การศึกษาการใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดในการปลูกถ่ายกระดูกในรอยแยกสันกระดูกเบ้าฟันของผู้ป่วยปากแหว่งเพดานโหว่โดยการใช้ภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีม

นางสาวอรินทรา ตาณะสุต

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล ภาควิชาศัลยศาสตร์
คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2556

STUDY OF THE PLATELET RICH FIBRIN IN ALVEOLAR CLEFT BONE GRAFT BY USING CONE BEAM COMPUTED TOMOGRAPHY

Miss Arintara Thanasut

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Oral and Maxillofacial Surgery
Department of Oral and Maxillofacial Surgery
Faculty of Dentistry
Chulalongkorn University
Academic Year 2013

Thesis Title	STUDY OF THE PLATELET RICH FIBRIN IN ALVEOLAR CLEFT BONE GRAFT BY USING CONE BEAM COMPUTED TOMOGRAPHY
By	Miss Arintara Thanasut
Field of Study	Oral and Maxillofacial Surgery
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(Associate Professor Chaiwat Pinnoi)

อรินทรา ตาณะสุต : การศึกษาการใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดในการปลูกถ่ายกระดูกในรอยแยกสันกระดูกเบ้าฟันของผู้ป่วยปากแหว่งเพดานโหว่โดยการใช้ภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีม. (STUDY OF THE PLATELET RICH FIBRIN IN ALVEOLAR CLEFT BONE GRAFT BY USING CONE BEAM COMPUTED TOMOGRAPHY) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ. ทญ. ดร.เกศกัญญา สัพพะเลข, 72 หน้า.

วัตถุประสงค์ของการวิจัย เพื่อเปรียบเทียบการหายของกระดูกที่ได้รับการปลูกถ่ายในรอยแยกสันกระดูกเบ้าฟันของผู้ป่วยปากแหว่งเพดานโหว่ ระหว่างกลุ่มที่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดร่วมกับกลุ่มที่ไม่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือด

วิธีวิจัย ศึกษาในผู้ป่วยปากแหว่งและเพดานโหว่ 13 ราย (15 รอยแยกเบ้าฟัน) ที่ต้องเข้ารับการปลูกถ่ายกระดูกด้วยกระดูกพรุนจากสะโพกในรอยแยกเบ้าฟัน โดยแบ่งเป็น 2 กลุ่มคือ กลุ่มที่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดร่วมด้วยจำนวน 8 รอยแยกและกลุ่มที่ไม่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดร่วมด้วยจำนวน 7 รอยแยก ทำการถ่ายภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีมก่อนผ่าตัดและหลังผ่าตัด 6 เดือน ถ่ายภาพรังสีรอบปลายรากที่ระยะก่อนผ่าตัด 1 3 และ 6 เดือนภายหลังการผ่าตัด วิเคราะห์ร้อยละของปริมาตรและความหนาแน่นสัมพัทธ์ของกระดูกที่ปลูกถ่ายด้วยสถิติแมนน์-วิทนีย์ ยูและสถิติฟรีดแมนที่ระดับนัยสำคัญน้อยกว่าหรือเท่ากับ 0.05 และประเมินตำแหน่งของกระดูกที่ปลูกถ่ายโดยใช้มาตรวัดของเชลซี

ผลการวิจัย จากการศึกษาด้วยภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีมไม่พบความแตกต่างของร้อยละปริมาตรกระดูกและความหนาแน่นสัมพัทธ์ของกระดูกที่ปลูกถ่ายที่เวลา 6 เดือนหลังผ่าตัดระหว่างทั้ง 2 กลุ่ม ($p = 0.817$ และ 0.908 ตามลำดับ) การศึกษาจากภาพรังสีรอบปลายราก พบว่าค่าความหนาแน่นสัมพัทธ์ของบริเวณที่ได้รับการปลูกถ่ายกระดูกของทั้ง 2 กลุ่ม ไม่มีความแตกต่างกันที่ระยะเวลาก่อนผ่าตัดและหลังผ่าตัด 1 3 และ 6 เดือน ($p = 0.249$, 0.775, 0.570 และ 0.949 ตามลำดับ) ในขณะที่ความหนาแน่นสัมพัทธ์ของบริเวณที่ได้รับการปลูกถ่ายกระดูกในกลุ่มที่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดเพิ่มขึ้นมากกว่ากลุ่มที่ไม่ใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดที่เวลา 3 เดือน (0.175 ± 0.21 และ 0.239 ± 0.14 ตามลำดับ) และ 6 เดือนหลังผ่าตัด (0.034 ± 0.2 และ 0.090 ± 0.36 ตามลำดับ) แต่อย่างไรก็ตามไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติ ($p = 0.173$ และ 0.465 ตามลำดับ) การประเมินตำแหน่งของกระดูกที่ปลูกถ่ายโดยใช้มาตรวัดเชลซีที่ระยะเวลา 6 เดือนหลังผ่าตัด พบว่าทั้งสองกลุ่มมีความใกล้เคียงกัน

สรุปผลวิจัย การใช้ไฟบรินที่อุดมไปด้วยเกล็ดเลือดไม่มีผลต่อการหายของกระดูกที่ปลูกถ่ายในรอยแยกสันกระดูกเบ้าฟันของผู้ป่วยปากแหว่งเพดานโหว่ที่ระยะเวลา 6 เดือน โดยการประเมินด้วยภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีมและภาพรังสีรอบปลายราก

ภาควิชา ศัลยศาสตร์ ลายมือชื่อนิสิต .....

สาขาวิชา ศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก .....

ปีการศึกษา 2556

5475825632 : MAJOR ORAL AND MAXILLOFACIAL SURGERY
KEYWORDS: PLATELET RICH FIBRIN (PRF) / BONE HEALING / ALVEOLAR CLEFT BONE GRAFTING / CONE BEAM COMPUTED TOMOGRAPHY (CBCT)

ARINTARA THANASUT: STUDY OF THE PLATELET RICH FIBRIN IN ALVEOLAR CLEFT BONE GRAFT BY USING CONE BEAM COMPUTED TOMOGRAPHY. ADVISOR: ASST. PROF. KESKANYA SUBBALEKHA, Ph.D., 72 pp.

Objective To compare the healing of the PRF-combined bone graft in alveolar cleft with the non-PRF-combined group

Materials and methods Thirteen cleft lip and palate patients with 15 alveolar clefts scheduled for iliac cancellous bone graft were classified into 2 groups. PRF group consisted of 8 cleft sites which PRF was added. Non-PRF group was 7 cleft sites grafted without PRF. CBCT was performed before surgery and 6 months after surgery. Periapical radiograph was evaluated before surgery, 1, 3 and 6 months after surgery. The volume percentage and relative density of filled bone were analyzed by Mann-Whitney U test and Friedman test (p-value < .05). Moreover, the position of filled bone was classified by Chelsea scale. Results From CBCT, there was no statistical difference of the volume percentage and relative density change at the 6th month post-operation between 2 groups (p = 0.817 and 0.908, respectively). From periapical radiographs, the relative density of filled bone at the 1st, 3rd and 6th month displayed no statistical difference between 2 groups (p = 0.775, 0.570 and 0.949, respectively). Relative density change in the PRF group increased more than those of the non-PRF group at the 3rd month post-operation (0.175 ± 0.21 and 0.239 ± 0.14, respectively) and at the 6th month post-operation (0.034 ± 0.27 and 0.090 ± 0.36, respectively). However, no statistical difference was found between both groups (p = 0.173 and 0.465, at the 3rd and 6th month respectively). The position of filled bone, classified by Chelsea scale, at the 6th month post-operation revealed to be similar in both groups.

Conclusion PRF did not show the effect on bone healing at 6 months after alveolar cleft bone grafting assessed by CBCT and periapical films.

Department:	Oral and Maxillofacial Surgery	Student's Signature	.....
		Advisor's Signature	.....
Field of Study:	Oral and Maxillofacial Surgery		
Academic Year:	2013		

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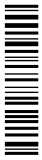

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CHAPTER I
INTRODUCTION

Background and Rationales

Cleft lip and palate is a congenital disorder related to craniofacial development. The defect of tooth bearing bone of cleft lip and palate patient, called alveolar cleft, needs to be repaired by bone grafting. The reasons of placing bone in the alveolar cleft are to restore the continuity thus stabilize the alveolus and the maxilla at the piriform rim, prevent collapse of the alveolar segments, preserve the health of dentition, provide bone for eruption of canine and/or lateral incisor, maintain bony support of the teeth adjacent to cleft, and promote the closure of oronasal fistula.(1, 2) The success of alveolar bone grafting depends on many factors such as type of cleft lip and palate, type of grafted bone, timing of procedure, duration of surgery, surgical technique, amount of initial defect, host immune status, physiological stress and growth factors.

Platelet-rich fibrin (PRF) is a new generation biomaterial of immune and platelet concentrate. The preparation process is uncomplicated and no chemical agent is needed. The fibrin membrane harbors all the blood constituents favorable to healing and immunity,(3) including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), fibroblast growth factor-basic (FGFb). Therefore, PRF can promote healing from the mechanisms of these growth factors including angiogenesis, immune control, harnessing the circulating stem cells, and wound protection by epithelial cover.(3) Furthermore, the fibrin provide supporting matrix for bone morphogenic protein (BMP) which has angiotrophic, hemostatic, and osseous conductive properties.(4) Moreover, this autologous blood component prepared at the time of surgery eliminates the concern about disease transmission and immunologic reactions, which associate with allogenic or xenogenic preparations.(5) From these benefits, PRF is used in many dental treatments such as bone grafting and sinus lift for dental implant, periodontal regeneration. However, the advantage of PRF in alveolar cleft bone graft has never been reported. We hypothesized that PRF could promote healing of alveolar cleft bone grafting and result in higher success rate.

In evaluation the success of bone grafting, the radiograph is used along with the clinical outcome. Although the conventional radiograph is routinely used for evaluation the success of bone graft.(6, 7) It displays only two dimensional and fails

to evaluate the volume, morphology and bony architecture. Moreover, the two dimensional radiograph was up to 25% under- or over-estimation concerning bone support when compared with computerized tomography (CT) scan which displays three dimensions.(8) The disadvantages of conventional radiograph also include distortion, lack of the reliable landmarks and superimposition of the nearby structures.(9) Nowadays, CT plays more roles in many fields including oral and maxillofacial surgery. Cone beam CT (CBCT) is used in this study due to the advantages over conventional radiograph and other type of CT. CBCT has total radiation approximately 20% of conventional CTs. It displays three dimension of alveolar bone cleft defect and provides the estimation of volume of bone graft needed. Moreover, the actual dimension of grafted area can be analyzed.

The purpose of this study is to compare the volume, density and level of grafted bone in alveolar cleft between the PRF addition and non-PRF addition group.

Research questions

Does the volume, density and level of grafted autologous iliac bone mixing with PRF differ from the one without PRF?

Objectives

To compare the volume, density and level of the PRF-combined bone graft in alveolar cleft with the non-PRF-combined group

Hypothesis

Hypothesis I

The bone volume of alveolar cleft bone grafting of the PRF group is significantly different from the non-PRF group.

Hypothesis II

The bone density of alveolar cleft bone grafting of the PRF group is significantly different from the non-PRF group.

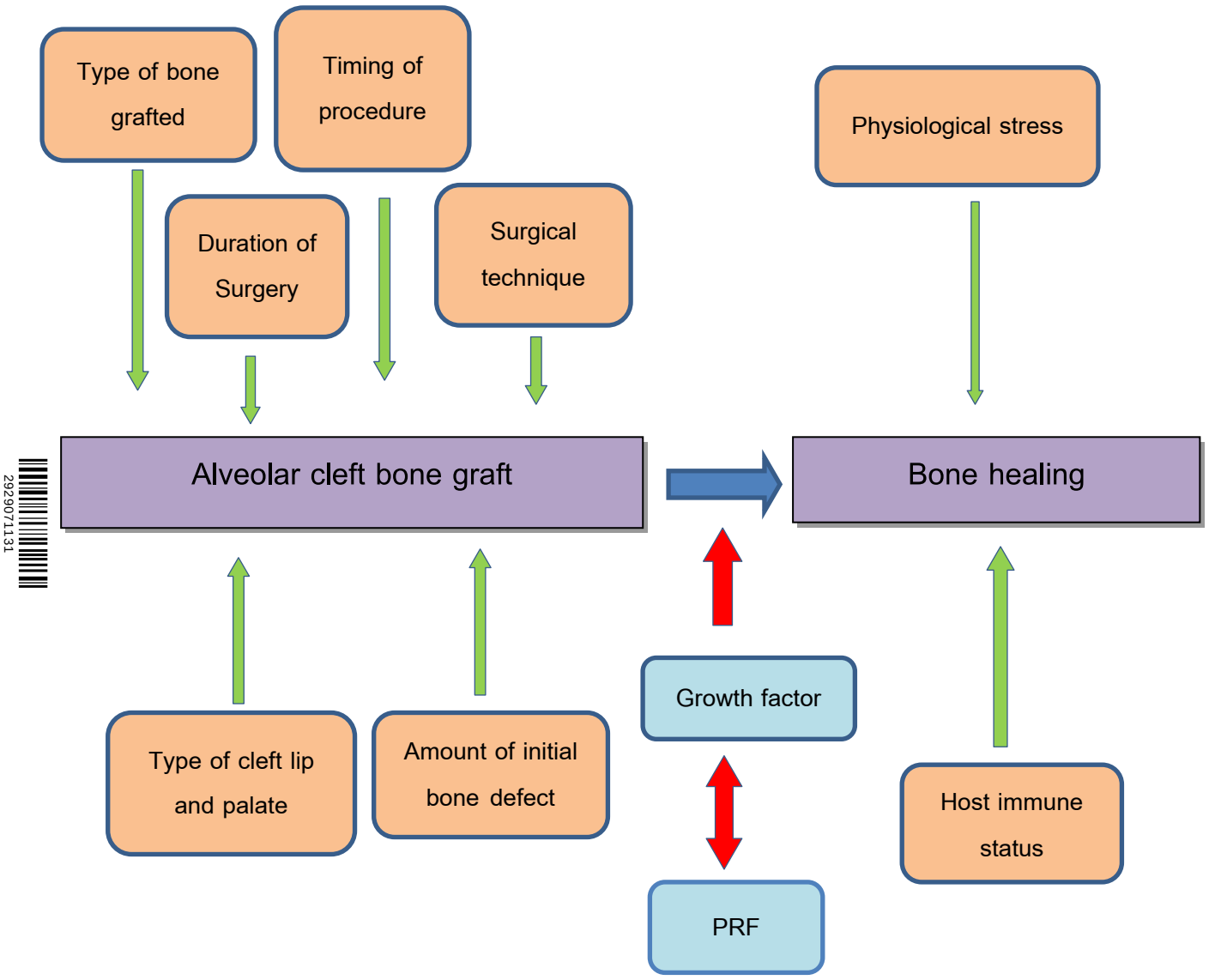
Hypothesis III

The bone level of alveolar cleft bone grafting of the PRF group is significantly different from the non-PRF group.

Expected benefits

The result from this research may show the effectiveness of PRF in alveolar cleft bone grafting. It may give some benefits in determining the proper condition for alveolar cleft bone grafting procedure. Moreover, it may be the database for the forthcoming researches in cleft lip and palate treatments.

Conceptual framework



CHAPTER II

REVIEW AND RELATED LITERATURES

I. ALVEOLAR CLEFT

Cleft of lip and palate is the most common congenital craniofacial abnormality found approximately 1 in 700 live births.(10) About 75% of cleft lip and palate patients have clefting of the maxilla and alveolus,(11-13) called alveolar cleft. For uniting and stabilizing the segments of maxilla, bone graft is an important procedure. Bone graft in the alveolar cleft is classified by timing into two most common intervals. Early reconstruction which is performed in very young patients, has been associated with maxillary growth disturbance, requiring orthognathic surgery.(11, 14) Secondary alveolar bone grafting has more advantage in orthodontic and restorative treatments.(15) Moreover, it also benefits in closing oronasal fistula, restoring the alveolar ridge, and improving craniofacial development. However, the ultimate goal is to provide bone support for spontaneous eruption of the adjacent teeth especially canine and lateral incisor, so this technique should be performed in mixed dentition.(6, 16) There are many sources of bone graft such as autografts, allografts, xenografts and alloplastic grafts. Autogenous bone is the most preferred because less risk of immunological reaction and transmission of the diseases. Moreover, autogenous bone has osteoinductive, osteogenic and osteoconductive properties. The autogenous bone can be harvested from iliac crest(11), calvarial bone(17), rib(18)or tibia(19). Cancellous bone is preferable to cortical or osteochondral bone due to the more osteoprogenitor cells.(20)

Reconstruction of alveolar cleft

Rationale for Bone Grafting

Although some authors have advocated nongrafting techniques(21) or prosthodontic approaches, the general consensus is that achieving continuity between the cleft alveolar segments has significant advantages, regardless of how and when this is accomplished. Potential advantages of bone graft in the alveolar cleft include the following(22):

1. Achieving stability of the arch and prevention collapse of the alveolar segments. This improved orthodontic stability.
2. Preservation the health of the dentition. Bone grafting provides bone bed for the canine and lateral incisor to erupt into stable alveolar bone and maintains bony support of teeth adjacent to the cleft.(1, 2)
3. Restoration the continuity of the alveolus and the maxilla at the piriform rim which supports the ala of the nose. This may have a direct esthetic benefit and may also prove to be of long-term benefit when formal rhinoplasty procedures are performed.(1)
4. Closure of oronasal fistula. Palatal and nasolabial fistulas are often present even following palatoplasty. Grafting of the alveolar defect provides an opportunity for the surgeon to address the residual oronasal fistula. This benefit both hygiene and speech. Many cleft patients suffer from chronic upper respiratory and sinus disease, which may be related to reflux into the nasal cavity and sinus. The residual fistula, whether labial or palatal can have an effect on speech articulation and nasality. The closure of the fistula and grafting the cleft defect can improve nasal emission and nasality as well.(23)

Outcome Measurement

Bergland and colleagues described a semiquantitative approach that classified grafted alveolar cleft into four types based on alveolar crest height.(6) The Bergland scale(6) is well-known to classify the bone septum formed after surgery into 4 types (Figure 1). The prerequisite for the use of this scale is the presence of the permanent canine in its final position in the dental arch.

Type I Bone septum of approximate normal height, up to the amelocemental junction

Type II Septum height at least 3/4 of normal height

Type III Septum height less than 3/4 of the normal height

Type IV No continuous bony bridge across the cleft, ie, surgical failure

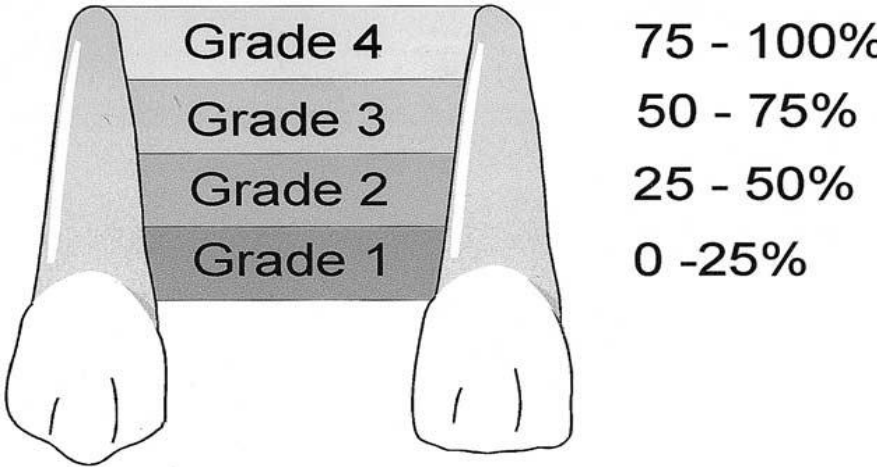


Figure 1 Scale for categorizing the osseous resorption in relation to the interalveolar bone height.(24)

A modification of the Bergland scale that measures both occlusal and basal bone height may be a better tool for evaluating graft success. However, most patients are in the age that canines have not erupted in the maxillary arch. Therefore, the Chelsea scale(7) is preferred. This scale classify grafted alveolar cleft into 6 groups (Figure 2), A to F, according to the position of bone tissue in relation to the teeth adjacent to the cleft area.

Group A Presence of bone tissue at the amelocemental junction and at least 75% of both roots covered with bone

Group B Presence of bone tissue in the amelocemental junction and in at least 25% of both roots

Group C Presence of bone tissue across at least 75% of the cleft roots from an apical direction

Group D Presence of bone tissue across at least 50% of both roots from an apical to coronal direction

Group E Presence of a bridgelike bone tissue in any area of the cleft except apically and coronally

Group F Presence of bone tissue 25% or less across both roots from an apical direction

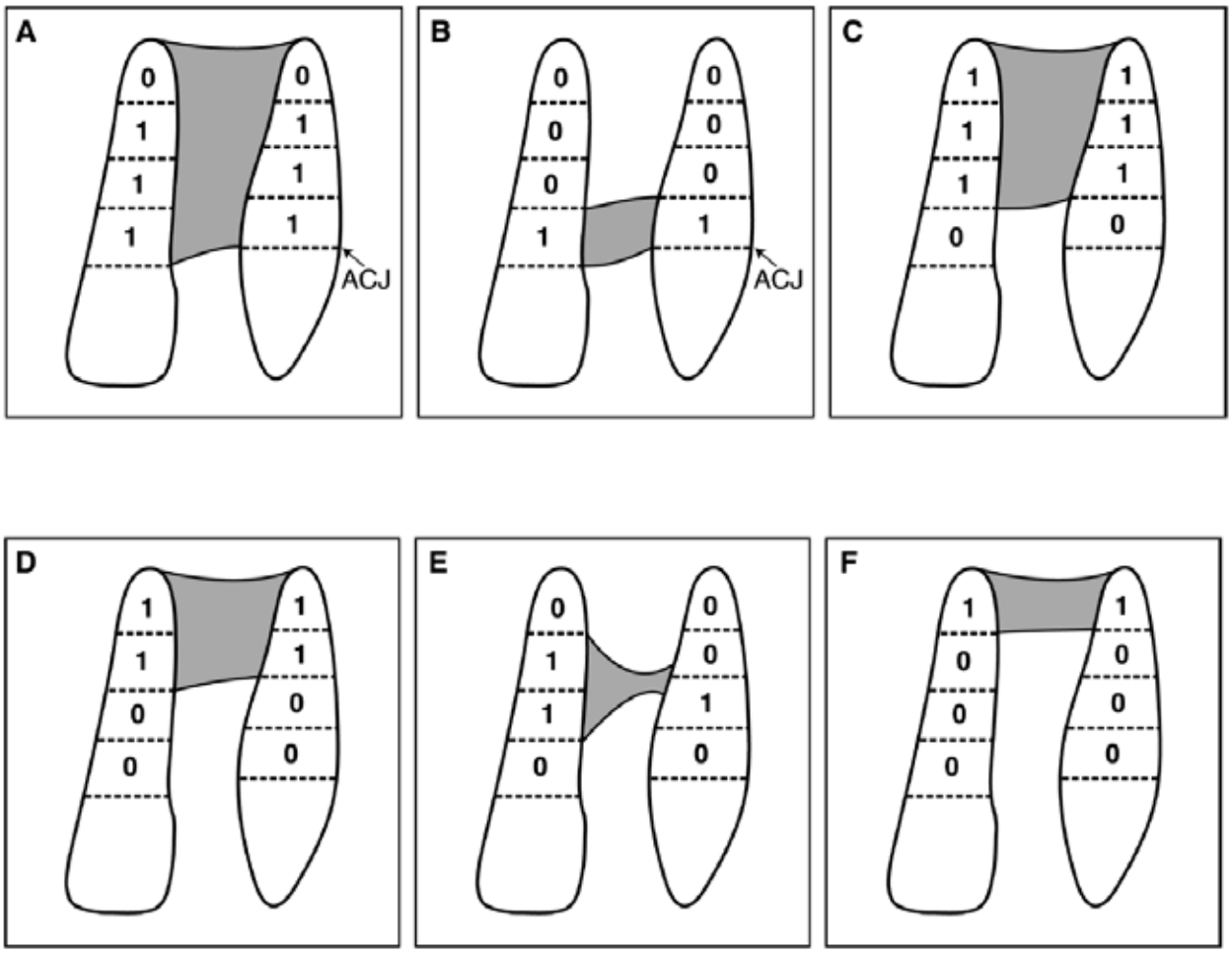


Figure 2 A-F: Chelsea scale classification

Alveolar Graft Timing

Primary grafting

Some defined primary alveolar bone grafting as that which is performed simultaneously with lip repair.(25) Others stated that any grafting that is performed

at less than 2 years of age or before repairing the palate is considered primary grafting.(26, 27) A prosthesis is placed before the lip is closed to mold the alveolar segments into close proximity. Then, the closure of the lip further aids in molding the segments. The segments must be in close proximity with good arch form before grafting onlay rib graft is placed across the labial surface of the cleft in a subperiosteal tunnel that is developed by limited dissection. However, primary grafting performed after closure of the lip and before closure of the palate has proven successful in a limited number of centers when a very specific protocol is followed.(26, 27)

Secondary Grafting

Early Secondary Grafting

Grafting after the child reaches 2 years of age and before 6 years is considered early secondary grafting. The literature does not support early secondary grafting.

Secondary Grafting During the Mixed Dentition

Alveolar reconstruction with grafting during the eruption of the permanent dentition may be the best for various reasons. Rationales for grafting during this time period include the following:

1. There is minimal maxillary growth after age 6 to 7 years. The effect of grafting at this time will result in minimal to no alteration of facial growth.(28, 29)
2. Cooperation with orthodontic and perioperative care is predictable.
3. The donor site for graft harvesting is of acceptable volume for predictable grafting with autogenous bone.
4. Grafting during this phase allows placement of the graft before eruption of permanent teeth into the cleft site, which achieves one of the primary goals of grafting — to enhance the health of teeth in and adjacent to the alveolar cleft.

5. Bone volume may be improved by eruption of the tooth into the newly grafted bone.(30)

Several studies support that grafting in the mixed dentition achieves many of the goals of reconstruction of alveolar cleft reconstruction including achieve stability of the arch, preserve the health of the dentition, provide bone for the canine and lateral incisor to erupt, maintain bony support of teeth adjacent to the cleft.(1, 2, 6, 11, 24, 31) The ideal patient is between 8 and 12 years with a maxillary canine root develop about one-half to two-thirds. However, some authors have suggested that earlier grafting should be considered as a means of preserving the lateral incisor as well.(32, 33) This suggested timing is as early as 6 years of age. Despite clear indications that grafting in the mixed dentition is preferable to either primary, early secondary, or late secondary grafting, it is not entirely clear whether this grafting should be performed early (age 6–8 years) or late (age 8–12 years).

Late Secondary Grafting

This delayed grafting does allow for increasing option with regard to donor site for graft material, as harvest of the mandibular symphysis becomes possible. Such graft is difficult in the mixed dentition stage where it is difficult to obtain adequate bone without damaging unerupted teeth. Late secondary grafting has received some support; however, data shows that when all the goals of alveolar reconstruction are considered, it has a less acceptable outcome. Patients older than 12 years of age who undergo grafting have been reported to have decreased success when evaluated by the Bergland scale,(6, 34) loss of osseous support of teeth adjacent to the cleft,(30) and increased morbidity.(35) There is less opportunity to salvage the lateral incisor, and there is a delay in correction of the orthodontic condition.

II. PLATELET RICH FIBRIN (PRF)—A NATURAL FIBRIN MATRIX

PRF was first developed in France by Choukroun et al.(36) for specific use in oral and maxillofacial surgery. This technique requires no anticoagulant, thrombin, gelling agent or any other additions, which avoids all the restrictions of the French law related to blood-derived product reimplantation. The PRF protocol is very simple: the blood sample is taken in 10-mL tube without anticoagulant, then immediately centrifuged at 3000 rpm for 10 minutes. The absence of anticoagulant implies the activation in a few minutes of most platelets of the blood sample in contact with the tube walls and the release of the coagulation cascades. Fibrinogen is initially concentrated in the high part of the tube, before the circulating thrombin transforms it into fibrin. A fibrin clot is then obtained in the middle of the tube, just between the red corpuscles at the bottom and acellular plasma at the top (Figure 3).

Figure 3 PRF clot blood centrifugation immediately after collection allows the composition of a structured and resistant fibrin clot in the middle of the tube, just between the red corpuscles at the bottom and acellular plasma at the top.

Platelets are theoretically trapped massively in the fibrin meshes. The success of this technique entirely depends on the speed of blood collection and transfer to the centrifuge. Indeed, without anticoagulant, the blood samples start to coagulate almost immediately upon contact with the glass surface of the tube, and it

takes a few minutes of centrifugation to concentrate fibrinogen in the middle and upper part of the tube. Quick handling is the only way to obtain a clinically usable PRF clot. The overly long duration while transferring the blood to centrifuge cause failure of PRF formation. The fibrin will polymerize in a diffuse way in the tube and only a small blood clot without consistency will be obtained. In conclusion, the PRF protocol makes it possible to collect a fibrin clot charged with serum and platelets. By driving out the fluids trapped in the fibrin matrix, the very resistant autologous fibrin membrane.

Angiogenesis, natural support to immunity and epithelial cover properties of fibrin are the 3 keys to healing and soft tissue maturation. The membranes of PRF are able to simultaneously support the development of these 3 phenomena.

Angiogenesis property of fibrin(3)

Fibrin is the natural guide of angiogenesis, the formation of new blood vessels inside the wound. An extracellular matrix allows migration, division, and phenotype change of endothelial cells. The fibrin matrix leads directly to angiogenesis,(37) from the 3-dimentional structure of the fibrin gel and by the simultaneous action of cytokines trapped in the meshes.(38) Fibroblast growth factor basic (FGFb), vascular endothelial growth factor (VEGF), angiopoı¨etin and platelet-derived growth factor (PDGF) are included in fibrin gel. Some studies indicate that FGFb and PDGF can bind to fibrin with high affinity.(39, 40) Moreover, the structure and mechanical properties of the fibrin clot are also important factors.(41) The rigidity of the matrix considerably influences the capillary formation by endothelial cells in response to FGFb or VEGF stimulation. These differences in the fibrin matrix configuration are crucial for understanding the differences of biologic kinetics between fibrin glue, concentrated platelet-rich plasma (cPRP), and PRF.(3) Finally, an important phase of angiogenesis is avb3 integrin expression by endothelial cells, allowing the endothelial cells to bind to fibrin, fibronectin, and vitronectin. Fibrin, fibrinogen, and vitronectin are major extracellular matrix (ECM) constituents. ECM-integrin interactions promote angiogenesis.

Fibrin constitutes a natural support to immunity(3)

Fibrin and fibrinogen degradation products (FDP) stimulate the migration of neutrophil and increase the membrane's expression of CD11c/CD18 receptor. This receptor permits adhesion of the neutrophil to endothelium and fibrinogen as well as the transmigration of neutrophils.(42) Moreover, the phagocytosis of neutrophils and the enzymatic degradation process are modulated by FDP.(43) It has been demonstrated that the wound colonization by macrophages is controlled by fibronectin via the chemical and physical properties of fibrin and by chemotactic agents trapped in its meshes.(44) For example, FDP D-dimer added to the culture medium of human promonocytic cell lines increases the interleukin (IL)-1 and plasminogen activator (uPA) secretion.(45) This implies a positive feedback of fibrin in inflammatory events

Fibrin and wound coverage(3)

Fibrin matrix effect the metabolism of epithelial cells and fibroblasts to coverage the injured tissue. Around the wound margin, epithelial cells lose their basal and apical polarity and produce basal and lateral extensions toward the wound side. The epithelial cells subsequently migrate on the transitory matrix made by fibrinogen, fibronectin, tenascin, and vitronectin. This migration is like a genuine matrix degradation. Moreover, Fibrin, fibronectin, PDGF, and transforming growth factors (TGF-b) are essential to modulate integrin expression, fibroblast proliferation, and their migration inside the wound.(46) These can be bound directly with fibrin by different integrins, of which avb3 integrin is primary. The expression of 2 plasminogen activators let fibroblasts develop an important proteolytic activity to move within the fibrin clot. After migration and degradation of fibrin, fibroblasts start the collagen synthesis.(47) Then, the healing process of injured tissue occurred.

Fibrin and osseous tissue(3)

Direct interactions between fibrin and osseous cells during healing are insufficiently documented. On the other hand, numerous animal studies deal with the fibrin effect on osseous healing. The results are contradictory; osseous healing is either improved or remains unchanged.(48) These divergences may be caused by differences between the models used: animal type, osseous defect, and fibrin gel. Nevertheless fibrin is a recognized support matrix for bone morphogenetic protein (BMP) transplants. Therefore, the fibrin matrix associated with BMPs has angiotrophic, hemostatic, and osseous conductive properties.(4) BMPs enmeshed in the fibrin matrix are progressively released, and when transplanted intramuscularly they are able to induce bone.

Other biomaterials such as platelet-rich plasma (PRP) and bone morphogenic protein-2 (BMP-2) are used for alveolar cleft bone grafting. BMP-2 has many advantages such as shortening of the operation time, absence of donor site morbidity, shorter hospital stay and reduction of overall cost but BMP-2 is very expensive. The result of BMP-2 in alveolar cleft bone grafting showed skeletally mature patients showed better results in the BMP-2 group in terms of bone quantity, less complications and less adverse events compared to patients in the mixed dentition.(49) PRP has controversial in alveolar bone grafting. The study showed no significant different were found between autogenous bone combined with PRP and autogenous bone alone on bone regeneration.(50) On the other hand, showed less mean bone loss at 6, 12 months in PRP-combined group compare to non-PRP group.(51) However, there is not any report about using PRF in bone grafting of the alveolar cleft.

III. Cone beam computed tomography (CBCT)

CBCTs for dental, oral and maxillofacial surgery and orthodontic indications were designed to counter some of the limitations of the conventional CT scanning devices. The radiation source consists of a conventional low radiation. X-ray tube and the resultant beam is projected onto a Si/CsI flat panel detector (FPD) or a charge coupled device (CCD) with an image intensifier. FPD has been shown in the literature to have a high spatial resolution.(52) The cone-beam produces a more focused beam. It has a fixed area and volume on a detector and much less radiation scatter compared to the conventional fan-shaped CT devices.(53) This significantly increases the X-ray utilization and reduces the X-ray tube capacity required for volumetric scanning.(54) It has been reported that the total radiation is approximately 20% of conventional CTs and equivalent to a full mouth periapical radiographic exposure.(55) CBCT can therefore be recommended as a dose-sparing technique compared with alternative standard medical CT scans for common oral and maxillofacial radiographic imaging tasks.(56) The images are comparable to the conventional CTs and may be displayed as a full head view, as a skull view or regional components.

In the maxillofacial region, CBCT is used for evaluation of impacted teeth(57), implant treatment planning(58), diagnosis of the temporomandibular joint (TMJ)(59), simulations for orthodontic and surgical planning, etc.(60). In complex orthodontic cases (canine impactions and clefts), in which 3D imaging is mandatory, CBCT is the method of choice. Furthermore, in cleft patients and those undergoing combined orthodontic and maxillofacial therapy, CBCT provided more information than conventional images.(61) Before routine use in orthodontics, however, further studies are needed.(62) It has been demonstrated that CBCT is accurate to identify apical periodontitis.(63) A recently suggested CBCT-aided method for the determination of root curvature radius allows more reliable and predictable endodontic planning, which reflects directly on a more efficacious preparation of curved root canals.(64) CBCT provides better diagnostic and quantitative information on periodontal bone levels in three dimensions than conventional radiography.(65) CBCT can also be used for maxillofacial growth and development assessment and

dental age estimation.(66) Therefore, CBCT is used in this study for evaluating the cleft size, volume of bone graft needed and healing after alveolar cleft bone grafting.

CHAPTER III

MATERIALS AND METHODS

Sample selection

Twenty cleft lip palate patients who were undergoing secondary alveolar cleft bone grafting procedure at Faculty of Dentistry, Chulalongkorn University (Bangkok, Thailand) were recruited. The operations were done by three surgeons that has board certified with the same technique. The subjects were classified into 2 groups. The control group includes 10 alveolar clefts treated with autogenous bone graft without PRF. The study group consists of 10 alveolar clefts treated with autogenous bone graft with PRF.

Inclusion criteria

- Age : 8-15 years old
- All types of cleft lip and palate patients who attend secondary alveolar cleft bone grafting
- Patients are healthy and do not have other craniofacial anomalies

Exclusion criteria

- Patients cannot attend all duration of this study

The patients were provided informed consent which was approved by the ethic committee, Faculty of Dentistry, Chulalongkorn University (Approval number 030/ 2012).

PRF preparation

PRF preparation was performed in the operating room, Hospital of Dentistry, Faculty of Dentistry, Chulalongkorn University.

PRF was prepared at the time patient receiving operation. Approximately 20 ml of autologous blood was drawn from anti-cubital vein before giving any drugs intravenously. Then, it was divided into 2 plastic tubes and immediately centrifuged by automatic blood centrifugation (Dynamica Velocity 14R centrifuge®, Victoria, Australia, Figure 4A) at 2500 rpm, 25°c for 10 minutes. The PRF from one tube was mixed with the particulate cancellous bone and marrow (PCBM) , harvested from iliac crest and the other tube was left to form PRF membranes (Figure 4B).

A B

Figure 4 (A) The automatic blood centrifugation machine (Dynamica Velocity 14R centrifuge®, Victoria, Australia), (B) PRF extracted from patient.

Surgical procedures

The surgical procedure for alveolar cleft bone grafting was performed following a standard procedure. Briefly, the incision was made along the alveolar cleft, the gingival mucoperiosteal flaps were reflected into the nasal side and the oral side. The nostril floor was closed in the water-tight manner. The alveolar space was filled with PCBM harvested from the anterior ridge of the iliac crest. In the study group, PCBM mixed with PRF was placed into the cleft and covered with a PRF membrane. In the control group, only PCBM was placed. Then the flaps of oral side were closed in the water-tight manner to prevent oral fluid leakage into the grafted area.

Computed tomographic evaluation

Computed tomography (CT) scan was taken before and 6 months after alveolar cleft bone grafting at Department of Radiology, Faculty of Dentistry, Chulalongkorn University by Dentomaxillofacial Cone-beam X-ray CT system (Hitachi CB MercuRay, Hitachi Medical Corporation, Tokyo, Japan) & Imager (Fuji DryPix 3000, FUJIFILM Corporation, Japan). Each patient received a computerized axial tomography of the skull. Patient positioning was standardized with the maxillary alveolar crest parallel to the plane of the scan.

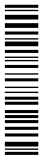
Measurement of alveolar cleft and bone forming volume

The volume was calculated by area multiply with height of alveolar cleft in every 2.1 mm-intervals from alveolar crest to floor of nose in axial view, using CBworks 2.12 software (Hitachi, Japan). The volume of alveolar cleft defect before operation was recorded. The bone forming in the cleft site at 6 months after surgery was measured. The percentage of formed bone in the cleft was a ratio of post-operative bone volume in the gap and pre-operative cleft volume.

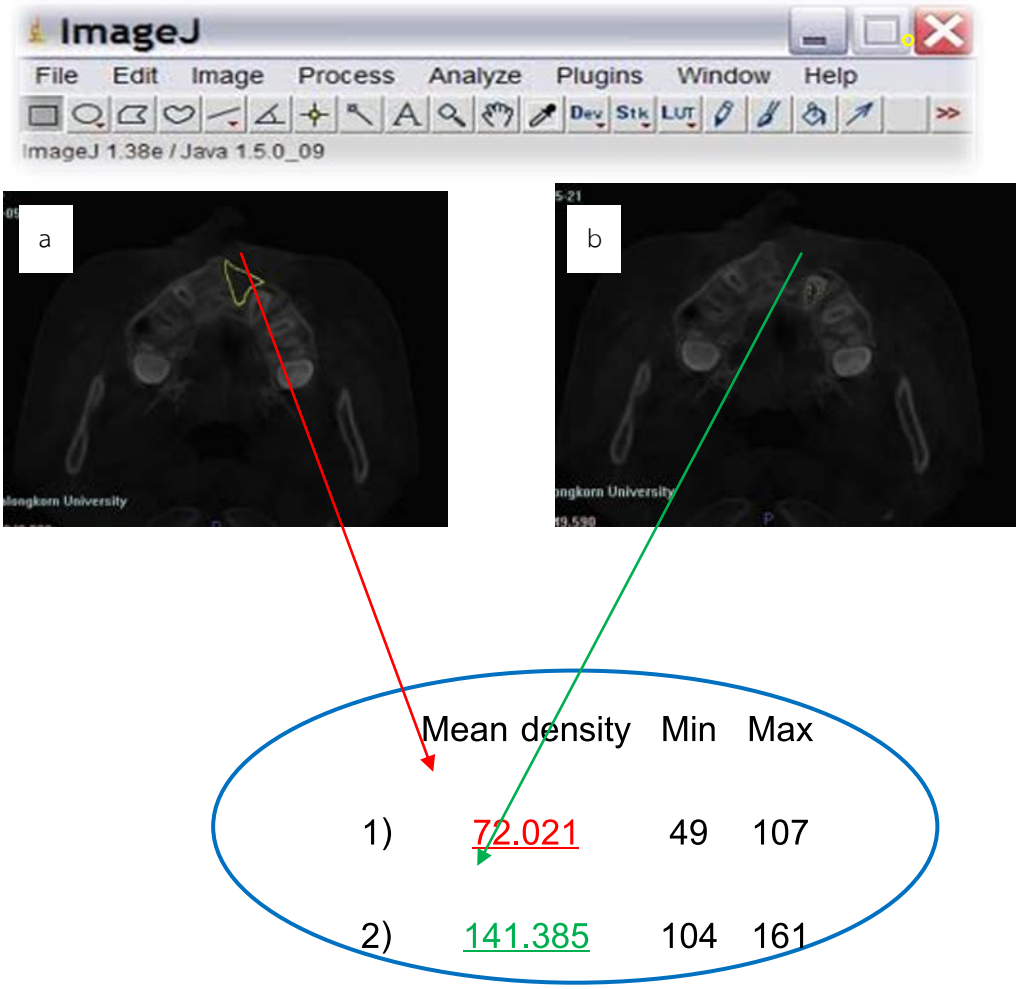
Bone density assessment

In every follow up periods, The ImageJ software (National Institutes of Health (NIH), United states) was used (Figure 5A). The density in cleft area was traced and

measured. The density of adjacent tooth was used as a reference. In each cross-sectional plane, the relative density was calculated by mean density at the cleft site area divided by mean density of adjacent tooth area. The average values from these all cross-sectional slices were attributed to the defined region. Then, we compared the average of relative density of cleft site area at pre-operative and 6 months post-operative between 2 groups



A



$$\text{Relative density} = \frac{\text{Mean density of cleft area}}{\text{Mean density of adjacent tooth}} = \frac{72.021}{141.385}$$

Figure 5 (A) Method to analyze density of cleft area by CT scan in each cross-sectional view (a) tracing area at cleft site, (b) tracing area of adjacent tooth

Periapical radiograph evaluation

The periapical film was taken at pre-operation and 1, 3, 6 months post-operation. The reproducible position was confirmed by using polyvinyl siloxane impression material as a occlusal index for each patient (Figure 6).

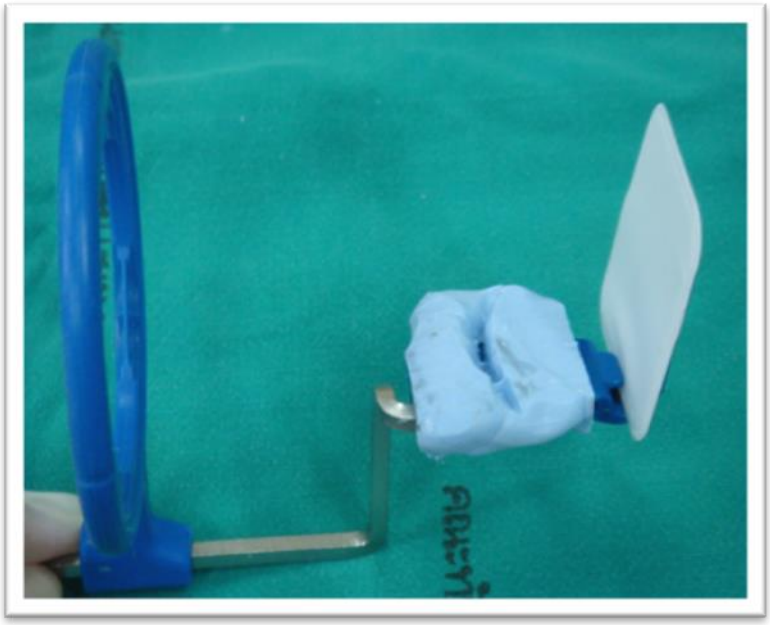


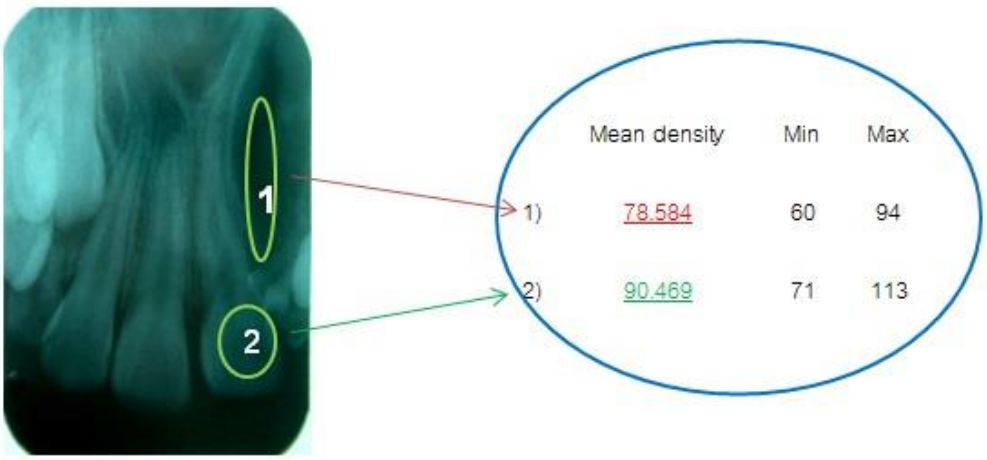
Figure 6 Polyvinyl siloxane impression material as a occlusal index

Bone density assessment

The ImageJ software was used to assess mean density. The cleft area was outlined and measured. The density of an adjacent tooth was also measured and used as a reference. Due to different contrast in each periapical film, we traced area at the junction between dentin and pulp to represent both radiopacity and radiolucency. While chose “set measurement” button in ImageJ and selected program to showed area, minimum, maximum and mean density of traced areas, these values were displayed automatically (Figure 7).

The relative density was calculated by mean density at the cleft site area divided by mean density of adjacent tooth area.

Then, we compared the relative density of cleft site area at pre-operative, 1, 3 and 6 months post-operative between 2 groups.



$$\text{Relative density} = \frac{\text{Mean density of cleft area}}{\text{Mean density of adjacent tooth}} = \frac{78.584}{90.469}$$

Figure 7 Method to analyze density of bone filled by periapical film

Level of bone tissue assessment

Level of filled bone in cleft site at 6 months post-operative was evaluated according to Chelsea scale (Figure 2).

Statistical analysis

All data was analyzed by SPSS software for Windows version 17.0 (IBM Corporation, Somers, NY). A p-value of < 0.05 was considered to be statistically significant. Demographic data was summarized by descriptive statistics. Data were tested normal distribution by One-Sample Kolmogorov-Smirnov test.

- The percentage of fbone volume was compared between PRF and non-PRF group by using Mann-Whitney U test because the population was independent but the means of two groups were not normally distributed (non-parametric test).

- Filled bone relative density using CBCT was compared between PRF and non-PRF group by using Mann-Whitney U test because the population was independent but the means of two groups were not normally distributed (non-parametric test).

- Filled bone relative density using periapical film was compared between two groups at pre-operation, 1, 3 and 6 months by using Mann-Whitney U test because the population was independent but the means of two groups were not normally distributed (non-parametric test).

- Filled bone relative density using periapical film in each group was compared from pre-operation to 6 months post-operation by using Friedman's test because the population was dependent but the means of two groups were not normally distributed (non-parametric test).

- The level of bone tissue in both groups were classified by Chelsea scale and summarized by descriptive statistics.

CHAPTER IV

RESULT

Part I: Demographic Information

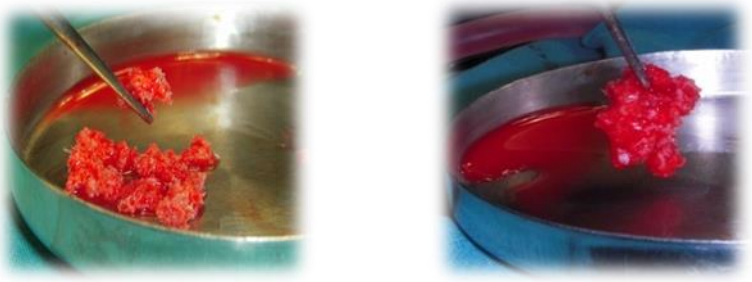
In 20 alveolar cleft patients supposed to be operated were recruited. Two patients were cancelled surgical treatment and one patient denied to participate this study. However, 4 patients were excluded due to unable to attend all radiographic examination. Therefore, only 13 patients, 15 alveolar cleft sites were attended in this study. Nine patients were male and four patients were female. They were classified into two groups, PRF group and non-PRF group. The PRF group consisted of six male patients. The age ranged from 9 to 13 years, the mean age was 9.83±1.60 years, There was two bilateral cleft lip (66.67%) and palate and four unilateral cleft lip and palate (33.33%) patients. The non-PRF group consisted of three male patients (42.86%) and four female patients (57.14%). The age ranged from 8 to 14 years, the mean age was 10.29±1.89 years. There was seven unilateral cleft lip and palate, three right sites and four left sites (Table 1).

Table 1 Demographic characteristics of the patients

	PRF Group (n = 6)				**Non-PRF Group (n = 7)**			
	male		female		Male		female	
	UCLP	BCLP	UCLP	BCLP	UCLP	BCLP	UCLP	BCLP
No. of patient (%)	4 (66.67%)	2 (33.33%)	0 (0%)	0 (0%)	3 (42.86%)	0 (0%)	4 (57.14%)	0 (0%)
Total	6		0		3		4	
Age average (years)	9.83±1.60				10.29±1.89			

Abbreviation: UCLP, unilateral cleft lip and palate ; BCLP, bilateral cleft lip and palate

PRF benefits in handling particulate bone for grafting. It made the harvested bone particle become aggregate and glutinous thus easily to be carried (Figure 8).



A B

Figure 8 (A) The harvested particulate cancellous bone from iliac crest (B) The mixture of particulate cancellous bone and PRF appeared as gelatinous aggregation

Part II: Comparison of filled bone volume between before and 6 months after surgery by using CBCT

In PRF group, the volume of alveolar cleft before grafting ranged from 234.78 to 547.05 mm^3, the mean ± SD was 369.51 ± 110.52 mm^3. In non-PRF group, the cleft volume ranged from 363.60 to 688.80 mm^3, the mean ± SD was 441.76 ± 112.00 mm^3. Then the filled bone volume in cleft site at the 6^{th} month post-operation was measured. In PRF group, the filled bone volume ranged from 142.80 to 369.18 mm^3, the mean mean ± SD was 230.99 ± 73.48 mm^3. In non-PRF group, the filled bone volume ranged from 147.72 to 489.51 mm^3, the mean mean ± SD was 298.78 ± 114.11 mm^3. Mann-Whitney U test showed no statistical significance in cleft volume and filled bone volume between two groups (P = 0.203 and 0.203, respectively).

In PRF group, the percentage of filled bone volume ranged from 41.31 to 93.39, the mean ± SD was 64.87 ± 19.63. In non-PRF group, the percentage ranged from 67.74 to 18.73, the mean ± SD was 64.87 ± 19.63. Mann-Whitney U test showed no statistical significance in the percentage of filled bone volume between two groups (P = 0.817). (Table 2, Figure 9)

Table 2 Volume analysis by CBCT in PRF and non-PRF group

	PRF Group (n = 8)			Non-PRF Group (n = 7)			
	Mean ±SD	min	max	Mean ±SD	Min	max	p-value
Cleft volume at pre-operation (mm^3)	369.51±110.52	234.78	547.05	441.76±111.99	363.60	688.80	0.203
Filled bone volume at 6 months (mm^3)	230.99±73.48	142.80	369.18	298.78±114.91	147.72	489.51	0.203
Percentage of filled bone	64.87±19.63	41.31	93.39	67.74±18.73	40.57	90.28	0.817

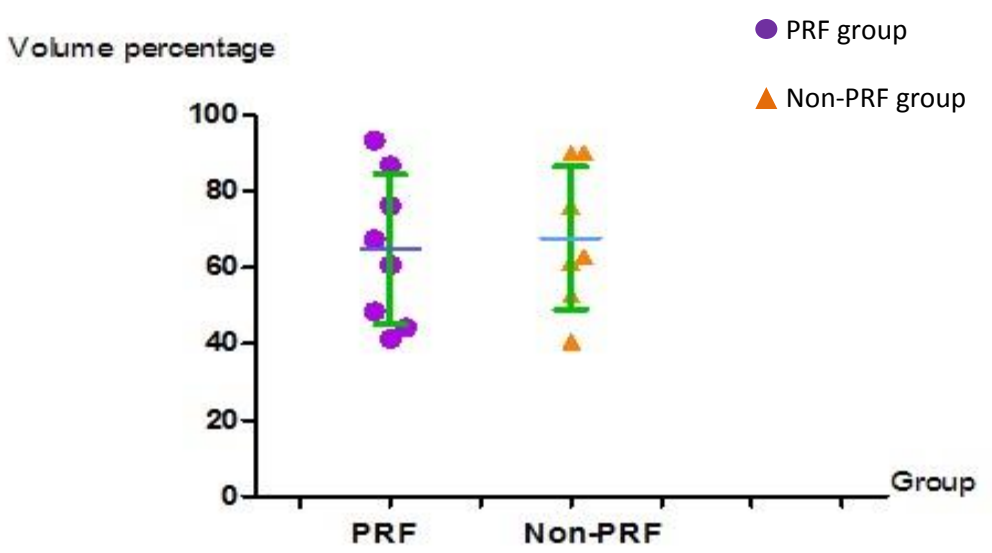


Figure 9 The percentage of filled bone between two groups using CBCT

Part III: Comparison of relative density between before and 6 months after surgery by using CBCT

In PRF group, the relative density of alveolar cleft before grafting ranged from 0.415 to 0.717, the mean ± SD was 0.578 ± 0.12. In non-PRF group, the cleft relative density ranged from 0.477 to 0.691, the mean ± SD was 0.595 ± 0.08. Then the bone filled relative density in cleft site at the 6th month post-operation was measured. In PRF group, the filled relative density ranged from 0.641 to 0.923, the mean ± SD was 0.744 ± 0.10. In non-PRF group, the filled relative density ranged from 0.661 to 0.855, the mean ± SD was 0.759 ± 0.08. Mann-Whitney U test showed no statistical significance in cleft relative density and filled bone relative density between two groups (P = 0.728 and 0.562, respectively).

In PRF group, the change of filled bone relative density ranged from 0.024 to 0.498, the mean ± SD was 0.172 ± 0.15. In non-PRF group, the change of filled bone relative density ranged from 0.030 to 0.378, the mean ± SD was 0.164 ± 0.12. Mann-Whitney U test showed no statistical significance in change of filled bone relative density between two groups (P = 0.908). (Table 2, Figure 10)

Table 3 Relative density analysis by CBCT in PRF and non-PRF group

	PRF Group (n = 8)			Non-PRF Group (n = 7)			p-value
	Mean ±SD	min	max	Mean ±SD	Min	max	
Relative density of cleft site at pre-operation	0.578±0.12	0.415	0.717	0.595±0.08	0.477	0.691	0.728
Relative density of filled bone at the 6th month	0.744±0.10	0.641	0.923	0.759±0.08	0.661	0.855	0.562
Change of relative density	0.172±0.15	0.024	0.498	0.164±0.12	0.030	0.378	0.908

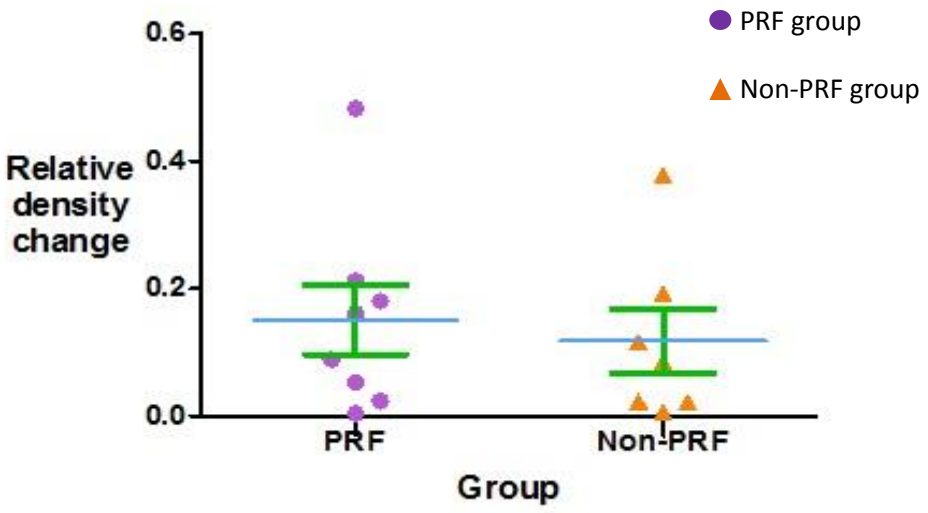


Figure 10 The change of relative density between two groups using CBCT

Part IV: Comparison of relative density between before, 1, 3 and 6 months after surgery by using periapical radiographs

In PRF group, the relative density of alveolar cleft before grafting ranged from 0.321 to 0.588, the mean ± SD was 0.461 ± 0.10. In non-PRF group, the cleft relative density ranged from 0.421 to 1.023, the mean ± SD was 0.707 ± 0.29. Then the bone filled relative density in cleft site at the 1st, 3rd and 6th month post-operation were measured.

At the 1st month post-operation, in PRF group, the filled relative density ranged from 0.289 to 1.1123, the mean was 0.707 ± 0.28. In non-PRF group, the filled relative density ranged from 0.382 to 1.782, the mean ± SD was 0.845 ± 0.45.

At the 3rd month post-operation, in PRF group, the filled relative density ranged from 0.158 to 0.876, the mean ± SD was 0.669 ± 0.24. In non-PRF group, the filled relative density ranged from 0.566 to 0.796, the mean ± SD was 0.668 ± 0.12.

At the 6th month post-operation, in PRF group, the filled relative density ranged from 0.531 to 0.979, the mean ± SD was 0.745 ± 0.18. In non-PRF group, the filled relative density ranged from 0.340 to 1.579, the mean ± SD was 0.807 ± 0.41.

Mann-Whitney U test showed no statistical significance in cleft volume at pre-operation and bone filled relative density of cleft site at the 1st, 3rd, 6th month post-operation between 2 groups (P = 0.249, 0.775, 0.570 and 0.949, respectively). (Table 4, Figure 11)

Table 4 Relative density analysis by periapical film in PRF and non-PRF group

Relative density	PRF Group (n = 8)			Non-PRF Group (n = 7)			p-value
	Mean ±SD	min	max	Mean ±SD	min	max	
Cleft site at pre-operation	0.461±0.10	0.321	0.588	0.707±0.29	0.421	1.023	0.249
Filled bone at 1 month	0.707±0.28	0.289	1.124	0.845±0.45	0.382	1.782	0.775
Filled bone at 3 months	0.669±0.24	0.158	0.876	0.668±0.12	0.566	0.796	0.570
Filled bone at 6 months	0.745±0.18	0.531	0.980	0.807±0.41	0.340	1.579	0.949

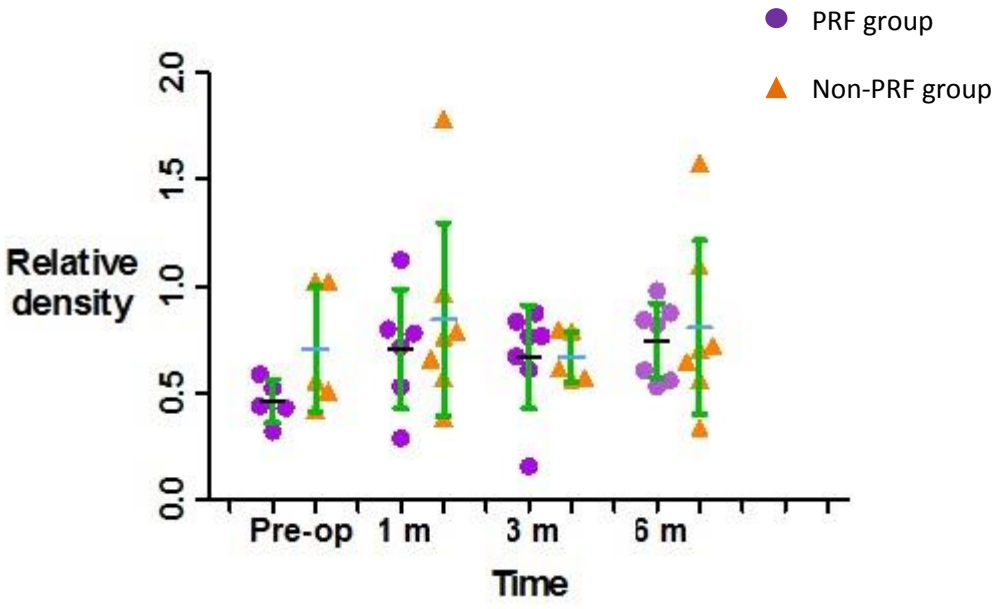


Figure11 The relative density between two groups at different time

Part V: Comparison of the change of relative density in each group from pre-operation to 6 months post-operation by using periapical radiographs

In PRF group and non-PRF group (Figure 12), Friedman test showed no statistical significance in change of filled bone relative density from pre-operation to 6 months post-operation (P = 0.122 and 0.960, respectively).

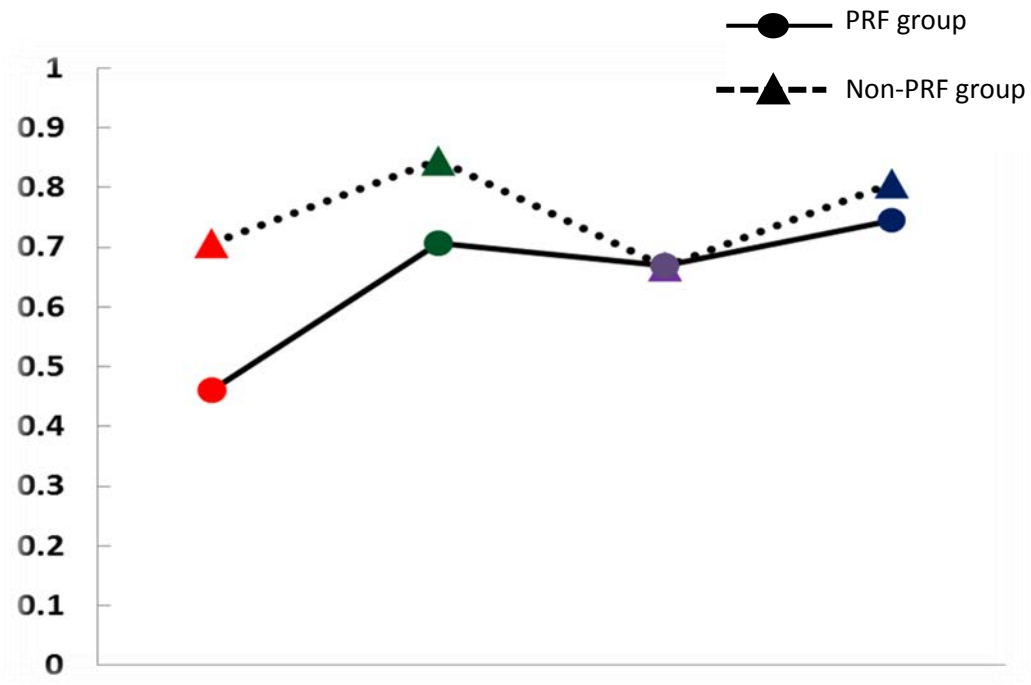


Figure 12 The filled bone relative density in both groups from pre-operation to the 6th month post-operation

In PRF group, the mean ± SD of the change of filled bone relative density from pre-operation to the 1st month post-operation was 0.124 ± 0.15, from pre-operation to the 3rd month post-operation was 0.175 ± 0.21 and from pre-operation to the 6th month post-operation was 0.239 ± 0.14. In non-PRF group, the mean ± SD of the change of filled bone relative density from pre-operation to the 1st month post-operation was 0.151 ± 0.38, from pre-operation to the 3rd month post-operation was 0.034 ± 0.27 and from pre-operation to the 6th month post-operation was 0.090 ± 0.36. Mann-Whitney U test showed no statistical significance in change of filled bone relative density between two groups from pre-operation to the 1st month post-operation, from pre-operation to the 3rd month post-operation and from pre-operation to the 6th month post-operation (P = 0.655, 0.173 and 0.465, respectively).(Table 5)

Table 5 Change of relative density analysis by periapical film in PRF and non-PRF group

Change of relative density	**PRF group (n=8)**	**Non-PRF group (n=7)**	p-value
	Mean ±SD	Mean ±SD	
Pre-operation to the 1st month	0.124±0.15	0.151±0.38	0.655
Pre-operation to the 3rd month	0.175±0.21	0.034±0.27	0.173
Pre-operation to the 6th month	0.239±0.14	0.090±0.36	0.465

Part VI: Position of filled bone at 6 months post-operation classified by Chelsea scale using periapical radiographs

In overall 15 cleft sites, the position of filled bone at 6 months post-operation were classified by Chelsea scale. (Table 6, Figure 13) In PRF group, five cleft sites (71.42%) were classified in grade A, one cleft site (14.29%) was classified in grade C and one cleft site (14.29%) was classified in grade D. There was one cleft site that could not classified because it did not have periapical radiograph at 6 months after surgery. In non-PRF group, three cleft sites (42.86%) were classified in grade A and four cleft sites (57.14%) were classified in grade C.

Table 6 Chelsea scale classification

	Grade A (Clefts)	**Grade C** (Clefts)	**Grade D** (Clefts)
PRF group (n=7)	5	1	1
(% in group)	(71.42%)	(14.29%)	(14.29%)
*missing data in 1 cleft			
Non-PRF group (n=7)	3	4	-
(% in group)	(42.86%)	(57.14%)	(0%)

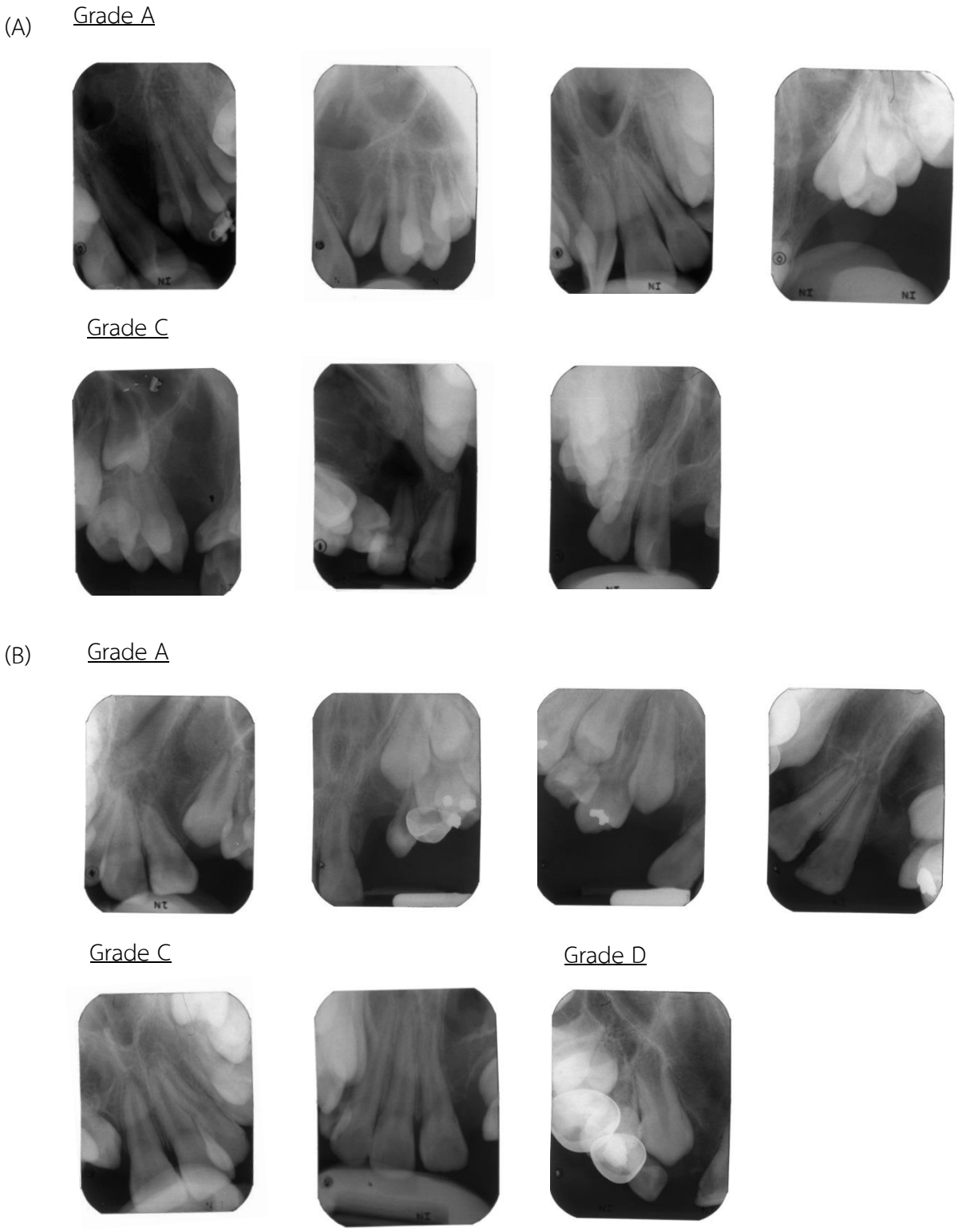


Figure 13 The position of filled bone classified by Chelsea scale (A) Non-PRF group, (B) PRF group

CHAPTER V
DISCUSSION AND CONCLUSION

Alveolar bone grafting is an essential procedure for management cleft lip and palate patients. It does not only facilitate the tooth eruption but also stabilize the maxillary arch. Autogenous iliac cancellous bone is preferable bone graft material because of higher osteoinductive property and more osteogenic cells than other grafting materials. Moreover, it can be harvested easily in adequate amount. However, partial bone resorption and inadequate of alveolar width or height was found postoperatively.

Factors influencing postoperative bone resorption have been reported including the age of patient, width of alveolar cleft, volume of grafted bone, and position of canine teeth as the major factors.(15, 67, 68) Growth factors, such as VEGF, PDGF and FGFb, also have influence of promote healing. These growth factors aid in angiogenesis, wound healing by epithelial cover and controlling circulating stem cells. Due to the richness of growth factors favorable to healing of PRF, we were interested in the benefit of PRF on bone graft healing. The outcome of grafted bone was measured by volume, density and position of filled bone in alveolar cleft at the 6th month after surgical procedures. However, iliac cancellous bone mixed with PRF failed to show higher prosperity. This study, we used plastic tubes to prepare PRF. After centrifuge, the PRF was coagulum. It did not form PRF membrane immediately like PRF preparation from the glass tube. We mixed bone particles with PRF in stainless steel plate. Then after 20-30 minutes, the particulate bone particles were glutinous aggregation. Interestingly, PRF aided in handling the graft particles by gluing them. Since no one reported about this property of PRF, we could claim that we were the first authors declared this advantage of PRF in making the bone particles stick together like a gelatinous composition.

There are many methods for post-operative evaluation of grafted bone. In this study, we assessed both qualitative and quantitative of filled bone by using periapical radiographs and cone beam computed tomography (CBCT). From the study of Jayasankar V. Valiyaparambil, et al.(69) reported that had trend of decreasing CBCT gray values of the edentulous sites with bone quality type from type 1 to type 4 classified by Lekholm and Zarb classification(70). However, this could not categorizing bone into 4 types because the range of CBCT gray values for type 2 and

type 3 were partly overlapped. They concluded that CBCT gray values can be used to infer bone density and help to predict bone quality at implant sites. This conformed to Salimov F, et al(71) that reported bone density assessment using CBCT is efficient method and significantly correlated with implant stability parameters and Lekholm and Zarb index(70). Due to the concerning of radiation exposure to pediatric patients and the costs of CBCT, we did not performed CBCT at immediate post-operation.

In this study, we did not find statistical difference between two groups but in PRF group had more slightly change of relative density than non-PRF group (0.172 and 0.164, respectively).

While the study of E. Marukawa et al.(51) reported quantitative aspect of the effect of platelet rich-plasma (PRP) by investigated bone resorption in width and height. It showed PRP group was less bone width resorption than non-PRP group, but did not differ in bone height resorption at 1 week, 1 month or 6 months.(51) However, we could not sort out the opacity of filled bone at 6 months whether it was the grafted bone or regenerated bone. Thus we assumed all of this opacity area of alveolar cleft in these CBCT images as healing bone graft.

To make the same position of taking periapical radiograph, we used impression material as the occlusal index in each patient. However, the eruption of teeth may affect the minimal position change.

In both groups, there were same tendency of the change of filled bone relative density. From pre-operation to the 1st month post-operation, the values of filled bone relative density were increased, then little decreased from the 1st month to the 3rd month post-operation and then were increased from the 3rd month to the 6th months post-operation. PRF group had lower relative density than non-PRF group at pre-operation and the 1st month post-operation but then increased to same level as non-PRF group at the 3rd month post-operation.

As previous described, the relative density at pre-operation in PRF group was lower than non-PRF group so we compared the change of relative density in both groups. The change of relative density at the 3rd month and the 6th month in PRF group were higher than non-PRF group. Although no statistical difference was found in the relative density change, we could assume that PRF might give some benefit in bone healing. Conformed to the study of E. Marukawa et al.(51) that the relative density of bone grafts in PRP group was lower than non-PRP group at 1 week after surgery. Then the relative density of bone grafts in PRP group gradually increased to the same level as non-PRP group from 1 month to 1 year after surgery.(51)

Moreover, we assessed position of filled bone at the 6th month post-operation. It classified by Chelsea scale.(7) This scale was first described by Witherow, et al in 2001. It has advantages over previously introduced scales that makes the filled-bone within the alveolar cleft to be measured in mixed dentition before canine erupted.(7) In this study, we found position of filled bone was classified to grade A and C in 13 cleft sites that referred the success of bone graft. Although one cleft site in PRF group was classified in grade D (50% of filled-bone) but it had sufficient bone to stabilized alveolar cleft and did not required further alveolar cleft bone grafting. However, at surgical operation, we could not place particulate iliac cancellous bone graft in tooth bearing area due to soft tissue stiffness and anatomical discrepancy. So we may not find the position of filled bone in that area in periapical radiographs.

However, we needed for further investigation on the effect of PRF improve in bone healing rate. Although the filled bone in the cleft showed no statistical difference between PRF and non-PRF group, PRF aided in handling the particulate bone. After mixing the PRF to the harvested particulate cancellous bone, the bone was more gelatinous aggregation.

Cone beam CT (CBCT) was used in this study due to the advantages over conventional radiograph as previously described. Especially the actual dimension of grafted area can be achieved. This conformed to our study, we found 75% of filled bone by using periapical radiographs at the 6th month post-operation classified by Chelsea scale, while in CBCT images had about 40% of filled bone in the same patient. Nowadays, it is evaluated success of bone graft by using only index from conventional radiographs, thus further investigation should create the specific index for three dimensional radiographs to assess the outcome after alveolar cleft bone grafting more precisely.

This study had many limitations including time, cost, and small sample size. We need further investigations about treated alveolar cleft bone grafting with PRF in long term follow up and more samples.

In conclusion, we found that at the 6th month post-operation quantitative value in PRF group was less than non-PRF group. In the other hand qualitative value in PRR group was more than non-PRF group. However, there was not statistical difference in both quantitative and qualitative aspects.

REFERENCES

1. Kalaaji A LJ, Friede H. Bone grafting at the stage of mixed and permanent dentition in patients with clefts of the lip and primary palate. Plast Reconst Surg. 1994;93:690-6.
2. Teja A PR, Omnell ML. Periodontal status of teeth adjacent to nongrafted unilateral alveolar clefts. Cleft Palate Craniofac J. 1992;29:357-62.
3. Choukroun J DA, Simonpieri A, et al. Platelet-rich fibrin (PRF): A second generation platelet concentrate. Part IV: Clinical effects on tissue healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endodont. 2006;101:E56-60.
4. Kawamura M UM. Human fibrin is a physiologic delivery system for bone morphogenic protein. Cln Orthop. 1998;235:302-10.
5. Marx RE CE, Eichstaedt RM, et al. Platelet-rich plasma: Growth factors enhancement for bone grafts. Oral Surg Oral Med Oral Pathol Oral Radiol Endodont. 1998;85:638-46.
6. Bergland O SG, Abyholm FE. Elimination of the residual alveolar cleft by secondary bone grafting and subsequent orthodontic treatment. Cleft Palate Craniofac J. 1986;23:175-205.
7. Witherow H CS, Jones E, Carr R,Waterhouse N. A new scale to assess radiographic success of secondary alveolar bone grafts. Cleft Palate Craniofac J. 2002;39(3):255-60.
8. Rosenstein SW LJR, Dado DV, Vinson B, Alder ME. Comparison of 2-D calculations from periapical and occlusal radiographs versus 3-D calculations from CAT scans in determining bone support for cleft-adjacent teeth following early alveolar bone grafts. Cleft Palate Craniofac J. 1997;34:195-8.
9. Van der Meji AJ BJ, Prahl-Andersen B, Valk J, Kostense PJ, Tuinzing DB. Bone volume after secondary bone grafting in unilateral and bilateral clefts determined by computed tomography scans. Oral Surg Oral Med Oral Pathol Oral Radiol Endodont. 2001;92:136-41.
10. Talvora MM CJ. Classification and birth prevalence of orofacial clefts. Am J Med Genet. 1998;75:126-37
11. Boyne PJ SN. Secondary bone grafting of residual alveolar and palate clefts J Oral surg. 1972;30:87-92.
12. DR M, editor. Cleft craft: the evolution of its surgery. Alveolar and palatal deformities. Boston: Little, Brown; 1980.

13. JC P, editor. The staging of cleft lip and palate reconstruction: infancy through adolescence. Philadelphia: WB Saunders; 2000.
14. S P. Presurgical orthopedics and bone grafting for infants with cleft lip and palate: a dissent. Cleft Palate J. 1964;1:164.
15. Enemark H K-SE, Schramm JE. Secondary bone grafting in unilateral cleft lip and palate patients: indications and treatment procedure. Int J Oral Surg. 1985;14:2-10.
16. Brattstrom V MJ, Larson O, Semb G. Craniofacial development in children with unilateral cleft of the lip, alveolus, and palate treated according to four different regimens, III: the soft tissue profiles at 16-18 years of age. Scand J Plast Reconstr Surg Hand Surg. 1992;26:197-202.
17. P. T. Autogenous bone grafts taken from the calvarium for facial and cranial applications. Clin Plast Surg. 1992;9:531-88.
18. Rosenstein SW MC, et al. The case for early bone grafting in cleft lip and palate. Plast Reconstr Surg. 1982;70:297-309.
19. Kalaaji A LJ, Elande A, Friede H. Tibia as donor site for alveolar bone grafting in patients with cleft lip and palate: long-term experience. Scand J Plast Reconstr Surg Hand Surg. 2001;35:35-42.
20. Borstlap WA HK, Freihofer HP, Kuijpers-Jagtman AM. Early secondary bone grafting of alveolar cleft defects: a comparison between chin and rib grafts. J Cranio Maxillofac Surg. 1990;18:201-5.
21. Santiago PE GB, Cutting CB, et al. Reduced need for alveolar bone grafting by pre-surgical orthopedics and primary gingivoperiosteoplasty. Cleft Palate Craniofac J. 1998;35:77-80.
22. Horswell BB HJ. Secondary osteoplasty of the alveolar cleft defect. J Oral Maxillofac Surg. 2003;61:1082-90.
23. Bureau S PM, McFadden L. Speech outcome after closure of oronasal fistulas with bone grafts. J Oral Maxillofac Surg. 2001;59:1408-13.
24. Abyholm RE BE, Semb G. Secondary bone grafting of alveolar clefts. Scand J Plast Reconstr Surg. 1981;15:127-40.
25. Vig KWL TT, Fonseca RJ, editor. Orthodontic and surgical considerations in bone grafting in the cleft maxilla and palate. Philadelphia: WB Saunders; 1996.
26. B E. Alveolar cleft bone grafting (part 1): Primary bone grafting. J Oral Maxillofac Surg. 1996;54:74-82.
27. SW R. Early bone grafting of alveolar cleft deformities. J Oral Maxillofac Surg. 2003;61:1078-81.

28. B W. The reconstruction of anterior residual bone defects in patients with cleft lip, alveolus and palate: a review. J Maxillofac Surg. 1985;13:197-208.
29. Daskalogiannakis J RR. Effect of alveolar bone grafting in the mixed dentition on maxillary growth in complete unilateral cleft lip and palate patients. Cleft Palate Craniofacial J. 1997;34:455-8.
30. Dempf R TT, Kramer FJ, Hausamen JE. Alveolar bone grafting in patients with complete clefts: a comparative study between secondary and tertiary bone grafting. Cleft Palate Craniofac J. 2002;39:18-25.
31. SN BP. Combined orthodontics surgical management of residual palatoalveolar cleft defects. Am J Orthod. 1976;70:20-37.
32. Kwon JK WD, Stickel FR, Chisholm T. The management of alveolar cleft defects. J Am Dent Assoc. 1981;102:848-53.
33. PJ B. Bone grafting in the osseous reconstruction of alveolar and palatal clefts. Oral Maxillofac Clin North Am. 1991;3:589-97.
34. Brattstrom V MJ. The influence of bone grafting age on dental abnormalities and alveolar bone height in patients with unilateral cleft lip and palate. Eur J Orthod. 1989;11:351-8.
35. Hall HD WJ. Conventional alveolar cleft bone grafting. Oral Maxillofac Clin North Am. 1991;3:609-16.
36. Choukroun J AF, Schoeffler C, Vervelle A. Une opportunite´en paro-implantologie: le PRF. Implantodontie. 2000;42:55-62.
37. Dvorak HF HV, Estrella P, Brown LF, McDonagh J, Dvorak AM. Fibrin containing gels induce angiogenesis. Implications for tumor stroma generation and wound healing. Lab Invest. 1987;57:673-86.
38. van Hinsbergh VW CA, Koolwijk P. Role of fibrin matrix in angiogenesis. Ann N Y Acad Sci. 2001;936:426-37.
39. Feng X CR, Galanakis D, Tonnesen MG. Fibrin and collagen differentially regulate human dermal microvascular endothelial cell integrins: stabilization of alphav/beta3 mRNA by fibrin1. J Invest Dermatol. 1999;113:913-9.
40. Sahni A OT, Francis CW. Binding of basic fibroblast growth factor to fibrinogen and fibrin. J Biol Chem. 1998;273:7554-9.
41. Nehls V HR. The configuration of fibrin clots determines capillary morphogenesis and endothelial cell migration. Microvasc Res. 1996;51:347-64.
42. Loike JD SB, Cao L, Leucona S, Weitz JI, Detmers PA, et al. CD11c/CD18 on neutrophils recognizes a domain at the N terminus of the A alpha chain of fibrinogen. Proc Natl Acad Sci USA. 1991;88:1044-8.

43. Kazura JW WJ, Salata RA, Budzynski AZ, Goldsmith GH. Modulation of polymorphonuclear leukocyte microbicidal activity and oxidative metabolism by fibrinogen degradation products D and E. J Clin Invest. 1989;83:1916-24.
44. Lanir N CP, Van de Water L, McDonagh J, Dvorak AM, Dvorak HF. Macrophage migration in fibrin gel matrices. II: Effects of clotting factor XIII, fibronectin, and glycosaminoglycan content on cell migration. J Immunol. 1988;140:2340-9.
45. Hamaguchi M MY, Takahashi I, Ogura M, Takamatsu J, Saito H. FDP D-dimer induces the secretion of interleukin-1, urokinase-type plasminogen activator, and plasminogen activator inhibitor-2 in a human promonocytic leukemia cell line. Blood. 1991;77:94-100.
46. Gray AJ BJ, Reeves JT, Laurent GJ. A alpha and B beta chains of fibrinogen stimulate proliferation of human fibroblasts. J Cell Sci. 1993;104:409-13.
47. Tuan TL SA, Chang S, Younai S, Nimni ME. In vitro fibroplasia: matrix contraction, cell growth, and collagen production of fibroblasts cultured in fibrin gels. Exp Cell Res. 1996;223:127-34.
48. Soffer E OJ, Anagnostou F. Fibrin sealants and platelet preparations in bone and periodontal healing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003;95:521-8.
49. Wouter M. M. T. van Hout ea. Reconstruction of the alveolar cleft: can growth factor-aided tissue engineering replace autologous bone grafting? A literature review and systematic review of results obtained with bone morphogenic protein-2. Clin Oral Invest. 2011;15:297-303.
50. Ramon Luaces-Rey ea. Is PRP useful in alveolar cleft reconstruction? Platelet-rich plasma in secondary alveoloplasty. Med Oral Patol Oral Cir Bucal. 2010 Jul 1;15(4):e619-23.
51. Eriko Marukawa ea. Reduction of bone resorption by the application of platelet-rich plasma (PRP) in bone grafting of the alveolar cleft. Cranio-Maxillo-Facial Surgery. 2011;39:278-83.
52. Baba R KY, Ueda K, et al. Comparison of flat-panel detector and image-intensifier detector for cone-beam CT. Comput Med Imaging Graph. 2002;26(3):153-8.
53. Mah J HD. Current status and future needs in craniofacial imaging. Orthod Craniofac Res. 2003;6:10-6.
54. P S. Cone beam computed tomography in craniofacial imaging. Orthod Craniofac Res. 2003;6:31-6.

55. Mah JK DR, Bumann A, et al. Radiation absorbed in maxillofacial imaging with a new dental computed tomography device. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003;96(4):508-13.
56. Ludlow JB IM. Comparative dosimetry of dental CBCT devices and 64-slice CT for oral and maxillofacial radiology. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;106(1):930-8.
57. Nakajima A SG, Arai Y, et al. Two- and three dimensional orthodontic imaging using limited cone beam computed tomography. Angle Orthod. 2005;75(6):895-903.
58. Madrigal C OR, Meniz C, et al. Study of available bone for interforaminal implant treatment using cone-beam computed tomography. Med Oral Patol Oral Cir Bucal. 2008;13(5):E307-12.
59. Honda K LT, Maruhashi K, et al. Osseous abnormalities of the mandibular condyle: diagnostic reliability of cone beam computed tomography compared with helical computed tomography based on an autopsy material. Dentomaxillofac Radiol. 2006;35(3):152-7.
60. Maki K IN, Takanishi A, et al. Computer-assisted simulations in orthodontic diagnosis and the application of a new cone beam X-ray computed tomography. Orthod Craniofac Res. 2003;6(1):95-101.
61. Korbmacher H K-NB, Sch¨ollchen M, et al. Value of two cone-beam computed tomography systems from an orthodontic point of view. J Orofac Orthop. 2007;68(4):278-89.
62. Silva MA WU, Heinicke F, et al. Cone-beam computed tomography for routine orthodontic treatment planning: a radiation dose evaluation. Am J Orthod Dentofacial Orthop. 2008;133(5):640e1-5.
63. Estrela C BM, Leles CR, et al. Accuracy of cone beam computed tomography and panoramic and periapical radiography for detection of apical periodontitis. J Endod. 2008;34(3):273-9.
64. Estrela C BM, Sousa-Neto MD, et al. Method for determination of root curvature radius using cone-beam computed tomography images. Braz Dent J. 2008;19(2):114-8.
65. Mol A BA. In vitro cone beam computed tomography imaging of periodontal bone. Dentomaxillofac Radiol. 2008;37(6):319-24.
66. Yang F JR, Willems G. Dental age estimation through volume matching of teeth imaged by cone-beam CT. Forens Sci Int. 2006;159(suppl 1):S78-83.
67. Giudice G ea. The role of functional orthodontic stress on implants in residual alveolar cleft. Plast Reconst Surg. 2007;119:2206-17.

68. Shima K ea. Evaluation of postoperative resorption of transplanted bone after secondary autogeneous particulate cnacellous bone and marrow grafting in alveolar cleft. J Jpn Cleft Palate Assoc. 1998;23:203-13.
69. Jayasankar V. Valiyaparambil ea. Bone Quality Evaluation: Comparison of Cone Beam Computed Tomography and Subjective Surgical Assessment. Int J Oral Maxillofac Implants. 2012;27:1271-7.
70. Lekholm U ZG. Patient selection and preparation:In: Branemark PI, Zarb GA, Albektsson T (eds). Tissue Integrated Prostheses: Osseointegraion in Clinical Dentistry. Chicago: Quintessence. 1985:199-209.
71. Salimov F ea. Evaluation of relationship between preoperative bone density values derived from cone beam computed tomography and implant stability parameters: a clinical study. Clin Oral Impl Res. 2013:1-6.

APPENDIX

APPENDIX A

Informed Consent Sheet for All Participants (in Thai)

Consent Form for All Participants (in Thai)

Withdrawal Form in Case Drop-out is Demanded (in Thai)

เอกสารข้อมูลคำอธิบายสำหรับอาสาสมัครที่เข้าร่วมในการวิจัย
(Patient/Participant Information Sheet)"

1. โครงการเรื่อง การศึกษาการใช้ลิ่มเพลตเลตริชไฟบรินในการปลูกถ่ายกระดูกในรอยแยกเบ้าฟัน โดยการใชhภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีม
2. ชื่อผู้วิจัยหลัก นางสาวอรินทรา ตาณะสุต
   สถาบันที่สังกัด ภาควิชาศัลยศาสตร์ช่องปากและแม็กซิโลเฟเชียล
   แหล่งทุนวิจัย ศูนย์ความเป็นเลิศทางการฟื้นฟูบูรณะช่องปากและใบหน้า
3. วัตถุประสงค์ของโครงการ เพื่อศึกษาถึงประสิทธิผลของลิ่มเพลตเลตริชไฟบรินต่อการหายของกระดูกในการปลูกถ่ายกระดูกในรอยแยกเบ้าฟัน
4. สถานที่ดำเนินการวิจัย คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
5. วิธีการที่เกี่ยวข้องกับการวิจัย โดยสรุป สั้นๆ กระชับ ได้ใจความ และใช้ภาษาที่เข้าใจง่าย ควรหลีกเลี่ยงศัพท์ทา วิชาการ

การศึกษาเปรียบเทียบผลการหายของกระดูกของกลุ่มอาสาสมัครที่ใช้ลิ่มเพลตเลตริชไฟบรินจากตัวอาสาสมัครเองกับกลุ่มอาสาสมัครที่ได้รับการผ่าตัดที่ไม่มีการใส่ลิ่มเพลตเลตริชไฟบริน โดยลิ่มเพลตเลตริชไฟบริน ได้มาจากเลือดของอาสามสมัครก่อนการผ่าตัดปลูกถ่ายกระดูกบริเวณรอยแยกเบ้าฟัน ซึ่งไม่ได้มีการเติมสารเคมีใดๆเข้าไป แล้วทำการถ่ายภาพรังสี CT scansและภาพรังสีปลายรากฟัน ติดตามผลที่ก่อนผ่าตัดและหลังผ่าตัดที่ 1, 3 และ 6 เดือน โดยมีเพียงการถ่ายภาพรังสี CT scans เพิ่มเติมจากการรักษาปกติที่ก่อนผ่าตัดและที่หลังผ่าตัด 6 เดือน

6. เหตุผลที่เชิญเข้าร่วมเป็นอาสาสมัครในโครงการ.(เช่น "เนื่องจากท่านเป็นผู้ป่วยโรค....." หรือ "เนื่องจากคาดว่า
   ท่านเป็นอาสาสมัครที่มีสุขภาพดี")..

เนื่องจากท่านเป็นผู้ป่วยปากแหว่งเพดานโหว่ที่เข้ารับการผ่าตัดปลูกถ่ายกระดูกรอยแยกบริเวณเบ้าฟัน

7. ความรับผิดชอบของอาสาสมัคร และ ระยะเวลาที่อาสาสมัครจะอยู่ในโครงการ

ขอให้ท่านปฏิบัติตามที่ผู้วิจัยแนะนำโดยการมาถ่ายภาพรังสีติดตามผลการรักษาเป็นระยะเวลา 6 เดือน

8. ประโยชน์ของการวิจัยที่อาสาสมัครและ/หรือผู้อื่นที่อาจได้รับ

ท่านจะไม่ได้รับประโยชน์ใด ๆ ในการร่วมการวิจัยครั้งนี้ แต่ผลการวิจัยที่ได้จะเป็นประโยชน์ในการปรับปรุงและพัฒนาการผ่าตัดปลูกถ่ายกระดูกรอยแยกบริเวณเบ้าฟันต่อไป

9. ความเสี่ยงหรือความไม่สะดวกที่อาจจะเกิดขึ้นแก่อาสาสมัคร และในบางกรณีแก่ทารกในครรภ์หรือทารกที่ดื่มนมมารดา

อาสาสมัครอาจได้รับปริมาณรังสีมากขึ้นและต้องใช้เวลาในการมาติดตามผลการรักษาเป็นระยะ

10. ค่าใช้จ่ายที่อาสาสมัครจะต้องจ่าย หรืออาจจะต้องจ่าย

ค่าใช้จ่ายเพิ่มเติมของอาสาสมัครเป็นค่าถ่ายภาพรังสี CT scan 2 ครั้ง ครั้งละ 3,000 บาท แต่หากขบวนการวิจัยนั้นมีการรักษาหรือตรวจมากเกินกว่ามาตรฐาน ผู้วิจัยและผู้สนับสนุนการวิจัยต้องออกค่าใช้จ่ายส่วนเกินทั้งหมด

11. การชดเชยใดๆ และการรักษาที่จะจัดให้แก่อาสาสมัครในกรณีที่ได้รับอันตรายซึ่งเกี่ยวข้องกับการวิจัย

หากท่านได้รับอันตรายจากการทำวิจัย ผู้วิจัยจะดำเนินการให้ท่านได้รับการรักษาโดยผู้วิจัยและผู้สนับสนุนการวิจัยจะเป็นผู้รับผิดชอบค่าใช้จ่ายของการรักษา

12. การจ่ายค่าเดินทาง ค่าเสียเวลา (ถ้ามี) ซึ่งต้องกำหนดไว้เป็นรายครั้ง แก่อาสาสมัครที่เข้าร่วมในการวิจัย (ทั้งนี้ต้องไม่มีข้อแม้หรือเงื่อนไขใดๆ ทั้งสิ้นในการจ่ายเงิน)

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13. เหตุการณ์ที่อาจจะเกิดขึ้น หรือเหตุผลซึ่งผู้วิจัยจะต้องยกเลิกการเข้าร่วมในโครงการวิจัยของอาสาสมัคร

ผู้วิจัยจะยกเลิกการเข้าร่วมในโครงการวิจัยของอาสาสมัครต่อเมื่ออาสาสมัครไม่สามารถมาถ่ายภาพรังสีติดตามผลการรักษาได้ครบตลอดระยะเวลาที่กำหนด

14. การกำกับดูแลและควบคุมการดำเนินโครงการ

ผู้กำกับดูแลการวิจัย ผู้ตรวจสอบ คณะกรรมการพิจารณาจริยธรรม และคณะกรรมการที่เกี่ยวข้อง สามารถเข้าไปตรวจสอบการดำเนินโครงการ รวมทั้ง ตรวจสอบบันทึกข้อมูลของอาสาสมัคร เพื่อเป็นการยืนยันถึงขั้นตอนในการวิจัยทางคลินิกและข้อมูลอื่นๆ โดยไม่ล่วงละเมิดเอกสิทธิ์ในการปิดบังข้อมูลของอาสาสมัคร ตามกรอบที่กฎหมายและกฎระเบียบได้อนุญาตไว้ นอกจากนี้ โดยการลงนามให้ความยินยอม อาสาสมัครหรือ ผู้แทนตามกฎหมายจะมีสิทธิตรวจสอบและมีสิทธิที่จะได้รับข้อมูลด้วยเช่นกัน

15. จริยธรรมการวิจัย

การดำเนินการโครงการวิจัยนี้ ผู้วิจัยคำนึงถึงหลักจริยธรรมการวิจัย ดังนี้

1. หลักความเคารพในบุคคล (Respect for person) โดยการให้ข้อมูลจนอาสาสมัครเข้าใจเป็นอย่างดีและตัดสินใจอย่างอิสระในการให้ความยินยอมเข้าร่วมในการวิจัย รวมทั้งการเก็บรักษาความลับของอาสาสมัคร

2. หลักการให้ประโยชน์ไม่ก่อให้เกิดอันตราย (Beneficence/Non-Maleficence) โดยระบุในข้อ 8 และ 9 ว่าจะมีประโยชน์หรือความเสี่ยงกับอาสาสมัครหรือไม่

3. หลักความยุติธรรม (Justice) คือมีเกณฑ์คัดเข้าและคัดออกชัดเจน มีการกระจายความเสี่ยงและผลประโยชน์อย่างเท่าเทียมกัน โดยวิธีสุ่มเข้ากลุ่มศึกษา

16. ข้อมูลที่อาจนำไปสู่การเปิดเผยตัวของอาสาสมัครจะได้รับการปกปิด ยกเว้นว่าได้รับคำยินยอมไว้โดยกฎระเบียบและกฎหมายที่เกี่ยวข้องเท่านั้น จึงจะเปิดเผยข้อมูลแก่สาธารณชนได้ ในกรณีที่ผลการวิจัยได้รับการตีพิมพ์ ชื่อและที่อยู่ของอาสาสมัครจะต้องได้รับการปกปิดอยู่เสมอ และอาสาสมัครหรือผู้แทนตามกฎหมายจะได้รับแจ้งโดยทันท่วงที ในกรณีที่มีข้อมูลใหม่ซึ่งอาจใช้ประกอบการตัดสินใจของอาสาสมัครว่าจะยังคงเข้าร่วมในโครงการวิจัยต่อไปได้หรือไม่

17. หากท่านมีข้อสงสัยต้องการสอบถามเกี่ยวกับสิทธิของท่านหรือผู้วิจัยไม่ปฏิบัติตามที่เขียนไว้ในเอกสารข้อมูลคำอธิบายสำหรับผู้เข้าร่วมในการวิจัย ท่านสามารถติดต่อหรือร้องเรียนได้ที่ ฝ่ายวิจัย คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ตึกสมเด็จย่า 93 ชั้น 10 หรือที่หมายเลขโทรศัพท์ 0-2218-8816 ในเวลาราชการ

18 หากท่านต้องการยกเลิกการเข้าร่วมเป็นอาสาสมัครในโครงการนี้ ให้ท่านกรอกและส่งเอกสารขอยกเลิกมาที่

นางสาวอรินทรา ตาณะสุต **ที่ทำงาน** คลินิกทันตกรรมโปรเด็นท์ **โทรศัพท์** 02-776599044
ที่อยู่ปัจจุบัน 250/413 ม.กรีนวิลล์ ซอย ¾ ถนนพุทธมณฑลสาย 2 ศาลาธรรมสพน์ ทวีวัฒนา กรุงเทพมหานคร 10170 **โทรศัพท์** 086-1623880

19. อาสาสมัครสามารถติดต่อผู้วิจัยได้ตลอด 24 ชั่วโมง ที่:

นางสาวอรินทรา ตาณะสุต **ที่ทำงาน** คลินิกทันตกรรมโปรเด็นท์ **โทรศัพท์** 02-776599044
ที่อยู่ปัจจุบัน 250/413 ม.กรีนวิลล์ ซอย ¾ ถนนพุทธมณฑลสาย 2 ศาลาธรรมสพน์ ทวีวัฒนา กรุงเทพมหานคร 10170 **โทรศัพท์** 086-1623880

.....

(นางสาวอรินทรา ตาณะสุต)

ผู้วิจัยหลัก

วันที่...../...../.....

เอกสารยินยอมเข้าร่วมการวิจัย (Consent Form)

เอกสารยินยอมเข้าร่วมการวิจัย (Consent Form)

การวิจัยเรื่อง การศึกษาการใช้ลิ่มเพลตเลตริชไฟบรินในการปลูกถ่ายกระดูกในรอยแยกเบ้าฟันโดยการใชhภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีม

"ข้าพเจ้า (นาย, นาง, นางสาว, เด็กชาย,เด็กหญิง).....

อยู่บ้านเลขที่.....ถนน.....ตำบล/แขวง.....

อำเภอ/เขต.....จังหวัด.....รหัสไปรษณีย์.....

ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้ ข้าพเจ้าได้รับเอกสารข้อมูลคำอธิบายสำหรับอาสาสมัครที่เข้าร่วมในการวิจัยแล้ว 1 ฉบับ รวมทั้งได้รับการอธิบายจากผู้วิจัยถึงวัตถุประสงค์ของการวิจัย วิธีการทำวิจัย อันตรายหรืออาการที่อาจเกิดขึ้นจากการทำวิจัยหรือจากยาที่ใช้ รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยรับรองว่าจะตอบคำถามต่าง ๆ ที่ข้าพเจ้าสงสัยด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าพอใจ

ข้าพเจ้าเข้าร่วมโครงการวิจัยนี้โดยสมัครใจ ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยนี้เมื่อใดก็ได้และการบอกเลิกการเข้าร่วมการวิจัยนี้จะไม่มีผลต่อการรักษาโรคที่ข้าพเจ้าจะพึงได้รับต่อไป

ผู้วิจัยรับรองว่าจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับ และจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่าง ๆ ที่เกี่ยวข้องกระทำได้เฉพาะกรณีจำเป็น ด้วยเหตุผลทางวิชาการเท่านั้น และผู้วิจัยรับรองว่าหากเกิดอันตรายใด ๆ จากการวิจัยดังกล่าว ข้าพเจ้าจะได้รับการรักษาพยาบาลโดยไม่คิดมูลค่า

ข้าพเจ้าได้อ่านเอกสารและข้อความข้างต้นแล้ว มีความเข้าใจดีทุกประการ และได้ลงนามในใบยินยอมนี้ด้วยความเต็มใจ

ข้าพเจ้าได้รับสำเนาเอกสารใบยินยอมที่ข้าพเจ้าลงนามและลงวันที่ และเอกสารยกเลิกการเข้าร่วมวิจัย อย่างละ 1 ฉบับ เป็นที่เรียบร้อยแล้ว

ลงนาม..... ผู้ยินยอม

(.....)

วันที่.....เดือน.....พ.ศ.....

ลงนาม..... พยาน

(.....)

วันที่.....เดือน.....พ.ศ.....

ลงนาม..... ผู้วิจัยหลัก

(.....)

วันที่.....เดือน.....พ.ศ.....

ข้าพเจ้าไม่สามารถอ่านหนังสือได้ แต่ผู้วิจัยได้อ่านข้อความในใบยินยอมนี้ให้แก่ข้าพเจ้าฟังจนเข้าใจดีแล้ว ข้าพเจ้าจึงลงนาม หรือประทับลายนิ้วหัวแม่มือขวาของข้าพเจ้าในใบยินยอมนี้ด้วยความเต็มใจ

ลงนาม.....ผู้ยินยอม
(.....)
วันที่.....เดือน.....พ.ศ.....

ลงนาม.....พยาน
(.....)
วันที่.....เดือน.....พ.ศ.....

ลงนาม.....ผู้วิจัยหลัก
(.....)
วันที่.....เดือน.....พ.ศ.....

ในกรณีที่ผู้ถูกทดลองยังไม่บรรลุนิติภาวะ จะต้องได้รับการยินยอมจากผู้ปกครองหรือผู้อุปการะโดยชอบด้วยกฎหมาย

ลงนาม..... ผู้ยินยอม
(.....)
วันที่.....เดือน.....พ.ศ.....

ลงนาม..... พยาน
(.....)
วันที่.....เดือน.....พ.ศ.....

ลงนาม..... ผู้วิจัยหลัก
(.....)
วันที่.....เดือน.....พ.ศ.....

เอกสารยกเลิกการยินยอมเข้าร่วมวิจัย (Withdrawal Form)

การวิจัยเรื่อง การศึกษาการใช้ลิ่มเพลตเลตริชไฟบรินในการปลูกถ่ายกระดูกในรอยแยกเบ้าฟันโดยการใชh ภาพรังสีส่วนตัดอาศัยคอมพิวเตอร์ชนิดโคนบีม

เหตุผลในการยกเลิกการยินยอมเข้าร่วมวิจัย

- ❑ ย้ายภูมิลำเนา
- ❑ ไม่สะดวกในการเดินทาง
- ❑ เหตุผลอื่น.....

.....

ลงนาม.....ผู้ยกเลิกการยินยอม
(.....)
ลงนาม.....พยาน
(.....)
ลงนาม.....พยาน
(.....)
ลงนาม.....หัวหน้าโครงการวิจัย
(.....)
วันยกเลิกการยินยอมเข้าร่วมวิจัย วันที่.....เดือน.....พ.ศ. .....

APPENDIX B

Statistic Output

Table 1 Descriptive analysis in the gender of PRF and non-PRF groups

Group * Gender Crosstabulation

			Gender		
			1	2	Total
Group	PRF	Count	6	0	6
		% within Group	100.0%	.0%	100.0%
		% within Gender	66.7%	.0%	46.2%
		% of Total	46.2%	.0%	46.2%
	non PRF	Count	3	4	7
		% within Group	42.9%	57.1%	100.0%
		% within Gender	33.3%	100.0%	53.8%
		% of Total	23.1%	30.8%	53.8%
Total		Count	9	4	13
		% within Group	69.2%	30.8%	100.0%
		% within Gender	100.0%	100.0%	100.0%
		% of Total	69.2%	30.8%	100.0%

Table 2 Descriptive analysis in the cleft side of PRF and non-PRF groups

Group * Side Crosstabulation

			Side		
			Right	Left	Total
Group	PRF	Count	4	4	8
		% within Group	50.0%	50.0%	100.0%
		% within Side	57.1%	50.0%	53.3%
		% of Total	26.7%	26.7%	53.3%
	non PRF	Count	3	4	7
		% within Group	42.9%	57.1%	100.0%
		% within Side	42.9%	50.0%	46.7%
		% of Total	20.0%	26.7%	46.7%
Total		Count	7	8	15
		% within Group	46.7%	53.3%	100.0%
		% within Side	100.0%	100.0%	100.0%
		% of Total	46.7%	53.3%	100.0%

Table 3 and 4 Descriptive analysis in the age of PRF and non-PRF groups

Report

Age

Group	Mean	N	Std. Deviation	Range	Minimum	Maximum
PRF	9.83	6	1.602	4	9	13
non PRF	10.29	7	1.890	6	8	14
Total	10.08	13	1.706	6	8	14

Group * Age Crosstabulation

			Age						Total
			8	9	10	11	13	14	
Group	PRF	Count	0	4	1	0	1	0	6
		% within Group	.0%	66.7%	16.7%	.0%	16.7%	.0%	100.0%
		% within Age	.0%	80.0%	25.0%	.0%	100.0%	.0%	46.2%
		% of Total	.0%	30.8%	7.7%	.0%	7.7%	.0%	46.2%
	non PRF	Count	1	1	3	1	0	1	7
		% within Group	14.3%	14.3%	42.9%	14.3%	.0%	14.3%	100.0%
		% within Age	100.0%	20.0%	75.0%	100.0%	.0%	100.0%	53.8%
		% of Total	7.7%	7.7%	23.1%	7.7%	.0%	7.7%	53.8%
Total		Count	1	5	4	1	1	1	13
		% within Group	7.7%	38.5%	30.8%	7.7%	7.7%	7.7%	100.0%
		% within Age	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	7.7%	38.5%	30.8%	7.7%	7.7%	7.7%	100.0%

Table 5 and 6 Descriptive analysis in the cleft side of PRF and non-PRF groups

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
Pre-op. volume * Group	15	100.0%	0	.0%	15	100.0%
The 6th post-op.volume * Group	15	100.0%	0	.0%	15	100.0%
Percentagel * Group	15	100.0%	0	.0%	15	100.0%

Group		Pre-op. volume	6th month Post op .volume	Percentage
PRF	Mean	369.5113	230.9887	64.8713
	N	8	8	8
	Std. Deviation	110.52245	73.47848	19.62990
	Range	312.27	226.38	52.08
	Minimum	234.78	142.80	41.31
	Maximum	547.05	369.18	93.39
non PRF	Mean	441.7643	298.7829	67.7400
	N	7	7	7
	Std. Deviation	111.99490	114.90578	18.72947
	Range	325.20	341.79	49.71
	Minimum	363.60	147.72	40.57
	Maximum	688.80	489.51	90.28
Total	Mean	403.2293	262.6260	66.2100
	N	15	15	15
	Std. Deviation	113.46916	97.89652	18.57958
	Range	454.02	346.71	52.82
	Minimum	234.78	142.80	40.57
	Maximum	688.80	489.51	93.39

Table 7 and 8 Comparison in the value of pre-operation volume, the 6th month post-operation volume and percentage of filled bone using CBCT between two groups by Mann-Whitney test

Mann-Whitney Test

Ranks

	Group	N	Mean Rank	Sum of Ranks
Pre-op.volume	PRF	8	6.63	53.00
	non PRF	7	9.57	67.00
	Total	15		
6th month Post-op.volume	PRF	8	6.63	53.00
	non PRF	7	9.57	67.00
	Total	15		
Percentage	PRF	8	7.75	62.00
	non PRF	7	8.29	58.00
	Total	15		

Test Statistics[b]

	Prevolume	Postvolume	Ratiovol
Mann-Whitney U	17.000	17.000	26.000
Wilcoxon W	53.000	53.000	62.000
Z	-1.273	-1.273	-.231
Asymp. Sig. (2-tailed)	.203	.203	.817
Exact Sig. [2*(1-tailed Sig.)]	.232[a]	.232[a]	.867[a]

a. Not corrected for ties.

b. Grouping Variable: Group

Table 9-11 Descriptive analysis in the relative density using CBCT in the cleft site at pre-operation and the 6th month post-operation

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum
CTdensitypre	15	.58247	.102551	.415	.717
CTdensity6m	15	.75093	.087853	.641	.923
ChangeCT	15	.16853	.130624	.024	.498
Group	15	1.47	.516	1	2

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
CTdensitypre * Group	15	100.0%	0	.0%	15	100.0%
CTdensity6m * Group	15	100.0%	0	.0%	15	100.0%
ChangeCT * Group	15	100.0%	0	.0%	15	100.0%

Report

Group		CT density pre-op.	CT density 6th month	Change of density
PRF	Mean	.57813	.74350	.17213
	N	8	8	8
	Std. Deviation	.124266	.095784	.150454
	Minimum	.415	.641	.024
	Maximum	.717	.923	.498
	Range	.302	.282	.474
non PRF	Mean	.59514	.75943	.16443
	N	7	7	7
	Std. Deviation	.078561	.084544	.115616
	Minimum	.477	.661	.030
	Maximum	.691	.855	.378
	Range	.214	.194	.348

Total	Mean	.58247	.75093	.16853
	N	15	15	15
	Std. Deviation	.102551	.087853	.130624
	Minimum	.415	.641	.024
	Maximum	.717	.923	.498
	Range	.302	.282	.474

Table 12 and 13 Comparison in the value of pre-operation, the 6th month post-operation and change of filled bone relative density using CBCT between two groups by Mann-Whitney test

Mann-Whitney Test

Ranks

	Group	N	Mean Rank	Sum of Ranks
CT density pre-op.	PRF	8	7.63	61.00
	non PRF	7	8.43	59.00
	Total	15		
CT density 6th month	PRF	8	7.38	59.00
	non PRF	7	8.71	61.00
	Total	15		
Change of density	PRF	8	7.88	63.00
	non PRF	7	8.14	57.00
	Total	15		

Test Statistics[b]

	CT density pre-op.	CT density 6th month	Change of density
Mann-Whitney U	25.000	23.000	27.000
Wilcoxon W	61.000	59.000	63.000
Z	-.347	-.579	-.116
Asymp. Sig. (2-tailed)	.728	.562	.908
Exact Sig. [2*(1-tailed Sig.)]	.779[a]	.613[a]	.955[a]

a. Not corrected for ties.

b. Grouping Variable: Group

Table 14 and 15 Descriptive analysis in the relative density using periapical films in the cleft site at pre-operation and the 1st, 3rd, 6th month post-operation

Case Processing Summary

	Cases					
	Included		Excluded		Total	
	N	Percent	N	Percent	N	Percent
Density pre-op. * Group	10	66.7%	5	33.3%	15	100.0%
Density 1st month * Group	13	86.7%	2	13.3%	15	100.0%
Density 3rd month * Group	12	80.0%	3	20.0%	15	100.0%
Density 6th month * Group	14	93.3%	1	6.7%	15	100.0%

Report

Group		Density pre-op.	Density 1st month	Density 3rd month	Density 6th month
PRF	Mean	.46068640	.70650950	.66923514	.74470957
	N	5	6	7	7
	Std. Deviation	.101457883	.280509715	.242882567	.176748947
	Minimum	.320854	.289059	.158129	.530600
	Maximum	.587996	1.123569	.875800	.979748
	Range	.267142	.834510	.717671	.449148
non PRF	Mean	.70676720	.84522243	.66791120	.80653343
	N	5	7	5	7
	Std. Deviation	.292379389	.452052498	.116925120	.408145795
	Minimum	.421259	.381629	.566079	.340414
	Maximum	1.022570	1.782151	.795579	1.579155
	Range	.601311	1.400522	.229500	1.238741
Total	Mean	.58372680	.78120108	.66868350	.77562150
	N	10	13	12	14
	Std. Deviation	.243699960	.374355156	.192741630	.303861905
	Minimum	.320854	.289059	.158129	.340414
	Maximum	1.022570	1.782151	.875800	1.579155
	Range	.701716	1.493092	.717671	1.238741

Table 16 and 17 Comparison in the relative density in cleft site at pre-operation and the 1st, 3rd, 6th month post-operation using periapical film between two groups by Mann-Whitney test

Mann-Whitney Test

Ranks

	Group	N	Mean Rank	Sum of Ranks
Density pre-op.	PRF	5	4.40	22.00
	non PRF	5	6.60	33.00
	Total	10		
Density 1st month	PRF	6	6.67	40.00
	non PRF	7	7.29	51.00
	Total	13		
Density 3rd month	PRF	7	7.00	49.00
	non PRF	5	5.80	29.00
	Total	12		
Density 6th month	PRF	7	7.43	52.00
	non PRF	7	7.57	53.00
	Total	14		

Test Statistics[b]

	Density pre-op.	Density 1st month	Density 3rd month	Density 6th month
Mann-Whitney U	7.000	19.000	14.000	24.000
Wilcoxon W	22.000	40.000	29.000	52.000
Z	-1.152	-.286	-.568	-.064
Asymp. Sig. (2-tailed)	.249	.775	.570	.949
Exact Sig. [2*(1-tailed Sig.)]	.310[a]	.836[a]	.639[a]	1.000[a]

a. Not corrected for ties.

Test Statistics[b]

	Density pre-op.	Density 1st month	Density 3rd month	Density 6th month
Mann-Whitney U	7.000	19.000	14.000	24.000
Wilcoxon W	22.000	40.000	29.000	52.000
Z	-1.152	-.286	-.568	-.064
Asymp. Sig. (2-tailed)	.249	.775	.570	.949
Exact Sig. [2*(1-tailed Sig.)]	.310[a]	.836[a]	.639[a]	1.000[a]

a. Not corrected for ties.

b. Grouping Variable: Group

Table 18 Descriptive analysis in the relative density in the cleft site using periapical films of non-PRF group from pre-operation to the 6th month post-operation

NPar Tests non-PRF

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum
Density pre-op.	4	.6278165	.26912114	.42126	1.02257
Density 1st month	4	.6272868	.19072666	.38163	.79099
Density 3rd month	4	.6359943	.10694563	.56608	.79274
Density 6th month	4	.6020993	.17746797	.34041	.72239

Table 19 and 20 Comparison in the relative density in cleft site in non-PRF group using periapical films from pre-operation to the 6th month post-operation by Friedman test

Friedman Test

Ranks

	Mean Rank
Density pre-op.	2.25
Density 1st month	2.50
Density 3rd month	2.75
Density 6th month	2.50

Test Statistics[a]

N	4
Chi-Square	.300
df	3
Asymp. Sig.	.960

a. Friedman Test

Table 21 Descriptive analysis in the relative density in the cleft site using periapical films of PRF group from pre-operation to the 6th month post-operation

NPar Tests PRF

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum
Density pre-op.	3	.4777773	.13956076	.32085	.58800
Density 1st month	3	.6018717	.27405537	.28906	.79972
Density 3rd month	3	.5998127	.38646393	.15813	.87580
Density 6th month	3	.7864263	.21246737	.55895	.97975

Table 22 and 23 Comparison in the relative density in cleft site in PRF group using periapical films from pre-operation to the 6th month post-operation by Friedman test

Friedman Test

Ranks

	Mean Rank
Density pre-op.	1.67
Density 1st month	2.00
Density 3rd month	2.33
Density 6th month	4.00

Test Statistics[a]

N	3
Chi-Square	5.800
df	3
Asymp. Sig.	.122

a. Friedman Test

Table 24 Descriptive analysis in the Chelsea scale using periapical films at the 6th month post-operation in both groups

Group * Chelsea scale Crosstabulation

			Chelsea scale			
			A	C	D	Total
Group	PRF	Count	3	1	1	5
		% within Group	60.0%	20.0%	20.0%	100.0%
		% within Chelsea scale	50.0%	20.0%	100.0%	41.7%
		% of Total	25.0%	8.3%	8.3%	41.7%
	non PRF	Count	3	4	0	7
		% within Group	42.9%	57.1%	.0%	100.0%
		% within Chelsea scale	50.0%	80.0%	.0%	58.3%
		% of Total	25.0%	33.3%	.0%	58.3%
Total		Count	6	5	1	12
		% within Group	50.0%	41.7%	8.3%	100.0%
		% within Chelsea scale	100.0%	100.0%	100.0%	100.0%
		% of Total	50.0%	41.7%	8.3%	100.0%

Table 25 and 26 Comparison in the change of filled bone relative density in cleft site at pre-operation and the 1st, 3rd, 6th month post-operation using periapical film between two groups by Mann-Whitney test

Group		Pre-1m	Pre-3m	Pre-6m
PRF	Mean	.12433	.17500	.23860
	Std. Deviation	.154053	.205558	.135055
non PRF	Mean	.15140	.03420	.09040
	Std. Deviation	.375433	.266051	.358380
Total	Mean	.14125	.10460	.16450
	Std. Deviation	.295838	.236105	.267002

Test Statistics[b]

	Pre-1m	Pre-3m	Pre-6m
Mann-Whitney U	6.000	6.000	9.000
Wilcoxon W	21.000	21.000	24.000
Z	-.447	-1.362	-.731
Asymp. Sig. (2-tailed)	.655	.173	.465
Exact Sig. [2*(1-tailed Sig.)]	.786[a]	.222[a]	.548[a]

a. Not corrected for ties.

b. Grouping Variable: Group

VITA

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