted or discontinuous forces compared to continuous forces and OIIRR. A pause in tooth movement is believed by many authors to allow the resorbed cementum to heal and thus many conclude that discontinuous force causes less root resorption (Acar et al., 1999; Dougherty, 1968; Levander et al., 1994; Maltha & Dijkman, 1996; Oppenheim, 1930; Oppenheim, 1942; Reitan, 1964; Weiland, 2003). There are a number of

studies with varying durations and frequencies of interruption in the applied forces which have led to varied results. One Scanning Electron Microscopy (SEM) study involved human premolar teeth in a split-mouth set up (Acar et al., 1999). The authors found that a discontinuous force of 100 cN, 12 hours per day resulted in less OIIRR than the same force applied 24 hours per day. A study involving young adult beagle dogs was conducted to compare continuous (24 hours/day) to discontinuous (16 hours/day) forces (Maltha & Dijkman, 1996). Although there was great variation in the force level (10 to 200 cN) and the treatment duration (4 to 100 days) in that study, histological and histomorphometric evaluation revealed that the discontinuous regime of force application caused significantly less resorption than the continuous force. Another histological study (Owman-Moll et al., 1995a) involving human premolar teeth where one force was not reactivated over three weeks, whilst the other “constant force” was reactivated every week over three week. After an additional week of “recovery”, it was found to have no histological evidence of a significant difference in the amount of OIIRR.

Excessive forces generated from both removable and fixed appliances can provoke OIIRR. It is well accepted that the force pattern for removable appliances is intermittent and is in distinct contrast to that of fixed appliances where continuous force is exerted. One radiographic study established that fixed appliances are more detrimental to the roots of upper incisors than “activators and spring plate” removable appliances (Linge & Linge, 1983). Another radiographic study by the same authors (Linge & Linge, 1991) involved a comparison of patients treated with full fixed

edgewise appliances with Class II elastics and rectangular wires and patients treated with activators, plates with clasps and vertical elastics. The patients treated with fixed appliances had notable OIIRR whilst the latter group of patients was found to have no OIIRR.

Until recently, the detection of OIIRR has mainly been achieved through two-dimensional measurement techniques such as radiographs (Ketcham, 1927; Ketcham, 1929), light microscopy (Reitan, 1974) and SEM (Jones & Boyde, 1972; Kvam, 1972a; Kvam, 1972b). Whilst two-dimensional radiography remains the most conservative diagnostic tool for the clinical detection of root resorption in patients, three-dimensional techniques such as stereoimaging SEM measurements (Chan & Darendeliler, 2005; Chan & Darendeliler, 2004; Chan et al., 2004) and X-ray microtomography (Micro-CT) (Foo et al., 2005; Harris et al., 2005) may allow more accurate and reliable measurements for researchers. However, its high cost and high radiation exposure to the patient limit its clinical use (Ngan et al., 2003).

The aims of this study were to investigate quantitatively, via Micro-CT, the amount of OIIRR induced by intermittent and continuous forces on human premolar teeth and to identify the surfaces where root resorption is more prevalent after controlled orthodontic buccal movement.

This study is a sequel of the series of studies investigating the physical properties of root cementum and root resorption developed at the University of Sydney, Australia.

4.3 MATERIALS AND METHODS

4.3.1 Clinical Model and Force Loading

Sixteen maxillary first premolars were collected bilaterally from 8 patients who required extractions as part of their orthodontic treatment (Ethical approval – Project 5/98 of Human Ethics Review Committee - CSHAS). The patients selected (2 males and 6 females, mean age of 16.5 years (range 13.4 – 18.6 years) were ready to start comprehensive orthodontic treatment. Due to the differences in bone density and root anatomy between the maxilla and mandible, and in order to allow comparison with previous studies, only maxillary upper premolars were used for this study.

Patients were selected following strict criteria described previously (Malek et al., 2001b) and completed a written informed consent. The subjects were then given a heavy continuous orthodontic force of approximately 225cN on one side and a heavy intermittent orthodontic force of the same magnitude on the contra-lateral side. The heavy continuous force and heavy intermittent force were randomly assigned to either the right or left premolars to eliminate any allocation bias. The forces were designed to facilitate a buccal tipping tooth movement.

After taking initial study models and digital photographs, each subject had the experimental appliances placed. The experimental appliance consisted of 0.022”

SPEEDTM brackets (Strite Industries, Canada) bonded to the buccal surfaces of the maxillary first molars and the buccal surface of the maxillary first premolars on working models. They were then transferred to the patient using an indirect bonding method with light cured adhesive (Transbond, 3M UnitekTM, USA). Occlusal stops (Transbond, 3M UnitekTM, USA) were placed on the occlusal surface of mandibular first molars to avoid occlusal interferences, allowing free buccal tipping of the first premolar teeth and helping to minimize spring deformation (Srivicharnkul et al., 2005) (Figure 1).

A 225 cN buccally directed force was applied to the maxillary first premolars by a β -titanium molybdenum alloy (TMA) 0.017"x0.025" (3M UnitekTM, USA) sectional wire attached to the bracket on the first molars. The wire was activated by bending buccally in the transverse plane. The force magnitude was measured to the nearest 5 cN with a strain gauge (Dentaurum, Germany).

After the initial activation, both sides were activated to 225cN force and an interval of 14 days was set to allow for the lag phase associated with tooth movement. The subjects then were recalled and commenced the intermittent phase of force loading. At this visit, the segmental wire on the intermittent side was removed and the subject released. The subject returned 3 days later to have the wire re-activated to 225 cN force. The wire on the contra-lateral side was also measured for any force decay and adjusted as necessary to maintain 225 cN force. The amount of force decay was noted for further analysis. After 4 days of further activation, the wire was again removed on

the intermittent side and the above regime was repeated another 5 times. The total duration of the study was 8 weeks (56 days) and each patient was seen a total of 15 times, including the initial consultation to ascertain suitability.

The maxillary first premolars were then extracted by Specialist Paediatric Dentists at the Sydney Dental Hospital with specific instructions outlined in a previous study (Chan et al., 2004) to avoid surgical trauma to the root cementum. Immediately after extraction, the teeth were stored in individually marked containers with Milli-Q® (deionised water) which has been established as a suitable medium for storage (Malek et al., 2003). Removal of periodontal ligament and tooth disinfection were conducted using a previously described method (Harris et al., 2005) where the teeth were subjected to an ultrasonic bath for 10 minutes, followed by disinfection in 70% alcohol for 30 minutes and then stored in Milli Q®. The teeth were bench dried prior to the imaging process.

4.3.2 Examination Of Root Resorption Via Micro-CT

Micro-CT is a variant of a medical computed tomography scan system that allows imaging of the interior microstructure of materials to be obtained non-destructively and with high spatial resolution (Stock, 1999a). The software enables the reconstruction of the complete internal microstructure of the teeth and it is able to reproduce fully three-dimensional data sets with isotropic sample spacing down to approximately 1 μm .

In this study, the sample quantification by Micro-CT was carried out following the same methodology as described in a previous study (Harris et al., 2005), using the updated SkyScan-1172 X-ray desk-top microtomographer and soft-ware (Sky Scan-1172, SkyScan, Aartselaar, Belgium).

4.3.2.1 Imaging Acquisition

Only one tooth was scanned at a time. During cone beam acquisition, the tooth rotated over 180 degrees and at each position an X-ray absorption radiograph (shadow image) was acquired. All teeth were scanned with a magnification equivalent to sixteen times (17.08 μm pixel size) using a rotation step of 0.45° and exposure time of 1.904 seconds. A total of 420 shadow images were acquired for each tooth during this first step and saved as 16 bit TIFF (Tagged Image File Format) files.

After acquisition was completed, axial slice-by-slice reconstruction was undertaken using a specific software implementation of the Feldkamp cone-beam algorithm (Feldkamp, 1984) (Cone beam reconstruction 1.4.2 – Skyscan –1172, Belgium).

The 16-bit TIFF shadow images generated a raw reconstructed cross-section data by using the reconstruction algorithm. The individual axial slices were generated as

1024x1024 pixel bitmap (BMP) images having an 8-bit gray-scale dynamic range. The gray-values in each dataset were calibrated so that the 8-bit range fully mapped the variation between the pixels with maximum X-ray attenuation (i.e. the most opaque) and those with minimum X-ray attenuation (i.e. transparent). A total of one thousand two-dimensional axial images for each tooth were generated.

4.3.2.2 Three-Dimensional Image Visualization

The three-dimensional reconstruction of the tooth images was carried out with VG Studio Max. 1.2 software (Volume Graphics GmbH, Germany), which allowed visualization of all aspects of the scanned tooth (Figure 2). The buccal and lingual surfaces of the teeth were analysed, each surface being further divided into thirds (cervical, middle and apical). Each root resorption crater was identified, its position on the tooth recorded and its coordinates noted. The craters were isolated and saved as separate files of BMP image stacks.

4.3.2.3 Volumetric Measurements Of The Root Resorption Craters

The volumetric measurement was obtained using convex hull software (CHULL2D) that was developed by the Electron Microscope Unit at the University of Sydney. Each crater was measured individually from its BMP image stack and then, the sum for the root resorption volume for each tooth and for each surface was calculated.

A minor limitation associated with the volume estimation software used in this study relates to the way in which the craters are closed by the convex hull algorithm. In general a convex hull creates a surface closure that is a local minimum in terms of its surface area. This effectively creates a flat closure that approximates the original tooth surface to a greater or lesser extent depending on the curvature of the tooth surface at the site of the crater. Where tooth surface is convex, a flat closure will be more likely to under estimate the crater volume. The converse is also true in that the software will over estimate the volume in areas of concavity. This small error is mitigated however by the fact that this method of crater volume measurement is based on a direct imaging of the tooth as a three dimensional object. Hence, the error in volume estimate was considered to be negligible.

4.3.3 Statistical Analysis

Univariate Analysis of Variance (ANOVA) was performed on the raw root resorption data utilizing the programme Statistical Package for Social Sciences (SPSS for Windows, version 12, SPSS Inc, Chicago III). Root resorption crater volumes were summed to obtain totals for each tooth as a whole, for each surface (buccal, lingual), vertical thirds (coronal, medial, apical) and for each position (combination of surface and vertical thirds). The volumes of the resorption cavities were transformed into cuberoot volume readings, a methodology used in previous three-dimensional volume root resorption studies (Chan et al., 2004; Foo et al., 2005; Harris et al., 2005). Thus the unit of measurement was $\sqrt[3]{}$ of voxels, which was pixels and may be converted to

$^3\sqrt{\text{mm}^3}$, or mm. Boxplots (including clustered boxplots) were used to provide a visual summary of the data.

Analyses of variance models were constructed for the various (cuberoor) volumes, with force and surface, vertical thirds or position as fixed factors and subjects as a random factor. Where a factor was significant and had more than two levels (e.g. position), mean values were compared using a Bonferroni adjustment for multiple comparisons.

4.4 RESULTS

The factors used in the first ANOVA analysis were subject (random factors) and force (fixed factors) which included continuous and intermittent forces (Table 1). It was found that force was significant ($p < 0.05$) but the subjects were not, with the mean cuberoot total volume of intermittent force being 47.7 pixels and 57.6 pixels for continuous force (Table 2). This is also demonstrated by the boxplots in Figure 3.

The factors used in the second ANOVA analysis were subject (random factor) with fixed factors of force and position. The root surface was divided into regions according to the location of the resorption. There were three vertical thirds; apical (A), middle (M) and cervical (C) and two surfaces; buccal (B) and lingual (L), giving a total of six positions.

The mean cuberoot volumes of each position are displayed in Table 3 and Figure 4, showing at least a twofold greater amount of root resorption in the buccal-cervical (BC) position than any other position. Analysis by position also showed buccal-cervical position to have significantly higher amounts of root resorption than the other positions ($p < 0.001$), with no other significant differences (Table 4).

4.5 DISCUSSION

It has been proposed that if the force which induces orthodontic movement is greater than the partial pressure of the periodontal capillaries (26g/cm^2), periodontal ischaemia will occur (Reitan, 1974) which will lead to root resorption (Brudvik & Rygh, 1993b; Brudvik & Rygh, 1994b; Harry & Sims, 1982; Reitan, 1974). It has also been stated that when pressure decreases to below this threshold, root resorption ceases (Schwartz, 1932). Many animal studies (Dellinger, 1967; King & Fischlschweiger, 1982; Vardimon et al., 1991) and human studies (Casa et al., 2001; Darendeliler et al., 2004; Faltin et al., 1998; Faltin et al., 2001; Harris et al., 2005; Harry & Sims, 1982) have agreed that the force magnitude is directly correlated with the severity of OIRR. However, there are other studies that disagree with this contention (Owman-Moll & Kurol, 1998; Owman-Moll et al., 1996b; Stenvik & Mjor, 1970). These studies were histological, involving two-dimensional measurements of a three-dimensional phenomenon and therefore may not be as accurate and reliable as three-dimensional measurement tools such as X-ray microtomography (Chan & Darendeliler, 2004).

Previous resorption studies undertaken at the University of Sydney (Barbagallo et al., 2006; Chan et al., 2004; Harris et al., 2005) selected 25cN force as a light force level and 225 cN as a relatively heavy force level. It was decided to use heavy forces of 225cN in this study to ensure there would be adequate OIRR to allow a comparison. The results could also be directly compared with our previous resorption studies.

The duration of this study was 56 days, which was chosen to cover the individuals who may require more than 10-35 days for the resorption craters to appear (Harry & Sims, 1982; Reitan, 1974; Rygh, 1977; Stenvik & Mjor, 1970) as well as allowing comparison with other root resorption studies that have been conducted at the University of Sydney choosing durations of 28 days and 56 days of force application.

As part of subjects inclusion screening, the upper first premolars of all of the patients who participated in the study were examined via panoramic radiography first. All teeth had completed apexification and there was no pre-treatment root shortening that was visible prior to the study. The patient selection process prohibited the selection of participants that were predisposed to pre-existing root resorption (Malek et al., 2001a), however previous studies have shown that teeth with no forces applied also have minor resorption (Chan & Darendeliler, 2005; Chan et al., 2004; Harris et al., 2005).

Although force loading design for this study was consistent with our previous studies (Barbagallo et al., 2006; Chutimanutskul et al., 2006), force decay was found to be significant, with the force decaying on the continuous side to approximately two thirds its initial activation level after just 7 days. As a result, we modified the established protocol where no reactivation was implemented during the experimental period, instead reactivating the force to 225cN at every subsequent visit. By doing so, we maintained a continuous force but not at a constant level.

Resorbed lacunae in root cementum following orthodontic tooth movement appear mainly in regions of compression (Gaudet, 1970; Reitan, 1964; Reitan, 1974; Reitan, 1985; Rygh, 1977), and rarely in regions of tension (Williams, 1984). Our analysis of the six positions of the root surfaces demonstrated an increased resorption distribution pattern in the buccal-cervical region which corresponds with increased pressure in this region generated by a tipping tooth movement. These findings are consistent with another three-dimensional root resorption study (Chan et al., 2005) in which more resorption craters were identified in the buccal-cervical area than any other location when the tooth was pulled buccally.. It must be noted however, that the patients who participated in the study had teeth that were in malocclusion e.g. being rotated or over tipped. Therefore, despite the best attempts, a buccal force direction might not have been applied perpendicular to the long axis of the tooth. Also, the crowding of the adjacent teeth might have influenced the amount and the exact direction of the movement actually occurred.

A potential area of concern was achieving an intermittent force that required no compliance by the patient. To this end we decided to have an operator control the force applications. In order to maintain a very high level of cooperation from the subjects, it was extremely important to make these appointments as convenient as possible for the patient. As a result, we chose the regimen of three days of rest followed by four days activation for compliance rather than any specific biological purposes. Even with these compromises it was extremely difficult to obtain willing participants, resulting in the relatively small sample size.

Although this study found less OIIRR with intermittent force when compared to continuous force which was in agreement with other studies (Acar et al., 1999; Maltha & Dijkman, 1996), it should be noted that many questions remain unanswered and that in fact, this could be seen as the beginning point for many more studies. Ideally we would like to increase our sample size to see if any other trends were noticeable. It remains to be seen, by increasing either the duration of the resting period or the activation, what effects these two force patterns would have on the amount and distribution of OIIRR. We used heavy forces but what effect would a lighter force have under the same regimen? We did not measure tooth movement in this study, so we can not be sure which force produced the most movement. It may be that although the teeth showed less root resorption with the intermittent force, it may not produce clinically useful tooth movement.

4.6 CONCLUSIONS

To quantify OIIRR with Micro-CT has recently been established in the literature as an accurate method for identifying root resorption. In the interest of extending our series of studies on which factors may influence root resorption, we used this technique to examine the differences in OIIRR produced by heavy continuous and heavy intermittent forces.

The results of our study revealed that buccally directed intermittent forces produce significantly less root resorption ($p < 0.05$) than a similarly directed continuous force of the same magnitude.

We also found that the greatest root resorption was found in the buccal-cervical area of the root, with at least twice the amount of any other region ($p < 0.001$). This area is thought to be under compression as a result of the tipping force.

This report represents a starting point in understanding the difference between continuous and intermittent forces with regard to root resorption, however there are many aspects requiring further investigation. These may include variations of the not only of the force magnitude, but also of the durations of both the resting and active periods.

Compared to continuous force, intermittent orthodontic activation may be safe to avoid significant root resorption. This regimen of force however, may compromise the efficiency of tooth movement.

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Figure 1: Experimental Appliance.

Figure 2: 3-D images showing root resorption craters A Continuous force Buccal view, B. Continuous force Lingual view, C. Intermittent force Buccal view, D. Intermittent force Lingual view.

Figure 3: Total Cuberoot volume of the resorption cavities produced by intermittent and continuous forces.

Figure 4: Cuberoot volume of the resorption cavities for each position of the root surfaces produced by the intermittent and continuous forces.

Figure 1: Experimental Appliance

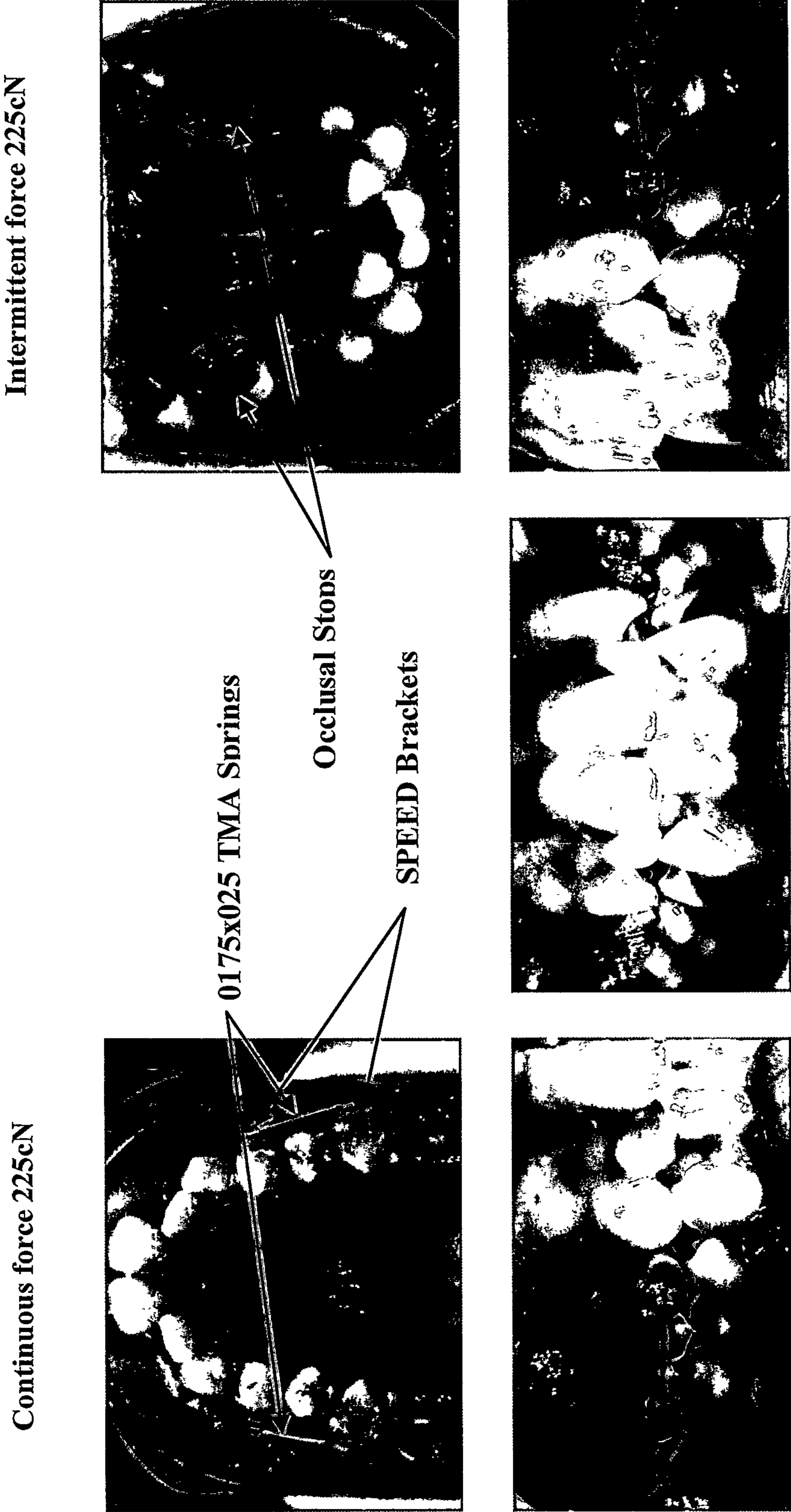


Figure 2: 3-D images showing root resorption craters A. Continuous force Buccal view, B. Continuous force Lingual view, C. Intermittent force Buccal view, D. Intermittent force Lingual view.

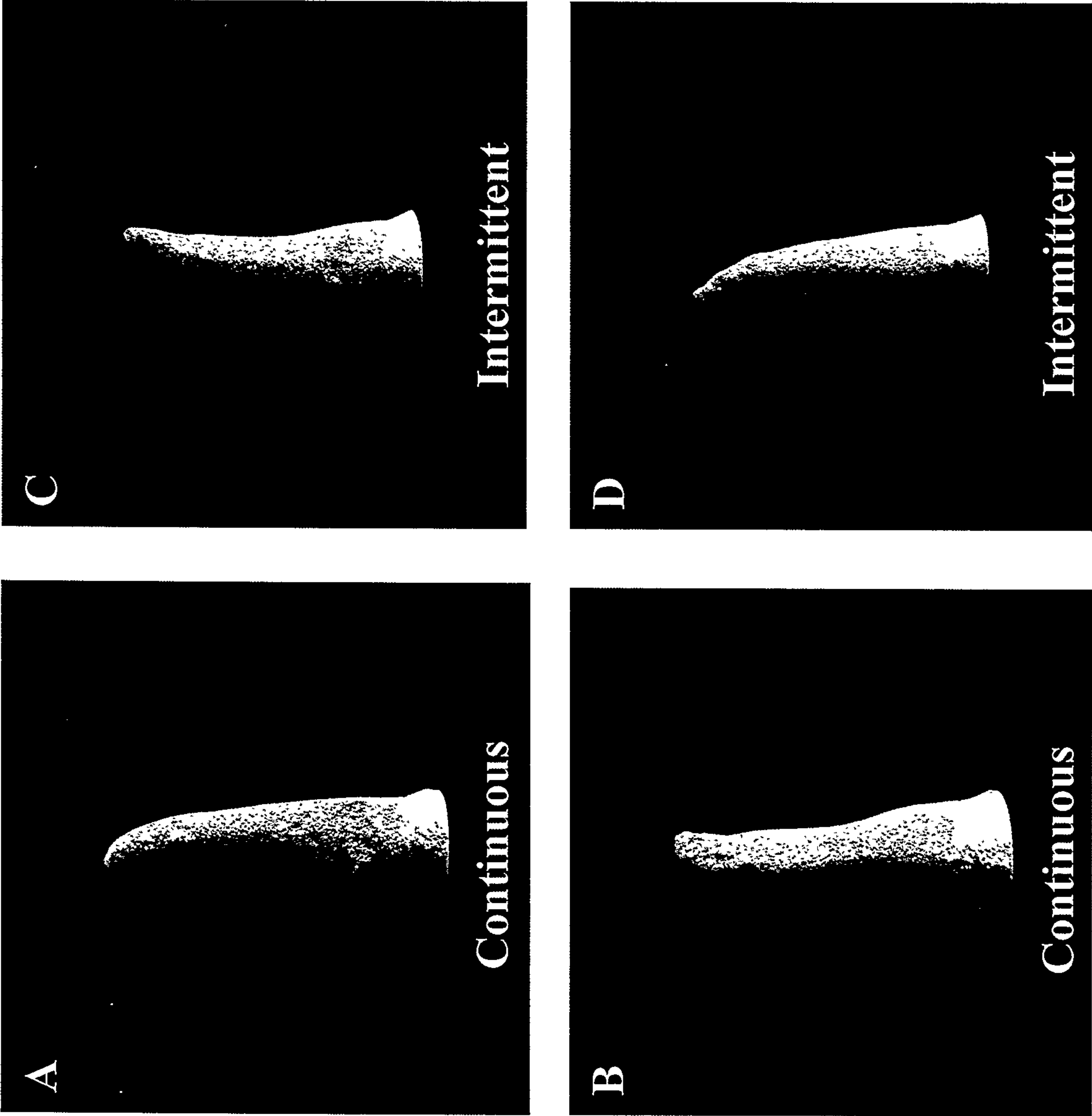


Figure 3: Total Cuberoot volume of the resorption cavities produced by intermittent and continuous forces.

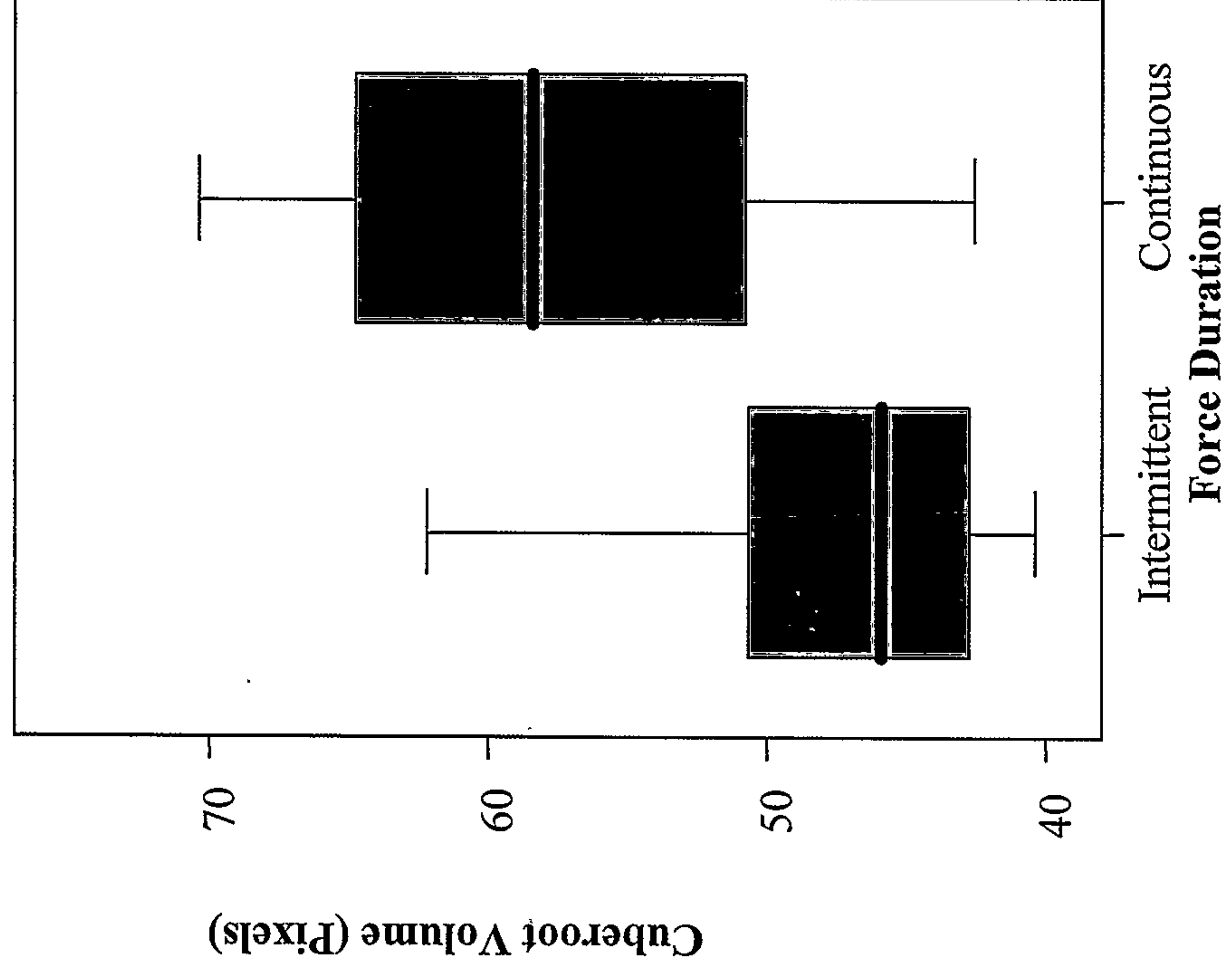
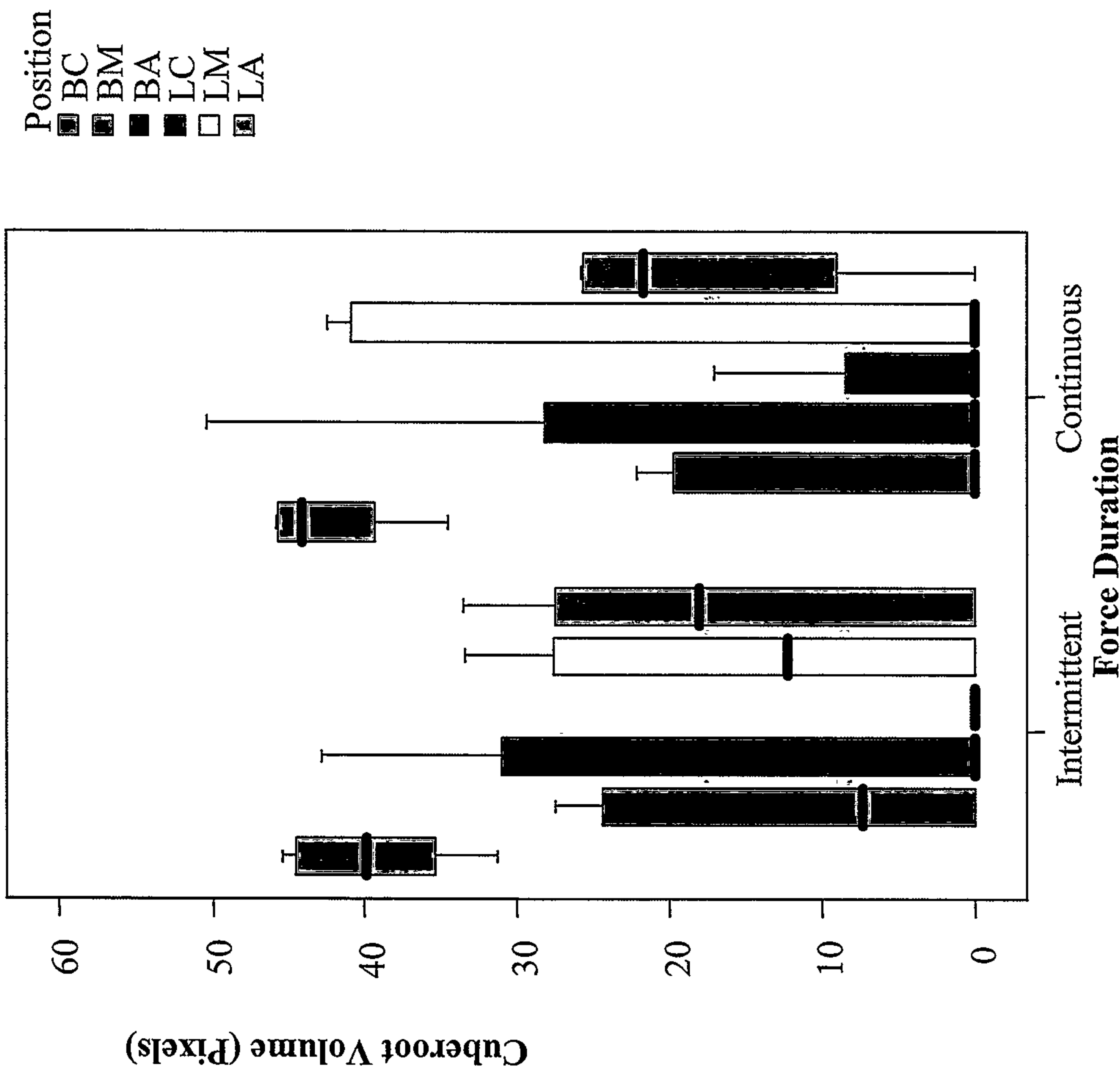


Figure 4: Cuberoot volume of the resorption cavities for each position of the root surfaces produced by the intermittent and continuous forces.



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Table 1: Tests of Between-Subjects Effects

Table 2: The Estimated Marginal Mean OIIRR for each of the two forces.

Table 3: The Estimated Marginal Mean OIIRR at each position on the root surface.

Table 4: Pairwise comparisons of root resorption values between the six positions.

Table 1: Tests of Between-Subjects Effects

Dependent Variable: Cuberoot volume total

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	Hypothesis	44366.292	1	44366.292	412.617	.000
	Error	752.668	7	107.524(a)		
Force	Hypothesis	392.089	1	392.089	11.662	.011
	Error	235.355	7	33.622(b)		
Subject	Hypothesis	752.668	7	107.524	3.198	.074
	Error	235.355	7	33.622(b)		

a MS(Subject)

b MS(Error)

Table 2: The Estimated Marginal Mean OIRR for each of the two forces.

Dependent Variable: Cuberoot volume total

Force	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Intermittent	47.708	2.050	42.860	52.556
Continuous	57.609	2.050	52.761	62.456

The volumes of the resorption cavities were transformed into cuberoot volume readings. Thus the unit of measurement is $\sqrt[3]{}$ of voxels, which is pixels, which may be converted to $\sqrt[3]{\text{mm}^3}$, or mm. The magnification setting for the Micro-CT was 16.00, resulting in a 0.01709mm pixel size. The mean values for cuberoot volume of the resorption cavities can thus be converted to mm by multiplying by 0.01709. For example the mean cuberoot volume of the continuous force resorption cavities was $57.609 \times 0.01709 = 0.985\text{mm}$.

Table 3: The Estimated Marginal Mean OIIRR at each position on the root surface.

Dependent Variable: Cuberoot volume

Position	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
BC	41.794	3.671	34.491	49.097
BM	11.632	3.671	4.329	18.935
BA	13.254	3.671	5.950	20.557
LC	5.269	3.671	-2.034	12.572
LM	14.852	3.671	7.549	22.155
LA	18.444	3.671	11.141	25.747

BC = Buccal-Cervical region

BM = Buccal-Middle region

BA = Buccal-Apical region

LC = Lingual-Cervical region

LM = Lingual-Middle region

LA = Lingual-Apical region

Table 4: Pairwise comparisons of root resorption values between the six positions.

Dependent Variable: Cuberoot volume

Position (I)	Position (J)	Mean Difference (I-J)	Std. Error	Sig.(a)	95% Confidence Interval for Difference(a)	
					Lower Bound	Upper Bound
BC	BM	30.162(*)	5.192	.000	14.464	45.860
	BA	28.540(*)	5.192	.000	12.842	44.238
	LC	36.525(*)	5.192	.000	20.827	52.223
	LM	26.942(*)	5.192	.000	11.244	42.640
	LA	23.350(*)	5.192	.000	7.652	39.048
BM	BC	-30.162(*)	5.192	.000	-45.860	-14.464
	BA	-1.621	5.192	1.000	-17.319	14.077
	LC	6.363	5.192	1.000	-9.335	22.061
	LM	-3.220	5.192	1.000	-18.918	12.478
	LA	-6.812	5.192	1.000	-22.510	8.886
BA	BC	-28.540(*)	5.192	.000	-44.238	-12.842
	BM	1.621	5.192	1.000	-14.077	17.319
	LC	7.985	5.192	1.000	-7.713	23.683
	LM	-1.599	5.192	1.000	-17.297	14.099
	LA	-5.191	5.192	1.000	-20.889	10.508
LC	BC	-36.525(*)	5.192	.000	-52.223	-20.827
	BM	-6.363	5.192	1.000	-22.061	9.335
	BA	-7.985	5.192	1.000	-23.683	7.713
	LM	-9.583	5.192	1.000	-25.281	6.115
	LA	-13.175	5.192	.196	-28.873	2.523
LM	BC	-26.942(*)	5.192	.000	-42.640	-11.244
	BM	3.220	5.192	1.000	-12.478	18.918
	BA	1.599	5.192	1.000	-14.099	17.297
	LC	9.583	5.192	1.000	-6.115	25.281
	LA	-3.592	5.192	1.000	-19.290	12.106
LA	BC	-23.350(*)	5.192	.000	-39.048	-7.652
	BM	6.812	5.192	1.000	-8.886	22.510
	BA	5.191	5.192	1.000	-10.508	20.889
	LC	13.175	5.192	.196	-2.523	28.873
	LM	3.592	5.192	1.000	-12.106	19.290

Based on estimated marginal means

* The mean difference is significant at the .05 level.

a Adjustment for multiple comparisons: Bonferroni.