THE EFFECT OF PIEZOCISION AND MECHANICAL VIBRATION ON ORTHODONTICALLY INDUCED ROOT RESORPTION OF FIRST PREMOLARS FOLLOWING THE APPLICATION OF ORTHODONTIC FORCES.

Dr Eunice Park

BDent (USyd), MRACDS (GDP)

Discipline of Orthodontics and Paediatric Dentistry

Faculty of Dentistry

University of Sydney

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Dedication

To my mum – For all the sacrifices you have made for me. For your unconditional love, strength, and belief in me.

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Candidate Certification

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

Dr Eunice Park

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Abbreviations

OIIRR	Orthodontically induced inflammatory root resorption
OTM	Orthodontic tooth movement
RR	Root resorption
PDL	Periodontal ligament
CBCT	Cone Beam Computed Tomography
2D	Two Dimensional
3D	Three Dimensional
LLLT	Low-level laser therapy
MOP	Micro-osseous Perforation
RAP	Regional Acceleratory Phenomenon
HFV	High-frequency vibration
CF	Compressive force
COX-2	Cyclooxygenase-2
UMIS	Ultra Micro Indentation System
IL-1β	Interleukin-1 beta
NSAID	Non-Steroidal Anti-Inflammatory Drug
CT	Computed Tomography
RCT	Randomized controlled trial
SNP	Single Nucleotide Polymorphism
IL-1RN	Interleukin-1 Receptor Antagonist
RANK	Receptor Activator of Nuclear Factor Kappa-B
IRAK1	Interleukin-1 Receptor-Associated Kinase 1

1. Literature Review

Part 1: Introduction

Orthodontically induced inflammatory root resorption (OIIRR) associated with orthodontic tooth movement (OTM) has been documented as early as the early 1900s, with reports by Sandstedt in 1904[1], Ottolengui in 1914[2], Ketchman in 1927[3], and Schwarz in 1932[4]. OIIRR refers to the loss of mineralized cementum and dentine from the root.[5] This process arises when orthodontic forces compress the periodontal ligament (PDL), resulting in cell death. The subsequent clearance of necrotic tissue triggers root resorption (RR).[6,7] OIIRR is an iatrogenic complication of orthodontic treatment that can lead to tooth loss if severe.[8]

OIIRR is influenced by patient-related and treatment-related factors.[8] Maxillary premolars are more susceptible compared to mandibular premolars.[9,10] Treatment variables such as duration, premolar extractions, force magnitude, and the method of force application significantly influence OIIRR risk.[8] Continuous heavy forces increase the likelihood of OIIRR, especially in regions experiencing high pressure, such as the buccal cervical and lingual apical areas.[9,10] Additionally, compression zones are more prone to resorption than tension zones.[11]

OIIRR is a significant concern during orthodontic treatment, particularly when high forces are applied. However light force may result in slower tooth movement, as there is a direct relationship between the force applied and the rate of tooth movement.[12]

Prolonged orthodontic treatment duration heightens the risk of OIIRR, particularly in adults. This has driven research into techniques to accelerate tooth movement while minimizing associated risks.[13] Both surgical and non-surgical acceleration methods have gained popularity in recent years.[14]

Piezocision is a surgical technique that accelerates tooth movement by creating small incisions in the bone, facilitating PDL distraction and promoting osteogenesis.[13,14] Studies on piezocision have shown mixed results: some suggest piezocision may increase OIIRR[15-17], while others find no significant difference compared to controls[18-20].

Patterson et al.[15] observed that piezocision combined with orthodontic forces heightened the risk of iatrogenic root resorption, while Strippoli et al.[17] reported notable anterior tooth OIIRR and a reduction in alveolar bone height in piezocision-assisted orthodontic treatments. In contrast, Charavet et al.[19] found no significant difference in root length between patients treated with piezocision and those who underwent standard orthodontic treatment from start to finish. Similarly, a study by

Alhaija et al.[18] reported no adverse effects of the piezocision procedure on the periodontium.

While some studies have associated piezocision-induced periodontal inflammation with an increased risk of OIIRR, others propose that the reduced bone density following piezocision enhances osteoclastic activity. This reduction in bone density may help alleviate the pressure on tooth roots, potentially minimizing OIIRR.[18]

Dibart et al.[21] stated there is no strong evidence suggesting an increased risk of OIIRR due to piezocision.

The use of mechanical vibration during orthodontic treatment has been suggested as a method to shorten treatment time and minimize OIIRR; however, there is insufficient evidence to confirm the effectiveness of this approach.[22]

Mechanical vibration induces an osteogenic response through piezoelectric charges on alveolar bone, but its effectiveness, especially for initial alignment, has been questioned.[14] However, Mayama et al.[23] found that combining vibration with static force increased tooth movement during canine retraction without added pain, discomfort or OIIRR.[23]

DiBiase et al.[24] reported that mechanical vibration had no impact on OIIRR in the maxillary central incisors. Similarly, Nishimura et al.[25], in a histological study on rat molars, found that mechanical vibration did not influence OIIRR. Both Yeoh et al.[26] and Yilmaz et al.[22] concluded that vibration, even with orthodontic force applied, does not affect the extent of resorption. A trial by Tangtanawat et al.[12] showed that high frequency vibration (HFV) with orthodontic force enhanced tooth movement in a rat model without inducing OIIRR.

Vibration appears to accelerate tooth movement without increasing OIIRR[24,25], but more research is needed across different tooth types and positions.

Both methods of acceleration (piezocision and mechanical vibration) show promise in shortening treatment time and reducing discomfort, potentially mitigating risks like dental complications and OIIRR.[27] However, the comparative effects of piezocision and vibration on OIIRR remain unclear.

There is a lack of research showing the combined effect of piezocision and mechanical vibration or their comparative effect on OIIRR.

Part 2: The biology of tooth movement

2.1 Definition

OTM is achieved through alveolar bone change due to mechanical straining of the periodontium creating zones of compression and tension that drive the physiological response within the periodontium.[7,10] The periodontium's molecular and cellular responses to tension and compression are fundamentally inflammatory, resulting in localized changes that influence the blood supply and prompt the release of neurotransmitters, growth factors, and cytokines.[10,28] PDL cells serve as vital mechanoreceptors and primary shock absorbers, responding to both constant and intermittent loads. When activated, PDL cells exhibit specific expression patterns that drive changes in cellular behaviour. These cells play a crucial role in periodontal remodeling, bone resorption, and facilitating tooth movement.[10] The movement leads to both bone formations, bone resorption and subsequent tooth movement. This is explained by the Pressure-Tension theory, originally formulated by Sandstedt in 1904[1], Oppenheim in 1911[29], and Schwartz in 1932[4], which suggested that when force is applied on teeth, this induces areas of pressure and tension within the PDL. Cellular activity is influenced by chemical messengers released in response to changes in blood flow within the PDL leading to remodelling of alveolar bone and tooth movement.[30] The pressure-tension theory in tooth movement biology remained unclear until Schwarz proposed that effective tooth movement occurs within a blood capillary pressure range of 7 to 26 grams per square centimetre.[4] Excessive orthodontic force above 26 grams can lead to reduced blood flow in the periodontal tissues, potentially causing OIIRR.[11]

2.2 Theories

2.2.1 Pressure Tension Theory

The pressure-tension theory proposes that chemical messengers play an important role in bone resorption and apposition. The change in homeostasis in PDL cause movement of immune cells accompanied by the various cytokines, prostaglandins, and growth factors. Hence the immune cells orchestrate the inflammatory reaction of OTM.[5] The cascade of events that explain the alveolar bone remodelling and tooth movement starts with alterations in PDL blood flow that affects the chemical environment, stimulating the release of these messengers.[30]

2.2.2 Bone Bending Theory

The bond bending theory suggested that changes in bone metabolism are governed by electrical signals produced when the alveolar bone bends in response to applied forces.[31]

When orthodontic forces are applied, they are distributed to the tooth, alveolar bone, and surrounding tissues, resulting in deformation of these structures. Since bone is more flexible, it tends to bend more easily. This observation led Grimm to propose that alveolar bone bending plays a key role in OTM. He suggested that this bending of the alveolar bone triggers remodeling and reorganization processes, ultimately influencing the position of the tooth. The remodeling activity accelerates when the bone remains in its deformed state over time.[31]

2.3 Physiology

The rate of OTM is determined by the modeling and remodeling processes of the alveolar process while adapting to the external stimulus.[32] Li et al. theorised that when the tooth is moved, the PDL is compressed in some areas and stretched in other area.[7] The compression of tissues and change in blood flow leads to sequence of chemical changes and undergoes sterile necrosis, resulting in the formation of hyaline tissue.[26] Tooth movement is facilitated as hematopoietic resorptive cells migrate from the marrow vasculature in the surrounding bone, clearing the obstructing alveolar bone and hyalinized tissue.[26] The reduced vascularity on the pressure side prompts the osteoclasts to resorb bone.[30] The reduced blood flow meads decreased oxygen level and increased carbon dioxide present in the tissue, thus creating an acidic environment.[30] This triggers the release of prostaglandins and cytokines, such as Interleukin-1 Beta (IL-β), thereby activating osteoclasts. Conversely on the tension side, the periodontal fibers are stretched, and osteoblasts are triggered to promote bony apposition.[30]

2.4 Heavy and light forces

Sandstedt's research involved application of heavy and light forces to cause tooth movement in dogs.[1,30] Light forces caused PDL to compress, leading to direct resorption of alveolar bone by osteoclasts.[30] Whereas, heavy forces caused more intense PDL compression, result in ischaemic necrosis in the PDL due to loss of blood supply.[6] These localized areas devoid of cells are referred to as hyalinized zones of the cementum.[5] These areas were subsequently infiltrated by phagocytic cells like macrophages and osteoclasts. Schwartz linked these findings to capillary blood pressure, which suggested that forces higher than the capillary blood pressure led to tissue necrosis and hyalinization, while forces lower than this threshold triggered no reaction within the PDL. Schwartz hypothesised that force creates changes in PDL width which increases cellular activity and thus tissue remodelling.[30]

In short, tooth movement can be explained in three stages:[30]

1. Initial tissue compression leading to reduced blood flow due to PDL pressure
2. Generation of chemical messengers
3. Stimulation of osteoblasts and osteoclasts, resulting in alveolar bone remodelling.

2.5 Optimal force

Storey et al.1952[33] and Reitan 1967[34] suggested that each type of tooth has a specific optimal force that enables the highest rate of movement while minimizing tissue damage. When this optimal force is exceeded, increasing the force does not lead to faster tooth movement. Studies, such as those by Quinn and Yoshikawa in 1985[35], indicate that the rate of movement is highly responsive to changes in force magnitude. However, this relationship is believed to be linear only up to a certain threshold. Beyond this point, higher stress levels do not produce any significant increase in the rate of tooth movement.

At lower force levels, there is a direct relationship between the force applied and the rate of tooth movement. However, once the force exceeds the optimal threshold, it no longer accelerates tooth movement. In studies with rats, the rate of tooth movement increased proportionally up to a force of 10 g, but beyond this point, further increases in force did not lead to more movement. Additionally, different magnitudes of light force (1.2, 3.6, 6.5, and 10 g) were found to promote bone remodeling through frontal bone resorption. However, a force of 1.2 g was less effective at promoting tooth movement compared to the other force magnitudes.[12]

The optimal force required for the fastest tooth movement remains uncertain for different types of tooth movement. Clinically, it is challenging to precisely regulate the ideal stress and strain across all areas of the PDL for specific movements. As a result, light force is often recommended as a safer alternative in orthodontic treatment to minimize the risk of OIIRR caused by excessive stress and strain in the PDL.[12,36]

Part 3: Cementum

3.1 Definition of Cementum

Cementum is primarily an avascular tissue, with its nutrition supplied by the surrounding PDL. The PDL is composed of collagen fibers, blood vessels, and interstitial fluid. Cementum is a dynamic biological material with a non-uniform structure that evolves over a lifetime. It does not possess a consistent structure or fixed values for hardness and elastic modulus throughout its entire depth.[37]

3.2 Role of cementum

Cementum, a specialized mineralized connective tissue covering the root surface, shares several characteristics with bone. It plays a dual role by anchoring PDL fibers and facilitating the repair of root surfaces affected by orthodontic tooth movement. [37]

3.3 Types of cementum

Morphologically, cementum is categorized into cellular and acellular types. Cellular cementum, which is less densely mineralized, is typically found on the apical third of the root, whereas acellular cementum, composed of mineralized layers, covers the cervical two-thirds of the root.[37]

3.4 Composition of cementum

The incremental layers of cementum exhibit variations in width, reflecting fluctuations in its formation rate over time. Its chemical composition can also differ.[37] Unlike dentine and enamel, cementum is less densely mineralized. It lacks blood vessels and does not undergo physiological remodeling, yet it continues to thicken throughout a person’s life. In humans, cementum exists in various physiological forms, each differing in structure, location, function, and formation rate.[37]

The hardness and elasticity of cementum are influenced by its structural orientation and mineral composition. The cervical two-thirds of the root is covered by acellular extrinsic fiber cementum, characterized by mineralized layers. In contrast, apical cementum is primarily cellular, less densely mineralized, and exhibits lower hardness and elastic modulus compared to the acellular cementum in the middle and cervical thirds. Research has consistently shown a positive correlation between the degree of mineralization and the mechanical properties of mineralized tissues.[38] Due to its lower level of calcification, cellular cementum exhibits reduced hardness and elastic modulus compared to the more highly mineralized acellular cementum.[39] Significant variability in cementum hardness has been reported, which may result from natural differences or inconsistencies in sampling methods.[37] Alteration in mineral content of cementum can be induced by heavy orthodontic forces.[38]

The study by Chutimanutskul et al. 2006[39] demonstrated a gradual decrease in hardness and elastic modulus from the cervical to the apical third in both buccal and lingual surfaces, independent of the orthodontic force applied.[39] This trend can be attributed to the inherent structural characteristics of human cementum or the influence of orthodontic forces. In untreated human premolar teeth, apical cementum is known to have the lowest hardness and elastic modulus values. These variations within the tooth are influenced by the structural orientation and differences in mineral content within the cementum.[39]

Several literature reviews have proposed that the physical properties of cementum, such as hardness and elastic modulus, may play a role in determining the resistance or susceptibility of the OIIRR. These properties could offer valuable insights into the characteristics of OIIRR.[39] An earlier study by Darendeliler et al. 2004[40] comparing the hardness and elastic modulus of cementum across three groups—control (0 cN), heavy force (225 cN), and light force (25 cN)—found no significant differences in these properties among the groups.[40] The results of this study may be influenced by individual variations, differences in the sample selection of upper and lower premolar teeth, and ethnic variations. There were considerable individual differences in terms of the occurrence, surface extent, and depth of OIIRR, which could have contributed to the lack of significant findings.[39]

3.5 Characteristics of Cementum

Cementum is a biologically derived material with a heterogeneous and evolving structure. Unlike synthetic engineering materials, it does not have uniform or fixed values for mechanical properties such as hardness and elastic modulus. These properties can vary significantly depending on the specific layer or region of cementum being tested. To assess these properties at the microscale, the Ultra Micro Indentation System (UMIS), particularly the UMIS-2000 model, is used. This device functions as a microprobe that measures mechanical characteristics in surface layers of materials. However, it is limited in its ability to penetrate deeply—only reaching up to one-third of the 20-μm indentation radius, which equates to approximately 6–7 μm in depth. Accurate measurements also depend on having a flat and smooth sample surface, which is difficult to obtain when working with human cementum due to its naturally irregular and textured surface. Furthermore, because the indentation points are placed randomly, they may not align with areas of interest such as resorption sites, which can result in inconsistent or non-representative data.[39]

Cementum formation is more pronounced at the root apex compared to the cervical region. Additionally, its thickness varies notably among different tooth groups and surfaces. Cementum tends to accumulate in concave areas of the root surface, leading to thicker deposits in root grooves and the furcation regions of multirooted teeth.[37]

Studies have identified variations in the hardness and elastic modulus of cementum across different regions of a premolar root. Specifically, the cementum in the apical third exhibits lower hardness and elastic modulus compared to the cementum found in the middle and cervical thirds.[37]

Research has shown that cementum on teeth extracted from female subjects tends to be harder than that from male subjects.[37] However, no differences in cementum hardness were observed between maxillary and mandibular premolars, buccal and lingual root surfaces, or between first and second premolars. Similarly, the elastic modulus of human cementum appears unaffected by factors such as sex, dental arch, tooth position, or tooth surface.[37]

There were no significant differences in the hardness or elasticity of cementum when comparing maxillary versus mandibular premolars, or between the buccal and lingual surfaces of premolar roots.[39] Consistent with other studies, this research also observed a gradient of decreasing hardness and elasticity in cementum from the cervical to the apical third in both groups.[37]

Further studies are needed to better understand the differences in the physical properties of untreated human first premolar cementum between the left and right sides, as well as the intraindividual variations in the mineral composition of cementum following the application of orthodontic forces.[39]

3.6 Development, Structure and Function of Cementum

Collagen fibers oriented both radially and circumferentially relative to the tooth's longitudinal axis were identified in human samples.[41]

In humans and rats, primary cementum is primarily composed of radially oriented collagen fibers. The structure of secondary human cementum, however, is characterized by a twisted plywood arrangement, exhibiting an alternating lamellar pattern. The structure of secondary cementum in both humans and rats can be likened to a woven fabric, composed of broad radial collagen fibers interwoven with narrower circumferential collagen fibers. Collagen fibers oriented in the longitudinal Z direction traverse the gaps between radial and circumferential fibers, connecting the woven fabric-like planes and contributing to a three dimensional (3D) architecture. This structure not only accommodates varying mechanical loads across species but also enhances tissue porosity and permeability.[41]

The hypomineralized, glycosaminoglycan-rich primary or radial fibers traverse the bulk of the cementum and anchor into the root dentin.[41]

The cementum-dentin junction in both humans and rats can be characterized as a zone of interspersed collagen fiber bridges that form during development following the disintegration of Hertwig’s epithelial root sheath.[41]

Histological analysis of human specimens has revealed 15- to 30-µm-wide collagen fiber bridges connecting cementum to root dentin. Through atomic force microscopy the behavior of the 10- to 50-µm-wide human cementum-dentin junction was distinguished by comparing its swelling in wet conditions to its appearance as a valley under dry conditions, in contrast to the surrounding predominantly mineralized tissues of cementum and root dentin.[41]

The pores observed in all three imaging techniques across different species may represent remnants of Hertwig's epithelial root sheath following its disintegration, also referred to as epithelial rests of Malassez. These structures resemble pore-like formations located between the bulk cementum and root dentin.[41]

Clark (1997) concluded that there were no significant differences in the hardness and elastic modulus of cementum between buccal and lingual surfaces or between maxillary and mandibular teeth. Additionally, it was assumed that the physical properties of cementum did not vary between left and right teeth. However, no prior studies had specifically investigated or compared the physical properties of cementum between the left and right sides.[39]

The comparable physical properties of cementum on the maxillary right and left first premolars indicate that intra-arch comparisons are suitable for studying OIIRR induced by orthodontic forces.[37]

Part 4: Root resorption

4.1 Introduction

OIIRR is a process, either physiological or pathological, characterized by the loss of cementum and dentine. OIIRR occurs when the mineralized tissue and matrix surfaces align or when the pre-cementum layer is mechanically disrupted or removed. Unmineralized tissues such as osteoid, pre-cementum, and pre-dentine are initially resistant to resorption and can act as protective barriers against root tissue loss. However prolonged or continuous pressure can overcome this resistance and OIIRR starts when osteoclasts gain access to the mineralized tissue through a disruption in the protective layer of formative cells.[39]

4.2 Orthodontically induced inflammatory root resorption (OIIRR)

4.2.1 History and Definition

OIIRR is a well-recognized and clinically significant complication associated with OTM.[10] OIIRR develops as a result of mechanical stress in both humans and animals and it is defined as more than 4mm of root loss or reduction by one-third of the original root length.[10,22] It is a complex pathological process involving multiple factors that lead to the loss of mineralised cementum and dentine of the root.[5,10,42] With longer duration and higher orthodontic force, an increase in OIIRR has been observed.[9,36] Varying methods of pressure application are linked to differing levels of OIIRR severity.[10] Historically, OIIRR has been primarily associated with the magnitude of applied force, with lighter forces being widely advocated to minimize undesirable tissue responses.[36,39]

The OIIRR is caused by active removal of the hyalinized necrotic tissue.[6] This means the compression of PDL results in cell death and lack of osteoclast differentiation which leads to removal of lamina dura and eventual resorption.[7] Contrastingly, the decompression of the PDL will initiate the repair process of the damaged cementum.[43]

4.2.2 Aetiology

The aetiology of OIIRR is believed to be multifactorial, stemming from both biological and treatment-related factors. Biological influences include genetic predisposition, allergies, medications, dental anomalies, atypical root morphology, bone density variations, and a prior history of root resorption. On the other hand, treatment mechanics contributing to OIIRR encompass factors such as the force magnitude, treatment duration, direction of tooth movement, and the extent of tooth displacement.[26]

Continuous force placed on teeth leads increased unwanted rotational movement and OIIRR. The rotational movement correlates with elevated levels of OIIRR observed particularly in the middle third level of the tooth root.[32]

In 2006, Chan et al.[11] conducted a study using volumetric measurements to quantify the extent of OIIRR in human teeth subjected to both light and heavy orthodontic tipping forces, focusing specifically on areas under compression and tension. Chan et al. classified forces around 25 g are classified as light, while those near 225 g are regarded as heavy.[11] A clinical trial by Chan et al discovered that the group subjected to heavy-force experienced greater resorption as measured through volumetric analysis compared to both the light-force and control groups.[40] Considerably higher levels of resorption were observed on the buccal cervical and lingual apical regions of the root surfaces, indicating that areas subjected to high pressure are more prone to resorption.[9,44] Additionally, OIIRR was observed to be more prominent in areas experiencing compression compared to those under tension.[11]

Chutimanutskul et al. 2006[39] concluded that heavy forces result in a greater reduction in the elasticity of cementum compared to light forces. Also, heavy forces lead to a more significant decrease in the hardness of cementum compared to light forces.[39]

4.2.3 Risk factors contributing to OIIRR:

OIIRR is a multifactorial condition influenced by a wide range of patient-specific, local, treatment-related, and biological factors. The following table categorises the key risk factors associated with OIIRR based on current literature.[10]

1. Patient-Related Risk Factors[10]
    - Demographics:
        - Race
        - Chronological and dental age
        - Sex
    - Genetic Predispositions
    - Health Conditions:
        - Asthma
        - Diabetes
    - Lifestyle and Systemic Factors:
        - Nutrition
        - Medications
2. Local Factors[10]
    - Malocclusion:
        - Type and severity
    - Habits:
        - Bruxism, tongue thrust, finger sucking, nail-biting

- Dental History:
    - Previous trauma
    - Endodontically treated teeth
- Root Morphology:
    - Developmental characteristics
- Bone and Tooth Factors:
    - Alveolar bone density and turnover rate
    - Specific tooth vulnerabilities

3. Treatment-Related Factors[10]
    - Treatment Duration
    - Force Characteristics:
        - Magnitude, direction, and type (continuous vs. intermittent)
    - Movement Mechanics:
        - Distance, type, and direction of movement
    - Appliances and Treatment Philosophy:
        - Appliance types and materials used to modify resorption
        - Extraction vs. non-extraction treatments
    - Other Mechanical Factors
4. Dental and Biological Risk Factors[10]
    - Pre-existing Conditions:
        - Resorption, trauma, periodontal status, and anomalies
    - Tooth and Root Development:
        - Dental age, stage of root development

The susceptibility to OIIRR can be influenced by both patient-related and orthodontic treatment-related risk factors.[8] Characteristics of root structure, including cementum hardness, elastic modulus, and mineral content, have been identified as potential risk factors affecting the root's resistance or susceptibility to resorption.[39] This variability of the physical properties of root cementum is a key factor in determining an individual's susceptibility to root resorption, whether or not orthodontic treatment is involved.[39] Such differences also impact the prevalence, extent, and depth of OIIRR.[39] Abnormalities in tooth root morphology, a history of previous root resorption, prior dental trauma and previous endodontic treatment are considered patient-related risk factors.[8] OIIRR was more likely to occur in the maxillary premolars compared to the mandibular premolars.[9]

On the other hand, orthodontic-related risk factors include the duration of treatment, extraction of premolars, the intensity of applied forces, and the method of force application.[8] Differences in hardness and elastic modulus of cementum may arise from variations in the application of orthodontic forces. Factors contributing to these variations include: [39]

1. The concentration of forces at the root apex, as OTM is rarely entirely translatory, with the fulcrum typically located occlusal to the apical half of the root[39,45]
2. The distinct orientation of PDL fibers near the apical region, which may result in increased stress in this area.[39]

The magnitude of orthodontic force is thought to play a critical role in both the extent of tooth movement and the potential damage to dental root tissues. Excessive force is often associated with increased tissue damage, including OIIRR. [9] Several studies have found a correlation between higher force magnitudes and greater OIIRR. However, contrasting research has shown that the application of heavy forces does not necessarily result in a significant increase in OIIRR.[39]

The study by Chutimanutskul et al. 2006[39] demonstrated significant differences in hardness and elastic modulus between the light force and heavy force groups. These findings align with previous research by Darendeliler et al. 2004[40], suggesting that if greater hardness of cementum correlates with reduced OIIRR, teeth with higher hardness may experience less resorption under orthodontic forces.[40] Conversely, if reduced hardness increases susceptibility to resorption, applying lighter orthodontic forces is advisable to minimize the risk of OIIRR.[40,44]

It is important to note that while this intraindividual study identified a strong correlation between the hardness and elastic modulus of cementum and the magnitude of orthodontic force, these properties may also vary significantly between individual teeth and across different regions of the same tooth. The unique structural arrangement of cementum can differ for each tooth. Research by Rautiola and Craig 1961[46] and Malek et al. 2001[47] highlighted substantial variations in hardness within different areas of the same cementum on a single tooth. This inherent characteristic of cementum allows for both natural variability and location-specific differences within its layers.[39]

With age, it is reported that there is tendency for increased mobility in teeth with severely resorbed roots, especially if the root length has resorbed to less than 10 mm.[8]

Increased occurrence of OIIRR observed in several studies including those involving roots with periapical pathology, hypofunctional teeth and periodontium, as well as teeth with a history of trauma to the surrounding periodontium in both human and animal studies.[10]

Immature roots experience less OIIRR compared to mature teeth, which may be attributed to lower expression levels of Jagged1, Notch2, IL-6, and Receptor Activator of Nuclear Factor Kappa B Ligand (RANKL) signaling. This pattern has been observed in low-risk human studies, although higher-risk animal studies show different findings.[28]

Systemic fluoride is considered a protective factor against OIIRR.[10]

Medications have been identified as an additional risk factor for OIIRR in animal studies. Strong evidence links strontium ranelate intake to increased OIIRR severity, while corticosteroids and 4-hexylresorcinol medications are associated with moderate to low evidence of contributing to this condition.[10,48]

Oral contraceptive use has been shown to reduce the severity of OIIRR, likely due to its impact on hormonal levels, which influence periodontal tissue and cementum metabolism.[49] This finding suggested that evaluating individual bone metabolism before orthodontic treatment could provide insights into the potential rate and severity of OIIRR.[10,49]

Similarly, studies in rats with reduced steroid-sex hormone plasma levels demonstrated a decrease in bone turnover, correlating with reduced OIIRR.[50] Additionally, moderate evidence suggested that higher caffeine intake may lower OIIRR occurrence, possibly by inhibiting osteoclast formation, which in turn reduces bone turnover and resorption.[10,51]

Occlusal abnormalities, including increased overjet and Angle's Class II malocclusion, are strongly associated with more severe OIIRR.[52] This may be attributed to prolonged treatment durations or higher levels of applied force.[10,52]

Increased incisal inclination and obstacles hindering root movement, such as impacted teeth or greater cortical bone thickness, can create additional stress on the root. This, in turn, enhances odontoclastic activity, as supported by high-quality human studies.[10]

The impact of biological sex on OIIRR remains controversial. In the systematic review done by Dawood et al.[10], four studies with strong evidence reported higher OIIRR in males compared to females, while other studies with moderate evidence found no significant difference related to sex. Higher age has been linked to increased OIIRR in human observational studies, including four high-quality studies.[10] However, three studies with low to medium evidence reported no such association. Age-related OIIRR may result from a greater susceptibility to iatrogenic damage caused by orthodontic forces.[10]

To mitigate the risk of OIIRR in adults, specific strategies should be considered, such as extending the interval between visits, applying lighter forces[36], and ensuring proper oral hygiene during treatment. High-quality randomized controlled trials are necessary to address this ongoing debate.

The relationship between asthma and OIIRR remains inconclusive.[10] However, factors such as initial root size, length, shape, and width have been identified as significant in some observational studies of varying quality. Variations in outcomes may stem from differences in methodologies, treatment durations, and measurement techniques.[10]

Additionally, numerous studies have highlighted the potential genetic influence on OIIRR, supporting the idea that genetic variations may contribute to differences in OIIRR severity between individuals, even when other factors are consistent.[10]

The majority of animal studies lacked clarity on whether randomization and blinding of assessors were implemented.[10]

A significant challenge in in vivo studies is the selection of radiographic techniques for assessing OIIRR. Since OIIRR is a 3D process, it can affect more than just root length, typically reported as apical resorption in most two dimensional (2D) radiographic studies.[8,10] It may also manifest as reductions in root thickness, cervical resorption, and the formation of coves, lacunae, or microcracks, which become more pronounced with the application of orthodontic biomechanics. These changes are not detectable using 2D imaging methods such as periapical, panoramic, or cephalometric radiographs.[8,10,53-55]

Another limitation of non-standardized radiographs is the variability in magnification, angulation, and the superimposition of surrounding structures, which reduces the reliability of the data.[53-55] Additionally, periapical results may overestimate the extent of OIIRR. In contrast, 3D imaging techniques such as Cone Beam Computed Tomography (CBCT) and scanning electron microscopy offer more accurate and detailed data on OIIRR.[10,53-55]

Genetic studies on OIIRR have yielded controversial findings. Emerging evidence indicates that a single nucleotide polymorphism (SNP) within a gene is unlikely to solely determine the condition or its severity. Instead, other genetic factors, such as gene-gene interactions, as well as environmental and lifestyle factors (including gene-lifestyle, gene-environment, and lifestyle-environment interactions), may contribute to the development and severity of OIIRR.[10]

Genetic studies have identified only a small fraction of relevant genes, and structural variations in genetic variance pose additional challenges. Discovering the missing SNP risk factors remains difficult without a comprehensive understanding of the primary contributing elements.[10]

The risks for increased OIIRR should be approached cautiously, with contributing factors including occlusion, prior trauma, tooth shape, allergies, low bone turnover, and medications such as corticosteroids, strontium ranelate, and 4-hexylresorcinol. Genetic polymorphisms, including IL-1 β, Interleukin-1 Receptor Antagonist (IL-1RN), RANK, osteoprotegerin, and the vitamin D receptor TaqI polymorphism, also play a role.[10]

Conversely, certain factors appear to reduce the rate of OIIRR, such as oral contraceptives, baicalin, high caffeine intake, root-filled teeth, and polymorphisms in osteoprotegerin and Interleukin-1 Receptor-Associated Kinase 1 (IRAK1).[10]

In vitro studies examining various force types and mechanical regimes on PDL cells have offered insights into their impact on biological behavior and genetic expression.[10] These studies suggest that extracellular matrix gene expression, cell adhesion, osteotropic cytokines, growth factors, and the regulation of osteoblastic/cementoblastic differentiation and proliferation in PDLs are influenced by mechanical forces. Additionally, autophagy has emerged as a novel mechanism involved in regulating the clinical processes of OTM and OIIRR.[10]

4.2.3.1 Biological Factors:

1) Individual Variation: OIIRR varies among individuals.[56]
2) Genetics: Shorter root lengths and familial predisposition are linked to resorption, with siblings being a reliable indicator.[57] Harris et al.1997[58] reported heritability for resorption at 70%, highest in maxillary central incisors and lowest in mandibular incisors.
3) Systemic Conditions: Disorders like hypothyroidism, hypopituitarism, and hyperpituitarism are associated with root resorption.[59] Asthmatics are more prone to external apical resorption of first molars compared to controls.[60]
4) Age: Older patients show greater resorption due to reduced vascularity and narrowed PDL. Younger individuals are less susceptible. Linge et al. 1983 stated that patients who began treatment after the age of 11 exhibited a markedly higher level of OIIRR compared to those who started at a younger age.[61]
5) Dental Age: Incompletely formed roots are less prone to resorption and can achieve near-normal root length, unlike fully formed roots.[62]
6) Sex: No significant differences between males and females.[58,63]
7) Pre-treatment Resorption: Radiographic evidence of pre-existing resorption is the most reliable predictor of risk during orthodontics.[64]
8) Habits: Behaviours such as finger-sucking[65] and nail-biting[66] may contribute to resorption.
9) Tooth Morphology: Blunted or pipette-shaped roots and dilacerated roots are more prone to resorption.[67]
10) Trauma History: Previous trauma, particularly to upper anterior teeth, significantly correlates with root shortening.[65]
11) Endodontic Treatment: Teeth with prior endodontic treatment are more resistant to resorption unless previously traumatized.[68]
12) Bone Density: Reitan 1985 discovered that OIIRR was more likely to occur in areas with denser alveolar bone.[69]
13) Malocclusion: Class III malocclusions, especially post-surgical cases, show significant resorption in lower incisors due to strong forces after mandibular surgery.[70] Class II/II cases experience resorption when incisors are torqued against cortical plates.
14) Specific Teeth: Maxillary lateral incisors are most prone to resorption (1.4 mm on average), followed by central incisors and canines in the upper jaw. In the mandible, the order is canines, lateral incisors, and central incisors. Brezniak and Wasserstein 1993 identified the maxillary lateral and central incisors, mandibular incisors, distal roots of mandibular first molars, mandibular second premolars, and maxillary second premolars as most affected.[71]

4.2.3.2. Mechanical Factors

1) Orthodontic Appliances: The use of rectangular wires and Class II elastics is linked to increased OIIRR.[65] While Sameshima 2001[67] found no significant differences in mechanical factors, he observed variations between practices.
2) Type of Movement: Intrusion movements result in more OIIRR compared to buccal movements.[67]
3) Force Application: Areas of compression are more susceptible than areas of tension.[11]

4) The study by Chan et al.[11] highlighted the effects of light and heavy forces on root surface areas under compression and tension:
   - Compressive forces on the PDL result in greater OIIRR compared to combined compressive and tensile forces or tensile forces alone.
   - Heavy compressive forces on the PDL lead to more OIIRR than lighter compressive forces when both are controlled.
   - Similarly, heavy tensile forces on the PDL cause greater OIIRR than controlled light tensile forces.
   - During buccal tipping forces, the higher compressive stress in the lingual apical regions produces OIIRR per unit area comparable to that in the buccal cervical regions.[11]
5) Force Magnitude: Heavier forces cause more resorption than lighter forces.[36] When light forces are applied, no significant increase in OIIRR is observed within the first 8 weeks. However, with heavy forces, there is a notable rise in resorption between 4 and 8 weeks.[36]
6) Cortical Plate Interaction: Torquing teeth against cortical bone increases the risk of resorption.[72]
7) Treatment Duration: Longer treatment times are associated with increased resorption[67]. Between 8 and 12 weeks, OIIRR significantly increases with both light and heavy orthodontic forces.[36]

4.2.3.3 Causal Factors

1) Tooth Movement: Both physiological and OTM can lead to resorption.[69]
2) External Pressures: Impacted teeth, tumors, or cysts can exert pressure that induces resorption.[69]
3) Infections: Periapical or periodontal infections are known contributors.[69]
4) Tooth Reimplantation: Implantation or reimplantation of teeth can result in resorption.[69]
5) Occlusal Trauma: Excessive occlusal forces may also contribute.[69]
6) Systemic and Metabolic Factors: Various underlying conditions can play a role.[69]
7) Idiopathic Cases: Some instances of resorption occur without an identifiable cause.[69]
8) Bone and Alveolar Changes: Decreases in alveolar bone, bone loss, thinning of bony plates, or expansion of the maxillary sinus are additional factors.[69]

4.2.4 Pathogenesis

Inadequate supply of oxygen at the tissue or cellular level is called hypoxia and this can induce PDL cell death.[5,8] Hypoxia along with loading-induced fluid flow can be considered as the start of signalling to induce the cascade of response that conclude in orthodontic tissue remodelling.[7] Upon teeth movement, interstitial fluid travels through the osteocytes which are mechanoreceptor cells of the bone.[7] This causes strain to the bone extracellular matrix and disrupting the integrins (the transmembrane protein).[7] Integrin stimulation releases intracellular molecules that changes in the gene expression of osteocytes.[7] Hence the formation and resorption of the bone is due to the differentiation of osteoblasts and osteoclasts as a reaction to the osteocyte gene expression.[7] Osteoclasts induce mineral resorption of the cementum and dentine.[5,8]

The cementoid serves as a protective layer on the root surface, resisting clastic cell activity.[12] The outer surface of the root consists of cementoblast layer.[32] Cementoid typically thins out on the compression side. Research has shown that significantly more cementum accumulates on the tension side than on the pressure side of root surfaces during orthodontic movement in monkeys.[11] Heavy forces can lead the PDL on the compression side leading to formation of necrotic tissue.[26] Necrotic tissue attracts macrophage-like cells to degrade the cementoid.[12]The signals generated by the sterile necrotic hyaline tissues activates osteoclasts.[26]

During the remodeling phase of the hyalinized zone, phagocytic cells—including macrophages, foreign body giant cells, and osteoclasts—clear necrotic tissues. This cellular activity can inadvertently damage the adjacent outer surfaces of the root and alveolar bone wall through osteoclastic resorption. Additionally, the exposure of unprotected areas of the cementoid layer on the root and bone leaves these surfaces vulnerable to resorptive cells.[8,11,26]

Resorption begins at the edge of the hyalinized zone, targeting the surrounding cell-free tissue. Research by Brudvik and Rygh[73] revealed that the removal of hyalinized tissue and the resulting resorption are primarily carried out by multinucleated, giant clast-like cells with ruffled borders.[11]

In orthodontics, varying levels of compressive forces influence the type of bone resorption during tooth movement. When compressive forces are high, blood vessels within the PDL at the pressure site become completely obstructed. This blockage can lead to the development of a sterile necrotic area, referred to as hyalinization, which may increase the risk of root surface resorption.[8] Conversely, under lighter physiological compressive forces, the blood vessels are only partially compressed, preventing hyalinization of the PDL. Hyalinization of the PDL in areas subjected to high compressive forces has been observed to last for 1 to 2 weeks. Within this period, a zone of sterile necrosis forms, with no cementoclastic activity detected. OIIRR is primarily developed during the third and fourth weeks of the study.[11] The size of resorption craters is influenced by both the intensity and duration of the applied force.[36]

Under increased stress, the metabolic changes on the compression side were found to be similar to those on the tension side. Both sides showed an increase in cell replication and a decrease in collagen synthesis. However, greater resorption was observed with higher compressive stress levels. Assuming comparable cellular changes between the compression and tension sides, the study revealed more extensive OIIRR in regions subjected to heavy tension compared to those under light tension.[9,11,36]

4.2.4.1 Role of PDL cells

Studies have shown that compressive force (CF) increases the expression of interleukin-6 (IL-6), interleukin-1β, ADAMTS1, cyclooxygenase-2 (COX-2) and osteocalcin. Both constant and intermittent CF elevate SOST, TGFB1, and HEY1 mRNA expression. However, HES1 mRNA and TGF-β signaling, which influence osteogenic differentiation, are enhanced by intermittent CF but not by constant CF.[10]

Additional experiments have reported decreased levels of alkaline phosphatase, a marker of new bone formation, under various force conditions. A reduction in FOXM1 expression under CF was found to promote osteoclastic differentiation and increase the RANKL/OPG ratio. Furthermore, activation of COX-2 and induction of prostaglandin E2 were associated with elevated RANKL levels.[10]

Conversely, cyclic tension upregulated OPG mRNA expression, which inhibits osteoclastogenesis. Transferring this gene to the periodontal area was shown to reduce OTM.[10]

The smaller surface area of apical regions may result in greater stress concentration. In our study, the cervical region exhibited higher OIIRR per unit area compared to apical region; however, this difference was not statistically significant. It was found that increasing the magnitude of force significantly amplified the severity of OIIRR.[11]

Unlike root resorption, bone remodeling operates differently due to the absence of an unmineralized cementoid layer and the presence of immature PDL collagen, which is more conducive to resorption and reorganization.[12] The resorption will stop when the orthodontic force on the tooth is decreases or until the hyaline tissue is all removed.[74] The cementum has the ability to repair itself unless the defect is substantial, which means the damage cannot be fully repaired leading to sustained OIIRR. Unrepaired OIIRR lacunae can lead to sequestration of the apex, and as the apex is resorbed, this process results in external apical root resorption.[8]

OIIRR is involved during hyaline zone elimination.[8,23] The necrotic tissue formed due to orthodontic force application are sterile, therefore activating Macrophage-like cells that lack tartrate-resistant acid phosphatase activity without ruffled borders.[23] Macrophages belong to the hematopoietic lineage and function as scavenger cells to clear necrotic tissues.[23]

While the hyaline (necrotic) tissue is removed, it also destroys the cementoblast layer covering the cementoid which is on the surrounding outer surface of the root.[5]

The hyalinised tissue is removed by the phagocytic cells.[5,8] Due to the indiscriminate action against both necrotic tissue and healthy root tissue, most of the root apex cementum and dentine are resorbed by macrophages, odontoclasts and osteoclasts.[5] The scavenging cells eliminate cementoid and mature collagen which exposes cementum that is susceptible to attack by odontoclastic cells.[8]

Tissue remodelling due to orthodontic loading starts with fibroblasts which is a mechanosensor in the PDL and gingiva.[7] Stress from orthodontic movement of the tooth produces integrins by the fibroblasts and disrupts the extracellular matrix.[7] This leads to signals to alter the gene expression that control proliferation and differentiation that dictates gingival tissue remodelling.[7]

Wei et al.[75] discovered 53 miRNAs with altered expression in PDL cells subjected to pressure compared to those without mechanical force. Of these, 26 were upregulated, while 27 were downregulated. Their findings indicated that changes in miRNA expression profiles are linked to the activation or suppression of osteogenesis, influencing both gene transcription and the production of osteogenic proteins. The mechanical tension exerted on PDL cells impacts miRNA levels, leading to the downregulation of certain genes, which subsequently inhibits bone formation.[10,75]

4.2.4.2 The role of the lncRNA and miRNAs expression

Important findings have highlighted the role of lncRNAs in cell differentiation, development, and osteogenesis pathways, as well as the impact of mechanical forces on their expression levels. LncRNAs are known to function as sponges for microRNAs (miRNAs), potentially interacting with them to regulate their downstream targets. Under mechanical pressure, lncRNAs facilitate osteogenesis by activating several key pathways, including the focal adhesion kinase pathway, the mitogen-activated protein kinase pathway, the TGF-β1/Smad3/HDAC signaling pathway, and by downregulating ANCR expression. Additionally, lncRNAs regulate mRNA expression by enhancing the binding affinity of miRNAs. Wang et al. introduced a novel insight into the complex network involving lncRNAs, miRNAs, and mRNAs in PDL stem cells under tension.[76]

4.2.5 Incidence and Prevalence of OIIRR

During comprehensive orthodontic treatment, the average OIIRR of maxillary incisors is typically less than 1.5 mm. However, approximately 5% of adults and 2% of adolescents may experience resorption exceeding 5 mm in at least one tooth during active treatment.[77] Anterior teeth, particularly maxillary central and lateral incisors, are at a greater risk of OIIRR compared to posterior teeth.[6] Around 7% of patients have at least one tooth with OIIRR exceeding 4 mm, though no more than three teeth per patient are affected to this extent.

Yong et al. 2022 states that OIIRR occurs in 80% of the orthodontically treated patients.[5] Histologically, it may be more than 90%.[8] Radiographic detection methods report a prevalence ranging between 44% and 91%.[8]

Yeoh et al. noted that the occurrence of OIIRR has been documented in 22–100% of orthodontic patients, with an average root length loss of 1–2 mm.[26] In most cases, root shortening does not exceed 2 mm. Severe OIIRR, defined as a loss exceeding one-quarter of the root length or more than 5 mm, is uncommon and affects only 1–5% of patients undergoing orthodontic treatment.[22,26]

Before treatment, 15% of incisors exhibit root resorption, which increases to 73% following orthodontic treatment.[78] Ten years after orthodontic therapy, radiographic analysis shows OIIRR in 28% of incisors overall, with 42% affecting upper central incisors, 38% involving upper lateral incisors, and 17% seen in lower incisors. In comparison, the control group shows only 3% root resorption.[79]

4.2.6 Classification and Grading of OIIRR

4.2.6.1 The Three levels of severity of OIIRR:

1) The resorption of the outer cemental surfaces of the root which later gets remodelled or fully regenerated.[23]
2) The resorption of the cementum and outer layer of the dentin. The repair process may not result in the final shape of the root to be same as the initial root form.[23]
3) The circumferential resorption of the apical root leading to shortened root. The hard tissues of the root apex beneath the cementum are lost therefore cannot be regenerated. The cemental layer repair overtime.[23]

4.2.6.2 The Four grades that categorises the level of root resorption:

This was introduced by Malmgren et al. in 1982 to quantitatively assess OIIRR detected through radiography:[8]

1) Grade 1 signifies a detection of irregular root contour
2) Grade 2 indicates minor resorption totalling less than 2 mm from the root apex,
3) Grade 3 represents severe resorption ranging from 2 mm to one-third of the original root length
4) Grade 4 reflects extreme resorption exceeding one-third of the original root length.[8]

4.2.7 Location of OIIRR

The apical third of the root is notably prone to iatrogenic damage due to orthodontic procedures.[8] This is because periapical cementum is more fragile and susceptible to injury, when subjected to excessive forces leading to vascular stasis.[8] The apical portion of the cementum shows decreased hardness and elastic modulus compared to the cervical region, which makes it more susceptible to OIIRR.[8]

4.3 Management

Management of OIIRR involves several key strategies to minimize risks and address potential issues during orthodontic treatment. Patients should be informed about the risk of OIIRR before treatment begins, ensuring they understand the potential outcomes. It is important to obtain informed consent after reviewing the patient’s medical and dental history, as well as assessing risk factors such as a family history of OIIRR or evidence of pre-existing resorbed roots.

Close monitoring is essential, with regular radiographic evaluations, such as orthopantomograms, recommended every six months.[80] Studies by Smale and Artun 2005[81] show that OIIRR can become evident as early as nine weeks into treatment, and those who display early signs are more likely to experience severe resorption. Levander and Malgren 1988[80] also suggest taking OPGs every six to nine months to ensure thorough monitoring. If resorption is detected, an additional radiograph should be taken three months later to monitor its progression.[80]

In cases of extensive OIIRR, incorporating treatment pauses into the orthodontic plan may allow time for tissue recovery, as suggested by Acar et al.[82].

To further reduce risks, treatment duration should be minimized when possible, even if it means accepting slightly compromised results, as Brezniak and Wasserstein 1993[71] recommend. Additionally, the use of lighter forces and the avoidance of intermaxillary elastics are crucial to decrease jiggling forces and reduce the likelihood of occlusal trauma, as highlighted by Linge 1991[65].

By implementing these management strategies, orthodontic treatment can be adjusted to mitigate the risks associated with OIIRR while still achieving favourable outcomes.

4.4 Pharmacological interventions

Research into the prevention of OIIRR during orthodontic treatment has explored several pharmacological interventions, with varying outcomes. Animal studies done by Haugland et al. 2018[74] showed that use of fluoride, thyroxine and steroids decreased OIIRR.[43]

Low doses of L-thyroxine have been shown to significantly reduce OIIRR by 50% in rats, as reported by Loberg et al.1994.[83] Similarly, bisphosphonates have demonstrated a dose-dependent inhibitory effect on OIIRR following force application in rats, according to studies by Igarashi et al. 1994.[84] However, other research indicates that bisphosphonates may, in some cases, increase the risk of OIIRR.[85]

Orthodontic treatment takes longer for patients undergoing bisphosphonate therapy because these medications hinder osteoclastic resorption.[86] Corticosteroids have also been studied, with their effects on OIIRR appearing dose-dependent. High doses, such as 15 mg/kg administered to rats, were found to increase OIIRR, while lower doses, such as 1 mg/kg, reduced it. These findings suggest that certain medications may have potential in mitigating OIIRR, though further research is needed to establish safe and effective protocols for clinical use.[43]

4.5 Prevention

Identifying OIIRR at an early stage is essential, as it has the potential to reverse once the contributing orthodontic forces are eliminated.[8] A decreased crown-to-root ratio caused by significant OIIRR can notably affect the long-term viability of the affected teeth, potentially resulting in tooth loss and negatively impacting the patient's quality of life, particularly when periodontal issues or trauma are present.[10,22,28,87]

Various strategies have been suggested to mitigate the risk of OIIRR. These include conducting a thorough pretreatment evaluation of familial and medical history.[26]

Prevention of OIIRR can be achieved by lowering the patient-related risk variables by employing lighter orthodontic forces, non-extraction approach when appropriate, extending activation intervals, reducing the active treatment duration, and radiographic monitoring 6 months after the initiation of orthodontic treatment.[8,26] Pausing the treatment for two to three months by applying a passive archwire in specific cases to facilitate repair[8] has also been recommended if early signs of OIIRR seen.[8] Studies have also explored the use of intermittent forces to minimize OIIRR. However, this method often results in less effective tooth movement and inconvenient for patients in clinical setting as intermittent force regimens require frequent reactivations daily or weekly.[32]

Study by Ozkalayci et al. 2018[32] showed that continuous force, when applied over a span of 15 weeks, results in a higher degree of OIIRR compared to an intermittent force regimen of 28 days on and 7 days off. For individuals susceptible to OIIRR, adopting the intermittent force approach of 28 days on and 7 days with the use of passive archwires during inactive periods has been strongly recommended.[32]

4.6 Research Methods for Investigation and Evaluation of OIIRR

As OIIRR is an iatrogenic damage that is considered an undesirable side effect of orthodontic treatment which in severe case, can result in tooth loss therefore, early detection is important.[8] If OIIRR is detected early, the treatment can be paused, and the OIIRR process may potentially be reversed.[8] Yazid et al. 2020 used both radiographs and biological markers to detect OIIRR.[8] Traditional radiographic techniques for diagnosing OIIRR have notable limitations[55], including structural superimposition, magnification errors, repeated exposure to ionizing radiation, and an inability to detect early-stage OIIRR.[8] Due to these drawbacks, researchers have proposed biomarkers as a potentially more accurate, sensitive, and safer diagnostic alternative.[8]

4.6.1 Biomarkers

Biomarkers can be regarded as a safer and more sensitive option for the early detection of OIIRR. The molecules—such as inflammatory cytokines, osteoprotegerin (a key regulator of bone metabolism), and dentine sialophosphoprotein—are released during orthodontic tooth movement (OTM) and serve as valuable biological indicators of tissue response. Common sampling techniques, such as analyzing whole saliva and gingival crevicular fluid, are utilized to isolate and identify these biomarkers.[8,88]

4.6.2 Radiography

This is the most common and the primary method to investigate OIIRR. Periapical or panoramic film is taken of patients at risk of OIIRR, however 3D imaging such as CBCT scans are not recommended unless specifically indicated due to concerns regarding radiation exposure and associated costs.[8]

4.6.2.1 Panoramic radiograph

Panoramic radiograph is easily accessible, offers cost-effective and time efficient method of detection of pathology.[8] It has relatively lower radiation exposure compared to a CBCT scan. It has its limitations in assessment of the severity of OIIRR.[89] When compared to periapical radiographs, a panoramic film was more challenging in evaluating root morphology and showed higher overall level of OIIRR in the apical region in comparison to periapical films.[8,89] The quality of panoramic films depends on the patient positioning by the clinician, which can result in unfocused or invisible root apices and palatal structures.[55] This is seen particularly in the anterior regions due to the narrow focal trough in the incisor area.[8,55] In cases where patients have excessively proclined or retroclined teeth, the roots of the anterior teeth may appear either shortened or magnified because the labial segments cannot fit into the focal trough.[90] This can lead to a misleading positive result, creating a false impression of more extensive OIIRR in the labial segments.[8]

4.6.2.2 Periapical radiographs

Periapical radiographs are commonly used to evaluate the degree of root resorption.[22] However, their reliability and precision can be compromised by several factors, particularly the positioning of the film and the alignment of the X-ray tube.[22,90]

However, periapical radiographs can capture find details of the root surface and has reduced distortion compared to panoramic films. Therefore, periapical radiographs offered greater precision and accuracy than panoramic films in quantifying the extent of OIIRR.[8]

Regularly obtaining identical radiographs poses a challenge in orthodontics because teeth undergo movement throughout treatment, and alterations in angulation can lead to projection errors.[8,55]

4.6.2.3 Lateral cephalograms

Lateral cephalometry is a highly reproducible radiographic technique for displaying the lengths of the upper and lower incisors. However, it has the drawback of overlapping the left and right sides, which makes it less effective for diagnosing OIIRR.[8]

Lateral cephalograms are subject to an inherent magnification of approximately 5–12% as a result of radiographic projection geometry.[90] In a retrospective study assessing OIIRR of upper central incisors with pre- and post-treatment lateral cephalograms, it was observed that the majority of participants (84%) had only minor root loss following orthodontic treatment.[8]

The authors acknowledged that accurately identifying the worn edges of the upper incisors and the root apices on the radiograph was challenging due to the superimposition of adjacent teeth.[8]

4.6.3 Cone Beam Computed Tomography (CBCT)

A CBCT is superior and more precise technique for detection of OIIRR as it is less technique sensitive when it comes to patient positioning variations and free from the anatomical structure overlap which allows accurate measurement of the OIIRR.[8,54,55]

CBCT images can detect and quantify OIIRR linearly. CBCT images surpass periapical radiographs as it could generate distortion-free and reproducible images, particularly beneficial for single-rooted teeth.[8,55]

In a prospective study examining the incidence and severity of OIIRR across all tooth roots, from incisors to molars, using CBCT, it was found that 91% of 152 patients showed some degree of root shortening.[8,54] Additionally, 15% of the palatal root surfaces exhibited slanted OIIRR, which could only be detected using 3D imaging.[54] While large resorptive areas were easily identified by all imaging techniques, low-grade resorption, particularly Grade 1, was only detectable with CBCT.[8,54]

A study[53] evaluated the accuracy of 2D imaging techniques (periapical and panoramic radiographs) versus 3D imaging (CBCT) by using a histologically analyzed extracted deciduous canine as the reference standard.[8,53] While all techniques were capable of diagnosing large defects, only the CBCT scan was able to detect low-grade OIIRR.[8,53]

However, CBCT has its drawbacks, including higher costs compared to conventional 2D radiographs.[53] Furthermore, the detection of minor resorption defects may not be clinically significant.[53] Therefore, it is essential to weigh the risks and benefits before opting for a CBCT scan, and it should generally be reserved for higher-risk patients.[8,53]

Continuously monitoring OIIRR necessitates repeated radiation exposure for patients, and CBCT has higher radiation dosage compared the 2D radiographs. This pose concerns for children and adolescents. Their heightened tissue metabolism renders them more sensitive to the risk of radiation-induced carcinogenesis.[8]

4.6.4 Histologic analysis (2D)

In a clinical trial by Owman-Moll et al.[91], an intraindividual design was used to assess the effects of light (50 cN) and heavy (100 cN) orthodontic forces on adverse tissue responses, such as OIIRR, in maxillary first premolars. Histological analysis revealed no significant difference in the extent or depth of resorption between the two force levels. The discrepancies between the findings of Owman-Moll et al. and those of the present study may be attributed to methodological differences. While recent studies have assessed the mechanical properties of root cementum—such as hardness and elasticity—across all regions to evaluate susceptibility to resorption, the study by Owman-Moll et al. relied on a limited number of tooth sections and two-dimensional observations, which may not have fully captured the extent of OIIRR.[39]

Chan and Darendeliler 2004[92] critiqued the methodology used by Owman-Moll et al. 1996[91], highlighting the potential for inaccuracies in assessing OIIRR craters. They noted that due to significant variations in the size and depth of resorption craters, irregular C-shaped craters and smaller craters might have been partially or entirely overlooked or inaccurately measured. This limitation could have affected the reliability of the conclusions regarding OIIRR.[39]

Part 5: Accelerated Tooth Movement

5.1 Introduction

The risk of OIIRR gets higher with longer orthodontic treatment times.

In recent years, both surgical and non-surgical adjunctive procedures within orthodontics to reduce treatment time has become increasingly common. This is particularly evident in cases involving adult patients, such as managing ectopic canines and closing extraction spaces, where treatment duration tends to be prolonged.[13] There are few accelerated orthodontic treatment methods to reduce treatment times. The current available methods can be divided into surgical or non-surgical interventions.[14]

5.2 Methods to accelerate orthodontic treatment

Various methods to accelerate tooth movement have been proposed, categorized into biological, surgical, and physical approaches:[12]

1. Biological Methods: Involve injecting key molecules into the periodontium to promote paradental tissue remodeling. However, this requires multiple injections and increases the risk of OIIRR.[12]
2. Surgical Methods: Based on the Regional Acceleratory Phenomenon (RAP) theory, these techniques aim to enhance tissue remodeling and reduce bone density. While effective, they carry risks of surgical complications such as pain, swelling, and potential loss of tooth vitality.[18]
3. Physical Approaches: Include Low-level laser therapy (LLLT) or vibration. Although their efficacy remains debated, these methods are noninvasive, painless, and free from significant complications, making them appealing alternatives.[12]

5.3 Non-surgical Method with Pharmacological agents

Pharmacological agents have the potential to influence the biochemical mechanisms underlying tooth movement. By targeting the hormones and mediators responsible for bone remodeling, calcium regulation, and inflammatory processes, it is possible to accelerate tooth movement. This is achieved by enhancing osteoclastic activity or suppressing osteoblastic activity.[14]

Animal studies showed that increase in tooth movement have been observed in orthodontic treatment involving corticosteroid hormones, vitamin D3, parathyroid hormone and thyroxin. However, the pain after weekly injection of the drugs is a strong deterrent of its use in orthodontics.[14]

5.3.1 Parathyroid hormone

A key regulator of bone remodeling and calcium homeostasis has been shown in animal studies to significantly speed up orthodontic tooth movement. Continuous global infusion or chronic local injections of this hormone have increased the rate of movement by 1.6 to 2 times while also elevating osteoblast numbers.[93]

5.3.2 Vitamin D3

1,25-dihydroxy vitamin D3, plays a role in calcium absorption in the intestines and bone remodeling. Animal research has demonstrated that local injections of vitamin D3 can accelerate tooth movement by 1.2 to 2.5 times.[94,95] Histological studies reveal that vitamin D3 promotes osteoclast formation in a dose-dependent manner, synergizing with mechanical force to cause notable alveolar bone resorption. At the same time, osteoblast activity and bone formation are elevated, creating a balanced effect on bone remodeling.[96]

5.3.3 Prostaglandins

Prostaglandins are local lipid inflammatory factors, which play a critical role in regulating bone remodeling.[97] Research on animals has demonstrated that localized application of prostaglandins such as PGE1, PGE2, or their analogues significantly accelerates orthodontic tooth movement.[98] Human studies, including trials involving the application of prostaglandins, suggest a similar potential for faster tooth movement.[98] Submucosal injections of PGE1 in human patients have been shown to speed up tooth movement by approximately 1.6 times.[97] However, clinical use of prostaglandins raises concerns, particularly regarding pain induction and the potential for increased OIIRR alongside accelerated movement. Moreover, drugs that inhibit prostaglandin action, such as Non-Steroidal Anti-Inflammatory Drug, have been found to slow down tooth movement, as shown in additional animal studies.[14,99]

5.3.4 Autologous platelet-rich plasma (PRP)

PRP is injected submucosally to orthodontically accelerate teeth movement[14] by leveraging platelets' role in initiating soft and hard tissue healing. Submucosal injections of PRP have been used to accelerate tooth alignment in cases of anterior crowding. While this technique has shown promising results in speeding up tooth movement, approximately 15% of patients reported experiencing severe pain following the injection.[14]

5.3.5 Growth factors

Platelet-derived growth factor, transforming growth factor, and endothelial growth factors are in platelets which assist in bone healing and formation. However, patients felt severe discomfort after injection.[14]

5.3.6 Limitations Pharmacological agents

Pharmacological methods for accelerating OTM remain largely unsuitable for routine clinical use. This is due to several challenges, including concerns about their practical application, variability in effectiveness, and potential risks to general health and safety.[100]

5.4 Low-intensity laser/ low-level laser therapy (LLLT)

LLLT at the cellular level, stimulates an increase in RANKL within the PDL.[14,100] This promotes the differentiation of precursor cells into activated osteoclasts, potentially accelerating OTM[14] Several clinical trials reported a beneficial impact of laser irradiation on the speed of canine movement into premolar extraction sites.[14,100] However, when employing different laser application protocols with lower energy density compared to other studies, contradictory findings resulted.[14,101] These studies found no discernible difference between the laser-treated groups and control groups regarding the rate of OTM.[101] Another important factor to consider is that the energy output of the laser may vary across different animal species used in clinical trials.[14,100,102]

LLLT, also referred to as photobiomodulation, utilizes red or near-infrared lasers with wavelengths ranging from 600 to 1000 nm.[14,30] This wavelength range enables the laser to penetrate deeply into tissues without generating heat or causing discomfort.[30,103,104] Photobiomodulation exerts biostimulatory or bioinhibitory effects, offering therapeutic advantages such as alleviating pain and enhancing tissue healing.[104,105]

LLLT works by transferring light energy into deeper tissues, where it modulates specific biological processes.[103,106] This therapy stimulates cellular activity, enhancing metabolism and promoting overall biostimulation.[30,106] It also improves blood circulation and induces vasodilation, facilitating better oxygen and nutrient delivery to the tissues.[103,104] Additionally, LLLT increases adenosine triphosphate (ATP) production within cells, providing them with the energy required for repair and regeneration.[104,107] Beyond these effects, LLLT also has an analgesic impact, offering pain relief, and exhibits anti-inflammatory and anti-edematous properties, which help reduce swelling and inflammation in treated areas.[104-106,108]

When a laser interacts with target tissue, it emits photons that are absorbed by cellular components, particularly cytochrome C within the mitochondria.[109] This interaction influences various cellular pathways.[109] In the inflammation pathway, LLLT enhances the production of nitric oxide (NO), which promotes vasodilation and increases the delivery of oxygen, nutrients, and other metabolites to the affected area, aiding in the resolution of inflammation.[106,108] Regarding the pain pathway, LLLT has a selective inhibitory effect on pain receptors, creating a reversible neural blockade.[105,106] It also stimulates the production of endogenous pain-relieving substances such as nitric oxide, serotonin, acetylcholine, and opioids.[105,106] In terms of healing, LLLT stimulates mitochondrial activity, boosting the production of ATP, the primary energy source for cells.[105,107] This reduces oxidative stress and accelerates the healing process.[105] Recent studies have also highlighted LLLT's ability to accelerate tooth movement by influencing the RANK/RANKL/OPG system, which regulates osteoclast differentiation and plays a critical role in bone remodeling.[30,104]

5.4.1 Animal Studies

LLLT has been studied extensively in animal models to evaluate its effects on bone remodeling during orthodontic tooth movement.[30] Kawasaki et al.[110] conducted a study using a Gallium-Aluminium-Arsenide laser with a wavelength of 830 nm at 100mW. The laser was applied at three points for three minutes each (a total of 9 minutes and 54 Joules) over a 12-day period. The results showed a 1.3-fold increase in tooth movement.[110] On the compression side, there was a 1.6-fold increase in the number of osteoclasts, while the tension side exhibited enhanced bone formation and cellular proliferation. These findings suggest that LLLT facilitates bone remodeling by increasing cellular activity in response to mechanical forces.[110]

Altan et al.[111] further explored LLLT's effects by examining metrical and histological changes during tooth movement. Their study revealed a significant increase in osteoclasts, osteoblasts, inflammatory cells, capillary vascularization, and new bone formation in the laser-treated group (Group II) compared to controls ($p < 0.05$).[111] Immunohistochemical staining also demonstrated stronger RANKL immunoreactivity in the treated group, indicating enhanced osteoclastic activity. These findings support the idea that LLLT accelerates the bone remodeling process by promoting the proliferation and function of osteoblasts and osteoclasts.[111] However, while the results indicated a positive effect on bone remodeling, the small sample size limited the reliability of the findings.[30]

5.4.2 Human Studies

Mistry et al.[30] conducted a triple-blind, split-mouth, randomized controlled trial to evaluate the effects of LLLT on the rate of orthodontic tooth movement.[30] The study used a gallium aluminium arsenide (GaAlAs) laser with a wavelength of 808 nm, power output of 0.2 W, and an irradiance of 1.97 W/cm² in continuous wave mode, delivering 13 J per session. Laser applications were performed every 4 weeks, with measurements taken after 12 weeks.[30]

The study included 21 participants, and the laser was applied at 8 points—4 on the buccal surface and 4 on the palatal surface.[30]

Results showed no significant difference in the amount of tooth movement between the LLLT group (2.55 ± 0.73 mm) and the control group (2.30 ± 0.86 mm) over the 12-week period. Additionally, no differences were observed in anchorage loss or canine rotation between the two groups.[30]

Ge et al.[112] conducted a systematic review and meta-analysis to evaluate the efficacy of LLLT in accelerating OTM. The review analyzed 9 studies, of which 5 were classified as having a medium risk of bias and 4 as having a high risk of bias.

The results indicated that LLLT could accelerate orthodontic tooth movement. Specifically:

- At 7 days, the mean difference was 0.19 mm/month (95% CI [0.02, 0.37], p = 0.03).
- At 2 months, the mean difference was 1.08 mm (95% CI [0.16, 2.01], p = 0.02).
- Marginal significance was observed at 3 months, with a mean difference of 0.49 mm (95% CI [0.00, 0.98], p = 0.05).

The study also noted that relatively lower energy densities, such as 5 and 8 J/cm², appeared to be more effective than higher doses, such as 20 and 25 J/cm². However, the optimal energy dose for LLLT remains undetermined.

Additionally, the cumulative tooth movement was significantly greater in all low-energy density subgroups, while no significant difference was found between the LLLT group and the control/placebo group in the high-energy density subgroups.[112]

5.5 Other non-surgical methods for orthodontic treatment

This includes photobiomodulation (PBM), electromagnetic fields, and direct electrical currents.[14]

More high-quality research is needed to confirm the effectiveness and safety of these techniques. Therefore, dual therapy—combination of adjunctive methods with conventional orthodontic treatment—is not yet considered standard practice and remains experimental at this stage.[14]

5.6 Surgical Methods

The definition of surgically assisted orthodontics aimed at accelerating orthodontic treatment is any surgical technique involving the operation on the interseptal bone, alveolar bone, and cortical bone to facilitate distraction of the PDL and osteogenesis at the osteotomy site.[13]

5.6.1 Micro-osteoperforations (MOP)

MOP represent one of the less invasive methods for inducing trauma by perforating the mucosa and adjacent bone near the teeth that require accelerated movement.[14] This is typically done using a disposable stainless-steel screw, targeting three locations adjacent to the teeth intended for movement. A randomized clinical trial by Alikhani et al. 2013[113] reported a 2.3-fold acceleration in canine retraction using this method.[113] However, contrasting results were noted in a study conducted with dogs, where no difference in the rate of tooth movement was found.[14] However, the effect of micro-osteoperforations was only confined to cortical bone rather than the medullary bone.[14]

5.6.2 Piezocision

Piezocision involves making an incision in the buccal gingiva, followed by further incisions using a Piezo surgical knife into the buccal cortical bone.[14,27,114] It is a variation of corticotomy that is less invasive.[115] Recent studies have demonstrated that piezocision can speed up tooth movement with results comparable to those of corticotomy, while also offering the advantage of being less invasive.[13,16,116]

5.6.3 Corticotomies

The clinician makes shallow perforations or cuts in the cortical alveolar bone during corticotomy procedure, while leaving the trabecular or medullary bone intact. This differs from an osteotomy, where the bone is cut completely through.[14] Studies by Aboul-Ela et al. (2011) and Leethanakul et al. (2014) found that three months after the corticotomy procedure, tooth movement increased by an average of 2.03 mm compared to non-surgical methods.[13]

5.6.4 Osteotomies/PDL distraction

A less invasive osteotomy method involves reducing the interseptal bone in an extraction socket distal to the tooth intended for retraction.[14] A study employing a split-mouth design reported approximately 1.5 times faster canine movement over three months compared to a contralateral control side. However, once the surgical effect subsided, any further accelerated retraction of teeth, aside from canines, was unlikely without additional surgery.[14]

An alternative, more invasive osteotomy approach involves rapid canine retraction through dentoalveolar distraction.[14] This method includes extracting a premolar as well as removal of its overlying buccal bone. The larger osteotomies are employed to completely mobilize the alveolar segment, including the canine, by fracturing the surrounding spongy bone around its root from the lingual or palatal cortex.[14] However, both techniques have limitations as they are mainly suitable for retracting canines after the extraction of first premolars. They cannot be broadly applied to the movement of multiple teeth.[14]

5.7 Macrosurgery: Corticotomy

A corticotomy is defined as a surgical procedure in which only the cortical bone is cut, perforated, or mechanically altered.[117] The concept of corticotomy-facilitated orthodontics was first described by Kole in 1959[118]. Kole introduced the term “bony block” to describe the presumed mechanism of tooth movement following corticotomy.[118]

Decades later, Wilcko et al.[119] revisited this concept using Computed Tomography (CT) imaging and proposed a different explanation for the rapid tooth movement observed with corticotomy-facilitated orthodontics.[119] Wilcko demonstrated that the process was more likely due to a demineralization and remineralization cycle associated with the initial phase of the RAP.[119] This phase is characterized by increased cortical bone porosity and higher turnover of trabecular bone surfaces due to elevated osteoclastic activity.[119]

The Wilcko brothers played a significant role in popularizing the corticotomy procedure for orthodontic tooth movement.[119] Through their technique, known as "Periodontally Accelerated Osteogenic Orthodontics (PAOO)", they claimed a reduction in total treatment time to one-quarter to one-third of conventional non-extraction and extraction methods.[119]

5.7.1 Technique:

The PAOO procedure begins with the raising of labial and lingual full-thickness flaps to fully expose the alveolar bone. A bur is then used to create labial and lingual "decorticating" incisions in the alveolar bone cortical plates of the anterior and premolar regions. Once the decortication is complete, a bone allograft is applied to the decorticated areas, and the flaps are closed.[119]

Gil et al.[120] done a systematic review on Alveolar Corticotomies for Accelerated Orthodontics. Their review reported a mean total treatment time of 8.85 months (range: 4–20 months) for corticotomy-facilitated orthodontic cases, compared to 16.4 months (range: 7.8–28.3 months) for control groups.[120] This demonstrates a significant reduction in treatment duration for corticotomy cases.[120]

Gil et al. concluded that corticotomy-facilitated orthodontics was found to decrease overall treatment time.[120] However, the evidence supporting this conclusion is of low quality. The systematic review included only three randomized controlled trials (RCTs), as well as prospective randomized clinical trials and case series, highlighting the need for more robust research in this area. [120]

Fleming et al.[13] completed a review on surgical methods to speed up orthodontic treatment. This analysis included four RCTs with a total of 57 participants aged between 11 and 33 years, focusing primarily on the speed of tooth movement. They found that surgically assisted orthodontic treatments showed a slight increase in the rate of tooth movement compared to standard treatments over one- and three-month periods.[13]
However, the reliability of these results is limited due to the small sample size and the low quality of the included studies.

5.7.2 Other Side effects

Throughout the treatment period, Wilcko et al.[119] reported no notable periodontal complications were detected. Tooth vitality remained intact, there were no alterations in alveolar crest height, and the periapical radiographs showed no significant evidence of apical root resorption.[121]

5.7.3 Potential Complications

However, while corticotomy-assisted OTM is known for its effectiveness and predictability, it is a highly invasive approach.[121] The procedure requires substantial flap elevation and bone surgery, which may result in post-operative discomfort and potential complications.[121] There was increase in OIIRR detected on animals with corticotomy performed during treatment.[43]

5.8 Microsurgery: Micro-osseous Perforation (MOP)

MOP is a minimally invasive technique that involves creating small perforations in the cortical bone using tools such as a miniscrew, without requiring a surgical flap. This procedure, which can be performed by orthodontists using standard orthodontic tools, aims to accelerate the rate of tooth movement.[113]

The technique was first developed by a research team at New York University, who conducted and published several animal studies on its effectiveness. This was followed by a small clinical trial, published by Alikhani et al.[113]. The approach is now commercially marketed under the brand name "Propel".[113]

Shahabee et al.[122] completed at systematic review on the effect of MOP on the Rate of Orthodontic Tooth Movement.

This systematic review included six randomized controlled trials that were analyzed in the meta-analysis. Most studies focused on the rate of canine retraction over a four-week period, with sliding mechanics used in all trials to retract the canine. The MOPs were applied distal to the canine teeth.[122]

There was considerable variation in how MOPs were performed, with some studies using the PROPEL device (PROPEL Orthodontics; 25 Corporate Drive, Suite 110, Burlington, MA 01803, USA) and others employing miniscrews to induce trauma. Additionally, no two trials used the same method to measure tooth movement.[122]

Findings: The MOP group showed a significantly faster rate of canine retraction, with a mean difference of 0.45 mm per month. This increased rate was consistent regardless of malocclusion type, jaw location, or the method of MOP application. Patients did not report significant differences in pain levels after undergoing MOP. However, a systematic review by Dab et al.[123] assessed root resorption six months following accelerated osteogenic orthodontic treatment. The study found a statistically significant increase in root resorption within the intervention group.[15,122,123]

Sivarajan et al.[124] completed at systematic review on micro-osteoperforations and its effect on rate of orthodontic tooth movement.[124]

This systematic review included eight randomized controlled trials, with a meta-analysis conducted on two homogenous studies.[124]

The meta-analysis of these two low-risk-of-bias studies found no significant effect of a single application of MOPs over a short observation period. However, the overall quality of the evidence was low. Evidence regarding the impact of MOPs on total treatment duration, the formation of black triangles, and the risk of bacteremia remains insufficient.[124]

Additionally, low-quality evidence suggested that MOPs do not influence pain levels, gingival recession, or OIIRR.[124]

5.9 Other Clinical Factors to Consider

The "surgery first" approach leverages the RAP by performing orthognathic surgery first, followed by orthodontic appliance therapy shortly afterward.[14] This approach initiates RAP, enabling more rapid tooth alignment.[14] However, this effect diminishes after two to three months. While numerous case reports describe the benefits of this method, there is currently no high-quality evidence to support its efficacy.[14]

Part 6: Mechanical vibration

6.1 Introduction

Two key theories underpin this concept: piezoelectricity within the alveolar bone and the pressure-tension theory within the PDL.[12,14] Piezoelectric forces, generated by orthodontic stress, cause bending in the alveolar bone, producing an electrical charge that triggers an osteogenic response.[14] Notably, these charges are created only during the application and release of stress, suggesting that continuous orthodontic forces may not be optimal for maximizing this effect.[12,14] Vibrational appliances, which apply and release forces rapidly, could help generate stress-induced electrical charges more effectively.[12,14]

6.2 Definition

Mechanical vibration of teeth involves rapid application and release of forces. A piezoelectric charge is formed when a pulsating, non-continuous stress is applied and released on alveolar bone which leads to osteogenic response.[14] In theory, vibration appliances induce these electrical charges to accelerate orthodontic movement.

6.3 Mechnism of Action

Mechanical vibration has been proposed as a potential method for accelerating OTM.[22] Vibration impacts bone remodeling in two primary ways: it stimulates both osteogenesis (bone formation) and osteoclastogenesis (bone resorption).[12]

Vibration is considered a safe medical technique to stimulate osteogenesis, aiding in the prevention of bone loss and the improvement of bone density in long bones.[12,14]

However, its effectiveness in promoting osteoclastogenesis and speeding up tooth movement during orthodontic treatment remains uncertain and debated.[12]

HFV has been found to enhance the release of inflammatory cytokines and boost osteoclast activity, leading to faster tooth movement in animal studies. Low-frequency vibration has been shown to have no impact on tooth movement in animal models.[12]

Mechanical vibration helps distribute stress within the PDL and promotes increased expression of receptor activator of nuclear factor kappa-B ligand (RANKL) in fibroblasts and osteoclasts, which Yilmaz et al. suggested the potential to lessen the occurrence of OIIRR.[22]

In vitro study has shown that mechanical vibration enhances the expression of PGE2, RANKL, interleukin-6 (IL-6), and interleukin-8 (IL-8) in compressed human PDL cells.[22] Additionally, a clinical study found that applying light force combined with HFV increases Interleukin-1 beta secretion in gingival crevicular fluid, facilitating faster tooth movement.[12]

6.4 Effects of Mechanical Vibration in OTM

6.4.1 Animal studies

Darendeliler et al.[125] investigated the impact of high-frequency, low-magnitude vibration on bone metabolism in 44 Wistar rats using magnets and a pulsed electromagnetic field. They hypothesized that, given prior evidence showing increased anabolic activity in bone under similar conditions, vibration might also enhance the rate of tooth movement. Similarly, Nishimura et al.[25] demonstrated in a rat model that molar vibration significantly accelerated tooth movement compared to a non-vibration control group. These findings suggest that vibration-induced stimulation holds promise as a tool for increasing the efficiency of orthodontic treatments.

6.4.2 Human studies

Recent cochrane review and randomised control trials of the mechanical vibration appliance showed no significant supportive evidence that vibrational force could notably accelerate the process of initial tooth alignment.[14,22]

El-Angbawi et al.[126], through a Cochrane review, evaluated non-surgical adjunctive methods aimed at accelerating tooth movement in patients undergoing fixed orthodontic treatment. This review included two studies that examined the effects of devices applying light vibrational forces. The first study investigated the "Tooth Masseuse," (DynaFlex; 8050 Hawk Ridge Trail, Lake St. Louis, MO 63367, USA) used during alignment in patients with conventional fixed appliances, while the second focused on "OrthoAccel," (OrthoAccel Technologies, Inc.; 6575 West Loop

South, Suite 200, Bellaire, TX 77401, USA) employed during space closure with fixed appliances.

Both studies assessed three primary outcomes: the rate of tooth movement, patient-reported pain and discomfort, and potential unwanted side effects. However, the review highlighted a significant gap in high-quality clinical research on the effectiveness of non-surgical approaches to accelerating orthodontic treatment. The existing evidence is of very low quality, making it inconclusive whether the application of vibrational forces has a beneficial or detrimental impact on the rate of tooth movement, treatment duration, or patient experience.[126]

Lyu et al.[127] conducted a systematic review to evaluate the effectiveness of vibrational forces in reducing orthodontic pain. The review included 15 randomized controlled trials and concluded that there is insufficient evidence to support the claim that supplemental vibrational forces provide a clinical advantage in enhancing tooth movement, alleviating orthodontic pain, or minimizing OIIRR.[127]

Similarly, Aljabaa et al.[128] performed a systematic review to investigate whether vibrational devices could accelerate OTM or reduce pain associated with treatment. This review included six studies derived from five RCTs. The findings revealed that, with the exception of one study,[129] there was no significant benefit observed from using vibrational devices during orthodontic treatment.[128]

6.5 Effects of Mechanical Vibration in OIIRR

6.5.1 Animal studies

In a split-mouth study involving 36 male Wistar rats, Tangtanawat et al. demonstrated that applying HFV promotes faster tooth movement without inducing OIIRR. When combined with light force, HFV accelerates tooth movement more effectively than optimal force alone, while still preventing OIIRR in rats.[12]

Using a frequency of 70 Hz with a 15 g force in a rat model showed no differences in OIIRR area compared to the application of force alone.[12]

Tangtanawat et al. found that mechanical vibration at 125 Hz alongside light force can effectively accelerate tooth movement without inducing OIIRR.[12]

Study revealed that applying the optimal force, both with and without HFV, was linked to a significantly greater OIIRR area compared to light force application.[12]

This combination of HFV and light force offers potential advantages in orthodontic treatment by enhancing tooth movement while maintaining a higher safety profile.[12]

Several limitations should be noted, as this study was conducted using a rat model. There are notable differences between human and rat bone remodeling processes. In humans, the bone remodeling cycle lasts from 1-2 weeks to 2-3 months, while in rats, it occurs within approximately 6 days.[12]

Nishimura et al. reported that applying a resonance vibration frequency of 60 Hz to rat molars not only enhanced tooth movement but also showed no further OIIRR in vibrated teeth. However, studies investigating the impact of mechanical vibration on OIIRR remain limited.[25]

Yeoh et al. did a study on rats with a heavy force of 100 g, which was deliberately selected to emphasize the potential of mechanical vibration in mitigating severe OIIRR. The findings showed no statistically significant differences between the vibration-treated groups and the positive control group. This outcome may be attributed to the extensive OIIRR craters caused by the heavy orthodontic force, which likely exceeded the tissue's ability to repair.[26]

Moreover, raising the mechanical vibration frequency from 30 Hz to 60 Hz did not result in any significant variation in the degree of OIIRR observed in orthodontically loaded molars.[26]

This outcome contrasts with Nishimura et al.'s findings, which proposed that mechanical vibration could mitigate the ischemic response and restore blood flow in the compressed PDL. The discrepancy may be attributed to the younger age of the rats (six weeks old) in their study, as immature roots typically exhibit a greater capacity for repair.[26]

6.5.2 Human studies

Mayama et al. [23] conducted a double-blind prospective randomized controlled trial using split-mouth design on patients with malocclusion.[23] The study revealed no notable variance in pain, discomfort, or OIIRR between the two groups.[23] These findings suggest that incorporating supplementary vibration alongside static orthodontic force significantly increased tooth movement during canine retraction thereby reducing the number of visits without adverse effects.[23]

Yilmaz et al concluded that mechanical vibration did not influence the degree of OIIRR.[22] A split-mouth, RCT done on 40 maxillary first premolars from 20 patients by Yilmaz et al. comparing the average total resorption between the force and no-force groups showed no statistically significant difference between the vibration and control sides.[22] In this study, there was similarly no significant difference in resorption between the control and vibration sides within the no-force group. Additionally, the comparison of total OIIRR volume on the vibration side, across various surfaces and levels of the root, with the control side (the force application side) showed no statistically significant difference. This suggested that vibration, even with force applied, does not affect the extent of resorption.[22]

6.6 Protocols

The impact of vibration on tooth movement remains a topic of debate, with the ideal vibration protocol to enhance tooth movement yet to be established. For the research done by Tangtanawat et al., the optimal force was determined to be 10 g, and light force was set at 5 g.[12]

Studies have shown that low-frequency vibration does not influence tooth movement in animal models.[12] Multiple animal studies have demonstrated that HFV positively influences tooth movement, enhances osteoclastogenesis, and elevates levels of inflammatory mediators. Research using a rat model compared frequencies ranging from 58–278 Hz, identifying 120 Hz as the frequency that resulted in the most significant tooth movement.[12]

The duration of exposure was not a key factor in enhancing tooth movement; therefore, the study utilized the shortest effective exposure time of 5 minutes. Findings from this rat model confirmed that combining HFV (125 Hz, 5 minutes per day) with orthodontic force accelerated tooth movement without causing OIIRR.[12]

Part 7: Piezocision

7.1 Definition

Peizocision is a type of surgical method to move teeth faster by balancing and modifying the resorption and apposition of bone tissue.[121]

The aim of peizocision is to accelerate OTM while not to causing irreversible damage to periodontium.[121]

7.2 Introduction & History

Dibart et al. introduced a minimally invasive, flapless technique using a piezocision tool. Under local anesthesia, small vertical incisions are made on the buccal side between the teeth, extending through the periosteum but below the interdental papilla. This space enables a piezoelectric knife to access the cortical bone in the interproximal region.[18]

Dibart et al[121] stated that the deliberate surgical injury to the cortical bone (i.e. corticotomy), has been one of the most reliable and effective methods for accelerating tooth movement.[121] By triggering an early and robust osteoclastic response, this procedure speeds up the bone resorption process.[121] The roots of this surgically enhanced orthodontic technique can be traced back to the late 19th century.[121]

Compared to selective surgical decortication as a method to accelerate OTM, piezocision is significantly less invasive.[121] Clinically, the healing process is more predictable, with patients experiencing less pain, leading to a smoother and more acceptable recovery.[121] Tissue regeneration appears to be fully restored, and bone turnover remains unaffected when piezocision is combined with OTM animal studies. Moreover, there is no evidence suggesting an increased risk of OIIRR, which is a potential concern with surgical techniques.[121]

7.3 Mechnism of Action

Piezocision-assisted tooth movement has been proposed to reduce the typical delay seen after initial tooth displacement in conventional orthodontics.[27] It has been suggested that it facilitates a smoother transition from the initial displacement phase to accelerated and sustained tooth movement.[21] Unlike conventional methods, during treatment for adult patients, Dibart et al noticed an increase in tooth mobility due to temporary bone loss caused by the procedure. This is confirmed by the level of demineralization observed in animal studies.[121]

When treating adult patients with this technique, the constant pressure applied to the teeth keeps the alveolar bone mechanically stimulated. This prolongs the temporary state of bone loss, giving the clinician a longer opportunity to move the teeth more quickly before the bone begins to remineralize. The combination of piezocision and tooth movement works together to extend this effect, since the temporary bone response (RAP) can be maintained through ongoing stimulation of both the teeth and bone.[121]

The elevated tissue turnover caused by surgery is limited to the areas directly involved in the procedure. It is crucial to make bony incisions only around the teeth designated for movement. Consequently, the anchorage value of teeth located away from the surgical site remains high, while the anchorage value of adjacent teeth is reduced. The orthodontist plays a key role in the team, determining, after comprehensive assessment and treatment planning, the specific locations where the surgeon should perform piezocision or grafting. This approach aims to create a biological environment conducive to the controlled, rapid, and safe movement of the teeth, whether partially or completely.[121]

A localized increase in osteoclastic and osteoblastic activity occurs, leading to reduced bone density and heightened bone turnover.[121] The kinetics of the OTM primarily constrained by the activity of osteoclasts, which break down the cortical lamina dura of the alveolus.[121] This resorption triggers bone remodeling, where osteoblasts are then stimulated to promote new bone formation.[121]

Corticotomies and perforations were designed to intentionally inflict maximal trauma to the alveolus and stimulate considerable bleeding.[121] Tooth movement after surgical intervention is essentially due to a demineralization–remineralization process.[121] The trauma to the bone is caused by peizocision triggers inflammation-induced osteopenia which leads to series of biological events called RAP.[115,121] The RAP effect is a healing process, which is directly proportional to the severity of the surgical injury, and typically begins a few days after the injury, reaches its peak within 1-2 months, and continues for 2-4 months.[115,121]

7.4 Regional Acceleratory Phenomenon (RAP)

Surgical approaches leverage the RAP, where injury to the tissue initiates the healing process and elevates inflammatory mediators. RAP refers to a localized increase in the activity of osteoclasts and osteoblasts, initially leading to reduced bone density and elevated bone turnover. Additionally, making surgical cuts near the teeth targeted for movement reduces bone density, thereby accelerating the OTM process.[18]

This temporary state of osteoporosis enhances the efficiency of tooth movement.

There is typically a 3–4 month period during which teeth can move more quickly through the demineralized bone matrix before the alveolar bone undergoes remineralization. However, Dibart et al. 2009 observed that RAP effects may extend up to 6 months.[21] This was notably evident in patients undergoing Piezoecision-assisted Invisalign (Align Technology, Inc.; 2820 Orchard Parkway, San Jose, California 95134, USA) treatments, where aligners were changed every 5 days instead of the usual 2-week interval.[21]

Animal studies have indicated a potential 50% reduction in overall treatment duration, findings that align with clinical observations. Additionally, RAP has been proposed as a method for achieving differential anchorage, potentially eliminating the need for supplementary anchorage devices.[121]

The effects of RAP can be reactivated in the same area through repeated applications of Piezocision.[21]

7.5 Effects of Peizocision in OTM

Current literature indicates that piezocision appears to accelerate tooth movement in the short term, but the evidence is limited and of low quality.[16]

Hawkins et al[115] found no significant difference in OTM in the piezocision group compared to control whereas study by Abbas et al[130] and Aksakalli et al[131] showed more accelerated OTM with piezocision. This can be explained as RAP effect is more intensified due to different surgical protocol.[115,121] Research has demonstrated that a more extensive injury leads to a stronger RAP response[121,132]

The systematic review analyzed the efficacy of piezocision in accelerating orthodontic tooth movement.[16] In their systematic review, Yi et al. reported that the use of piezocision was associated with accelerated tooth movement and a significant reduction in overall treatment duration.[16]

No adverse effects on periodontal health, pain perception, patient satisfaction, OIIRR, or anchorage control were observed in the reviewed studies.[16]

Dibart et al.[121] stated that the advantage of piezocision-facilitated tooth movement is the integration of minimally invasive surgery with orthodontics, serving as an advanced and effective technique for the modern dental team.[21,27,114,121] Its versatility lies in its ability to incorporate both soft and hard tissue grafting, which helps to enhance the volume and dimensions of the jaw tissues during tooth movement.[114] This approach is particularly beneficial in preventing or correcting pre-existing periodontal issues, such as bony fenestrations, dehiscences, and gingival recessions, which might otherwise be exacerbated by conventional orthodontic treatments.[21,27,114,121] Another key feature of this technique is that it involves operating on only one side of the alveolus, typically the buccal side.[27] Unlike earlier corticotomy-facilitated tooth movement methods, there is no need to perform surgery on the palate or the lingual aspect of the teeth.[21] This makes the procedure less invasive while still effectively facilitating tooth movement.[21,27,114,121]

Dibart et al.'s study in 2013 demonstrated that combining buccal interproximal micro-incisions with localized piezoelectric decortication produces significant demineralization around teeth in areas undergoing movement.[121] The extent of demineralization achieved through Piezocision eliminates the need for additional lingual or palatal intervention, reducing trauma and discomfort while improving patient acceptance.[21,27,114,121] This technique presents an appealing alternative to the more invasive conventional approach, which involves large full-thickness periodontal flaps and the use of high-speed handpieces with surgical burs.[27,121]

Although the overall evidence supporting piezocision as a safe and effective adjunct for accelerating tooth movement is weak in systematic reviews, the author suggested it is beneficial, particularly in the short term.[16,114] However, significant variations in piezocision protocols were noted across the studies, and there was a high risk of bias, including selection, performance, and detection bias.[16] The included studies also encompassed both extraction and non-extraction cases, contributing to heterogeneity.[16,115]

7.5.1 Animal studies

Dibart et al. conducted an animal study using rats to assess the effects of piezocision, both with and without tooth movement.[121] For the piezocision procedure on rats, a vertical incision was made on the palate, both mesial and distal to the first molar, using a microsurgical blade.[121] A piezotome was then inserted through this small opening to create an injury to the alveolar bone, penetrating the cortical bone to a depth of 0.5 mm on both sides.[27] At the same time, for tooth movement, the wires were activated during the piezocision surgery.[27,114,121] To move the left maxillary first molar mesially, a 25 g Sentalloy stainless steel coil spring was attached to its buccal surface. The coil was stretched 10 mm and secured around both the left maxillary first molar and the incisors.[121] The rats were then sacrificed for histomorphometric analysis to count the number of osteoclasts present.[121]

Dibart et al. stated that piezocision group showed alveolar bone resorption more than non-piezocision group.[21,27,114,121] Piezocision caused a rapid rise in osteoclastic activity, with a more pronounced effect in demineralization of the bone surrounding the teeth in the group that received both piezocision and OTM.[21,27,114,121] This suggested that OTM may have an additional contributory role in osteoclastic activity.[121]

Piezocision triggers RAP which facilitates faster tooth movement compared to traditional orthodontic methods.[21,27,114,121] Dibart et al concluded that, through the animal model observations, the teeth treated with piezocision move at double the speed of those treated without it.[121]

7.5.2 Human studies

Gibreal et al.[133] focused on adult patients with severe mandibular crowding requiring the extraction of two lower first premolars. The mean time to alignment of the lower anterior teeth was significantly shorter in the piezocision group, averaging 53 days (1.7 months), compared to 121 days (4.3 months) in the control group. This represents a 59% reduction in alignment time.

The greatest effect of piezocision was observed within the first month of treatment. Importantly, there were no reports of tooth vitality loss or OIIRR associated with the procedure.

The study concluded that piezocision, with regular reviews every two weeks, can significantly reduce the time required to achieve alignment of the lower anterior teeth. However, it could not be determined whether piezocision leads to a reduction in the total duration of orthodontic treatment.[133]

Study by Charavet et al.[19] evaluated the effect of piezocision combined with CAD/CAM customized appliances on treatment time in cases of mild to moderate crowding. A total of 24 adult patients with mild to moderate crowding were included, with piezocision performed two weeks after the placement of fixed appliances.

The treatment duration in the piezocision group was significantly shorter, averaging 278 days, compared to 393 days in the control group. This represents a 3.8-month reduction in treatment time.[19]

Overall, treatment with piezocision was 1.6 times faster than conventional treatment, translating to a 36% reduction in total treatment time.[19]

7.6 Effects of Peizocision in OIIRR

7.6.1 Human studies

Piezocision has been proposed to reduce the risk of OIIRR by promoting increased osteoclastic activity and lowering bone density.[18]

Patterson et al.[15] investigated the impact of piezocision on OIIRR associated with orthodontic forces using a microcomputed tomography (Micro-CT) approach. A total of 28 maxillary first premolars were extracted bilaterally from 14 patients (6 males and 8 females; mean age: 16 years and 2 months).[15]

The study employed a split-mouth design, with one side receiving piezocision and the other serving as the control. Due to limited interradicular space between some premolars and canines, the side with the least risk of root damage was chosen for piezocision, resulting in a non-randomized study design.[15]

Orthodontic forces of 150 g were applied to induce buccal tipping using 0.017 x 0.025-inch TMA cantilever springs extending from the molars to the first premolars. Piezocision was performed as described by Dibart et al., involving two vertical buccal incisions apical to the interdental papilla, measuring 5–7 mm in length, with corticotomy cuts 4–5 mm in length and 2–3 mm in depth. TMA springs were left in place for four weeks to induce buccal tipping.[15]

Micro-CT analysis revealed that teeth subjected to piezocision exhibited 44% more OIIRR compared to the control teeth, with resorption observed on all root surfaces. Additionally, five participants experienced significant damage from the surgical piezocision procedure. Although Patterson's[15] study concluded that piezocision combined with orthodontic forces heightened the risk of iatrogenic OIIRR, the study's limitations included a small sample size, lack of randomization, and absence of blinding, which may have influenced the results.[15,18]

Additionally, research by Patterson et al.[15] has not specifically examined OIIRR following orthodontic forces. For instance, Abbas et al.[130] focused on changes before and after canine retraction, while Charavet et al.[19] analyzed OIIRR before and after comprehensive orthodontic treatment.[18,19,130]

Strippoli et al.[17] also reported notable OIIRR in anterior teeth and a reduction in alveolar bone height in piezocision-assisted orthodontic treatments.[17,18]

However, Charavet et al. found no significant difference in root length between piezocision and non-piezocision groups from the beginning to the end of treatment.[18,19]

The clinical trial by Alhaija et al. 2023[18] was the first to evaluate and compare the effects of piezocision on periodontal tissues and OIIRR of mandibular second molars during their protraction. They found no adverse impacts of the piezocision procedure on the periodontium.[18]

This study had several limitations, including an imbalance in the female-to-male ratio, the use of 2D imaging for assessing OIIRR, and the evaluation being limited to the mesial root of the second molar. The mesial root was specifically analyzed due to its proximity to the piezocision incision and its interaction with the denser bone in the first molar extraction site during protraction.[18]

The effect of piezocision on OIIRR following orthodontic forces is still unclear as certain studies have linked piezocision-induced periodontal inflammation to increased OIIRR, others suggest that the decreased bone density following piezocision alleviates the pressure exerted on tooth roots, thereby potentially minimizing OIIRR.[18,134]

7.6.2 Protocols

Piezocision is typically performed one week after brackets are placed, with wire adjustments made every two weeks thereafter. Piezocision can be applied to the entire dentition or focused on specific segments, and it can be repeated as needed in localized areas to reactivate the RAP.[121]

Hawkins et al used a minimally invasive approach using a soft tissue laser was utilized to make the initial mucosal incisions, reducing postoperative bleeding and ensuring simultaneous coagulation.[115] Also to minimize the risk of iatrogenic injury and enhance patient comfort, a single bone cut was made distal to the canine.[115] Hawkin's study extracted the premolars before placement of fixed appliance.[115] The surgical protocol is contrasting to the study by Abbas et al[130] and Aksakalli et al[131].

A 3 mm vertical incision on the distal to the canine and 4 mm incision that is apical to the interdental papilla is made on the buccal soft tissue during piezocision.[115] A vertical corticotomy cuts of 4-5 mm in length and 3 mm in depth is made with a piezocision blade by inserting the blade into the incision site to penetrate into the buccal cortical bone.[115] The depth was measured using the millimeter markings on the piezosurgery knife for accuracy. By maintaining a minimum 3 mm gap between adjacent teeth, this approach aimed to prevent iatrogenic root damage while effectively triggering the RAP effect.[115]

The surgical technique of Wilcko et al. 2001[119] was the improved version of the protocol that was started in late 19th century.[121] Labial and lingual alveolar flaps of full thickness were elevated, with decortication only reaching the medullary bone close to the roots of the teeth planned for movement.[121] One week after surgery, tooth movement was initiated, and orthodontic appliances were tightened every two weeks until the malocclusion was fully corrected.[119,121]

Kim et al.[135] introduced the corticision technique as a minimally invasive alternative without the need for flap elevation. This method uses a reinforced scalpel and mallet to cut through the gingiva and cortical bone directly, without raising any flaps. This technique was used to create enough trauma to the bone to trigger the RAP, however the downside was that gingival or bone grafting was not possible during the procedure.[135]

Dibart et al.[21] introduced a new minimally invasive method called "Piezocision" which allowed soft or hard tissue grafting by selective tunneling, making it effective for treating gingival recession or correcting inadequate bone structure in patients. This technique involved making tiny incisions in the buccal gingiva, through which a piezoelectric knife is used to decorticate the alveolar bone, triggering the RAP.[21]

These mid-level incisions provide access for the insertion of a piezoelectric knife, allowing a 3 mm deep corticotomy to be performed using a piezotome. The procedure triggers the RAP, enhancing bone remodeling in the operated areas. In contrast, non-treated regions maintain higher anchorage values as they are unaffected by the demineralization process.[21]

For optimal results, the decortication must extend beyond the cortical bone into the medullary bone to fully activate the RAP effect. The procedure is typically carried out one week after orthodontic appliances are placed. Following surgery, the appliance is activated at intervals of 1–2 weeks to leverage the temporary phase of demineralization, which promotes accelerated tooth movement.[21]

7.7 Applications and Considerations

7.7.1 Usage

Piezocision can be performed either in a localized area or as a generalized approach, and it can also be applied sequentially to address specific orthodontic needs.[16]

7.7.2 Indications

Piezocision is indicated in the treatment of Class I malocclusions with moderate to severe crowding, whether managed with or without extractions.[21] It is also suitable for selected cases of Class II or Class III malocclusions.[131] This technique can be used to correct deep bites or open bites, assist in molar distalization, and palatal expansion.[133] Additionally, it is particularly effective in rapid orthodontic treatment in adults, clear aligner therapies and the rapid intrusion or extrusion of teeth.[21] Piezocision can be used for simultaneous correction of osseous and mucogingival defects, prevention of mucogingival issues that might arise during or after orthodontic treatment, and to assist in bone remodeling when exposing impacted teeth.[27,121]

7.7.3 Contraindications

Piezocision is contraindicated in patients with medical conditions that impair healing or compromise bone health.[114] It should not be used in patients who are taking medications that affect normal bone metabolism, such as corticosteroids or bisphosphonates.[27] The presence of bony pathologies, pre-existing root resorption or ankylosed teeth, or patient non-compliance with treatment protocols also precludes the use of this technique.[121]

7.7.4 Potential Complications

The potential complications associated with piezocision include root damage, the risk of infection, and the development of mucogingival defects.[121]

Part 8: Indication for research

OIIRR is a significant side effect in orthodontic treatment, which prompts investigation into the OIIRR associated with effective methods for accelerating tooth movement.

Research showed that the use of piezocision or vibration during orthodontic treatment showed accelerated tooth movement.

Yi et al.[16] stated that there is insufficient evidence to support that the piezocision is a safe method to accelerate OTM. Patterson et al[15] conducted a split-mouth study[14] on patients and stated that there was a notable amount of OIIRR seen, averaging of 44% increase, on the section piezocision was done compared to the control section.[15]

However, a recent controlled clinical trial done by Arana et al.[20] showed a contrasting perspective, that there were no differences among the groups in terms of the amount of root shortening observed with or without piezocision during their orthodontic treatment. The authors found that piezocision integrated within orthodontic treatment does not increase the risk of OIIRR.[20] However, the study's limited sample size and focus on mandibular incisors and canines emphasize the need for further research to validate these results from larger sample size and different tooth types and positions.

Nishimura et al[25] suggested that vibration can be used as a potential adjunct to orthodontic treatment to accelerate OTM without additional OIIRR damage. A randomized controlled trial done by DiBiase et al[24] also supports this notion. The authors stated that vibrational force during orthodontic treatment does not affect OIIRR[24]. However, this study exclusively examined the vibrational effects on maxillary central incisors, therefore warrants further studies into its possible side effects on different tooth types following the application of vibration during orthodontic treatment.

Additionally, Lund et al.[54] reported no statistically significant correlation between treatment duration and the degree of OIIRR.

Both piezocision and vibration are two common modalities sometimes used by orthodontists to accelerate tooth movement thus reducing treatment duration and enhancing patient satisfaction by shortening the postoperative discomfort experienced[23,27,114,127]. Reduced treatment time is beneficial for patient’s oral health as patients will likely to have less incidence of dental complications such as dental caries, decalcification, gingivitis, and OIIRR associated with prolonged orthodontic appliance wear.[136]

OIIRR is one of the most common complications associated with orthodontic treatment and is considered irreversible.[12] Thus, exploring methods to speed up tooth movement while avoiding OIIRR could significantly enhance orthodontic treatment outcomes.[12]

Overall, there is a clear need for higher-quality evidence across all methods. Future research should focus on reducing bias, implementing rigorous testing protocols, including larger sample sizes, and adopting standardized methodologies to ensure more reliable and generalizable findings.

The current literature reveals a notable gap in our understanding, especially the comparative effects of mechanical vibration and piezocision on OIIRR on teeth following OTM. There is no split-mouth randomised controlled trials comparing the effect of mechanical vibration and piezocision on OIIRR of first premolars. Addressing this gap through a split-mouth randomized controlled trial is imperative for dentists and orthodontist to provide evidence-based clinical practice to patients and optimize treatment outcomes for orthodontic patients by accelerating tooth movement while minimizing associated risks.

The objective is to compare the effect of piezocision and mechanical vibration on orthodontically induced inflammatory root resorption of human first premolars following application of orthodontic forces.

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2. Manuscript

THE UNIVERSITY OF SYDNEY

Physical properties of root cementum: Part 30.

THE EFFECT OF PIEZOCISION AND MECHANICAL VIBRATION ON ORTHODONTICALLY INDUCED ROOT RESORPTION OF FIRST PREMOLARS FOLLOWING THE APPLICATION OF ORTHODONTIC FORCES.

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Eunice Park

BSc, BDent, MRACDS

Doctor of Clinical Dentistry (Orthodontics) student

Discipline of Orthodontics and Paediatric Dentistry

Faculty of Dentistry

University of Sydney, Australia

Alice Wong

BDS, DClinDent(Orth), MOrth RCSEd MRACDS (Orth)

Lecturer

Discipline of Orthodontics and Paediatric Dentistry

Faculty of Dentistry

University of Sydney, Australia

Peter Petocz

PhD

Professor

Statistician

Macquarie University

Oyku Dalci

DDS, PhD

Senior Lecturer

Discipline of Orthodontics and Paediatric Dentistry

Faculty of Dentistry

University of Sydney, Australia

Selma Elekdag-Turk

BSc, DDS, PhD

Professor

Department of Orthodontics

Faculty of Dentistry

University of Ondokuz Mayis, Samsun, Turkey

Matthew Foley

PhD

Deputy Facility Manager, Analysis & X-Ray Microscopy Manager

Sydney Microscopy & Microanalysis.

University of Sydney

M. Ali Darendeliler

BDS, PhD, Dip Ortho, Certif. Orth, Priv. Doc, MRACDS (Ortho), FICD

Professor and Chair

Discipline of Orthodontics and Paediatric Dentistry

Faculty of Dentistry

University of Sydney, Australia

Tamer Turk

DDS, PhD

Professor and Chair

Department of Orthodontics

Faculty of Dentistry

University of Ondokuz Mayis, Samsun, Turkey

ABSTRACT

Introduction

The aim was to compare the effect of piezocision and mechanical vibration on orthodontically induced inflammatory root resorption (OIIRR) of human first premolars following application of orthodontic forces.

Methodology

Forty-one orthodontic patients (aged 13–18) requiring first premolar extractions were treated with a 225g buccal force on both maxillary first premolars for four weeks. Premolars were divided into control (C), piezocision (P), vibration (V), or a combination (PV) through randomization. A total of 82 premolars were extracted, and OIIRR crater volumes were measured using X-ray microtomography and Fiji software to compare OIIRR across the groups.

Results

OIIRR crater volumes were analyzed using a cube root transformation (crt) by treatment (C, P, V, PV) and location. While the mean crt for PV (0.75mm) was slightly higher than for C (0.65mm), V (0.71mm), and P (0.65mm), there were no statistically significant differences among treatments ($p=0.33$). The location analysis showed statistically significant differences ($p<0.001$), with the highest OIIRR on the buccal middle (0.44mm) and the lowest on the palatal cervical (0.07mm).

Conclusions

The study found no significant differences in mean crtRR volumes between treatments (C, P, V, PV), suggesting piezocision and vibration may not impact OIIRR following the application of heavy orthodontic forces. OIIRR levels varied by location, with the highest on the buccal middle root surface.

Ethics Approval

Ethic approval was obtained from the Ondokuz Mayis University (Decision number OMU KAEK 2013/507) and the University of Sydney (Project No. 2022/451)

Protocol

The protocol was not published before trial commencement.

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Author/s

Eunice PARK[a], Selma ELEKDAG-TURK[b], Alice WONG[a], Matthew FOLEY[c], Peter PETOCZ[d], Oyku DALCI[a], Mehmet Ali DARENDELILER[a], Tamer TURK[b]

Organisation or Affiliation

[a]Faculty of Medicine and Health, Department of Orthodontics, Discipline of Orthodontics

and Paediatric Dentistry, School of Dentistry, University of Sydney,

Sydney Dental Hospital, Sydney Local Health District, Sydney, New South Wales,

Australia.

[b]Department of Orthodontics, Faculty of Dentistry, Ondokuz Mayis University, Samsun, Turkey

[c]Sydney Microscopy & Microanalysis, University of Sydney, Sydney, Australia

[d]Macquarie University, Sydney, Australia

Address for Correspondence

M. Ali Darendeliler

Department of Orthodontics

Sydney Dental Hospital

Lvl 2, 2 Chalmers Street

Surry Hills, NSW 2010

Australia

Phone +61 2 93518314

Fax +61 2 9351 8336

Email: ali.darendeliler@sydney.edu.au

Introduction

Orthodontically induced inflammatory root resorption (OIIRR)

OIIRR is an inevitable pathological complication of orthodontic tooth movement (OTM).[1] This condition is recognized as a multifactorial process that leads to the degradation of the permanent root surface to varying extents.[1] In severe cases, OIIRR can significantly compromise the long-term health and stability of the affected teeth, potentially resulting in tooth loss.[2]

Pathogenesis

Orthodontic loading compresses the periodontal ligament, inducing hypoxia and interstitial fluid flow through the osteocyte network, which generates mechanical strain on the bone matrix and initiates tissue remodelling.[3,4] This disrupts integrins and alters gene expression, leading to bone formation and resorption of cementum and dentine by osteoblasts and osteoclasts.[3,5] OIIRR occurs during the removal of the hyaline zone,[6] as phagocytic cells clear the necrotic tissue. This often causes macrophages, odontoclasts, and osteoclasts to indiscriminately resorb root apex cementum and dentine from the root.[3,4]

Aetiology

Longer treatment duration and heavy orthodontic force of 225g during orthodontic treatment correlate with heightened OIIRR with maxillary premolars more vulnerable than mandibular ones.[7,8] Continuous, especially heavy orthodontic force increases OIIRR, particularly in high-pressure areas like the buccal cervical and lingual apical regions.[9-11] Compression areas are more prone to resorption than tension areas.[12]

Methods to accelerate orthodontic treatment

Orthodontic treatment duration increases the risk of OIIRR, especially in adults with prolonged treatment.[13,14] To address this, accelerated methods, such as piezocision and mechanical vibration have been utilised by clinicians.[15]

Piezocision is a surgical technique that involves creating small incisions in the bone without raising a flap.[16] This procedure accelerates tooth movement by stimulating alveolar bone remodeling.[16] This process is driven by osteoclastic activity initiated after surgery and amplified by the synergistic effect between piezocision and orthodontic forces.[13,15,16] Patterson et al.[17] reported that combining piezocision with orthodontic forces increased the risk of OIIRR. In contrast, Charavet et al.[18] and Alhaija et al.[19] found no significant differences in root length or adverse periodontal effects of the piezocision procedure compared to standard orthodontic treatment. Dibart et al.[20] concluded that there is no strong evidence linking piezocision to an elevated risk of root resorption.

Mechanical vibration induces an osteogenic response through piezoelectric charges on alveolar bone.[15] Mayama et al.[6] found that combining vibration with static force increased tooth movement during canine retraction without added pain, discomfort, or OIIRR. Tangtanawat et al[21] and Nishimura et al.[22] reported that vibration accelerates tooth movement without inducing root resorption in animal models. Similarly, DiBiase et al.[23], Yeoh et al.[24] and Yilmaz et al.[25] concluded that vibration, even with orthodontic force, does not influence root resorption.

Indication for research

Studies on piezocision and vibration have shown mixed results: some suggest piezocision may increase OIIRR,[14,17] while others propose no significant difference when compared to controls.[18,19,26] Vibration appears to accelerate tooth movement without increasing OIIRR,[6,21-25] however more research is needed. Both methods show promise in shortening treatment time and reducing discomfort, potentially without the additional OIIRR.[6,21,27-29] The comparative effects of piezocision and vibration on OIIRR remain uncertain. There are currently no randomised control trials examining either their combined influence or a direct comparison of their impact on OIIRR following heavy orthodontic forces.

Aims

The primary aim of this study was to compare the effect of piezocision and mechanical vibration on orthodontically induced inflammatory root resorption of human first premolars following application of orthodontic forces. Secondary outcomes were to compare the extent of OIIRR across different root surface locations.

Materials and Methods

Type of study:

A prospective experimental study investigating the volume of OIIRR craters of the extracted premolars using microcomputed tomography scanning (Micro-CT). This was a single-centre, block randomization with a 1:1 allocation ratio, parallel-group study.

Trial design, participants, eligibility criteria and settings

Ethic approval was obtained from the University of Ondokuz Mayis (Decision number OMU KAEK 2013/507) and the University of Sydney (Project No. 2022/451). Written and informed consent was obtained from all subjects participating in the study.

The sample size was estimated by G*Power (version 3.1.7) according to a 2012 study by Aras et al. on OIIRR with 2 or 3 weekly reactivated continuous or intermittent orthodontic forces (80% power; 5% significance level; 2-tailed).[30] The OIIRR volume of 3 weekly reactivated continuous or intermittent groups were 1.13 ± 0.46 mm3 and 0.76 ± 0.32 mm3, respectively.[30] A minimum sample size of 13 in each group was required to detect a significant difference between the groups.[30] The sample size was increased to 14 patients in each group, to account for dropouts. Therefore, a total of forty-two patients presenting with Class II malocclusion, moderate to severe anterior crowding, and a Class I or II skeletal base—requiring bilateral maxillary first premolar extractions, moderate anchorage, and fixed appliance treatment—were recruited from the orthodontic patient waiting list at Ondokuz Mayis University in Samsun, Turkey. The participants had an age range of 13 to 18 years. The patient sampling method and inclusion criteria were as follows: (1) Permanent Dentition, (2) Normal root development, (3) Apexification completed, (4) No previous orthodontic or orthopedic treatment, (5) No craniofacial anomaly present, (6) No history of trauma, bruxism or parafunction, (7) No previous reported or observed dental treatment of the maxillary and mandibular first premolars, (8) No past and present signs and symptoms of periodontal disease, (9) No significant medical history or medication that would adversely affect the development or structure of the teeth and jaws as well as any subsequent tooth movement.

Randomization

This study followed a split-mouth randomized controlled clinical trial design. 42 patients were randomly allocated to 3 groups (Fig 1.). For the allocation of the patients, a computer-generated list of random numbers was used.[31] One patient had to be excluded due to medical treatment in group 1. Within each group, randomization of 1:1 for right and left sides of the maxillary arch were designated as Side A and Side B for each patient. Sides A and B were further randomly allocated as seen in Fig 1. No modifications were made after the commencement of the trial.

Blinding

Blinding was implemented for the investigator responsible for identifying OIIRR craters and measuring their volumes, achieved by storing the teeth in coded vials with the identifying information obscured by a staff member uninvolved in the trial. However, blinding was not feasible for both patients and the clinician providing orthodontic treatment. Concealment of the vials and information of each patient's allocation were securely stored in a folder until all measurements of the OIIRR craters and statistical analysis were completed.

Intervention

The orthodontic setup (Fig. 2) involved bonding 0.022” x 0.028” Self-ligating SPEED brackets (Strite Industries, Cambridge, Ontario, Canada) to the first permanent molar and first premolar teeth[11,31]. A 0.017” x 0.025” Beta-titanium molybdenum alloy (TMA; Ormco, Glendora, California, USA) cantilever springs were inserted into the maxillary first molar and first premolar brackets, skipping the maxillary second premolar, to apply 225g buccally directed force bilaterally to the first premolars to achieve buccal tipping.[11,32] The magnitude of force was precisely measured to the nearest gram using a strain gauge (Dentaurum, Ispringen, Germany). Unobstructed tipping of the premolars were facilitated by preventing its occlusal interferences with the opposing teeth with occlusal stops (Transbond Plus Light Cure Band Adhesive; 3M Unitek) which were placed on the mesiobuccal cusps of the mandibular first molars during the experiment.(Fig. 2)

All appliances were administered and patients were treated consecutively by a single operator. The springs were activated in accordance with the manufacturer's instructions. This application was maintained for the entire duration and no reactivation of the springs occurred throughout the 4-week experimental duration (28 days).

Group 1 (n = 13)		Group 2 (n = 14)		Group 3 (n = 14)	
Side A Subgroup 1	Side B Subgroup 2	Side A Subgroup 3	Side B Subgroup 4	Side A Subgroup 5	Side B Subgroup 6
Positive Control (Force application only)	**Piezocision + Vibration + Force application**	**Piezocision + Force application**	**Piezocision + Vibration + Force application**	**Vibration + Force application**	**Piezocision + Vibration + Force application**

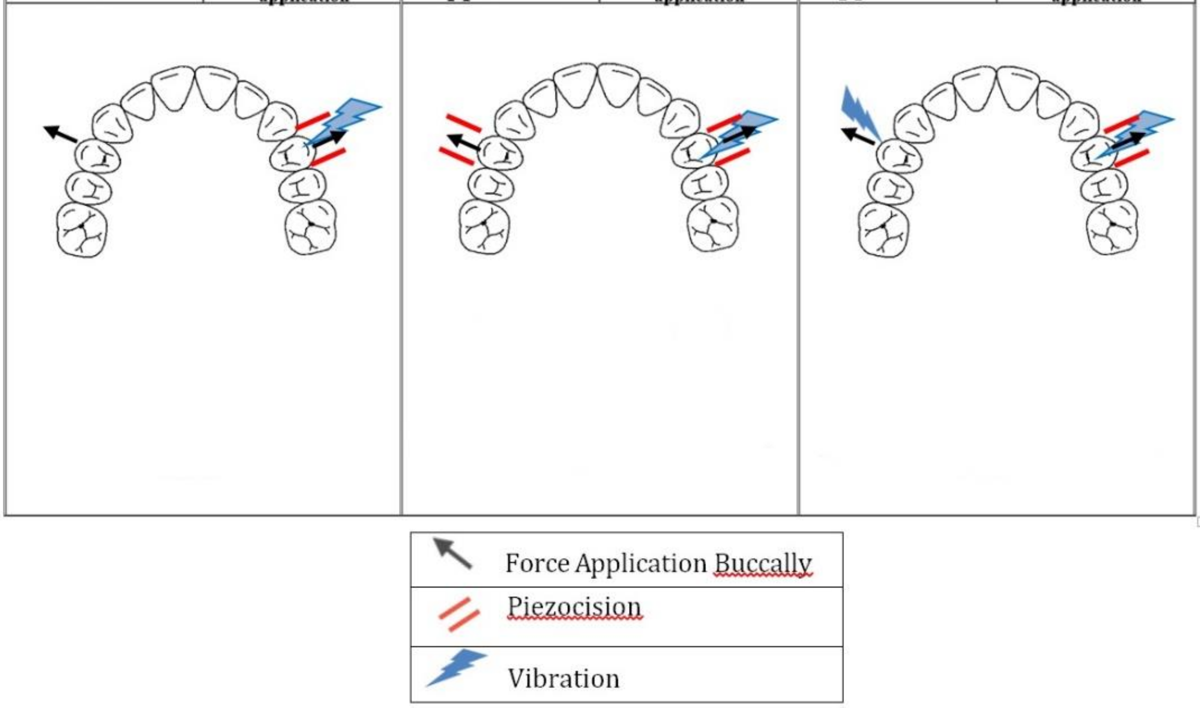

Figure 1. Group 1: Side A (Control) received only orthodontic force, while Side B received piezocision, vibration treatments, and orthodontic force. **Group 2:** Side A received piezocision with orthodontic force, while Side B received piezocision, vibration treatments, and orthodontic force. **Group 3:** A received vibration treatment with orthodontic force, while Side B received piezocision, vibration treatments, and orthodontic force.

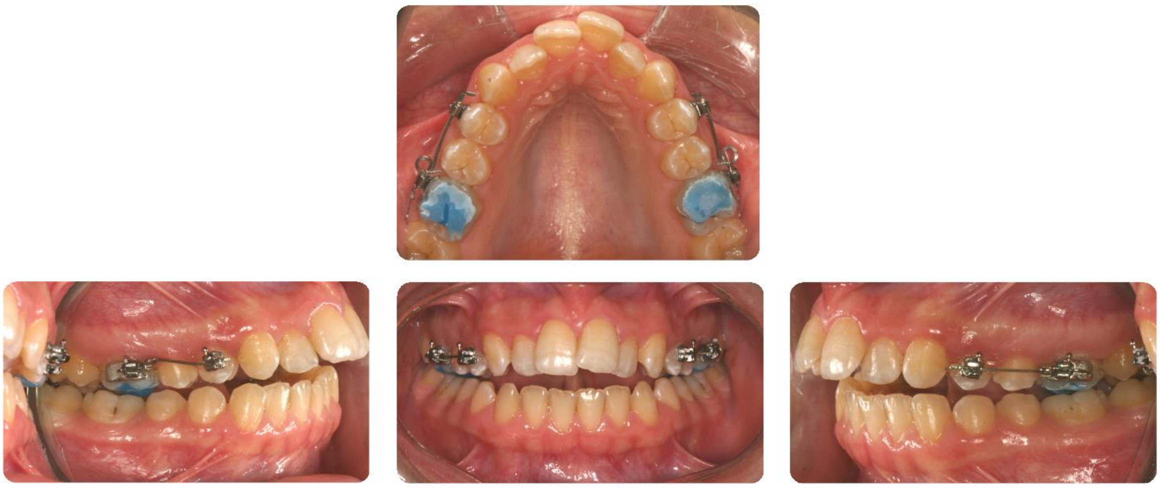

Figure 2. Orthodontic set up with 0.017” x 0.025” Beta-titanium molybdenum alloy cantilever springs inserted.

Piezocision was carried out following bracket placement by the same clinician. For the piezocision protocol, to ensure unimpeded access to the surgical site, the springs were removed from the brackets. In a surgical setup under local anesthetic, the piezocision procedure was performed following the technique outlined by Dibart et al[33] which involved the use of a piezoelectric knife (VarioSurg Ultrasonic Bone Surgery System; NSK Nakanishi, Tochigi, Japan). Sterile scalpel blades were used to make vertical Incisions 5 to 7 mm in length, apical to the interdental papilla, into the interproximal gingiva on the mesial and distal aspects of the first maxillary premolars. The piezocision blade was inserted into the soft tissue incision to create vertical aveolar bone corticotomy cuts, 2-3 mm deep penetrating the buccal cortical bone and reaching into the medullary bone between the mesial and distal aspects of the first maxillary premolars. Caution was taken when deciding the depth of the corticotomy cut near the maxillary first premolar root if it neared the canine or second premolar root, to avoid inadvertent iatrogenic root damage. No sutures were placed on the vertical soft tissue incision sites following the completion of the piezocision procedure. The calibrated cantilever springs were then replaced and remained in situ for 4 weeks without reactivation.

The vibration protocol required vibration to be applied on the buccal surface of the premolar for 10 min/day for 28 days, using an Oral B (USA) Humming Bird Vibrating Unit (The Procter & Gamble Company; 1 Procter & Gamble Plaza Cincinnati, OH 45202, USA).[25,34] (Fig. 3)

Patients were instructed to follow this regimen diligently. Daily communication was established through WhatsApp (WhatsApp LLC, a Delaware Limited Liability Company. 1 Meta Way, Menlo Park, California 94025, United States) messages to monitor compliance. Patients reported that they were 100% compliant with the vibration protocol.

Quality control measures focused on two key areas: oral hygiene and appliance integrity. To preserve data integrity and consistency, any patients who sustained damage to brackets, archwires, or springs during the clinical trial period were planned for exclusion from the study.

Throughout the 28-day observation period, patients maintained good oral hygiene, and there were no instances of appliance breakage.

Figure 3. Oral B (USA) Humming Bird Vibrating Unit

Specimen collection

Specimen collection occurred after 4 weeks (28 days). The cantilever springs and occlusal stops were removed, and atraumatic extractions of the first maxillary premolars was performed by the same surgeon under local anaesthesia. To remove blood and tissue remnants from the teeth after extraction, they were washed with a non pressurized isotonic solution without touching the root surfaces, then each tooth was placed in a 5-ml sterile tube containing 10% formalin solution (Sarstedt Ag & Co., Nümbrecht, Germany). After 2 weeks, the formalin solution was changed and no other procedure was applied until examination of the roots.

Outcomes and sample analysis

Resorption assessment was conducted using micro-computed tomography (micro-CT). Each tooth specimen was wrapped in parafilm (Fig.4) to keep the tooth from drying and was scanned using a desktop x-ray microtomography machine (SkyScan 1272; Bruker, Aartselaar, Belgium) (Fig. 5).

Scanning of each tooth from the crown to the root apex was performed with source conditions of 90 kV and 111uA, a pixel size of 12μm, and over a full 360° rotation around the vertical axis (Fig. 6). A filter was used (0.5mm Al + 0.038mm Cu) to minimise beam hardening artefacts.

Reconstruction of the axial cross-sections was achieved using NRecon (version 2.2.0.6; Bruker Corporation, Aartselaar, Belgium) (Fig. 7). All 82 teeth were reconstructed using the same reconstruction parameters and saved as 8-bit bitmap files. Consequently, a comprehensive three dimensional (3D) representation of internal microstructure and density over a specified height range in the transmission image was generated. Following reconstruction, cross sections, along with a realistic 3D image featuring options for rotation and slicing the object model, could be presented. This model enabled the computation of internal morphological parameters.

Detection and quantification of OIIRR craters were conducted using the imaging software program FIJI[35] (version 2.14.0/1.54f; available at https://imagej.net/Fiji) in conjunction with a custom macro (Enigma; Sydney Microscopy and Microanalysis, University of Sydney). Each image slice was thresholded to a binary format (black and white) to distinguish between tooth mineral and air before crater detection (Fig 8.). The assessment of OIIRR craters was conducted through the examination of axial image stacks for each tooth root. Craters were visually identified by an operator on a slice-by-slice basis. Once detected, the crater bounding positions were recorded in a rectangular box around the crater which was defined using an x-y coordinate system across the relevant Z-stack slices. The number of images in the stack through which the crater extended provided information for defining the crater in the third dimension (Fig 8.). This segmented data, along with the coordinate information, was then fed into the Enigma script. The resulting output calculated the volume of each crater in cubic millimeters. Enigma utilized the convex hull method to calculate the volume of the crater. To minimize error and bias, the same operator conducted all measurements.

Craters were categorized based on their location on the buccal or palatal surface, with the three vertical locations identified as cervical, middle, or apical third of the root. A total of six regions were investigated and measured, which were labelled as Buccal-Cervical, Buccal-Middle, Buccal-Apical, Palatal-Cervical, Palatal-Middle, and Palatal-Apical regions (Fig. 6).

The total OIIRR volume was also documented for each tooth.

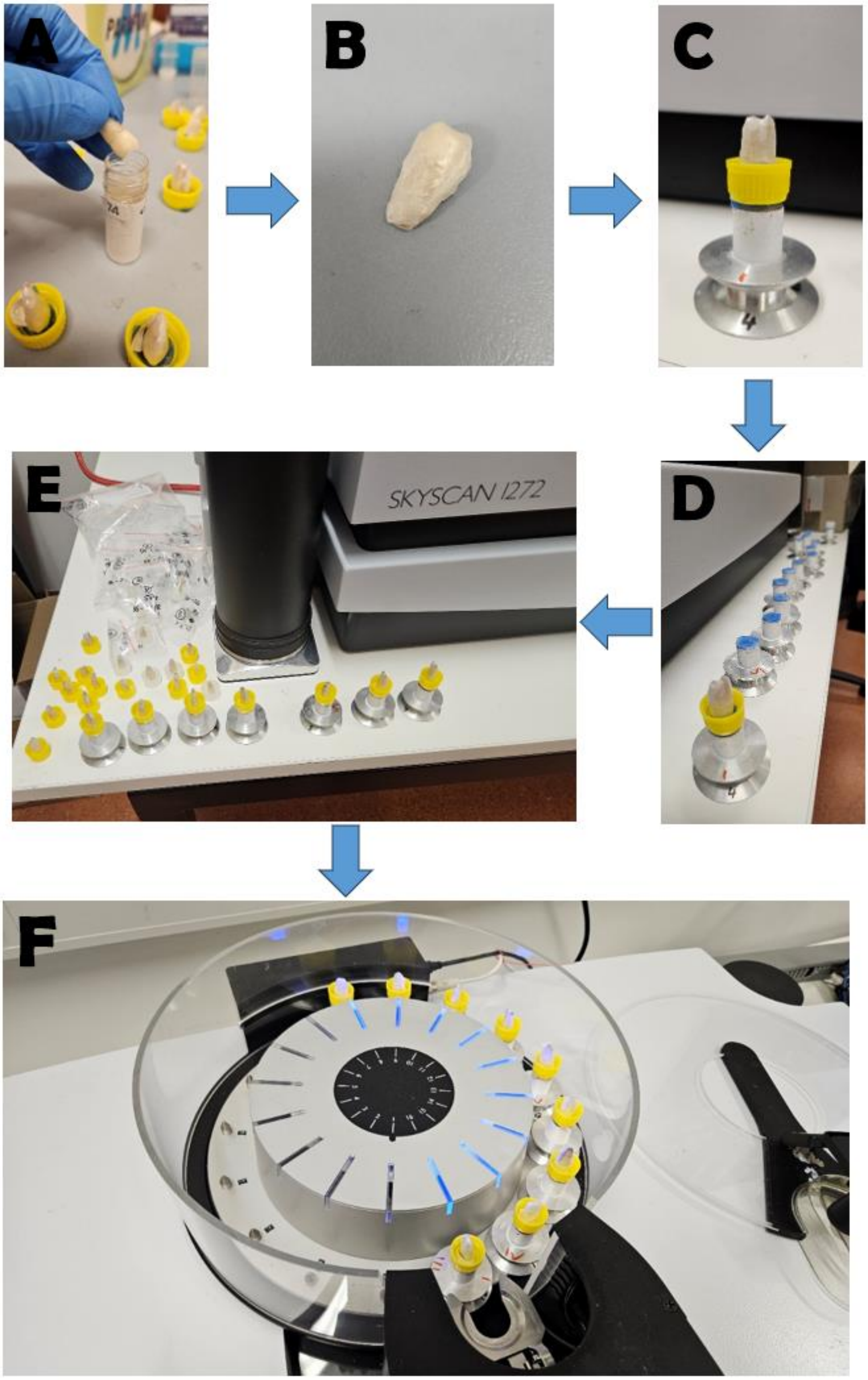

Figure 4. Photographs of specimens **(A)** taken out of each vial (**B**) wrapped in parafilm and **(C), (D), (E)** mounted on discs. (**F**) Each scan cycle had 16 specimens loaded onto Skyscan 1272.

Figure 5. A photograph of the desktop x-ray microtomography machine (SkyScan 1272)

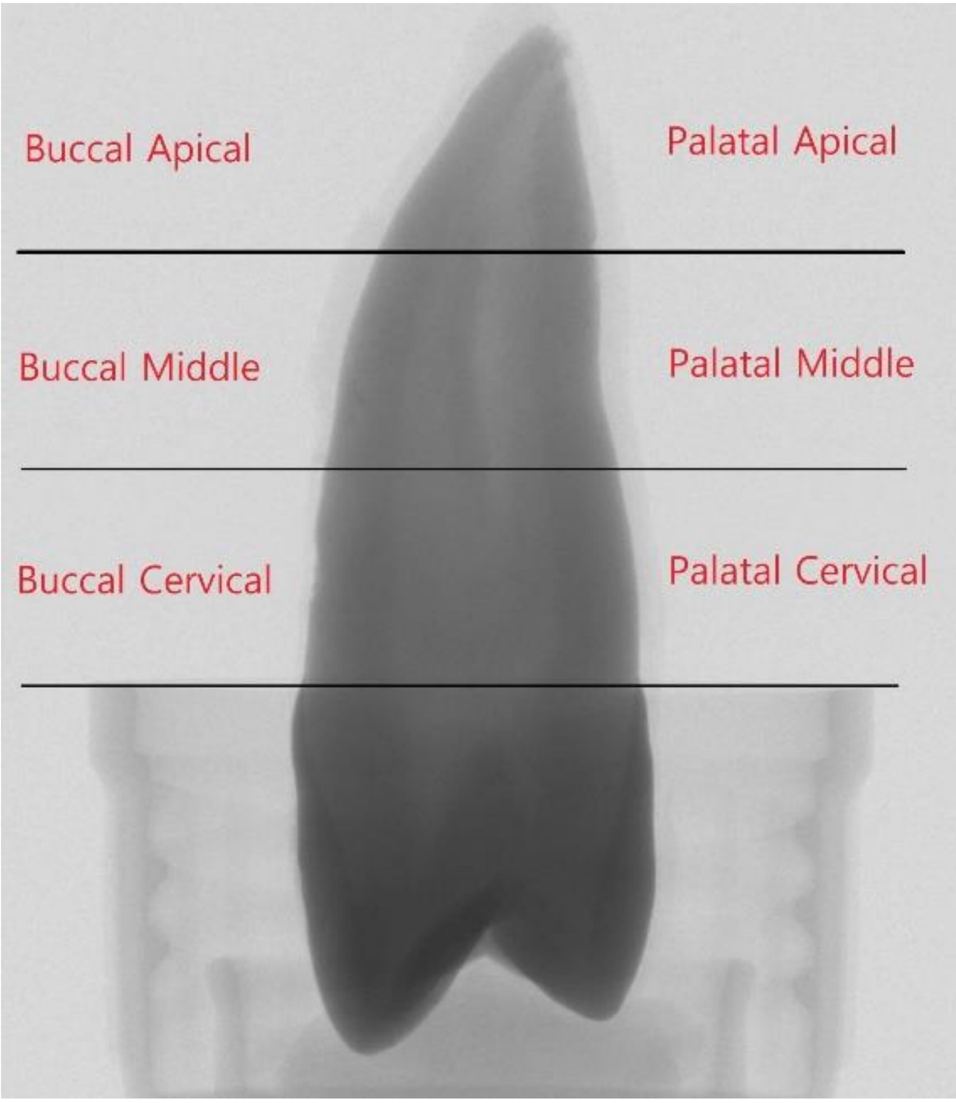

Figure 6. Micro-CT scan of a premolar

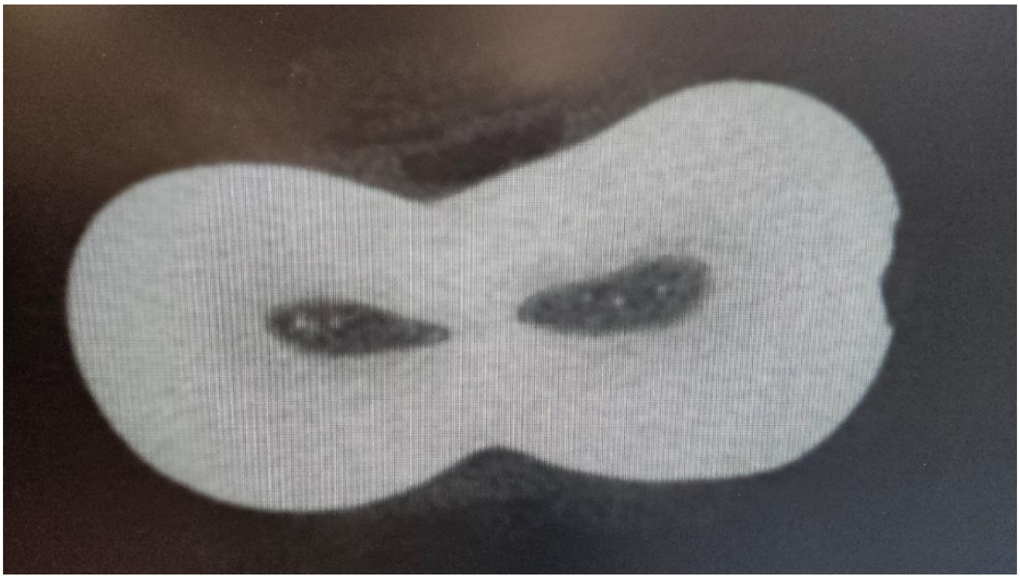

Figure 7. Axial cross-section of the tooth. The 3D data obtained from micro-CT were transformed into an image stack consisting of multiple 2D axial slices. The measurements were taken for the resorption craters in these regions.

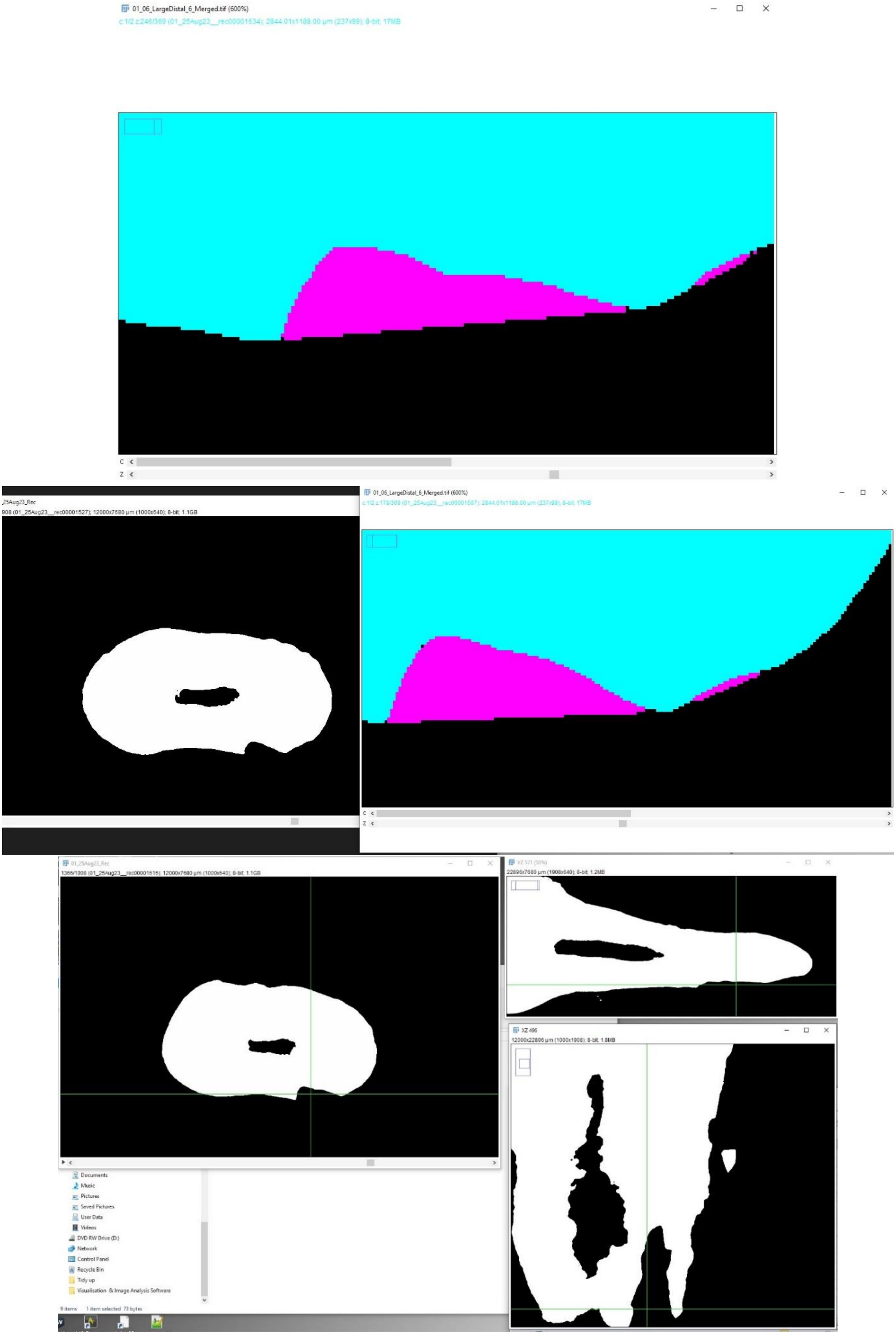

Figure 8. Visual representation of the crater detection

Statistical Analysis

IBM SPSS Statistics software version 29 (IBM Corporation, Armonk, NY, USA) was used for the statistical analysis.

The OIIRR crater volumes were quantified in mm³ for analytical purposes.

Total resorption values per tooth were calculated by combining the measured volumes of OIIRR craters. The buccal and palatal aspects of the roots were divided into three height levels: cervical, middle, or apical third. As a result, the positions of the OIIRR craters were categorised into six surfaces: Buccal cervical, Buccal middle, Buccal apical, Palatal cervical, Palatal middle, and Palatal apical.

Statistics were calculated including means and Standard Deviations (SD). Results are given in the form of means and standard errors (of means), based on the normality assumptions used in the analyses. The boxplots (Figs 12, 14) show that the values of crtRR used still have a certain amount of skew (non-normality), though that varies from group to group. They also show the medians and inter-quartile ranges. Nevertheless, the important aspect for the analyses is that the residuals from the models are approximately normal; this was checked and found to be satisfied (as shown in P-P plots). Additionally, linear models were employed to investigate the association between the extent of OIIRR and the treatment groups (C, P, V, PV). This analysis was carried out both collectively for each tooth and for each of its six surfaces.

All measurements were performed by a sole operator who was blinded to the allocation of treatment types to individual teeth. To assess measurement reliability, the reconstructed root images of 8 teeth were randomly selected for repeated measurements OIIRR crater volumes 4 weeks after the initial assessments, aiming to determine the overall standard error of measurement and coefficient of variation (CV%).

The OIIRR values for each entire tooth, as well as for each of its six surfaces, were all positively skewed. This suggests that analysing differences would be more appropriate on a transformed scale rather than the original linear scale[7,11,32,36-38]. A commonly utilized transformation, such as the logarithm, may be suitable for such scenarios, although adjustments would be necessary to accommodate the frequent occurrence of zero values for resorption.

Past research has applied the cube root transformation (crt), in which each crater volume - whether total per tooth or per surface - is substituted with its cube root[7,11,32,36-38]. Essentially, this transformation converts the volume measurement of resorption (per tooth or per surface) into a linear measurement, representing a constant multiple of the diameter of an equivalent hemispherical crater, thereby converting measurements from mm³ to mm. Graphs depicting the cube-root transformed values show reduced skewness. Residuals from the model utilized in the analyses demonstrate approximately normal distribution, suggesting the effectiveness of the crt.[7,11,32,36-38]

Each volume set (comprising total root surface or segmented by the six locations of the root) underwent analysis employing a mixed general linear model. Treatment (C, P, V, PV) served as the independent factor for total analyses, as well as location (for surfaces and heights). Subject was included as a random factor. To allow for the effect of multiple comparisons, significance was represented by p-values less than 0.01.

Results

Participant flow

41 patients completed the study with 82 teeth eligible for scanning and inclusion in the study as displayed with the CONSORT flow diagram. (Fig.9)

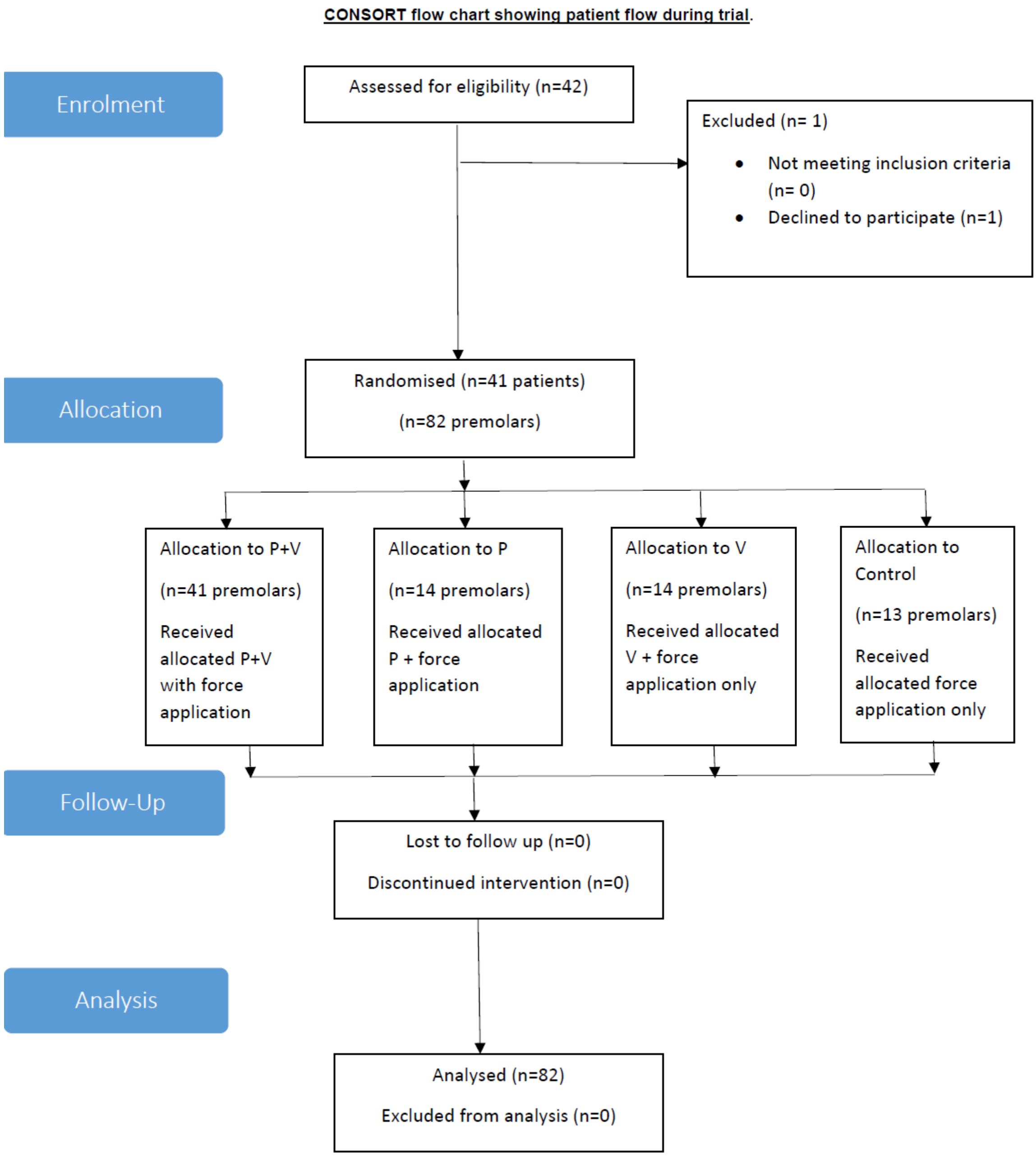

Figure 9. Consort Flow Chart showing patient flow during Trial

Baseline data

The patients had an age range of 13 to18 years. Baseline data such as age and sex were gathered.

Group 1 (n = 13)	
Side A Subgroup 1	**Side B** Subgroup 2
Control (Force application only)	**Piezocision** **+** **Vibration** **+** **Force**

No	**14 4**	**24 4**	**Sex**	**Age Year/month/day**	**decimal conversion**
1	P + V	C	male	17 year 3 months 10 days	17.28
2	C	P + V	male	15 year 3 months 15 days	15.29
3	C	P + V	male	14 year 1 months 24 days	14.15
4	P + V	C	female	17 year 8months 24 days	17.73
5	C	P + V	female	16 year 7 months 26 days	16.65
6	P + V	C	female	17 year 11 months 25 days	17.99
7	C	P + V	male	18 year 1 months 28 days	18.16
8	C	P+ V	female	12 year 10 months 27 days	12.91
9	P + V	C	female	16 year 1 months 10 days	16.11
10	P + V	C	female	12 year 9 months 6 days	12.77
11	C	P + V	female	17 year 1 months 14 days	17.12
12	P + V	C	male	15 year 8 months 24 days	15.73
13	This patient had to be discarded from the study due to medical reasons.				
14	P + V	C	female	14 year 3 months 24 days	14.32
				Mean age	15.86

Group 2 (n = 14)	
Side A Subgroup 1	**Side B** Subgroup 2
Piezocision **+** **Force**	**Piezocision** **+** **Vibration** **+** **Force**

No	**14 4┘**	**24 └4**	**sex**	**Age Year/month/day**	**decimal conversion**
1	P + V	P	female	16 year 10 months 14 days	16.87
2	P	P + V	male	14 year 2 months 17 days	14.21
3	P + V	P	female	14 year 7 months 20 days	14.64
4	P	P + V	male	14 year 5 months 20 days	14.47
5	P + V	P	female	15 year 11 months 0 days	15.93
6	P	P + V	female	15 year 0 months 2 days	15.01
7	P + V	P	female	16 year 7 months 9 days	16.61
8	P	P + V	female	16 year 2 months 3 days	16.17
9	P+ V	P	female	12 year 6 months 1 days	12.5
10	P	P + V	female	14 year 4 months 4 days	14.34
11	P + V	P	female	17 year 3 months 10 days	17.28
12	P	P+ V	female	17 year 1 months 12 days	17.12
13	P + V	P	female	16 year 0 months 25 days	16.07
14	P	P + V	female	15 year 6 months 3 days	15.51
				Mean age	15.48

Group 3 (n = 14)	
Side A Subgroup 1	**Side B** Subgroup 2
Vibration **+** **Force**	**Vibration** **+** **Piezocision** **+** **Force**

No	**14** **4**	**24** **4**	**sex**	**Age** **Year/month/day**	**decimal conversion**
1	V + P	V	female	13 years 10 months 29 days	13.91
2	V	V + P	female	13 years 10 months 2 days	13.84
3	V + P	V	female	12 years 7 months 19 days	12.64
4	V	V + P	female	17 years 2 months 5 days	17.18
5	V + P	V	male	16 years 0 months 15 days	16.04
6	V	V + P	female	13 years 0 months 25 days	13.07
7	V + P	V	male	13 years 4 months 25 days	13.4
8	V	V + P	female	17 years 7 months 21 days	17.64
9	V	V + P	male	16 years 7 months 27 days	16.66
10	V + P	V	female	14 years 9 months 26 days	14.82
11	V	V + P	female	17 years 4 months 18 days	17.38
12	V + P	V	female	16 years 1 months 5 days	16.1
13	V	V + P	female	14 years 4 months 22 days	14.39
14	V + P	V	female	12 years 7 months 17 days	12.63
				Mean age	14.98

Numbers analysed for primary outcome and subgroup analysis

The mean total crtRR per entire tooth for each treatment type (PV, P, V, C) was analysed. (Fig. 10)

The mean crtRR for PV was 0.75mm (95% CI 0.687, 0.821mm) was larger than for C (0.65mm; 95% CI 0.492, 0.801mm), V (0.71mm; 95% CI 0.564, 0.859mm) and P (0.65mm; 95% CI 0.505, 0.801mm). However the total analysis indicated that treatments were not statistically significant (p=0.33). This means that, while there were differences, they were not large enough to be definitively attributed to the treatments rather than to the effects of chance. (Fig 10.)

			95% Confidence Interval	
Treat	Mean	Std. Error	Lower Bound	Upper Bound
P	.653	.073	.505	.801
V	.712	.073	.564	.859
PV	.754	.033	.687	.821
C	.646	.076	.492	.801

Figure 10. crtRR per whole tooth for each treatment. Dependent Variable: crtRR; Subject as random factor

The analysis of OIIRR per location for each treatment confirmed that treatments were not statistically significantly different (p=0.94). The mean crtRR values by treatment (adjusted for surfaces) were much closer: between 0.23mm for P (95% CI 0.167, 0.295mm), 0.24mm for V (95% CI 0.173, 0.301mm), 0.25mm for PV (95% CI 0.220, 0.278mm) and 0.26mm for C (95% CI 0.189, 0.323mm). (Fig.11). This is represented in the boxplot (Fig. 12).

			95% Confidence Interval	
Treat	Mean	Std. Error	Lower Bound	Upper Bound
P	.231	.033	.167	.295
V	.237	.033	.173	.301
PV	.249	.015	.220	.278
C	.256	.034	.189	.323

Figure 11. crtRR per location for each treatment. Dependent Variable: crtRR

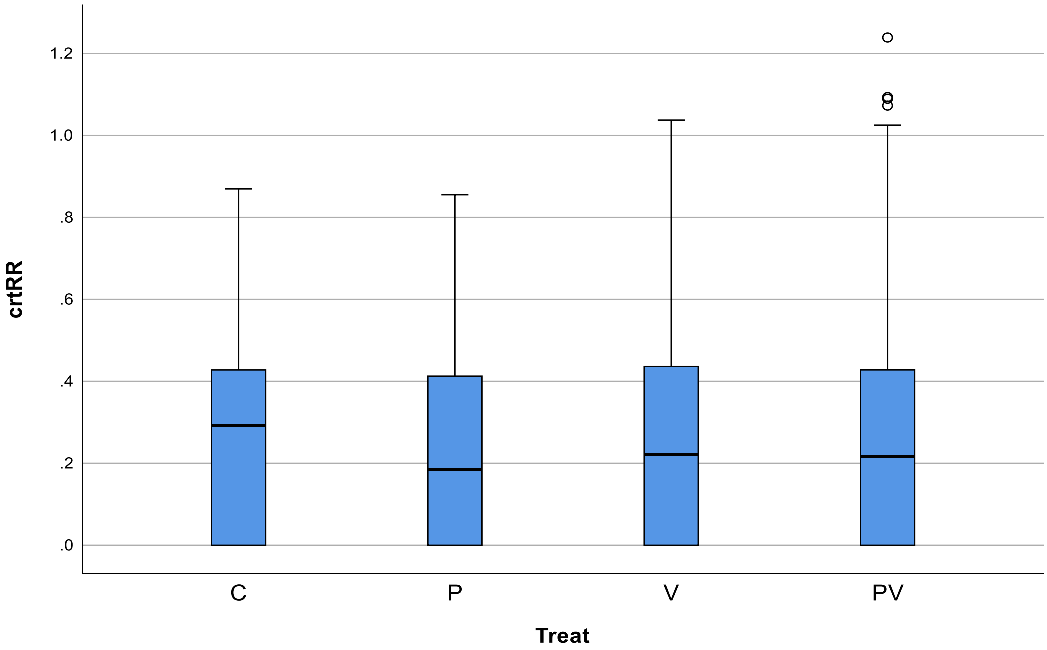

Figure 12. A boxplot for the total results shows the distribution of values of crtRR per location (surface/height) for teeth subjected to each of the different treatments. Each boxplot shows the middle half of values (blue box) with a line indicating the median, as well as vertical lines going out to the minimum and maximum values. In some cases, unusually high values are shown individually (circles), and in other cases, the vertical line showing the lowest quarter of values is combined with the lower end of the box (in cases where there were substantial numbers of zero readings).

Secondary Outcomes

The mean total crtRR values of each location of the root was analysed and compared (i.e. Buccal-Cervical, Buccal-Middle, Buccal-apical, Palatal-cervical, palatal-middle, palatal-apical). The locations were statistically significantly different ($p<0.001$). The mean values for locations ranged from 0.07mm (palatal-cervical) to 0.44mm (buccal-middle) (Fig 13). The box plot (Fig. 14) displays mean crtRR being highest on buccal middle, followed by palatal middle, palatal apical and buccal cervical root surfaces. with most crtRR on the buccal cervical and mid locations and the palatal mid and apical locations. The buccal middle had significantly more resorption than the other regions. (Fig. 13, 14)

			95% Confidence Interval	
Locn	Mean	Std. Error	Lower Bound	Upper Bound
BuccCerv	.213	.026	.162	.265
BuccMid	.442	.026	.391	.494
BuccApic	.192	.026	.140	.243
PalCerv	.073	.026	.022	.124
PalMid	.279	.026	.228	.330
PalApic	.261	.026	.210	.312

Figure 13. crtRR by treatment and (surface, height and interaction). Dependent Variable: crtRR

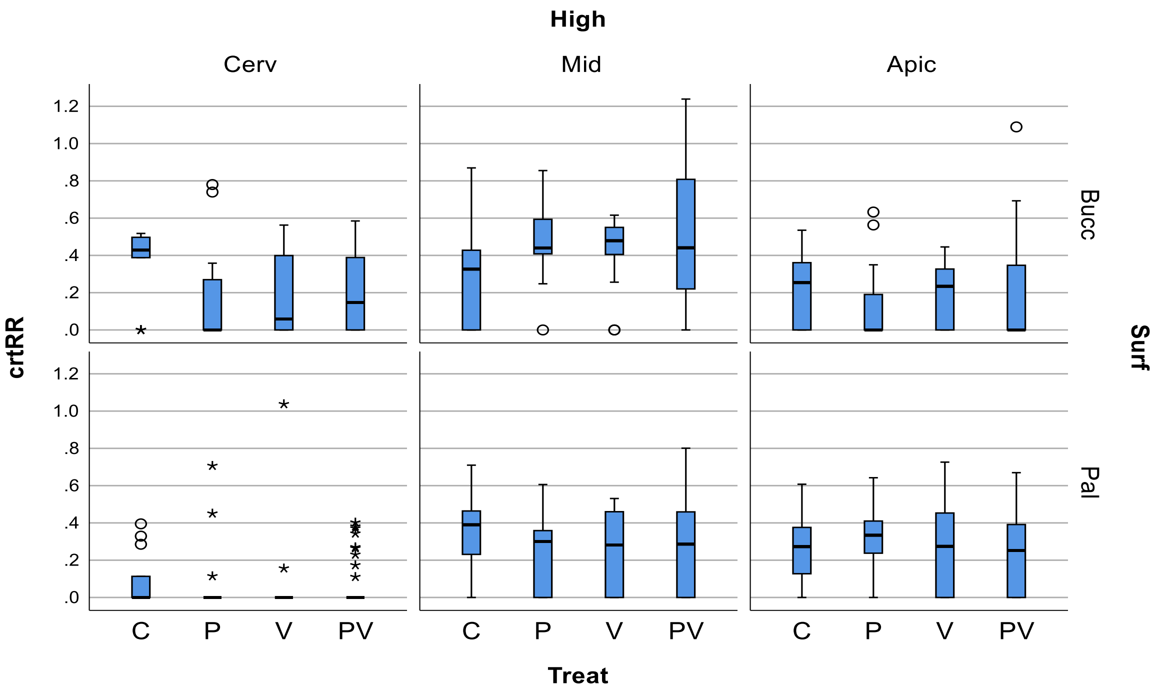

Figure 14. A panelled boxplot for the location results depicting the distribution of the data.

Error

Repeated measurements of randomly selected 8 teeth were completed and the root mean square error of measurement was 0.0023 and the coefficient of variation was 0.48%.

Harms

No harm or adverse effects were observed during piezocision, vibration or force applications during orthodontic treatments.

Discussion

Main findings in the context of the existing evidence, interpretation

This split-mouth randomised controlled trial investigated the effect of mechanical vibration and piezocision on the amount of OIIRR of upper first premolars following orthodontic force application.

This prospective clinical trial marks the pioneering utilization of microcomputed tomography in investigating the comparative impact of piezocision and vibration subsequent to orthodontic forces. Additionally, it delves into the combined influence of piezocision and vibration on the OIIRR process, setting a precedent in the field.

There was higher mean OIIRR recorded in the combined piezocision and vibration group compared to the other 3 groups. However, no discernible differences of clinical or statistical significance were observed among the control group, the vibration group, the piezocision group and the combined piezocision and vibration group.

The outcome of the trial showing no statistically significant difference in OIIRR among the groups might be due to the tissue's inability to repair itself after reaching a certain level of extensive root resorption craters caused by heavy orthodontic forces.[24]

In the investigation conducted by Grove et al.[39], findings indicated that employing the Oral B HummingBird unit for vibration notably diminished the level of resorption in comparison to the non-vibration condition[39]. Conversely, Tan et al.[40] reported in their research that the application of Acceledent did not demonstrate a statistically significant difference in the magnitude of OIIRR craters in maxillary first premolars subjected to a buccally directed force for four weeks[40]. The differences in response to vibration could potentially influence these outcomes. It is conceivable that individuals manifest varying degrees of reactivity in skeletal and periodontal tissues and cells to vibratory stimuli.[40] Patients have different types of bone quality and remodeling patterns which can subsequently result in divergent treatment outcomes.[40]

Utilizing Micro CT imaging, this investigation showed no statistically significant evidence indicating disparities between the vibration-only group compared to combined vibration and piezocision group, the control group and piezocision-only groups. However noteworthy individual variation in both the extent and location of OIIRR was observed within the study sample. This variability could potentially be attributed to individual susceptibility to OIIRR and the orientation of force application.[40]

The influence of piezocision procedures on OIIRR has been examined in a limited number of studies.[17,19,26] From the available literature, it appears that there is no consistent agreement regarding the impact of piezocision procedures on OIIRR compared to conventional orthodontic treatment without piezocision. Some studies suggest that piezocision does not lead to increased OIIRR[19,26], while others indicate the opposite[17]. However, the reliability of these findings may be questioned due to the small sample sizes in previous studies, such as Patterson et al.'s randomized controlled trial in 2017[17], which included only 28 premolars. In contrast, this current trial boasts a larger sample size of 82 premolars, thereby providing adequate statistical power to detect any potential significant differences in the primary outcome.

The reliability of utilizing periapical radiographs in Alhaija et al.[19] can be questioned due to the inherent limitations of traditional 2D radiography in accurately diagnosing and evaluating orthodontically induced OIIRR. These limitations encompass issues such as the superimposition of adjacent structures, magnification discrepancies, limited assessment capability restricted to mesial and distal root surfaces perpendicular to the x-ray beam, as well as a notable deficiency in reproducibility and sensitivity. These constraints inherent to 2D imaging modalities often lead to the detection of only advanced stages of OIIRR and apical root loss, thus compromising the comprehensive assessment of orthodontically induced OIIRR.

DiBiase et al. stated that incorporating additional vibrational force during the alignment phase of fixed appliance therapy did not yield a substantial impact on OIIRR as measured at the maxillary right central incisor.[23] The authors observed comparable levels of OIIRR across all groups investigated, including the Accel group, the Accel-sham group, and the fixed-only group indicating that the application of vibrational force did not exert any discernible influence on its occurrence.[23] Similar to Alhaija et al., Dibiase et al. utilized periapical radiographs to quantify OIIRR, a method constrained by the limitations inherent in 2D radiography.[19,23]

The OIIRR levels assessed by DiBiase et al.[23] at the maxillary central incisor remained unaffected by various patient factors, including age, sex, initial root length, history of dentoalveolar trauma during treatment, duration of the alignment phase, and pain experienced during this period.

OIIRR was observed on both the buccal and palatal surfaces. Notably, the greatest mean volume of OIIRR occurred on the buccal-middle surface, followed by palatal-middle, palatal-apical and buccal-cervical regions. These findings align with prior research investigating OIIRR under buccal tipping forces, indicating a consistent pattern across studies[11].

Limitations

A primary limitation of this split-mouth study design was the inability to blind both the patients and the operators, which could introduce bias. Additionally, potential iatrogenic damage[17] during piezocision procedures might be misinterpreted as OIIRR, posing a challenge for accurate assessment.

Limitations in the study of root resorption would be the idiopathic individual differences, particularly in subjects' metabolic responses. Additionally, while some areas displayed single large resorption craters, others contained numerous smaller craters that collectively accounted for the total resorption volume in those regions. These factors likely contributed to the significant variability in the measurements of the craters and standard deviations of the results.[12]

Generalizability

In clinical practice, the level of resorption remains challenging to detect using 2D radiographs, especially when it involves the buccal and lingual surfaces.[11]

In this clinical trial, through the extraction of the maxillary first premolars, it became feasible to acquire comprehensive insights into the OIIRR craters with the use microcomputed tomography[17]. Upper first premolars were specifically selected due to their frequent extraction in orthodontic treatment planning.

Arana et al.[26] used CBCT scans when OIIRR was assessed and the study concluded that the combination of orthodontic treatment with piezocision does not elevate the risk of OIIRR in mandibular incisors and canines[26].

Chan et al.[11] observed a greater volume of resorption in the heavy-force group (225g) compared to both the light-force group (25g) and the control group.[11] However, according to Chan et al.[11] the disparity in resorption volume between the light-force and control groups did not reach statistical significance.[11] A buccal tipping heavy-force of 225 g was selected for this study as it represents a clinically relevant magnitude, documented in earlier OIIRR investigations conducted at the University of Sydney by Chan et al[11].

These prior studies also determined that a 4-week experimental timeframe was appropriate for facilitating the development of detectable OIIRR craters, ensuring ethical and practical considerations for the study participants, such as minimizing the risk of breakage [11,17].

The short timeframe of 28 days compared to standard orthodontic treatment protocols aligns with prior studies.[11,17,39,40] Hence, this study employed a heavy force of 225g to examine whether piezocision, vibration, or a combination of piezocision and vibration would influence the OIIRR that is predetermined to occur on premolars under such intense force application for 28 days.

Conclusions

In the investigation of OIIRR across diverse modes of acceleration methods (Piezocision, Vibration, or combined Piezocision and Vibration) subsequent to orthodontic forces, no statistically significant differences were observed. This suggests that the utilization of piezocision and vibration may not substantially contribute to OIIRR. While this current trial has revealed a higher mean OIIRR with piezocision compared to alternative treatments and there are prior studies noting higher OIIRR volume with piezocision compared to controls[17], This study did not ascertain any statistically significant variance in OIIRR between teeth treated with vibration and piezocision when compared with the control group.

The utilization of vibration and/or piezocision to accelerate OTM may offer advantages for individuals exhibiting increased susceptibility to OIIRR during orthodontic treatment.

The findings indicate a statistically significant increase in resorption observed specifically on the buccal middle region of the root surfaces compared to other regions. This suggests that areas experiencing higher pressure are more prone to undergoing resorption.[11]

Future directions

The findings of this study suggest that the incorporation of piezocision and/or vibration into orthodontic treatment does not elevate the likelihood of OIIRR in upper first premolars when compared to orthodontic treatment devoid of acceleration techniques. Nevertheless, given the constraints associated with the sample size in the present investigation, further studies with larger sample sizes than 82 samples, and longer study designs are warranted to corroborate and strengthen the obtained results. Subsequent comprehensive investigations are imperative to understand the impact of piezocision and vibration on tooth OIIRR.

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