THE EFFICACY OF MODIFIED FLAPLESS CORTICOTOMY USING PIEZOCISION PROCEDURE TO ACCELERATE ORTHODONTIC TOOTH MOVEMENT IN PREMOLAR EXTRACTION CASES

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2021

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by

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A thesis submitted in fulfilment of the requirements
for the degree of
Doctor of Philosophy

June 2021

ACKNOWLEDGMENT

بِسْمِ اللهِ الرَّحْمٰنِ الرَّحِيْمِ

First and foremost, I would like to thank Allah, the most gracious the most merciful. I relied on Him entirely, my sincere gratitude for all the blessings bestowed upon me during my whole life, including the period of study in Malaysia.

I would like to convey my most profound acknowledgement to my mentor, Dr. Norma Ab Rahman, for her continuous support and guidance throughout my studies and research. My deepest and sincere gratitude to my co-supervisors, Dr. Basaruddin Ahmad, and Dr. Siti Lailatul Akmar Zainuddin, for their valuable support and advice.

My sincere special thanks to Dr. Jawaad Ahmed Asif from Oral and Maxillofacial Surgery Unit, School of Dental Sciences, Universiti Sains Malaysia (USM). I have learned the piezocision operative procedure from his excellent expertise. Also, I would like to show my gratitude to Yanty Suarni Bustaman, Siti Nur Akhirah Hasmi, and Roslinda Mohd. Noor staff of Orthodontic Specialist Clinic, Hospital Universiti Sains Malaysia (HUSM), for all the technical support during clinic time.

Many thanks to my parents, my siblings for their unconditional love, support, patience, and encouragement, without which I would never have gotten this far.

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LIST OF ABBREVIATIONS

ACF	Alveolar-crest fibres
AF	Apical fibres
ANOVA	Analysis of variance
AOO	Accelerated osteogenic orthodontics
ARF	Activation, resorption, formation
BGP	Bone Gla protein
BMC	Bone mineral content
BMD	Bone mineral density
BMU	Basic multicellular unit
BP	Bone matrix
BVF	Bone volume fraction
CAD-CAM	Computer-aided design and computer-aided manufacturing
CBCT	Cone-beam computed tomographic
CF	Circular fibres
CFO	Corticotomy-facilitated orthodontics
CI	Confidence interval
CONSORT	Consolidated Standards of Reporting Trials
COVID	Coronavirus disease
CTR	Calcitonin receptor
DFDBA	Demineralized freeze-dried bone allograft
DGF	Dentogingival fibres
DPF	Dentoperiosteal fibers
ELISA	Enzyme-linked immunosorbent assay
EPT	Electric pulp tester
Er: YAG	Erbium-doped yttrium aluminium garnet
Er, Cr: YSGG	Erbium, chromium-doped yttrium, scandium, gallium, and garnet
FDA	Food and Drug Administration
Ga-Al-As	Gallium-aluminum-arsenide

GF	Gingival fibres
HF	Horizontal fibres
HGF	Hepatocyte growth factor
HUSM	Hospital Universiti Sains Malaysia
HVJ	Hemagglutinating virus of Japan
ICC	Intra-class coefficient
IL-1β	Interleukin-1β
IRF	Interradicular fibres
IQR	Interquartile range
LA	Local anaesthesia
LAFC	Laser-assisted flapless corticotomy
LAO	Light accelerated orthodontics
LFMV	Low-frequency mechanical vibration
LII	Little's Irregularity Index
LIPUS	Low-intensity pulsed ultrasound
LLLT	Low-level laser therapy
MCO	Movement control order
MBT	McLaughlin Bennett Trevisi prescription brackets
M-CSF	Macrophage-colony stimulating factor
MOTIS	Movement of teeth by trauma-induced stimulation
MOP	Micro-osteoperforation
Nd: YAG	Neodymium-doped yttrium aluminium garnet
NRS	Numeric rating scale
NSAID's	Non-steroidal anti-inflammatory drugs
OF	Oblique fibres
OPG	Osteoprotegerin
OPG	Orthopantomograph
OTM	Orthodontic tooth movement
PAOO	Periodontally accelerated osteogenic orthodontics
PG	Prostaglandin
RAP	Regional acceleratory phenomenon

RANKL	Receptor activator of nuclear factor-kappa β ligand
RCT	Randomized clinical trial
SADc	Selective alveolar decortication
SD	Standard deviation
TF	Transseptal fibres
TNF	Tumour necrosis factor
TM	Tooth movement
TRAP	Tartrate resistant acid phosphatase
USM	Universiti Sains Malaysia
VAS	Visual analogue scale

LIST OF SYMBOLS

%	Percentage
~	Around
<	Less than
±	Plus, minus
≤	Less than or equals to
α	Level of significance
ß	Power of the study
δ	Difference in population means
µm	Micrometre
Al	Aluminium
gms	Grams
ml	Millilitre
mm	Millimetre
N	Sample size
kHz	Kilohertz

KEBERKESANAN KAEDAH KORTIKOTOMI MENGGUNAKAN CARA PIEZOCISION UNTUK MEMPERCEPATKAN PERGERAKAN GIGI BAGI KES CABUTAN GERAHAM KECIL PERTAMA DALAM RAWATAN ORTODONTIK

ABSTRAK

Kajian ini bertujuan untuk mengkaji keberkesanan prosedur piezocision yang diubahsuai untuk mempercepatkan tahap penjajaran dan keselarasan di dalam rawatan ortodontik untuk kes cabutan gigi geraham kecil pertama rahang atas dan rahang bawah, serta menilai kesannya terhadap kemelesetan gusi, kedalaman poket periodontal, vitaliti gigi dan skor kesakitan serta kepuasan. Sampel terdiri daripada 16 pesakit dengan Indeks Ketidakteraturan Little (LII) antara 7-9 mm pada gigi insisor rahang atas dan rahang bawah yang memerlukan cabutan gigi geraham kecil pertama di kedua-dua rahang. Subjek diagihkan secara rawak ke dalam kumpulan kawalan dan kumpulan piezocision dan subjek dibahagikan kepada dua kumpulan selari dengan nisbah peruntukan 1:1. Kedua-dua kumpulan menerima braket preskripsi McLaughlin Bennett Trevisi (MBT) slot 0.022 inci. Kumpulan eksperimen menerima pembedahan piezocision pada hari pemasangan yang sama. Model kajian untuk rahang atas dan rahang bawah diambil pada selang waktu bulanan untuk menilai keseluruhan waktu penjajaran, perubahan pada LII, dan kadar penjajaran. Parameter periodontal (kemelesetan gusi dan kedalaman poket) dan ujian daya hidup pulpa juga dinilai. Persepsi pesakit terhadap tahap kesakitan dan tahap kepuasan dengan skala penilaian numerik juga dinilai untuk prosedur piezocision. Sebanyak 13 pesakit (7 kawalan dan 6 piezocision) di rahang atas telah selesai kajian, manakala untuk rahang bawah sejumlah 10 pesakit (7 kawalan dan 3 piezocision) menyelesaikan kajian tersebut. Masa rawatan keseluruhan untuk meratakan dan menjajarkan gigi jauh lebih pendek pada kumpulan piezocision berbanding dengan kumpulan kawalan di rahang atas (perbezaan min = 31.5, 95% CI: 6.5, 56.5; P = 0,018), sedangkan, pada rahang bawah hasilnya tidak signifikan. Perubahan LII dan kadar penjajaran lebih ketara pada dua bulan pertama untuk kumpulan piezocision berbanding dengan kumpulan kawalan untuk rahang atas, tetapi tidak ada perbezaan yang signifikan pada rahang bawah. Kemelesetan gusi, kedalaman poket, dan daya hidup pulpa gigi rahang atas dan rahang bawah tetap stabil pada kedua-dua kumpulan sepanjang tempoh pemerhatian kajian ini. Pesakit telah melaporkan skor nyeri yang ringan hingga tidak ada, dan skor memuaskan mengenai prosedur piezocision. Piezocision boleh dikategorikan sebagai kaedah yang berkesan untuk mengurangkan keseluruhan masa meratakan dan menyelaraskan serta mempercepatkan pergerakan gigi ortodontik. Walau bagaimanapun, keberkesanan yang ketara hanya terdapat pada rahang atas dan keberkesanan yang tidak begitu meyakinkan untuk rahang bawah. Prosedur piezocision tidak memberikan kesan buruk pada struktur periodontal dan daya hidup gigi, dan ia juga merupakan pendekatan pembedahan yang kurang menyakitkan dan memuaskan.

THE EFFICACY OF MODIFIED FLAPLESS CORTICOTOMY USING PIEZOCISION PROCEDURE TO ACCELERATE ORTHODONTIC TOOTH MOVEMENT IN PREMOLAR EXTRACTION CASES

ABSTRACT

This study aimed to investigate the efficacy of modified piezocision procedure to accelerate the levelling and alignment stage in orthodontic treatment with first premolar extraction cases of the maxilla and mandible and evaluate its effects on the gingival recession, periodontal pocket depth, tooth vitality, pain, and satisfaction score. The sample comprised 16 patients with Little's Irregularity Index (LII) between 7-9 mm in the maxillary and mandibular incisors and require extraction of first premolars for both jaws. The subjects were randomly allocated into the control group, and the piezocision group and the recruited subjects were divided into two parallel groups with a 1:1 allocation ratio. Both groups received McLaughlin Bennett Trevisi (MBT) prescription brackets of the 0.022-inch slot. The experimental group received piezocision surgery on the same bonding day. Maxilla and mandibular study cast were taken at a monthly interval to assess the overall alignment time, changes in the LII, and alignment rate. The periodontal parameters (gingival recession and pocket depth) and pulp vitality test were evaluated. Patient perception of the pain level and level of satisfaction with a numeric rating scale was assessed following the piezocision procedure. A total of 13 patients (7 control and 6 piezocision) in the maxilla completed the study, whereas, in the mandible, a total of 10 patients (7 control and 3 piezocision) completed the study. The overall treatment time to complete the levelling and alignment was significantly shorter in the piezocision group compared to the control group in the maxilla (mean difference = 31.5, 95% CI: 6.5, 56.5; P = 0.018), whereas, in the mandible, the result was non-significant. In the maxilla, changes of LII had significantly reduced at the second month and alignment rates were significantly faster in the first two months in the piezocision group compared to the control group, but no significant difference in the mandible. Gingival recession, pocket depth, and pulp vitality of the maxillary and the mandibular teeth remained stable in both groups throughout the observation period of this study. Patients had reported a mild to no pain score and a satisfactory score about the piezocision procedure. Piezocision seems to be an effective method to decrease the overall levelling and alignment time and accelerating orthodontic tooth movement. However, the significant efficacy was found only in the maxilla and convincing efficacy to the mandible. The piezocision procedure did not produce any adverse effects on periodontal structure and vitality on the tooth; also, it seems a less painful and satisfactory surgical approach.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Orthodontic treatment is a costly and tedious treatment method, which takes 18-30 months to finish the entire treatment depending on the severity of malocclusion, treatment choices and orthodontic appliances (Buschang *et al*., 2012). The advantage of orthodontic treatment is not only correct the malocclusion of the teeth but also help individuals who are experiencing a diverse sort of dentofacial and malocclusion problem by accomplishing appropriate dentofacial form with a balanced occlusion. Based on experience, orthodontic patients are always concerned about the short duration of the treatment time with the best outcome of the result, and these days many patients are also worried about the social discomfort related to carrying braces and the sheer number of appointments.

Over the years, various attempts have been made to accelerate orthodontic tooth movement (OTM) with minimal adverse effects, including non-surgical and surgical methods. Non-surgical methods use pharmacological or chemical agents such as prostaglandins (Yamasaki *et al*., 1982, 1984), local receptor activator of nuclear factor-kappa β ligand (RANKL) gene transfer (Kanazaki *et al*., 2006), vitamin D (Collins *et al*., 1988), corticosteroids (Ashcraft *et al*., 1992, Kalia *et al*., 2004), osteocalcin (Kobayashi *et al*., 1998, Glowacki *et al*., 2004) and parathyroid hormone (Soma *et al*., 2000) administration locally and systemically. Other non-surgical approaches include movement of teeth by trauma-induced stimulation (MOTIS), such as low-level laser therapy involving Gallium-Aluminum-Arsenide (Ga-Al-As)/diode laser (Kawasaki *et al*., 2000), mechanical vibration (Nishimura *et al*., 2008), application of therapeutic ultrasound (El-Bialy *et al*., 2011) and light-accelerated orthodontics (LAO) involves photobiomodulation or low-level light therapy (Kau *et al*., 2013) which applied together with orthodontic force to accelerate OTM. These procedures are less invasive and also have shown less adverse effects during acceleration of OTM (Kawasaki *et al*., 2000, El-Bialy *et al*., 2011). Although the pharmacological approaches manifest the rapid movement of the tooth, evidence shows some adverse effects also such as local pain, severe root resorption, and systemic side effects (Brudvik *et al*., 1991, Leiker *et al*., 1995, Sekhavat *et al*., 2002, Yamaguchi *et al*., 2005). For this reason, researchers turned towards finding a new approach, MOTIS, without any adverse effects.

The surgical approach includes more extensive corticotomy and less extensive flapless corticotomy procedures to accelerate OTM. The theory behind these procedures is a regional acceleratory phenomenon (RAP) of wound healing that starts in alveolar bone with an initial burst of osteoclastic activity, decreasing bone density, followed by enhanced bone remodelling (Frost, 1983). The extensive corticotomy surgical technique involves intentional surgical trauma on the cortical bone with reflecting full thickness of mucoperiosteal flap by performing dental or periodontal distraction (Liou, 1998), selective alveolar decortication with the enhancement of cortical bone termed as periodontally accelerated osteogenic orthodontics (PAOO) (Wilcko *et al*., 2001), corticotomies (Moon *et al*., 2007), osteotomies (Sebaoun *et al*., 2007, 2008). Whereas, the less invasive or flapless corticotomy surgical technique involves intentional surgical trauma on the cortical bone without reflecting gingiva and named corticision (Park *et al*., 2006), piezocision (Dibart *et al*., 2009), perforation (Seifi *et al*., 2012, Cheung *et al*., 2016) puncture alveolar bone (Alikhani *et al*., 2013, Kim *et al*., 2013) and latest discision (Yavuz *et al*., 2018).

However, extensive surgical approach such as dental distraction, PAOO, corticotomies, osteotomies, has been increased the risk of postoperative pain, subcutaneous hematomas of the face and neck, scarring on the gingiva, loss of attached gingiva, interdental bone loss, and periodontal defects such as a reduction in alveolar bone height (Dorfman *et al*., 1979, Kwon *et al*., 1985, Ozturk *et al*., 2003, Hassan *et al*., 2010). This possibly explains the lack of enthusiasm from both patients and orthodontists to adopt these techniques, and the trend has turned towards finding less invasive techniques. The details about the extensive or flapless corticotomy procedure and their outcome is describing in the literature review chapter.

These days, the use of piezoelectric ultrasonic blades is an alternative tool to the traditional bur, Dibart *et al*. (2009) have been introduced a modified flapless corticotomy by using piezotome tools and termed as piezocision for the first time. The procedure involved inducing transient RAP; therefore, rapid tooth movement can be achieved without injury of nerves, blood vessels, mucosa, periosteum, periodontal ligament, and other soft tissues (Dibart *et al*., 2009, Sebaoun *et* al., 2011, Ruso *et al*., 2014, Dibart *et al*., 2015). Orthodontists are often interested in conducting the less invasive corticotomy in their professional practice. If the treatment time rate reduces 30-50 %, the patient is also interested in undergoing a flapless corticotomy procedure and willing to pay higher monthly fees to reduce treatment time (Uribe *et al*., 2014). Therefore, to accomplish faster OTM without the downside of an extensive and traumatic surgical approach, one can use a less invasive piezocision procedure to decrease overall orthodontic treatment time.

1.2 Problem statement

Based on the literature review reports, there are a few randomized clinical trials (RCT), where researchers performed piezocision procedure to investigate the overall time required for orthodontic treatment to eliminate moderate crowding in the anterior maxilla and mandibular arch in non-extraction cases (Charavet *et al*., 2016, Uribe *et al*., 2017, Yavuz *et al*., 2018, Charavet *et al*., 2019). So far, there is only one clinical trial that reported overall treatment time to complete levelling and alignment of lower anterior severe crowding case required premolar extraction (Gibreal *et al*., 2018). Another few RCT studies reported the time required for only canine retraction or en-masse retraction stage of orthodontic treatment by performing piezocision procedure (Aksakalli *et al*., 2016, Abbas *et al*., 2016, Tuncer *et al*., 2017, Alfawal *et al*., 2018). Up to date, there is no study about the time required to reach the complete levelling and alignment stage of both maxilla and the mandible separately in first premolar extraction cases by performing piezocision procedure.

There is also insufficient evidence about the influence of piezocision on surrounding tooth structure, i.e., gingival recession, periodontal pocket depth, and pulp vitality. The dimensions of the piezocision cut and follow up visit vary between clinical trials; there were five different lengths × depth of corticotomies found between nine clinical trials, and patient recall visit also varied between 2-5 weeks to activate the orthodontic appliance to stimulate the RAP effects, which naturally remain short term (Charavet *et al*., 2016, Aksakalli *et al*., 2016, Abbas *et al*., 2016, Uribe *et al*., 2017, Tuncer *et al*., 2017, Alfawal *et al*., 2018, Yavuz *et al*., 2018, Gibreal *et al*., 2018, Charavet *et al*., 2019). However, among these studies, two of the studies did not find a significantly shorter duration of the orthodontic treatment time (Uribe *et al*., 2017, Tuncer *et al*., 2017). Besides that, in the clinical orthodontic practice, it is not feasible to recall a patient every two weeks to spare time from daily busy life due to the long duration of orthodontic treatment outcome; patients also feel exhausted from frequent visits in the clinic (AlSadhan, 2013). Even difficult for doctors to manage all patients for a long time schedule.

Hence a well-designed randomized clinical trial is needed to investigate the efficacy of modified piezocision procedure to accelerate OTM in alignment and levelling stage of first premolar extraction cases following the regular recall interval 4-5 weeks. Besides that, it is also necessary to evaluate the changes of surrounding tooth structure and the patient's response to the treatment procedure due to the influence of piezocision during the alignment and levelling stages of orthodontic treatment.

1.3 Justification of the study

Conventional corticotomy procedure requires a full mucoperiosteal flaps reflection at both buccal and palatal sides of the teeth and extends beyond the apices of the teeth that need to be moved. Selective decortications may be performed on both buccal and lingual sides using a diamond round bur or piezoelectric blade (Wilcko *et al*., 2001). This intentional surgical trauma stimulates the RAP as a wound healing process, which is transient in nature and the most influential factor to accelerate tooth movement (Wilcko *et al*., 2001, Mostafa *et al*., 2009, Huang *et al*., 2014). The whole procedure increases the risk of postoperative pain, swelling, infection, scarring, attached gingiva loss, pulp vitality loss, root damage, and interdental bone loss (Dorfman *et al*., 1979, Kwon *et al*., 1985, Ozturk *et al*., 2003, Hassan *et al*., 2010).

In light of the current limitations, the development of a less invasive method to get the most out of RAP to accelerate the tooth movement, minimize the risk and maximize the efficacy is essential (Kim *et al*., 2009, Dibart *et al*., 2009). Piezocision procedures have been proposed as a less invasive and effective tool to accelerate OTM (Kim *et al*., 2009, Dibart *et al*., 2009). Most of the in vivo animal study found encouraging results about piezocision procedure and perform repeated piezocision procedure 2-3 weeks later or 1-2 months later with 0.25-0.5mm depth of corticotomies to re-activate the RAP and utilize the phenomenon effect to accelerate the tooth movement (Kim *et al*., 2009, Safavi *et al*., 2012, Murphy *et al*., 2014). But in humans, every two weeks, repeated piezocision procedures could be difficult and will not be accepted by the patient.

Despite the significant results obtained from the animal studies, the evidence to support the piezocision procedures has been limited to some clinical trials. To date, only seven clinical trials found that the piezocision procedure significantly shortens the orthodontic treatment time (Charavet *et al*., 2016, Aksakalli *et al*., 2016, Abbas *et al*., 2016, Alfawal *et al*., 2018, Yavuz *et al*., 2018, Gibreal *et al*., 2018, Charavet *et al*., 2019) and others two clinical trials found piezocision procedure was not so effective to accelerate orthodontic tooth movement (Uribe *et al*., 2017, Tuncer *et al*., 2017). These conflicting results may be explained by the difference in corticotomy depth and frequency of recall visits to activate orthodontic appliances performed in each study.

Therefore, based on the previous study report, the current study performed a pilot study before starting the clinical trial, to see the efficacy of piezocision procedure and modified the approach of piezocision design that include minimum interproximal vertical cut than the original methods described by Dibart et al. (2009, 2010, 2015) with adequate depth of corticotomies to reach the medullary bone to get the full effect of the regional acceleratory phenomenon for the piezocision group, and follow up visit for orthodontic appliance activation on every 4-6 weeks instead of 2 weeks interval and bone grafting will not be considered, which is similar to Uribe et al. (2017). Hence, there is a need for well-designed RCTs to investigate the merit of this modified approach to accelerate OTM in the alignment and levelling stage in extraction cases.

This randomized controlled clinical trial was designed to investigate the efficacy of the modified piezocision procedure to accelerate OTM in the levelling and alignment stage of first premolar extraction cases. Besides that, this study has also investigated the influence of modified piezocision flapless corticotomy surgical approach on surrounding tooth structure such as gingival recession, periodontal pocket depth, tooth vitality, and changes of Little's Irregularity Index. Most patients experience pain and discomfort during orthodontic treatment (Ngan *et al*., 1989, Scheurer *et al*., 1996, Erdinc *et al*., 2004, Giannopoulou *et al*., 2006). Therefore, patients might be concerned about the pain after the piezocision procedure. However, there is a lack of evidence in patient perception of pain and satisfaction after piezocision procedures; this study was also being investigated pain level and level of satisfaction score among patients regarding piezocision procedure.

1.4 Research questions

How long does it take to complete the leveling and alignment stage of orthodontic treatment of first premolar extraction cases by using the modified method of piezocision procedure?

1.5 Research hypothesis

This study hypothesized that the modified method of flapless corticotomy using piezocision procedure could induce the RAP effect, thereby accelerate the tooth movement and reduce the treatment time of levelling and alignment stage than conventional orthodontic treatment. In addition, this modified approach is expected to result in minimal changes to the surrounding tooth structures, which are comparable to the conventional orthodontic method, with limited pain experience and optimum satisfaction in the piezocision group.

1.6 General objective

- The study aims to investigate the efficacy of modified flapless corticotomy using piezocision to accelerate the levelling and alignment stage in orthodontic cases that require first premolar extraction.

1.7 Specific objectives

1. The study aims to determine the time duration required to complete the levelling and alignment of maxillary and mandibular anterior teeth (canine to canine) in the modified piezocision and conventional orthodontics group.
2. The study aims to compare the time duration required to complete the levelling and alignment of the maxillary and mandibular arch between the modified piezocision and conventional orthodontics group.

3. The study aims to evaluate and compare the changes in Little's Irregularity Index during levelling and alignment of maxillary and mandibular teeth in piezocision and conventional orthodontics groups.
4. The study aims to evaluate and compare the changes in alignment rate during levelling and alignment of maxillary and mandibular teeth in piezocision and conventional orthodontics groups.
5. The study aims to assess and compare the changes of surrounding tooth structure (gingival recession, pocket depth, and pulp vitality) during levelling and alignment of maxillary and mandibular teeth in piezocision and conventional orthodontics groups.
6. The study aims to assess the patient perception about pain level and level of satisfaction about the surgical procedure in the piezocision group.

CHAPTER 2

LITERATURE REVIEW

2.1 Tooth supporting tissues

Periodontium modification occurs while tooth movement starts during orthodontic treatment, depending on the force level, direction, and duration of force applied (Graber *et al*., 2011). The periodontium is derived from ectomesenchyme of the first branchial arch and is composed of connective tissue that protects the tooth. It is a highly vascularized soft tissue that helps to attach the roots of teeth with the jaw bone and keep the masticatory mucosa integrity of the oral cavity. The periodontium consists of the alveolar bone, gingiva, root cementum, and periodontal ligament (PDL). Depending on age, function, morphology, and oral environment, tooth movement can trigger changes in supporting structures of the tooth (Lindhe *et al.*, 2003, Graber *et al*., 2011).

2.1.1 Gingiva

The gingiva is a part of the masticatory mucosa that covers the alveolar process and encircles the cervical portion of the teeth. Gingiva can be distinguished into the free gingiva, which is coral pink and in a coronal direction. The attached gingiva is dark red in colour and demarcated by the mucogingival junction in an apical direction (Lindhe *et al*., 2003). Typically, the free healthy gingiva is in proximity with the enamel surface and has a coronal margin of 0.5 to 2mm at the cementoenamel junction after the tooth eruption has been completed. The attached gingiva is firmly attached by connective tissue fibres to the underlying alveolar bone and cement and is thus fairly immobile with the underlying tissue.

The principal element of the gingiva is the connective tissue, which contains nerves, blood vessels, collagen fibres, fibroblasts, and matrix. The bundles of collagen fibrils provide the elasticity needed to maintain its architectural form and the strength of the dentogingival attachment. The group of collagen fibrils is directed towards the tooth structure, such as circular fibres covering the free gingiva and the teeth. In contrast, the dentogingival fibres are embedded in the cementum of the supra-alveolar portion of the root and extend from the cementum into the free gingival tissue in a fanlike configuration (Figure 2.1). Dentoperiosteal fibres are immersed in the same portion of the cementum as the dentogingival fibres but end up in the tissue of the attached gingiva, while trans septal fibres are guided directly across the interdental septum and embedded in the adjacent teeth cementum. (Lindhe *et al*., 2003, Graber *et al*., 2011).

2.1.2 Periodontal ligament

The PDL is a highly vascular, cellular, and soft connective tissue that encircles the roots of the teeth and attaches to the cementum of the root with a socket wall. The PDL is located around the roots of the teeth and the alveolar bone proper. The width of the PDL range between 0.2-0.4mm. The principal fibres of PDL are alveolar crest fibres, horizontal, oblique, apical, and inter-radicular fibres (Figure 2.2). The presence of a periodontal ligament permits physiologic tooth movement within its socket, which makes it possible to distribute and resorb the forces generated during masticatory function and other tooth contacts are essential for the movement of the teeth in orthodontic treatment (Lindhe *et al*., 2003, Graber *et al*., 2011).

The PDL fibrils are embedded in a ground substance with polysaccharides of the connective tissue (glycosaminoglycan's), which differ with age. For older people, the tissue's reaction to orthodontic forces, including the transfer of collagen fibres and cell mobilization, is considerably slower than in children and adolescents. The field content with collagen has a greater regeneration than the fibres (Graber *et al*., 2011).

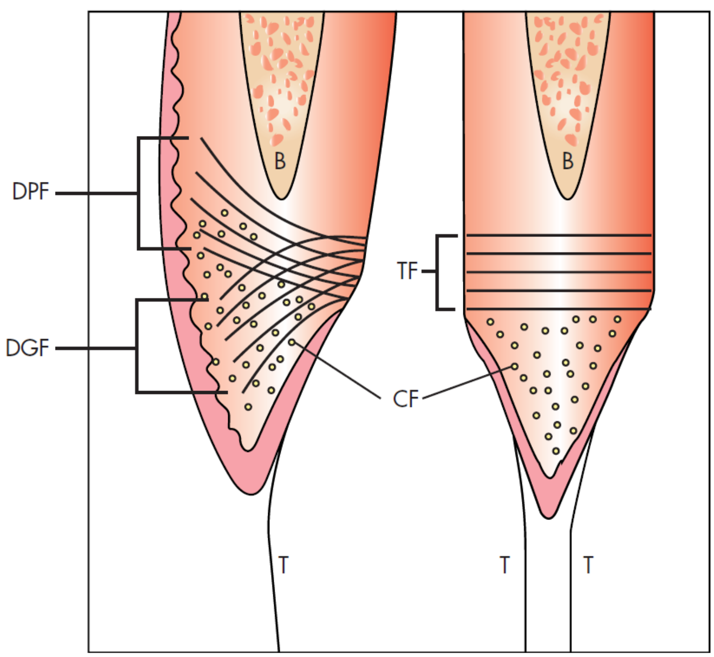

Figure 2. 1: Different collagen bundles in the gingival showing circular fibres (CF), dentogingival fibres (DGF), dentoperiosteal fibres (DPF), and transseptal fibres (TF) (Graber *et al*., 2011).

2.1.3 Cementum

The root cementum is a dense, mineralized tissue that has no blood vessels. By gradual apposition, the different types of cementum increase in thickness over the lifespan. In the apical segment of the root, the cementum is comparatively wider than in the cervical part, where the thickness is only 20-50μm, and the cementum is often 150-250μm wide in the apical root portion. Cementum connects the PDL fibres to the root and contributes to the repair process following root surface damage (e.g., during orthodontic treatment) (Lindhe *et al*., 2003). Besides, as the cementum surface resorption arises due to orthodontic force, it is completely regenerated or remodelled. When the cementum is resorbed together with the outer layers of dentin, the cementum itself is repaired, and morphological alterations are obtained. However, if the root loses an apical portion beyond cementum, regeneration will not be possible. After two weeks, the reparative process begins when the orthodontic force is withdrawn, and the results become apparent within 6-8 weeks by acellular cementum is laid down in initial stages followed by cellular cementum (Brezniak *et al*., 2002).

2.1.4 Alveolar bone

The outside of the alveolar bone is very thick and termed cortical bone, and the inner side of the bone is named cancellous bone covered by the periosteum. The alveolar process forms and supports the tooth sockets within the maxillary and mandibular bones. The alveolar bone is a densely connective tissue consisting of inorganic (67%) and organic (33%) components and is capable of continuous remodelling in response to functional requirements. Bone-forming osteoblasts and osteoclasts, cells involved in resorption, are responsible for this remodelling process. These cells are present on the socket walls toward the periodontal membrane, on the inside of the cortical bone toward the marrow spaces, and the bone trabeculae's surface in cancellous bone (Lindhe *et al*., 2003, Graber *et al*., 2011).

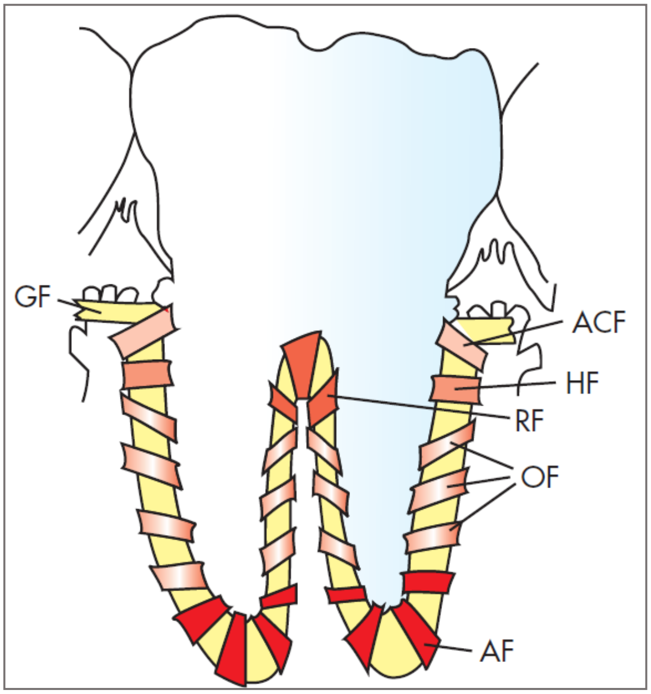

Figure 2. 2: The PDL fibres: alveolar-crest fibres (ACF), apical fibres (AF), gingival fibres (GF), horizontal fibres (HF), oblique fibres (OF), and inter radicular fibers (RF) (Graber *et al*., 2011).

2.2 Healing process of hard and soft tissues:

2.2.1 Bone remodelling

Bone remodelling is an integral part of the healing process, which involves the apposition and deposition of a discrete, identifiable bundle of cortical or trabecular bone (Robling *et al*., 2006). Cells originating from different sources are referred to as the basic multicellular unit (BMU) that controls the sequences of bone remodelling events. BMUs are responsible for continuous bone remodelling by resorbing degraded bone to create a resorption cavity filled with new bone. This cycle is commonly referred to as ARF (activation, resorption, formation) (Robling *et al*., 2006).

The remodelling rate depends on osteoblast cell lineage, which is also responsible for activating osteoclast precursors cells (Takahashi *et al*., 1998). However, the induction of osteoclastogenesis had happened due to an intermediary factor on the osteoblastic surface. This factor is a member of the tumour necrosis factor (TNF) superfamily and was termed receptor activator of nuclear factor κβ ligand (RANKL) (Hsu *et al*., 1999). In the presence of macrophage-colony stimulating factor (M-CSF), RANKL binding to its cognate receptor RANK, which is present on the surface of osteoclast progenitor cells, induces osteoclastogenesis and rapid differentiation and proliferation of hematopoietic osteoclast precursors to mature osteoclasts resulting in increased bone resorption (Hsu *et al*., 1999, Nakagawa *et al*., 1998). Nonetheless, RANKL also can bind to osteoprotegerin (OPG), a soluble decoy receptor protein that attaches competitively to the cell surface membrane-bound RANKL proteins and inhibits osteoclastogenesis activation by RANKL, therefore, decreases bone resorption (Simonet *et al*., 1997) (Figure 2.3).

A key determinant of the recruitment rate and activation of immature osteoclasts is believed to be the ratio of RANKL / OPG expression by osteoblasts. Production of RANKL and OPG proteins was observed in human periodontal cells. In periodontitis tissues, pathologically lymphocytes and macrophages show associations with RANKL protein production, and endothelial cells have correlations with OPG production. From an orthodontic viewpoint, variations in pressure changes in the tooth socket's microenvironment may induce up and down-regulation of the RANKL and OPG genes to modulate protein production, and eventually, bone remodelling (Hasegawa *et al*., 2002).

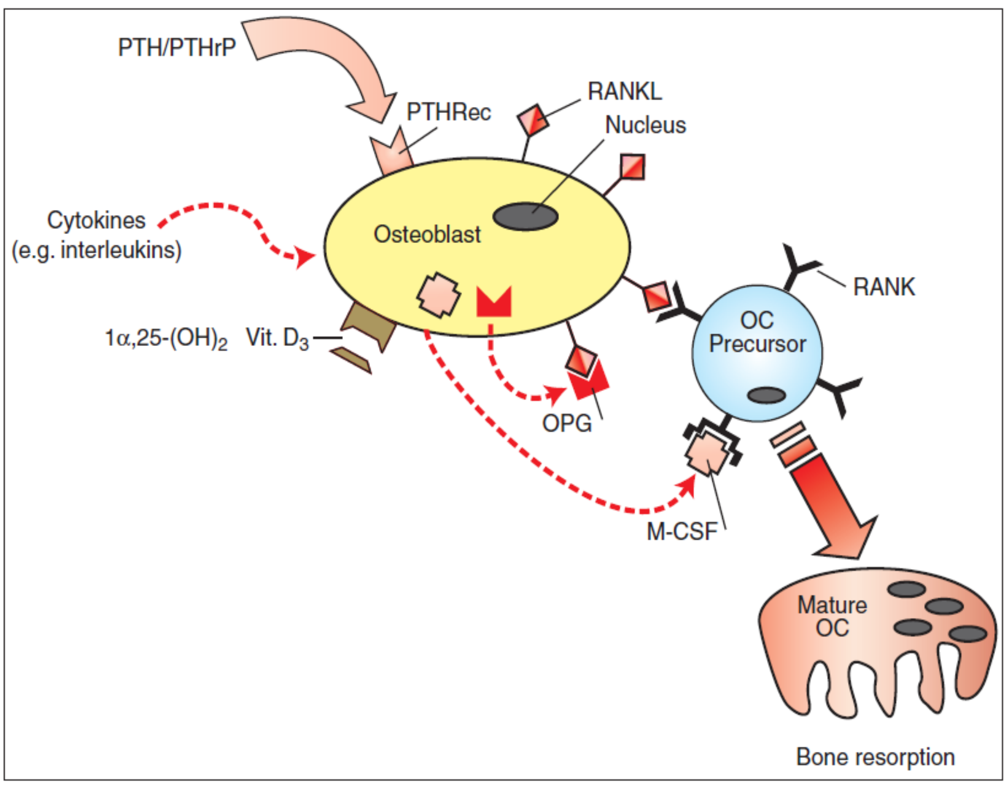

Figure 2. 3: Theoretical regulation of osteoclastogenesis by osteoblasts (Nanda 2005).

2.2.2 Periodontal soft tissue healing

The soft tissue healing process starts immediately after tissue injury or surgical insult by initiating blood coagulation or the hemostatic phase. There is an activation of extravasated platelets, red blood cells, and neutrophils in the blood clot, known as blood coagulum. The extracellular matrix mainly consists of newly formed fibrin meshwork that includes other cell adhesion proteins, such as fibronectin and vitronectin (Sculean *et al*., 2014). These fibrin-rich matrices will be replaced by granulation tissue later. The inflammatory response starts at 6/7 days, an increase in vascularization of the flap's remaining connective tissue. Chemokines attract the neutrophil, and by peptides released during the separation of fibrinogen. Neutrophils kill invading bacteria and clean the wound site as they release proteases before eliminated via phagocytosis (Sculean *et al*., 2014).

The stage of new tissue formation is initiated by the "granulation tissue" development, a morphologic term that depicts highly vascularized tissue made of an extracellular matrix and fibroblast. A complex process involving at least three types of cells requires activation of the catabolic transition to the anabolic phase: endothelial cells, epithelial cells, and fibroblasts. Such myofibroblasts can pull together the wound edges and are, therefore, essential components of wound healing (Sculean *et al*., 2014). The flap is reattached to the tooth and bone after 12 days, while the gingiva's oral epithelium tends to be keratinized. At around four weeks, dense, structured, connective tissue re-attaches the flap to the tooth. The tissues seem to be completely regenerated at five weeks and do not exhibit differences compared to barren sites (Sculean *et al*., 2014).

2.3 Orthodontic tooth movement

2.3.1 Theories of orthodontic tooth movement

Biology of the tooth movement and biomechanics are required to understand how to accelerate the orthodontic tooth movement (OTM). The biomechanics of orthodontic is mainly aimed at tooth movement by bone remodelling and functional alterations in tooth-supporting tissues, including dental pulp, based on force magnitude, types, and duration of the force (Proffit *et al*., 2013). OTM varies from physiological tooth eruption. Since the process of physiological tooth movement is slow and covers only a short period in life, that occurs mainly in the frontal direction into trabecular bone due to compact jawbones' growth. In contrast, OTM can appear rapidly or slowly, depending on the physical characteristics of the applied force, pressure distribution per area, and the PDL's biological response (Krishnan *et al*., 2006).

When the orthodontic force is applied to the tooth, different types of tooth movement create such as tipping, torque, bodily movement, rotation, intrusion, and extrusion, depends on the direction, amount, and application of the force. Therefore, the applied orthodontic force distribution within the PDL is different, and consequently, the pressure of PDL also differs with different types of tooth movement (Proffit *et al*., 2013). Force applied for OTM mediated strains modify the PDL's vascularity and blood flow resulting in local increased expression of many main molecules, such as cytokines, neurotransmitters, growth factors, and arachidonic acid metabolites. Such molecules can boost several cellular responses in and around the teeth through different cell types, offering a preferred microenvironment for deposition or resorption of tissue, thus reshaping the bony alveolar contour (Krishnan *et al*., 2006).

2.3.1(a) The pressure-tension theory

Classic histologic research led to the development of the pressure-tension hypothesis stated by Sandstedt, Oppenheim, and Schwarz, that is, when orthodontic force applies on the tooth, it creates a "pressure side" and a "tension side" in the periodontal ligament space and causes the tooth to move within the PDL space (Krishnan *et al*., 2006). Blood flow is decreased in compressed PDL space on the pressure side, which leads to decreased cellular activity and decreases fibre production. In contrast, on the tension side, blood flow is maintained or increased, stretching of the PDL fibres results in increased cellular activity and increased fibre production. Therefore, during orthodontic therapy, forces should be applied between 20-25gm/cm2 of root surfaces so that it could not damage or necrosed the capillary bed blood pressure due to compressed periodontium (Krishnan *et al*., 2006).

These chemical changes stimulating the release of other biologically active agents, thereby promoting cellular differentiation, begin within PDL. When light force is applied, tooth movement beginning as osteoclast/ osteoblast remodel at the lamina dura of the bony socket immediately adjacent to the ligament, known as frontal resorption (Figure 2.4). Application of heavy force level leads to cell death in the compressed area and the formation of sterile necrosis known as hyalinization. In this case, cell differentiation and bone resorption occur in adjacent marrow spaces underside the lamina dura of the alveolar bone, termed as undermining resorption (Proffit *et al*., 2013, Krishnan *et al*., 2006). The phenomenon of the recurrent pattern starts from applying force to the regulation of cellular activity and the bone's response forming the fundamental theme of the 'pressure-tension hypothesis.'

2.3.1(b) Bioelectric signals in orthodontic tooth movement

Bassett and Becker (1962) described that there is the propagation of electric potential in the stressed tissues in response to applied mechanical forces. Hence these electric potentials might charge macromolecules that interact with specific cell membrane sites or mobilize ions across cell membranes (Krishnan *et al*., 2006). The bioelectric theory proposes that when alveolar bone flexes and bends, it causes changes in bone metabolism controlled by the electric signals and produced tooth movement. The bending of the bone causes small electrical charges. This phenomenon has been observed in the bending of dry bone and therefore hypothesized that these electric signals might stimulate orthodontic tooth movement (Fukada *et al*., 1957).

Zengo et al. (1974) described that after orthodontic treatment, the treated bone of the concave side is filled with electronegative ions and shows more osteoblastic activity. In contrast, the convex areas filled with electropositive ions revealed with increased osteoclastic activity experiment in a dog. It has been supported by another study Davidovitch et al. (1980), who use the feline model, demonstrated that near the electronegative side (PDL compression site) increases the bone resorption and bone formation near the electropositive side (tension side).

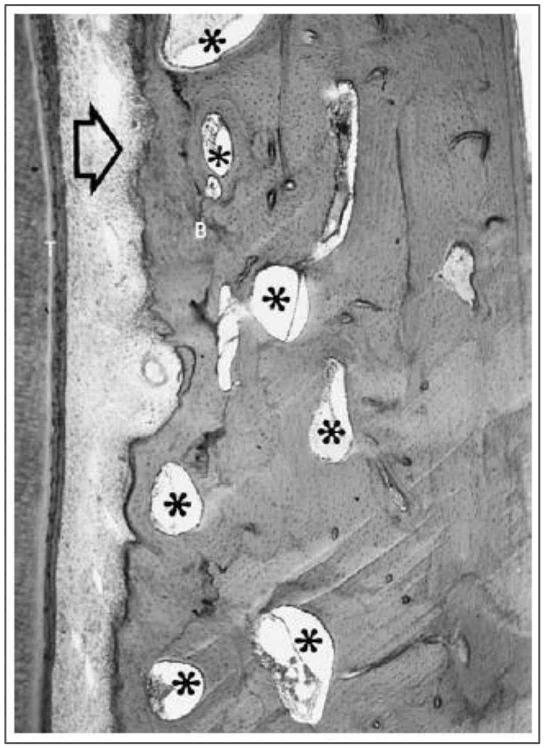

Figure 2. 4: Demineralized histologic section of human periodontium reveals the modelling and remodelling mechanisms of progressive tooth movement through a dense cortical bone (Graber *et al., 2011*).

2.3.1(c) Bone bending theory

In the OTM pressure-tension principle, Baumrind acknowledged a logical error. According to Pascal's rule, the PDL is a continuous hydrostatic device, and therefore any force applied to it would be distributed to all regions uniformly. The author found out that the only portion of the periodontium where differential stresses could occur as indicated by the principle of pressure-tension was in the hard tissues, namely the bone and the tooth (Krishnan *et al.*, 2006). When a force is applied, it results in the bone bending that reacts most elastically by inducing bone turnover via cellular processes activation. The bone reorganization is not limited solely to the alveolus lamina dura but stretches to the trabeculae level. The force applied to the tooth results in stress lines being formed, and the biological reaction arises in cells perpendicular to the stress lines. The overall result of cellular activities is a change in bone shape and internal structure (Baumrind *et al*., 1969). The bone bending principle can clarify some clinical findings, including the apparent slowness of teeth en-masse retraction, tooth progression speed to an extraction site, and the speed of the OTM has increased in children who have fewer calcified bones compared to adults (Grimm *et al*., 1972).

2.4 Phases of tooth movement

Burstone (1962) was first identified and outlined tooth movement stages after the force was applied during orthodontic therapy. He suggested three different tooth movement phases, such as initial strain or initial phase, lag phase, and linear or progressive tooth movement. Right following application of force, the initial stage is marked by the rapid movement of the tooth within the PDL with cellular and tissue reactions begins, bone strain, and extrusion (Figure 2.5). This reaction differs due to occlusion, the width, quality of the PDL, length of the tooth root, and amount of bone resorption. Typically, this phase lasting 1-2 days (Burstone, 1962).

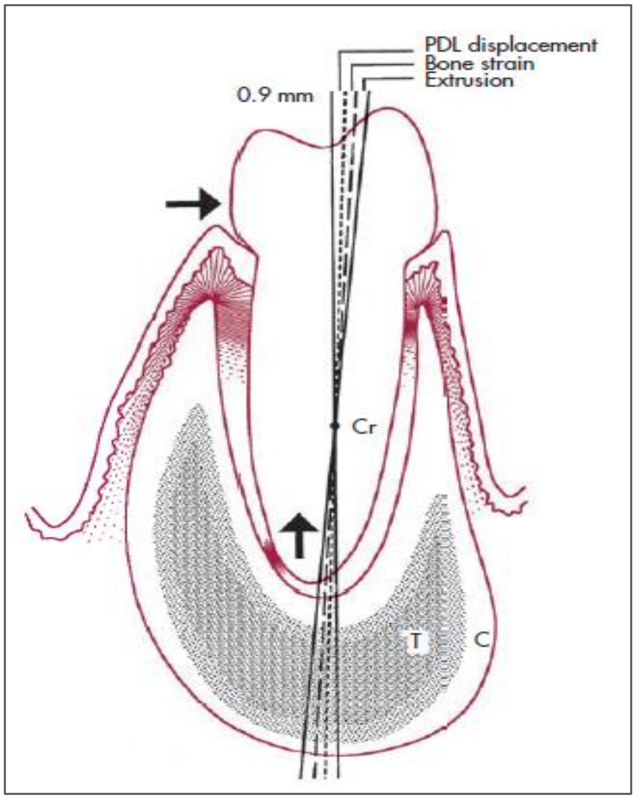

Figure 2. 5: Phases of tooth movement: initial displacement (1 to 3 days) of a tooth exposed to tipping (horizontal) load usually is about 0.5 mm but maybe as much as 0.9 mm for slightly mobile teeth, periodontally compromised, or heavily loaded. The three components are (1) displacement of the root in the periodontal ligament (PDL); (2) bone strain caused by bending and creep; and (3) extrusion caused by the inclined plane effect of the tooth root pressing against a tapered alveolus (Graber *et al., 2011*).

There is a lag period immediately after the initial phase due to hyalinization of the PDL located in compression areas. No further movement of the tooth continues until the cells destroying the necrotic tissues completely. This phase is marked by a deterioration of the PDL on the stress side that contributes to an interruption of the blood flow that can activate the hyalinised region and interrupt the teeth' movement. Hence, the elimination of the hyalinised layer is viewed histologically as a cell-free