ADJUNCTIVE BUCCAL AND PALATAL CORTICOTOMY FOR MAXILLARY EXPANSION IN A SHEEP MODEL

LE HUY THUC MY

FACULTY OF DENTISTRY
UNIVERSITY OF MALAYA
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ADJUNCTIVE BUCCAL AND PALATAL CORTICOTOMY FOR MAXILLARY EXPANSION IN A SHEEP MODEL

ABSTRACT

The prevalence of transverse maxillary deficiency is high and the number of adults seeking treatment is increasing in the recent years. Untreated patients suffer from psychological and functional problems which resulted in them experiencing inferior quality of lives. Currently, both conventional maxillary expansion and surgically assisted maxillary expansion could not fulfill the needs of the patients as well as the outcomes expected by the clinicians. The purpose of this project is to explore the potential of adjunctive buccal and palatal corticotomy (ABPC) as an alternative intervention for adult maxillary expansion by using a sheep model. Cone beam computed tomography (CBCT) scan has been shown to produce accurate images and 3D volume rendering, thus this study utilised CBCT images to evaluate the dental and skeletal changes before and after intervention and compared the differences of the intervention effects between ABPC assisted rapid maxillary expansion (ABPC + RME group or Group 1), conventional rapid maxillary expansion (conventional RME group or Group 2) and those receiving no intervention (control group or Group 3). Our findings suggested that ABPC + RME allows for both skeletal and dental expansion, with the amount of dental expansion exceeding that of skeletal expansion at the alveolar crest and hard palate levels by two and three folds, respectively. Moreover, skeletal and dental expansion in the ABPC + RME group were approximately three times greater than that of the conventional RME group. As the quality of bone might affect the stability of teeth in their new positions, this study employed micro-computed tomography to assess the bone microstructure recovery at 4- and 12-week retention. After 4 weeks retention, bone volume fraction at the third premolar area were at the lowest value (54.4%-60.39% of the control value) and highest at the first premolar of ABPC + RME group (80.44% of the control value).

After 12 weeks post-retention, the bone volume fraction value increased up to around 80% of control value. Furthermore, pooled bone volume fraction of the banded teeth in Group 1 was significantly higher than that of Group 2. Therefore, ABPC assisted expansion is less detrimental to the supporting bone of the banded teeth while conventional RME seemed to be harmful to this bone. Histomorphological analysis showed that new bone formation area in Group 1 is around two to three times that of Group 2 and control group. Microvascularisation in the furcation of premolars in Group 1 was significantly higher than that of Group 2 at 4-week. At 12-week retention, this value in Group 1 was still slightly higher than that of Group 2. In conclusion, ABPC + RME allows for both skeletal and dental expansion. Moreover, it also promoted bone remodelling after the intervention. Therefore, ABPC could be a potentially good alternative to the currently available interventions in enhancing the outcomes of maxillary expansion in non-growing subjects.

Keywords: adult maxillary expansion, adjunctive buccal and palatal corticotomy, palatal expander, cone-beam computed tomography, micro-computed tomography

ADJUNCTIVE BUCCAL DAN PALATAL CORTICOTOMY UNTUK PENGEMBANGAN MAKSILA ENGGUNAKAN MODEL KAMBING BIRI-BIRI

ABSTRAK

Kadar prevalensi *tranverse maxillary deficiency* di kalangan orang dewasa semakin meningkat setiap tahun. Sekiranya, pesakit ini tidak menerima rawatan yang sepatutnya, mereka akan menghadapi masalah psikologi dan fungsi yang dapat menyebabkan rasa rendah diri. Buat masa ini rawatan '*conventional rapid maxillary expansion* (RME)' dan 'surgically assisted mmaxillary expansion (SARME)' belum dapat memenuhi kehendak para pesakit dan pakar perubatan sepenuhnya. Tujuan projek ini adalah untuk menilai sama ada *adjunctive buccal* dan *palatal corticotomy* (ABPC) dapat menjadi rawatan alternatif untuk pengembangan maksila dengan menggunakan model haiwan iaitu, kambing biri-biri. Pemeriksaan *cone-beam computed tomography* (CBCT) telah digunakan dalam analisis pengimejaan yang dapat memberikan keputusan tepat untuk kerja penyelidikan berkaitan imej 3 dimensi. Kajian ini menggunakan imej CBCT untuk menganalisa perbezaan di antara tulang dan keadaan gigi sebelum dan selepas rawatan serta perbandingan rawatan di antara ABPC dengan *conventional rapid maxillary expansion* (RME). Kajian ini telah menunjukkan rawatan secara ABPC boleh mengembangkan tulang rahang maksila dan kedudukan gigi 2-3 kali ganda melebihi pengembangan tulang pada *alveolar crest* dan kedudukan lelangit keras. Tambahan pula, pengembangan rahang dan bahagian gigi secara APBC adalah 2-3 kali lebih banyak dari cara RME. *Micro-computed tomography* (µCT) adalah dianggap sebagai alat piawai untuk pemeriksaan 'ex-vivo bone microstructure'. Oleh itu adalah penting untuk memeriksa kestabilan gigi di tempat baharu, dengan menggunakan µCT yang dapat melihat keadaan kualiti tulang selepas rawatan pada minggu ke-4 dan -12. Kajian ini telah menunjukkan kuantiti 'bone volume fraction' pada kedua-dua kumpulan eksperimen menjadi rendah daripada kumpulan kontrol pada minggu keempat. Pada minggu ke 4, kuantiti ‘bone volume fraction’ pada premolars ketiga adalah merupakan yang paling rendah (54.4%-60.39% dari paras awal) dan golongan tertinggi pada premolar pertama Kumpulan 1 (80.44%). Pada minggu ke-12 *retention,* kuantiti ‘bone volume fraction’ meningkat ke 80% daripada aras kawalan dan terendah pada *anchorage* premolar ketiga dalam golongan RME (60.71% di aras kawalan). Keputusan histomorfologi menunjukkan vaskularisasi pada furkasi akar gigi premolar di Kumpulan 1 adalah tinggi daripada kumpulan lain pada minggu retensi ke 4 dan 12. Pengembangan tulang dan gigi pada golongan ABPC + RME menjadi dua kali ganda dari kumpulan RME, tulang sokongan pada golongan ABPC sembuh lebih baik daripada Kumpulan 2. Kesimpulannya, *adjunctive buccal* dan *palatal corticotomy assisted expansion* boleh mengembangkan tulang dan gigi dan tambahan pula ianya boleh meningkatkan *bone remodelling* selepas rawatan. Oleh itu, rawatan ini adalah berpotensi untuk meningkatkan keberhasilan rawatan *maxillary expansion* di kalangan pesakit dewasa.

Keywords: adult maxillary expansion, adjunctive buccal and palatal corticotomy, palatal expander, cone-beam computed tomography, micro-computed tomography

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LIST OF SYMBOLS AND ABBREVIATIONS

ABPC	:	Adjunctive buccal and palatal corticotomy
AOO	:	Accelerated Osteogenic Orthodontics
BV/TV	:	Ratio of bone volume to the total volume in the ROI
CBCT	:	Cone-beam computed tomography
CSF-1	:	Colony stimulating factor
CO	:	Compression osteogenesis
Cr-Cr	:	Transverse dental arch width at the crest level
CT	:	Computed tomography
Cu-Cu	:	Transverse intercuspal width at the cusp level
EDTA-2Na	:	Ethylene diamine tetra-acetic acid
FOV	:	Field of view
G1	:	Group 1 (ABPC + RME group)
G2	:	Group 2 (Conventional RME group)
G3	:	Group 3 (Control group)
H&E	:	Hematoxylin and eosin
HP level	:	Transverse dental arch width at hard palatal level
IACUC	:	Institutional Animal Care and Use Committee
ICC	:	Intraclass correlation coefficient
LLLT	:	Low level laser therapy
M1	:	First molar
MicroCT/µCT	:	Micro-computed tomography
µm	:	Micro-meter
mm	:	Milimeter
MARPE	:	Microimplant-assisted rapid palatal expansion

MMPs	:	Matrix metalloproteinases
NB	:	New bone
NBF	:	New bone fraction
NBV/mm^2	:	Number of blood vessels per mm^2
NHANES	:	National Health and Nutrition Survey
OBF	:	Old bone fraction
OHRQoL	:	Oral-health-related-quality of life
OPG	:	Osteoprotegerin
TBF	:	Total bone fraction
TNBF	:	Total new bone fraction
OB	:	Old bone
P1	:	First premolar
P2	:	Second premolar
P3	:	Third premolar
PAOO	:	Periodontally Accelerated Osteogenic Orthodontics
PDL	:	Periodontal ligament
PEMF	:	Pulsed electromagnetic field
PTH	:	Parathyroid hormone
Pu-Pu	:	Transverse interdental width at the central pulp level
RANKL	:	Receptor activator of nuclear factor kappa-β ligand
RAP	:	Regional acceleratory phenomenon
RME	:	Rapid maxillary expansion
ROI	:	Region of interest
R-R	:	Transverse root apex distance
SARME	:	Surgically assisted rapid maxillary expansion
SME	:	Slow maxillary expansion

T0	:	Before treatment
T1	:	After treatment
Tb.N	:	Trabecular number
Tb.Sp	:	Trabecular separation
Tb.Th	:	Trabecular thickness
Teeth inclination	:	Changes of the teeth axis to the nasal plane in the coronal plane
TMJ	:	Temporomandibular joint
TGF- β	:	Transforming growth factor β
TB	:	Total bone
TOBF	:	Total old bone fraction
TRAP	:	Tartrate resistant acid phosphatase
TT	:	Total tissue
UPM	:	University Putra Malaysia
WSI	:	Whole slide imaging

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CHAPTER 1: INTRODUCTION

1.1 The prevalence of transverse maxillary expansion

The most common clinical manifestations of transverse maxillary deficiency are crowding and crossbite (Kennedy & Osepchook, 2005; McNamara, 2000). In the United States of America, a national survey (n = 9044) revealed that approximately 40% of individuals, between 15 to 50 years old, had moderate crowding and 17% had severe crowding (Buschang & Shulman, 2003). In Iceland, anterior crowding and molar crossbite were the second (20.5%) and the third (11.9%) most frequent malocclusions in a group of 829 adult subjects (Jonsson et al., 2007). Recent surveys reported a high percentage of adults with crossbite. Helsen et al. (2003) reported that 29.7% of German adults (n = 1777) manifested posterior crossbite (Hensel et al., 2003). In Turkey, a study on 1554 subjects between 4 to 25 years old showed that the highest frequency of posterior crossbite was in the permanent dentition compared to that of the primary and mixed dentition; 20.7% in permanent dentition compared to 1.2% in primary and 12.7% to 17.8% in mixed dentition. Bilateral crossbite frequency was 51% and unilateral crossbite frequencies on the right and left sides were 47.3% and 53.6%, respectively (Gungor et al., 2016). Among the adults seeking orthodontic treatment, crossbite prevalence was high, 31.5% in Turkey and 36.3% in Bangladesh (Celikoglu et al., 2010; Rahim, et al., 2012).

1.2 The consequences of transverse maxillary deficiency on the teeth, facial skeleton and individual's quality of life

Crossbite, a condition produced by an abnormal occlusion could lead to aberrant development of teeth, skeletal bone and also the adaption of muscle in the long term (McNamara, 2000; McNamara, 2002; Petren et al., 2003). The most detrimental consequence of posterior crossbite is lateral displacement of the mandible to the crossbite side. This condition could start from the primary or mixed dentitions stage and spontaneous self-correction only occurs in less than 10% of the cases (Allen et al., 2003; Kennedy & Osepchook, 2005; Kutin & Hawes, 1969). Other authors have described an asymmetric condyle position and occlusal interferences between the left and right side of patients with posterior discrepancy (Ishizaki et al., 2010; Kennedy & Osepchook, 2005). Several studies have supported the correlation between posterior crossbite and temporomandibular joint (TMJ) disorder (Egermark-Eriksson et al., 1990; Fushima et al., 1994; Riolo et al., 1987; Williamson & Simmons, 1979; Alamoudi, 2000). The main TMJ dysfunction signs and symptoms were joint crepitus, pain and muscular tenderness (Alamoudi, 2000). When the mandible shifted to one side, the corresponding condyle is likely to experience higher compression in the glenoid fossa and will be prone to internal derangement (Ishizaki et al., 2010). Fushima et al. (1994) reported that TMJ disorders were observed in 65% of patients (n = 64) having the lateral mandibular displacement. The prevalence of TMJ symptoms in the affected side was significant higher than that of the normal side (84.6% vs. 23.1% respectively) (Fushima et al., 1994). Unusual chewing patterns in patients with crossbite have been reported by Lewin since 1985 (as cited in Piancino et al., 2006) and followed by other authors such as Piancino, Throckmorton (Piancino et al., 2006; Throckmorton et al., 2001).

Maxillary deficiency does not only affect the normal masticatory function, but also the facial aesthetics. Allen et al. (2003) found that maxillary deficiency patients usually have greater lower face height, this could be due to the clockwise rotation of mandible relative to the cranial base. A small maxilla might be associated with upper airway obstruction and results in mouth breathing (Allen et al., 2003). The functional shift of the mandible leads to the deviation of the chin and the discrepancies of dental and skeletal midline. When an untreated posterior crossbite condition persists during and beyond the development stage of mandible, it might lead to the mandible being asymmetrical. Other authors reported that posterior crossbite could cause occlusal plane inclination and facial asymmetry (Ishizaki et al., 2010; Kennedy & Osepchook, 2005).

Abnormal occlusal conditions and dentofacial deformities can also generate a negative impact on the individuals' psychological well-being as well as social acceptance and interpersonal relationships (Chen et al., 2015; Masood & Newton, 2014; Rusanen et al., 2010). Traebert & Peres (2005) established the positive correlation between dental crowding and the quality of life in Brazilian young adults (n = 414) (Traebert & Peres, 2005). The levels of overall oral-health-related quality of life (OHRQoL) were reported to be significantly lower in adults with dentofacial deformities who were bullied compared to those without these conditions. People with malocclusion and dentofacial deformities usually experience low self-esteem, low social competence and negative self-perspective of their body image (Seehra et al., 2011). Other related emotional and behaviour disorders are shyness, social complications, avoidance of smiling and feeling worn out (de Paula Junior et al., 2009). Zhou et al. (2001) showed that approximately 50% of the patients (n = 140) were given a nickname related to their dentofacial deformities and the majority of them (80%) felt distressed about their nicknames (Zhou et al., 2001). Consequently, previous studies have established a strong relationship between malocclusion and low physical, social and psychological health greatly affecting the quality of life of the involved patients (Chen et al., 2015; de Paula Junior et al., 2009; Feu et al., 2010; Klages et al., 2015; Obilade et al., 2016; Silvola et al., 2012; Torkan et al., 2012).

In 2014, Masood et al. assessed the consequences of posterior crossbite on OHRQoL according to five orders of impact in the following increasing degree sequences: impairment, functional limitation, pain/discomfort, disability and handicap (Masood et al., 2014). Compared to the control, the functional limitation and psychological discomfort in young people (n = 145) aged from 15 to 25 were found to have the most impact on OHRQoL with the highest mean scores of 3.89 (±1.95) and 3.45-4.24 (±1.56 - ±1.69) respectively. Functional limitation was related to functional restrictions such as difficulty when chewing. Psychological discomfort referred to physical and psychological difficulties. The least degree of impact was observed in the handicap domain with the mean score of 3.11 (±2.07). Handicap was associated with isolation from the society at large. Moreover, the patients with higher education level had greater impairment of OHRQoL than ones with a lower level of education (Masood et al., 2014).

1.3 Treatment approaches for adults with transverse maxillary deficiency and their limitations.

A simple type of treatment for transverse maxillary deficiency is nonsurgical approach, utilising expansion appliances such as a Quad helix, Haas appliance and Hyrax appliance. This treatment modality has been shown to be very successful in children with the success rates from 84% to 100% (Bjerklin, 2000; Erdinc et al., 1999; Kurol & Berglund, 1992; Lagravere et al., 2005; Thilander & Lennartsson, 2002). It is not costly, associated with minimal complications and usually well tolerated by most children (Kennedy & Osepchook, 2005). According to Gurel et al. (2010), the interpremolar and intermolar width could be expanded up to 7 mm or more in children less than 13 years old (Gurel et al., 2010). However, this dimension reduced by 2 to 3 mm after 2 to 7 years post treatment. Similar findings have been revealed by McNamara et al. (McNamara et al., 2003). Handelman (2000) reported that the mean transarch width increase in a group of children with a mean age of 9.5 years old (n = 47) was 4.6 ± 2.8 mm for the molars and 5.9 ± 3.6 mm for the premolars (Handelman et al., 2000). Therefore, nonsurgical maxillary expansion has been suggested as a routine treatment modality in growing patients (Bishara & Staley, 1987; Lagravere et al., 2005).

In nonsurgical procedures, both removable appliances and fixed appliances have been used, coupled with rapid (0.5-1 mm/day) or slow (1 mm/week) expansion protocol. For many decades, rapid maxillary expansion (RME) with a Hyrax appliance has become the most popular protocol. The main theory supporting the use of rapid maxillary expansion technique is that with abrupt force applied on the premolar and molar teeth, resulted in a force being transferred to the midpalatal suture and this suture would open up while the teeth moved only minimally relative to their supporting bone. (Kennedy & Osepchook, 2005; Lagravere et al., 2005; Proffit et al., 2007). Therefore, this technique emphasizes on the opening of the midpalatal suture and most clinicians believed that skeletal expansion itself attributed dominantly to the final outcome (Baydas et al., 2006; Kennedy & Osepchook, 2005).

However, some authors proved that the outcome of maxillary expansion are not primarily contributed by the midpalatal suture opening (Handelman, 2011; Handelman et al., 2000; Schilling et al., 1998). Since 1959, Krebs has proposed this hypothesis. Two studies have subsequently been carried out on the midpalatal suture opening using metallic implants as markers. The results showed that sutural expansion contributed to only 50% of the total expansion for patients less than 13 years old. When a child reached the age of 14 or older, this ratio dropped dramatically to 30% or lesser (Krebs, 1959; as cited in Northway, 2011; Handelman, 2011). Iseri and Ozsoy (2004) also concurred and they reported similar results; that basal bone expansion was only 40% in a group of patients (n = 40) with a mean age of 14.5 years old. Handelman (2011) concluded that the total resultant of expansion in children was an amalgamated contribution of approximately 50% of the midpalatal suture widening and 50% of displacement of the dental alveolar complex (Handelman, 2011). Using more modern imaging technology such as cone-beam computed tomography, Garrett et al. (2008) reported that skeletal expansion was 55% at the premolar region and only 38% at the first molar region, and the remainder was due to dentoalveolar changes. Their experimental subjects were adolescents at a mean age of 13.8 ± 1.7 years old (n = 30) (Garrett et al., 2008). Therefore, it has been suggested that dentoalveolar displacement contributed significantly to the maxillary arch expansion (Handelman, 2011; Garrett et al., 2008; Iseri & Ozsoy, 2004).

In 1970, Haas proposed that the nonsurgical maxillary expansion technique could possibly be used to open the midpalatal suture of patients up to the age of 16 or 17 years old (Haas, 1970). As the patient matures, the midpalatal suture becomes increasingly tortuous and begins to fuse (Melsen, 1975). Application of nonsurgical expansion seems to be inappropriate as separating the tightly interdigitated suture will be challenging. For this reason, most clinicians tend to choose surgically assisted rapid maxillary expansion (SARME) in patients with skeletal maturity (Betts, 2016; Melsen, 1975; Mommaerts, 1999; Suri & Taneja, 2008; Timms & Vero, 1981). In addition, several authors advocated that nonsurgical maxillary expansion modality should be limited to mild transverse discrepancies of less than 5 mm, and any expansion beyond this limit, SARME was suggested as a more suitable treatment of choice (Betts, 2016; Silverstein & Quinn, 1997; Suri & Taneja, 2008).

It is believed that SARME is more beneficial for adult patients with moderate and severe transverse maxillary discrepancies (more than 5 mm) (Betts, 2016; Northway, 2011; Suri & Taneja, 2008). Typically, it is a combination of several surgical procedures such as splitting midpalatal suture, buccal corticotomy or Lefort 1 osteotomy with/without pterygoid separation followed by maxillary expansion using palatal expanders (Suri & Taneja, 2008; Betts, 2016). It is believed that SARME provides predominantly skeletal effects. Lagravere and co-workers (2006) in their literature review highlighted that the mean skeletal expansion from previous studies ranged from 1.7 to 5 mm. The mean dental expansion at the first premolar and first molar regions was approximately between 7.1 and 8.7 mm (Lagravere et al., 2006). With a surgical approach, the resistance from the surrounding sutures could be released, thus, the skeletal expansion has been reported to be more stable in the long term. However, Chamberland and Proffit showed that 24% of the outcome of dental expansion decreased over time. Moreover, 64% of patients experienced relapse of more than 2 mm over 6 months period (Chamberland & Proffit, 2008, 2011). Other studies reported the relapse rate varied from 5% to 51% (Suri & Taneja, 2008; Bays & Greco, 1992; Berger et al., 1998; Mommaerts, 1999; Betts, 2016). Kretschmer et al. (2010) demonstrated that Le Fort I osteotomy in combination with expansion of more than 4 mm increased the risk of a vascular sequelae. Among the complications that patients may experience are significant hemorrhage, facial swelling, root resorption, postoperative pain and devitalization of teeth (Mommaerts, 1999; Harada et al., 2004; Ozturk et al., 2003; Handelman, 2011; Suri & Taneja, 2008). These complications may be of concern to patients and such they may not wish to follow this line of treatment.

Although the nonsurgical expansion approach is favourable in children, it is not considered as an appropriate treatment for adults (Baydas et al., 2006; Bishara & Staley, 1987; Proffit et al., 2007). However, there are some authors who have continuously advocated for its use (Cao et al., 2009; Handelman, 2011; Handelman et al. 2000; Handelman, 1997). These authors showed that they could gain the transverse interpremolar and intermolar width of approximately 4 to 5.5 mm. Nevertheless, skeletal expansion using a conventional expander (Haas expander) was reported to be rather low at 0.9 mm compared to 1.7 to 5 mm with a surgical approach. Consequently, it is believed that in adult patients, the expansion was typically due to the displacement of the dental alveolar complex (Handelman, 2011). In cases where the alveolar displacement did not occur, patients would have had perforation of the buccal plate of the posterior alveolus (Handelman et al., 2000; Northway, 2011; Timms & Moss, 1971). Other unwanted side effects reported includes buccal root resorption (Barber & Sims, 1981; Langford & Sims, 1982; Timms & Moss, 1971), fenestration of the buccal cortex (Timms & Moss, 1971; Handelman et al., 2000), lateral tipping of posterior teeth (Timms, 1980), pain and instability of expansion (Haas, 1980; Wertz, 1970; Zimring & Isaacson, 1965; Handelman et al., 2000).

Currently, the prevalence of adult patients with a posterior crossbite seeking orthodontic treatment is high, 31.5% to 36.3% (Celikoglu et al., 2010; Rahim et al., 2012). Malocclusion and dentofacial deformities does not only affect normal function, physical and psychological health but also isolate from the society (Masood et al., 2014). Clinicians face the dilemma when treating transverse maxillary deficiency for adults, of offering nonsurgical and surgical treatment options. Therefore, the protocol for treatment of maxillary deficiencies in adults is still controversial (Baydas et al., 2006; Handelman, 2011; Northway, 2011). Most clinicians prefer skeletal expansion over dental expansion as the latter is likely to relapse and is prone to adverse side effects as mentioned previously (Kennedy & Osepchook, 2005). Therefore, an alternative protocol for maxillary expansion in adults is timely.

1.4 Possibilities for corticotomy as an alternative treatment for adults with transverse maxillary deficiency

In recent years, corticotomy facilitated orthodontics has become a promising procedure. Although the modern techniques originated from the procedures developed by Köle and Suya (as cited in Choo et al., 2011), The Wilcko brothers have disseminated the procedure widely (Kim et al., 2013). Köle believed that the cortical bone was the primary resistance to tooth movement. Following corticotomy, the movement of a tooth was accompanied with their supporting bone in a block, thus markedly reducing orthodontic treatment duration (Kole, 1959). However, Wilcko and co-workers disagreed with this hypothesis (Murphy et al., 2009; Sebaoun et al., 2007; Wilcko et al., 2009; Wilcko & Wilcko, 2013). They reported demineralisation on the surface of cortical bone after flap elevation, thus, the bone matrix, not the bone block moved together with the roots. From this observation, they proposed the "Accelerated Osteogenic Orthodontics" technique, which was later changed to "Periodontally Accelerated Osteogenic Orthodontics" (PAOO) (Wilcko et al., 2009). Their technique was based on the "Regional acceleratory phenomenon" (RAP) occurring at the injured bone (Murphy et al., 2009; Sebaoun et al., 2007; Wilcko et al., 2009; Wilcko & Wilcko, 2013; Wilcko et al., 2001).

Another reported application of corticotomes is during retraction anterior segment developed by the Koreans (Choo et al., 2011; Chung et al., 2009; Lee et al., 2007). This technique is known as "Speedy surgical orthodontics" (Chung et al., 2007). Chung and co-workers performed perisegmental decortication around the incisors and canines. Then they inserted a C-palatal retractor on the palate and retracted a protrusive dentoalveolar segment within only 4 to 6 months. Chung and co-workers believed that decortication reduced the rigidity of cortical bone, thus the force applied to the decorticotomised segment could deform the medullary bone (Chung et al., 2001; Chung, et al., 2007; Chung et al., 2009).

During maxillary expansion, several authors reported that the hindrance of dental arch expansion was not solely due to the increasing interdigitation of midpalatal suture and the surrounding sutures. Persson and Thilander (1977) demonstrated that ossification increased with ages, but the obliteration index was usually lower than 5% in patients aged less than 25 years. A suture with obliteration index less than 5% can be opened by physiologic forces (Persson & Thilander, 1977). The obliteration value is typically age-independent in spite of the growth of sutural interdigitation with age (Basdra, 2005; Knaup et al., 2004). However, the bone density recorded within the suture correlates to chronological age until 30 years old with the highest value of 53.2%. After 30 years old, bone density starts to decrease due to physiological osteoporosis (Korbmacher et al., 2007). Korbmacher et al. (2007) assumed that the increasing bone density at midpalatal suture accounted for the difficulty of its opening. Investigating the other sutures surrounding the maxilla complex, Kokich concluded that synostosis within these sutures generally does not occur throughout the eighth decades of human life. Only 6.7% of these sutures displayed complete ossification at 70 years, 26.7% at 80 years and 55% at 90 years (Kokich, 1976). Hence, difficulty in employing expansion in adults is multifactoral and includes increasing interdigitations within sutures which diminishes the bone elasticity as well as a higher value of bone density within sutures which increases the suture resistance.

Corticotomy surgery might have the potential to overcome the rigidity of the maxillary complex. In 2015, Echchadi et al. showed that this technique could facilitate expansion in a 14 years old girl with skeletal maturity (Echchadi et al., 2015). Their technique involved perforations on the buccal surface cortex of the maxillary premolars and molars using a piezo device. By this way, the dental arch was wider significantly and 9 mm of crowding was resolved within less than six months. Additionally, the outcome was stable throughout a three years follow-up. In comparison to SARME, corticotomy assisted expansion is less invasive, less costly and has less surgical complications (Hassan et al., 2015; Kim et al., 2011; Lines, 1975; Robiony et al., 2007). Moreover, it might be more stable in the long term (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013). Hence, corticotomy assisted expansion may be a preferred options by patients.

The idea of this research is to explore an alternative approach which is less risky but still feasible to expand maxilla to certain amount adequate to compensate bone discrepancies in adults. Corticotomy assisted maxillary expansion might overcome dentition limitations resulting from the rigidity of alveolar bone and enhance the outcomes of dental and skeletal expansion for this age group. Also, this method may meet the requirements of patients who need widening of the alveolar segment only, without changing their harmonized nose. By utilising adjunctive buccal and palatal corticotomy, maxillary expansion in adults might be achievable and stable in the long term.

To date, there is no literature on the application of corticotomy to facilitate maxillary expansion. The aim of this research was to evaluate the potential of adjunctive buccal and palatal corticotomy (ABPC) in widening of the dental arch in a sheep model. The null hypothesis is ABPC cannot produce dental and skeletal changes after maxillary expansion in a sheep model.

Our specific objectives were as follows;

i. To compare the dental and skeletal changes using the intervention among Group 1, Group 2 and Group 3 at different retention periods.
ii. To assess the type of tooth movement and skeletal displacement produced by ABPC + RME and conventional RME at 4- and 12-week retention.
iii. To assess the changes of microCT and histological features of the buccal alveolar bone in ABPC + RME group and conventional RME group in comparison to the control at 4- and 12-week retention.
iv. To evaluate the bone microstructural changes in ABPC + RME group, conventional RME and control group at 4- and 12-week retention.

v. To evaluate the amount of new bone and old bone component in the supporting tissue in ABPC + RME group, conventional RME group and control group at 4- and 12-week retention

vi. To evaluate the microvascular changes in medullary bone in ABPC + RME group, conventional RME and control group at 4- and 12-week retention.

CHAPTER 2: LITERATURE REVIEW

2.1 Maxillary expansion

2.1.1 Maxillary transverse deficiency and aetiology

2.1.1.1 The importance of maxillary expansion in solving transverse maxillary deficiency prior to orthodontic treatment.

According to McNamara (2000), the maxillary arch can adequately accommodate teeth of average size without crowding or spacing when transpalatal width was approximately 30 to 39 mm, measured between upper first molars. On the contrary, if this width is less than 31 mm, some forms of malocclusion could occur such as crowding and a crossbite (McNamara, 2000).

Clinical manifestations of transverse maxillary deficiency are diversified ranging from a narrow palatal vault and accentuated curve of Wilson to easily recognisable clinical features such as crossbites and dental crowding (Kennedy & Osepchook, 2005; McNamara, 2000; Kutin & Hawes, 1969) (Table 2.1). Unlike the skeletal imbalances in the anteroposterior and vertical dimension, which are usually treated early, most transverse maxillary deficiencies are ignored. Therefore, the possibilities of treatment for patients with transverse skeletal problems are limited in the later stages (McNamara, 2000).

Transverse maxillary deficiency may occur in the deciduous, mixed or permanent dentition. It may occur in combination of Class I, Class II or Class III malocclusions (Guyer et al., 1986). Sultana et al. (2015) described the prevalence of crossbite, one of the typical signs of transverse maxillary deficiency, was presented in 60.7% of Class I, 22.7% of Class II and 14.7% of Class III malocclusion (Sultana et al., 2015).

Table 2.1: Clinical manifestations of transverse maxillary deficiency (sources: Kennedy & Osepchook, 2005; McNamara, 2000; Kutin & Hawes, 1969)

Teeth protrusion.
Dental crowding.
Accentuated curve of Wilson.
Narrow and tapered maxillary arch.
Anterior crossbite alone or combined with posterior crossbite.
Unilateral buccal crossbite.
Unilateral lingual crossbite with/without deviation of midlines.
Bilateral buccal crossbite.
Bilateral lingual crossbite with/without deviation of midlines.
Dark spaces at the corner of mouth during smiling.
Arch width discrepancy between maxilla and mandible.
Functional shift of jaw towards the affected side.
Discrepancy between centric occlusion and centric relation.
Laterally flared maxillary posterior teeth in the absence of crossbite.
Class III malocclusion due to mild-to-moderate maxillary skeletal retrusion.
Lower position of lingual cusps of the upper posterior teeth in relation to the occlusal plane.
Mild-to-moderate Class II malocclusion with maxillary skeletal retrusion, obtuse nasolabial angle and a steep mandibular plane angle.

In orthodontic practices, protrusion and crowding are among the most prevalent orthodontic problems, which are due to the disharmony between the size of teeth and the perimeter of the dental arch (McNamara, 2000). Bimaxillary protrusion is usually believed as a condition in which the positions of teeth in the maxilla and mandible were too far forward compared to their basal bone. However, this condition might also be caused by hypoplastic maxilla, which could not accommodate the whole dentition, thus, the teeth flare out to compensate (Lewis, 1943). According to Howe et al. (1983), dental crowding was more likely associated with a reduced maxillary arch width than with larger teeth. When the maxillary and mandibular dentition camouflage for the skeletal deficiency, clinical manifestation of crowding can be observed without the presence of a crossbite; otherwise, if the maxillary dentition reflects the underlying skeletal disharmony, a crossbite often occurs (McNamara, 2000). Similarly, Hwang and co-workers (2004) showed that the dental arch widths measured at the premolars and molars region were smaller in the crowding group than in a non-crowded group. Consequently, when treating crowding cases, further arch development may be a beneficial treatment option. For young patients, this option can be feasibly achieved by various appliances such as a Hyrax expander, Quad helix appliance or Haas expander (Howe et al., 1983; McNamara, 2000).

Maxillary expansion may be helpful in treating a substantial number of Class III cases (McNamara, 2000). Class III malocclusions can be derived from maxillary retrusion, mandibular prognathism or a combination of these two forms. The majority of Class III cases (26%-45.2%) are caused by maxillary retrusion whilst the mandible is normal (Guyer et al., 1986). When treating Class III patients, the true aetiology should be recognised from an early age and a suitable treatment option should be discussed. If maxillary retrusion is the cause and not severe, it is advisable to simply widen the maxilla or combining the expansion with a facemask during the mixed dentition stage. Thus, dental arch expansion with RME is often effective in treating this type of skeletal discrepancy, especially for young patients. In more severe conditions or in adults, more complex treatment is required (McNamara, 2000).

Maxillary deficiency occurs in many cases of Class II malocclusions. Previous studies demonstrated that the prevalence of maxillary skeletal retrusion in Class II patients was as much as 30% while maxillary protrusion was less than 15% (McNamara, 2000;

McNamara, 1981). Tollaro and co-workers (1996) showed that a transverse skeletal discrepancy (when the maxillary arch was about 3 to 5 mm narrower than the mandible) was often found in Class II patients (Tollaro et al., 1996). Other authors reported maxillary width was 2.5 mm smaller in the Class II group when compared with the a non-treatment ideal group (Franchi & Baccetti, 2005). Al-Khateeb et al. (2006) found that Class II division 1 malocclusion had the narrowest maxillary arch in comparison to other types of malocclusion. As Class II malocclusions are traditionally considered typically sagittal and vertical problem, arch expansion was not usually indicated (McNamara, 2000). However, McNamara (2000) reported that widening the dental arch in the early mixed dentition stage led to spontaneous correction of the buccal molar relationship during the retention period. Moreover, this early intervention eliminated the possibilities of crossbite progression in the permanent dentition and created a favourable condition for mandibular growth. Subsequently, the sagittal occlusal relationship was improved and the outcome was stable in the long term (McNamara, 2000). In parallel to a previous study, a recent study (n=17) demonstrated that RME treatment improved the molar relationship in 75% children with Class II division 1 malocclusions and transverse maxillary deficiency during the retention period (Baratieri et al., 2014; Weissheimer et al., 2011). Hence, maxillary expansion should be indicated and treated in certain cases of Class II malocclusions (McNamara, 2000).

2.1.1.2 Aetiology of maxillary transverse deficiency

Transverse maxillary deficiency may result from developmental, congenital, traumatic or iatrogenic conditions (Table 2.2) (Suri & Taneja, 2008; Bishara & Staley, 1987). A thorough history, clinical examination and speak test should be performed prior to treatment planning for orthodontic treatment including assessment of the maxillary arch dimensions.

Table 2.2: Aetiology of transverse maxillary deficiency (sources: Suri & Taneja, 2008; Bishara & Staley, 1987)

- Thumb sucking or pacifier sucking habits.
- Obstructive sleep apnea, mouth breathing.
- Iatrogenic condition (cleft repair).
- Palatal dimensions and inheritance.
- Muscular condition.
- Syndromes:
    - Klippel-Feil syndrome.
    - Cleft lip and palate.
    - Congenital nasal pyriform aperture stenosis.
    - Marfan syndrome.
    - Craniosynostosis (Apert's. Crouzon's disease, Carpenter's).
    - Osteopatia striata.
    - Treacher Collins.
    - Duchenne muscular dystrophy.
    - Acromegaly.
- Nonsyndromic palatal synostosis.
- Functional origins.
- Multifactorial phenomena related to genetic, congenital, environmental factors.
- Others: retained deciduous tooth, congenitally missing teeth, abnormal size and shape of teeth, occlusal prematurity, delayed eruption, low tongue position, tongue thrusting.

2.1.2 History of maxillary expansion

In 1859, Westcott was the first clinician applying mechanical forces to the maxilla. However, Emerson C. Angell was the first author to publish a case report of maxillary expansion in the Dental Cosmos journal in 1860 (as cited in Timms, 1999). The maxillary expansion was performed using a jackscrew in a 14-year-old girl for two weeks. Although the paper still raised doubts about the true effects of expansion on craniofacial structures, the maxillary expansion appliance with jackscrew was then widely used with successful results (as cited in Timms, 1999). Nevertheless, in 1889, this method was almost prohibited in the United States of America because the maxillary expansion with jackscrew was considered a forceful procedure and it was believed its effects could be achieved by conventional appliances (Timms, 1999; Haas, 1965). The debate was probably due to the dissemination of the functional concept of development during the last half of the 19th century (Haas, 1965). In 1956, the maxillary expansion modality was revived in the United States of America by Dr. Andrew J. Haas, who also introduced the Haas expander. A variety of expansion effects such as the opening of midpalatal sutures, increase in arch and nasal width, and lowering of the mandibular position along with bite opening have been reported (Haas, 1961; Haas, 1965; Timms, 1999). Together with the application of cephalometric analysis, the possible detrimental effects of maxillary expansion were highlighted. In later decades, other clinicians contributed to the development of various expansion appliance designs such as the Quad Helix (Ricketts, 1979), the Hyrax appliance (introduced by Biederman in 1968 (as cited in Agarwal & Mathur, 2010)) and bonded type appliance (Cohen and Silverman, 1973). Nowadays, maxillary expansion is widely accepted and used routinely to manage transverse skeletal deficiency (Bjerklin, 2000; Erdinc et al., 1999; Kurol & Berglund, 1992; Lagravere et al., 2005; Thilander & Lennartsson, 2002).

2.1.3 The characteristics of maxillary suture and circummaxillary sutures.

2.1.3.1 Sutures of maxilla

The maxilla forms the central part of the midface composed of two halves of maxillary bones fused at the intermaxillary suture. Each half includes a body and four processes (zygomatic process, the frontal process, the alveolar process and the palatine process). Each maxilla articulates with ten bones in total including two cranial bones (the frontal and ethmoid) and eight facial bones which are the nasal, zygomatic, lacrimal, inferior nasal concha, palatine, vomer and the other half of maxilla. There are numbers of sutures resulting from these articulations which are the nasomaxillary suture, frontomaxillary suture, zygomaticotemporal suture, lacrimomaxillary suture, ethmoidomaxillary suture and intermaxillary suture (Figure 2.1) (Bishara & Staley, 1987).

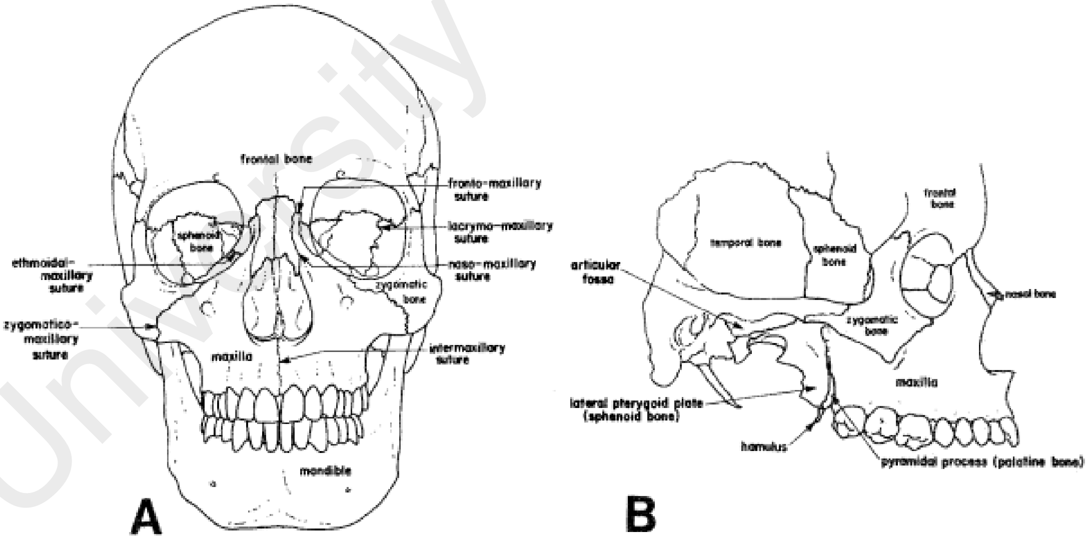


Figure 2.1: Circummaxillary sutures.
A, Frontal view; B, Lateral view (source: Bishara & Staley, 1987)

2.1.3.2 Characteristics related to maturation of maxillary sutures and circummaxilary sutures.

Maxillary expansion has been shown to be favourable in children with constricted maxilla (Bjerklin, 2000; Erdinc et al., 1999; Kurol & Berglund, 1992; Lagravere et al., 2005; Thilander & Lennartsson, 2002). It has been proposed that the midpalatal suture plays the main role in dental arch widening. However, as the patients mature, the successful opening of the midpalatal suture become more difficult by RME (Northway, 2011; Baydas et al., 2006). Thus, understanding the characteristics related to maturation of maxillary sutures is necessary to explain the difficulty in opening the midpalatal suture.

A widespread hypothesis for failure of midpalatal suture splitting among adults is due to the increasing interdigitation of the midpalatal suture in the later age of life. As maxillary growth in human is nearly completed (approximately 95%) by the age of seven years old, most people assumed that the intermaxillary suture would also fuse (Melsen, 1975; Lux et al., 2004).

In 1975, Melsen reported the three stages development of midpalatal suture morphology from infantile to adulthood under histological examination. In the infantile ages, the suture is wide-opened and Y-shaped with short crossing bony spicules. In the next stage, the suture becomes curvier and starts to fuse during juvenile-hood; and when reaching the adolescent period, pronounced tortuous bony bridges appear distinctly and lock the two halves of the maxilla tightly (Figure 2.2). Therefore, the midpalatal suture would barely open in adults unless these firmly interdigitated bony bridges were disrupted (Melsen, 1975).

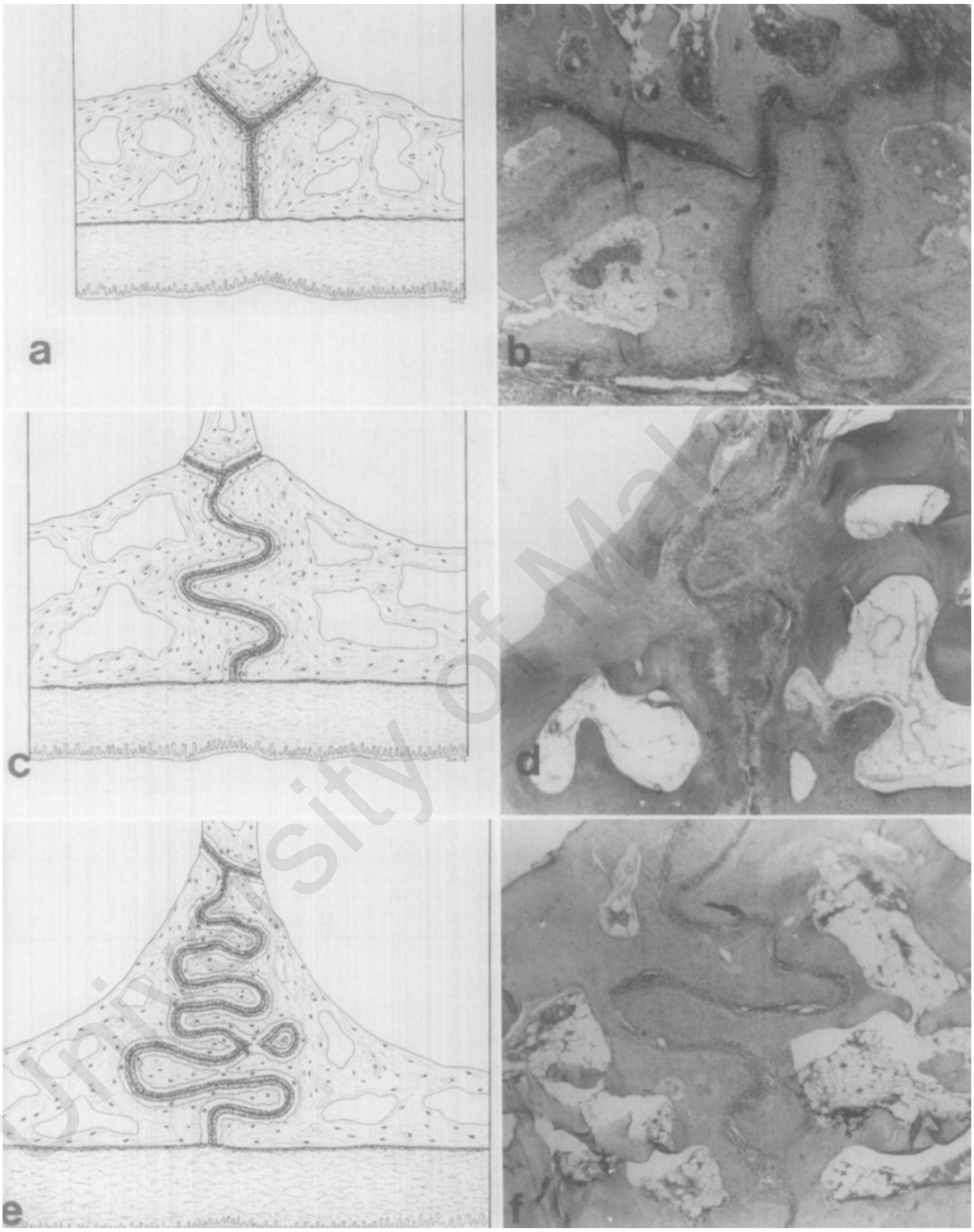


Figure 2.2: Morphologic development of the midpalatal suture from infantile to adolescent.
A, B the suture is broad and Y-shaped at infantile stage; C, D, the suture is longer in the vertical aspect at juvenile stage; E, F, the suture is very tortuous at adolescent stage (source: Melsen, 1975)

In 1977, Persson and Thilander proposed the resistance to midpalatal splitting during adulthood might not be only attributed by too tight interdigitation of the mid palatal suture. A study was performed to quantify the obliteration of the midpalatal suture on human necropsy specimens collected from 24 subjects (15 to 35 years) (Persson & Thilander, 1977). The earliest obliteration was observed in a 15-year-old girl, whereas the oldest person without any synostosis was observed in a 27-year-old woman. It was demonstrated that a suture with obliteration index lower than 5% can be easily split by physiologic forces (Persson & Thilander, 1977). The closure of the midpalatal suture started posteriorly towards the anterior part of the midpalatal suture. Although the ossification advances with age from juvenile, a noticeable union is rarely observed in people younger than 30 years of age (Persson & Thilander, 1977). In parallel to previous findings, Knaup et al. (2004) demonstrated that the obliteration value in the midpalatal suture was low in all subjects. The median value of the obliteration in a group of 26 to 63 years old subjects was only 3.11%, while the maximum ossification was about 13% in a 44-year-old man (Knaup et al., 2004). The advancement in microCT technology permits the examination of midpalatal suture and bone density quantification at a micro level (Korbmacher et al., 2007). Generally, the obliteration value is age-independent throughout human life. The highest bone density was recorded at just 53.2% in the younger age group (<30 years old). It has been demonstrated that the bone density within the suture was evidently correlated to chronological age until middle-aged (less than 30 years). The density slightly decreases after reaching 30 years old which is probably related to osteoporosis (Korbmacher et al., 2007). As the bone density constitutes 50% to 60% of the bone strength, it might be a possible contributing factor for the difficulty in opening midpalatal suture in the skeletally mature patients (Goldstein et al., 1993; Keaveny et al., 1994).

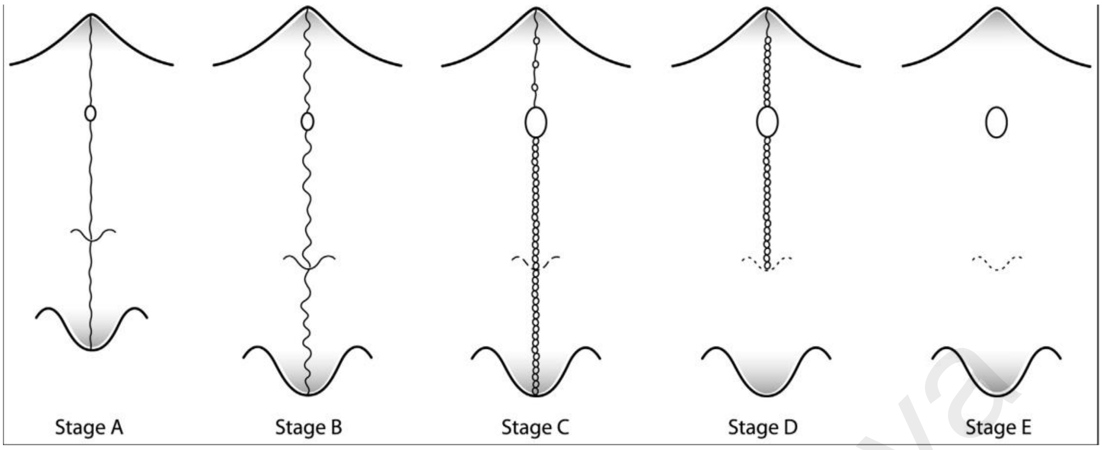


Figure 2.3: Schematic drawing showing the maturation stages of the midpalatal suture.
Stage A, midpalatal suture is almost straight with no or little interdigitation; stage B, midpalatal suture increases its interdigitation; stage C, midpalatal suture has a straight or irregular feature with two parallel scalloped lines; stage D, fusion occurred in the palatine bone; stage E, completely fusion in the entire part of maxilla (source: Angelieri et al., 2013)

Angelieri et al. (2013) classified the midpalatal suture maturation using CBCT. The classification comprised five stages from stage A to stage E. Stage A is characterised by a distinctly straight sutural line and almost no obliteration. Stages B and C have increased the scalloping of the suture. Stage D has fusion in the palatine region, and stage E is characterised by entire fusion at both anterior and posterior of the palate (Figure 2.3). The two first stages are usually found in children up to 13 years, while a substantial number of adolescents are found in stage C. Stage C may start early in girls at 11 years old but 21% of female adults are still identified in stages B and C. Additionally, stages D and E are only observed in 58% of girls and 23% of boys from 11 to 19 years old (Angelieri et al., 2013). Thus, midpalatal suture should possibly be opened by RME during adolescent-hood especially in boys.

The hypothesis associated with tightly interdigitated sutures cannot be the only reason why it is difficult to employ nonsurgical expansion in adults. Other studies have advocated that the resistance to maxillary expansion derives from the surrounding maxillary sutures. Two prominent ones are zygomatic buttress and sphenoid bones (Kokich, 1976). In 1976, Kokich inspected the frontozygomatic suture changes according to age from 20 to 95 years in 61 cadaver specimens by an amalgamation of radiographic and histologic techniques. Unexpectedly, it was found that synostosis within frontozygomatic suture generally did not occur by the age of 95 years in the majority of subjects. Only 6.7% displayed entire ossification at 70 years, 26.7% at 80 years, and 55% at 90 years (Kokich, 1976).

The sphenoid bone constitutes the midsagittal part of the cranial base. Although the sphenoid bone does not directly connect to the maxilla, its body's position is just superior and posterior to maxillary complex and it does not have a midsagittal suture. The sphenoid parts known as the pterygoid plates lie bilaterally to the maxilla and articulate to the pyramidal processes of the palatine bones which are then fused to the maxilla anteriorly. Such rigid structures probably limit the lateral movements of maxillary complex and decrease the possibility of transverse expansion in the posterior region of the maxilla (Bishara & Staley, 1987) (Figure 2.4).

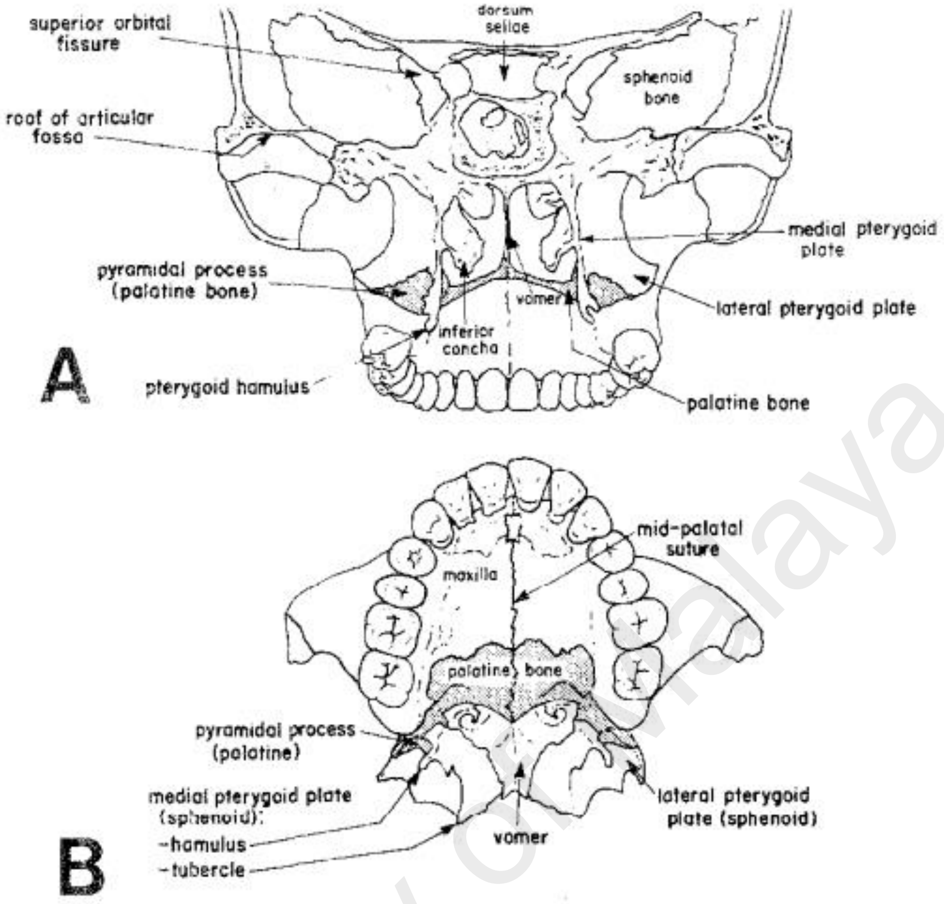


Figure 2.4: Anatomy of the sphenoid bone.
The sphenoid bone does not have a midsagittal suture. The lateral and medial pterygoid plates of the sphenoid bone interlocked the pyramidal processes of the palatine bones and then limited the lateral movement of the maxilla posteriorly.
A, posterior view; B, occlusal view (source: Bishara & Staley, 1987).

2.1.3.3 Does advancing rigidity of the craniofacial complex increase the difficulty in expanding the maxilla in adults?

Bone tissue, in general, comprises 65% mineral and 35% organic components in mass. Cortical and trabecular bones were the mineral components, made from hydroxyapatite (a crystal of calcium compound). The organic parts are water, cells, collagen, and vessels.

The bone matrix is primarily made from collagen type I. The proportion of inorganic and organic components varies in regions and types of bone (Currey et al., 1996).

Cortical bone is highly resistant to bending and torsion forces. The cortical bone forms the outer layer of all cranial and skeleton bones. It is dense and compact. Thus, its crucial functions are to support the skeletal activities and protect various internal organs. Cortical bone has a low turnover rate, but it can act as a mineral reservoir responding to the metabolism need when the mineral deficiency is severe. Cortical bone occupies a large proportion of the skeletal mass (80%), while the trabecular bone just makes up the remaining 20% (Currey et al., 1996). Trabecular bone constitutes the inside part of maxilla, mandible and other bones. It is less dense and more elastic compared to the cortical bone. It is responsible for mechanical support. Besides, trabecular bone also plays a major role in the regulation of the mineral metabolism (Hadjidakis & Androulakis, 2006).

The maxilla develops primarily from the membranous ossification centres in the mesenchyme of the maxillary process, and secondarily from the malar cartilage in the zygomatic process. After birth, the maxilla grows mainly by surface remodelling. The remodelling rate is approximately 25% per year in the cancellous bone and 3% in the cortical bone. During the adolescence period, bone apposition surpasses bone resorption. As a result, the total bone mass starts to accumulate and reaches its peak at the age of 25 to 30 years (Boskey & Coleman, 2010; Hanschin & Stern, 1995; Lau & Adachi, 2011). In addition, the mineral crystal component undergoes maturation by increasing the size and perfection during this period. Subsequently, the bone matrix is strengthened. Bone mass determines 75% to 85% of the ultimate bone strength (Schonau, 2004). Consequently, the increase of the bone strength or rigidity of maxilla during the adolescent period appears to concur with the stage that maxillary expansion becomes unfeasible.

The size and shape of bone also contribute to the bone strength (Ammann & Rizzoli, 2003; Boskey & Coleman, 2010; Jepsen, 2009; Wang & Seeman, 2008). The shape of the maxillary body looks like two halves of the semi-sphere connecting each other at the palate. One semi sphere is thick alveolar bone containing teeth, while the other is the maxillary sinus wall with the supports from the zygomatic processes.

2.1.4 Types of maxillary expansion

Depending on the jackscrew turning protocol, nonsurgical expansion can be divided into two main types including rapid and slow maxillary expansion (Proffit et al., 2007). In addition, SARME is also widely recommended in non-growing people (Suri & Taneja, 2008).

2.1.4.1 Rapid maxillary expansion (RME)

RME refers to a protocol in which the jackscrew is turned at the rate of 0.5 to 1 mm/day. The most common schedule is two turns each day (0.5 mm/day), one in the morning and one in the afternoon. The treatment can be completed within one to four weeks (Proffit et al., 2007). According to Isaacson and co-workers, the force created by RME technique from the first activation of jackscrew ranges from three to ten pounds. The incorporated force from consecutive days of activation maybe up to 20 pounds or more (Isaacson et al., 1964; Zimring & Isaacson, 1965). Such a high magnitude force has been believed to be adequate to overwhelm the interlocking suture. Therefore, RME was proposed to maximise the orthopaedic separation of the midpalatal suture before any considerable tooth movement can take place (Haas, 1961; Haas, 1965; Haas, 1970; Haas, 1980; Wertz, 1970; Proffit et al., 2007). Krebs (1964) reported that 50% of the total expansion outcome is skeletal in young patients (8-12 years old) when using nonsurgical expanision. This ratio drops to 30% in an older group of 13 to 19 years old (as cited in Northway, 2011). However, the dental and skeletal changes produced by RME are reported to be higher than those produced by SME (Bell, 1982; Brunetto et al., 2013).

Rapid maxillary expanders can be categorised into tissue-borne expanders, tooth-borne expanders and implant-supported expanders (Proffit et al., 2007; Brunetto et al., 2017; Carlson et al., 2016). Tissue-borne expander has been proposed to provide more orthopedic effect than tooth-borne expander (Handelman, 2000; Handelman, 2011). However, Weissheimer et al. (2011) demonstrated a greater orthopedic effects and less tooth tipping in Hyrax group (tooth-borne expander) when compared with the Haas group (tissue-borne expander). Other authors reported that both of these appliances produce similar skeletal effects (Garib et al., 2005; Huynh et al., 2009). Recently, implant supported expanders have been reported to be a potential treatment modality for skeletally mature patients (Brunetto et al., 2017; Carlson et al., 2016).

2.1.4.2 Slow maxillary expansion (SME)

In the SME procedure, the rate of expansion is one mm per week or one turn each other day. It takes two to six months to achieve the desired amount of expansion (Proffit et al., 2007). Some popular appliances used in SME are the Quad helix and the W-spring (Bell, 1982; Bishara & Staley, 1987). The force delivered by these appliances is from several ounces to two pounds (Hick, 1978; Bell & LeCompte, 1981; Ricketts, 1979). SME is often indicated for patients in the deciduous or mixed dentition stage (Haas, 1961; Hicks, 1978). The low magnitude of force produced by SME is considered insufficient to overcome the tensile strength of sutural tissue in the permanent dentition stage (Hicks, 1978; Ricketts, 1979). Thus, the midpalatal suture can be barely opened and the percentage of tooth movements will be greater (Hicks, 1978).

Previous studies have reported the orthopaedic effect of SME. A study showed that 20% orthopaedic change could be achieved by SME (Bell, 1982). Similarly, Hicks (1978) found that the orthopaedic contribution ranged from 24% to 30% of the total arch width changes in children (less than 11 years old). Nevertheless, this ratio decreases dramatically to 16% in the older group of 14 to 15 years old (Hick, 1978). In comparison to RME, the force produced by SME is more physiologic to the sutural tissue (Bell, 1982; Proffit et al., 2007). Histological findings demonstrated that sutural tissue reorganised well within 30 days and stabilised in the third month. Thus, the three-month retention for SME is adequate (Bell & LeCompte, 1981**;** Hicks, 1978), while it takes between three to six months for RME (Krebs, 1959; Wertz, 1970; Bell, 1982). However, SME was reported to cause significantly greater vertical and horizontal bone losses than RME (Brunetto et al., 2013)

2.1.4.3 Surgically assisted rapid maxillary expansion (SARME)

(a) ***Overview***

In the 1900s, the increasing tortuosity in midpalatal suture had been proven to be the main cause of failure for nonsurgical maxillary expansion in adults (Melsen, 1975). To overcome this difficulty, Brown proposed a surgical technique involving midpalatal splitting to assist maxillary expansion (as cited in Taylor & Johnson, 2017). As not all the cases were successfully treated with midpalatal splitting, the circummaxillary sutures were suggested to be the dominant resistant areas. The piriform aperture pillars in the anterior area, zygomatic buttresses in the lateral sides and pterygoid junctions in the posterior areas were all thought to be involved in resisting expansion (Taylor & Johnson, 2017). Kole (1959) proposed the combination of vertical corticotomy incisions and horizontal osteotomies for treating several malocclusion cases (Kole, 1959). Converse and Horowitz (1969) advocated a technique involving both buccal and palatal cortical osteotomies, also known as LeFort I surgery, to release the buccal resistances (Converse & Horowitz, 1969; Buchanan & Hyman, 2013; Suri & Taneja, 2008). Several incision designs have been proposed to treat various skeletal deficiency cases such as LeFort I surgery, with or without pterygoid disjunctions, combined with midpalatal splitting, and LeFort I surgery sparing the pyriform pillars (Suri & Taneja, 2008; Taylor & Johnson, 2017).

The surgical approaches for maxillary expansion can be categorised into two groups; surgically assisted maxillary expansion (SARME) and segmental or total maxillary osteotomy (Suri & Taneja, 2008; Taylor & Johnson, 2017). Up to now, consistency of the procedure for SARME has not been confirmed. The extent of incisions depends on the severity of the malocclusion and the experience of surgeons (Suri & Taneja, 2008).

(b) ***Indications for SARME***

A consensus on the suitable age of patients for SARME has not been defined. Mommaerts (1999) recommended that patients over 14 years old could be subjected to SARME. Some other authors extend age limit to 20 to 25 years i.e. also depends on gender (Timms & Vero, 1981; Mossaz et al., 1992; Alpern & Yurosko, 1987). It has been reported that chronological age is not a good predictor for skeletal maturation (Suri & Taneja, 2008). Skeletal age itself is possibly a good predictor in determining the appropriate age for SARME (Melsen, 1975). SARME has been recommended to treat skeletal maxillomandibular transverse discrepancies. Recently, SARME is also indicated to reduce the black buccal corridors and broaden a patient’s smile (Woods et al., 1997; Koudstaal et al., 2005; Suri & Taneja, 2008) (Table 2.3).

Table 2.3: Indications for surgical assisted rapid maxillary expansion (SARME) (source: Betts, 2016).

Skeletal maxillomandibular transverse discrepancy greater than 5 mm.
Significant transverse maxillary deficiency associated with a narrow maxilla and wide mandible
Failed orthodontic or orthopedic expansion
Necessity for a large amount (> 7 mm) of expansion, or preference to avoid the potential increased risk of segmental osteotomies
Extremely thin, delicate gingival tissue or preence of significant buccal gingival recession in the canine bicuspid region of the maxilla
Significant nasal stenosis
Need for widening of maxillary arch when no other skeletal deformity is present
Widening of the arch to provide space for dental alignment without requiring maxillary extractions to create space
Widening of the arch after collapse associated with the cleft palate deformity.

2.1.5 Types of expanders

2.1.5.1 Tooth-borne expander

A popular tooth-borne expander is Hyrax the name of which was derived from “Hygienic Rapid Expander” (Asanza et al., 1997). This appliance was introduced by William Bidermann in 1968 (as cited in Agarwal & Mathur, 2010). It comprises a jackscrew in the middle of the palate with stainless-steel arms connected to bands placed on premolars and molars (Asanza et al., 1997). When the jackscrew is activated, teeth are the main components bearing the loading force (Agarwal & Mathur, 2010; Garib et al., 2005). The advantages of tooth-borne appliances are greater comfort, easier hygiene, and less ulceration to the palatal mucosa (Garib et al., 2005; Agarwal & Mathur, 2010).

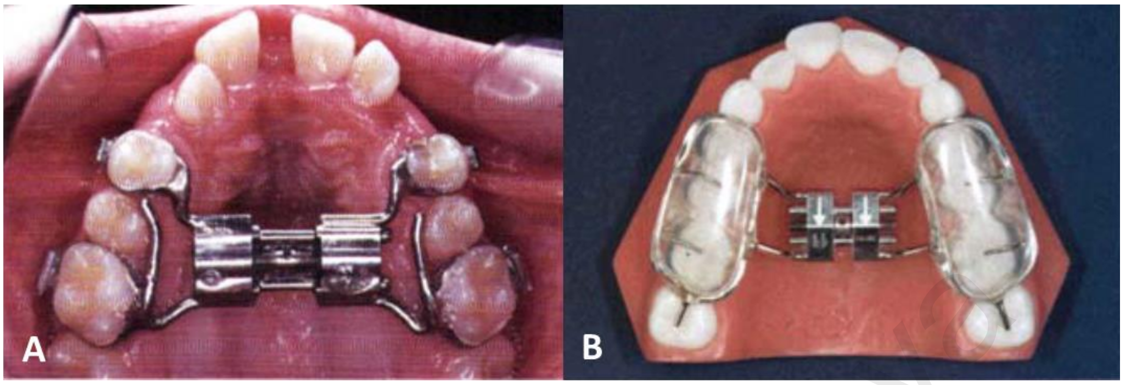


Figure 2.5: Tooth-borne appliances
A, banded expander; B, bonded expander (source: Proffit, Fields & Sarver, 2007)

Tooth-borne expanders might be bonded or banded to the teeth (Asanza et al., 1997) (Figure 2.5). Two types of appliances were demonstrated to produce similar dental and skeletal effects, but the bonded appliance with acrylic occlusal coverage could better control the vertical dimension (Alpern & Yurosko, 1987; Sarver & Johnston, 1989; Asanza et al., 1997). Besides, the sturdy frame of the appliance is believed to produce a controlled expansion force (Garib et al., 2005). Thus, the tooth-borne expander is thought to be more effective in opening the midpalatal suture compared to the tissue-borne appliance (Weissheimer et al., 2011). However, this appliance might cause cortical fenestration, loss of anchorage, and root resorption (Mommaerts, 1999).

2.1.5.2 Tooth tissue-borne expander

The Haas expander is the representatives of tooth tissue-borne appliance. Andrew J. Haas introduced the Haas expander in 1961 (Haas, 1961) (Figure 2.6). This appliance includes a jackscrew in the middle of the palate and acrylic pads on the alveolar ridge (Agarwal & Mathur, 2010). The bearing force produced by Haas expander is dissipated directly to the tissue underneath the appliance (Garib et al., 2005). It is believed that this appliance produces more bodily skeletal movement, greater apical base expansion, less relapse and dental tipping (Haas, 1961; Haas 1965, 1970, 1980). However, this appliance may easily cause food trapping and exerts pressure on the palatal mucosa (Agarwal & Mathur, 2010).

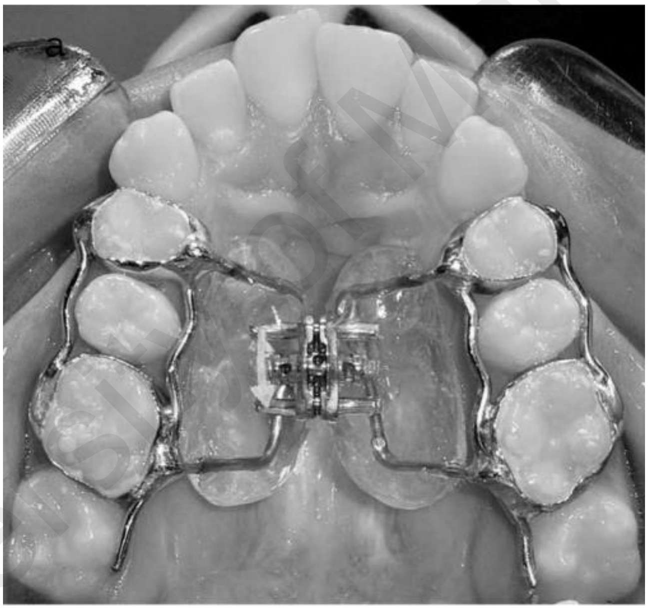


Figure 2.6: Haas appliance- a typical type of tooth-tissue expander (source: Garib et al., 2005)

2.1.5.3 Other types of appliance:

Some authors proposed other types of bone-borne appliances such as a transpalatal distractor (Mommaerts, 1999), Magdenburg palatal distractor (Gerlach & Zahl, 2003), and Rotterdam palatal distractor (Koudstaal et al., 2006) (Figure 2.7). These appliances attach to the alveolar bone and produce a greater orthopaedic effect (Suri & Taneja, 2008). Every appliance has its own properties; hence, it is important for clinicians to follow the manufacturer's instructions (Koudstaal et al., 2006).

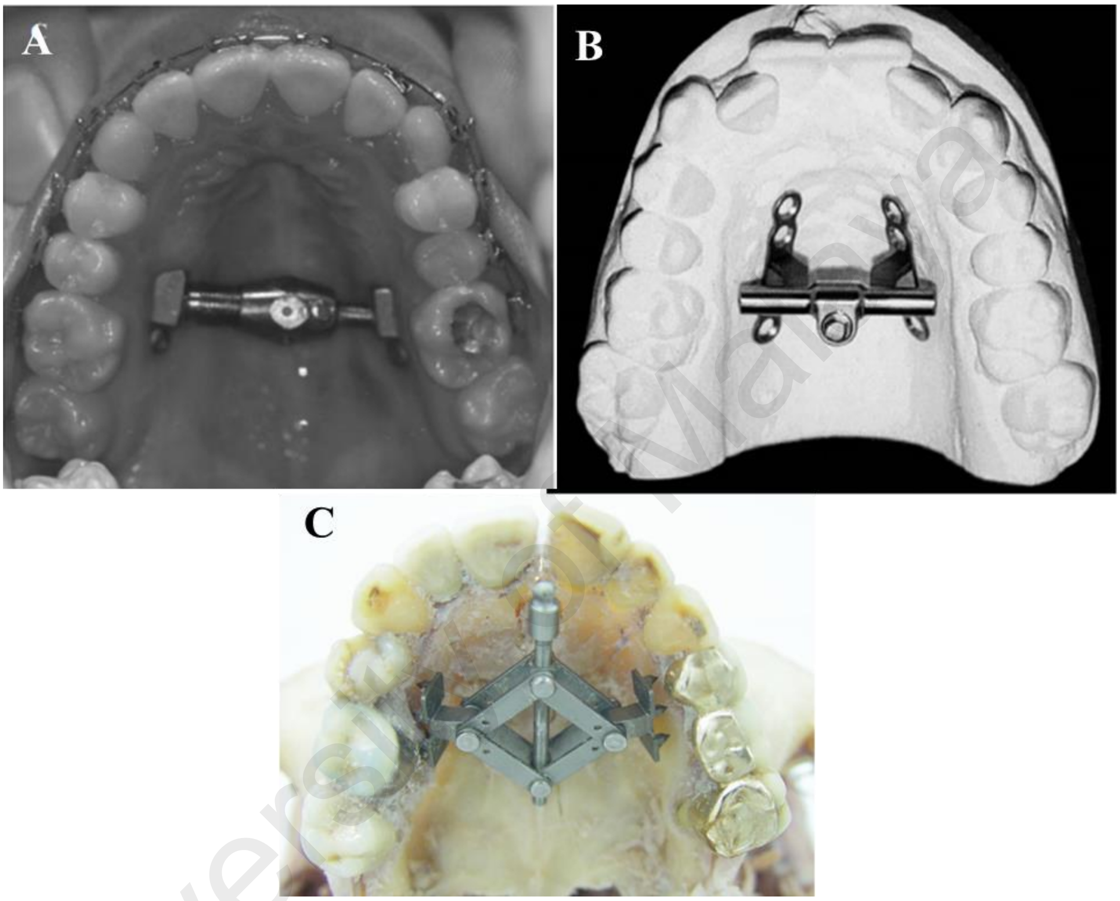


Figure 2.7: A type of bone-borne appliance
A, transpalatal distractor (Mommaerts, 1999); B, the Magdenburg palatal distractor (Gerlach & Zahl, 2003); and C, Rotterdam palatal distractor (Koudstaal et al., 2006)

The Rotterdam palatal distractor (Figure 2.7) does not require any screw fixation to the alveolar bone. Thus, the risk of damaging tooth's root can be minimised (Koudstaal et al., 2006). The Rotterdam palatal distractor is attached to the palatal bone by two the abutment plates. This appliance is stabilized at its target position by the nails protruding to the abutment plates. In addition, the placement and removal of this appliance are easy. The disadvantage of this appliance is that the food remnants are easily trapped in the device. In addition, this appliance should not be indicated for patients with Class II deep bite (Koudstaal et al., 2006).

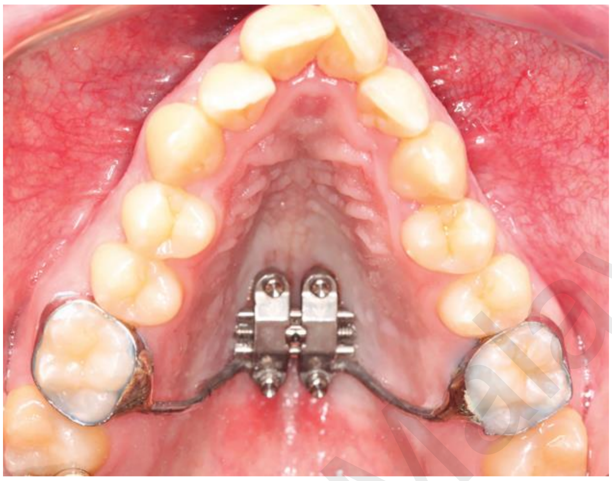


Figure 2.8: Microimplant- assisted rapid palatal expansion (MARPE) (source: Carlson et al., 2016)

Recently, implant-supported expansion has become more popular. This appliance includes two to four mini-implants to support the expansion screw or acrylic frame. In 2016, Moon and co-workers introduced a technique known as microimplant-assisted rapid palatal expansion (MARPE) (Figure 2.8) (Brunetto et al., 2017; Carlson et al., 2016). The force produced by MARPE is directly transmitted to the implants and induces midpalatal suture opening. It was reported that this appliance could produce a large amount of skeletal effect without performing osteotomies (Brunetto et al., 2017; Carlson et al., 2016).

2.1.6 Effects of RME on the maxillary complex

In RME, the generated force from the jackscrew will directly produce pressure on the anchorage teeth and/or palatal tissues. This pressure influences not only the adjacent structures but also the distant ones. The possible changes produced by expansion force are teeth tipping, alveolar displacement and midpalatal suture separation (Bishara & Staley, 1987).

2.1.6.1. Maxillary posterior teeth

When the anchor teeth were subjected to pressure, they tipped labially until the force was completely dissipated to the alveolar bone and suture. The angulation between the long axis of the right and left posterior teeth increased by 1° to 14° under the expansion force. In addition, tooth extrusion was observed during the tipping movement (Byrum, 1971; Hicks, 1978).

2.1.6.2. Alveolar processes

The alveolar processes could displace laterally following the teeth tipping movements because bone is resilient. The expansion force was reported to be completely dissipated within five to six weeks. When the force is released, the alveolar bone tends to return to the previous position (Isaacson et al., 1964). Therefore, overcorrection of the maxillary deficiency is necessary to compensate the rebound (Haas, 1965; Wertz, 1970).

2.1.6.3 Midpalatal suture separation and arch perimeter

The expansion force displaces the alveolar processes and subsequently opens the midpalatal suture (Haas, 1961). The amount of midpalatal separation is approximately half that of the dental expansion in children and lesser in older patients. The midpalatal opening is usually double the gap between the incisors (Krebs, 1959; Bishara & Staley, 1987).

2.1.6.4 Maxillary halves and palatal vault

According to Krebs, the two halves of the maxilla rotated downward and forward following maxillary expansion (Krebs, 1959). The magnitude of tipping displacement between the two halves was reported to be -1° to +8° (Hicks, 1978). This rotation resulted in a lower position of the palatal vault and less skeletal increment at the palatal vault level than at the dental level (Haas, 1961; Wertz, 1970). Also, the stability of the new position of maxillary halves was unpredictable because they tend to return partially or completely to the previous position (Haas, 1970; Wertz, 1970).

2.1.6.5 Maxillary incisors

When the midpalatal suture is separated, patients usually notice a diastema between the central incisors. This gap would bother some patients and their parents. Thus, clinicians need to inform them of the possible occurrence of the diastema before performing the intervention (Bishara & Staley, 1987). Central incisors are likely extruded and upright or tipped buccally (76% of the cases) during the expansion procedure (Haas, 1965; Wertz, 1970).

2.1.6.6 Palatal tissue and periodontium

When the midpalatal suture opens, the palatal mucosa is stretched (Bishara & Staley, 1987). As a result, two bodies of the maxilla might rebound to their original position partly or completely post treatment (Cotton, 1978). Besides, the pressure force applied on the anchorage tooth might cause detrimental effects on the alveolar bone and tooth root (Barber & Sims, 1981; Langford, 1982; Langford & Sims, 1982). Some authors reported a noticeable loss of alveolar bone crest and root resorption in some cases (Barber & Sims, 1981). However, these defects were likely to be repaired during the retention period (Bishara & Staley, 1987).

2.1.6.7 Effects of RME on the mandible and mandibular teeth

When the maxillary posterior teeth extrude and tip buccally, the mandible tends to rotate downward and backwards. This phenomenon should be carefully considered in patients with a steep mandibular plane or open bite malocclusion (Bishara & Staley, 1987). By contrast, most of mandibular teeth remain in their position or slightly upright (Haas, 1965; Haas, 1970). In some cases, the mandibular teeth upright, and the intermolar widths slightly increase up to 1 mm (Gryson, 1977).

2.1.6.8 Effects of RME on the surrounding structures

Most of the studies described an increase in the nasal cavity width especially at the floor of nose next to the midpalatal suture. The average of nasal width increment was 1.9 mm but could be up to 4 mm (Wertz, 1970). As a result, the nasal airflow increases and the patients feel less obstructed (Gray, 1975). However, the indication of maxillary expansion for the purpose of solving nasal obstruction should be considered carefully because the increment of nasal volume may be just temporary and depends on the cause, location, and the severity of the nasal obstruction (Bishara & Staley, 1987).

RME may have an influence on distant structures. All craniofacial bones directly connected to the maxilla were reported to be displaced under the expansion force (Bishara & Staley, 1987). In an animal study, Gardner and Krohman (1971) showed that the lambdoid and parietal bones were also moblilised. Therefore, the effect of RME is not only limited to the palate and dentoalveolar complex (Bishara & Staley, 1987).

2.1.7 Type of tooth movements and forces in orthodontics

In orthodontics, teeth movements can be mainly divided into torque, uncontrolled tipping, controlled tipping, bodily movement (Proffit et al., 2007). Torque refers to a movement in that the crown of a tooth is nearly restrained and the root moves more than the crown does. The centre of rotation in this movement is displaced incisally (Figure 2.9D). Pure tipping is the movement that tooth rotates around the centre of resistance with the crown and its root move in opposite direction (Figure 2.9A). In controlled tipping, the inclination of teeth changes, the centre of rotation moves apically to the centre of resistance and the root and crown move in the same direction (Figure 2.9B). Bodily movement is related to tooth movement in which crown and root moved equally (Figure 2.9C). During maxillary expansion, as the force is applied at the crown, tipping movement is more likely to occur than the other movements (Proffit et al., 2007).

The distribution of compression and tension areas depends on the type of tooth movement. When a tooth moves, some parts of the PDL are compressed and other parts are under tension. The pressure areas undergo bone resorption while the tension areas undergo bone apposition. Tipping, a simplest type of tooth movement, occurs when a single force is placed at the crown. In this movement, the PDL is compressed at the root apex on the same side of the force application and at the alveolar crest on the opposite side of the force (Figure 2.10A). The other areas in the PDL receive the tension. In translation movement, the pressure area is a rectangle region situated on the opposite side of the force application (Figure 2.10B). Therefore, the magnitude of force should be adjusted according to the type of tooth movement (Table 2.4) (Proffit et al., 2007).

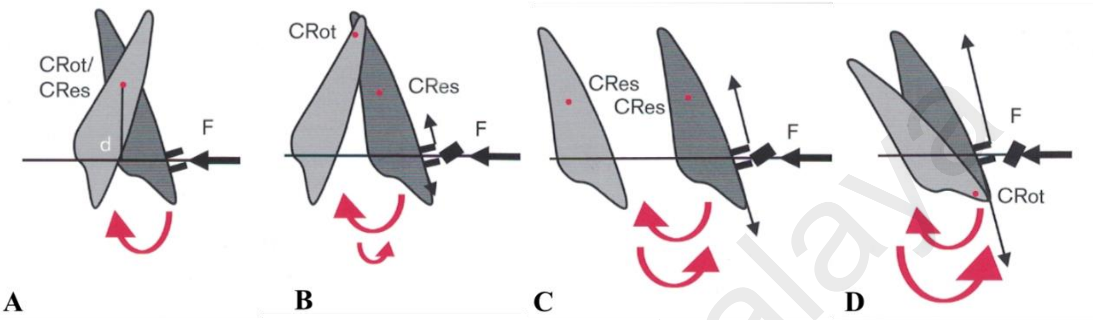


Figure 2.9: Types of tooth movement
A, pure tipping movement: tooth rotates around the centre of resistance; B, controlled tipping: centre of rotation moves apically to the center of resistance; C, bodily movement: crown and root move equally; D, root torque: the crown is retained and root moves more than the crown (source: Nanda & Tosun, 2010).

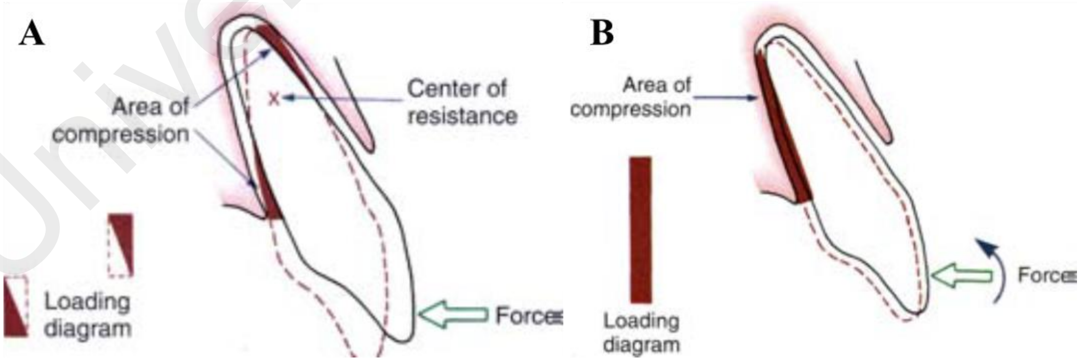


Figure 2.10: The distribution of compression areas according to the types of tooth movement.
A, tipping movement: the compression areas are two triangles (red) at the cervical and the apex of the tooth; B, translation movement: the compression area is a rectangle (red) at one side of the root (source: Proffit et al., 2007)

Table 2.4: Optimum forces for tooth movement in orthodontics (source: Proffit et al., 2007)

Type of tooth movement	Force (gm)
Tipping	35-60
Bodily movement (translation)	70-120
Root uprighting	50-100
Rotation	35-60
Extrusion	35-60
Intrusion	10-20

2.1.8. Nonsurgical vs. surgical assisted expansion in adults.

RME has been proven to be effective in treating maxillary deficiency in children. Nevertheless, the success of RME in adults has not been well-documented (Baydas et al., 2006; Bishara & Staley, 1987; Proffit et al., 2007). Currently, nonsurgical and surgical approaches for treatment maxillary deficiency in adults is still a controversy (Figure 2.11) (Handelman, 2011; Northway, 2011).

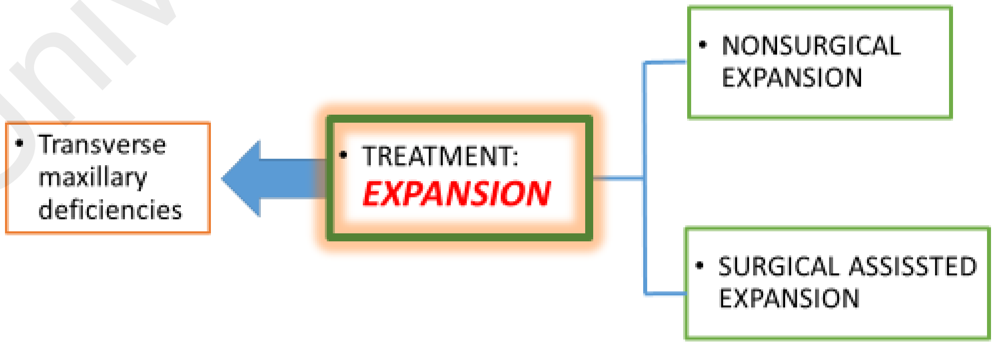


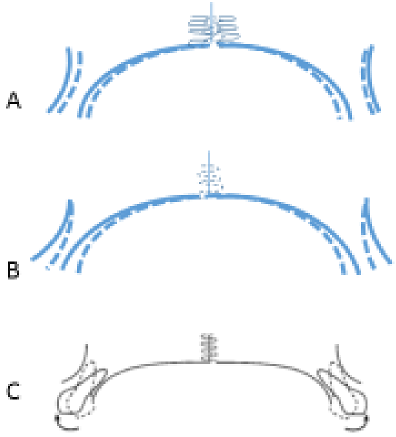
Figure 2.11: Types of treatment modality for transverse maxillary deficiencies in adults (sources: Handelman, 2011; Northway, 2011)

2.1.8.1. Nonsurgical expansion approach in adults

Studies on nonsurgical expansion approaches in adults are limited. Handelman and co-workers demonstrated that this modality is efficacious in many adults (18 to 49 years). The average amount of dental expansion is 4.6 to 5.5 mm at the premolars and first molars region (Handelman et al., 2000; Handelman, 1997). Lin et al. (2015) reported similar results during late adolescence (mean age at 17.4 years). Transverse interpremolar and intermolar widths increased only 4 mm post-intervention despite the appliance being activated over 7 mm (Lin et al., 2015). Chen et al. (2016) studied miniscrews to assist maxillary expansion in 69 patients aging from 18 to 28 years. In this study, the increase widths of interpremolar and intermolar distance were between 6 and 8 mm. However, the measurement decreased to 4.5 mm after debonding (Chen et al., 2016). Therefore, it is recommended that a nonsurgical approach should be indicated when the maxillary deficiency is less than 5 mm (Betts, 2016).

Most authors reported little or no significant skeletal changes with nonsurgical expansion approach. The skeletal changes were 0.9 mm at the palatal vault and 5.1 mm at the cervical level (Handelman et al., 2000). Cao et al. (2009) found no skeletal changes on cephalometric radiographs after SME in an adult group. In a late adolescent group (averaged 17.4 years), Lin et al. (2015) found that the hard palatal width increased by 1.14 to 1.71 mm in the group treated with Hyrax expander. The expansion of the palate was more significant in implant-supported expansion group (1.78 to 3.08 mm) compared to the Hyrax group. Similarly, Chen and co-workers reported 2 mm skeletal expansion when using mini-implant supported expanders (Chen et al., 2016).

Some authors favour SME to treat maxillary deficiency in adults. This paradigm is believed to cause less tissue resistance and more physiological response at to the midpalatal tissue. Moreover, adult patients feel less pain and can better adapt to the SME protocol (Cao et al., 2009; Handelman, 2011; Handelman et al., 2000).



- *Children ≤ 14 years old*: 40%-55% suture opening + 45%- 60% (alveolar bending + teeth tipping)
- Adult: ≤ 30% suture + ≥ 70% (alveolar bending + teeth tipping)

Figure 2.12: The nature of maxillary expansion in children and adults. Total effect of nonsurgical maxillary expansion results from A: midpalatal suture opening; B alveolar displacement and C: teeth tipping. These contributions are different in children and adults (sources: Garrett et al., 2008; Iseri & Ozsoy, 2004; Krebs, 1959; Handelman, 2011, Northway, 2011).

The nature of the expansion is different in adults when compared to children (Figure 2.12). In children, skeletal changes resulted from the opening of midpalatal sutures, accounting for approximately 50%-60% of the total expansion. The remaining half was attributed to the displacement of the dentoalveolar complex (Handelman, 2011). When patients were in the early adolescents, the percentage of skeletal contribution to total changes dropped dramatically to 30% (Northway, 2011). According to Handelman, the displacement of alveolar bone is the cornerstone for the successful of nonsurgical treatment in adults. Handelman also advocated Haas expander to be the key appliance since it was thought that the acrylic plates could displace the alveolus and enhance the skeletal effects. In adults, the skeletal change at the palatal roof was 18% of the total alveolus displacement (Handelman et al., 2000). Although this amount was much less than that of in children, satisfactory outcomes have been achieved in many adults (Handelman, 2011; Handelman, 1997; Handelman et al., 2000).

In adults, greater skeletal effects could be achieved when nonsurgical expansion is combined with mini-implants. Although the skeletal expansion has been reported to contribute up to 43.34% of the total expansion (Chen et al., 2016; Kim & Helmkamp, 2012), this modality could not split the midpalatal suture in all maxillary deficiency cases (Chen et al., 2016).

The long term stability of nonsurgical expansion in adults has not been well-documented. A slightly decrease in the intercuspal width at 0.5 mm to 0.6 mm was observed over 5 years post treatment. Using the Haas expander and long term retention are suggested to be helpful to prevent relapse of the nonsurgical expansion treatment (Handelman, 2011; Handelman et al., 2000).

The expansion force produced by RME is adequate to deform bone. Following alveolus deformation, the alveolar bone underwent remodelling. Bone apposition took place on the concave surface (buccal surface), whereas bone resorption occurred on the convex side. As a result, the alveolar bone was displaced buccally (Epker & Frost, 1965; Handelman 2011).

2.1.8.2. Surgical approach for maxillary expansion in adults

Most clinicians advocate the surgical approach in adults because the surgical approach is proposed to produce a great amount of dental and skeletal expansion. Another advantage is that it improves dental and skeletal stability. In addition, it causes less iatrogenic effects on the periodontium (Northway, 2011). The noteworthy feature of a surgical approach for maxillary expansion in adults is that the skeletal effect is maximised (Suri & Taneja, 2008; Northway, 2011; Betts, 2016).

The dental changes after SARME have been reported in the literature. The mean intermolar width increment immediately after the intervention was approximately 8 mm with the maximum amount being 13 mm (Lagravère et al., 2006). A similar amount of change was recorded for transverse width increase in the interpremolar widths. In the long term, such a large amount of expansion declined gradually. Chamberland and Proffit (2011) showed that the average percentage relapse was 24% (or 1.83 mm) of the total dental changes (7.6 mm), regardless of a 6-month retention. In addition, relapse of 2 mm occurred in 42% of subjects and 22% of patients had a decrease of more than 3 mm (Chamberland & Proffit, 2011). Meanwhile, a larger amount of dental relapse (36%) was reported, even though the retainers were maintained for six months (Byloff & Mossaz, 2004). Other studies showed various relapse rates ranging from 5% to 25% (equivalent to 0.5 to 3 mm) (Bays & Greco, 1992; Berger et al., 1998; Mommaerts, 1999; Suri & Taneja, 2008; Betts, 2016).

SARME produces remarkable skeletal expansion. The average amount of skeletal change varies from 1.7 mm to 5mm with up to 8 mm reported (Lagravère et al., 2006) . As a result, skeletal change contributes approximately half of the total maxillary width change. The skeletal changes are more stable in the long term compared with the dental changes (Chamberland & Proffit, 2011; Lagravère et al., 2006; Betts, 2016).

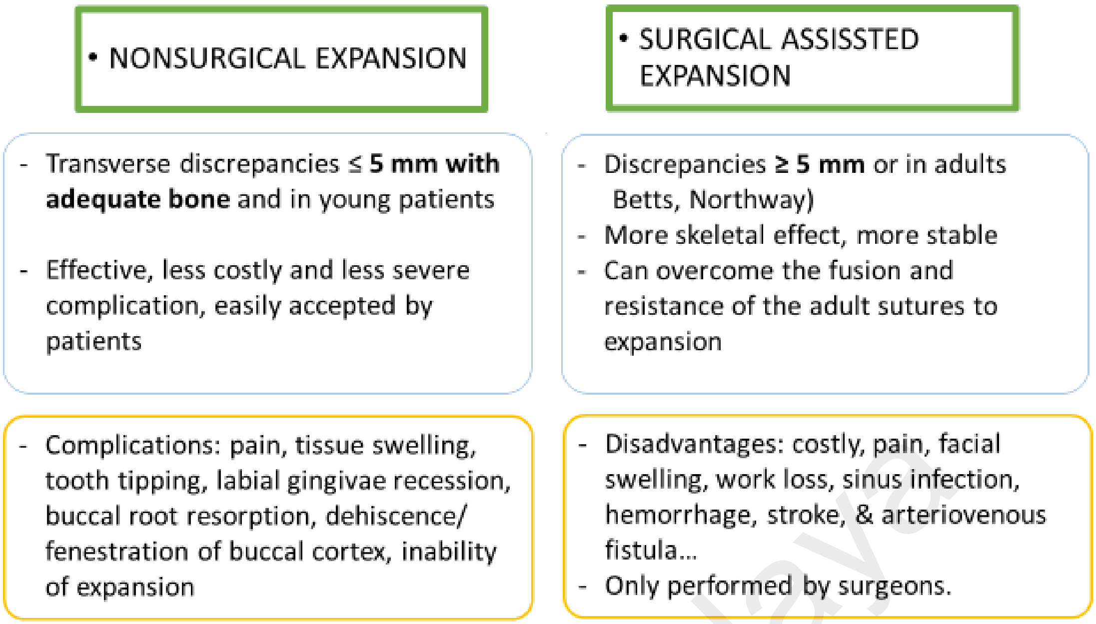
SARME has been proposed to cause less teeth tipping due to the buccally movement of two halves of maxilla. The premolars and molars tipped by 6.48° and 7.04° to 9.63°, respectively (when patients were treated with a tooth-borne appliance) (Lagravère et al., 2006; Verstraaten et al., 2010). Other authors described a larger amount of tipping in the molar region at 9.6° (ranging from 2.2° to 17°) (Byloff & Mossaz, 2004).

Horizontal alveolar loss probably occurs although most clinicians assume that this iatrogenic effect is of little consequent. Gauthier et al. (2011) stated that clinical gingival recession seemed to be minimal but a significant loss of alveolar crest occurred. In this study, osteotomies were performed at all resistance centres such as at the maxillary sinus wall, midpalatal suture, nasal septum and pterygoid plates. However, the height of alveolar crest decreased considerably (2.4 to 3.3 mm) (Gauthier et al., 2011).

Several other complications related to SARME have been reported. Severe problems can include epistaxis and skull base fracture. The others were less serious including hemorrhage, postoperative pain, sinusitis, gingival recession, infection and injury to the maxillary nerves (Carmen et al., 2000; Handelman, 2011; Suri & Taneja, 2008).

2.1.9. What is the most suitable treatment for maxillary deficiency in adults?

The most suitable modality for treating transverse maxillary deficiency in adults is still a controversial subject. Both nonsurgical and surgical approaches have their own potential advantages and disadvantages (Figure 2.13). Successful outcomes from both approaches could be achieved with some limitations and accompanied with certain iatrogenic effects (Handelman, 2011; Northway, 2011). Recently, mini-implant supported expansion has been reported as an alternative treatment choice (Brunetto et al., 2017; Carlson et al., 2016). Another option is corticotomy assisted expansion (Echchadi et al., 2015).



• NONSURGICAL EXPANSION

- Transverse discrepancies ≤ **5 mm with adequate bone** and in young patients
- Effective, less costly and less severe complication, easily accepted by patients

- Complications: pain, tissue swelling, tooth tipping, labial gingivae recession, buccal root resorption, dehiscence/ fenestration of buccal cortex, inability of expansion

• SURGICAL ASSISSTED EXPANSION

- Discrepancies ≥ **5 mm** or in adults Betts, Northway)
- More skeletal effect, more stable
- Can overcome the fusion and resistance of the adult sutures to expansion

- Disadvantages: costly, pain, facial swelling, work loss, sinus infection, hemorrhage, stroke, & arteriovenous fistula…
- Only performed by surgeons.

Figure 2.13: Summary of reports on indications, advantages and disadvantage of nonsurgical and surgical approaches (sources: Betts, 2016; Suri & Taneja, 2008; Handelman, 2011; Northway, 2011)

2.2 Corticotomy

2.2.1 Definition of the term “corticotomy”

A corticotomy is a minor surgical procedure involving only the cortical bone, while the penetration into medullary bone is only minimal. The surgical insults on the cortical bone include incisions, perforations, and mechanical alterations (Alghamdi, 2010; Cano et al., 2012; Hassan et al., 2015; Uzuner & Darendeliler, 2013).

Corticotomy surgery should be differentiated from osteotomy, ostectomy and coticoectomy. Osteotomy is a surgical procedure involving a complete bone cut through both the cortical and cancellous bones. Ostectomy involves a removal a part of both cortical and medullary bones. Finally, corticoectomy is a surgical procedure which only takes a portion of cortical bone without penetrating into cancellous bone (Uzuner & Darendeliler, 2013).

2.2.2. Historical background

Prolonged treatment duration is one of the main consequences for patients receiving orthodontic treatment. Since the early 1800s, some clinicians have proposed osteotomies to surgically assist orthodontic tooth movement resulting in a short treatment duration. Osteotomies include incisions performed through the whole thickness of alveolar bone. As a result, the separated segment could be mobilised to the new position in a much shorter time than which could be done by conventional orthodontic therapy alone. Nonetheless, this technique was considered as a traumatic procedure and not routinely accepted by patients and clinicians. Common complications included infection, necrosis of bone, bony dehiscence, and devitalisation of involved teeth. (Kole, 1959; Kim et al., 2013; Alghamdi, 2010).

Corticotomies were introduced at the end of the 19th century. Bryan and Cunningham were the first pioneers who employed corticotomies in orthodontics. Bryan described a cortictomy technique in an orthodontic textbook name “Orthodontia: Or Malposition of the Human teeth, its prevention and remedy” in 1893, while Cunningham presented it in a dental conference in Chicago in the same year. However, most of the corticotomy procedures used nowadays are an adopted or modified of the original technique introduced by Köle (as cited in Vargas & Ocampo, 2016; Sirisha et al., 2014; Uzuner & Darendeliler, 2013).

In 1959, Heinrick Köle, an influential orthodontist, performed a combination of corticotomy and osteotomy techniques on an alveolar ridge to treat several types of occlusal abnormalities (Kole, 2959). The corticotomy cuts were made vertically involving the entire interdental alveolar height to one centimetre above the apex of the teeth. These cuts were performed on the buccal and palatal sides of the maxilla. The depth of the incisions were limited to the cortical bone only and the cancellous bone was left intact or minimally involved. The replacement of the vertical osteotomy by corticotomy incisions would allow the maintenance of sufficient blood supply to the dentition. The vertical cuts were then connected with the horizontal osteotomies placed above the apex of a single tooth or a group of teeth. By this way, blocks of bone were created and could be moved somewhat independently to the remaining bone. The crowns of teeth acted as points of applications receiving the orthodontic forces and bringing along their bony blocks. Although Kole's procedure was similar to an osteotomy in nature, it provided more support to the dentition and periodontium (Kole, 1959; as cited in Vargas & Ocampo, 2016; Sirisha et al., 2014).

Köle (1959) employed the corticotomy technique to solve various severe orthodontic problems. These severe cases would take a long treatment duration when treated with conventional orthodontic modality. Otherwise, they would require a combination of complex surgical procedures, followed by a conventional orthodontic treatment. The average active treatment duration was shown to be between 6 and 12 weeks with the rate of tooth movement at 0.5 mm per day. Köle believed that the rigidity of the cortical plate was the primary resistance to the tooth movement. Thus, by disrupting the integrity of cortical bone, when a force was applied, the segment of teeth could be moved to a new position in a shorter period of time. The important point in Kole's hypothesis was that the block of bone was moved with its tooth rather than moving individual tooth through the alveolar bone. Unfortunately, Köle's seminal contributions did not gain the enthusiasm from his colleagues, and the technique was not widely accepted during his time (Kole, 1959; Vargas & Ocampo, 2016; Sirisha et al., 2014; Kim et al., 2013).

In 1991, Suya resuscitated the academic interest into this topic by reporting the successful use of the corticotomy technique in 395 Japanese patients. Suya substituted the horizontal osteotomies at the buccal and lingual subapical areas in Köle's technique for horizontal corticotomy incisions, which did not penetrate deeply into medullary bone. The vertical cuts initiated at least 2 mm above or below the alveolar crest to preserve the health of periodontium. Although the bony blocks were less mobilised, 69% of the cases could be finished within only 4 months and the remainder were completed in less than 1 year. The term “corticotomy-facilitated orthodontics” was used to describe this technique. The majority of tooth movements were recommended to be completed within three to four months, before the block of bone began to fuse to the basal bone. In addition, the advantages of this technique were increased stability, lower incidence of resorption, and increased patient comfort (as cited in Kim et al., 2013; Cano et al., 2012; Choo et al., 2011).

It was not until 2000 that the well-recognised revival of corticotomies took place by the two Wilcko brothers. They introduced Wilckodontics which was initially referred to as “Accelerated Osteogenic Orthodontics” (AOO). In 2008, the name was changed to “Periodontally Accelerated Osteogenic Orthodontics” (PAOO) (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013; Wilcko et al., 2001; Kim et al., 2013). The Wilcko brothers filed a patent for their novel idea. The innovative feature of Wilckodontics is the combination of an alveolar bone graft into the corticotomy treatment modality. In PAOO, the corticotomy procedure also involved a full flap reflection, followed by the circumscribing decortication cuts buccally and lingually around the targeted teeth (Figure 2.14). Additional buccal perforations on the cortical layer were performed to maximise the trauma to the bone surface and to enhance bleeding into the grafting material. Most of corticotomised areas were recommended to be grafted to strengthen the periodontium and prevent bony dehiscence and fenestration. Grafting materials used in their studies were decalcified dried bone allograft, deproteinised bovine bone or a mixture of both. Tooth movement were recommended to start two weeks after surgery. The fixed appliances were adjusted in two weeks intervals- ranging from one to three weeks. The advantages of alveolar augmentation were that the thin bone layer covering the prominences of the roots was maintained, and the bony fenestrations were prevented. In some cases, the thickness of alveolar bone increased post treatment (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013; Wilcko et al., 2001; Kim et al., 2013; Sirisha et al., 2014).

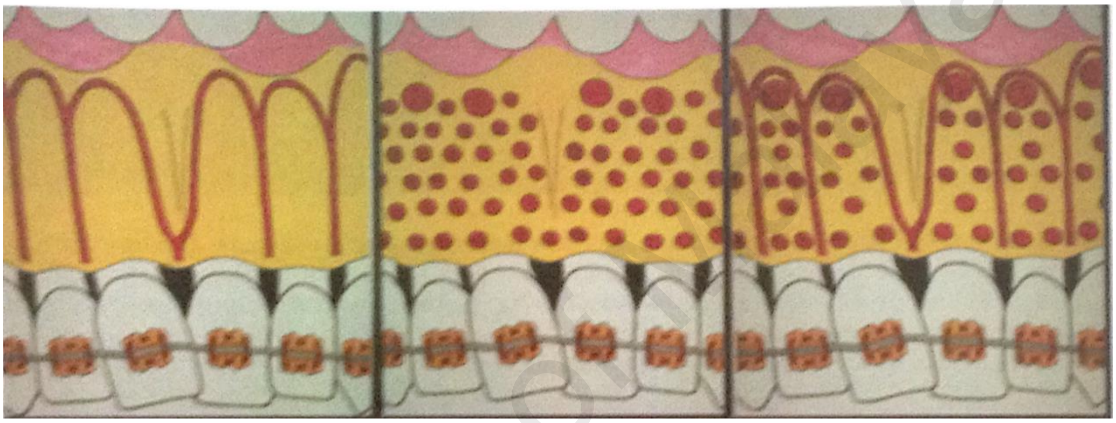


Figure 2.14: Wilcko technique. Corticotomy incisions were performed around the anterior roots in combination with perforations on the buccal alveolar cortex (source: Wilcko et al., 2001).

Wilcko and co-workers showed several treated cases using Wilckodontics. They advocated employing PAOO for moderate crowding with and without extraction. The average treatment time was only one-third (around 6 months) of the routine orthodontic treatment time (Table 2.5). Retainers were recommended to be worn immediately after bracket debonding. By this way, teeth would be maintained in the new position until the surrounding bone matrix fully remineralises (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013; Wilcko et al., 2001).

Table 2.5: Advantages of "Periodontally Accelerated Osteogenic Orthodontics" (PAOO) (source: Wilcko et al. 2008)

Safe, efficacy.
Less root resorption.
Short treatment time.
No risk of pulp necrosis.
No risk of periodontal pocket formation.
Decreasing the risk of bony dehiscence and fenestrations.
Eliminating the need for extraction and orthognathic surgery.
Correction of bony dehiscence and fenestrations if they exist before treatment.
Reshaping the alveolar bone and improving the patient's profile for certain cases.

Another noteworthy feature is that Wilcko brothers were not in agreement with previous pioneers on the nature of tooth movement produced by corticotomy. When comparing CBCT images pre- and post-treatment, Wilcko and co-workers reported some demineralisation on the buccal alveolar surface of the moved teeth (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013). When the roots were retained in the new position, the collagenous bone matrix was gradually remineralised. From these observations, Wilcko and co-workers hypothesised that "bone matrix" instead of the "bony block" would be transported together with the roots. Thus, the demineralisation-remineralisation phenomenon could be a more precise explanation for the accelerated tooth movement (Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013).

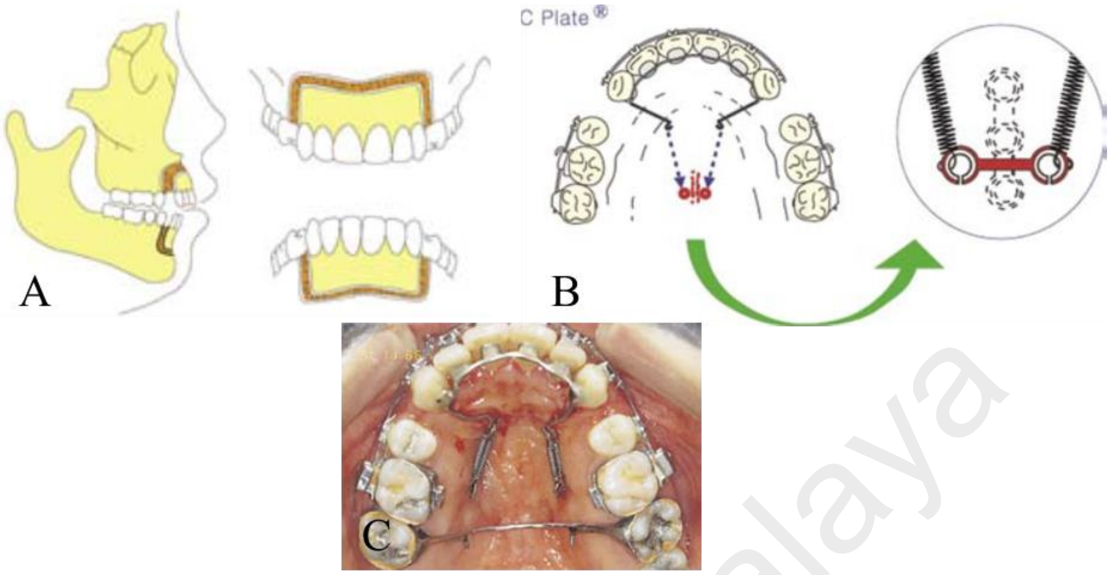


Figure 2.15: Speedy surgical orthodontics.
Three key components in this concept are a perisegmental corticotomy around the anterior segment (A) in combination with orthopaedic traction (B, C) (source: Chung et al., 2007).

At the same time as the introduction of Wilckodontics, Korean orthodontists proposed a technique known as “Speedy surgical orthodontics” (Chung et al., 2007; Chung et al., 2009; Kim et al., 2011; Kim et al., 2012; Kim et al., 2009). The essential theme of this novel concept was the combination of corticotomy surgery and orthopaedic traction force. The three key components in this concept were a perisegmental corticotomy around the incisor and canine segment, a C-palatal miniplate inserted at the hard palate, and a C-palatal retractor for pulling backwards of the anterior bone block (Chung et al., 2007) (Figure 2.15). This novel technique was shown to be effective and could replace orthognathic surgery partly in treating severe bimaxillary protrusion in adults. Speedy surgical orthodontics technique does not only enhance the treatment outcomes, but also reduces treatment time (Chung et al., 2007). Chung et al. (2009) reported that the retraction of the anterior segment only took 4 to 6 months, and subsequent 2 to 3 months for finishing. The common associated complications were swelling and contusion. However, these complications depend on the suturing skill of the surgeons, physical constitution of the patients, and adherence to post-operative instructions; ie. using cold pack (Chung et al., 2009). Therefore, most patients treated with this modality were satisfied with their final profile and shorter treatment time (Chung et al., 2007).

Speedy surgical orthodontics involves a wider incision around a whole block of anterior teeth. This feature is different to Wilckodontics and corticotomy facilitated orthodontics, which include narrower cuts around individual teeth and with punctures on the cortical layer. Another crucial feature is that a bone-bending effect can be created when a heavy orthopaedic traction force is applied to the separated block of bone and teeth. This possibility of bone-bending is due to the high elastic capacity of medullar bone at the decortication sites. The medullary bone is the main region that bears the force and can be easily deformed under the loading force. A high force (1,500 to 1,800 grams) could be applied without detrimental effects to the soft tissue when the corticotomy and orthodopaedic forces were combined. The bone-bending effect plays a crucial role in shortening the treatment duration. It is recommended that orthodontic treatment should be started immediately after surgery to prevent bone reunion at the borders of the cutting lines. The wide cutting line employed in Speedy surgical orthodontics was used to delay the reunion between the bone edges at the incisions. The nature of the treatment duration reduction by PAOO is due to the regional acceleratory phenomenon (RAP). However, the hypothesis in shortening treatment duration produced by Speedy surgical orthodontics is primarily based on the compression osteogenesis (CO). When the cortical bone is insulted, medullary bone resorption is induced (Chung et al., 2009; Kim et al., 2011; Kim et al., 2012; Kim et al., 2009). Moreover, the cancellous bone possesses the poroelastic and viscoelastic properties (Birmingham et al., 2013; Metzger et al., 2015). These properties play an important role on the mechanical response of the tissue (Sandino et al., 2015). Under the loading force, the medullar bone can be deformed and sustain the pressure (Ferguson & Wilcko, 2016). When the cortical bone continuity was disrupted, the elasticity of the corticotomised alveolar segment would increase and this bony segment can be feasibly deformed (Chung et al., 2001; Kim et al., 2011). Compression osteogenesis encompasses both RAP phenomenon and bone-bending effect (Chung et al., 2009; Kim et al., 2011; Kim et al., 2012; Kim et al., 2009).

2.2.3. Phenomena produced by corticotomy surgery

The advantages of the corticotomy surgery together with orthodontics have gradually gained recognition from clinicians. The emerging advantages are the reduction in treatment duration, especially in complex cases, and the possibilities of negating the need for orthognathic surgery. As a result, clinicians can broaden the boundaries of treatment. Three theories related to phenomena produced by corticotomy have been suggested (Kim et al., 2011):

i. Regional acceleratory phenomenon (RAP). RAP includes two sides: the remineralisation to heal the injury; and the demineralisation occurring at the surgically insulted site and its adjacent bone. Hence, RAP is an intensified response of the local bone to an injury, in which the bone turnover is faster than the normal regional regeneration process (Kim et al., 2011).

ii. “Bone matrix transportation”. Corticotomy triggers the RAP, resulting in the decrease of the cortical bone density. As a result, the mechanical resistance of the cortex reduces, and the orthodontic tooth movement is accelerated. The nature of the accelerating tooth movement is proposed to be due to the transportation of bone matrix together with the root (Sirisha et al., 2014; Wilcko et al., 2009; Wilcko et al., 2001).

iii. “Bone-bending effect”. This phenomenon results from the compression osteogenesis (CO) phenomenon (Chung et al., 2007; Kim et al., 2009).

2.2.3.1. Regional acceleratory phenomenon (RAP)

In 1983, Harold Frost, a well-known orthopaedic surgeon, noticed that the healing of a bone injured by a surgical process was different from the normal activity of the local tissues (Frost, 1989). The reorganising activity in this bone area was two to ten times higher than that of the other ribs. Frost termed these events as a regional acceleratory phenomenon (RAP) (as cited in Kim et al., 2011; Kim et al., 2013; Wilcko et al., 2009; Wilcko et al., 2001; Frost, 1989; Roberts et al., 2006; Sirisha et al., 2014).

The RAP is a series of local healing events in response to a noxious stimulus. It occurs not only in hard tissues but also in soft tissues. It is the protective mechanism of the human body. In this event, normal cellular activities are accelerated to facilitate the healing process and shorten the healing duration. The dominant features of RAP are the burst of anabolic and catabolic events at the injured sites. These activities lead to the demineralisation of the local bone. The duration and intensity of the anabolic and catabolic processes depend on the type and magnitude of the stimulus, as well as the type of the insulted tissues. RAP may occur following a surgery, bone fraction, tooth extraction, implant insertion, orthodontic tooth movement, or alveolar bone exposure by flap elevation (Frost, 1989; Roberts et al., 2006; Kim et al., 2013; Sebaoun et al., 2008; Sirisha et al., 2014).

The typical healing process in a rat’s tibia comprises of two phases: woven bone formation and resorption phase (Ferguson & Wilcko, 2016; Sirisha et al., 2014). The first phase was characterised by the formation of woven bone, which formed a bony bridge and gradually covered the defect. This woven bone was the true new bone. It reached maximal thickness at day 7. After day 7, the majority of woven bone in the cortical area was remodelled into the lamellar bone. In contrast, the woven bone in the marrow space underwent resorption. The bone strength decreased immediately after the injury. However, bone strength started to increase when the woven bone transformed to lamellar bone. The formation of woven bone did not follow the routine control pathways of endocrine or nutritional factors. It was found to follow a "high priority" regulatory mechanism to meet the local mechanical demands (Ferguson & Wilcko, 2016; Sirisha et al., 2014).

In 1994, Yaffe et al. observed that the resorption resulted from RAP was first detectable after 10 days of flap elevation in a rat's mandible (Yaffe et al., 1994). The surface of the cortical bone and the buccal alveolar bone proper facing to the buccal side of roots underwent marked resorption. Therefore, tooth movement through the bone cortex during the demineralisation phase may lead to bone dehiscence. The alveolar bone returned to normal mineralisation levels within 120 days after injury. The resorption event might account for the increasing teeth mobility after periodontal surgery (Yaffe et al., 1994). RAP in human was believed to be initiated within a few days following the injury. RAP reached its maximum activity within one to two months, and diminished after 6 to 24 months (Frost, 1989). Therefore, it is recommended that orthodontic appliances should be activated more frequently within the first six months to take the advantage of this phenomenon (Kim et al., 2011).

Sebaoun et al. (2007) examined the RAP duration in a rat model. In this study, the decortications were performed on the buccal and palatal bone surfaces of the upper left molars. A 0.2 mm diameter bur was used to make several dots on the alveolar bone (5 dots in the buccal and 5 dots in the palatal side). The catabolic and anabolic rates were reported to peak at the third week post decortication, by two to three-fold compared to the normal level. The rates at the trabecular bone surface in the surgery group reduced by two-folds at the third week, but recovered equal to that of the control sites at week 11. In parallel to the resorption events, the highest number of osteoclasts and preosteoclasts stained by tartrate resistant acid phosphatase (TRAP) were observed at the third week. The number of osteoclasts subsided to the baseline levels at the 11th week. However, the highest apposition of new bone on the lamina dura was recorded at the 4th week. This was due to the augmentation of the number of osteoclasts and osteoblasts during this period. Meanwhile, lymph, precursors, supporting cells, and blood capillaries also increased at the insulted area (Sebaoun et al., 2007).

In orthodontics, the benefit of RAP in increasing bone turnover has been utilised to accelerate the tooth movement. This benefit has been proven in several humans and animals studies (Sebaoun et al., 2007; Kim et al., 2011; Sanjideh et al., 2010; Aboul-Ela et al., 2011). The rate of tooth movement in the corticotomy treated sides was double that of the control sides. However, this benefit was not maintained in the long term. The highest speed of tooth movement in foxhounds was observed between 22 and 25 days. Subsequently, the velocity of tooth movement decreased gradually. Additional surgery at the 28th day helped to maintain the high rate of tooth movement in an extending period (Sanjideh et al., 2010). Similarly, Aboul-Ela et al. (2011) examined the duration of RAP during maxillary canine retraction in 13 adults. The velocity of tooth movement in the corticotomy side was two times higher than the control during the first two months. Nevertheless, this velocity diminished to 1.6 times in the third month, and returned to the control level by the fourth month. Consequently, the advantage of RAP in the accelerating tooth movement lasted only 4 months in spite of that the true end of this phenomenon may exist in a longer duration (Aboul-Ela et al., 2011).

The nature of tooth movement is based on the cellular activities. When a force is applied to a tooth, it will be transmitted to the root and surrounding periodontal ligament (PDL). One side of the PDL is under tension, while the other side is compressed. On the compression side, the high pressure occludes the blood vessels and causes necrosis areas known as hyalinisation zones. This hyalinisation zone interferes the tooth movement because it inhibits the bone resorption. In the following days, macrophages were recruited to the compression areas, and the hyaline areas will be removed gradually. The removal of hyalinisation zones allows the contact of osteoclasts to the bone surface, and tooth starts to move (Proffit et al., 2007).

In an experiment in dogs, the hyalinisation in the sham group was observed to remain in the PDL up to 4 weeks (Iino et al., 2007). The number of the osteoclasts and preosteoclasts gradually increased from the first week, and peaked at the end of the second week; subsequently, decreasing to the end of the experiment. In parallel with these events, the tooth stopped moving in the first two week as a result of hyalinisation in the PDL (lag phase). Following the removal of hyaline, the tooth started to move from the third week. In contrast, in the corticotomy treated group, the hyaline regions were removed quite early within the first week after the orthodontic force generation. This was due to the increase in the number of osteoclasts, which were dramatically higher during the first week. Therefore, teeth in the experimental side started to move from the end of the first week. Additionally, the lag phase was not detected in corticotomy treated side, because the hyaline was removed as early as the first week. Moreover, the velocity of the tooth movement in the experimental side was two to five times that of the control side. These findings confirmed that corticotomy is enable to accelerate the tooth movement (Iino et al., 2007) Other reseach in cats and rats also showed similar results (Kim et al., 2009; Tomizuka et al., 2007).

2.2.3.2. Bone matrix transportation

In 2001, Wilcko and co-workers reported that the rapid alignment of anterior teeth resulted from demineralisation/remineralisation processes occurring after corticotomy surgery (Wilcko et al., 2001). Wilcko and co-workers (2001) reported the outcomes of two cases with Class I moderately to severely crowding and constricted maxillary arches, which were treated with the PAOO technique. Flaps were elevated, followed by a corticotomy surgery and bone graft augmentation. The appliances were adjusted 2 weeks after surgery in a 2-weeks interval schedule. A demineralisation status of the alveolar bone after the treatment was observed in CT images. However, these demineralised bones underwent various degrees of remineralisation after two years (Figure 2.16). Moreover, it was reported that new bone formation can be induced from the decalcified bone matrix (Wilcko et al., 2001). From these observations, Wilcko and co-workers disagreed on using the concept of “bony block” movement to explain the acceleration of tooth movement. The localised demineralisation/remineralisation condition was proposed to be responsible for the high rate of tooth movement. The bone matrix moved together with the roots to the new position. When the tooth was retained in the new position, the bone matrix underwent remineralisation (Ferguson & Wilcko, 2016; Murphy et al., 2009; Wilcko et al., 2008; Wilcko et al., 2009; Wilcko & Wilcko, 2013; Wilcko et al., 2001).

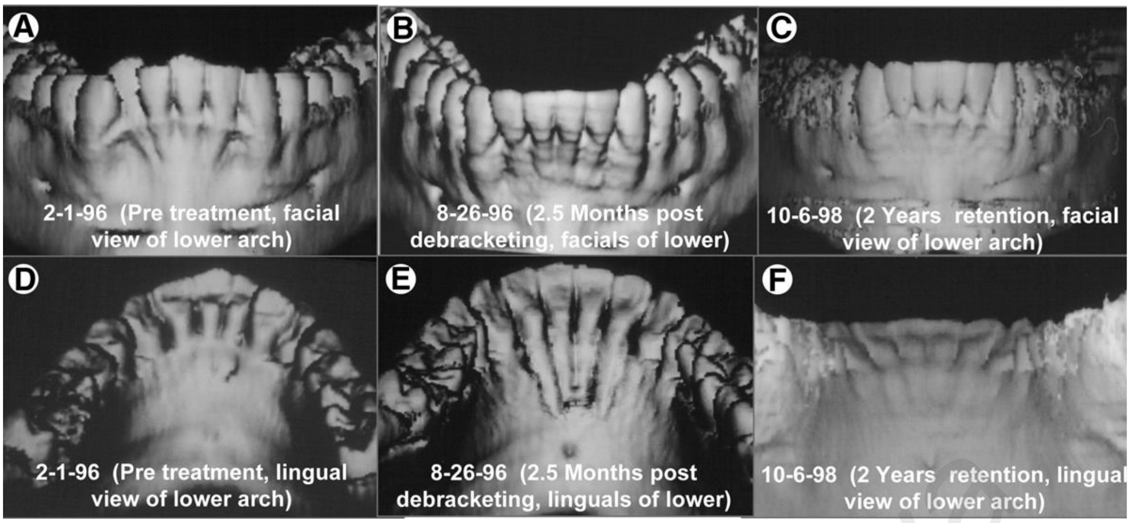


Figure 2.16: Cone-beam computed tomography (CBCT) images of the alveolar bone in a patient treated with "Periodontally Accelerated Osteogenic Orthodontics" (PAOO)

A, B, the feature of normal cortical bone pre-treatment; B, E, a transient decalcification of the alveolus was reveald at 2.5 months post- treatment; C, F, regeneration of cortical bone after 2 years retention (source: Wilcko et al., 2008).

2.2.3.3. Compression osteogenesis (CO)

In the beginning of the 21st century, Chung and co-workers proposed the Speedy surgical orthodontics technique (Chung et al., 2001). The new aspect of this technique is the combination of the segmental corticotomy and orthopaedic forces. The compression osteogenesis theory was utilised to explain the shorter duration in retraction of the anterior teeth segment, when compared to the conventional orthodontic modality (Chung et al., 2007). Compression osteogenesis is based on the concept of distraction osteogenesis, but different in the direction of force application and the amount of cortical bone removal. In compression osteogenesis, more extensive cortical bone is removed, and the two cut-ends are compressed closer to each other (Chung et al., 2007). The compression force induces the resorption and demineralisation in the medullar bone at the decortication sites. As a result, this bone segment can be easily deformed to the direction of force (Chung et al., 2001, Chung et al., 2007). Chung and co-workers called this phenomenon as "bending CO" (Chung et al., 2001, Chung et al., 2007) (Figure 2.17). In speedy surgical orthodontics, the perisegmental corticotomy is performed around the incisors and canines. Then, a heavy orthopaedic force is used to retract this segment backwards. Following the resorption of the medullary bone at the corticotomy area, the alveolus can be deformed easily by a heavy traction force and the treatment duration is reduced (Choo et al., 2011; Chung et al., 2001; Chung et al., 2009; Chung et al., 2009; Kim et al., 2011).

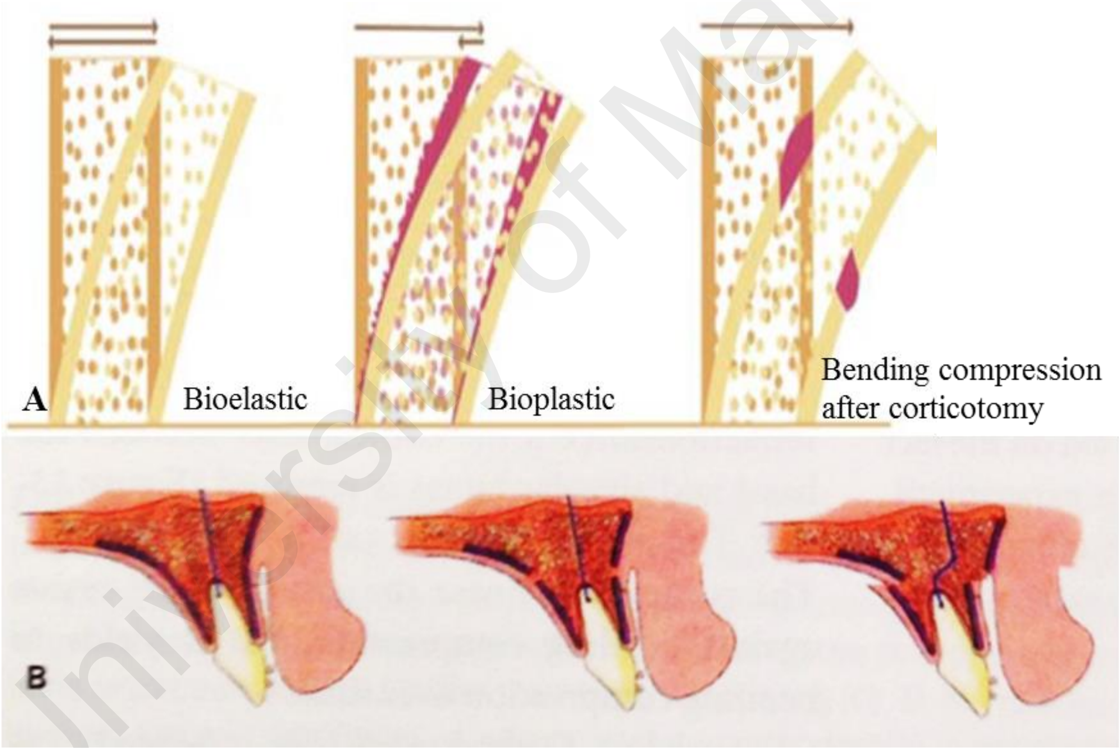


Figure 2.17: Compression osteogenesis theory applied in Speedy surgical orthodontic.

A, schematic illustration of the different forms of bone deformation. "Bioelastic" refers to the possibility of bone to return to the previous position when the applied force is release. "Bioplastic" means the partial deformation of bone. Bending compression oseogenesis implies that the bone deformation was permanent when the decortication bone was ossified; B, the anterior segment could be retracted without difficulty when the perisegmental corticotomy was performed (source: Chung et al., 2007)

2.2.4. Perspective possibilities for maxillary expansion:

Echchadi et al. (2015) utilised corticotomies to assist RME in a skeletally mature girl. An ultrasonic tip of a piezo-surgical device was used to elevate the flap and perform corticotomy perforation on the buccal side of maxillary alveolar bone (Figure 2.18). The palatal expander was installed and activated 1 mm immediately after the surgery. The expander was continuously activated at the rate of 1 mm per week. The fixed appliance was bonded after two months. Echchadi et al. (2015) demonstrated 9 mm maxillary crowding was solved only within six months. This novel surgical design was reported to derive from Fischer and Wilcko's concept but without the bone graft (Echchadi et al., 2015).

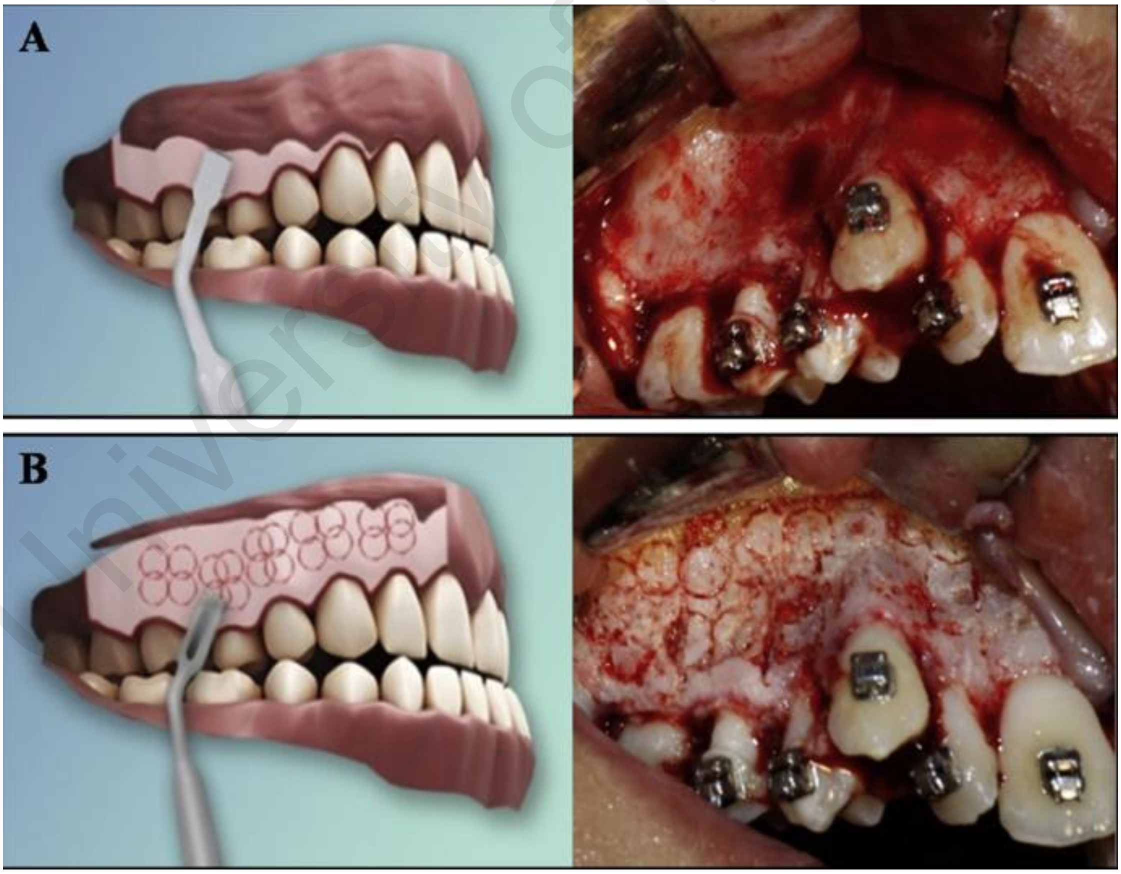


Figure 2.18: Corticotomy assisted maxillary expansion using piezo device
A, Buccal flaps elevation; B, Perforations with piezo device on the buccal surface of the alveolar bone (source: Echchadi et al., 2015).

2.3 Other adjunctive interventions for accelerating tooth movement in orthodontics

Other adjunctive interventions to accelerate the rate of tooth movement can be divided into two categories, i.e., nonsurgical and surgical approaches (Kalemaj et al., 2015). Some types of nonsurgical approach are mechanical vibration, electrical current and low level laser therapy (LLLT) (El-Angbawi et al., 2015) (Tables 2.5). Mechanical vibration has been showed to be a potential treatment modality, but the evidence is of low quality (El-Angbawi et al., 2015). LLLT is a safe therapy to the PDL and root health, but its effectiveness is not adequately high to be clinically relevant (Kalemaj et al., 2015; Long et al., 2012). In a recent systemic literature review, El-Angbawi et al. (2015) concluded that the available research is not convincing to prove the positive effect of nonsurgical methods in accelerating the tooth movement (El-Angbawi et al., 2015).

Surgical interventions include corticotomy, dentoalveolar distraction, and periodontal distraction. Corticotomy can be performed by using burs, piezoelectric scalpel or a Propel device with or without flap elevation. The methodology used in the studies related to dentoalveolar or periodontal distraction was reported to be unreliable, but the results showed promising application. Overall, it is agreed that corticotomy is safe and can significantly accelerate tooth movement at least in the short-term (Kalemaj et al., 2015; Long et al., 2012). Recent Cochrane literature review on the effectiveness of surgical adjunctive procedures also showed quicker tooth movement in surgically assisted orthodontics group compared to conventional treatment group (Fleming et al., 2015). However, further research need to be carried out to confirm these possible benefit (Fleming et al., 2015).

Table 2.6: Nonsurgical adjunctive interventions for accelerating orthodontic tooth movement (sources: El-Angbawi et al., 2015; Aldrees et al., 2016)

Interventions	Definition
Low level laser therapy (LLLT)	Laser beam delivered to the mucosa of the moved teeth by a laser device.
Mechanical vibration.	A device inserted in a mouthpiece produces cyclic vibrational forces directly to teeth.
Pulsed electromagnetic field (PEMF)	An integrated circuit inserted in a removable denture to produce pulsed electromagnetic field.
Electrical current	An electrical appliance used to produce electrical current to the oral mucosa around the moved teeth.
Injected substances	Some substances such as RANKL (receptor activator of nuclear factor kappa β ligand), PGE1 or PGE2 (prostaglandins) are injected into the alveolar bone

2.4 The biology of bone remodelling

2.4.1 Bone remodelling process

Bone remodelling process involves several phases, types of cells, and molecular mechanisms. Basically, the bone remodelling process can be divided into five distinct phases: activation, resorption, reversal, formation, and termination (Figure 2.19) (Raggatt & Partridge, 2010).

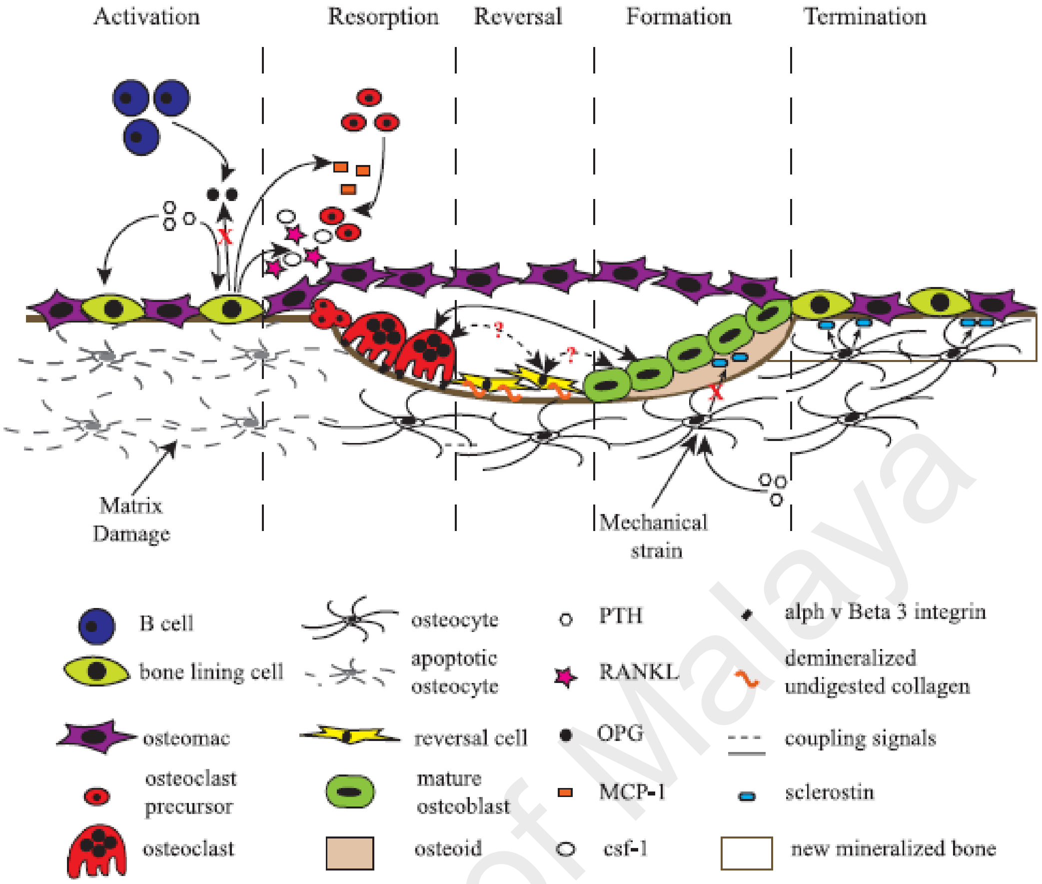
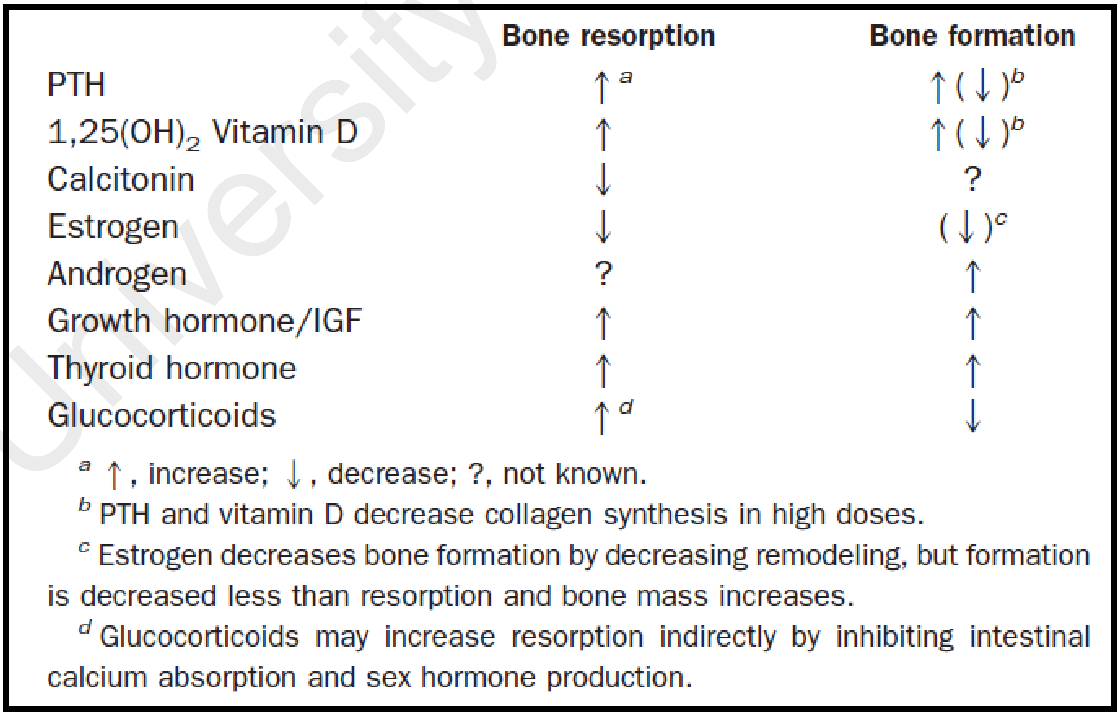


Figure 2.19: Schematic illustration of bone remodelling process.
The figure illustrated the associated cells and signaling molecules involved in the process of bone remodelling (source: Raggatt & Partridge, 2010).

The first phase in bone remodelling is the activation phase, which is mainly associated with the detection of the remodelling signal. The remodelling signals might be as a result of direct damage to the bone, a hormonal change or a systemic disease (Raggatt & Partridge, 2010). The bone damage leads to the exposure of collagen to extracellular fluid and release of prostaglandins (PGs), interleukin, and other inflammation cytokines, which in turn attracts the immune cells. T cells produce the receptor activator of nuclear factor kappa-B ligand (RANKL), which proceeds the osteoclastogenesis (Roberts et al., 2006). Under normal conditions, transforming growth factor β (TGF- β) secreted by osteocytes restrains osteoclast formation. The apoptosis of osteocytes due to injury decreases the

TGF- β level, and induces osteoclast formation (Figure 2.20). Additionally, when the serum calcium decreases, the parathyroid hormone (PTH) secreted by the parathyroid glands binds to its specific receptor (seven transmembranes G-protein-coupled receptor) on the surface of osteoblast, and subsequently activates the production of chemokine MCP-1 (monocyte chemoattractant protein-1) in this cell. MCP-1 then initiates the calcium intracellular signalling pathways. This pathways play an important role in maintaining the calcium homeostasis. PTH regulates the production and recruitment osteoclast precursors, and the differentiation and activation of osteoclasts. The mature osteoclasts are responsible for the bone resorption (Raggatt & Partridge, 2010) (Table 2.7).

Table 2.7: Systemic regulation of bone remodelling (source: Raisz, 1999).



	Bone resorption	Bone formation
PTH	↑ ^{a}	↑ (↓)^{b}
1,25(OH)$_2$ Vitamin D	↑	↑ (↓)^{b}
Calcitonin	↓	?
Estrogen	↓	(↓)^{c}
Androgen	?	↑
Growth hormone/IGF	↑	↑
Thyroid hormone	↑	↑
Glucocorticoids	↑ ^{d}	↓

^{a} ↑, increase; ↓, decrease; ?, not known.

^{b} PTH and vitamin D decrease collagen synthesis in high doses.

^{c} Estrogen decreases bone formation by decreasing remodeling, but formation is decreased less than resorption and bone mass increases.

^{d} Glucocorticoids may increase resorption indirectly by inhibiting intestinal calcium absorption and sex hormone production.

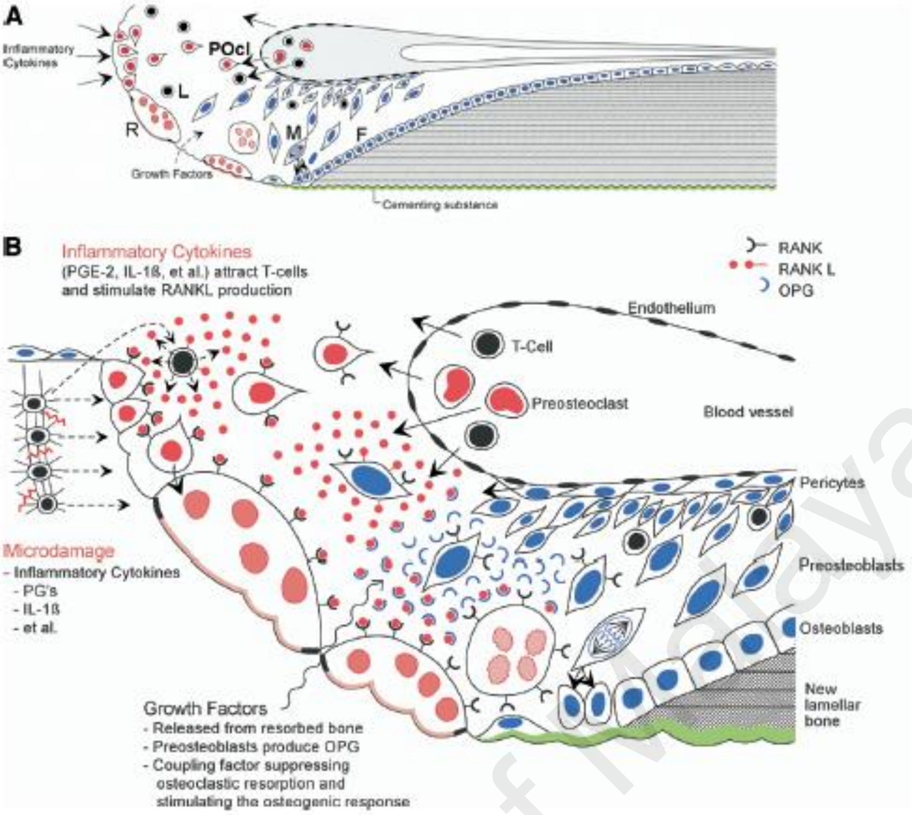


Figure 2.20: Schematic illustration of the mechanism for controlling the bone remodelling process.
A: localised inflammation initiates bone remodelling. B. magnified view of the A illustrating the mechanism involved in bone remodelling (source: Roberts, 2006)

In the resorption phase, the osteoclast precursors are recruited to the remodeling site by the osteoblast/stromal cells, immune cells and chemokines such as MCP-1. Two important factors involved in osteoclastogenesis are osteoclast differentiation factor (RANKL/OPGL/TRANCE) and macrophage colony stimulating factor (CSF-1) (Udagawa et al., 1999). The role of CSF-1 is to stimulate the growth of osteoclast precursor. Meanwhile, RANKL facilitates the transformation of osteoclast precursors to osteoclast, enhances the resorption activity and promotes the survival of osteoclast. Osteoprotegerin (OPG) is a decoy receptor of RANKL and thus, it inhibits the osteoclast and bone resorption activity (Ma et al., 2001). Matrix metalloproteinases (MMPs) secreted from osteoblasts demineralizes the osteoid on the bone surface and exposes

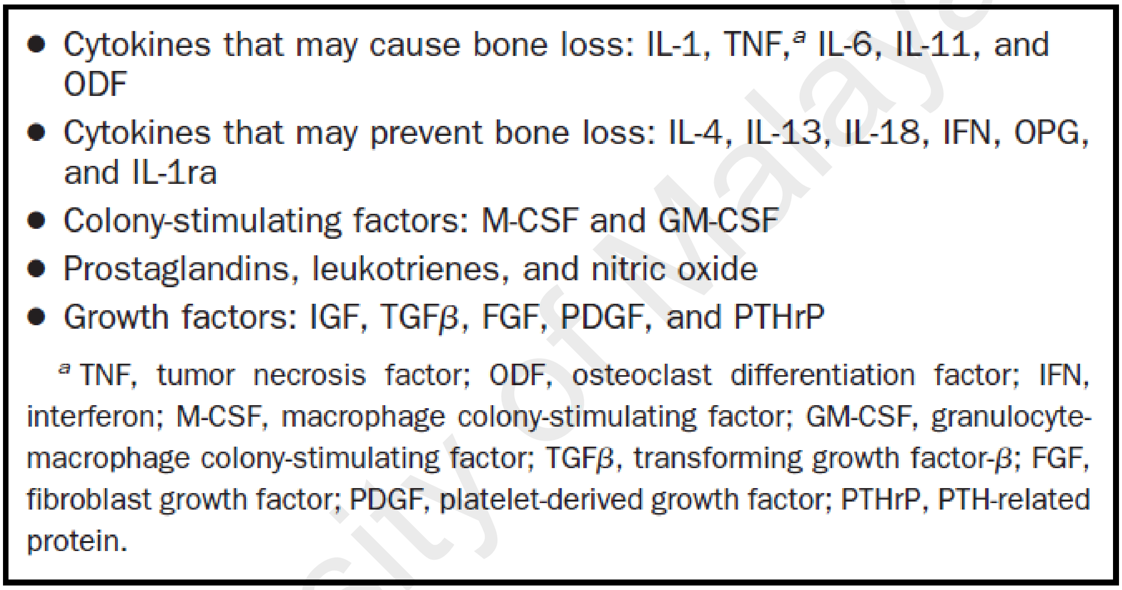
RGD-binding sites for osteoclast to attach. The attachment of osteoclasts stimulates the pumping of hydrogen ions into remodeling sites and creates an acidic microenvironment. The acidic microenvironment causes the dissolution of mineralized matrix and creates Howship lacunae (Teitelbaum, 2000). The organic bone matrix is later degraded by collagenolytic enzymes (Saftig et al., 1998).

The subsequent reversal phase is characterized by the activities of mononuclear “reversal cells” in removal of collagen matrix debris and preparation of bone surface for bone formation in the next phase (Everts et al., 2002). Previously, “reversal cells” were assumed to be a phagocyte (Tran Van et al., 1982). However, recently, this cell was reported to originate from the osteoblast lineage (Everts et al., 2002). The mesenchymal bone-lining cells and macrophages also participates in this reversal phase to remove collagen remnants (Newby, 2008; Takahashi et al., 2004). Finally, the reversal cells might facilitate the transition from bone resorption to bone formation by coupling signals (Everts et al., 2002; Raggatt & Partridge, 2010).

The fourth stage of bone remodelling is the formation phase. In this phase, a series of coupling signals are produced to inhibit bone resorption and promote the return of mesenchymal stem cells and osteoblast progenitors. Some important coupling molecules are insulin-like growth factors I and II and TGF- β, which recruit the mesenchymal stem cell to the remodelling sites (Raggatt & Partridge, 2010). Sphingosine 1-phosphate facilitates the recruitment of osteoblast precursor and prolongs the life of mature osteoblasts (Pederson et al., 2008). EphB4 ephrin-B2 bidirectional signalling enhances the differentiation of osteoblasts and suppresses the differentiation of osteoclast via c-Fos/NFATc1 which inhibits the bone resorption (Zhao et al., 2006). Osteoblasts secret the necessary molecules such as collagen type I and proteoglycans to form a bone matrix and then hydroxylapatite is deposited to form the new bone (Murshed et al., 2005).

Finally, when the bone resorption lacunae was completely filled with the new bone, the remodelling cycle is terminated. So far, the termination signals have not been well-documented. Osteocytes might play an important role in this termination phase (Raggatt & Partridge, 2010).

Table 2.8: Summary of local factors acting on the skeleton (source: Raisz, 1999)



- Cytokines that may cause bone loss: IL-1, TNF,[a] IL-6, IL-11, and ODF
- Cytokines that may prevent bone loss: IL-4, IL-13, IL-18, IFN, OPG, and IL-1ra
- Colony-stimulating factors: M-CSF and GM-CSF
- Prostaglandins, leukotrienes, and nitric oxide
- Growth factors: IGF, TGFβ, FGF, PDGF, and PTHrP

[a] TNF, tumor necrosis factor; ODF, osteoclast differentiation factor; IFN, interferon; M-CSF, macrophage colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; TGFβ, transforming growth factor-β; FGF, fibroblast growth factor; PDGF, platelet-derived growth factor; PTHrP, PTH-related protein.

2.4.2 Cells and molecular mechanisms associated with the bone remodelling

2.4.2.1 Osteoclasts:

During bone remodelling, the osteoclast is mainly responsible for bone resorption. The osteoclastogenesis is regulated by CSF-1 and RANKL (Udagawa et al., 1999) (Table 2.7). RANKL might be produced by T-cells (Roberts et al., 2006), or osteoblasts/stromal cells (Udagawa et al., 1999). OPG is a competitor ligand for RANK, which deactivates osteoclasts, and thus it acts as a negative regulator of bone resorption activity.

Kanzaki et al. (2006) investigated the role of the local RANKL gene in accelerating the tooth movement when this gene was transferred to the PDL of Wistar rats. An inactivated hemagglutinating-virus of Japan envelope vector containing the RANKL was injected to the palatal side of PDL of the first molars being moved palatally. The result showed that the tooth in the experimental side moved significantly faster than the control side. The local RANKL gene transferred stimulated the osteoclastgenesis. Therefore, RANKL might be a potential tool in accelerating tooth movement (Kanzaki et al., 2006).

2.4.2.2 Osteoblasts

Osteoblasts play an essential role in bone remodeling, i.e., expression of factors for suppression of osteoclasticgenesis, secretion necessary protein for bone matrix formation, and bone mineralization (Karsenty, 2008**)**. Osteoblastic cells originate from mesenchymal stem cells. The differentiation of osteoblasts is regulated by a runt-related transcription factor 2 (RUNX2) (Franceschi et al., 2003).

2.4.2.3 Osteocytes

When an osteoblasts is engulfed into the mineralised bone matrix, it is called osteocytes (Bonewald, 2007). Osteocytes communicate with each other, and other osteoblasts on the bone surface by long dendrite-like processes (Kamioka et al., 2001). These cells are believed to be responsible for detecting mechanical strain and micro-fractures within the bone. They also initiate the remodelling process to repair the damage (Verborgt et al., 2002).

2.4.2.4 T-cell and B-cells

The role of T-cells and B-cells in bone remodelling has not been thoroughly investigated. Li et al. (2007) showed a positive correlation between the lack of these cells and osteoporosis. Thus, these immune cells might be involved in the bone homeostasis maintenance. It was reported that B-cell produced a large proportion of OPG which is assumed to play an important role in inhibiting osteoclast formation process. T-cells might cooperate with B-cells in stimulating the OPG production via CD40/CD40L (Li et al., 2007; Raggatt & Partridge, 2010).

2.4.2.5 Megakaryocytes

Megakaryocytes develop from hematopoietic stem cells. It has been suggested that these cells play a role in both bone resorption and bone formation. Lack of factors GATA-1 and NF-E2 (nuclear factor, erythroid derived 2) lead to increase megakaryocytes numbers and bone volume (Kacena et al., 2004). In addition, megakaryocytes stimulate the proliferation, and differentiation of osteoblast, and the expression RANKL and OPG (Lorenzo et al., 2008).

2.4.2.6 Osteomacs

Osteomacs play an important role in the full functional differentiation of osteoblasts and maintaining osteoblasts (Chang et al., 2008).

2.5. Relapse problem and what do we know?

Maintaining teeth in the desired position after orthodontic treatment has been a long term problem for all orthodontists (E. W. King, 1974; Little, 2009; Vaden et al., 1997). Until now, how long a patient should wear a retainer is still an unanswerable question (Johnston & Littlewood, 2015). Most clinicians advise patients to wear the retainer as long as possible.

The extent of relapse is difficult to predict even in well-treated cases. From a well-documented survey comprising 800 cases post treatment at the University of Washington, Little (2009) reported a high percentage of relapse in all types of treated malocclusion over 10 to 20 years post-retention. In extracted cases, only one third of the samples maintained acceptable alignment over 10 years. This ratio reduced continuously to only 10% over 20 years post-retention. For cases treated with either fixed or removable appliance to increase arch length in the mixed dentition, only 11% maintained satisfactory arch width increase over the follow-ups period (Little, 2009).

The instability tendency of orthodontic outcomes comes from intrinsic and extrinsic factors (van Leeuwen et al., 2003). The intrinsic factors result from the alveolar bone and PDL. The extrinsic factors are associated with surrounding tissue, physiological process, and orthodontic treatment. Some authors reported that the arch width and length tend to decrease throughout the human life (Johnston & Littlewood, 2015; Littlewood et al., 2016). Even in untreated patients, arch constriction continues actively after the cessation of growth, and up to 30 years of life (Johnston & Littlewood, 2015; Littlewood et al., 2016). After this age, arch constriction tendency almost stabilises (Johnston & Littlewood, 2015; Littlewood et al., 2016). However, arch constriction tendency varies in patients and cannot be predicted precisely. Additionally, as orthodontic treatment brings the teeth to a new position, it changes the relationship between tooth and surrounding tissues and the balance of that area. The instability of teeth in a new position may be due to the soft tissue pressure, occlusal contacts, limits of dentition, and reorganisation of PDL and gingival fibres. However, how these factors influence the alveolar bone is unclear. Relapse comes from multifactor and it is hard to eliminate it completely (Johnston & Littlewood, 2015; Littlewood et al., 2016).

Whatever the aetiology of relapse, bone remodelling might play an important part in the relative stability of teeth in the new position. Regarding to anatomy, teeth are housed in alveolar bone with a thin layer of PDL between them. When a tooth moves, bone resorbs on the pressure side and apposes on the opposite side (van Leeuwen et al., 2003). After active treatment, the teeth must be retained by some types of retention appliances for a prolonged period, which is long enough for bone to model and remodel to the normal mineralisation level. How much is the minimum amount of bone quality value to retain the teeth in new position partly and completely? How long does it need for the bone quality return to the normal level? Although most of procedures require patients to wear retainer for 6 months full time and next 6 months night time, there is insufficient information on the necessary time for bone modelling and remodelling currently.

From 1959, Köle believed that cortical bone interfered with movement of teeth. By performing corticotomies, the resistance of the cortical bone would be reduced and teeth would move faster to a new position. Moreover, the regional acceleratory phenomenon (RAP) resulting from corticotomies might increase the bone turnover and consolidate the bone around the roots (Kole, 1959). Following this, Wilcko and co-workers who hypothesised that the PAOO technique may enhance stability post treatment (Einy et al., 2011; Wilcko et al., 2008; Wilcko et al., 2009). However, how the corticotomy affected the stability of the orthodontic treatment outcomes is still unknown, but it might be a potential modality to overcome the current relapse problem.

2.6. Computed tomography (CT) and cone beam computed tomography (CBCT)

Imaging technologies have progressed over the last ten decades. These advances provide a powerful tool for diagnostic and clinical research in dentistry.

Initial two dimensional conventional radiographs such as periapical, bitewing, and occlusal radiograph are the backbone of imaging in dentistry. Periapical radiographs are routinely clinically indicated for examining in detail the teeth and surrounding tissues such as root canal morphology, periodontal status, crown and root fractures, and periapical abnormalities. Bitewing provides information of interproximal surfaces simultaneously which is useful in detecting interproximal caries. Occlusal radiographs are taken to evaluate a larger portion of dentition or abnormalities such as cyst, supernumerary and foreign bodies (Shah et al., 2014; Vandenberghe et al., 2010).

Panoramic radiographs image the entire maxilla and mandible using a specialized tomographic technique and usually indicated as a screening film. The disadvantages of panoramic radiographs include superimposition, unequal geometric magnification and image distortion (Shah et al., 2014; Vandenberghe et al., 2010). Overall, these radiographs are only able to provide images in a two dimensional plane. Three dimensional (3D) imaging techniques are helpful in providing accurate information for complex cases (Shah et al., 2014; Vandenberghe et al., 2010). Thus, the demand of 3D imaging technology is necessary and imminent to the development of imaging diagnosis in dentistry especially for implant diagnosis and planning, as well as in orthognathic planning, location of impacted teeth (Shah et al., 2014; Vandenberghe et al., 2010).

Computed tomography has evolved along with advancements in computer science. In 1963, Cormack- a South Africa physicist- was the pioneer applied reconstructive tomography into medicine (Boerckel et al., 2014; Shah et al., 2014). In 1972, Hounsfield made a breakthrough by successfully inventing the first computed tomography (CT) with a British firm EMI Ltd (Boerckel et al., 2014; Shah et al., 2014). This discovery was immediately acclaimed by the medical community and has become the crucial tools in diagnostic radiology. Housefield and Cormack both went on to receive Nobel Prize in 1979 for their contribution in Medicine (Boerckel et al., 2014; Shah et al., 2014).

A CT scanner unit comprises of an X-ray tube head, a series of detectors and a bed for the patient to lie on inside the gantry. The tube head and its detectors may either rotate around the patient simultaneously or stay stationary while the radiographic tube moves following the orbit of the detector ring (Shah et al., 2014).

Until now, there are four generations of CT scan machine. The first generation by Hounsfield used one detector and a pencil shaped beam. The second generation which was introduced in 1975 use multiple detectors and a small fan shaped beam (Shah et al., 2014). These detectors rotate around the patients. The third generation scanner was launched in 1976 and has been widely used until today. The detector of this machine was large enough to acquire an image of the whole object without translation around the object. In the fourth generation, the detectors form a whole circle around the patient's table which allows the detectors to stay stationary while the radiographic tube rotates following the detector ring. This generation is expensive and disperses high radiation so it is not common in practice today (Shah et al., 2014).

CBCT system was introduced in dentistry in 1990s (Shah et al., 2014). Compared to CT scanner systems in medicine, dental CBCT machines are less bulky. This system produces a cone-shaped or pyramid shaped radiologic beam. The detector rotates around the patient's head and a series of two dimensional images were taken. Then, the 3D images are reconstructed from the two dimensional images based on an algorithm. The advantages of CBCT are fast scanning, shorter processing time, considerably lower radiation dose (compared to other CT scan systems), lower cost and capability to produce three dimensional images at high resolution (Shah et al., 2014). With these advantages, CBCT becomes a powerful tool not only for diagnostic purposes but also for clinical research in all fields of dentistry (Shah et al., 2014).

CBCT has been widely used in dentistry. High resolution and 3D visualization allow clinicians to examine, locate and evaluate the extension of disease, anomalies and injuries precisely. Recently, CBCT is most common used prior to implant surgery to evaluate bone quality including bone density and bone microstructure. In orthodontics, CBCT offers a 3D view of the whole dentition which facilitates the clinicians to examine and carry out measurements on the relation of upper and lower arch, the disturbance in eruption of teeth, teeth's roots angulation and skeletal abnormalities. In comparison to conventional radiographs, CBCT image is relatively free of distortion. Thus, the size and shape of an object can be measured and evaluated precisely. Recently, CBCT scan is used to evaluate root resorption before and after orthodontic treatment. However, it is not a routine practice to take pre and post-orthodontic CBCT scan. Together with various third party software, outcomes from various interventions can be predicted and planned; analyzed and presented to the patients (Horner, 2013; Shah et al., 2014).

The resolution of CBCT image is dependent on the scan setting selection such as the size of field of view (FOV) and voxel size. Smaller FOV produces better image resolution and lowers the radiation dose and vice versa. The size for large FOV ranges from 15-23 cm, medium FOV from 10-15 cm and small FOV is less than 10 cm (Horner, 2013; Shah et al., 2014; Vandenberghe et al., 2010). A small FOV is indicated for acquiring detail information while large FOV provides the overview of large areas. Metal objects such as jewelry, dentures, metal crown and filling may cause artifacts and influence the quality of images. Other parameters such as expose time, rotation arc, and dose of exposure also affect the image quality. Also maintaining patient still is important, or otherwise have “motion” artifacts (Horner, 2013; Shah et al., 2014; Vandenberghe et al., 2010).

In veterinary, Fidex CBCT scanner (Animage, LLC, Pleasanton, CA, US) has recently been introduced into animal research laboratories and veterinary clinics. It adopts all the newest advancement of computed tomography technology, thus facilitates researchers to replicate a similar process used in human. Now imaging research related to animals can be carried out with high quality and less distorted images. Pre- and post- treatment images can be preserved, retrieved and superimposed for comparison using modern imaging analysis software such as Mimics (Materialized, Leuven, Belgium).

2.7. Micro computed tomography (μCT or microCT)

The first CT systems could only render 2D reconstructions and the resolution of these systems was low. Thus, accurate assessment of bone microstructure was almost impossible to be achieved. In the 1980s, Lee Feldkamp from Ford Motor Company developed the first microCT machine based on the concepts of cone-beam x-ray source (Boerckel et al., 2014; Ritman, 2004). MicroCT comprises an x-ray tube, radiation filter, specimen stand, collimator and a camera. The X-ray beam geometry is a fan or cone-beam shape. Reconstruction of a 3D image is based on the collection of a series of 2D scan by rotating either the samples or the detectors around the samples in 180° or 360°. The voxel size of microCT can approach up to 1 μm which makes this system a superior resolution system than any other imaging techniques. The first scanned was performed at Henry Ford Hospital in the US using a small sample of a bone tissue from an iliac crest (Boerckel et al., 2014; Ritman, 2004). Since then, more microCT research have been carried out to study the bone microstructure (Boerckel et al., 2014; Ritman, 2004).

Currently, microCT has been widely used for clinical and bone research to evaluate osteoporosis, bone metabolism and in the gene-engineering field. As a non-destructive imaging analysis tool, microCT can acquire the results faster and less costly than the histomorphormetric approach. In addition, the 3D images of the structure provides thorough information on trabecular number, thickness, connectivity, orientation, total bone volume as well as bone density. Some authors demonstrated that measurement of bone parameters attained using microCT were not different from those by conventional 2D histomorphometry which has been used as a gold standard in this field (Genant & Jiang, 2006; Lespessailles et al., 2006). As a result, microCT has emerged its role as a gold standard tool for *ex-vivo* evaluation and quantitation of bone microstructure (Yip et al., 2004).

2.8 Animal studies about maxillary expansion

Various animals have been used in maxillary expansion research such as monkeys, rats, rabbits, cats, dogs, pigs, and sheep (Feng et al., 2014; Zhao et al., 2015; Ozan et al., 2015; Kara et al., 2011; Altan et al., 2013; Erdogan et al., 2015; Liu et al., 2014; Li et al., 2012; Romanyk et al., 2013; Parr et al., 1997; Brin et al., 1981; Vardimon et al., 2005; Santiago et al., 2012; Tong et al., 2017; Kretschmer et al., 2010; Sun et al., 2011; Hoffer & Walters, 1975; Vardimon et al., 1989; Murray & Cleall, 1971; Cleall et al., 1965; Cotton, 1978) (Table 2.9). The first studies on maxillary expansion were carried out in monkeys, i.e., *Macaca mulatta* and *Rhesus*. It was due to the common belief that there was close approximation of human morphology to monkey, and this would allow the best interpretation and application of the findings back to the human beings (Cleall et al., 1965; Cotton, 1978; Hoffer & Walters, 1975; Murray & Cleall, 1971; Vardimon et al., 1989). The maxillary expanders used in these studies were similar to those used in humans.

However, it was demonstrated that the midpalatal suture in monkey was distinctly different to that of human. The monkey has a separate premaxilla, which discontinues from the midline suture in the anterior part of the palate. The connections between the premaxilla and maxilla and two maxillary halves form a Y-shape suture (Cotton, 1978; Hoffer & Walters, 1975; Murray & Cleall, 1971; Vardimon et al., 1989) (Figure 2.21). Research in rodents such as mice, rats, and rabbits, helical springs have been used to separate the midpalatal suture (Altan et al., 2013; Erdogan et al., 2015; Feng et al., 2014; Kara et al., 2012; Liu et al., 2014; Özan et al., 2015; Zhao et al., 2015). Helical spring has not been used for maxillary expansion in human adults as it is unable to expand the tightly interdigitated maxillary suture (Romanyk et al., 2010). Except in monkeys, the palatal expander with jackscrew were only observed in the studies using larger animals such as cats, dogs and sheep (Brin et al., 1981; Vardimon et al. 2005; Kretschmer et al., 2010; Santiago et al., 2012; Tong et al., 2017; Vardimon et al., 1989). Among these large animals, sheep has been used successfully in research involving maxillary osteotomies and maxillary distraction osteogenesis (Kretschmer et al., 2010; Krawczyk et al., 2007; Rachmiel et al., 2002; Rachmiel et al., 2007). Similar to humans, the midpalatal suture in sheep is also at the center of the palate from anterior to posterior. In addition, it is difficult to standardize the experimental sample in breeds and quantity if using cats and dogs as it has to depend on the local availability (Santiago et al., 2012). Moreover, Dorper sheep is strong, highly adaptable to harsh environment and have a longer breeding season, therefore, it is easy to find suppliers for commercial stocks.

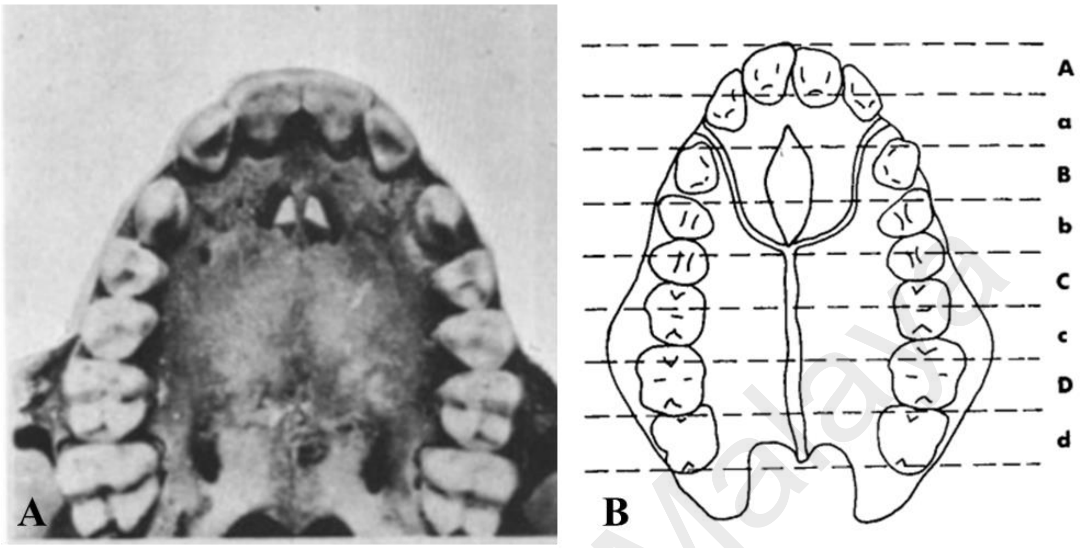


Figure 2.21: The feature of midline palatal suture in monkey.
A, the midline suture in monkey has the Y-shaped because the premaxilla is separated; B, schematic illustration of the midline suture in monkey (source: Murray & Cleall, 1971).

Table 2.9: Summary of animal studies on maxillary expansion (1/3)

Study	Animal used	Age, sex	Protocol of activation	Type of appliance
Feng et al. 2014	Sprague-Dawley rats	6 weeks old male rats	130-150 gr force, 5 days expansion	Helical spring from 0.018 inch SS wire inserted into the spaces between the 1st and 2nd molars.
Zhao et al. 2015	Wistar rats	6 weeks old male rats	0.98 N, 10 days expansion	Helical spring from 0.014 inch SS wire inserted into the spaces between the 1st and 2nd molars.
Ozan et al. 2015	Wistar albino rats	12 weeks male rats	30 gr force, 5 days expansion and 12 days retention.	Helical spring from 0.012-inch SS wire placed at maxillary incisors
Kara et al. 2011	Wistar albino rat	12 weeks male rats	30 gr force, 5 days expansion and 12 days retention.	Helical spring from 0.012-inch SS wire placed at maxillary incisors
Altan et al. 2013	Wistar albino rat	12 weeks male rats	30 gr force, 5 days expansion and 12 days retention.	Helical spring from 0.012-inch SS wire placed at maxillary incisors
Erdogan et al. 2015	Wistar albino rat	12 weeks male rats	30 gr force, 5 days expansion + 12 days consolidation	Helical spring from 0.012-inch SS wire placed at maxillary incisors
Liu et al. 2014	C57BL/6 mice	6 weeks male mice	70 gr force, 5 days expansion + 7-14 days consolidation	Custom manufactured NiTi wire spring bonded to the 1st and 2nd maxillary molars
Li et al. 2012	New Zealand white rabbits	12-13 weeks old	0, 10, 20 gr force, 5 days expansion with 2 turns/day in 10 days, retention 10 days.	An acrylic bonded device
Romanyk et al. 2013	New Zealand White rabbits.	12-13 weeks old.	Force: 50 gr, 100gr, 200gr, active expansion in 6 weeks.	Sentalloy® coil spring

Table 2.9: Summary of animal studies on maxillary expansion (2/3)

Study	Animal used	Age, sex	Protocol of activation	Type of appliance
Parr et al 1997	New Zealand White rabbits	Not stated	1 N-3 N force	Implant supported expander with open coil spring between two abutments, placed at the midface region.
Brin et al. 1981	Female cats	10-12 months (Group 1) and 36-48 months (Group 2).	A quarter turn once daily for 7 days and 2 quarter turn daily after 7th day for 0, 19 and 15 days	Expansion includes 14 mm jack screw embedded in acrylic plate with 0.9 mm SS retentive clasp
Vardimon et al. 2005	Inbred cats	1 year old adult male cat.	25 days with full turn screw (0.8 mm) every 3-4 day, and 60 days retention.	Bonded expander with jack screw
Santiago et al. 2012	Dogs (Canis Lupus familiaris)	6 months age dogs obtained from veterinary centre according to local availability, convenient sample.	Protocol: first 3 days: 2 quarter turns in morning and 2 quarter turns in the afternoon. Next 4 days, reduced to 1 quarter turn in morning and afternoon. 7 days of expansion.	Tooth borne hyrax type attached to 1st, 2nd and 3rd premolars
Tong et al. 2017	Beagle dogs	6 months male dogs	Activation in 4 weeks to achieve 6 mm.	The magnetic palatal expansion appliance and jackscrew expander.
Kretschmer et al. 2010	Adult sheep	Adult sheep	Hyrax appliance was turned to 4mm, 8 mm, 12 mm.	Le Fort I osteotomies + maxillary expansion with Hyrax screw

Table 2.9: Summary of animal studies on maxillary expansion (3/3)

Study	Animal used	Age, sex	Protocol of activation	Type of appliance
Sun et al. 2011	Domestic pig heads (*Sus scrofa*)	3-6 months (Heads obtained from Ohio state university laboratory animal resources and commercially from the Herman Falter packing Columbus)	Not stated	Jacksrew appliance
Hoffer et al. 1975	*Macaca mulatta* monkey	Females, 25 to 37 months determined by the method of Hurme	Activation to 6 mm. Initially activated by 7 turns with 6 additional turns each week for 3 weeks.	Jackscrew expander
Vardimon et al. 1989	*Macaca mulatta* monkey	3-3.5 years old	258 g - 360 g force	A tooth–borne acrylic plate appliance bonded directly to the canine to the 1st molar; indirect magnets and direct magnets appliances.
Murray et al. 1970	*Rhesus* monkeys	40 months female monkeys	Three quarter turns in the 1st activation, a quarter turn everyday thereafter for 1, 4, 7 and 14 days	Jackscrew appliance
Cleall et al. 1965	Macacus rhesus monkeys	30-40 months female monkeys	2 mm at 4 weeks interval for 12 weeks to achieve 6 mm of expansion	Jackscrew appliance
Cotton 1978	*Rhesus* monkeys (Macaca mulatta)	26-44 months male monkey	Not stated	Open coil spring expander

In summary, neither nonsurgical nor surgical approach is the most suitable modality for treating transverse maxillary deficiency in adults. Nonsurgical approach might expand the narrow maxilla up to 5 mm or may be more in certain patients. However, the skeletal effects was reported very less which raises the concern on buccal alveolar fenestration or failed orthopedic expansion. Currently, transverse discrepancy beyond 5 mm, SARME is more preferable. SARME is able to produce greater amount of skeletal expansion but it is accompanied with unwanted iatrogenic effects. In addition, the difficulty in widening the maxilla might derive from the increasing rigidity of the facial complex. Interestingly, corticotomy has showed to be able to break the rigidity of cortical bone clinically. Therefore, it might be the potential alternative treatment option for adult with transverse maxillary deficiency. In addition, other benefits of corticotomy are accelerating the tooth movement, increasing the bone turnover, less invasive and potential of increasing stability of orthodontic outcomes.

CHAPTER 3: MATERIALS AND METHODS

3.1 Experimental subjects and research design

This study was performed on adult Dorper male sheep with the age ranging from 20 to 48 months and the body weight from 50 to 60 kg. The experiment was carried out at the Animal Experimental Unit, Faculty of Veterinary Medicine, University Putra Malaysia (UPM), Malaysia. The protocol of this study was submitted and approved by the Institutional Animal Care and Use Committee (IACUC), UPM (No. UPM/IACUC/AUP-R031). Sheep were selected following these inclusion criteria:

(1) Good general health without any noticeable disease.
(2) Eruption of all six maxillary premolars.
(3) Absence of periodontal disease.
(4) Absence of any other intraoral infection.

Studies on animals have to follow the “3R” (reduction, replacement and refinement) rule which minimizes the number of animals used for experiments. According to Mead and co-workers, the sample size of the studies on animals should be calculated based on the following formula (Charan & Kantharia, 2013):

E = total number of animals – total number of groups

The sample is considered as adequate when E is between 10 and 20. If E is less than 10, the sample is small. If E is more than 20, sample is considered large and redundant (Charan & Kantharia, 2013). Our study included 18 sheep which were divided into 3 groups. As the result of E was 15, our sample size was sufficient. In the later analysis, every group was divided into 2 subgroups which made in total 6 subgroups. The result of E at this time was 12, our sample size was still adequate.

The codes on the ear tags of sheep, which were marked by suppliers, were recorded into a notebook. A research assistant flipped two identical coins to divide sheep into three groups. There were three possible outcomes of flipping two coins: two heads up where sheep were assigned into Group 1, two tails up where sheep were coded as Group 2, and one head and one tail up where sheep were allocated into Group 3. The coins were flipped until getting 6 sheep per group. The limitation of this simple randomization is that it could result in an unequal number of subjects among group and would take time to generate a randomization list. Our study included 18 sheep randomly divided into three groups as following (Figure 3.1):

- Group 1 (ABPC + RME, n = 6), where sheep were treated with adjunctive buccal and palatal corticotomy (ABPC) and followed by rapid maxillary expansion (RME).
- Group 2 (conventional RME, n = 6), where sheep were only treated with conventional RME;
- Group 3 (control, n = 6), where sheep received no treatment.

All sheep were kept in a raising wooden-floor pen one month prior to the procedure for acclimatization. They were fed daily with custom-formulated feed of commercial pellets and grass at the ratio 1:1 w/w, mineral salt lick and pipe water. In Group 1 and 2, the palatal expanders were activated to 8 mm (Figure 3.2). After the activation phase, self-cured acrylic was poured around two ends of the screw to prevent the screw from turning back. All appliances were still maintained on teeth for another 4 weeks or 12 weeks for retention. Then, in every group, three sheep were sacrificed at 4-week retention and the other three sheep were sacrificed at 12-week retention and processed to CBCT scan, microCT scan and histology procedure (Figure 3.1).

In literature review, retention protocols were reported from 8 weeks to 6 months (Bell et al.,1981; Cozzani et al., 2007; Godoy et al., 2011; Petren et al., 2011). Choosing longer retention period might affect sheep welfare. Moreover, it is more difficult to protect the expanders from being broken under strong chewing force of sheep. Therefore, 4- and 12-week retention periods were suitable for this experiments as these periods were not too long as well as too close to the activation phase, but would still reflect the bone quality changes during retention periods.

Figure 3.1 showed the flowchart of this study. CBCT scan was used to evaluate objective 1, 2; microCT for objectives 3, 4; and histology for objectives 3, 5, 6.

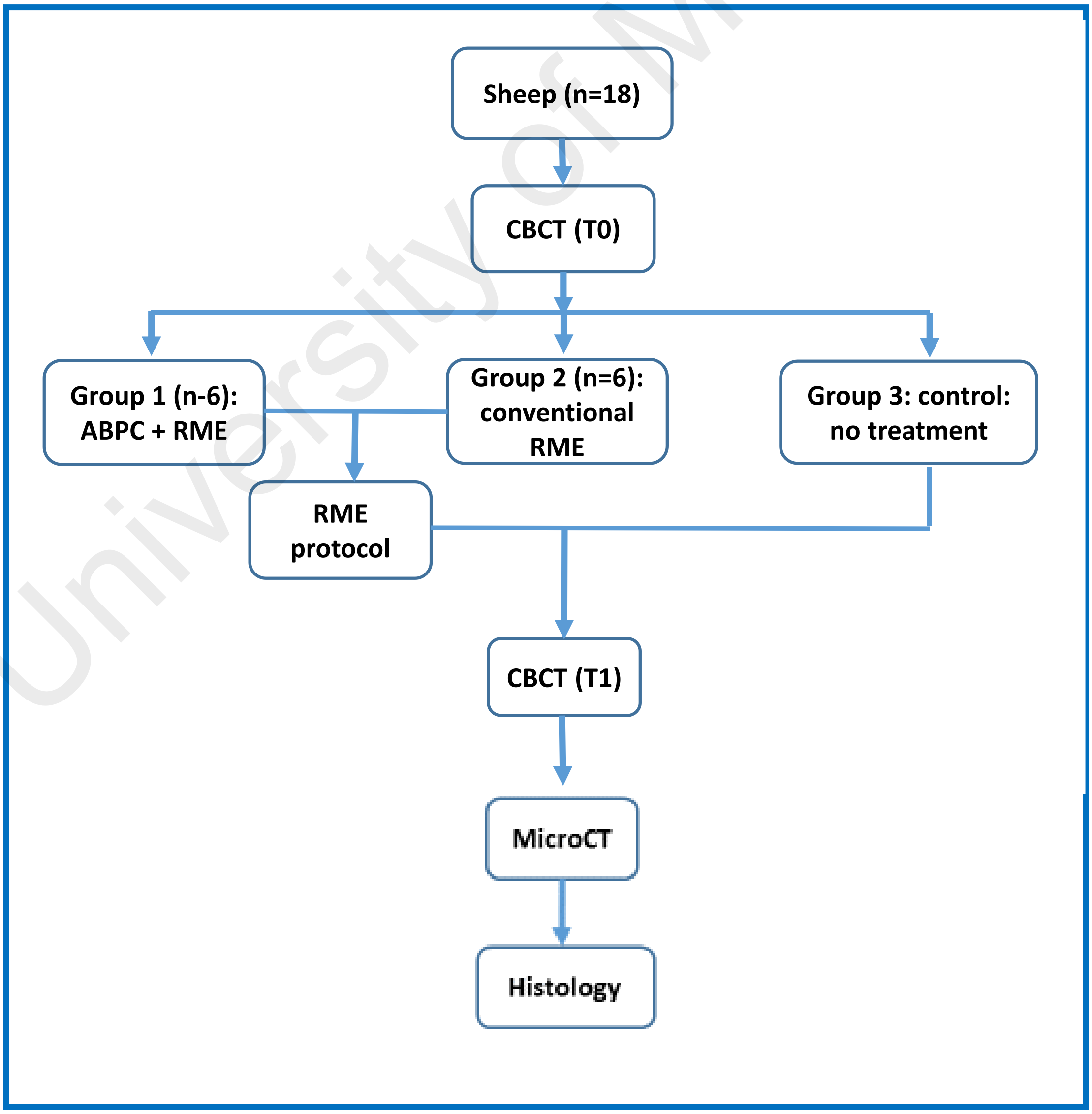


Figure 3.1. Flow chart of the research framework

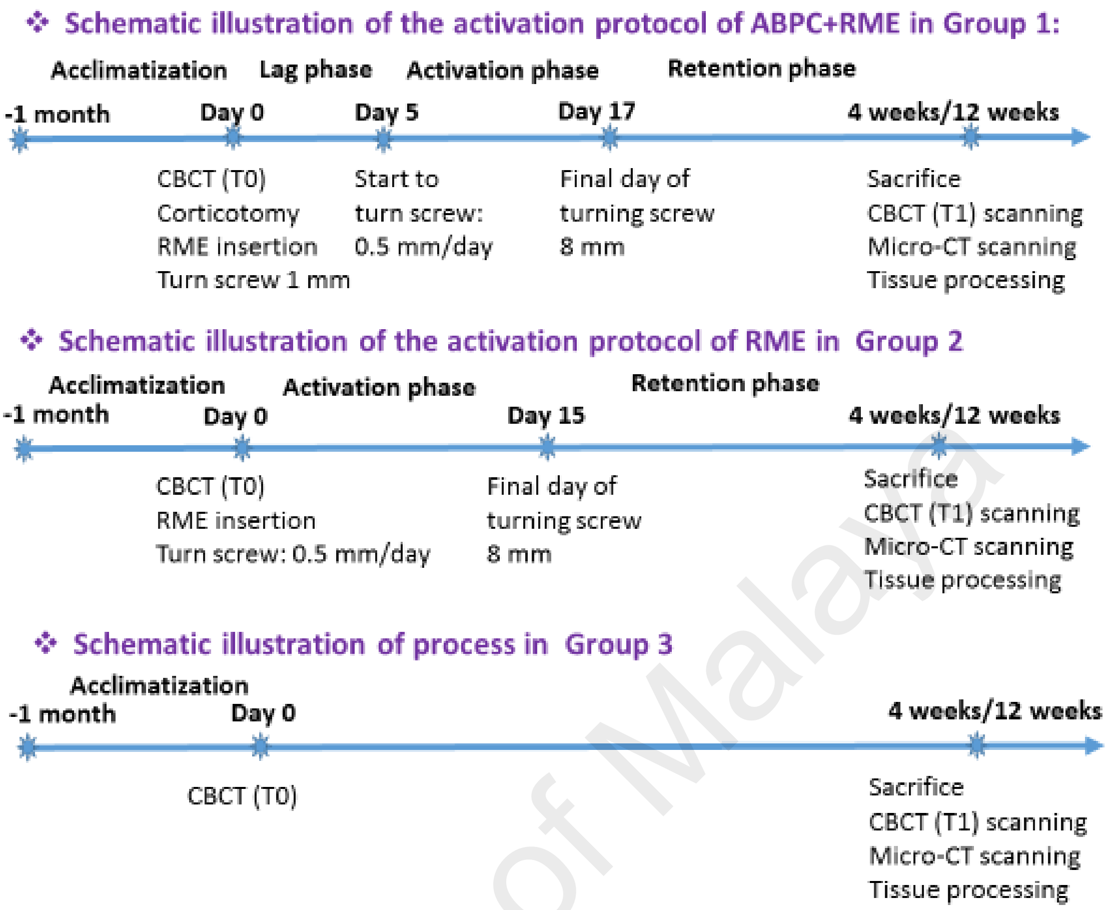


Figure 3.2: Schematic illustration of the activation protocol in Group 1 (ABPC + RME) and Group 2 (conventional RME) and Group 3 (control).

All procedures involving cone beam computed tomography (CBCT) scan, appliance fixation and corticotomy surgery were performed under general anesthesia. The sheep were made to fast 24 hours before anesthesia induction to minimize the risk of regurgitation. Anesthesia was induced with intravenous ketamine at the dose of 7mg/kg (Narketan® 10, Vetoquinol, Buckingham, UK) and Diazepam at the dose of 0.6 mg/kg (Diapine, Atlantic Laboratories Ltd, Bangkok, Thailand). Following endotracheal intubation, anesthesia was maintained with 2% to 3% isoflurane in 100% oxygen. Following corticotomy surgery, the animals were injected with one dose of intramuscular antibiotics and analgesics to prevent infection and make animals comfortable. Antibiotics were given in the following 7-10 days to prevent any infection or periodontal disease.

Intramuscular vitamin C and vitamin B were also administered daily to stimulate apatite formation and strengthen sheep's natural defense.

3.2 Hyrax-appliance design:

RME was performed using a Hyrax appliance comprising a 16-mm Super -Screw® (Great Lakes Orthodontics, Tonawanda, New York, USA) soldered on two bands placed on the first premolars and two bands placed on the third premolars. The Super-Screw® was positioned perpendicular to the midpalatal suture in the region of the second premolars. The expander fabrication procedure was similar to that in human. Sheep was anesthetized. Subsequently, bands were tried and impression was taken with customised trays and irreversible hydrocolloid impression material (Aroma fine plus, GC Corporation, Tokyo, Japan). The taken impressions were sent to orthodontic laboratory for reproduction working casts or models. On these models, customised expander for each sheep was fabricated. All appliances were fabricated by one experienced technician. The Hyrax appliance were cemented using glass ionomer luting cement (Ketac™ Cem Easymix; 3M Deutschland GmbH, Neuss, Germany) (Figure 3.3). This glass ionomer luting cement has been used popular in orthodontics.

In activation phase, the screw was turned with a screwdriver provided by supplier. The sheep mouth was kept opening with a customised plastic cylinder and the screw was turned 0.5 mm/day according to the manufacturer instructions.

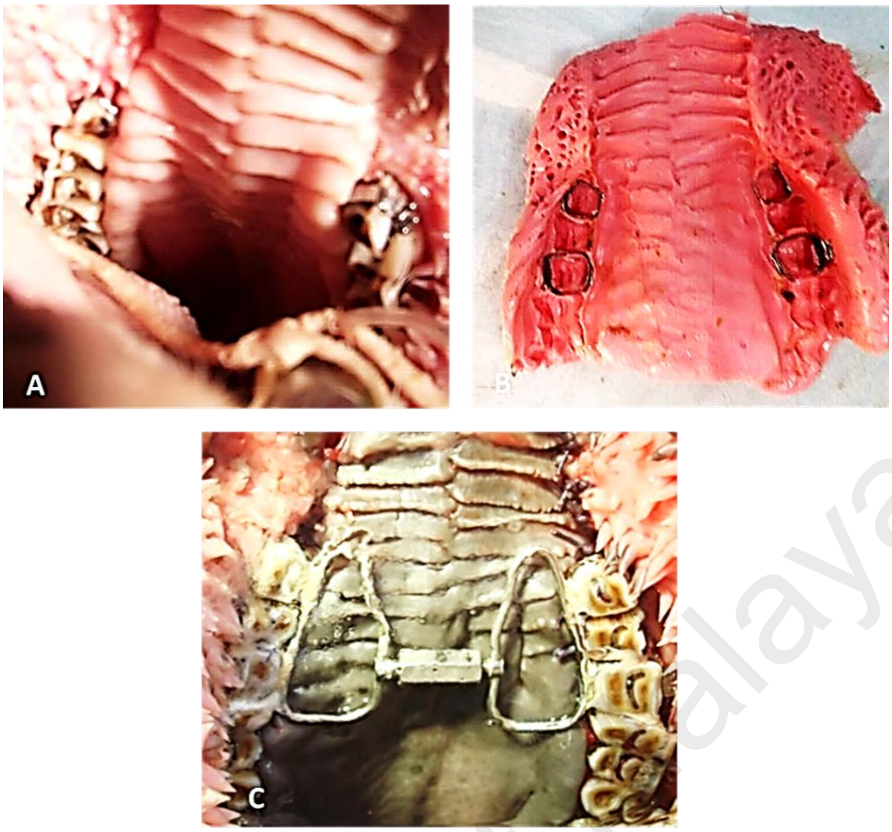


Figure 3.3: Clinical procedures for Hyrax expander fabrication.
A: trying bands, B: taking impression, C: cemented Hyrax.

3.3 Corticotomy protocol and activation protocol:

All sheep in ABPC + RME group underwent corticotomy involving the maxillary premolar segments. The buccal and palatal mucosa were infiltrated with lidocaine HCl 2% with epinephrine 1:100,000 (Lignospan, Septodont, Saint-Maur-des-Fossés, France). Bilateral cervicular mucoperiosteal incisions were made buccally and palatally along the gingival sulcus from the mesial of the first premolar to the mesial of the first molar, with the horizontal releasing incision at the mesial of the first premolar. A full thickness flap was raised using a periosteal elevator to expose the alveolar bone. A 2-mm diameter round bur was used to perform decortication up to a depth of 2 to 2.5 mm, which is the average thickness of cortical alveolar bone in sheep. On the buccal aspect, a vertical cut was made 5 mm from the mesial alveolar crest of the first premolar; extending upwards parallel to the axis of the first premolar. A second cut was made horizontally 2 to 5 mm above the premolars roots, and downward between the third premolar and first molar roots to the distal crest of the third premolar (Figure 3.4A). The vertical cuts on the palatal aspect were similar to those on the buccal aspect, with the horizontal lines placed approximately 5 mm from the cervical regions of the teeth (Figure 3.4B). The bone was cut under copious saline irrigation. The flaps were sutured using absorbable suture material (PDS™ Plus, 3-0, Ethicon, Sommerville, NJ, USA). Immediately after surgery, the hyrax appliance was cemented and the screw was turned 1 mm, followed a popular chosen protocol reported in literature review (Suri et al., 2008). After 5-days lag, the screw was turned by 0.5 mm/day for 14 days consecutively in order to achieve 8 mm of arch expansion. The appliance was removed at 4- week or 12- week retention followed by CBCT scans (Figure 3.1).

When an incision is placed on the bone, RAP occurs within a few days and accelerates the bone turnover. However, RAP also causes bone demineralisation (Ferguson & Wilcko, 2016). In our study, the expansion screw was only turned 1 mm immediately after surgery and no further turns until day 5 to take the advantage of demineralisation produced by RAP. After 5-days lag, the screw was continued to turn again at the rate of 0.5 mm/day (Figure 3.2).

It was reported that the bone healing process after injury includes two phases, i.e., woven bone formation and transformation of woven bone into lamellar bone. Woven bone started to form within a few days after injury and reached its peak of thickness at day 7. After day 7, the woven bone at the cortical area was remodelled to lamellar bone which resulted in the increase of bone strength (Ferguson & Wilcko, 2016). Thus, ceasing turning the expansion screw for 5 days was suitable because it could take the advantage of demineralisation produced by RAP but avoided the disadvantage of increasing bone strength.

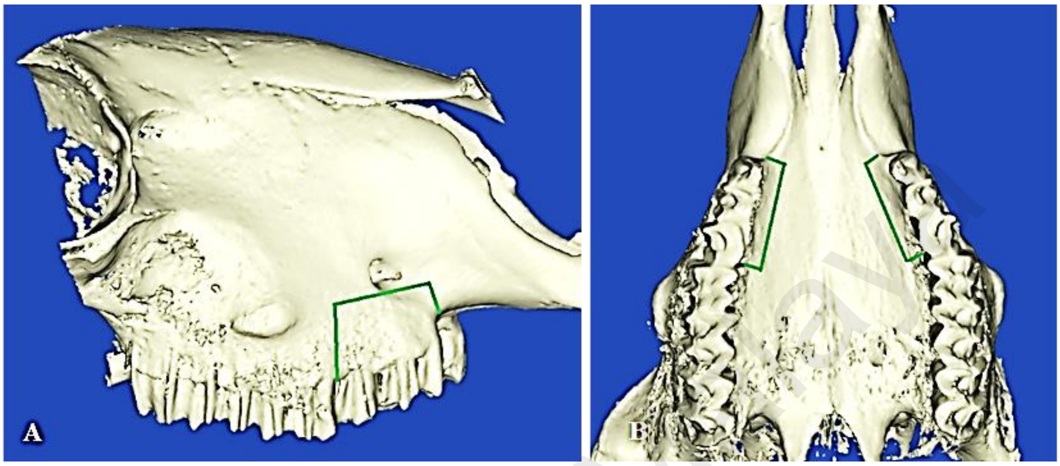


Figure 3.4: The corticotomy incisions.
Buccal view showing the corticotomy incisions from mesial of first premolar to distal of third premolar (A); Occlusal view showing the palatal aspect of the corticotomy incisions (B).

3.4 Conventional RME protocol

The expander were cemented in appropriate place for all sheep in Group 2 after CBCT scanning. Subsequently, the screws were turned at the rate of 0.5 mm/day at day 0 until achieving 8 mm of turning screw. The appliances were kept in place for 4 weeks or 12 weeks. Then, all sheep were sacrificed, and processed to CBCT scan the second time, microCT protocol and histology protocol (Figure 3.2).

3.5 CBCT scanning protocol

Cone beam computed tomography scans (CBCT) were performed using a CBCT machine (Fidex, Animage LLS, Pleasanton, CA, USA) with a voxel size of 0.3 mm, 110 kV energy and 0.15 mAs scanning time. The sheep were positioned with the anterior-posterior head's axis paralleled to the centre of the table. The scans were made before treatment (T0) and at 4-week or 12-week retention (T1).

Before performing any measurements, the transverse plane of all CT images was rotated to make it parallel to the palatal plane; the sagittal plane along the palatal suture and the nasal septum and coronal plane perpendicular to the nasal septum (Figure 3.5).

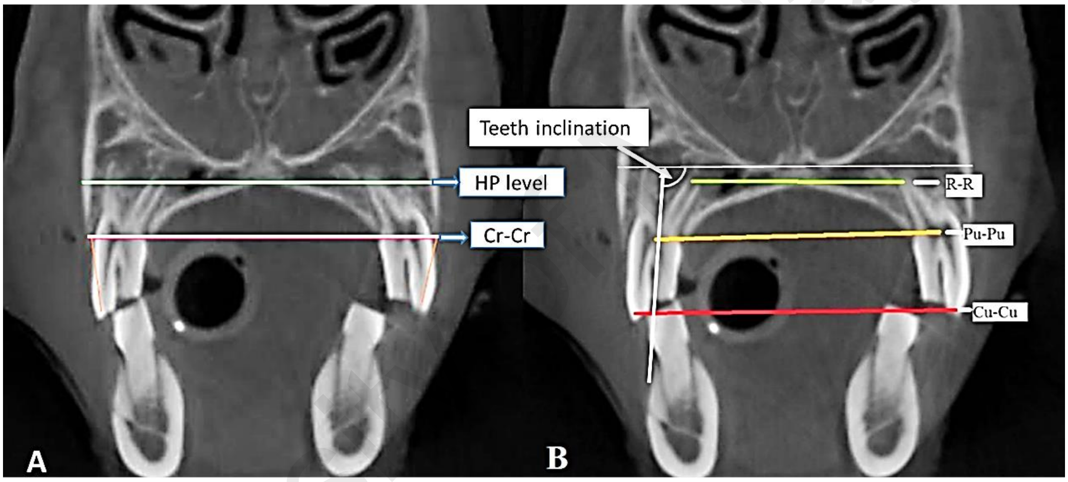


Figure 3.5: Measurements performed on cone-beam computed tomography (CBCT) images.
For skeletal changes (A): transverse alveolar width at alveolar crest level (Cr-Cr) and at hard palate level (HP level); For dental changes (B): tooth displacement at buccal cusp tip level (Cu-Cu), at central pulp level (Pu-Pu) and root apex level (R-R); and teeth inclination changes .

Linear and angle measurements, as defined in Table 3.1, were acquired using Fidex software (Fidex, Animage LLS, US). Skeletal changes were evaluated at the crest level (Cr-Cr) and hard palatal level (HP level). Dental changes were measured at the cusp level (Cu-Cu), centre of pulp chamber level (Pu-Pu) and lingual root apex level (R-R) (Figure 3.5).

Table 3.1: Definition of measurements on cone-beam computed tomography (CBCT) images.

Variables	Definitions	Measurements
Cr-Cr P1/P2/P3	Distance between the most occlusal point of the buccal alveolar crests of the left and right first premolars (P1), second premolars (P2), third premolar (P3).	Dental arch width at the alveolar crest level of premolars in coronal plane.
HP level P1/P2/P3	Distance between the intersections of a line tangent to the most inferior of hard palate (HP) and to the buccal alveolar cortex of left and right premolars.	Dental arch width at the hard palatal level of premolars in coronal plane.
Cu-Cu P1/P2/P3	Distance between buccal cusp tips of right and left maxillary premolars.	Tooth displacement in coronal plane at the cusp level.
Pu-Pu P1/P2/P3	Distance between the centre of pulp chambers of left and right premolars.	Tooth displacement at centre pulp level in coronal plane.
R-R P1/P2/P3	Distance between the lingual root apex of left and right premolars.	Root apex displacement in coronal plane.
Teeth inclination P1/P2/P3	The angle between teeth axis of premolars and nasal plane (the plane tangent to the nasal floor).	Changes of teeth axis to the nasal plane in coronal plane.

To observe the 3D dental and skeletal changes, Mimics software version 19.0 (Materialise NV, Leuven, Belgium) was used to superimpose the pre-treatment and post-retention images. The stack of images were loaded into Mimics software, then the segmentation process was used to create the 3D model for every maxilla. Segmentation process included thresholding, region growing, dynamic region growing, 3D calculating and editing to capture only the maxilla. The obtained 3D imgage was saved into STL format. Subsequently, two obtained STL images of pre-treatment and post-retention maxilla were loaded into Mimics software and rotated and superimposed so that the nose, palate and the skull were seen most simultaneously.

All animals were sacrificed using Dolethal (Pentobarbitone, Vetoquinol S.A France) injected at the cephalic vein. After CBCT scanning, the upper jaws of sheep (from the mesial of the first premolar to the mesial of the second molar segment) were separated by a sharp saw. All soft tissues were removed using a scalpel and surgical scissors. Only the bone and teeth were preserved. The obtained anatomic pieces were cleaned under running water and stored in 4% paraformaldehyde solution (1:10 volumes) for one month. Then, the samples were processed for micro-CT scanning and histology.

3.6 MicroCT scanning protocol

The three dimensional changes of bone microstructure were assessed using microCT. All sheep's maxillary samples were covered with Parafilm and scanned using Skyscan 1176 microtomography scanner (Skyscan NV., Kontich, Belgium). The purpose of covering the samples with Parafilm was to prevent dehydration during the long scanning duration. MicroCT scanning was performed using a resolution of 18 µm, 90 kV, 278 µA, 0.5 mm Aluminum filter and 360 degree rotation range.

All acquired images were reconstructed using NRecon software (NRecon, version 1.6.10.4, Skyscan, Belgium) with a Gaussian smoothing of 3, beam hardening correction of 40%, ring artefact reduction of 12. DataViewer (DataViewer version 1.5.2.4 64-bit, Skyscan, Belgium) was used to reorient the direction of reconstructed images to the sagittal plane. Subsequently, all images were imported into CTAn software (CT Analyser version 1.15.4.0+, Skyscan, Belgium) for bone microstructural analysis.

Each group comprised of 6 sheep in which 3 sheep were sacrificed at 4- week retention and the other 3 sheep were sacrificed at 12 week retention. As the left and right buccal segments were pooled together, in total 36 samples were collected; every group had 6 samples taken at 4- week retention and 6 samples taken at 12- week retention.

3.6.1 Change in buccal alveolar bone thickness at 4- and 12-week retention

The buccal alveolar bone thickness was measured on microCT images. To measure the buccal alveolar thickness, a point located 4 mm inferior the furcation area was determined. The centre of resistance of a tooth is at approximately midpoint of the embedded root in the alveolar (Proffit et al., 2007). Therefore, a point 4 mm inferior the furcation was close to the centre of resistance and did not depend on the alveolar height. In addition, this point was easy to locate when measurements were repeated. A line going through this point and perpendicular to the tooth axis was drawn. The measurement was performed from the most buccal point of the buccal cortical bone to the most inner point of the cancellous bone on this line and used as the buccal alveolar bone thickness (Figure 3.6). The measurements were carried out at three points (mesial, middle and distal of the teeth) and then the total of these values were averaged. This averaged value was used as the buccal alveolar bone thickness for every premolar. Every subgroup had 6 samples (three right sides and three left sides) taken at 4- week retention and 6 samples taken at 12- week retention.

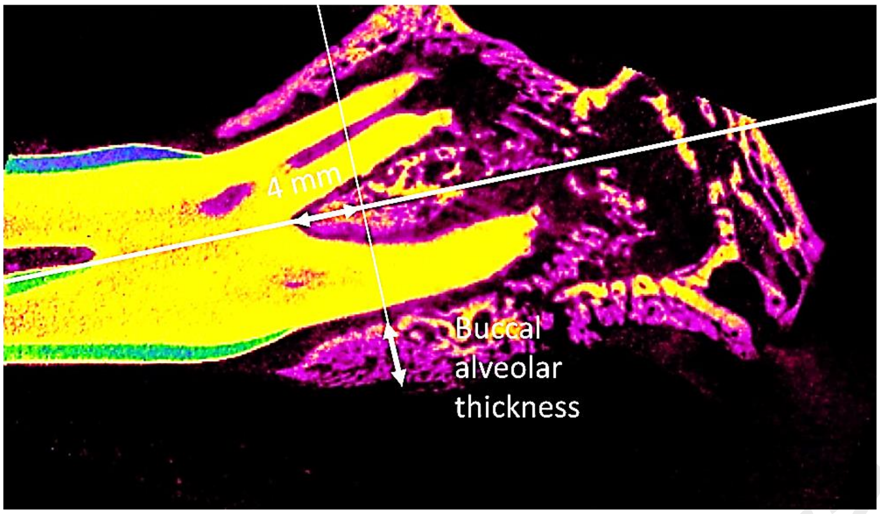


Figure 3.6: The measurement of the thickness of buccal alveolar bone. The thickness of buccal alveolar bone was measured from the most buccal point and the most inner point of the buccal alveolar bone (white arrow) on the line going through a point at 4 mm below the furcation and perpendicular to the tooth axis.

3.6.2 Bone microstructural changes at 4- and 12-week retention periods

The furcation bone areas enclosed by the buccal and lingual roots were defined as the region of interest (ROI) (Figure 3.7). When a tooth moves buccally, some buccal parts of the root are under pressure and the other parts are subject to tension. The pressure areas undergo bone resorption and the tension areas undergo bone apposition. In maxillary expansion, the furcation area comprises the palatal aspect of the buccal root and buccal side of palatal root. If teeth move bodily, the palatal side of buccal root bears the strain and buccal side of palatal root bears the pressure. In case tooth moves in tipping pattern, the stress and strain areas depend on the centre of rotation. In controlled tipping, the centre of rotation slightly moves towards apical to the centre of resistance. In uncontrolled tipping, tooth rotates around its centre of resistance (Proffit et al., 2007). Consequently, the apex half portion of the palatal side of the buccal root and the upper half portion of the buccal side of the palatal root receive pressure while the other parts receive tension. The bone microstructural changes at the furcation areas can reflect both bone resorption and apposition activity in the cancellous bone. Moreover, as determine the PDL (transparent areas) between the roots and alveolar at the furcation was easy, the reliability in defining this area and repeating the measurement was high.

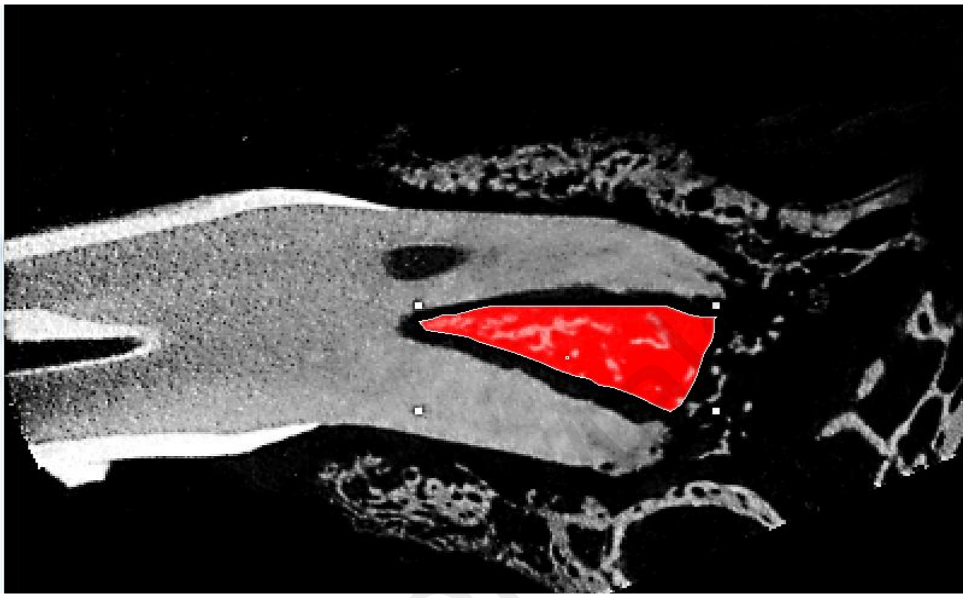


Figure 3.7: The region of interest (ROI) for bone microstructural measurement. The furcation areas enclosed by the buccal and lingual roots of premolars were defined as ROI for measuring bone microstructural changes after retention periods.

After ROIs were selected, the automatic (Otsu method) threshold was applied for all images during analysis. The bone structural microstructure parameters obtained from CTAn software (CT Analyser version 1.15.4.0+, Skyscan, Belgium) included bone volume fraction, trabecular thickness, trabecular separation and trabecular number (Table 3.2).

Table 3.2: Definition of bone microstructural parameters

Abbreviation	Parameters	Unit	Description
BV/TV	Bone volume fraction	%	Ratio of bone volume to the total tissue volume in the region of interest (ROI).
Tb.Th	Trabecular thickness	µm	Average of the thickness of trabecular.
Tb.Sp	Trabecular separation	µm	Average distance between trabeculae.
Tb.N	Trabecular number	1/µm	Average number of trabeculae per unit length.

3.7 Histology protocol

The obtained maxillary samples were separated into left and right sides with a sharp saw. A coin was flipped for every sample to choose the left or right side for histological analysis. Subsequently, for every left or right side, the second and third premolar were separated with a saw and processed for histology. In total 36 samples were collected which each group had 12 samples; 6 samples taken at 4-weeks retention and 6 samples at 12-weeks retention. Among these 6 samples, 3 samples were the second premolar blocks and the others were the third premolar blocks.

Maxillary samples were rinsed with a phosphate buffered saline solution and decalcified with 10% ethylene diamine tetra-acetic acid (EDTA-2Na) (pH 7.4) at 4°C in one month. Following decalcification, the tissue was dehydrated in ethyl alcohol of gradually increasing concentrations from 70% to 100% and embedded in paraffin. All samples were sagittally sectioned at 5 µm thickness through the second and third premolar roots using a microtome. Two slides were made for each area. Each area was sectioned so that it comprised mesio-buccal and lingual roots. Subsequently, all slides were stained with hematoxylin and eosin for histological examination (Appendix A).

The whole slide imaging (WSI) were digitized at 40x magnification using Pannoramic Desk slide scanner (3DHISTECH Ltd, Budapest, Hungary). The Pannoramic Viewer software (Pannoramic Viewer version 1.14.4, 3DHISTECH Ltd, Budapest, Hungary) was used to examine the obtained images.

3.7.1 Quantification of blood vessel number at 4- and 12-week retention.

Histomorphometric analysis was performed to examine the features of buccal cortical bone at 4-week and 12-week retention. Quantification of blood vessel number per mm square was carried out to evaluate the microvascularisation in the furcation area of the second and third premolars. Six regions (at the furcation crest, middle and apical level, two regions for each level) of interest were taken in the periodontal area for every slide at 800× magnification using Pannoramic Viewer (Figure 3.8). The vessel lumens were defined as thin endothelial lined lumens filled in with some blood cells. Very small cross-sectioned capillaries without clear lumen and completely ossified blood vessels were not counted. The areas of the region of interest were calculated using the same software and manual blood vessel number count was performed. The number of blood vessel per mm square was calculated by dividing the number of blood vessel in the region of interest by the area containing them.

Figure 3.8: Regions of interest (ROI) for blood vessel number quantification. ROI were 6 areas (the black boxes) between premolar roots at the furcation crest, middle and apical level**.**

3.7.2 Histomorphometric analysis of the new bone formation at 4- and 12-week retention in three groups

The quantification of the new bone and old bone area was performed using Pannoramic Viewer software (Pannoramic Viewer version 1.14.4, 3DHISTECH Ltd, Budapest, Hungary). The region of interest was the whole area of the tissue surrounding the second and third premolar tooth showed on the slide. New bone was defined as the amorphous eosinophilic material with porous bone and pale cement lines (Figure 3.9). Old bone was the bone with a compact feature and prominent cement lines (Figure 3.9). Table 3.3 presented the parameters used in quantification of the new bone, old bone, total bone and total tissue area and their definitions.

Table 3.3: Definition of parameters in quantification of new bone formation in the region of interest (ROI)

Abbreviation	**Parameters**	**Unit**	**Description**
NB	New bone	µm^2	The area of new bone in the ROI
OB	Old bone	µm^2	The area of old bone in the ROI
TT	Total tissue	µm^2	The area of the whole tissue surrounding the tooth.
TB=NB+OB	Total bone	µm^2	The area of new and old bone in the ROI
NBF=NB/TB	New bone fraction		The ratio of new bone to total bone area in ROI
OBF=OB/TB	Old bone fraction		The ratio of old bone to total bone area in ROI
TNBF=NB/TT	Total new bone fraction		The ratio of new bone to total tissue area in ROI
TOBF=OB/TT	Total old bone fraction		The ratio of old bone to total tissue area in ROI
TBF=TB/TT	Total bone fraction		The ratio of total bone and total tissue area in ROI

ROI: region of interest defined as the whole areas of the tissue surrounding the premolar tooth showed on the slide.

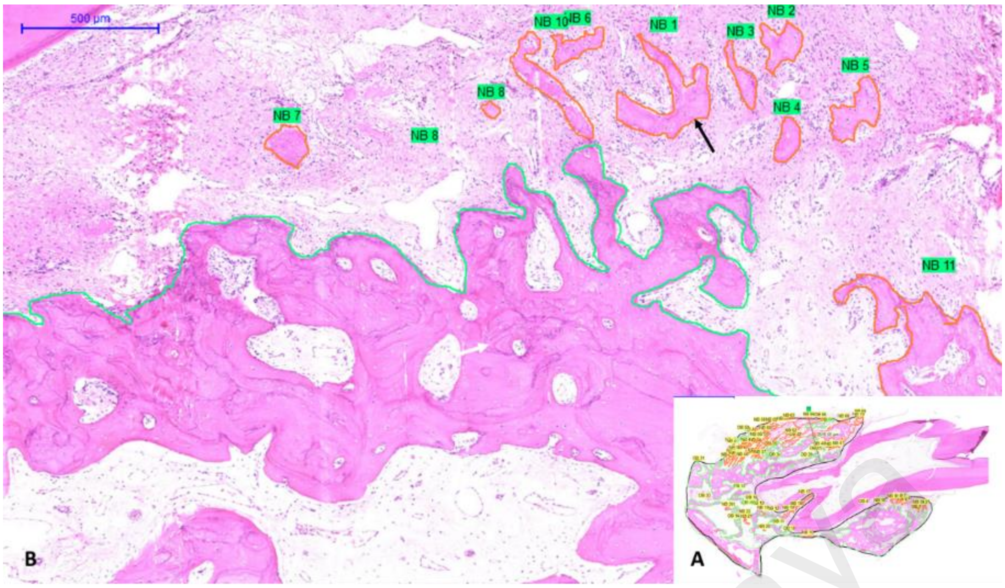


Figure 3.9: Histomorphometric analysis of bone remodelling. Photomicrograph showing new bone, old bone, total tissue area (TT).
A, the total tissue area (outline by black line) at 20× magnification; B, magnification at 200× showing feature of old bone with prominent cement lines and compact (white arrow); and feature of new bone with unclear cement lines and woven (black arrow).

3.8 Statistical analysis

All data were analyzed using SPSS® Statistics version 20.0 (IBM Co., Armonk, NY, US). The normality of data distribution was assessed using the Shapiro-Wilk test. Parametric tests were used to analyze the normal distributed data and the non-parametric tests were applied for the non-normal distributed data. A *p*-value of 0.05 was considered statistically significant.

All measurements were repeated after 30 days by the same rater. Intraclass correlation coefficient (ICC) was performed for Intrarater reliability test. ICC is to test how similar measures are that have been made for the same subject at different occasions. ICC is used for continuous data, measures the proportion of total variance of data measured by 1 rater that is due to differences between these data, and its size depends on the variability in the sample.

CHAPTER 4: RESULTS

4.1 Animal welfare

The welfare of sheep was monitored daily following the general guidelines for monitoring the sheep health (Ewing et al., 1999a, 1999b). A checklist was made based on this guidelines including the amount of diet, the speed of feed intake, the color of mucous membrane of eyes, ear, nose and mouth, other behaviors and weight (Appendix D).

During the experimental period, all sheep were fed two times daily (8-9 am and 15.30-16:30 pm) and fed by group with one kg pelleted feed/sheep/day and one to two kg of hay/sheep/day. Most of the sheep finished their feed quickly (approximately 30 minutes). In Group 1, sheep received corticotomy surgery finished their feed a little bit slower at the first day after surgery (approximately 3 hours). Therefore, they were kept in separated pens until they could take feed normally (approximately 2 days). Most of sheep recovered at the third day after surgery and there was no any problem in chewing recorded. With the restricted diet, no refused feed were recorded in all groups during the experimental period.

Sheep were also monitored on other behaviors and features. The sheep had very close contact, walked well, and moved freely and easily with no hesitation. Their eyes were clear, bright and alert. The mucous membranes of the eye, ear, nose, mouth were moist and pink. The hair was not shed and the skin was smooth and flexible. Feces looked like pellets and normal. No abnormal signs were recorded during the experimental period.

The weight of sheep was recorded before the intervention and at the end of the experimental periods. Tables 4.1 and 4.2 showed that the weight of sheep slightly increased over this period revealing that sheep were healthy during the experiment period.

Table 4.1: Change of sheep's weight in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention.

Weight (kg)	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Control (n=3) Mean ± SD
Initial weight	53.67 ± 2.75	54.20 ± 3.32	53.70 ± 4.25
Weight at 4 week	54.83 ± 2.51	55.53 ± 3.04	54.87 ± 4.25
Weight difference	1.16 ± 0.50	1.33 ± 0.29	1.17 ± 0.76

Table 4.2: Change of sheep's weight in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention.

Weight (kg)	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Control (n=3) Mean ± SD
Initial weight	55.67 ± 3.32	55.01 ± 2.78	54.30 ± 4.53
Weight at 12 week	58.78 ± 3.01	57.80 ± 2.52	58.27 ± 3.83
Weight difference	3.11 ± 1.15	2.79 ± 0.76	3.97 ± 1.61

4.2 Linear and angular dental and skeletal changes produced by ABPC + RME and conventional RME at 4- and 12-week retention period evaluated by using CBCT

In all CBCT images acquired after the experiment period, the midpalatal suture were examined in the transverse plane using Fidex software (Fidex, Animage LLS, US). Opening of midpalatal suture was not evident on any CBCT scan in all sheep (Figure 4.1).

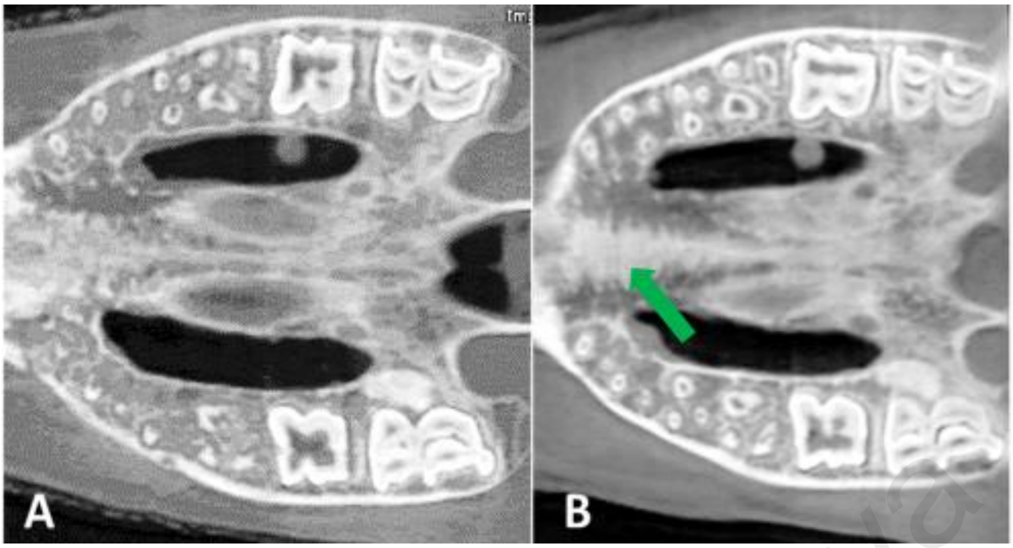


Figure 4.1: Cone-beam computed tomography (CBCT) images of midpalatal suture.
The opening of midpalatal suture was not evident before (A) and after (B) experiement periods (green arrow).

Shapiro-Wilk test showed that the data were normally distributed ($p > 0.05$). Thus, the parametric tests were applied for further analysis. Paired *t*-test was used to determine the dental and skeletal differences between before treatment and after retention periods in each group. Two-way ANOVA with Bonferroni post hoc was applied to compare the difference among groups after 4- and 12-week retention. ICC's were 0.90 for teeth inclination measurements and more than 0.93 for the others dental and skeletal linear measurements in three groups.

In control group, no significant differences in dental and skeletal changes between before and after treatment in all groups were detected for all parameters ($p > 0.05$, Table 4.3, 4.4). Thus, the growth of sheep in our study was already stable.

In Group 1 (ABPC + RME), all the mean measurements showed significant dental and skeletal differences between before the intervention and after each retention period ($p <$ 0.05, Table 4.3, 4.4).

In Group 2 (conventional RME), the results of a paired *t*-test showed significant increase in the mean interpremolar widths at the Cu-Cu level and Pu-Pu level ($p < 0.05$, Table 4.3, 4.4). In addition, the mean teeth inclination and the mean skeletal width changes at the Cr-Cr level were also significant ($p < 0.05$, Table 4.3, 4.4) over the retention period. Skeletal changes at the HP level were not significant over the retention periods ($p > 0.05$, Table 4.3, 4.4).

Table 4.3. Changes in dentoalveolar dimensions in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4 and 12-week retention

Measurement	Group 1		Group 2		Group 3	
	T2-T0 Mean ± SD	***p*-value***	**T2-T0 Mean ± SD**	***p*-value***	**T2-T0 Mean ± SD**	***p*-value***
Cr-Cr at						
P1-4w	3.94 ±1.02	s	2.29 ±0.90	s	-0.15 ± 0.45	ns
P2-4w	3.79 ±0.83	s	2.40 ±0.30	s	-0.06 ±0.54	ns
P3-4w	3.64 ±0.31	s	2.01 ±0.24	s	0.46 ±0.82	ns
P1-12w	4.92 ±1.20	s	4.18 ±0.58	s	-0.43 ±0.63	ns
P2-12w	4.54 ±0.71	s	2.41 ±0.24	s	-0.05 ±1.36	ns
P3-12w	3.74 ±0.16	s	2.15 ±0.83	s	1.16 ±0.91	ns
HP level at						
P1-4w	2.26 ±0.88	s	0.47 ± 0.51	ns	-0.20 ±0.33	ns
P2-4w	3.63 ±0.28	s	0.46 ±0.31	ns	0.11 ±0.15	ns
P3-4w	3.02 ±1.13	s	0.25 ±0.30	ns	0.44 ±0.38	ns
P1-12w	2.32 ±1.85	s	1.45 ±1.44	ns	0.09 ±1.16	ns
P2-12w	3.62 ±1.79	s	1.10 ±0.25	ns	-0.11 ±0.85	ns
P3-12w	3.22 ±0.65	s	0.48 ±0.40	ns	0.11 ± 0.52	ns

ns: non-significant difference ($p > 0.05$); s: significant difference ($p < 0.05$).
P1, first premolar; P2, second premolar; P3, third premolar.
4w, at 4-weeks retention; 12w, at 12-weeks retention.
See Table 3.1 for the definitions of each measurement. Cr-Cr: skeletal changes at crestal level; HP level: skeletal changes at hard palate level.
*pair *t*-test for comparison between before intervention and after retention periods

Table 4.4. Changes in dental dimensions in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4 and 12-week retention

	Group 1		**Group 2**		**Group 3**	
Measurement	**T2-T0 Mean ± SD**	***p*-value***	**T2-T0 Mean ± SD**	***p*-value***	**T2-T0 Mean ± SD**	***p*-value***
Cu-Cu at						
P1-4w	11.50 ± 2.29	s	6.17 ± 1.26	s	0.50 ± 0.77	ns
P2-4w	10.83 ± 1.44	s	4.33 ± 1.15	s	0.45 ± 0.56	ns
P3-4w	11.00 ± 1.00	s	4.67 ± 2.89	s	0.33 ± 0.22	ns
P1-12w	9.33 ± 0.58	s	8.67 ± 3.33	s	0.24 ± 0.27	ns
P2-12w	7.83 ± 1.04	s	7.00 ± 2.00	s	-1.08 ± 2.87	ns
P3-12w	7.33 ± 2.52	s	6.67 ± 2.52	s	-0.32 ± 1.58	ns
Pu-Pu at						
P1-4w	6.82 ± 0.38	s	4.04 ± 1.85	s	0.49 ± 0.74	ns
P2-4w	5.88 ± 0.29	s	3.50 ± 0.93	s	0.04 ± 0.29	ns
P3-4w	6.11 ± 1.02	s	2.63 ± 2.19	s	-0.24 ± 0.23	ns
P1-12w	6.01 ± 2.25	s	4.84 ± 0.89	s	0.22 ± 0.24	ns
P2-12w	4.98 ± 1.22	s	4.08 ± 1.63	s	0.69 ± 1.46	ns
P3-12w	5.53 ± 1.50	s	4.24 ± 2.78	s	0.02 ± 0.69	ns
R-R at						
P1-4w	1.85 ± 0.65	s	-0.90 ± 0.72	ns	0.10 ± 0.05	ns
P2-4w	2.53 ± 0.97	s	1.95 ± 3.73	ns	-0.05 ± 0.13	ns
P3-4w	2.49 ± 1.30	s	0.91 ± 0.62	ns	-0.19 ± 0.61	ns
P1-12w	3.64 ± 3.34	s	0.02 ± 1.73	ns	1.00 ± 0.83	ns
P2-12w	2.41 ± 2.10	s	2.00 ± 1.10	s	0.44 ± 0.29	ns
P3-12w	3.32 ± 2.60	s	2.63 ± 2.37	s	-0.88 ± 1.19	ns
Teeth inclination						
P1-4w	14.19 ± 3.50	s	9.23 ± 7.41	s	-0.12 ± 1.97	ns
P2-4w	12.55 ± 2.98	s	8.35 ± 1.73	s	0.43 ± 0.51	ns
P3-4w	11.39 ± 2.48	s	5.68 ± 7.22	s	0.58 ± 1.11	ns
P1-12w	11.18 ±0.26	s	14.5 ± 7.94	s	-1.00 ± 3.97	ns
P2-12w	7.13 ± 1.56	s	9.83 ± 4.54	s	-1.19 ± 2.44	ns
P3-12w	6.97 ± 3.16	s	7.00 ± 1.73	s	0.33 ± 2.08	ns

ns: non-significant difference ($p > 0.05$); s: significant difference ($p < 0.05$).
P1, first premolar; P2, second premolar; P3, third premolar.
4w, at 4-weeks retention; 12w, at 12-weeks retention.
See Table 3.1 for the definitions of each measurement. Cu-Cu: intercuspal width of premolars (dental changes at cusp level); Pu-Pu: distance between pulp centres of premolars (dental changes at pulp level); R-R: distance between lingual root apexes of premolars (dental changes at root apex level). Teeth angle: axis of premolar teeth to the nasal plane (a plane tangent to the nasal floor).
*pair *t*-test for comparison between before intervention and after retention periods.

Mean dental and skeletal changes were not significantly different among the first, second and third premolars over the retention periods ($p > 0.05$, Table 4.5, 4.6, 4.7, 4.8, and 4.9).

Dental changes at the first, second and third premolars in all groups at 4- and 12-week retention were presented in Table 4.5, 4.6, and 4.7. The mean dental expansion at the Cu-Cu level in Group 1 was approximately two times greater than that of the Group 2 at 4-week retention ($p < 0.05$, Table 4.5). Compared with the control group, the mean Cu-Cu values in two intervention groups were significantly higher ($p < 0.05$, Tables 4.5 and 4.6).

The mean dental change at the R-R level in Group 1 was statistically higher than the control groups at 4 and 12 weeks ($p < 0.05$, Tables 4.5 and 4.6). In Group 2, at 4-week retention, the root apex of the first premolar moved lingually while the other premolar roots moved buccally. The mean root movement was much less in Group 2 compared to Group 1 ($p > 0.05$, Table 4.5 and 4.6).

At 4-week retention, the mean Pu-Pu value in Group 1 was statically significant between the control as well as Group 2 ($p < 0.05$, Table 4.7). The mean Pu-Pu was approximately twice as high as that of Group 2 ($p < 0.05$, Table 4.7), but there was no significant difference between the two mean intervention groups at 12-week retention ($p > 0.05$, Table 4.7).

From 4- and 12-week retention, in ABPC + RME group, the Cu-Cu values decreased while the R-R values increased ($p > 0.05$). As a result, the tooth inclination values also decreased at 12-week retention compared with the previous period (Tables 4.5 and 4.6). In contrast, the crowns in Group 2 continued to move buccally and moved at a greater amount than the roots did. This movement led to greater buccal tipping of premolars and the teeth inclination increased correspondingly (Tables 4.5 and 4.6).

Table 4.5: Dental changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention.

Measurement	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Group 3 (n=3) Mean ± SD	*p*-value*
Cu-Cu (mm) at				
P1	11.50 ± 2.29	6.17 ± 1.26	0.50 ± 0.77	s[a]
P2	10.83 ± 1.44	4.33 ± 1.15	0.45 ± 0.56	s[b]
P3	11.00 ± 1.00	4.67 ± 2.89	0.33 ± 0.22	s[c]
Average	11.11 ± 1.47	5.06 ± 1.88	0.43 ± 0.53	s[d]
R-R (mm) at				
P1	1.85 ± 0.65	-0.90 ± 0.72	0.10 ± 0.05	s[e]
P2	2.53 ± 0.97	1.95 ± 3.73	-0.05 ± 0.13	ns
P3	2.49 ± 1.30	0.91 ± 0.62	-0.19 ± 0.61	s[f]
Average	2.29 ± 0.93	0.65 ± 2.29	-0.05 ± 0.34	s[g]
Teeth inclination (^{o})				
P1	14.19 ± 3.50	9.23 ± 7.41	-0.12 ± 1.97	s[h]
P2	12.55 ± 2.98	8.35 ± 1.73	0.43 ± 0.51	s[i]
P3	11.39 ± 2.48	5.68 ± 7.22	0.58 ± 1.11	ns
Average	12.71 ± 2.88	7.75 ± 5.48	0.30 ± 1.21	s[j]

ns: non-significant difference (*p* >0.05); s: significant difference (*p*< 0.05).
P1, first premolar; P2, second premolar; P3, third premolar.
G1: Group 1; G2: Group 2, G3: Group 3.
See Table 3.1 for the definitions of each measurement. Cu-Cu: intercuspal width of premolars (dental changes at cusp level); R-R: distance between lingual root apex of premolars (dental changes at root apex level). Teeth angle: axis of premolar teeth to the nasal plane (a plane tangent to the nasal floor).
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

[a] G1 > G3 (s);
[b] G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[c] G1 > G2 (s); G1 >G3 (s);
[d] G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[e] G1 > G2 (s); G1 > G3 (s);
[f] G1 > G3 (s);
[g] G1 > G3 (s);
[h] G1> G3 (s);
[i] G1 > G3 (s); G2 > G3 (s);
[j] G1 > G2 (s); G1 > G3 (s); G2 > G3 (s).

Table 4.6: Dental changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention period.

Measurement	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Group 3 (n=3) Mean ± SD	*p*-value*
Cu-Cu (mm) at				
P1	9.33 ± 0.58	8.67 ± 3.33	0.24 ± 0.27	s[a]
P2	7.83 ± 1.04	7.00 ± 2.00	-1.08 ± 2.87	s[b]
P3	7.33 ± 2.52	6.67 ± 2.52	-0.12 ± 0.55	s[c]
Average	8.17 ± 1.66	7.44 ± 2.49	-0.32 ± 1.58	s[d]
R-R (mm) at				
P1	3.64 ± 3.34	0.00 ± 1.73	1.00 ± 0.83	ns
P2	2.41 ± 2.10	2.00 ± 1.10	0.44 ± 0.29	ns
P3	3.32 ± 2.60	2.63 ± 2.37	-0.88 ± 1.19	ns
Average	3.12 ± 2.42	1.54 ± 1.97	0.18 ± 1.11	s[e]
Teeth inclination (°)				
P1	11.18 ±0.26	14.5 ± 7.94	-1.00 ± 3.97	s[f]
P2	7.13 ± 1.56	9.83 ± 4.54	-1.19 ± 2.44	s[g]
P3	6.97 ± 3.16	7.00 ± 1.73	0.33 ± 2.08	ns
Average	8.43 ± 2.72	10.44 ± 5.69	0.62 ± 2.81	s[h]

ns: non-significant difference (*p* >0.05); s: significant difference (*p*< 0.05).
P1, first premolar; P2, second premolar; P3, third premolar;
G1: Group 1; G2: Group 2, G3: Group 3.
See Table 3.1 for the definitions of each measurement. Cu-Cu: intercuspal width of premolars (dental changes at cusp level); R-R: distance between lingual root apex of premolars (dental changes at root apex level). Teeth angle: axis of premolar teeth to the nasal plane (a plane tangent to the nasal floor).
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

[a] G1 > G3 (s); G2 > G3 (s);
[b] G1 > G3 (s); G2 > G3 (s);
[c] G1 > G3 (s); G2 > G3 (s);
[d] G1 > G3 (s); G2 > G3 (s);
[e] G1 > G3 (s);
[f] G2 > G3 (s);
[g] G2 > G3 (s);
[h] G1> G3 (s); G2 > G3 (s).

Table 4.7: Dental changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4- and 12-week retention.

Measurement (mm)	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Control (n=3) Mean ± SD	*p*-value*
4-week retention				
Pu-Pu at				
P1	6.82 ± 0.38	4.04 ± 1.85	0.49 ± 0.74	s[a]
P2	5.88 ± 0.29	3.50 ± 0.93	0.04 ± 0.29	s [b]
P3	6.11 ± 1.02	2.63 ± 2.19	-0.24 ± 0.23	s [c]
Average	6.26 ± 0.71	3.39 ± 1.63	0.10 ± 0.52	s [d]
12-week retention				
Pu-Pu at				
P1	6.01 ± 2.25	4.84 ± 0.89	0.22 ± 0.24	s[e]
P2	4.98 ± 1.22	4.08 ± 1.63	0.69 ± 1.46	s[f]
P3	5.53 ± 1.50	4.24 ± 2.78	0.02 ± 0.69	s[g]
Average	5.51 ± 1.55	4.39 ± 1.71	0.31 ± 0.87	s[h]

ns: non-significant difference (p >0.05); s: significant difference (p< 0.05).
P1, first premolar; P2, second premolar; P3, third premolar.
G1: Group 1; G2: Group 2, G3: Group 3.
See Table 3.1 for the definitions of each measurement. Pu-Pu: distance between pulp centres of premolars (dental changes at pulp level).
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

[a]G1 > G3 (s); G2 > G3 (s);
[b]G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[c]G1 > G3 (s);
[d]G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[e]G1 > G3 (s); G2 > G3 (s);
[f]G1 > G3 (s);
[g]G1 > G3 (s);
[h]G1> G3 (s); G2 > G3 (s).

Tables 4.8 and 4.9 illustrated the skeletal changes at 4- and 12- week retention in three groups. The increase in transverse alveolar width at the HP level in Group 1 was approximately three folds or greater than that of Group 2 over the retention periods (p <

0.05). Skeletal alterations at the Cr-Cr level in Group 1 were around 1.5 times that of Group 2 (*p* > 0.05) over the retention periods. All changes in the two intervention groups were highly significant compared with control group (*p* < 0.05). From 4- to 12- week retention, the skeletal expansion increased slightly in the conventional RME while it was almost stable in ABPC + RME group (*p* > 0.05, Figures 4.2 and 4.3).

Table 4.8: Skeletal changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention.

Measurement (mm)	**Group 1 (n=3) Mean ± SD**	**Group 2 (n=3) Mean ± SD**	**Group 3 (n=3) Mean ± SD**	***p*-value***
Cr-Cr at				
P1	3.94 ±1.02	2.29 ±0.90	-0.15 ± 0.45	s[a]
P2	3.79 ±0.83	2.40 ±0.30	-0.06 ±0.54	s[b]
P3	3.64 ±0.31	2.01 ±0.24	0.46 ±0.82	s[c]
Average	3.79 ±0.68	2.23 ± 0.93	0.08 ±0.61	s[d]
HP level at				
P1	2.26 ±0.88	0.47 ± 0.51	-0.20 ±0.33	s[e]
P2	3.63 ±0.28	0.46 ±0.31	0.11 ±0.15	s[f]
P3	3.02 ±1.13	0.25 ±0.30	0.44 ±0.38	s[g]
Average	2.97 ± 0.94	0.39 ± 0.35	0.12±0.38	s[h]

ns: non-significant difference (*p* >0.05); s: significant difference (*p*< 0.05).
P1, first premolar; P2, second premolar; P3, third premolar.
G1: Group 1; G2: Group 2, G3: Group 3.
See Table 3.1 for the definitions of each measurement. Cr-Cr: skeletal changes at crestal level; HP level: skeletal changes at hard palate level.
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

[a] G1 > G3 (s);
[b] G1 > G3 (s);
[c] G1 > G3 (s);
[d] G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[e] G1 > G2 (s); G1 > G3 (s);
[f] G1 > G2 (s); G1 > G3 (s);
[g] G1 > G2 (s); G1 > G3 (s);
[h] G1 > G2 (s); G1 > G3 (s).

Table 4.9: Skeletal changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention.

Measurement (mm)	Group 1 (n=3) Mean ± SD	Group 2 (n=3) Mean ± SD	Group 3 (n=3) Mean ± SD	*p*-value*
Cr-Cr at				
P1	4.92 ±1.20	4.18 ±0.58	-0.43 ±0.63	s^a
P2	4.54 ±0.71	2.41 ±0.24	-0.05 ±1.36	s^b
P3	3.74 ±0.16	2.15 ±0.83	1.16 ±0.91	s^c
Average	4.39 ± 0.88	2.91 ± 1.09	0.023 ±1.14	s^d
HP level at				
P1	2.32 ±1.85	1.45 ±1.44	0.09 ±1.16	ns
P2	3.62 ±1.79	1.10 ±0.25	-0.11 ±0.85	s^e
P3	3.22 ±0.65	0.48 ±0.40	0.11 ± 0.52	s^f
Average	3.05 ±1.45	1.01 ±0.87	0.03 ±0.77	s^g

ns: non-significant difference ($p > 0.05$); s: significant difference ($p < 0.05$).
P1, first premolar; P2, second premolar; P3, third premolar.
G1: Group 1; G2: Group 2, G3: Group 3.
See Table 3.1 for the definitions of each measurement. Cr-Cr: skeletal changes at crestal level; HP level: skeletal changes at hard palate level.
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

[a]G1 > G3 (s); G2 > G3 (s);
[b]G1 > G3 (s);
[c]G1 > G3 (s);
[d]G1 > G2 (s); G1 > G3 (s); G2 > G3 (s);
[e]G1 > G3 (s);
[f]G1 > G2 (s); G1 > G3 (s);
[g]G1 > G2 (s); G1 > G3 (s).

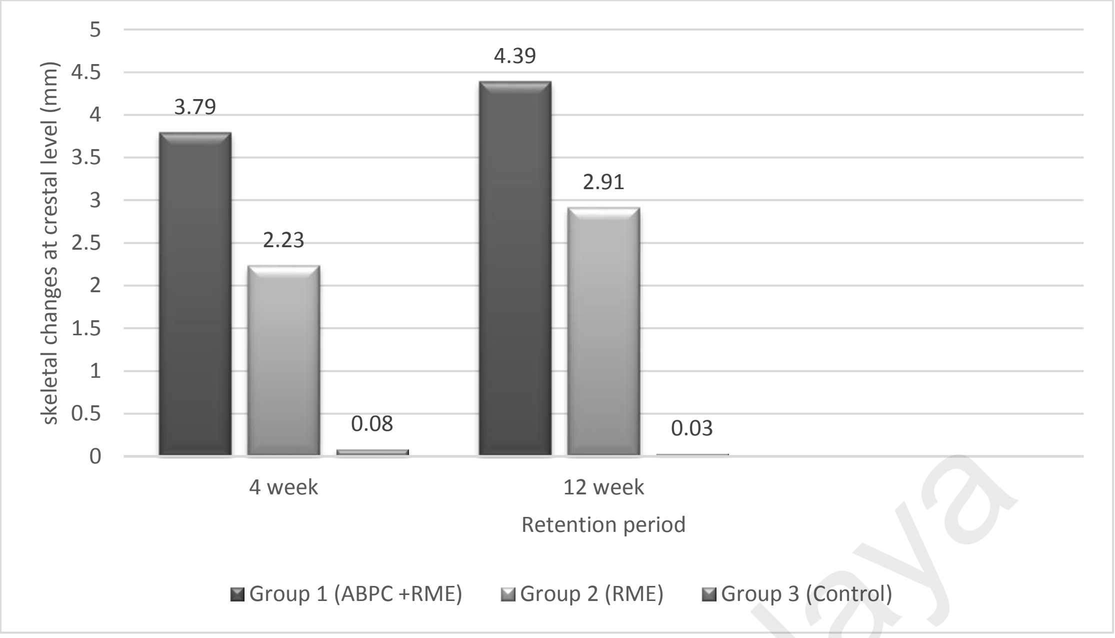


Figure 4.2: Skeletal changes at the crestal level (Cr-Cr) in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4- and 12- week retention.

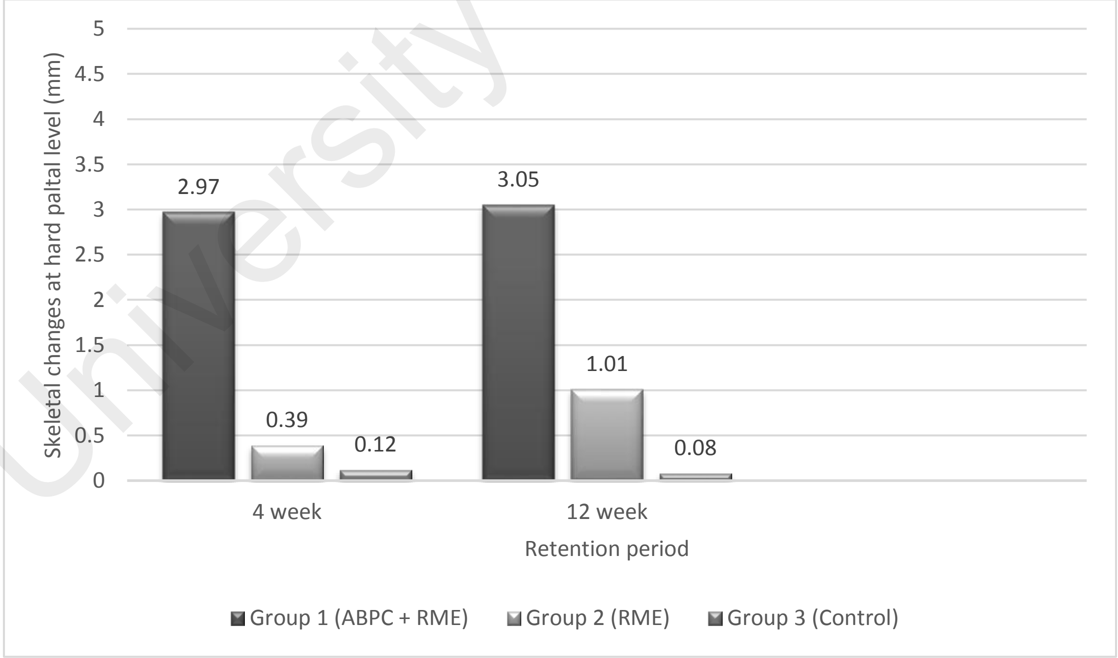


Figure 4.3: Skeletal changes at the hard palatal level (HP level) in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4- and 12-week retention.

Superimposition of CBCT images before treatment and after retention periods in Group 1 (ABPC + RME) were performed as showed in Figure 4.4 using Mimic Software version 19.0 (Materialise NV, Leuven, Belgium). The superimposition was performed at the palate and outer skull so that these sites superimposed most simultaneously. The pre-treatment image was coded in green while the post-retention image was coded in red. The surface differences at the intervention sites (buccal and palatal sides of the premolar segments) was recorded. The superimposed images revealed a clear change (red) at the surgical regions in the buccal sides showing the buccal displacement of the premolar segments. The skeletal changes occurred at most buccal areas starting from the cervical to hard palatal level in the corticotomized areas (Figure 4.4).

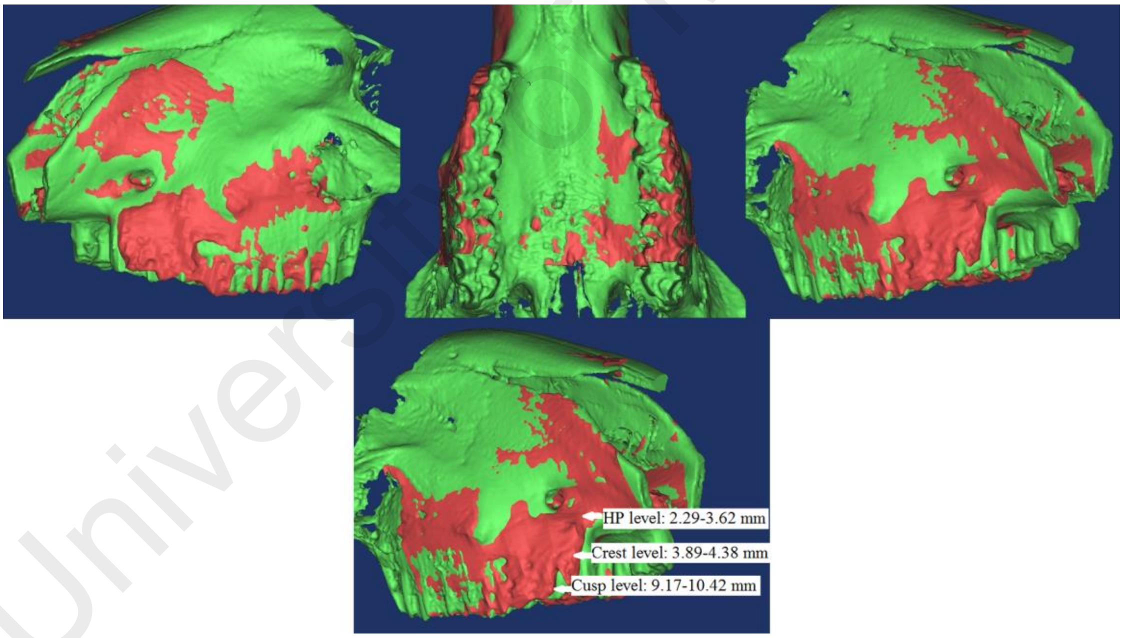


Figure 4.4: The dental and skeletal changes of transverse maxillary arch in Group 1 (ABPC + RME). Superimposition of images taken before intervention (green) and after retention period (red) in Group 1 using Mimic Software.

The red part revealed significant changes after retention period from left side view (A); occlusal view (B) and from right side view (C); and summarized mean transverse skeletal (at the hard palatal and alveolar crest level) and dental changes (at the cusp level) in the premolar regions from right side view (D).

CBCT images taken before treatment and after retention periods in Group 2 (conventional RME) were also superimposed using Mimic Software (Materialise NV, Leuven, Belgium). Skeletal changes occurred from alveolar crest to around middle of the buccal alveolar bone (Figure 4.5). The skeletal changes at the HP level in conventional RME group were not as obvious as in ABPC + RME group (Figures 4.4 and 4.5).

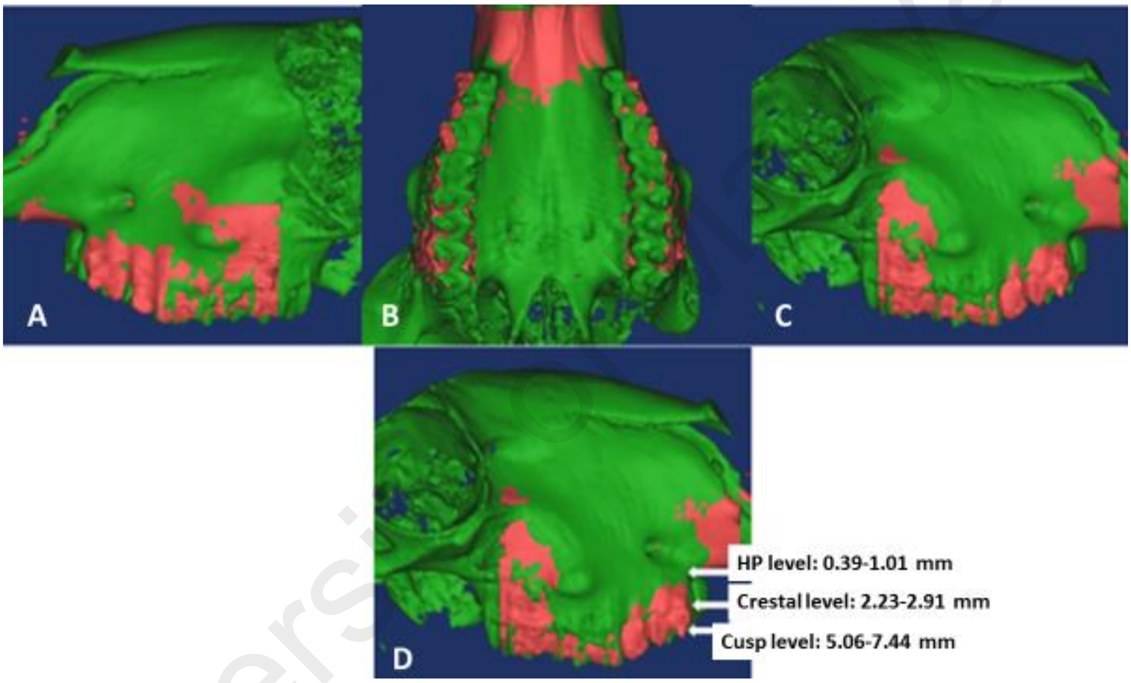


Figure 4.5: The dental and skeletal changes of transverse maxillary arch in Group 2 (conventional RME). Superimposition of images taken before intervention (green) and after retention period (red) in Group 2 using Mimic Software.
The red part revealed changes after retention period from left side view (A); occlusal view (B) and from right side view (C); and summarized mean transverse skeletal (at the hard palatal and alveolar crest level) and dental changes (at the cusp level) in the premolar regions from right side view (D).

4.3 Types of dental movement and skeletal displacement produced by ABPC + RME and conventional RME evaluated by using CBCT

The ratio between the amount of crown and root movements as well as between the skeletal segments can reflect the type and magnitude of the movement. The ratio with minus value showed an uncontrolled tipping in which crown and root move in different directions. If the ratio between crown and root components is positive and nearly 1, the tooth moves close to the bodily movement pattern. The other positive values of ratio reflect buccal tipping movement. Values above 1 indicates more crown tipping than root.

Tables 4.10 and 4.11 illustrated the ratio between the values of transverse interpremolars width change in ABPC + RME group and conventional RME group at 4- and 12-week retention.

Table 4.10: The ratio between dental parameter values in Group 1 (ABPC +RME group) and Group 2 (conventional RME group) at 4-week retention.

Tooth type	Cu-Cu /Pu-Pu		R-R/Cu-Cu		R-R/Pu-Pu	
	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)
P1	1.69	1.52	0.16	-0.15	0.27	-0.22
P2	1.84	1.24	0.23	0.45	0.43	0.55
P3	1.80	1.78	0.23	0.19	0.41	0.35
Average	1.78	1.51	0.21	0.16	0.37	0.23

P1: first premolar; P2: second premolar; P3: third premolar.
See Table 3.1 for the definitions of each measurement. Pu-Pu: distance between centre of teeth pulp (dental changes at centre of pulp level); Cu-Cu: transverse intercuspal width (dental changes at premolar cusp level); R-R: distance between lingual root apex (dental changes at root apex level).

At 4-week retention, all the mean ratio values (Cu-Cu/Pu-Pu, R-R/Cu-Cu, R-R/Pu-Pu) in the Group 1 were higher than that of Group 2 (Table 4.10). The amount of cusp movement was 1.78 times that of the centre of the pulp while it was 1.51 in Group 2. The root movement to its crown in Group 1 was 21% (R-R/Cu-Cu) and 37% (R-R/Pu-Pu) while it was less at 13% (R-R/Cu-Cu) and 19% (R-R/Pu-Pu) in Group 2. As the ratio between root and crown components was minus, the first premolar in Group 2 followed a pure tipping pattern (root and its crown move in opposite direction). The movements of the other teeth in two intervention groups were controlled tipping (root and its crown moved in the same direction but root moved much slower than its crown).

Table 4.11: The ratio between bony parameter values or bony and dental parameter values in Group 1 (ABPC +RME group) and Group 2 (conventional RME group) at 12-week retention.

Tooth type	Cu-Cu /Pu-Pu		R-R/Cu-Cu		R-R/Pu-Pu	
	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)
P1	1.55	1.79	0.39	0.01	0.61	0.01
P2	1.57	1.71	0.31	0.29	0.48	0.41
P3	1.38	1.57	0.45	0.39	0.62	0.62
Average	1.50	1.69	0.38	0.21	0.57	0.35

P1: first premolar; P2: second premolar; P3: third premolar.
See Table 3.1 for the definitions of each measurement. Pu-Pu: distance between centre of teeth pulp (dental changes at centre of pulp level); Cu-Cu: transverse intercuspal width (dental changes at premolar cusp level); R-R: distance between lingual root apex (dental changes at root apex level).

At 12-week retention, the ratio of root movement to its crown (R-R/Cu-Cu, R-R/Pu-Pu) increased in both intervention groups. The Cu-Cu/Pu-Pu ratio slightly decreased in Group 1 but it was increased in Group 2. At this period, the premolars in Group 2 continued to tip buccally while they were torque in Group 1. The root movement in the Group 1 was 38% and 57% that of the movement of its crown at the Cu-Cu level (R-R/Cu-Cu) and the Pu-Pu level (R-R/Pu-Pu) while these ratio were just 21% and 35% in Group 2 (Table 4.11).

Tables 4.12 and 4.13 presented the ratio between the values of bone parameters or the values of bone and dental parameters in Group 1 (ABPC + RME) and Group 2 (conventional RME) at 4- and 12- week retention.

Regarding to the skeletal displacement (HP/Cr-Cr), the changes of alveolar bone at the HP level in Group 1 was approximately 0.70 to 0.78 of the increment at the Cr-Cr while this ratio was low at 0.17 to 0.34 in Group 2 (Tables 4.12 and 4.13). Thus, the displacement of the buccal alveolar segment in ABPC + RME group was closer to the bodily displacement pattern compared to that of conventional RME group.

The HP/R-R ratio in Group 1 was approximately 1 (ranging from 0.98 to 1.3) illustrating that the buccal alveolar segment in this group displaced in accordance with the movement of the corresponding roots. In contrast, the displacement of the buccal alveolar segment in Group 2 was just 60% to 66% of the movement of the corresponding roots.

Table 4.12: The ratio between bony parameter values or bony and dental parameter values in Group 1 (ABPC +RME group) and Group 2 (conventional RME group) at 4-week retention.

Tooth type	HP/Cr-Cr		HP/R-R		Pu-Pu/Cr-Cr		Cu-Cu /Cr-Cr	
	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)
P1	0.58	0.21	1.22	0.52	1.73	1.76	2.92	2.69
P2	0.96	0.19	1.43	0.23	1.55	1.45	2.85	1.80
P3	0.80	0.12	1.21	0.27	1.68	1.18	3.03	2.32
Average	0.78	0.17	1.30	0.60	1.65	1.52	2.93	2.27

P1: first premolar; P2: second premolar; P3: third premolar.
See Table 3.1 for the definitions of each measurement. Cr-Cr: skeletal change at crestal level; HP level: skeletal change at hard palate level; Pu-Pu: distance between centre of teeth pulp (dental changes at centre of pulp level); Cu-Cu: transverse intercuspal width (dental changes at premolar cusp level); R-R: distance between lingual root apexes (dental changes at root apex level).

Table 4.13: The ratio between bony parameter values or bony and dental parameter values in Group 1 (ABPC +RME group) and Group 2 (conventional RME group) at 12-week retention.

Tooth type	HP/Cr-Cr		HP/R-R		Pu-Pu/Cr-Cr		Cu-Cu /Cr-Cr	
	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)	Group 1 (n=3)	Group 2 (n=3)
P1	0.47	0.35	0.64	0.01	1.22	1.16	1.90	2.07
P2	0.80	0.46	1.50	0.55	1.10	1.69	1.72	2.91
P3	0.86	0.22	0.97	0.18	1.43	1.97	1.96	3.10
Average	0.70	0.34	0.98	0.66	1.24	1.51	1.86	2.56

P1: first premolar; P2: second premolar; P3: third premolar.
See Table 3.1 for the definitions of each measurement. Cr-Cr: skeletal change at crestal level; HP level: skeletal change at hard palate level; Pu-Pu: distance between centre of teeth pulp (dental changes at centre of pulp level); Cu-Cu: transverse intercuspal width (dental changes at premolar cusp level); R-R: distance between lingual root apex (dental changes at root apex level).

The Pu-Pu/Cr-Cr ratio reflects the harmony between the displacement of the tooth and supporting bone. At 4-week retention, the tooth movements at the Pu-Pu level were around 1.5 times greater than the skeletal displacement at the Cr-Cr level in both intervention groups. The Pu-Pu/Cr-Cr ratio in ABPC + RME group was slightly higher than that of conventional RME group at 4- week retention (1.65 vs. 1.52) but then it decreased to nearly 1 (1.24) in the former group while it is stable in the latter group (1.51). Therefore, the tooth movement in ABPC + RME group was more proportional to the supporting bone.

Figures 4.6 and 4.7 showed superimposed images between before treatment and after retention period using Mimics software 19.0 (Materialise NV, Leuven, Belgium) in two intervention groups. These figure revealed the difference changes of skeletal segment in Group 1 and 2. In ABPC + RME group, as the skeletal increment occurred greatly at the HP level, the palatal vault in this group was U-shaped from the front view (Figure 4.7 C). On the other hand, the palatal vault in Group 2 was V-shaped because the increment of alveolar width at the HP level was obscured (Figure 4.7 D). From occlusal view, it is observed that the dental arch form at the premolar teeth become more U-shape in Group 1 while the shape of dental arch in Group 2 was still oval, similar to the original shape (Figure 4.7 G, H).

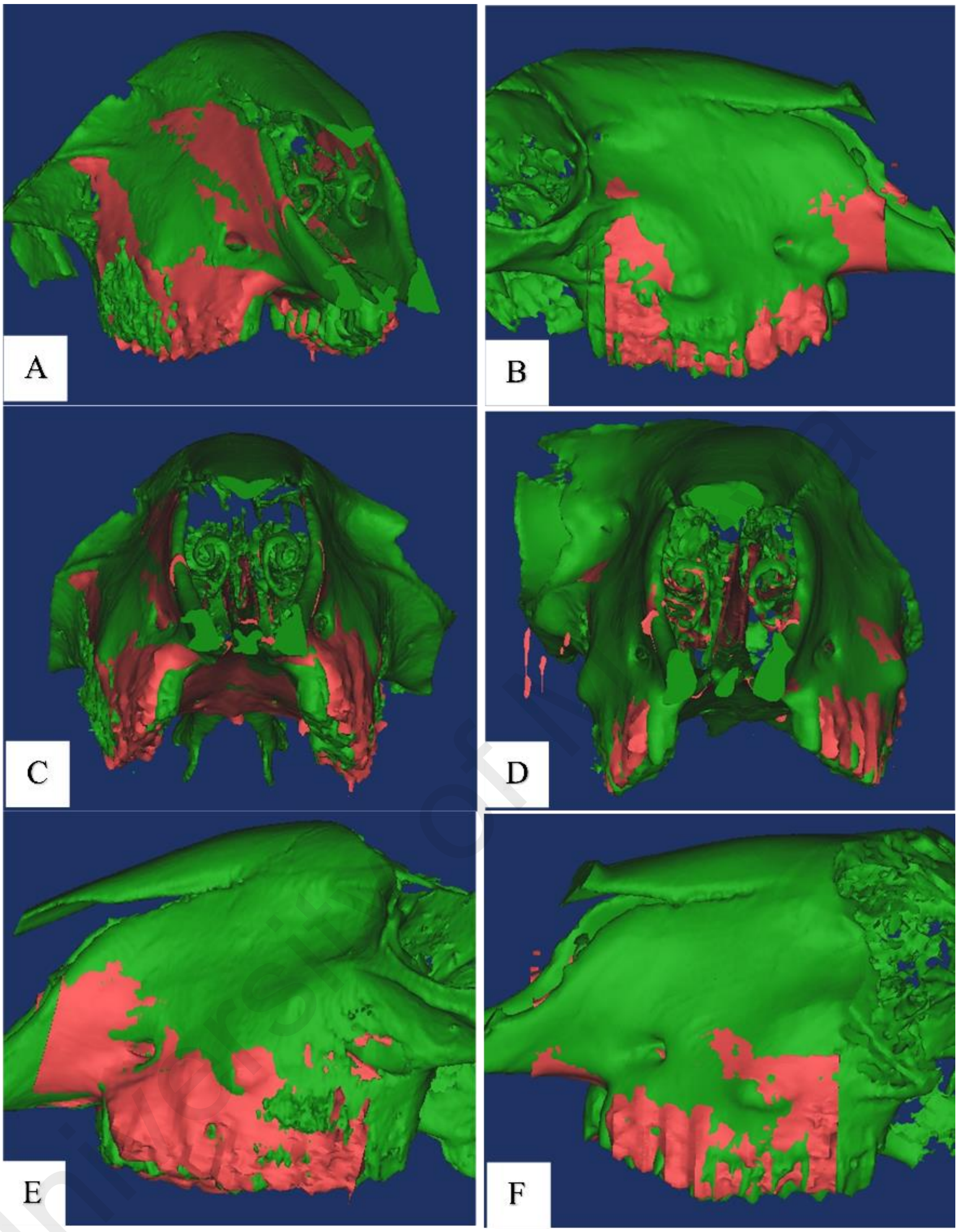


Figure 4.6: Comparison the skeletal changes of transverse maxillary arch in Group 1 (ABPC + RME) and Group 2 (conventional RME). Superimposition the sheep skull before treatment (green) and after retention period (red) revealed the difference in skeletal change pattern in Group 1 (A, C, E) and Group 2 (B, D, F) from right side (A, B), from front side (C, D), and left side (E, F). The buccal alveolar segment at the premolar regions in Group 1 increased greater than Group 2. The skeletal increment at the hard palatal level in Group 2 was very obscured.

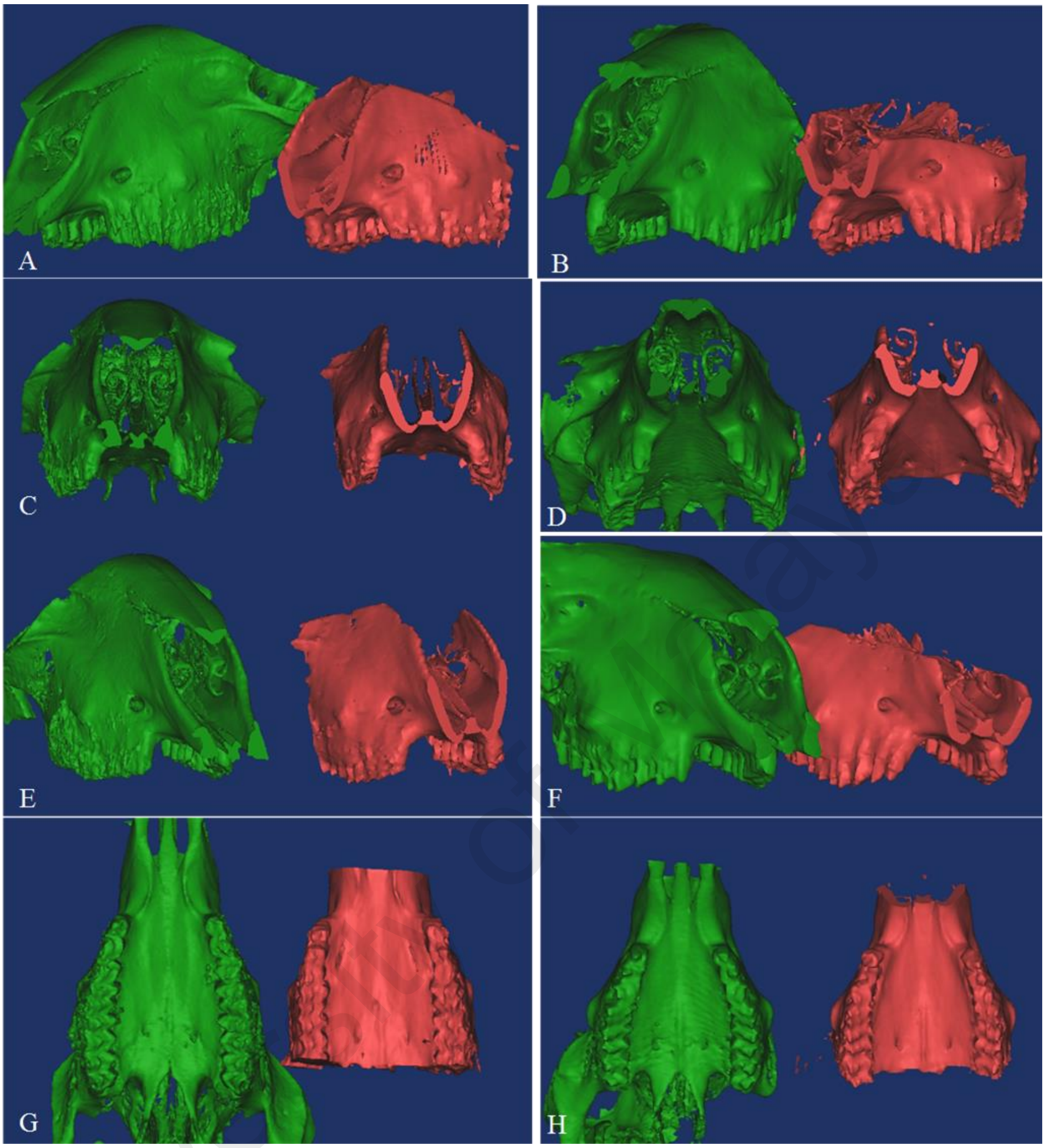


Figure 4.7: Comparison the dental and skeletal changes of transverse maxillary arch before and after retention period in Group 1 (ABPC + RME) and Group 2 (conventional RME).

Differences in before intervention (green) and after (red) retention period between Group 1 (A, C, E, G) and Group 2 (B, D, F, H) from left side (A, B), from front side (C, D), from right side (E, F) and from occlusal view (G, H). The palatal shape in Group 1 was U-shaped (C) while it was V-shaped in Group 2 (D). The premolar teeth in Group 1 arranged in parallel rows (G) whereas the shape of the dental arch from occlusal view in Group 2 was similar to the original shape (H).

4.4 MicroCT and histological features of the buccal alveolar bone at 4- and 12-week retention

4.4.1 Changes in buccal alveolar bone thickness at 4- and 12-week retention

The buccal alveolar bone thickness at the premolar regions measured on microCT images after the two retention periods in three groups are presented in Table 4.14. One-way ANOVA with Bonferroni post hoc was applied to compare the difference among groups after 4- and 12-week retention.

Table 4.14: Buccal alveolar bone thickness (measured on microCT images) in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4- and 12-week retention.

Buccal bone thickness (mm)	Group 1 (n=6) Mean ± SD	Group 2 (n=6) Mean ± SD	Group 3 (n=6) Mean ± SD	*p*-value*
4-week retention				
P1	1.99 ± 0.50	2.02 ±0.49	2.15 ±0.36	ns
P2	2.51 ±0.67	1.90 ± 0.85	2.53 ±0.75	ns
P3	2.35 ±0.78	2.00 ± 0.95	2.46 ±0.79	ns
Average	2.29 ±0.66	1.97 ±0.85	2.38 ±0.63	ns
12-week retention				
P1	1.89 ±0.54	1.24 ± 0.57	2.11 ±0.82	ns
P2	1.98 ±0.56	1.32 ±0.33	2.40 ±0.91	s[a]
P3	2.25 ±0.73	1.60 ±0.52	2.58 ± 0.49	s[b]
Average	2.04 ±0.59	1.38 ±0.48	2.36 ±0.74	s[c]

ns: non-significant difference (*p* >0.05); s: significant difference (*p*< 0.05).
P1, first premolar; P2, second premolar; P3, third premolar.
G1: Group 1; G2: Group 2, G3: Group 3.
*Anova with Bonferroni post hoc for comparison among groups.

[a] G2 < G3 (s).
[b] G2 < G3 (s).
[c] G1 > G2 (s); G2 < G3 (s).

At 4-week retention, the mean buccal alveolar bone thickness in the two intervention groups decreased slightly compared to that of control group ($p > 0.05$). At 12-week retention, this value in Group 2 decreased significantly compared to the other groups ($p < 0.05$). Although the mean buccal alveolar bone thickness decreased in Group 1 at 12-week retention, the mean still showed no significant difference to the control ($p > 0.05$).

4.4.2 MicroCT and histological features of the buccal alveolar bone at 4- and 12-week retention

MicroCT features of the buccal cortical bone in all groups after retention periods were illustrated in Figures 4.8, 4.9 and 4.10.

In the control group, the buccal cortex was thick, dense and dark yellow similar to the color of the dentine (Figure 4.8). In human body, the most highly mineralised substance is enamel, followed by dentine and bone. The mineralisation of the cortical bone is much higher than the inner cancellous bone. Therefore, the cortical bone showed a dense and dark yellow feature similar to the feature of the dentine while the cancellous bone was porous with lighter yellow, orange or slightly purple.

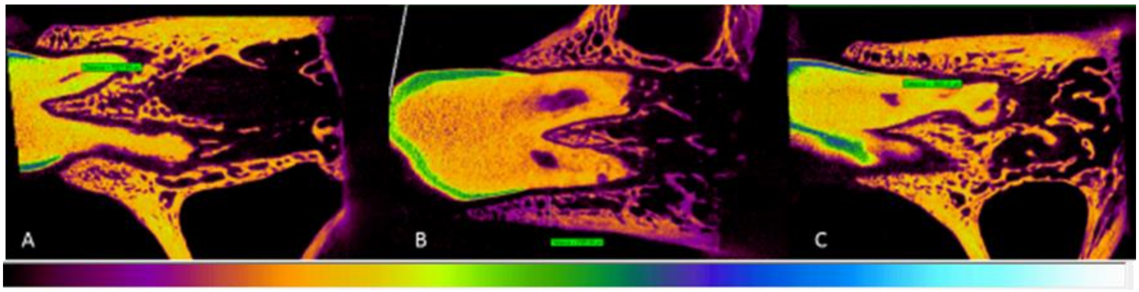


Figure 4.8: Normal cortical bone features in Group 3 (control) showed thick and dense cortical bone.

The cortical bone in APBC + RME group showed two features, i.e., the bone apposition and the bone resorption/demineralised features (Figure 4.9). The former feature had two layers of bone and the buccal cortex increased in thickness. The outside layer was purple, porous and thick lying on the old bone layer (Figures 4.9 A, B, D and E). The purple color was darker than that of the cancellous bone in the control group which showed less demineralised bone formed. The below old bone layer was dark yellow and denser which was similar to the normal feature of the control group. The second feature of the cortical bone in APBC + RME group was purple, porous and thinner compared to that of the control (Figures 4.9 C and F) which illustrated a resorption or demineralisation occurred.

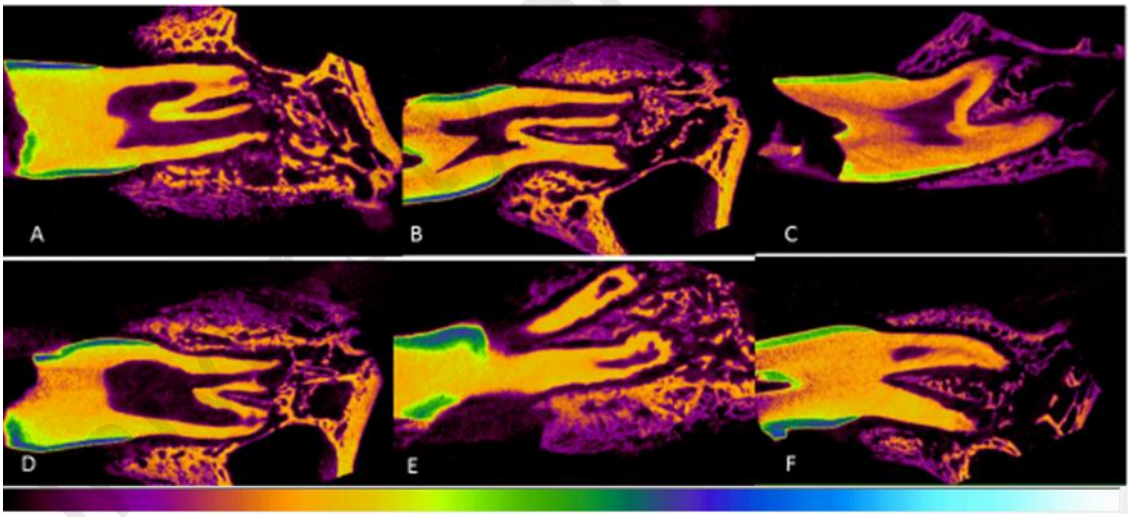


Figure 4.9: The buccal cortical bone features after retention period in Group 1 (ABPC + RME). It revealed two features: new bone apposition (purple colour in A, B, D, E images) on the surface of buccal cortex which increased the cortical thickness and resorption/demineralised feature (C, F), which decreased the thickness of buccal cortex.

In Group 2, the cortical bone was thinner and purple especially at the alveolar crest which showed that these areas underwent bone resorption and demineralisation when it was compared to the control (Figure 4.10).

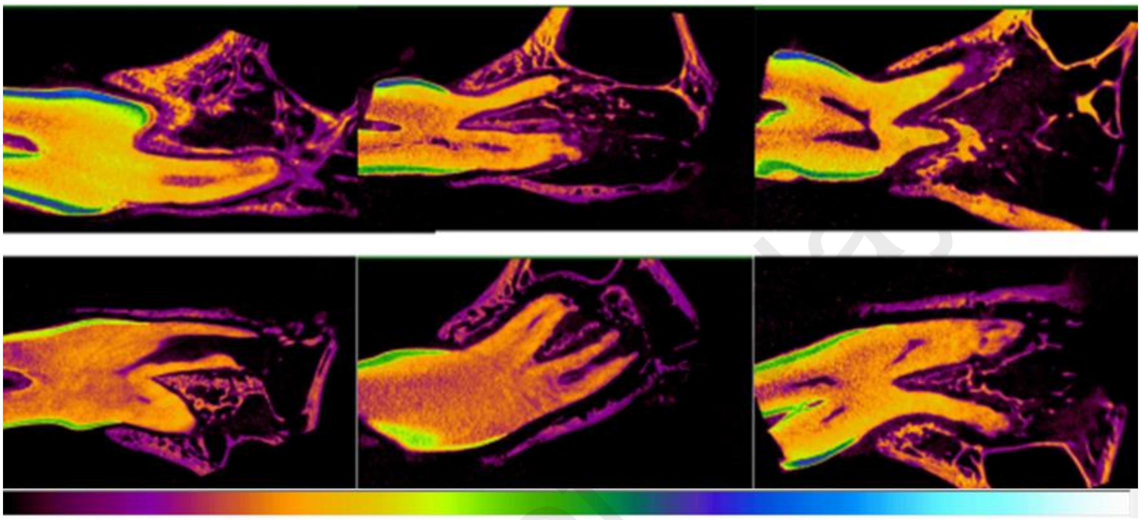


Figure 4.10: The buccal cortical bone features after retention period in Group 2 (conventional RME). Images showed that the cortical thickness became thinner or less mineralisation especially at the alveolar crest.

The histological changes of buccal cortical bone after the two retention period in all groups had similar features to those of microCT (Figures 4.11, 4.13 and 4.15). In the control group, the buccal alveolar bone was thick and dense (Figure 4.11) with clear cement lines (Figure 4.12)

Figure 4.11. Histological feature of the buccal cortex in Group 3 (control group).
Normal feature of the buccal cortical bone seen at 40x magnification (A, C) and at 10x magnification (B, D).

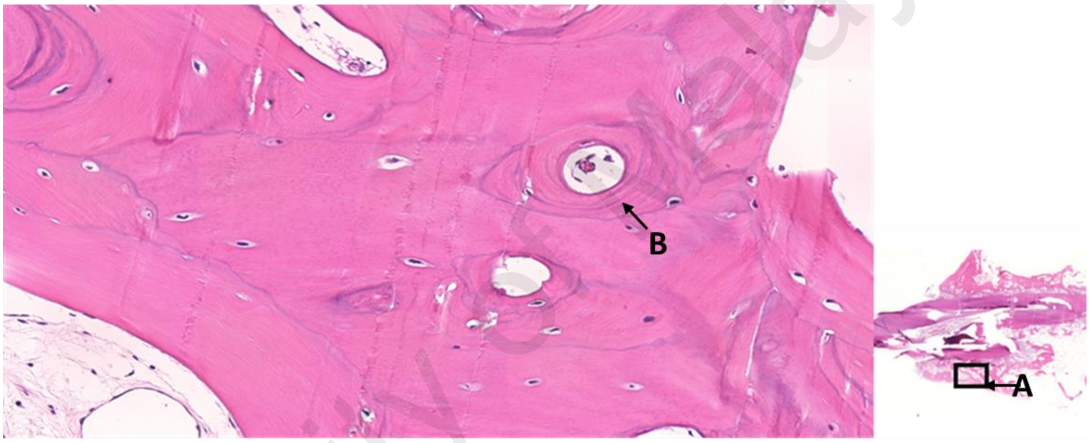


Figure 4.12: Normal feature of cortical bone in Group 3 (control group).
A: representative area (black rectangular); bone is compact with clear cement lines at 800x magnification (black arrow B).

In Group 1 (ABPC + RME), the buccal cortex showed two features: bone apposition at the surface of buccal cortex and resorption/demineralised feature. The former feature showed two clear layers- a layer of new bone formation on the old basal bone layer (Figures 4.13 A-H). The new bone was porous, woven and less compact (Figure 4.14 A) while the old bone below was compact with clear cement lines (Figure 4.14 B). The bone apposition increased the thickness of buccal alveolar bone. The latter feature included only one layer which showed a decrease in the thickness and density of the buccal alveolar bone (Figures 4.13 I-L).

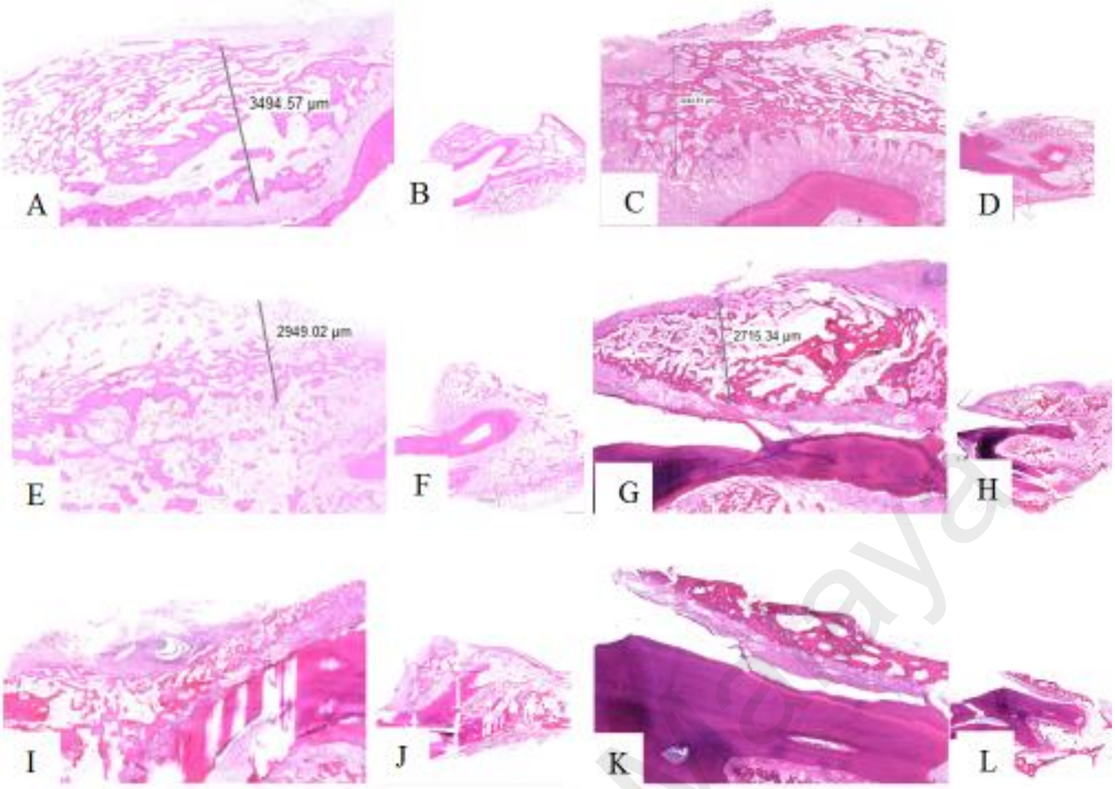


Figure 4.13: The feature of buccal cortical bone in Group 1 (ABPC + RME). The images showed two features: buccal bone apposition in two layers, new bone above and old bone below (A, B, C, D, E, F, G, H) and resorption/demineralisation (I, J, K, L). The buccal cortical bone of Figure B, D, F, H, J, L were magnified (A, C, E, G, I, K).

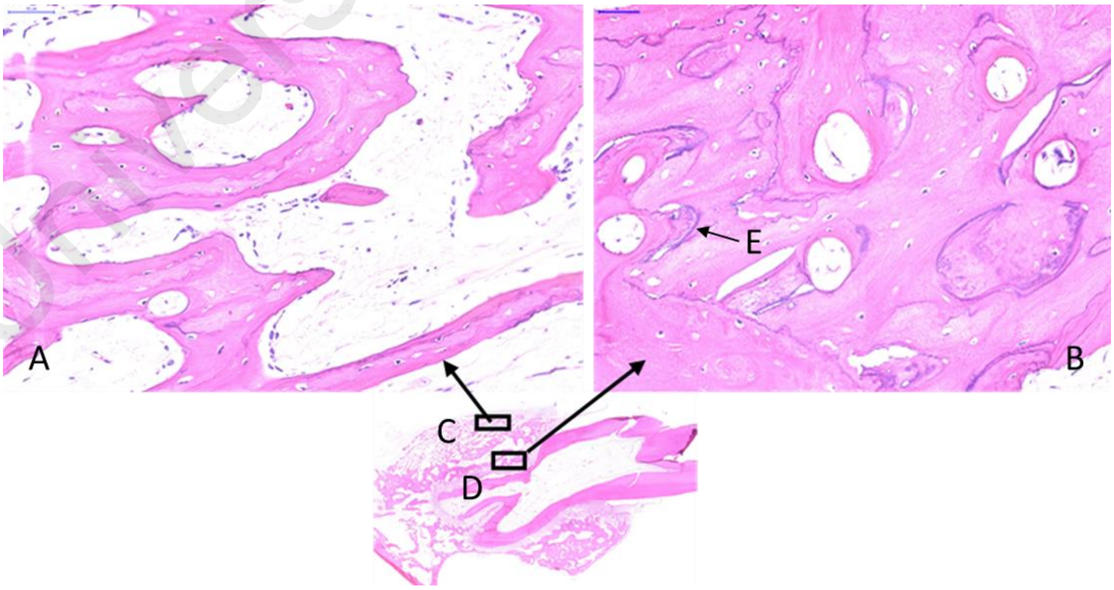


Figure 4.14: Histological feature of buccal cortex in Group 1 (ABPC + RME). A: magnified image from C showed feature of new bone; B: magnified image from D showed feature of old bone below. E: cement line in old cortical bone.

In conventional RME, buccal cortex was dense but thin especially at the alveolar crest region (Figure 4.15).

Figure 4.15: Histological feature of buccal cortex in Group 2 (conventional RME). The images showed thinner/demineralised feature especially at the alveolar crest region.

Table 4.15 illustrated the distribution of sheep according to the histomorphological changes of buccal cortical bone as presented in Figures 4.11, 4.13 and 4.15 in Group 1 and 2 at 4- and 12- week retention. In Group 1, two third of sheep showed bone apposition and the remaining had buccal bone resorption or demineralisation. In contrast, resorption/demineralisation was dominant in Group 2.

Table 4.15: Distribution of sheep according to histological changes of buccal alveolar cortical bone in Group 1 (ABPC + RME) and Group 2 (conventional RME) at 4- and 12-week retention.

Feature of cortical bone	Group 1		Group 2	
	4-week retention (n=3)	12-week retention (n=3)	4-week retention (n=3)	12-week retention (n=3)
New bone apposition	2	2	0	0
Bone resorption/Demineralisation	1	1	3	3

4.5 Bone microstructure changes in the furcation bone at 4- and 12-week retention

Shapiro-Wilk test demonstrated that the data were normally distributed ($p > 0.05$). Thus, parametric tests were applied for further analysis. Paired *t*-test was used to test the difference between before treatment and after retention period in each group. There was no significant difference between before intervention and after retention periods for all values (BV/TV, Tb.Th, Tb.Sp and Tb.N) ($p > 0.05$). Two-way ANOVA with Bonferroni post hoc was applied to compare the difference among groups at 4 and 12 weeks retention periods. ICC's were 0.95, 0.96, 0.97 and 0.94 for BV/TV, Tb.Th, Tb.Sp and Tb.N respectively.

BV/TV, Tb.Th, Tb.Sp and Tb.N in the control group were stable over the retention period ($p > 0.05$, Tables 4.16 and 4.17), thus these values can be considered as baseline to compare the changes in the other groups.

Bony microstructure changes at 4-week retention in the three groups were presented in Table 4.16. At this point of time, BV/TV in both intervention groups and at every premolar region decreased significantly compared to the control group ($p < 0.05$) except for the value of the first premolar in Group 1 ($p > 0.05$). Conspicuously, this value of first premolar in Group 1 was at the highest while this value of third premolars was at the lowest. Overall, BV/TV values at the first premolars regions were significantly higher than that of the third premolars ($p < 0.05$, Table 4.16). Therefore, there is a difference in BV/TV changes according to tooth position.

Table 4.16: Bony microstructural changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention.

Bone structural parameters (unit)	**4 weeks**			
	BV/TV (%) **Mean ± SD**	**TbTh (μm)** **Mean ± SD**	**TbSp (μm)** **Mean ± SD**	**TbN (1/μm)** **Mean ± SD**
Group 1 (n=6)				
P1	37.79 ± 6.01	88.11 ± 16.79	99.78 ± 10.43	0.0042 ± 0.0009
P2	33.07 ± 7.91^{b}	83.83 ± 13.99	108.92 ± 21.69	0.0039 ± 0.0006
P3	25.04 ± 8.70^{c}	74.17 ± 21.04^{d}	111.56 ± 30.08	0.0034 ± 0.0008
Group 2 (n=6)				
P1	31.46 ± 4.60^{a}	72.53 ± 14.50	127.08 ± 19.46	0.0044 ±0.00080
P2	33.66 ± 4.42^{b}	91.64 ± 11.48	146.27 ± 34.26	0.0038 ± 0.0010
P3	27.80 ± 7.51^{c}	93.25 ± 33.36	135.48 ± 31.99	0.0032 ± 0.0012
Group 3 (n=6)				
P1	46.98 ± 6.39^{a}	99.11 ±15.33	119.03 ± 23.91	0.0053 ± 0.0020
P2	48.17 ± 6.73^{b}	113.69 ± 25.21	134.69 ± 28.22	0.0051 ± 0.0029
P3	46.03 ± 8.90^{c}	119.39 ± 44.61^{d}	121.75 ± 24.71	0.0041 ± 0.0010
Source*p*-value*				
Teeth	0.029 (P1 vs P3)	0.435	0.326	0.174
Group	0.000 (G1 vs G3; G2 vs G3)	0.002 (G1 vs G3; G2 vs G3);	0.013 (G1 vs G2)	0.638
Teeth× Group	0.301	0.431	0.966	0.977

P1, first premolar; P2, second premolar; P3, third premolar; G1: Group 1; G2: Group 2, G3: Group 3.

See Table 3.2 for the definitions of each measurement; BV/TV: bone volume fraction; TbTh: trabecular thickness; TbSp: trabecular spacing; TbN: trabecular number.

*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

After 12-week retention, BV/TV, Tb.Th, and Tb.N values in all groups were higher than the values at 4-week retention ($p > 0.05$, Table 4.16 and 4.17). Although TbTh, TbSp and TbN values were not statistically different compared with those of control ($p > 0.05$), BV/TV values in both intervention groups were still significantly lower than that of the control ($p < 0.05$). Except for the first premolar (P1) in Group 1 and the third premolar in (P3) Group 2, BV/TV values in all groups and subgroups returned to approximately 80% relative to those of control at 12-week retention (Figure 4.16). This value was noticeably high in the first premolar region of Group 1 (92.10% of the control) (Figure 4.16). BV/TV values in the third premolar region (P3) in Group 2 increased very little from 4- and 12-week retention (from 27.80% to 28.73%, Table 4.16 and 4.17). After 12-week retention, this value was still far lower than the control value (just approximately 60.71% of the control) ($p < 0.05$, Figure 4.16).

Table 4.17: Bony microstructural changes in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention.

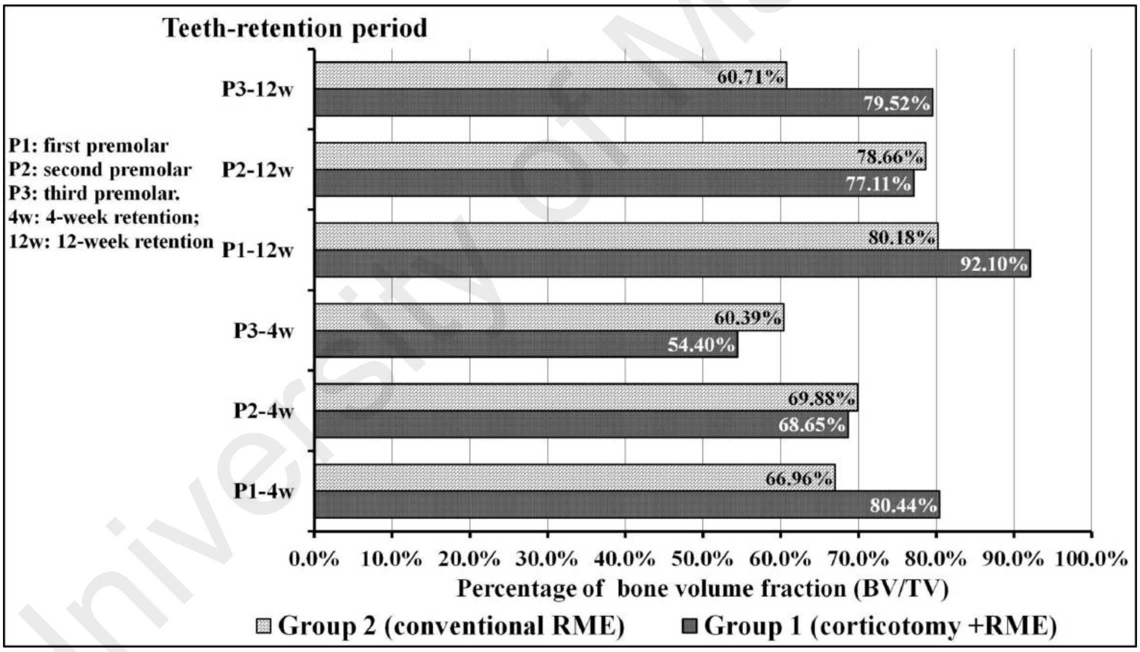
Bone structural parameters (unit)	12 weeks			
	BV/TV (%) Mean ± SD	**TbTh (µm) Mean ± SD**	**TbSp (µm) Mean ± SD**	**TbN (1/µm) Mean ± SD**
Group 1 (n=6)				
P1	43.95 ± 4.73	92.12 ± 11.18	87.62 ± 21.81	0.0048 ± 0.0006
P2	37.72 ± 9.85	100.98 ± 17.10	130.27 ± 40.33	0.0038 ± 0.0010
P3	37.63 ± 4.25	89.07 ± 18.57	102.32 ± 23.74	0.0043 ± 0.0014
Group 2 (n=6)				
P1	38.26 ± 6.17	86.69 ± 11.58	104.63 ± 18.07	0.0045 ± 0.0013
P2	38.74 ± 7.44	113.32 ± 30.61	149.70 ± 26.35	0.0037 ± 0.0011
P3	28.73 ± 4.34	92.49 ± 36.85	156.62 ± 27.87	0.0028 ± 0.0010
Group 3 (n=6)				
P1	47.72 ± 6.49	99.11 ± 13.61	116.44 ± 26.28	0.0054 ± 0.0023
P2	48.92 ± 7.06	114.75 ± 27.54	127.76 ± 16.17	0.0052 ± 00300
P3	47.32 ± 9.29	119.06 ± 21.47	118.55 ± 28.48	0.0049 ± 0.0022
Source*p*-value*				
Teeth	0.062	0.083	0.004 (P1 vs P2)	0.353
Group	0.000 (G1 vs G3; G2 vs G3);	0.067	0.010 (G1 vs G2)	0.567
Teeth× Group	0.248	0.570	0.179	0.519

P1, first premolar; P2, second premolar; P3, third premolar; G1: Group 1; G2: Group 2, G3: Group 3..

See Table 3.2 for the definitions of each measurement; BV/TV: bone volume fraction; TbTh: trabecular thickness; TbSp: trabecular spacing; TbN: trabecular number.

*Two-way ANOVA with Bonferroni post hoc for comparison among groups

Figure 4.16 illustrates the changes of BV/TV values to that of the control at 4- and 12-week retention. The relative values of BV/TV to the control for the second and third premolar regions in Group 1 were from 54.4% to 68.65% which were slightly less than those of Group 2 (60.39%-69.88%) (Figure 4.16). This value of the first premolar in Group 1 was 80.44% (Figure 4.16). Tb.Th and Tb.N values in both intervention groups were also lower than that of control but only the difference of the former was significant ($p < 0.05$). Tb.Sp value in Group 1 was significantly smaller than that of Group 2 ($p < 0.05$, Table 4.16).



P1: first premolar; P2; second premolar; P3: third premolar.
4w: 4-week retention; 12w: 12-week retention.

Figure 4.16: Relative percentage of bone volume fraction at premolar regions to the control in Group 1 (ABPC + RME) and Group 2 (conventional RME) at 4- and 12-week retention.

Figure 4.16 showed that the distinct difference in relative percentage of bone volume fraction were at the first and third premolar regions. Therefore, the bone microstructure data of the banded teeth (P1 and P3) in three groups was pooled and analyzed as shown in the Tables 4.18 and 4.19. At 4-week retention, pooled BV/TV and Tb.Th values in both intervention groups were significantly lower than that of the control ($p < 0.05$, Table 4.18).

Table 4.18: Difference in bony microstructural changes of banded teeth (P1+P3) in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention .

Bone structural parameters (unit)	4-week retention			*p*-value*
	Group 1 (n=12) Mean ± SD	Group 2 (n=12) Mean ± SD	Group 3 (n=12) Mean ± SD	
BV/TV (%)	31.41 ± 9.76	29.64 ± 6.24	46.50 ± 7.40	s^a
TbTh (um)	81.15 ± 19.56	82.89 ±26.81	109.25 ±25.22	s^b
TbSp (um)	105.67 ±22.33	131.28 ± 25.62	120.39 ±23.23	s^c
TbN (1/um)	0.0038 ±0.0009	0.0038 ±0.0012	0.0047 ±0.0016	ns

ns: non-significant difference (p >0.05); s: significant difference (p< 0.05).
P1, first premolar; P3, third premolar;
G1: Group 1; G2: Group 2, G3: Group 3.
P_p: *p* value of P1 and P3; P_{Gr}: *p* value of Group 1, Group 2 and Group 3.
See Table 3.2 for the definitions of each measurement; BV/TV: bone volume fraction; TbTh: trabecular thickness; TbSp: trabecular spacing; TbN: trabecular number.
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.
^{a}G1 < G3 (s); G2 < G3 (s);
^{b}G1 < G3 (s); G2 < G3 (s);
^{c}G1 < G2 (s).

However, at 12-week retention, only the pooled BV/TV value of Group 2 were significantly lower than that of Group 3 ($p < 0.05$, Table 4.19). At this point of time, the pooled BV/TV value of Group 1 was significantly higher than that of Group 2 and 3 ($p <$ 0.05, Table 4.19). The relative percentage of pooled BV/TV value of Group 1 to the baseline at 4-week was 67.5% which was slightly higher than that of Group 2 (63.74%). However, at 12-week retention, this value increased noticeably in Group 1 to 85.8% while it was still significantly lower, i.e., 70.47% in Group 2 ($p < 0.05$, Figure 4.16). As a result, the pooled BV/TV value of the banded teeth (P1 and P3) in ABPC + RME group was statistically higher than that of conventional RME group at 12-week retention ($p < 0.05$, Table 4.19).

Table 4.19: Difference in bony microstructural changes of banded teeth (P1+P3) in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention

Bone structural parameters (unit)	12-week retention			*p*-value*
	Group 1 n=12) Mean ± SD	Group 2 (n=12) Mean ± SD	Group 3 (n=12) Mean ± SD	
BV/TV (%)	40.78 ± 5.41	33.49 ± 7.11	47.52 ± 7.64	s^a
TbTh (um)	90.60 ±14.70	89.59 ±26.22	109.08 ±20.06	s^b
TbSp (um)	94.98 ±20.98	130.63 ±35.19	117.50 ± 26.15	s^c
TbN (1/um)	0.0045 ±0.0011	0.0038 ±0.0013	0.0052 ±0.0022	ns

ns: non-significant difference (p >0.05); s: significant difference (p< 0.05).
P1, first premolar; P3, third premolar;
G1: Group 1; G2: Group 2, G3: Group 3.
P_p: *p* value of P1 and P3; P_{Gr}: *p* value of Group 1, Group 2 and Group 3.
See Table 3.2 for the definitions of each measurement; BV/TV: bone volume fraction; TbTh: trabecular thickness; TbSp: trabecular spacing; TbN: trabecular number.
*Two-way ANOVA with Bonferroni post hoc for comparison among groups.
^{a}G1 > G2 (s); G2 < G3 (s);
^{b}G2 < G3 (s);
^{c}G1 < G2 (s).

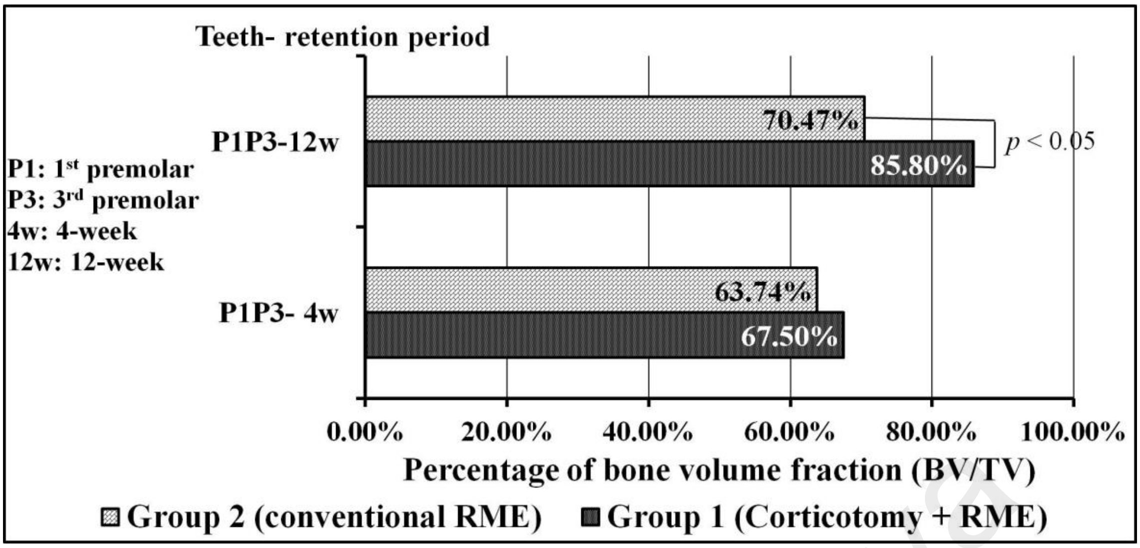


Figure 4.17: The relative percentage of bone volume fraction (BV/TV) to the control group of the banded teeth (first premolars and third premolars) in Group 1 (ABPC +RME group) and Group 2 (conventional RME group) at 4 and 12-week retention.

4.6 Histomorphometric analysis of the new bone formation in ABPC + RME group, conventional RME group and control group at 4- and 12-week retention

Histological changes of the new bone and old bone in area (µm^2) in the three groups at 4- and 12-week retention were illustrated in Table 4.18 and 4.19. Shapiro-Wilk test showed that the data were normally distributed ($p > 0.05$). Thus, two-way ANOVA with Bonferroni post hoc was applied to compare the difference among groups at 4- and 12-week retention. ICC's were 0.93, 0.96, and 0.97 for NB (new bone), OB (old bone) and TT (total tissue) respectively.

At 4 week retention, the ratio values related to new bone change (NBF and TNBF) of Group 1 were the highest and those of Group 3 were the lowest and vice versa for the ratio values related to old bone (OBF and TOBF) ($p < 0.05$, Table 4.20). Thus, new bone formation was very active in Group 1 at this point of time. The NBF and TNBF values in Group 1 were approximately two to four times those of Group 2 and 3. This difference might be due to the RAP which related to corticotomy surgery performed in Group 1. RAP plays an important role in increasing the bone turnover (Sebaoun et al., 2008). The new bone formation of Group 2 was just slightly higher than that of the control group ($p > 0.05$, Table 4.20). The TBF values in two intervention groups were significantly lower than that of control ($p < 0.05$, Table 4.20) which showed an overall decrease in the quantity of alveolar bone during experimental period.

Table 4.20: The new bone and old bone component in supporting tissue in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 4-week retention.

Ratio of bone parameters	**4 weeks**				
	NBF **Mean ± SD**	**OBF** **Mean ± SD**	**TNBF** **Mean ± SD**	**TOBF** **Mean ± SD**	**TBF** **Mean ± SD**
Group 1 (n=3)					
P2	0.199 ± 0.075	0.801 ± 0.075	0.003 ± 0.0002	0.013 ± 0.007	0.015 ± 0.006
P3	0.165 ± 0.059	0.835 ± 0.059	0.002 ± 0.0006	0.010 ± 0.003	0.012 ± 0.004
Group 2 (n=3)					
P2	0.055 ± 0.030	0.945 ± 0.030	0.001 ± 0.0003	0.018 ± 0.005	0.019 ± 0.005
P3	0.064 ± 0.032	0.936 ± 0.032	0.001 ± 0.0002	0.014 ± 0.011	0.015 ± 0.011
Group 3 (n=3)					
P2	0.035 ± 0.011	0.965 ± 0.011	0.001 ± 0.0002	0.031 ± 0.009	0.032 ± 0.009
P3	0.041 ± 0.018	0.959 ± 0.018	0.001 ± 0.0002	0.033 ± 0.016	0.034 ± 0.016
Source/P-value					
Teeth	0.777	0.777	0.043 (P2 vs P3)	0.753	0.709
Group	0.000 (G1 vs G2; G1 vs G3)	0.000 (G1 vs G2; G1 vs G3)	0.000 (G1 vs G2; G1 vs G3)	0.009 (G1vs G3; G2 vs G3)	0.011 (G1 vs G3, G2 vs G3)
Teeth× Group	0.650	0.447	0.152	0.883	0.859

P2, second premolar; P3, third premolar; G1: Group 1; G2: Group 2, G3: Group 3.

See Table 3.3 for the definitions of each measurement; NBF: new bone fraction; OBF: old bone fraction; TNBF: total new bone fraction; TOBF: total old bone fraction; TBF: total bone fraction.

*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

At 12-week retention, the amount of new bone formation in ABPC + RME group slightly decreased but it was still significantly higher than those of Group 2 and 3 ($p < 0.05$, Table 4.21). At this point of time, the ratio values related to new bone area (NBF and TNBF) were approximately two to three times that of Group 2 and 3. These ratio values in Group 2 was just slightly higher than that of control group ($p > 0.05$). Interestingly, it might be due to the high activity of new bone formation, the total bone fraction (TBF) of Group 1 was not significantly lower than that of control ($p > 0.05$) while this value in Group 2 was still rather low ($p < 0.05$). The TBF values in Group 1 followed a clear increase trend from 4-week to 12-week retention while the trend of this ratio in Group 2 was not clear.

Table 4.21: The new bone and old bone component in supporting tissue in Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group) at 12-week retention.

Ratio of bone parameters	**12 weeks**				
	NBF **Mean ± SD**	**OBF** **Mean ± SD**	**TNBF** **Mean ± SD**	**TOBF** **Mean ± SD**	**TBF** **Mean ± SD**
Group 1 (n=3)					
P2	0.116 ±0.046	0.912 ±0.036	0.003±0.0008	0.023 ±0.005	0.025 ±0.006
P3	0.125 ±0.045	0.875 ±0.045	0.002±0.0007	0.016 ±0.001	0.019 ±0.001
Group 2 (n=3)					
P2	0.081 ±0.054	0.919 ±0.055	0.001±0.0008	0.014 ±0.002	0.015 ±0.001
P3	0.056 ±0.026	0.944 ±0.026	0.001±0.0003	0.015 ±0.003	0.017 ±0.003
Group 3 (n=3)					
P2	0.031 ±0.016	0.971 ±0.018	0.001±0.0009	0.031 ±0.011	0.032 ±0.012
P3	0.032 ±0.010	0.968 ±0.010	0.001±0.0002	0.030 ±0.010	0.031 ±0.010
Source/P-value					
Teeth	0.78	0.766	0.356	0.523	0.517
Group	0.004 (G1 vs G3)	0.009 (G1 vs G3)	0.003 (G1vs G2; G1vs G3)	0.004 (G1 vs G3; G2 vs G3)	0.006 (G2 vs G3)
Teeth× Group	0.371	0.337	0.954	0.552	0.605

P2, second premolar; P3, third premolar; G1: Group 1; G2: Group 2, G3: Group 3.

See Table 3.3 for the definitions of each measurement; NBF: new bone fraction; OBF: old bone fraction; TNBF: total new bone fraction; TOBF: total old bone fraction; TBF: total bone fraction.

*Two-way ANOVA with Bonferroni post hoc for comparison among groups.

Figure 4.18 illustrated the changes in the total new bone formation (TNBF) at 4- and 12-week retention in three groups. Overall, this ratio in ABPC + RME group was three times that of Group 2 and 3.

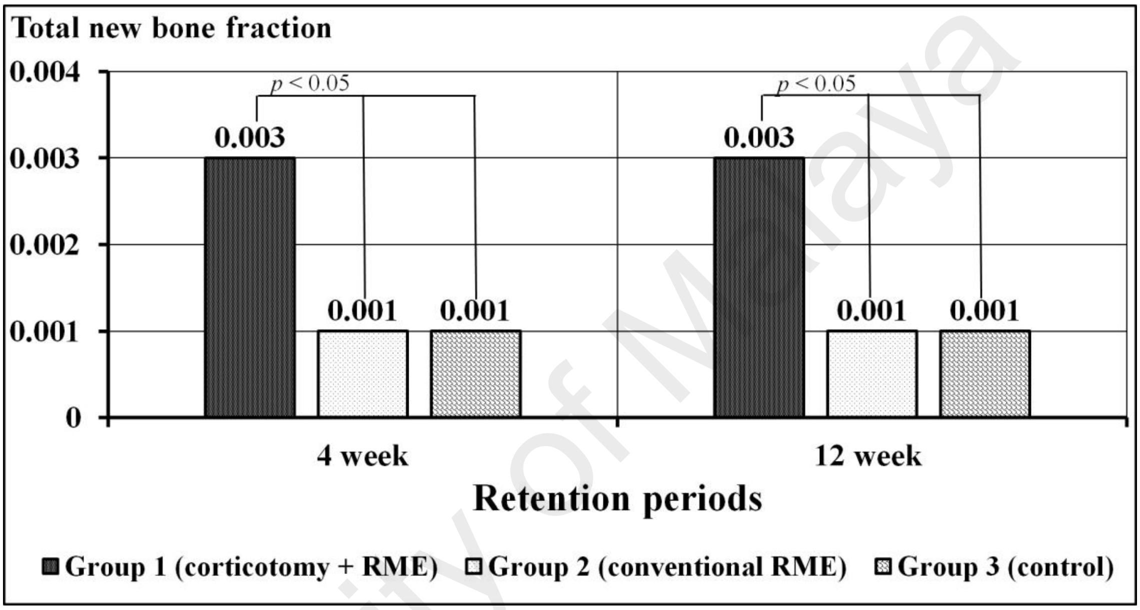


Figure 4.18: Changes in the total new bone fraction (the ratio of new bone to total tissue in the region of interest) in Group 1 (ABPC + RME), Group 2 (conventional RME) and Group 3 (control) at 4- and 12-week retention.

4.7. Quantification of blood vessels number in the furcation area at 4- and 12-week retention

The microvascular changes in the second and third premolar furcation region in three groups were presented in Table 4.22. Shapiro-Wilk test showed that the data were not normally distributed ($p < 0.05$). Thus, Kruskall Wallis test and pairwise comparisons were used to compare the difference among groups at 4- and 12-week retention. ICC's was 0.92.

Table 4.22 showed that the number of blood vessels in Group 1 at 4-week retention was statistically higher than that of Group 2 and 3 ($p < 0.05$). Subsequently, this value in Group 1 decreased at 12-week retention. Although the number of blood vessel in Group 1 was still higher than the other groups, no statistically significant was found at 12-week retention ($p > 0.05$, Table 4.20). In Group 2, the number of blood vessel was slightly higher than that of control throughout the retention period but showed no statistical difference compared with control group ($p > 0.05$).

Table 4.22: Comparison of microvascularisation in the second and third premolar furcation regions at 4- and 12-week retention between Group 1 (ABPC +RME group), Group 2 (conventional RME group) and Group 3 (control group).

	Group 1 (n=3) Mean ± SD (NBV/ mm^2)	**Group 2 (n=3) Mean ± SD (NBV/ mm^2)**	**Group 3 (n=3) Mean ± SD (NBV/ mm^2)**	***p*-value**
P2-4w	49.83 ± 12.41	34.67 ± 11.97	30.33 ± 9.31	G1 > G3 (s)
P2-12w	43.17 ± 10.98	34.33 ± 8.29	27.54 ± 5.04	ns
P3- 4w	61.50 ± 19.26	35.17 ± 6.55	31.83 ± 5.04	G1 > G2 (s) G1 > G3 (s)
P3-12w	44.00 ± 10.88	33.33 ± 7.17	28.75 ± 7.28	ns
P-value	ns	ns	ns	

ns: non-significant difference; s: significant difference.
P2: second premolar; P3: third premolar; G1: Group 1; G2: Group 2; G3: Group 3.
4w: at 4-week retention; 12w: at 12-week retention.
NBV/ mm^2: number of blood vessels per mm$^{2.}$
*Kruskal-Wallis test and pairwise comparisons to compare the difference among groups.

CHAPTER 5: DISCUSSION

5.1. Experimental set-up and animal selection

Selection of an appropriate animal model for maxillary expansion research is critical to allow the extrapolation of the findings to humans. Previous studies on maxillary expansion have been carried out on monkeys, rats, rabbits, cats, dogs, pigs, and sheep (Feng et al., 2014; Zhao et al., 2015; Li et al., 2012; Parr et al., 1997; Romanyk et al., 2013; Brin et al., 1981; Vardimon et al. 2005; Santiago et al., 2012; Tong et al., 2017; Kretschmer et al., 2010; Sun et al., 2011; Hoffer et al., 2075; Vardimon et al., 1989; Murray et al., 1970; Cleall et al., 1965; Cotton, 1978). The earliest studies investigating maxillary expansion were conducted in monkeys, because of the common belief that monkey had the most similar traits (morphology of the dentition) to human (Cleall et al., 1965; Cotton, 1978; Hoffer & Walters, 1975; Murray & Cleall, 1971; Vardimon et al., 1989). However, monkeys have a separated premaxilla and the midline suture does not run continuously throughout the palate. The connection between midline suture and two premaxillary-maxillary sutures has a Y-shape, which is different to that of human (Cleall et al., 1965; Cotton, 1978; Hoffer & Walters, 1975; Murray & Cleall, 1971; Vardimon et al., 1989). Thus, research findings based on monkeys would not reflect the effect of maxillary expansion in human beings.

Rodents such as mice, rats, and rabbits are very popular alternatives because of their small body size. Furthermore, these animals can be easily maintained in the laboratory environment. However, the small size of the palate of these animals could potentially hinder the insertion of screw-type maxillary expander intra orally. Therefore, studies related to maxillary expansion in rodents were performed using a helical spring design instead of an expansion screw (Altan et al., 2013; Erdogan et al., 2015; Feng et al., 2014; Kara et al., 2012; Liu et al., 2014; Özan et al., 2015; Zhao et al., 2015). However, the force produced by a helical spring is low, inconsistent and unreliable (Romanyk et al., 2010), thus this appliance is not suitable for maxillary expansion procedure in adult animals. In comparison to a helical spring, a screw-type maxillary expander is more stable and can deliver higher force, which is necessary to open the midpalatal suture particularly in mature subjects. Moreover, helical springs are not commonly used in humans (Romanyk et al., 2010). Hence, there is a need to utilise bigger animals with larger palate size such as cats, dogs and sheep which might allow the use of the bulky jackscrew (Brin et al., 1981; Kretschmer et al., 2010; Santiago et al., 2012; Tong et al., 2017; Vardimon et al., 1989). As cats and dogs have cone-shape teeth, the attachments need to be customized to ensure the stability of expander on the maxilla dentition (Santiago et al., 2012; Tong et al., 2017; Vardimon et al., 1989). Moreover, it is hard to find suppliers who breed and raise these animals for commercial stocks. Santiago et al. (2012) reported that they had to depend on the local availability of animals and accepted a convenient sample. Therefore, a standardized research methodology would be difficult to achieve.

In our study, the sheep was chosen as the animal of choice due to the size of its maxilla. Compared to those in rodents, the palate and dental arch in sheep are wider and more suitable for the planned procedures. In addition, as the shape of teeth in sheep were similar to that of humans, normal clinical bands could be utilized in fabricating the expanders. Moreover, this farm animal is easily sourced with required breed, age and weight. Our experiment was carried out at the Animal Experimental Unit, Faculty of Veterinary Medicine, UPM where the welfare of sheep were monitored systemically by experienced staff.

5.2. Linear and angular dental and skeletal changes produced by adjunctive buccal and palatal corticotomy for adult maxillary expansion.

The effectiveness and stability of maxillary expansion in adults have been the subject of discussions for many years. Tightly interdigitated midpalatal sutures and the increasing rigidity of the surrounding bones are reported to be the causes of failed orthopedic expansion in adult patients (Northway, 2011; Wertz, 1970; Bishara & Staley, 1987; Melsen, 1975). In 2001, Chung and co-workers suggested that decortication may overcome the rigidity of the surrounding bones with a technique known as “Speedy surgical orthodontics’. They reported successful treated adult with bimaxillary protrusion (Chung et al., 2001; Chunget al., 2009; Chung et al., 2009; Lee et al., 2007). Hence, this theory could be utilised in facilitating the maxillary expansion in non-growing subjects.

The control group in our study showed no meaningful alterations of the studied parameters before the treatment and post-retention, suggesting that the growth of the maxilla was relatively stable. This group was recruited in order to reduce bias or confounding factors related to the effect of the natural skull growth. In addition, the CBCT images taken at post-retention confirmed that there was no opening of the midpalatal suture as a result of the growth, suggesting that the net effect of expansion was due to the intervention employed, not the separation of the midpalatal suture.

According to the previous studies, conventional RME has been the treatment of choice for growing adolescent (Gurel et al., 2010; Lagravere et al., 2005; McNamara et al., 2003). However, nonsurgical maxillary expansion method has not been considered a viable option for adults because of the interdigitation of midpalatal suture. Accordingly, research on this approach for adults is rare. It was reported that the dental expansion by using nonsurgical method can be attained up to 5 mm without remarkable increase in transverse width at the basal bone (Cao et al., 2009; Handelman et al., 2000; Lin et al., 2015). Only one study reported that minimal expansion at the palatal roof (0.9 mm) was achieved when the gingival level was expanded up to 5.1 mm (Handelman et al., 2000). In general, the conventional maxillary expansion in adults can be achieved primarily by alveolar bending. The alveolar expansion at the palatal vault only contributed 18% of the total transarch increment (Handelman, 2011; Handelman, 1997; Handelman et al., 2000). Compared to the nonsurgical method in human (0.9 mm), the ABPC assisted expansion in our study showed a conspicuous basal bone expansion at the HP level (mean values: 2.9 mm at 4-weeks retention and 3.1 mm at 12-weeks retention). Transverse alveolar bone width at the Cr-Cr level expanded to 4.39 mm, thus, the increment at the HP level contributed to approximately 70% of the total bone expansion. The remaining 22-30% of the expansion was due to alveolar bending. Furthermore, the mean interpremolar width at 12-week retention increased by 8.17 mm, which was noticeably higher than the reported outcomes achieved by the nonsurgical approach. The percentage of basal bone enlargement to the dental expansion was 37.33% (3.05 mm/8.17 mm) at 12-week retention. Even in children, where it is believed that the skeletal expansion is dominant, this percentage is from 30% to 50% which is slightly higher than our results (Handelman, 2011; Handelman et al., 2000; Iseri & Ozsoy, 2004; Schilling et al., 1998). Therefore, the skeletal and dental expansions achieved by ABPC + RME in our study were conspicuously higher than those achieved by the conventional RME as reported in the literature.

In adults, SARME has been preferred by many clinicians for the treatment maxillary deficiency (Betts, 2016; Northway, 2011; Suri & Taneja, 2008). Currently, there are numerous reports on this modality. SARME can result in mean dental changes up to 12 mm with an average dental expansion of 8 mm (Lagravere et al., 2006). However, it has been suggested that expansion of more than 8 mm with SARME is not stable (Suri & Taneja, 2008, Chamberland & Proffit, 2011). Regarding skeletal changes, the amount of expansion at the maxillary base is 2 to 5 mm and 4 to 5 mm of expansion at the Cr-Cr level (Lagravere et al., 2006). The skeletal increment is achieved by complicated surgery including splitting midpalatal suture in combination with osteotomy, buccal corticotomy with/without pterygoid separation (Lagravere et al., 2006), then followed by maxillary expansion using a palatal expander. With ABPC, mean expansion at the HP level was 2.97 ± 0.94 mm at 4-week retention and still stable at 3.05 ± 1.45 mm at 12-week retention. The mean intercuspal width (Cu-Cu) in the present study was 11.11 ± 1.47 mm at 4-week retention but then reduced to 8.17 ± 1.66 mm at 12-week retention. Hence, the dental and skeletal expansion achieved by ABPC + RME in our study were slightly less than that achieved by SARME approach. However, SARME is not without adverse effect. Consistent clinical findings after SARME include widening of the nose which may be unfavourable in patients with a wide alar base (O'Ryan & Schendel, 1989). Other iatrogenic problems are facial swelling, sinus infection and severe haemorrhage (Handelman, 2011; Suri & Taneja, 2008).

Minor bone surgery has also been suggested to facilitate arch expansion (Echchadi et al., 2015; Lines, 1975). Corticotomy assisted maxillary expansion was first suggested by Lines in 1975 (Lines, 1975). This technique included the placement of a buccal incision at the maxillary sinus combined with splitting the midpalatal suture which resulted in the release of all resistance from the skull complexes. However, the dental and skeletal changes following this procedure were not described. Furthermore, this technique can be difficult for inexperienced surgeons. Recently, Echchadi et al. (2015) reported a simpler technique using piezo-bone perforations on the buccal alveolar for treatment of a maxillary transverse deficiency in a 14-year-old girl. They achieved 8.4 to 10.6 mm of dental expansion, which is approximately similar to our findings. In addition, changes in tooth inclination post treatment were also similar to our results (Echchadi et al., 2015)

(Table 4.3 and 4.4). Therefore, we believed that corticotomy can be used to enhance the treatment outcomes of RME in adults.

According to Chung and co-workers, when the cortical bone layer was interrupted around a targeted segment, the remaining medullary bone around that segment can be easily displaced by heavy force (Choo et al., 2011; Chung et al., 2001; Chung et al., 2009; Chung et al., 2007; Lee et al., 2007). With regard to nonsurgical maxillary expansion, alveolar displacement accounted for a large proportion of the total expansion, varying from 50% in children to 82% in adults (Handelman et al., 2000; Handelman, 2011). However, in adults, the cortical bone is more rigid; hence, expansion of the dental arch becomes more difficult with the nonsurgical approach. In our study, performing adjunctive buccal and palatal corticotomy breaks the continuity of the alveolar segment to the surrounding basal bone. As a result, the bony segments could be displaced buccally to compensate for any transverse maxillary deficiency and provide additional arch perimeter space. As the tooth apices were around the HP level, horizontal incisions on the buccal side were placed slightly higher than the HP level. Under the expansion force, the basal bone may act as a fulcrum for the outward movement of the alveolar bone. This could be the reason for the alveolar increments at the hard palatal level. Accordingly, our findings supported Chung’s theory for expansion of rigid alveolar in adults (Chung et al., 2001; Chung et al., 2007; Chung et al., 2009).

The recent development of ultrasonic device allows corticotomy to be performed under local anaesthesia. This device provides the advantages of minimal flap elevation for surgery, and less pain and associated risks (Robiony et al., 2007). However, the drawback is that the device is rather costly.

Our study has provided a new insight regarding the movement of a block of teeth in the lateral dimension for overcoming dental crossbites and transverse skeletal discrepancy in adults. However, further research needs to be carried out to clarify our finding because the craniofacial skeleton of sheep is evidently different from that of humans. In addition, variation in the rigidity and thickness of the cortical bone may have affected the results of our study. In our research, the intervention was carried out in a short period; hence, we were not able to assess the long term stability of the procedures in our study. Nevertheless, Chung and co-workers illustrated that fractured bone with adequate mineralisation would retain its final deformed shape permanently (Chung et al., 2001; Chung et al., 2007). Therefore, the remineralised decorticotomy segment is likely to be stable in its new buccal position and our outcomes are expected to be maintained in the long term.

In summary, adjunctive buccal and palatal corticotomy approach may be a potential treatment modality for moderate transverse maxillary deficiency in adults. In a sheep model, ABPC + RME showed a combination of skeletal and dental expansion. The dental expansion was approximately two to three times greater than the skeletal expansion. With the advantages of ABPC + RME, compensation treatment may be performed easily. ABPC might be performed at a selective segment of alveolar bone in treating unilateral maxillary deficiency. It can also provide the solution to expand the dental arch for bilateral maxillary deficiency cases. This procedure may also provide an increase in the vestibular region width, and widens the smile providing beneficial in selected cases. Furthermore, it may potentially minimize further enlargement of existing cleft defects, as it will not cause further enlargement of the existing cleft defects when expanding the alveolar segment.

5.3. Dental and skeletal changes produced by conventional RME.

Treating maxillary deficiency in adults with conventional RME has been a dilemma to orthodontists for many years. Until now, the controversy around the effectiveness and application of nonsurgical approach in adults still continues (Handelman, 2011; Northway, 2011). Conventional RME is believed to produce limited dental and skeletal expansion in adults (Handelman et al., 2000; Baydas et al., 2006; Bishara & Staley, 1987; Proffit et al., 2007). Moreover, it is painful and uncomfortable for some patients (Handelman et al., 2000).

Nonsurgical maxillary expansion has been employed in adults (Cao et al., 2009; Handelman, 2011; Lin et al., 2015). Filho and co-workers showed mixed results (maxillary expansion could achieve only in 81.5% of patients) when applying this approach in non-growing patients. Moreover, only moderate maxillary expansion was possible (Filho et al., 1996). Other authors found that the transverse interpremolar and intermolar widths increased by 4.7 mm at the cervical level and 5.9 mm at the cusp level. The average transverse alveolar expansion at the cervical level was 3.3 mm, while there was no increment at the basal bone or with a limited change was around 0.9 mm (Cao et al., 2009; Handelman et al., 2000). In our study, at 4-week retention, the mean interpremolar width increments were 5.06 ± 1.88 mm and 3.39 ± 1.63 mm at the Cu-Cu level and Pu-Pu level, respectively. These increment were slightly less than previous reports (Handelman, 1997; Handelman, 2000). However, the mean interpremolar widths at 12-week retention increased by 7.44 ± 2.49 mm at the Cu-Cu level and 4.39 ± 1.71 mm at the Pu-Pu level, which were greater than a previous study (Handelman et al., 2000). At 4-week retention, the mean transverse alveolar expansion at the Cr-Cr level was only 2.23 ± 0.93 mm and 0.39 ± 0.35 mm skeletal expansion at the HP level. Subsequently, at 12-week retention, the Cr-Cr value slightly increased to 2.91 ± 1.09 mm and the skeletal expansion at the HP level was 1.01 ± 0.87 mm, but the difference were not significant. Our findings of skeletal expansion at both evaluation periods were lower than previous studies (Handelman, 1997; Handelman et al., 2000). Therefore, nonsurgical expansion modality could produce dental changes in the non-growing subjects but only very little skeletal changes.

A protocol for successful application of conventional RME in adults was proposed by Chester Handelman, based on his cumulative experience (Handelman, 2011). Handelman and co-workers reported 47 successfully treated cases of adult patients between 18.8 and 49.3 years old with conventional RME using a Haas expander (Handelman, 1997; Handelman et al., 2000). After the active treatment phase, all patients were advised to wear the same appliances used in the active phase for eight to twenty-four weeks (averaged 12 weeks), followed by a removable retainer. The dental and skeletal changes post treatment in this study were also measured at the time of retention period. However, Handelman and co-workers followed a slower expansion protocol in which the screw was turned once daily. In case patients experienced pain or tissue swelling, they were instructed to stop turning the screw for one week (Handelman, 1997; Handelman et al., 2000). Overall, the successful treatment outcomes in this study might be due to long duration expansion as the accumulated force would slowly exert its effect during the retention periods when the cortical bone became thinner and more flexible. In parallel to the previous studies (Handelman, 1997; Handelman et al., 2000; Handelman; 2011), our results also showed that the maxillary expansion occurred slowly and for a longer duration. The dental and skeletal expansions in our study were higher at 12-week retention than at 4-week retention.

Cortical bone rigidity might influence the alveolar bone displacement. In humans, the total bone mass has been shown to be increased from adolescence to the middle-aged period (Boskey & Coleman, 2010; Hanschin & Stern, 1995; Lau & Adachi, 2011). Bone mass determines 75% to 85% of the ultimate bone strength (Schonau, 2004). Resistance to bending and torsion forces was demonstrated to be higher in the dense and compact bone than in the porous bone (Currey et al., 1996). Moreover, bone size and shape also contribute to bone strength (Ammann & Rizzoli, 2003; Boskey & Coleman, 2010; Jepsen, 2009; Wang & Seeman, 2008). In humans, the thickness of the buccal alveolar bone was reported to be approximately 2 mm (Brunetto et al., 2013; Rungcharassaeng et al., 2007), which is thinner than the sheep in our study (approximately 2.4 mm). Therefore, the buccal alveolar bone in sheep would be more rigid than that of humans. As a result, the dental and skeletal expansions in sheep were less than in the previous findings on humans (Handelman, 1997; Handelman et al., 2000). Brunetto et al. (2013) reported that major bone loss was found when a long duration of slow maxillary expansion (SME) was performed. In our study, buccal alveolar bone demineralisation and resorption features were observed by using microCT and histological images (Figures 4.9 and 4.12). The buccal alveolar bone was found to be thinner at 12-week retention than 4-week retention. The decrease in buccal alveolar thickness at 12-week might enhance greater teeth and alveolar bone displacements when compared to 4-week retention. Therefore, the buccal alveolar bone rigidity might explain why the expansion was rather difficult at the initial phase. When the cortex undergoes demineralisation, arch expansion in these patients might continue to take place.

The nature of maxillary expansion in adults has been extensively studied, however, the detailed mechanism has not been fully understood. According to Handelman et al. (2000), the displacement of the alveolar process primarily accounted for the possibility of maxillary expansion in adults. This expansion is referred as “rapid maxillary alveolar expansion”. A previous study showed that the expansion across the palatal vault increased by 18% at the palatal gingiva (Handelman et al., 2000). Similarly, results were found in our study, with a change of approximately 17% at 4-week retention and further increase to 34.7% at 12-week retention. Isaacson and Ingram (1964) demonstrated that it took five to six weeks for the expansion force to be completely dissipated to the tissues. Hyrax appliance used in our study was cemented to the crowns of premolars and the SuperScrew® was turned to 8 mm. At 4-week retention, the dental expansion was just approximately 5 mm, smaller than the amount of screw turning (8 mm). This observation suggested that the expansion force placed on the tooth crown might not be completely disseminated to the root and surrounding bone because of the high resistance of cortical bone in sheep. When the expander was retained on the crowns during the retention periods, pressure energy could be stored in the expander and gradually influenced the supporting bone in the subsequent weeks. Accordingly, the interpremolar and alveolar expanded more at 12-week retention compared to the previous time. The mean interpremolar width at the Cu-Cu level increased by 7.44 ± 2.49 mm at 12-week retention, which was very close to the amount of the screw turning (8 mm). However, the increase in interpremolar width at the Pu-Pu level and alveolar width at the Cr-Cr level was still reduced at 4.39 ± 0.88mm and 2.91 ± 1.09 mm, respectively. Accordingly, the nature of conventional RME expansion is primarily from the dentoalveolar complex displacement, which is in agreement with the previous findings (Handelman, 1997; Handelman et al., 2000).

In short, conventional RME can be achieved in non-growing subjects. Patient's adaptation to this modality depends on the alveolar cortex rigidity. Moreover, a slow expansion protocol might be more suitable, which would facilitate the cortical bone gradually adapting to the expansion force. Furthermore, it would make patients feel more comfortable as they would experience less pressure and pain. Handelman proposed that the screw should be turned less frequently at every other day interval or every third to the fifth-day interval (Handelman, 2011). However, the risk of fenestration is high (Brunetto et al. 2013). Hence, in order to avoid any adverse effect, this modality should be indicated in adults with transverse maxillary deficiency of less than 5 mm.

5.4. The differences in the linear and angular dental and skeletal effects achieved by ABPC + RME and conventional RME post-retention period and types of dental movement and skeletal displacement produced by interventions.

5.4.1. The differences in the linear and angular dental and skeletal expansions achieved by ABPC + RME and conventional RME.

Our study found that both ABPC + RME and conventional RME can be employed in non-growing subjects.

Differences in transverse dental expansion between two intervention groups were observed. At 4-week retention, the mean interpremolar widths at the Cu-Cu level and Pu-Pu level in ABPC + RME group expanded approximately two times greater than those in conventional RME (11.11 ± 1.47 mm vs. 5.06 ± 1.88 mm at the Cu-Cu level, and 6.26 ± 0.71 mm vs. 3.39 ± 1.63 mm at the Pu-Pu level, respectively). The amount of the buccal movement of the roots in the conventional RME group was approximately one-third of the other intervention group (0.65 ± 2.29 mm vs. 2.29 ± 0.93 mm). Therefore, at all measured levels, ABPC + RME group showed a larger amount of dental expansion compared with that of conventional RME group. The difference between two intervention groups was the addition of corticotomy procedure in Group 1. This corticotomy procedure disrupted the integrity of cortical bone along the segmental lines, decreased the alveolar rigidity, and subsequently enhanced the dental expansion in ABPC + RME group.

The amount of skeletal expansion in ABPC + RME group were higher than that of conventional RME at all different post-retention periods and measured parameters. The mean transverse alveolar width at the Cr-Cr level in Group 1 was approximately 1.5 times greater than that of Group 2 (3.79 ± 0..68 -4.39 ± 0.88 mm vs. 2.23 ±0.93 -2.91 ± 1.09 mm). At the HP level, this value in ABPC + RME group was approximately three to seven times greater than that of the other intervention group (2.97-3.05 mm vs. 0.39-1.01 mm). Our findings highlighted that corticotomy enhanced the expansion of the entire skeletal segment involved in decorticotomised surgery. In contrast, the displacement of skeletal segment in conventional RME group, especially at the HP level, was minimal. It was observed that the palatal vault in conventional RME group remained as V-shaped, while it was transformed to U-shaped in ABPC + RME group. Handelman believed that the outcomes of nonsurgical maxillary expansion mainly resulted from the dentoalveolar complex displacement (Handelman, 2011; Handelman, 1997; Handelman et al., 2000). Our findings were coincident to those of Handelman and co-workers.

The nature of expansion in the two intervention groups was different. The expansion force has previously been demonstrated to be slowly dissipated in the surrounding tissues over five to six weeks (Isaacson and Ingram, 1964), which was clearly reflected in the conventional RME group in our study. The interpremolar width increment values in conventional RME group were less than 5 mm at 4-week retention, which was much less than the amount of total screw turning (8 mm). These mean values were 7.44 ± 2.49 mm and 4.39 ± 1.71 mm at the Cu-Cu level and at the Pu-Pu level at 12-week retention, respectively. The skeletal expansion in the conventional RME group also had increased slightly at 12-week retention. In contrast, the mean dental expansion at the Cu-Cu level in Group 1 was more than 8 mm at two different intervals. The transverse alveolar width in ABPC + RME group was also found to be stable throughout the retention period. Therefore, the nature of expansion in this group is thought to be different. Ren et al. (2015) showed that cortical bone was highly resistant to bending and torsion forces. These characteristics may explain the limits of enlargement of the dental arch. On the other hand, the inside medullar bone represents the poroelastic and viscoelastic properties (Birmingham et al., 2013; Metzger et al., 2015). These properties play an important role in the tissue mechanical response (Sandino, McErlain, Schipilow, & Boyd, 2015). Under the loading force, the medullar bone can be deformed, thus, it can sustain the pressure as in the ABPC + RME group (Ferguson & Wilcko, 2016). When the cortical bone continuity was disrupted, the elasticity of corticotomised alveolar would increase and the bony segment can be readily deformed (Chung et al., 2001; Kim et al., 2011). As a result, the whole expansion force might be transmitted immediately after it was applied to the corticotomised segments. On the other hand, the greater dental and skeletal expansion at 12-week retention in the conventional RME group was due to the reduction of the buccal alveolar thickness. As the buccal alveolar bone rigidity decreased, the stored energy in the expander might gradually overcome the resistance of the cortical bone. Therefore, the corticotomy procedure resulted in a quicker and greater response of dental and skeletal segments in the ABPC + RME group compared to conventional RME.

In the present study, the bands were cemented at the central pulp level and the screw was turned up to 8 mm. Therefore, the mean transverse interpremolar widths at Pu-Pu levels are more accurate in reflecting the true dental movement than those at the cusp levels. The greater distance of intermolar width at Cu-Cu was due to further tooth tipping.

The higher amount of skeletal expansion in ABPC + RME group might also be contributed by RAP. In our study, a full thickness flap elevation triggered RAP on the entire cortical bone surface. The microCT and histological images revealed the apposition of new bone on the buccal cortical bone. Wilcko and co-workers demonstrated that the demineralised bone occurred due to RAP which later underwent remineralisation (Wilcko et al., 2009; Wilcko et al., 2001). Accordingly, buccal alveolar bone in the ABPC + RME group was not thinner than that of conventional RME group even though the dental expansion in ABPC group was two times greater than that of conventional group. Besides, Frost proposed that when the alveolar bends, bone apposition occurs on the concave surface (as cited in Roberts et al., 2004; Roberts et al., 2006). Hence, in our study, RAP and expansion force direction might induce the new bone apposition on the buccal surface. RAP is basically an inflammatory phenomenon that occurs in an injured bone to stimulate the healing process. As the intensity of inflammation varies from one subject to another, bone apposition might occur higher in one area than the other. In summary, the transverse alveolar width increment in ABPC + RME group might be the result of bone-bending effect and new bone apposition produced by RAP.

The dental expansion was different according to the type of expansion intervention and tooth position. In our study, the RME was designed as such that the bands were cemented to the first and third premolars with a wire connected to the bands resting on the palatal surface of the second premolars. In terms of pressure, higher forces may have been transmitted to the first and third premolars due to the increase surface contact area of the bands as compared to the small area of contact between the wire and the second premolar. Hence, the banded teeth in Group 1 may have moved towards the buccal side a greater amount than the wire-supported teeth. As expected, only the first premolars moved more than the other teeth in Group 2. However, these differences were not significant. The teeth and alveolar segment were not present anteriorly in sheep model. The first premolar teeth and their alveolar would move more freely while the other teeth were restricted by the neighbouring teeth and supporting bone. As a result, only the first premolar moved more than the other teeth in Group 2 despite of both first and third premolars were banded. In Group 1, as the corticotomy procedure was performed around the premolars segments, the banded teeth could move more than that of the wire-supported teeth. Accordingly, the flexibility of tooth and its surrounding bone influenced the amount of dental and skeletal expansion.

The limitation of this study is to completely control the periodontal disease which might occur during the experiment periods. In this study, antibiotics was given in Group 1 for 7 to 10 days to prevent any infection which may initiate for periodontitis. In other groups, the sheep mouth were checked daily for any lesion during this experiment, but no any intraoral lesion was detected. Vitamin C was also given daily to strengthen sheep's natural defenses as well as mucosa health.

In short, the dental and skeletal expansions achieved by ABPC + RME were significantly greater than those achieved by conventional RME at 4-week retention. At 12-week retention, the skeletal expansions in ABPC + RME group were still significantly larger than those in the conventional RME. The skeletal expansion occurred in the entire corticotomised segment in ABPC + RME group while it is limited in the conventional RME, especially at the hard palatal level. In addition, the nature of the increment of transverse alveolar width in ABPC + RME group attributed to the bone-bending effect and apposition of new bone produced by RAP.

5.4.2. Types of dental movement and skeletal displacement produced by ABPC + RME and conventional RME and their related effects on buccal alveolar bone thickness.

In orthodontics, there are four main types of tooth movements: uncontrolled tipping, controlled tipping, bodily movement, and torque. During maxillary expansion, as the force is subjected to the crown, tipping movement is most likely to occur. Pure tipping refers to the rotation of the tooth around its centre of rotation in which the crown and roots move in opposite directions. In controlled tipping and bodily movement, the crown and root move are in the same direction. However, the amount of crown and root movements are equal in bodily movement. Torque refers to movement in which the root apex moves further than the crown because the crown is retained (Proffit et al., 2007). The amount of crown and root expansion ratio can reflect the types and magnitude of the dental movement.

The tipping movement was observed at 4-week retention in both intervention groups. At 4-week retention, the ratios between the dental parameter values (Cu-Cu/Pu-Pu, R-R/Cu-Cu, and R-R/Pu-Pu) in Group 1 were higher than that of Group 2. The crowns in Group 1 tipped more than that of Group 2 (1.78 times vs. 1.49 times). However, the root movement in this group was also higher (21% to 37% vs. 13% to 19%). Only the first premolars in Group 2 followed an uncontrolled tipping pattern movement, while the other teeth in two intervention groups followed the controlled tipping pattern.

At 12-week retention, types of tooth movement were different between two intervention groups. At this point, the Cu-Cu/Pu-Pu ratio continued to increase in Group 2 but decreased in Group 1. The R-R/Pu-Pu ratio increased 22% more in Group 1 than in Group 2. These facts reflected that the premolars in conventional RME continued to tip buccally, whereas they were torqued in ABPC + RME group. In Group 1, as the expansion force was completely dissipated, the crown of premolars were retained by the bands, while the root continued to move buccally, causing the tooth to upright. This observation suggesting that the premolars in ABPC + RME group followed a root torque movement pattern. Continuous tipping in conventional RME group resulted in more detrimental effect to the supporting bone than in ABPC + RME group as was evident from the reduction in its buccal alveolar thickness. In this study, the microCT and histomorphological features of the cortical bone in the two intervention groups were in accordance with the findings from the CBCT images. Besides the cortical bone in conventional RME group becoming thinner, the bone also resorbed and demineralized throughout the retention periods. These detrimental effects were possibly due to the reduction in cortical bone integrity and rigidity, which resulted in a disharmony between the dental and skeletal displacements. Conversely, new bone apposition on the buccal aspect in ABPC + RME group would increase the cortical bone thickness. This event might have compensated the bone resorption caused by tooth tipping during the activation phase. In addition, the skeletal segment in this group moved in tandem with tooth segment as a result of corticotomy procedure.

The differences in the skeletal displacement were also observed. The HP/Cr-Cr ratio in Group 1 was from 70% to 78%, while in Group 2 it was only 17% to 34%. Thus, the buccal alveolar segment of ABPC + RME group was displaced in a bodily like pattern, in contrast to tipping movement in conventional RME group. The value of HP/R-R ratio in Group 1 was approximately 1 (0.98-1.3), illustrating that the movement of the buccal skeletal segment in this group was similar to the movement of the corresponding roots. In contrast, the HP/R-R ratio in Group 2 was just approximately 60% to 66%, displaying that the movement of bone and root were not disproportionate. Therefore, the corticotomy procedure facilitated the buccal movement of the entire corticotomised alveolar segment.

It is also crucial that the proportionate displacements of the tooth and its supporting bone (the Pu-Pu/Cr-Cr ratio) be analysed. If the tooth movement corresponds with the displacement of the bony segment, this tooth movement would cause less adverse effect to the supporting bone. The Pu-Pu/Cr-Cr ratio in Group 1 was slightly higher than that of Group 2 at 4- week retention (1.65 vs. 1.52), showing that the crowns movements in two intervention groups were not parallel to the skeletal displacement in the early stage. Nevertheless, at 12-week retention, the Pu-Pu/Cr-Cr ratio in Group 1 was close to 1 (1.24), while it was stable at 1.51 in Group 2. Therefore, the tooth movement in ABPC + RME group was less detrimental to the supporting bone in the long term than that of Group 2.

One of the limitation in using sheep as an animal model in record taking is that it was difficult for CBCT scan to be taken serially for the same subject without affecting animal welfare. Furthermore, when an X-ray beam passes through metallic materials of the bands and screw, the lower energy radiations will be absorbed partly or completely, thus the emerging beam contains mostly high energy particles. This event leads to the appearance of hypo/hyper-dense streaks around the metallic region, causing streak artefacts in the CBCT images (Nardi et al., 2015), and significantly decreased or increased the pixel values (Naitoh et al., 2013). Thus, the quality of CBCT image was low at the affected regions which in turn would influence the measurements performed in these areas (Naitoh et al., 2013). In addition, these artefacts occur more frequently in the horizontal than vertical direction (Nabha et al. , 2014). However, this absorption depends on the atomic number and thickness of metal materials. In addition, the removal of metal expander for serial CBCT scanning at different observation time points may cause relapse where the teeth might return to their original position and cause the measurements to be inaccurate. Therefore, the limitations of this study is that it could evaluate the results at 4-week retention or 12-week retention only.

An interesting point to note from this study was that during the retention period, minor tooth movement still takes place even though it is being held by the appliance. Hence, during the retention periods, the teeth are not quite stable in their new position. Tooth tipping and torque movements were observed in ABPC + RME group, while only tooth tipping occurred in the conventional RME group. The tooth movement in ABPC + RME group was in accordance with the skeletal displacements, while it was not in the conventional RME group. Moreover, the new bone apposition on the buccal aspect and torque movement during the retention periods minimised the detrimental effects to the buccal cortical bone in ABPC + RME group. Further tooth tipping occurred in conventional RME group might pose the risk of fenestration. Therefore, ABPC + RME may pose a lesser risk to the alveolar bone health in the long term than that of conventional RME group.

5.5. Bone microstructure changes at 4- and 12-week retention.

Relapse in orthodontics is believed to be originated from normal aging, PDL, and gingival fibres, occlusal factors, and soft tissue pressure (Johnston & Littlewood, 2015; Thilander, 2000). During arch expansion, movement of the teeth within the envelope of discrepancy of bony structures, as highlighted by Epker, is crucial in achieving the desired amount of expansion and improving the long term stability of the treatment outcomes. The cortical bone has been suggested as one of the determinants causing relapse (Kole, 1959; Wilcko et al., 2001; Wilcko et al., 2008), but how it affects the teeth position post orthodontic treatment is still not well understood. Hence, the benefits of corticotomy in the rehabilitation of bone quality in terms of bony microstructural changes during retention periods should be elaborated.

The BV/TV, Tb.Th, Tb.Sp and Tb.N values in the control group were stable for all teeth over 4- and 12-week retention. Therefore, these values can be considered as the baseline to compare the changes in the two intervention groups. In addition, the use of adult subjects eliminated the effect of growth factors that could influence the results. Similarly, two intervention groups were treated with the same conditions, type of expanders and the same amount of screw turning. Hence, any confounding factors from PDL, gingival fibres, soft tissue pressure, and occlusal force could be reduced.

At 4-week retention, the BV/TV values in the two intervention groups were still significantly lower than that of the control. The relative values of BV/TV to the control for the second and third premolar regions in Group 1 were from 54.4% to 68.7% which were slightly less than those of Group 2 (60.4%-69.9%). After 12 weeks retention, there was an increase in BV/TV, Tb.Th, and Tb.N values in the two intervention groups. The relative values of BV/TV to the control recovered to more than 77% in most of the regions, except for the third premolar region in Group 2 (60.7%). In addition, the pooled BV/TV value of Group 1 was significantly higher than that of Group 2 at 12-week retention. Therefore, the corticotomy procedure may have enhanced the recovery of bone microstructure in the ABPC + RME group.

Orthodontic tooth movement is the result of a series of biological responses within the PDL and surrounding bone. The behaviour of the PDL has been studied by numerous researchers, whereas the reaction of the supporting bone has not been well discussed in the literature (Verna et al., 1999; van Leeuwen et al., 2003). When a force is applied to a tooth, one side of the root absorbs the pressure while the other side reacts to the tension. This event led to the alterations in the PDL vascularisation, related cells and molecules matters. Subsequently, the alveolar bone would undergo resorption and apposition at certain sites to create space for tooth movement while maintaining the bone at the opposite sites (Krishnan & Davidovitch, 2006; Roberts et al., 2006; Proffit et al., 2007). It is believed that the slow reorganisation of the PDL and gingival fibres is the main reason which cause the teeth to return to their original positions. However, Orlowski demonstrated that the turnover of collagen in a rat's PDL was only 13.4 days and the half-life was 9.5 days (Orlowski, 1976, 1978). Other authors also agreed with these findings showing that the turnover rates of rats' PDL and gingival fibres were rather rapid. The PDL turnover was in around 5.7 days and transseptal ligament in 8.4 days (Deporter et al., 1984; Row & Johnson, 1990). It seems that the PDL adapts swiftly to any changes in the environment and might not be the main cause of relapse. In our experiment, two intervention groups was subjected to the same RME protocol; hence, the effect of PDL, if exists would be the rather similar. However, further experiments should be carried out to confirm this hypothesis.

Some studies have quantified the alveolar bone density after orthodontic tooth movement. Verna et al. (1999) showed that the mesial tooth movement in rats caused a reduction in bone volume fraction. The decrease occurred not only at the alveolar bone adjacent to the displaced teeth, but also extended to bone surrounding the neighbouring teeth (Verna et al., 1999). Recent studies in humans have also reported similar results (Chang et al., 2012; Hsu et al., 2011). The bone density was evaluated around the displaced roots after orthodontic treatment using a 250 µm voxel resolution CBCT scan. The total orthodontic treatment duration was seven months. They demonstrated that the alveolar density around the roots reduced by 20% to 29%. When the tooth moved more than 0.5 mm, the density reduction increased up to 59% to 69.1% (Chang et al., 2012; Hsu et al., 2011). However, these studies did not investigate the bone recovery during the retention period. In addition, Panmekiate and co-workers (2015) demonstrated that the value of bone quality parameters evaluated using CBCT images is less accurate when compared to microCT. Parsa et al (2015) reported that BV/TV measured using CBCT is smaller than by using microCT- even when the smallest FOV and the highest resolution scan mode (0.08 mm) was used. They reiterated that the measurement of bone density using CBCT was inaccurate (Parsa et al., 2015). Overall, the use of CBCT in bone microstructural measurement is likely to overestimate BV/TV, Tb. Th and Tb. Sp in comparison to microCT (Van Dessel et al., 2013). Although our study did not evaluate the bone quality changes immediately after the expansion, the BV/TV values at 4-week retention were around 60% that of the control group. This result showed that the bone quality would have decreased more than 60%, which could be due to a large tooth movement (more than 0.5 mm) during the expansion. Thus, our findings are in agreement with previous studies. Another advantage of our study was that the bone microstructure parameters were measured by using microCT to ascertain the measurement accuracy.

The bone quality changes following the relapse is not well reported in the literature. In a previous study, the mesial movement of the first maxillary molars was performed in 10 days, and then allowed to relapse from 1 to 21 days (Franzen et al., 2014). Franzen et al. (2014) reported that the molars relapsed very quickly from the first day and the amount of relapse was up to 73% of achieved tooth movement. The relapse rate started to stabilise after seven days and the total relapse after 12 days was very high at 93%. The bone volume fraction (evaluated by using microCT) increased from 17% to 25% within 21 days of follow-ups (Franzen et al., 2014). In our study, the appliance was activated over 16 days, which was longer than the study by Frantzen and co-workers. Following the active phase, the same expander was maintained on the teeth for 4 to 12 weeks without further activation. However, after 12 week retention, the bone microstructure in most of the regions recovered to just approximately 80% of the control level. According to Isaacson and Ingram, the expansion force was still dissipated to the surrounding tissues in the following five to six weeks (Isaacson and Ingram, 1964). This resulted in an unstable tooth position during retention. Hence, it is thought that the tooth movement during the retention period might retard the full recovery of the trabecular bone.

Studies on the effect of retention after the long term orthodontic treatment are scarce. Van Leeuwen and co-workers (2003) carried out a study in beagle dogs investigating the influence of continuous and discontinuous forces, with and without retention on the relapse. Teeth were moved in four months and then one group was allowed to relapse immediately after tooth movement but the teeth in the other group were retained in situ with the inactive appliance for three months (van Leeuwen et al., 2003). Teeth in the group without retention were reported to relapse immediately after orthodontic appliance removal. Conversely, teeth in the three-month retention group experienced a lesser amount of relapse and at a slower rate. Van Leeuwen and co-workers also suggested that retention was crucial when the tooth was moved greater than 4 mm. As the bone microstructural value at 12-week retention is higher than that of 4-week, our study showed that the retention period affected the recovery of the bone quality after orthodontic treatment. However, at 12-week retention, the bone quality only returned to approximately 80% of the baseline value. Therefore, a retention period more than three months is crucial to maintain the achieved treatment outcomes, as the 3-months retention is not enough for a remodelled alveolar bone to be completely rehabilitated.

The corticotomy procedure was found to play an important role in the restoration of bone microstructure. Although Group 1 had the double amount of dental expansion of Group 2 at 4-week retention, BV/TV value for the former group already approximately equaled to that of Group 2 (25%-33% vs. 27%-33%). Overall, BV/TV value at the first premolar regions was significantly higher than that of the third premolars. Therefore, there was a significant difference in BV/TV changes according to tooth position. The teeth and alveolar segment were not present anteriorly in the sheep model. As a result, the first premolar region is not limited by the neighbouring teeth and alveolar, and it may be more flexible than the second and third premolar segments. In addition, performing corticotomy incisions in Group 1 separated premolar segments to the surrounding bone, possibly making the decorticotomised segments more flexible. In general, when a force is applied to a tooth, it will be transmitted to the root and the surrounding bone. If the surrounding bone did not move corresponding to the tooth movement, the teeth would fenestrate through the bone. If the bone did not bend and the tooth is retained, the expansion energy would be stored and cause stress to the root and the adjacent bone. The accumulation of stress might lead to further resorption of root and bone. Some authors confirmed that the accumulated load from expanders caused root resorption even after the activation period (Langford, 1982; Ma et al., 2001). In addition, the banded and wire-supported teeth would bear different loads, thus the mechanical and biological response would be different (Martins et al., 2016). Corticotomy discontinued the cortical bone and might release the accumulative stress. Therefore, the bone surrounding the first premolars may have recovered more than the other sites in spite of this tooth moving more than the other teeth. In contrast, the third premolar in conventional RME group may experience more of the expansion force because it was restricted by the neighbouring teeth and bone. At 12-week retention, BV/TV values of all teeth returned to approximately 80% of control value except for that of the third premolar in the conventional RME group. The BV/TV values of the third premolar in Group 2 were just slightly higher than itself at 4-week retention. Zimring et al. reported that the expander loads remained active up to 5 to 7 weeks after the activation phase (Zimring et al., 1965). It seemed that the trabecular bone around this tooth may have been overloaded by the expansion force. Thus, the bone surrounding the third premolars healed slower. Corticotomy procedure may promote a higher bone microstructure restoration when compared to conventional RME.

The role of corticotomy in bone healing is more obvious for the banded teeth (first and third premolars). At 4-week retention, the pooled BV/TV value for the banded teeth in Group 1 was slightly higher than that of Group 2. The relative values of BV/TV to the control in Group 1 and 2 were 67.5% and 63.7%, respectively. Interestingly, at 12-week retention, the pooled BV/TV value in Group 1 was significantly higher than that of Group 2. The relative values of BV/TV in ABPC + RME group compared to the control group returned to 85.8% compared to only 70.5% in the conventional RME. Other parameter values such as Tb.Th and Tb.N accordingly increased. The Tb.Sp values in Group 1 were significantly lower than that of Group 2 at this point of evaluation. Therefore, the corticotomy procedure may have enhanced the rehabilitation of bone microstructure for the supporting bone around the banded teeth.

The benefits of corticotomy may be due to RAP and the bone-bending effect. Sebaoun et al. (2008) showed that the anabolic turnover increased by two to three folds after decortication in rats (Sebaoun et al., 2008). In our study, as Group 1 was treated with corticotomy, RAP might increase the bone turnover, thus promoting the bone modelling and remodelling in this group. Moreover, the corticotomy incisions could enhance the flexibility of the block of the tooth and its supporting bone. As a result, the accumulated stress was release and overloading the pressure on alveolar was prevented. Subsequently, it created a favourable environment for bone remineralisation. Consequently, the flexibility of the tooth segment during the maxillary expansion may have affected the bone modelling and remodelling during the retention period.

Until now, the bone quality change during the retention period especially after the maxillary expansion has not been well-documented. The present study revealed that bone quality in terms of the bone microstructure increased during the retention period. However, 3-months retention is not adequate for a complete rehabilitation of bone strength, which explains the possibilities of relapse after retention. Interestingly, corticotomy remarkably enhanced the restoration of bone quality, and thus it may have potential in increasing the stability of orthodontic outcomes.

5.6. The differences in the new bone formation and microvascularisation at 4- and 12-week retention in ABPC + RME (Group 1), conventional RME (Group 2) and control group (Group 3).

Histological examination of new bone fraction (total new bone area to total bone area) and total new bone fraction (total new bone area to total tissue area) revealed the bone remodelling and modelling activities.

Overall, the NBF and TNBF values in the control group were not significantly different at the two evaluation time points showing that the bone remodelling activity in normal status was low. By contrast, the NBF and TNBF values in Group 1 was three to fourth times greater than that of Group 2 at 4- and 12-week retention. There was no statistical difference in NBF and TNBF between Group 2 and the control group. Our findings revealed that the bone remodelling and modelling activities were remarkably higher in the ABPC + RME group over the retention periods while these activities were much slower in the conventional RME group. Following the high rate of new bone formation in Group 1, the total bone fraction (TBF) value increased clearly from 4- week to 12-week retention. In contrast, TBF value did not increase in Group 2. As a result, at 12-week retention, only the TBF value in Group 2 was significantly lower than that of the control. Our histological findings were in agreement with the results acquired from the microCT analysis. Therefore, the rehabilitation of the alveolar bone was higher in ABPC + RME group as compared to the conventional RME group.

In our study, due to the large size of the maxillary specimen, it took a long time for the paraformaldehyde to be absorbed completely to the whole tissue. Besides, microCT scanning needs to be carried out before the sample is processed for histological studies. It is well documented that Tartrate resistant acid phosphatase (TRAP) is a good marker for detecting osteoclasts in the catabolic examination but it requires quick analysis as it is not stable during storage (Fraser et al., 2013; Szulc & Delmas, 2008). Alkaline phosphatase (ALP) for staining osteoblasts could not be applied as the target enzyme was destroyed by paraformaldehyde preservation (Miao & Scutt, 2002). Therefore, this anabolic and catabolic examinations with TRAP and ALP cannot be performed due to the limitation in sample preparation.

The bone remodelling after corticotomy was studied by many researchers. From 1989, Frost described a phenomenon in which bone turnover noticeably increased following a bone injury. He referred it as 'regional acceleratory phenomenon' (RAP) (as cited in Kole, 1959). RAP occurs after tooth extraction, flap elevation, and cortictotomy incision. RAP is believed to occur within a few days after corticotomy and lasts up to four months (Ferguson & Wilcko, 2016; Kim et al., 2011). The anabolic rate at the corticotomy side was reported to be two to three times greater than that of the control side. The increased anabolic activity induces greater bone apposition in the trabecular bone around the upper first molar roots and the anabolic rate peaks at 3 to 4 weeks (Sebaoun et al., 2008). The findings of Sebaoun and co-workers were in agreement with a previous study by Bogosch and co-workers in which anabolic activity was described to dramatically increase at 4 weeks after corticotomy surgery on a long bone spongiosa (Bogoch et al., 1993a, 1993b). Surgical cuts were reported to enhance the bone remodelling activity. Subsequently, the bone surface area increased at 9 weeks evaluation (McBride et al., 2014). In parallel to previous study, the TNBF value in ABPC + RME group in our study was two to three times greater than that of the control. In addition, the new bone formation was higher at 4-week retention than at 12-week retention.

King and co-workers (1997) assessed the changes of the alveolar bone during orthodontic relapse without retention. In their study, the first maxillary molars on rats were moved mesially in 16 days with 40 grams of force. Following the tooth movement, rats were sacrificed at 1, 3, 5, 7, 10 and 14 days after the appliance removal (King et al., 1997). Their results revealed that the percentage of osteoclasts and osteoblasts was higher than that of the control in the first three to five days. On the mesial aspect, remineralisation at the bone surface increased to the control level on the ninth to the eleventh day. The mineralised apposition rate was higher than that of control group from the forth to twelfth day only. These results illustrated that the alveolar bone continued to undergo bone remodelling for several days after appliance removal, and the bone turnover rate returned to the control level by the 14th day. However, they did not report the amount of tooth movement after 16 days as well as the cumulative amount of relapse after the experimental period. The bone remodelling around the retained tooth would be different to the tooth let relapse immediately after orthodontic movement (King et al., 1997). In our study, the appliance was activated in 16 days which was similar to a previous study (King et al., 1997). However, the same expander was maintained on teeth for 4 to 12 weeks, passively. According to Isaacson and Ingram, the expansion force was still slowly dissipate to the surrounding tissues in five to six weeks (Isaacson and Ingram, 1964). Therefore, the bone remodelling continued and the bone turnover rate did not return to the baseline level after 12-week retention.

The rate of bone remodelling (based on NBF) in Group 2 was slightly higher than that of control. Although this increment was not statistically significant, it demonstrated that the protective mechanism was active to maintain the bone volume in this group. Thus, RAP also occurred in Group 2 but at a very low rate. The slow rate of RAP might not be strong enough to compensate for the bone resorption caused by tooth movement during the maxillary expansion because the bone remaining (based on TBF) did not show a clear increase.

The histological evidence on the microvascularisation revealed the difference in the healing process at the furcation bone between Group 1 and 2. As compared to the other groups, the number of blood vessels was significantly higher in ABPC + RME group at 4-week retention. This increment might be the result of RAP and the effect of corticotomy procedure. At 12-week retention, the microvascularisation in Group 1 decreased but was still higher than that of the other groups. RAP is believed to occur within a few days after corticotomy and last up to four months (Kim et al., 2011; Aboul-Ela et al., 2011). In contrast, the number of blood vessel in Group 2 was not significantly different to that of the control group.

Some authors proposed that there was an intimate relationship between the newly formed blood vessels and new bone formation (Wang & Boyapati, 2006; Winet, 1996). Blood vessels might be a crucial supply of osteoblasts, collagen and minerals substances for the bone remineralisation process. The higher density of blood vessels in Group 1 may partly explain the higher bone remineralisation in comparison to that of Group 2. In contrast, the blood vessels density in Group 2 was stable for all teeth over the retention period. Martins et al. (2016) suggested that the force loads would be different between the banded teeth and wire-supported teeth. In our study, the banded third premolar might bear more force and surrounding bone underwent demineralisation compared to the second premolar regions. Thus, the bone microstructure values at the third premolar regions in Group 2 healed poorly at 12-week retention because the normal vascularisation would not bring enough cells and mineral substances materials for bone remodeling.

In summary, parallel to the findings from the micoCT analysis, the new bone formation under histological examination in APBC + RME group was two to three times greater than that of Group 2 and 3 over the retention periods. It was found that only the TBF value in conventional RME was significantly lower than that of the control. Accordingly, the histology results further strengthened the usefulness of corticotomy procedure in increasing the rate of bone remodelling and enhancing the rehabilitation of bone quality during the retention periods.

CHAPTER 6: CONCLUSION

6.1 Summary and conclusions

The primary aim of this thesis was to explore the potential of adjunctive buccal and palatal corticotomy in widening the dental arch in non-growing sheep. Subsequently, various parameters associated with the dental and skeletal effects, tooth movement and skeletal displacements were evaluated using CBCT scanning. Further microCT analysis of the structural properties of trabecular bone and the features of cortical bone were helpful for estimating the potential for relapse and risk of detrimental effects to the surrounding bone. In addition, the histology examination revealed the rate of bone turnover for validating the probable advantages of ABPC + RME.

Within the limitation of the study, the following conclusions can be drawn:

- Adjunctive buccal and palatal corticotomy was able to create a combination of skeletal and dental expansions. The dental expansion was approximately two and three times greater than bony expansion at the alveolar crest and hard palate level respectively.

  The skeletal and dental expansions in ABPC + RME group were approximately two to three times greater than those of conventional RME group at 4 weeks retention, respectively. However, at 12-week retention, only the skeletal effects in ABPC + RME group were significantly higher than those of conventional RME. The skeletal expansion in group 1 was stable over the retention periods. On the other hands, more dental expansions were produced in group 2 which eliminated the difference of dental effects between the two intervention groups

  Conventional RME could be employed in non-growing sheep with moderate crowding (less than 5 mm). This modality mainly produced dental expansion whereas the skeletal expansion was minimal. The successful outcomes achieved by conventional RME might depend on the rigidity of the alveolar cortex. Moreover, SME might be a suitable protocol when using this technique. However, the potential of bone fenestration was high.

- The skeletal segment in ABPC + RME group was displaced in a likely bodily pattern while this segment in the conventional RME group primarily bent towards the buccal side.

  The teeth in conventional RME group tipped buccally, while the teeth in ABPC + RME group followed tipping and torque patterns of movement.

- There were two features of the cortical bone in ABPC + RME group: new bone apposition on the buccal cortex and resorption/demineralisation features. The new bone apposition might have compensated for the bone loss during the tooth tipping in the activation phase. In contrast, the cortical bone in conventional RME became thinner or more demineralized during the retention periods.
- Corticotomy remarkably enhanced the restoration of bone microstructure during the retention periods and might be a potential for increasing the stability of orthodontic outcomes. These advantages might be derived from the increasing bone flexibility and bone turnover produced by corticotomy and RAP. The flexibility of blocks of the tooth might release accumulated stress during the activation phase and RAP provided favourable microenvironment for bone remodelling.

  The quality of bone in terms of bone microstructure increased during the retention periods. Hence, a retention period of more than 3 months are required for a full rehabilitation of alveolar bone.

- Similar to microCT findings, the new bone formation in the histological analysis in ABPC + RME group was two to three times more than the conventional RME and control group. These results highlighted that bone modelling and remodelling activities in the ABPC + RME group was very active.
- The microvascularisation in ABPC + RME group was significantly higher than the other groups. The increase of blood vessel number might facilitate the bone remodelling process.

In conclusion, our study showed that adjunctive buccal and palatal corticotomy was able to create a combination of skeletal and dental expansion in non-growing sheep. The skeletal effects was stable over the retention periods. In addition, corticotomy evidently increased the rate of bone remodelling and the quality of bone recovery during the retention period, proving that corticotomy is a probable technique enhancing for the long term stability of orthodontic outcomes. Accordingly, adjunctive buccal and palatal corticotomy is a potential treatment for non-growing patients with transverse maxillary deficiency.

With the advantages of adjunctive corticotomy, compensation treatment may be performed easily. ABPC might be helpful for both unilateral and bilateral maxillary deficiency as it can be performed at a selective segment of alveolar bone or on the entire dental arch. This technique also provides an increase in the vestibular region width, and widen the smile providing beneficial in selected cases. Furthermore, it may potentially minimise further enlargement of existing cleft defects, considering that it may not lead to further enlargement of the defects.

The limitation of our study was that the long term stability of our findings could not be evaluated. In addition, various corticotomy techniques such as performing corticotomy without flap or using piezo device were not carried out in our study. Hence, we are not able to extrapolate the advantages of this least invasive technique for the same procedure.

6.2 Recommendations for future work

- Further studies to validate the effectiveness of the dental and skeletal expansion achieved by ABPC + RME for treatment maxillary deficiency should be performed in human as this treatment modality appears potentially useful for selected cases.
- The long term dental and skeletal stability after application of ABPC + RME should be investigated.
- Future studies on the incidence and the severity of root resorption caused by ABPC + RME compared with SARME and conventional RME should be carried out to investigate the potential risks and adverse effects.
- Comparing the different outcomes when using ABPC for maxillary expansion with flap and flapless should be further studied to optimize the technique.
- Future investigations on the effectiveness of ABPC + RME for the entire or unilateral dental arch expansion should be performed to validate the clinical indications.
- Comparing the dental and skeletal effects achieved by ABPC + RME using piezo-bone incisions and burs for decortication is necessary to develop an optimum technique which is potentially useful for this clinical practice.

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LIST OF PUBLICATIONS AND PAPERS PRESENTED

"Adjunctive buccal and palatal corticotomy for adult maxillary expansion in an animal models." This paper was published on March, 2018 in Korean Journal of Orthodontics (ISI-index).

"Alveolar restoration following rapid maxillary expansion with and without corticotomy: a microcomputed tomography study in sheep": under review.

25 February, 2017: Poster presentation at Association of Singaporean Orthodontic Congress 24-26 February, 2017 with the title "Widening dental arch with adjunctive buccal and palatal corticotomy- A new treatment approach'.

18 March, 2017: poster presentation at IADR Malaysian section with the title "Adjunctive buccal and palatal corticotomy for maxillary expansion in adults- a new treatment approach".

January, 2018: Travel Award for oral presentation at "7th Hiroshima Conference on Education and Science in Dentistry", Japan with the title "Adjunctive buccal and palatal corticotomy for adult maxillary expansion in an animal models."