EFFECTS OF LOW-LEVEL LASER THERAPY ON ORTHODONTIC TOOTH MOVEMENT: A RANDOMISED CLINICAL TRIAL

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APPENDIX E: Randomization plan

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LIST OF PUBLICATION

PUBLICATIONS

LIST OF ABBREVIATIONS

AB	Apical Buccal
AD	Arch Depth
AD	Apical Distal
AL	Arch Length
ALD	Arch Length Discrepancy
AM	Apical Mesial
ANOVA	Analysis of Factorial Variance
AP	Arch Perimeter
AP	Apical Palatal
C_1	Initial Crown Length
C_2	Crown Length After Levelling Alignment Stage
Camp	Cyclic Adenosine Monophosphate
CB*	Cervical Buccal
CB	Conventional brackets
CBCT	Cone Beam Computed Tomography
CCO	Cytochrome C Oxidase
CD	Cervical Distal
CD	Compact Disc
CEJ	Cemento Enamel Junction
CF	Correction Factor
CGMP	Cyclic Guanosine Monophosphate
CI	Confidence Interval
CM	Cervical Mesial

CO_2	Carbon Dioxide
CONSORT	Consolidated Standards of Reporting Trials
CP	Cervical Palatal
CT	Computed Tomography
DAI	Dental Aesthetic Index
DICOM	Digital Imaging and Communications in Medicine
DDM	Digital Dental Models
DPA	Dual-energy photon absorptiometry
DXA	Dual energy X-ray absorptiometry
Er-Cr:YSGG	Erbium-Chromium: Yttrium Scandium Gallium Garnet
FDA	American Food and Drug Association
FDI	Federation Dentaire Internationale
FOV	Field of View
Ga-Al-As	Gallium-Aluminum-Arsenic
GCF	Gingival Crevicular Fluid
GLA	Gamma Carboxyglutamic Acid
Group A	Self-Ligating Bracket Laser Group
Group B	Conventional Bracket Laser Group
Group C	Self-Ligating Bracket Non-Laser Group
Group D	Conventional Bracket Non-Laser Group
He-Ne	Helium-Neon
HLD	Handicapping Labio-Lingual Deviation
HREC	Human Research and Ethical Committee
HU	Hounsfield Units

ICC	Intra Class Correlation
ICW	Inter Canine Width
IEC	Electrotechnical Commission
IMW	Inter-Molar Width
IP3	Inositol Phosphatase 3
J/Cm^2	Joule/Square Centimetre^2
JEPeM	Jawatankuasa Etika Penyelidikan Manusia
LASER	Light Amplification by Stimulated Emission of Radiation
LED	Light Emitting Diodes
LII	Little Irregularity Index
LLLT	Low-Level Laser Therapy
Man	Mandibular
MAP	Mitigen Activated Protein
Max	Maxillary
MB	Middle Buccal
MBT	Mclaughlin Bennett Trevisi
MD	Middle Distal
MM	Middle Mesial
mm	Millimetre
MP	Middle Palatal
mRNA	Messenger Ribonucleic Acid
mW	Milliwatt
NiTi	Nickel Titanium
nm	Nanometre

NRS	Numerical Rating Scale
NSAIDs	Nonsteroidal Anti-Inflammatory Drugs
OP	Osteoprotegerin
OPG	Orthopantomogram
OTM	Orthodontic Tooth Movement
P	P Value
PA	Posterior Anterior
PAR	Peer Assessment Rating Index
PDL	Periodontal Ligament
PG	Prostaglandin
PGE2	Prostaglandin E2
PTH	Parathyroid Hormone
QCT	Quantitative computed tomography
R_1	Initial Root Length
R_2	Root Length After Levelling Alignment Stage
RANKL	Receptor Activator of Nuclear Factor Kappa-B Ligand
RG	Radiogrammetry
RP	Radiographic Photo densitometry
RR	Root Resorption
SD	Standard Deviation
SL	Self- Ligating
SPA	Single energy photon absorptiometry
SS	Stainless Steel
T_1	Pre-Treatment

T_2	After Levelling and Alignment
TM	Transportation Management
TMJ	Temporomandibular Joint
TNF	Tumour Necrosis Factor
USM	Universiti Sains Malaysia
VAS	Visual- Analog Scale
VEGF	Vascular Endothelial Growth Factor
vs	Versus
#	FDI notations
*	Significant Difference ($p<0.05$)
2D	Two-Dimensional
3D	Three-Dimensional

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KESAN TERAPI LASER PERINGKAT RENDAH TERHADAP PERGERAKAN GIGI ORTODONTIK: SATU PENILAIAN KLINIKAL SECARA RAWAK

ABSTRAK

Kajian ini bertujuan untuk menilai kesan terapi laser aras rendah (LLLT) terhadap Index Ketaktentuan Little (LII), keberkesanan penjajaran dan susunan gigi, perubahan dimensi lengkung alveolar gigi, persepsi kesakitan, inter radikular dan perubahan tulang bukolingual, resorpsi akar, ketumpatan tulang dan penggunaan masa untuk cabutan ortodontik menggunakan sistem pendakap pasang sendiri dan konvensional dengan penilaian tiga dimensi (3D) melalui pancaran kon tomografi berkomputer (CBCT) dan model pergigian digital (DDM). Satu ujian klinikal secara rawak telah dijalankan ke atas sejumlah tiga puluh dua pesakit (lapan orang bagi setiap kumpulan) yang mempunyai min umur 22.41 (4.18). Rekabentuk kajian ini digunakan sebagai kumpulan eksperimen dan kumpulan kawalan secara rawak. Pesakit kemudiannya dibahagikan pula kepada empat kumpulan secara rawak [A=Pendakap pasang sendiri laser (SLL), B = Pendakap konvensional laser (CBL), C = Pendakap pasang sendiri bukan laser (SLNL), D = Pendakap konvensional bukan laser (CBNL)]. Peranti laser dengan panjang gelombang 940nm digunakan dalam kajian ini. Penyinaran laser digunakan untuk kedua-dua gigi kacip atas dan bawah dan juga pada gigi taring selama 6 saat pada setiap titik (bahagian mesial dan distal apikal, tengah, bahagian mesial dan distal kawasan servikal) dimana hasil keluaran laser berukuran 100nW dan ketumpatan daya untuk setiap gigi adalah 7.5J/cm. Data pesakit semasa pra-rawatan dan pada peringkat akhir penyusunan dan penjajaran CBCTdan DDM

diambil dan dinilai menggunakan Perisian Planmeca Romexis TM 2.3.1 R (Helsinki, Findland). DDM menilai pemecutan pergerakan gigi dan perubahan dimensi lengkung. Resopsi akar, inter radikular, perubahan tulang bukolingual dan ketumpatan tulang pula diukur menggunakan data dari CBCT. Skala analog visual diberikan kepada pesakit supaya mereka dapat merekodkan peningkatan kesakitan selama tujuh hari. Kenormalan data dinilai melalui ujian Shapiro –Wilk. Ujian parametrik atau bukan parametrik dilaksanakan berdasarkan taburan data yang diperolehi. Ujian pekali kolerasi intrakelas digunakan untuk memeriksa kebolehpercayaan semua pembolehubah. Ujian t- berpasangan dan ujian taraf bertanda Wilcoxon dilaksanakan untuk membuat perbandingan dalam kumpulan. Statistik perihalan digunakan untuk menilai persepsi kesakitan yang berdasarkan penempatan dawai berlainan selama tujuh hari. Ujian t- tak bersandar dan ujian Mann Whitney dijalankan untuk membuat perbandingan antara kumpulan tanpa mengira penggunaan sistem pendakap atau LLLT. Untuk menilai perbandingan kesemua empat kumpulan, ANOVA sehala dengan pembetulan Post Hoc Bonferroni dan Kruskal Wallis telah dijalankan. Nilai kolerasi intra kelas untuk kebolehpercayaan intra pemeriksa dan kebolehpercayaan antara pemeriksa berada dalam julat kolerasi yang cukup bagus untuk semua pembolehubah. Kebanyakan pembolehubah menunjukkan perbezaan yang signifikan dalam perbandingan dalam kumpulan. Namun begitu terdapat juga beberapa pembolehubah yang menunjukkan perbezaan yang signifikan semasa perbandingan antara kumpulan tanpa mengira sistem pendakap yang digunakan (pemecutan pergerakan gigi, resopsi akar pada lateral kiri insisor, ketumpatan tulang CM11.AD11) dan penggunaan LLLT (lebar inter molar mandibular, kesakitan pada dawai .017×.025 NiTi dan ketumpatan pada MM33,CD31, CD 41, MP33). Perbandingan dengan kesemua empat kumpulan menunjukkan terdapat perbezaan yang signifikan dalam pemecutan pergerakan gigi, perubahan tulang inter radikular (42 ke 41 untuk CBNL vs CBL), kesakitan (.014 NiTi archwire), ketumpatan tulang (AM22, AD12, CP21, AM42, MM33) dan perbandingan masa. Pembolehubah lain menunjukkan tiada perbezaan yang ketara. Kesimpulanya, min masa kumpulan LLLT lebih rendah untuk melengkapkan penyusunan dan penjajaran berbanding kumpulan bukan LLLT. Namun begitu LLLT tidak memberi kesan kepada perubahan tulang bukolingual dento alveolus, perubahan tulang bukolingual dan inter radikular, resopsi akar dan ketumpatan tulang. Sistem pendakap tidak memberi kesan kepada pemecutan pergerakan gigi, perubahan dimensi lengkung dento alveolus, kesakitan ortodontik, inter radikular, perubahan tulang bukolinggual, resopsi akar dan ketumpatan tulang. Namun begitu, pendakap gigi pasang sendiri mengambil masa operasi yang lebih rendah berbanding pendakap konvensional.

EFFECTS OF LOW-LEVEL LASER THERAPY ON ORTHODONTIC TOOTH MOVEMENT: A RANDOMIZED CLINICAL TRIAL

ABSTRACT

The purpose of this study was to evaluate the effects of low-level laser therapy (LLLT) on Little Irregularities Index, acceleration of tooth movement, dental arch dimensional changes, pain perception, inter radicular and buccolingual bony changes, root resorption, bone densities and chairside time in orthodontic extraction cases using self-ligating and conventional bracket systems with three-dimensional (3D) evaluation via cone beam computed tomography (CBCT) and digital dental models (DDM). A randomised clinical trial was performed with a total of thirty-two patients (eight patients in each group) with the mean age of 22.41 (4.18) years. The patients were further divided in four groups randomly [A= self-ligating laser (SLL), B = conventional bracket laser (CBL), C = self-ligating non laser group (SLNL), D = conventional non laser bracket (CBNL)]. A 940 nm wavelength laser device (iLase; Biolase, Irvine, Calif) was used. Laser irradiation applied for both upper and lower incisors and canine tooth for 6 seconds at mesial and distal side of apical, middle, mesial and distal side of cervical area with 100mW laser output and energy density was 75J/cm^2 per tooth. Patient's pre-treatment and at the end of levelling and alignment stage, the CBCT and DDM acquisition were taken and measured via Planmeca Romexis^{TM} Software 2.3.1.R (Helsinki, Finland). DDM assessed the acceleration of tooth movement and dental arch dimensional changes. The root resorption, inter radicular, buccolingual bony changes and bone densities measured via CBCT acquisitions of patients. Visual analogue scale (VAS) was given to the patients to record their pain intensity for seven days. The normality of the data was evaluated with the Shapiro–Wilk test. Intra-class correlation (ICC) coefficient test was applied to check the reliability for all the variables. For the intragroup comparison, the paired sample t-test and Wilcoxon signed-rank test were performed. Descriptive statistic was applied for assessment of pain perception based on the different wire placement up to seven consecutive days. For the intergroup comparison, regardless of a bracket system and LLLT application, an independent t-test and Mann Whitney test were performed. One-way ANOVA with Post Hoc Bonferroni correction and Kruskal Wallis with pair wise comparison were performed to assess the comparison of four groups. The intra-class correlation (ICC) values for intra and inter-examiner reliability were in the range of excellent correlation of all variables. Most of the variables showed significant differences in intra group comparison. However, few variables exhibited significant differences during intergroup comparison regardless of the bracket system (acceleration of tooth movement, root resorption on 22, bone density on CM11, AD11) and LLLT application (mandibular IMW, pain on 0.017×0.025 NiTi wire and bone density on MM33, CD31, CD 41, MP33). Moreover, when comparing all four groups, significant difference ($P<0.05$) observed in accelerating tooth movement, inter radicular bony changes (42 to 41 for CBNL *vs* CBL), pain (0.014 NiTi archwire), bone density (AM22, AD12, CP21, AM42, MM33) and chairside time. Other variables showed no significant differences. In conclusion, LLLT group needed less mean time to complete levelling and alignment than the non LLLT group. LLLT does not affect dental arch dimensional changes, inter radicular and buccolingual bony changes, root resorption and bone density. Bracket system has no effects on the acceleration of the tooth movement, dental arch dimensional changes, orthodontic pain, inter radicular,

buccolingual bony changes, root resorption and bone density. Self-ligating bracket takes less chair side time compared to the conventional bracket.

CHAPTER 1

INTRODUCTION

1.1 Background of study

Improvement of dentofacial aesthetics is the most primary concern of any orthodontic patients then the other oral health benefits (Bishara and Saunders, 2001; Ackerman, 2007). Like every other intervention, fixed orthodontic treatment is not free from any risk or complications. For tooth movement, the disproportionate force might result in undesirable treatment consequences like root resorption, pain, loss of vitality of the tooth, delayed tooth movement (Talic, 2011). Different studies ascertained that orthodontic dental movement does not take place easily and involves obliteration of the alveolar bone or tooth root (Storey, 1973; Mohammed *et al.*, 1989).

Moreover, plaque accumulation around the bracket, periodontal problems, gingival inflammation, and difficulties in brushing were also deliberated as additional complications in fixed orthodontic treatments (Lau and Wong, 2006). Regardless of reasons, most of the adverse effects of orthodontic treatments are due to the longer time duration (Qamruddin *et al.*, 2017; Deshpande *et al.*, 2016). On average, 2 to 3 years are considered as the standard duration for any orthodontic treatment with fixed appliances (Fink and Smith, 1992).

Nevertheless, patients are not anticipating longer than 1.5 years of the orthodontic treatment (Sayers and Newton, 2007). Also, the England national health care system (NHS) and private practices discouraged the prolong treatment period (Turbill *et al.*, 2001). Hence, to shorten the treatment duration has always been a matter of apprehension for patients as well as for orthodontists (Jawad *et al.*, 2014).

Orthodontic tooth movement triggered by various factors such as vascular and neural networks, the periodontal ligaments and the biological reaction of alveolar bone (Krishnan and Davidovitch, 2009). Stress-strain dissemination in periodontal ligament changes due to the force applied in the tooth for the orthodontic tooth movement resulting in compression and tension site development. Regional osteoblastic and osteoclastic activity lead to bone apposition and resorption at the same time resulting in tooth movement through modelling and remodelling of alveolar bone (Yamaguchi, 2009). Orthodontists have tried various approaches to accelerate the tooth movement with force level, anchorage systems, biomechanics system, selection of brackets and an assortment of novel techniques (Limpanichkul *et al.*, 2006).

Different surgical and non-surgical procedures have been performed previously to accelerate tooth movements (Cruz *et al.*, 2004; Uzuner and Darendeliler, 2013). Surgical interventions such as distraction of periodontal ligament, corticotomy, alveolar decortication and the distraction of the dento alveolus have been a growing interest in the last ten years (Wilcko *et al.*, 2001; Alikhani *et al.*, 2013). However, these surgical procedures are highly invasive, and patients hardly give consent to undergo such surgical procedures. On the other hand, local administrations of biochemical for instance prostaglandin E2, osteocalcin and parathyroid hormones considered as non-surgical options for tooth movements. Nevertheless, have systemic effects on body mechanism, thus it is a challenge to use for tooth movement (Yamasaki *et al.*, 1982; Soma *et al.*, 1999; Hashimoto *et al.*, 2001).

Orthodontists have tried various approaches to make treatment mechanically more efficient for example, use of low friction and self-ligating brackets, pre-formed robotic archwires (Oliveira *et al.*, 2010) and use of micro-implants (Motoyoshi *et al.*, 2007). Bone remodelling is considered as another approach involving interventions to increase the velocity of orthodontic tooth movement. This intervention can be classified into three categories: (1) use of certain biochemical, (2) mechanical or physical stimulation of the alveolar bone which includes the use of magnets, cyclic vibration (Kau, 2011), or direct electrical current (Kolahi *et al.*, 2009), and (3) surgical interventions to accelerate tooth movement.

Local administration of biochemical have systemic effects on body metabolism therefore they are difficult to use for orthodontic tooth movement only. Further, the electric and pulsed electromagnetic field have no convincing evidence to be regarded as an effective modality for rapid tooth movement (Long *et al.*, 2012).

Therefore, researchers and orthodontists are continually seeking for safe, reliable and non-invasive interventions for not only accelerating the tooth movements but also eliminating the other complications of orthodontic treatment.

1.2 Low-level laser therapy (LLLT)

Low-level laser therapy (LLLT) is also known as ‘cold laser’ due to its stable temperature nature. It does not increase its temperature in tissues comparing with other types of lasers which were used in cutting or thermal coagulation of the tissues (Chung *et al.*, 2012).

The use of LLLT depends on either comprehensible light sources (lasers) or non-comprehensible light sources comprising light emitting diodes (LED) and sometimes combination of both. In medical sciences, the most common uses of LLLT are augmenting tissue repair, decreasing inflammation and pain, avoiding tissue damage, and helping the regeneration of different tissues and nerves (Chung *et al.*, 2012; Gupta *et al.*, 2013).

The mechanism of LLLT, which is related to cellular photobiostimulation, is not entirely understood yet. However, LLLT is influenced by the subcellular photoreceptor. Cellular metabolic processes increased due to the stimulation of these receptors, which then affects the electron transport chain, oxidation and the respiratory chain of mitochondria (Johar and Kirpa, 2011). LLLT has an extensive range of effects at the cellular, molecular and tissue levels. The basic biological mechanism of LLLT is assumed to be through the immersion of the red light by mitochondrial chromophores. The cytochrome c oxidase (CCO) convened in the respiratory chain which is located inside the mitochondria possibly by the photoreceptors in the plasma membrane of cells (Greco *et al.*, 1989; Karu *et al.*, 2004; Karu and Kolyakov, 2005).

Biostimulation effects of LLLT are most operative at 0.5-4 J/cm^2 (Mester *et al.*, 1985). Biological activities are stimulated with a low level of energy and bio inhibition is caused by higher energy. Therefore, low-level energies promote the healing process, whereas high energies suppress nerve sensitivity, which controls pain perception (Youssef *et al.*, 2008). LLLT first effect is to inhibit the release of arachidonic acid which means decreased levels of PGE2 which is a potent inflammatory mediator (Angelieri *et al*., 2011, Mizutani *et al*., 2004, Bicakci *et al*., 2012). Laser exposure induces the release of beta-endorphin, an endogenous opioid neuropeptide which produces potent analgesic effects (Arias and Marquez-Orozco, 2006). There is also neuronal effect of LLLT therapy which stabilizes membrane potential henceforth inhibits activation and transmission of the pain signal to the central nervous system (Sonesson *et al*., 2016).

Since pain and longer duration of orthodontic treatment are among the worst aspects of fixed appliance therapy, LLLT could be an ideal modality to address both concerns. Various authors have investigated the biostimulating and analgesic effects of LLLI in relation to orthodontic tooth movement (OTM) in animals and humans (Limpanichkul *et al.*, 2006; Seifi *et al.*, 2007; Qamruddin *et al.*, 2018). During orthodontic treatment, there is a different possible mode of action of LLLT on the inflammatory process; for instance, the release of a pro-inflammatory substance to speed up the tissue healing. Moreover, LLLT accelerates the osteoclastic and osteoblastic activity and stimulates collagen production, which is the major matrix protein in bone (Chung *et al.*, 2012). Studies proved that LLLT accelerates the bone regeneration in mid-palatal suture during the palatal expansion and at bone fractures as well as extraction site, respectively (Trelles and Mayayo, 1987; Takeda, 1988; Saito *et al.*, 1997). Additionally, different clinical trials have piled up evidence that LLLT accelerates the orthodontic tooth movement along with reducing the intensity of pain during orthodontic treatment (Limpanichkul *et al.*, 2006; Qamruddin *et al.*, 2017; Qamruddin *et al.*, 2018). On the other hand, some researchers also found that there were no significant differences in tooth movement using LLLT in animals (Seifi *et al.*, 2007; Gama *et al.*, 2010; Kim *et al.*, 2010; Rowan, 2010; Atlan and Cohen, 2012).

However, specifications of LLLT such as power output, wavelength, energy density, mode of delivery, power density, time interval during each application and duration of the experiments are still varied among different studies (Rowan, 2010).

1.3 Self-ligating brackets

In orthodontics, brackets integration in the ligation system has been practiced for a long time. The foremost edgewise attachment was designed in 1935, known as 'Russell Lock' (Stolzenberg, 1935). Very few bracket designs have become commercially available, though many have been patented. Many designs, for instance, TwinLock bracket, Time bracket and Damon self-ligating brackets appeared at the end of the 20th century. The fundamental feature of self-ligating bracket is its inbuilt mechanics, and metal clip which faced labially to the bracket slot to hold the archwires. Self-ligating brackets were developed based on faster ligation (Harradine, 2013a). Two main advantages of this bracket are low friction and diminished use of elastomeric ligatures (Kerfoot, 2010). Many researches proved that self-ligating brackets showed less friction compared to conventional bracket (Sims *et al.*, 1993; Harradine and Birnie, 1996; Kapur *et al.*, 1998; Pizzoni *et al.*, 1998; Thomas *et al.*, 1998; Harradine, 2013b). Researchers stated that in sliding mechanics, Damon self-ligating brackets work better in when rectangular wire is used compared to any other bracket system (Pizzoni *et al.*, 1998; Ehsani *et al.*, 2009). Due to the low friction, self-ligating brackets is proposed as the more efficient for clinical treatment (Damon, 1998; Qamruddin *et al.*, 2017). Conversely, higher cost for the brackets, the possibility of breakage the clips, more occlusal interference or lip uneasiness are the main disadvantages of self-ligating brackets (Ehsani *et al.*, 2009; Fleming and Johal, 2010;

Chen *et al.*, 2010). Self-ligating brackets are divided into two types according to the mechanism of closure, which is active and passive (Kerfoot, 2010). Active self-ligating brackets are used for controlling the rotation and torque of the archwire with a spring clip. In contrast, passive self-ligating brackets have a slide which can close without invading the slot lumen that applying an active force on archwires. Smart clip (3M Unitek, Monvoriac Calif) and Damon (Ormco, Glendora, Calif) are the most popular brand of passive self-ligating brackets, and these are mostly used in clinical orthodontic treatment (Chen *et al.*, 2010).

The main advantages of passive self-ligating brackets are better sliding mechanics (Damon, 1998), secure wire ligation (Harradine, 2003), reduce treatment time (Damon, 1998), possible anchorage conservation (Berger, 2008), less chairside time (Harradine, 2003), improved oral hygiene (Shivapuja and Berger, 1994), better infection control (Forsberg *et al.*, 1991), less patient discomfort (Damon, 1998; Berger, 2008) and fewer patient appointment (Eberting *et al.*, 2001).

Though many in vitro studies have been performed to investigate the low friction and the less force effect of self- ligating brackets (Pizzoni *et al.*, 1998; Khambay *et al.*, 2004; Griffiths *et al.*, 2005; Henao and Kusy, 2005; Kim *et al.*, 2008), very few clinical randomized controlled trials have addressed the tooth movement effects of this popular self-ligating brackets (Chen *et al.*, 2010; Qamruddin *et al.*, 2017). Therefore, most of these positive and negative claims are still controversial and need further researches.

1.4 Statement of problems

On average, two to three years are considered as the standard duration, for any orthodontic treatment with fixed appliances (Fink and Smith, 1992; Turbill *et al.*, 2001). Nevertheless, patients are not anticipating longer than one and half years of the orthodontic treatment (Sayers and Newton, 2007). Hence, to shorten the treatment duration which associate with accelerating the tooth movement has always been a matter of apprehension for patients as well as for orthodontists (Jawad *et al.*, 2014). In orthodontic treatment, 3 to 4 weeks are considered as the standard interval to recall patients (Jerrold and Naghavi, 2011b). Frequent visits for patients are challenging to manage due to time restriction and forgetfulness (AlSadhan, 2013b).

Studies on LLLT related to orthodontic treatment have documented that the laser was shot mostly daily or short duration between the applications (Limpanichkul *et al.*, 2006; Genc *et al.*, 2013; AlSayed Hasan *et al.*, 2016). However, it is difficult and not a feasible option for patients to manage time frequently in their day-to-day life. Study is needed to evaluate the effects of LLLT until levelling and alignment stage of orthodontic treatment and its effects on dental arch dimensional changes, inter radicular buccolingual changes, and bone density changes via cone beam computed tomography (CBCT) and digital dental models (DDM).

LLLT has never been studied for the bio-stimulating effects along with the passive self-ligating brackets until the levelling and alignment stage of orthodontic tooth movement. Different researchers claimed that passive self-ligating brackets have better mechanical force delivery system which accelerates orthodontic tooth movement (Damon, 1998; Kapur *et al.*, 1998; Eberting *et al.*, 2001; Henao and Kusy, 2005).

Moreover, it is essential to explore the effects of LLLT for the levelling and alignment stage of orthodontic treatment along with the self-ligating brackets and conventional brackets for root resorption, dental arch dimensional changes, inter radicular buccolingual bony changes, bone density and chairside time consumption.

1.5 Justification of the study

Nowadays, demand for orthodontic treatment is increasing day by day (Sonesson *et al.*, 2016). However, prolonged treatment duration and treatment-related discomfort are the major deterrents to treatment. Though few procedures have been familiarised to accelerate the tooth movement, most of them have either side effects or are invasive. Therefore, for the benefit of patients, it is essential to inspect various modalities to overcome these disputes.

LLLT applies as a non-invasive modality in medical science, and it is very promising without reporting any side effects (Jawad *et al.*, 2014). Uses of LLLT in routine orthodontic practice without disturbing patients' regular schedule may accelerate the tooth movement and reduce the treatment duration (Qamruddin *et al.*, 2018). Moreover, the velocity of tooth movement, treatment associated pain in case of the self-ligating bracket is always controversial. It is necessary to investigate the benefits of using passive self-ligating brackets and supplementary advantages of using LLLT with self-ligating brackets.

The effect of LLLT need to investigate in various variables such as dental arch dimensional changes, inter-radicular and buccolingual bony changes root resorption and bone density until the levelling and alignment stage of orthodontic treatment. The current study explored the effect of LLLT on the chair side time consumptions along with the self ligating brackets (SL) and conventional brackets (CB).

1.6 Novelty of the research

This research evaluated the effects of LLLT on orthodontic patients' management in terms of tooth movement using CBCT and DDM with conventional brackets and passive self-ligating brackets.

The results of the study contribute some knowledge to the clinicians regarding the effects of LLLT in orthodontic tooth movement, treatment-associated pain, understanding of three-dimensional (3D) CBCT acquisition and digital dental models evaluation. Moreover, the efficiency of self-ligating brackets and its association with LLLT have also enlighten the practitioners.

This research explored the effects of LLLT on various variables such as dental arch dimensional changes, inter-radicular and buccolingual bony changes, root resorption, bone density and chairside time consumptions along with the SL and CB until the levelling and alignment stage of orthodontic treatment which not yet done by others.

1.7 Objectives of the studies

1.7.1 General objective

The prime objective of this research was to study the effect of LLLT with 3D evaluation via CBCT and digital dental models in orthodontic extraction cases managed with conventional and self-ligation bracket system.

1.7.2 Specific objectives

The specific objectives for this study were:

1. To compare LLLT and non LLLT groups in relation to alignment efficacy (acceleration of tooth movement) for extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment.
2. To compare LLLT and non LLLT groups in relation to dental arch dimensional changes in extraction case management with the conventional and self-ligation system, via digital dental models acquisition until levelling and alignment stage of orthodontic treatment.
3. To compare LLLT and non LLLT groups in relation to pain perception for extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment.
4. To compare LLLT and non LLLT groups in relation to inter radicular and buccolingual bony changes in extraction cases management with the

conventional and self-ligation system until levelling and alignment stage of orthodontic treatment via 3D CBCT.

5. To compare LLLT and non LLLT groups in relation to root resorption for extraction case management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment via 3D CBCT.
6. To compare LLLT and non-LLLT groups in relation to bone densities from canine to canine, for extraction case management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment via 3D CBCT.
7. To evaluate the chair side time for orthodontic wires (engagement and disengagement) and LLLT application with conventional and self-ligation brackets until the levelling and alignment stage of orthodontic treatment.

1.8 Hypothesis

1. There is a significant difference in the effect of LLLT in relation to alignment efficacy to extraction case management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment.
2. There is a significant difference in the effect of LLLT and non-LLLT groups in relation to dental arch dimensional changes in extraction case management with the conventional and self-ligation system, via digital dental model acquisition until levelling and alignment stage of orthodontic treatment.
3. There is a significant difference in the effect of LLLT and non LLLT groups in relation to pain for extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment.

4. There is a significant difference in the effect of LLLT in relation to inter radicular and buccolingual bony changes in extraction case management with the conventional and self-ligation system until levelling and alignment stage of orthodontic treatment via 3D CBCT.
5. There is a significant difference in the effect of LLLT and non-LLLT groups in relation to root resorption for extraction case management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment via 3D CBCT.
6. There is a significant difference in the effect of LLLT and non-LLLT groups in relation to bone densities for extraction case management with the conventional and self-ligation system until levelling and alignment stage of orthodontic treatment via 3D CBCT.
7. There is a significant difference in the chair side time for orthodontic wires (engagement and disengagement) and LLLT application with conventional and self-ligation brackets until the levelling and alignment stage of orthodontic treatment.

1.9 Research Questions

1. What is the effect of LLLT in relation to alignment efficacy to extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment?
2. What is the effect of LLLT and non LLLT groups in relation to dental arch dimensional changes in extraction case management with the conventional and self-ligation system, via digital dental model acquisition until levelling and alignment stage of orthodontic treatment?

3. What is the effect of LLLT and non LLLT groups in relation to pain for extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment?
4. What is the effect of LLLT in relation to inter radicular and buccolingual bony changes in extraction cases management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment via 3D CBCT acquisition?
5. What is the effect of LLLT and non LLLT groups in relation to root resorption for extraction case management with the conventional and self-ligation system until the levelling and alignment stage of orthodontic treatment via 3D CBCT?
6. What is the effect of LLLT and non-LLLT groups concerning bone densities for extraction case management with conventional and self-ligation bracket system until the levelling and alignment stage of orthodontic treatment via 3D CBCT acquisitions?
7. Is there any difference in the chair side time for orthodontic wires (engagement and disengagement) and LLLT application with conventional and self-ligation brackets until the levelling and alignment stage of orthodontic treatment?

CHAPTER 2

LITERATURE REVIEW

2.1 Malocclusion

The majority of the people usually have a varying degree of malocclusion. Misalignment of teeth and disharmony between the upper and lower dental arches are termed as malocclusion (Proffit, 1985; Proffit, 2000; Bishara and Saunders, 2001). Malocclusion is considered an inherited condition, which means it can pass through generations (Proffit, 1985; Proffit, 2000). Edward H Angle (1899), father of orthodontics has classified malocclusion based on a permanent first molar. When a mesiobuccal cusp of permanent upper molar occludes in the mesiobuccal groove of the lower permanent molar with ideal relations is known as normal occlusion (Alam *et al.*, 2018). Malocclusion is divided into three classes: Class I, Class II and Class III (Angle, 1899).

The normal anterior, posterior relationship between both jaws is regarded as Class I skeletal relations. Class I malocclusion occurs when permanent molars of both jaws are in normal position, but malposition of the other teeth may appear (**Figure 2.1**) when the mandibular first molar distally placed about the maxillary first molar, it is termed as Class II malocclusion (Angle, 1899; Alam *et al.*, 2018). Though Angle emphasised the "distal" positioning of the mandibular molars yet most of the Class II malocclusion is observed with prognathic maxilla or retruded mandible. Moreover, "distal" referred only to the tooth's surface. Therefore, words such as posterior are more suitable. On the other hand, when there is a mesial relationship of the mandible to maxilla known as Class III malocclusion. The mesiobuccal cusp of the maxillary first molar occludes distal to the buccal groove of the mandibular first molar (Angle, 1899; Bishara and Saunders, 2001).

2.1.1 Class I malocclusion

Class I malocclusion is a normal anteroposterior relationship between both arches dropping in this class. The mesiobuccal cusp of the maxillary first permanent molar articulates in the buccal groove of the mandibular first permanent molar. The bony base supporting the mandibular dentition directly beneath that of the maxillary arch, and neither is too far anterior or posterior to the cranium (Alam *et al.*, 2018). Class I malocclusion occurs when maxillary and mandibular molars are in the appropriate position, but confined to malposition of the other teeth themselves which may be misaligned on their bony bases (dentoalveolar protrusion) (**Figure 2.1**).

Figure 2.1: Class I malocclusion (Adapted from Alam *et al.*, 2018)

2.1.2 Class II malocclusion

Angle assumed in his classification of malocclusion that first permanent molars are persistent to the arch. When the first permanent molar of maxilla positioned mesially to the mandibular first permanent molar is called Class II malocclusion (Angle, 1907). In addition, British Orthodontic Society (1992) publicised another classification of malocclusions, which based on incisal relationships. According to the incisal classification, Class II malocclusion occurs when mandibular incisor edges positioned back to the cingulum plateau of maxillary incisors (Williams and Stephens, 1992).

Angle’s classification is used widely due to its simplicity. Nevertheless, this classification is criticised by different authors due to its vertical and transverse considerations (Case, 1922; Williams and Stephens, 1992). Conferring to Angle’s classification, Class II malocclusion embraces diverse skeletal and dental mechanism which may differ from the perception of the normality. Skeletal disproportion is a consequence of growing resentment between mandible and maxilla which forms a convex facial profile. Class II malocclusion is of great apprehension for the fact that many patients having this malocclusion are treated routinely for the orthodontic purpose (McNamara Jr, 1981). Thus, concerns on the development of Class II subjects has become important because of the increasing awareness in enhancing treatment timing and planning in dentofacial orthopaedics.

2.1.2(a) Classification of Class II malocclusion

Class II malocclusion is divided into two divisions to explain the position of the anterior teeth (Graber *et al.*, 2016).

i. Class II Division 1:

   When the maxillary anterior teeth are proclined with a large overjet is termed as Class II Division 1 **(Figure 2.2**).

ii. Class II Division 2:

   When the maxillary anterior teeth are retroclined with a deep overbite is termed as Class II Division 2 (**Figure 2.3**) (Graber *et al.*, 2016).

Van der Linder (2014) further classified Class II Division 2 into three types (Singh, 2015).

a. Type A

   Upper central and lateral incisors are retroclined (**Figure 2.4**).

b. Type B

   Central incisors are retroclines and overlapped by the lateral incisors (**Figure 2.5**).

c. Type C

   Upper central and lateral incisors are retroclined and overlapped by the canines (**Figure 2.6**).

Figure 2.2: Class II Division 1

(Adapted from Alam *et al.,* 2018)

Figure 2.3: Class II Division 2

(Adapted from Alam *et al.,* 2018)

Figure 2.4: Class II Division 2 type A

Figure 2.5: Class II Division 2 type B

Figure 2.6: Class II Division 2 type C

(Above adapted from Orthodontic Specialist Clinic, PPSG, Hospital USM)

2.1.3 Class III malocclusion

The malocclusions in which there is a mesial relationship of the mandible to maxilla make up Class III malocclusion. The mesial groove of the mandibular first permanent molar articulates anteriorly to the mesiobuccal cusp of the maxillary first permanent molar (Singh, 2015; Graber *et al.*, 2016) (**Figure 2.7**).

Though Angle's classification is being used all over the world due to its simplicity, there are some controversies also. Successive cephalometric researches have not validated the Angle's hypothesis. Highlighting on the relationship of the first permanent molars have caused orthodontists to overlook the facial skeleton itself and to think only in terms of the tooth position. Consequently, faulty bone growth and muscles malfunction is often unnoticed. Even today, there is a tendency to centre too much attention on this one tooth relationship. The molar relationship alters during the different stages of development of the dentition. A better correlation could obtain if one uses the Angle groups to classify skeletal relationships.

Figure 2.7: Class III malocclusion (Adapted from Orthodontic Specialist Clinic, PPSG, Hospital USM)

2.2 Orthodontic tooth movement

A continuous and well-proportioned process of deposition and resorption of alveolar bone around the tooth results in proper orthodontic tooth movement. During orthodontic tooth movement, forces are applied on the teeth. Therefore, compression and stretching of the periodontal ligament (PDL) occur around the root area of the tooth which results in the remodelling of the bone and lead to teeth movement (Dolce *et al.*, 2002; Zainal Ariffin *et al.*, 2011).

The most important factor for orthodontic tooth movement is the optimal force. Literature showed that there is a debate about the force level, which results in optimal mechanical conditions within the periodontal ligament for orthodontic tooth movement. It is suggested that an optimal force system plays an important role in an adequate biological response in the periodontal ligaments (Burstone, 1989). Also, an optimal force associated with the root surface area (Storey, 1952; Boester and Johnston, 1974; Quinn and Yoshikawa, 1985) **(Table 2.1)**.

Table 2.1 Phases of orthodontic tooth movement (Kato *et al.*, 1996; Dolce *et al.*, 2002; Zainal Ariffin *et al.*, 2011)

Phases of tooth Movement	**Activity in days after force application.**	**Changes at the cell level**
Phase 1 (Initial)	24 hours to 2 days within the socket	The acute inflammatory response leads to vasodilation and migration of leukocytes, which release cytokine cell signalling molecules (metabolic product of paradental remodelling).
Phase 2 (Arrest)	20 -30 days Movement stops (Burstone, 1962).	In a second phase, treatment-related chronic inflammation occurs with the continuation of migration of leukocytes and periodontal remodelling happen.
Phase 3 (Acceleration)	40 days of accelerated tooth movement after the initial force of application	Phase three leads to another phase of acute inflammation
Phase 4 (Linear)	Orthodontic tooth movement	The recruitments of macrophages, fibroblasts, osteoblasts, osteoclast and alkaline phosphatase activity, lead to tooth movement.

2.2.1 Initial phase of orthodontic tooth movement

In the initial phase of orthodontic treatment, rapid tooth movement occurs within the alveolus. This displacement of the tooth in the PDL space occurred within 1 to 2 days after applying the force in the crown of the tooth. Following interrelated processes are taking place in the initial stages of tooth movement:

i. Deformation of crystalline structures of bone generating piezoelectric or bioelectric current (Shapiro *et al.*, 1979).
ii. Reduction of oxygen level in the compression area and increase the oxygen level in the tension area of PDL due to the alteration of the blood flow (Baumrind, 1969b; Gianelly, 1969).
iii. Distortion of nerve terminals and fibers results in releasing of different neurotransmitters (Kato *et al.*, 1996).
iv. PGE2 and leukotrienes releases due to the cell distortion by mechanical force.

The periodontal ligament has viscoelastic properties. It acts as a shock absorber and can resist the heavy intermittent forces, whereas it can be compressed by even light continuous prolonged application of forces. Cribriform plate or lamina dura connects the alveolar bone and the PDL in the lower two-thirds of the socket. These are low-pressure reservoirs, thus when the force exerted, tissue fluid and blood squeeze out from one reservoir to the other, causing elastic deformation of alveolar bone (Castelli and Dempster, 1965; Bien, 1966).

Application of the constant orthodontic force results in initial rapid and immediate movement of the tooth into the alveolus within 24 to 48 hours of force