การเปรียบเทียบผลของการใช้แผ่นเยื่อกีดขวางสองชนิดที่แตกต่างกันในการฝังรากเทียม
ร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกในบริเวณที่ต้องการความสวยงาม

นางสาวสิริดา อรุณเจริญสุข

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COMPARISON OF THE OUTCOMES OF GBR SIMULTANEOUS WITH DENTAL IMPLANTS IN THE ESTHETIC ZONE USING TWO DIFFERENT MEMBRANES

Miss Sirida Arunjaroensuk

A Thesis Submitted in Partial Fulfillment of the Requirements
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สิริดา อรุณเจริญสุข : การเปรียบเทียบผลของการใช้แผ่นเยื่อกีดขวางสองชนิดที่แตกต่างกันในการฝังรากเทียมร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกในบริเวณที่ต้องการความสวยงาม (COMPARISON OF THE OUTCOMES OF GBR SIMULTANEOUS WITH DENTAL IMPLANTS IN THE ESTHETIC ZONE USING TWO DIFFERENT MEMBRANES) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: รศ. ทพ. ดร.อาทิพันธุ์ พิมพ์ขาวขำ, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: รศ. ทพ. ดร.สุนทรา พันธ์มีเกียรติ, หน้า.

วัตถุประสงค์: เพื่อเปรียบเทียบผลของการใช้แผ่นเยื่อกีดขวางชนิดสังเคราะห์และชนิดคอลลาเจนในการฝังรากเทียมร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกในบริเวณที่ต้องการความสวยงาม

วิธีการศึกษา: รากเทียมที่ฝังร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกจำนวน 60 รากเทียม ถูกแบ่งออกเป็น 2 กลุ่ม (กลุ่มละ 30 รากเทียม) โดยใช้แผ่นเยื่อกีดขวางชนิดสังเคราะห์ในกลุ่มทดลองและชนิดคอลลาเจนในกลุ่มควบคุม เพื่อวิเคราะห์เปรียบเทียบผลทางคลินิกโดยใช้ความกว้างของเหงือกยึดและเสถียรภาพของการปลูกกระดูกภายหลังการผ่าตัดและ 6 เดือนภายหลังการผ่าตัดโดยใช้ความหนาของกระดูกด้านหน้าจากภาพถ่ายรังสีคอมพิวเตอร์แบบโคนบีมคอมพิวเตดโทโมกราฟฟีและระดับกระดูกด้านประชิดจากภาพถ่ายรังสีปลายราก

ผลการศึกษา: ความกว้างของเหงือกยึดและความหนาของกระดูกด้านหน้าลดลงไม่แตกต่างกัน แต่ระดับกระดูกด้านประชิดใกล้กลางลดลงอย่างมีนัยสำคัญทางสถิติ ในกลุ่มทดลองมากกว่ากลุ่มควบคุม (p=0.017) อย่างไรก็ตาม ไม่พบการสูญเสียรากเทียมตลอดการศึกษา

บทสรุป: แผ่นเยื่อกีดขวางชนิดสังเคราะห์สามารถนำมาใช้ในการฝังรากเทียมร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกได้ดีเช่นเดียวกันกับแผ่นเยื่อกีดขวางชนิดคอลลาเจน

ภาควิชา ศัลยศาสตร์ ลายมือชื่อนิสิต .....

สาขาวิชา ศัลยศาสตร์ช่องปากและแม็กซิลโลเฟเชียล ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

ปีการศึกษา 2558

5675821232 : MAJOR ORAL AND MAXILLOFACIAL SURGERY
KEYWORDS: DENTAL IMPLANT / GUIDED BONE REGENERATION / RESORBABLE MEMBRANE / FACIAL BONE THICKNESS / CONE BEAM COMPUTED TOMOGRAPHY

SIRIDA ARUNJAROENSUK: COMPARISON OF THE OUTCOMES OF GBR SIMULTANEOUS WITH DENTAL IMPLANTS IN THE ESTHETIC ZONE USING TWO DIFFERENT MEMBRANES. ADVISOR: ASSOC. PROF. ATIPHAN PIMKHAOKHAM, D.D.S., Ph.D., CO-ADVISOR: ASSOC. PROF. SOONTRA PANMEKIATE, D.D.S., Ph.D., pp.

Objective: To compare the outcomes of the synthetic membrane and collagen membrane using for implant placement with GBR.

Materials and Methods: a total of 60 dental implants in esthetic zone were enrolled in this study and randomly allocated to a simultaneous GBR using either synthetic resorbable membrane in study group (n=30) or a collagen resorbable membrane in comparison group (n=30). Clinical outcomes were assessed by the width of keratinized mucosa (KM). The stability of contour augmentation was analyzed by a facial bone thickness (FBT) using a cone beam computed tomographic (CBCT) image and the distance between the implant shoulder and the first bone-implant contact (DIB) using periapical film over 6 months.

Results: The mean change of KM and FBT change were similar decreased in both groups. However, the statistical significant difference was found between groups for only the DIB value change at mesial aspects (p=0.017). All implants were stable with existing facial bone and no implant loss was found over this study.

Conclusion: A synthetic resorbable membrane revealed similar outcomes to collagen resorbable membrane and suitable used for GBR simultaneous with dental implant placement.

Department:	Oral and Maxillofacial Surgery	Student's Signature .....
		Advisor's Signature .....
Field of Study:	Oral and Maxillofacial Surgery	Co-Advisor's Signature .....
Academic Year:	2015	

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CHAPTER I

INTRODUCTION

Background and Rationale

The dental implant has become an important treatment with greater popularity and highly success outcome for edentulous patients over more than past thirty years, [1, 2] and it has a well-documented with prospective long-term studies.[3, 4] Dental implant placement in an esthetic zone is challenging to the surgeon and dental clinicians because of the patient's esthetic concerns, difficult anatomical structure involved bone deficiencies, and various risk factors that can influence to a predictability of the outcome.[5]

The bone reduction of alveolar ridge is a phenomenon occurred immediately post-extraction and result in a decreasing of volume and morphologic change of alveolar ridge. The most of the ridge alteration estimated two thirds of bone resorption happens in the first quarter of the year after extraction, and results in a decrease of both horizontal and vertical dimensions approximately 50% reduction during the first 12 months[6, 7] After that, the progression of these changes resulted in 0.25 - 0.5% ridge reduction per year.[8] The dimensional alteration is greater on the buccal site of alveolar ridge due to the higher proportion of bundle bone that decomposed from the loss of blood supply from the periodontal ligament after tooth extraction.[9, 10]

Alveolar ridge change sometimes jeopardizes the implant placement in an optimal position and may results in a dehiscence or fenestration after implantation. Moreover, the deficient alveolar ridge endangers the esthetic outcome especially in the anterior maxilla. Therefore, many surgical techniques have been suggested for augment the alveolar ridge and to treat bony defect such as bone grafting, bone splitting, distraction osteogenesis and guided bone regeneration. One of the most frequently used and scientifically well documented techniques is guided bone regeneration (GBR).

The GBR technique has established to be a predictable and successful method of contour augmentation at site for implant placement. This procedure can be performed prior to or simultaneously with implant placement[11] and considered important for the esthetic outcome because of the establishment of sufficient facial bone thickness compensated for ridge resorption after tooth

extraction. The Principal concept of GBR is the use of bone particles combined with barrier membrane to inhibit the ingrowth of fast-growing connective tissue and allow the slower growing osteoblasts occupy the dehiscence or fenestration to accomplish the bone regeneration over the exposed implant surface. The stability of contour augmentation was represented for the success outcome of GBR technique and currently assessed using CBCT in many studies.[12-16]

Nowadays, a various bone grafting materials and membranes have been used in conjunction with GBR, autogenous bone grafts are appraised as a gold standard because it forms new bone by osteogenesis, osteoinduction, and osteoconduction. Furthermore, it has no risk of disease transmission.[17] The disadvantages of using autogenous bone grafts are the requirement of a second operative site, the limited availability of bone amount especially from intraoral donor site, the patient morbidity, and complications [18, 19] including neurosensory disturbance, wound dehiscence, and infection. Owing to these many disadvantages, recent clinical studies were directed toward the alternative bone grafting materials including allografts, xenografts and synthetic bone grafts. Among these, xenografts was approved as the gold standard at present time[20, 21] however possible transmission of prion-related diseases from animal products may occurred and occasionally reported.[22] Thus, the use of synthetic bone grafts, beta-tricalcium phosphate (β-TCP) and hydroxyapatite (HA), was more popular and many studies reported the equal result with xenografts.[23-26]

In order to achieve the success of GBR, barrier membrane plays an important role as well; the major studies related to non-resorbable membranes have involved expanded polytetrafluoroethylene (e-PTFE) membranes. This membrane is accepted as the gold standard[27, 28] for augmentation and reported an increase in new bone regeneration up to 5.5 mm.[29] However, the main disadvantage of this material is that the membrane has to be displaced so a second surgery was needed for the membrane removal. In addition, a frequent post-operative complication is membrane exposure resulting inflammatory response and bacterial colonization from its roughness, so a tension free primary flap closure is required for prevent membrane exposure to the oral environment.

To overcome these shortcomings, resorbable collagen membranes have become the optional membrane in various situations without necessity for a

second surgery for retrieval. Numerous studies [30-32] demonstrated the effectiveness of resorbable membrane composed of porcine collagen (Bio-Gide®) in bone regeneration procedures including simultaneous augmentation around implant placed in osseous defects. Collagen membrane often used in conjunction with deproteinized bovine bone mineral and was proper for accomplished in GBR for treat osseous defects surrounding dental implants as well as a non-resorbable membrane.[30, 31] Also, this membrane was confirmed as the gold standard of presently used. Notwithstanding, all collagen membranes originated from animal sources, which can be trouble for patient acceptance, immune responses, and a transmission of infectious agents. Furthermore, other potential drawbacks of collagen membranes are soft and not stable, so it can collapse during healing period. Moreover, collagen membranes are fast biodegradable, resulting in a loss of a barrier function, thus compromising the bone regeneration.[33]

The synthetic resorbable membranes were introduced to serve as alternative barrier membranes. The development of this membrane based on biocompatible synthetic material from polymers such as polylactic acid (PLA), polyglycolic acid (PGA), and trimethylene carbonate. These synthetic polymers have clear advantage over collagen membranes that these can be reproduced in unlimited quantities under controlled condition. Another advantage is the property of complete biodegradation to carbon dioxide and water. However, sufficient documentation of clinical studies using synthetic resorbable membrane is still lacking in dental literature and limited data are available reporting on the application of this membrane combined with the use of synthetic bone graft for ridge augmentation simultaneous with implant installation.

Hence, the purpose of this study is to compare the synthetic resorbable membrane with a resorbable collagen membrane in combination with a synthetic bone substitute material regarding in clinical outcomes and stability of contour augmentation in GBR.

Research Question

Does GBR using the synthetic membrane resulted in significantly better outcomes compared to collagen membrane in short-term period?

Objective

To compare the outcomes of the synthetic membrane and collagen membrane using for implant placement with GBR in term of clinical outcomes and stability of contour augmentation.

Definition of this study

Clinical outcomes

Clinical outcomes were examined by the clinical standard soft tissue parameters, the width of keratinized mucosa (KM) and clinical observation such as handling during surgery and post-operative complication.

The stability of contour augmentation

The stability of contour augmentation was examined by two radiographic parameters including facial bone thickness and the distance between the implant shoulder and the first bone-implant contact (DIB)

Hypothesis

Hypothesis 1

H_0: The change of the width of keratinized mucosa (KM) in patients whom GBR with the synthetic membrane is used is <u>not</u> higher than patient whom GBR with the collagen membrane is used.

H_1: The change of the width of keratinized mucosa (KM) in patient whom GBR with the synthetic membrane is used is higher than patient whom GBR the collagen membrane is used.

Hypothesis 2

H_0: The decreasing of a facial bone thickness in patient whom GBR with the synthetic membrane is used is <u>not</u> higher than patient whom GBR with the collagen membrane.

H_1: The decreasing of a facial bone thickness in patient whom GBR with the synthetic membrane is used is higher than patient whom GBR with the collagen membrane is used.

Hypothesis 3

H_0: The decreasing of the distance between the implant shoulder and the first bone-implant contact (DIB) in patient whom GBR with the synthetic membrane is used is not higher than patient whom GBR with the collagen membrane is used.

H_1: The decreasing of the distance between the implant shoulder and the first bone-implant contact (DIB) in patient whom GBR with the synthetic membrane is used is higher than patient whom GBR with the collagen membrane is used.

Research Design

Prospective Randomized clinical trial

Limitation

This study reported the short-term period outcomes 6 months after contour augmentation with GBR as a case series due to a restriction of timeframe for study. All data is still being recorded for further long-term evaluation.

Expected Benefit

A synthetic membrane together with a synthetic bone graft can be effectively used for GBR contour augmentation. This technic considered to be an alternative treatment for implants with guided bone regeneration.

Conceptual Framework

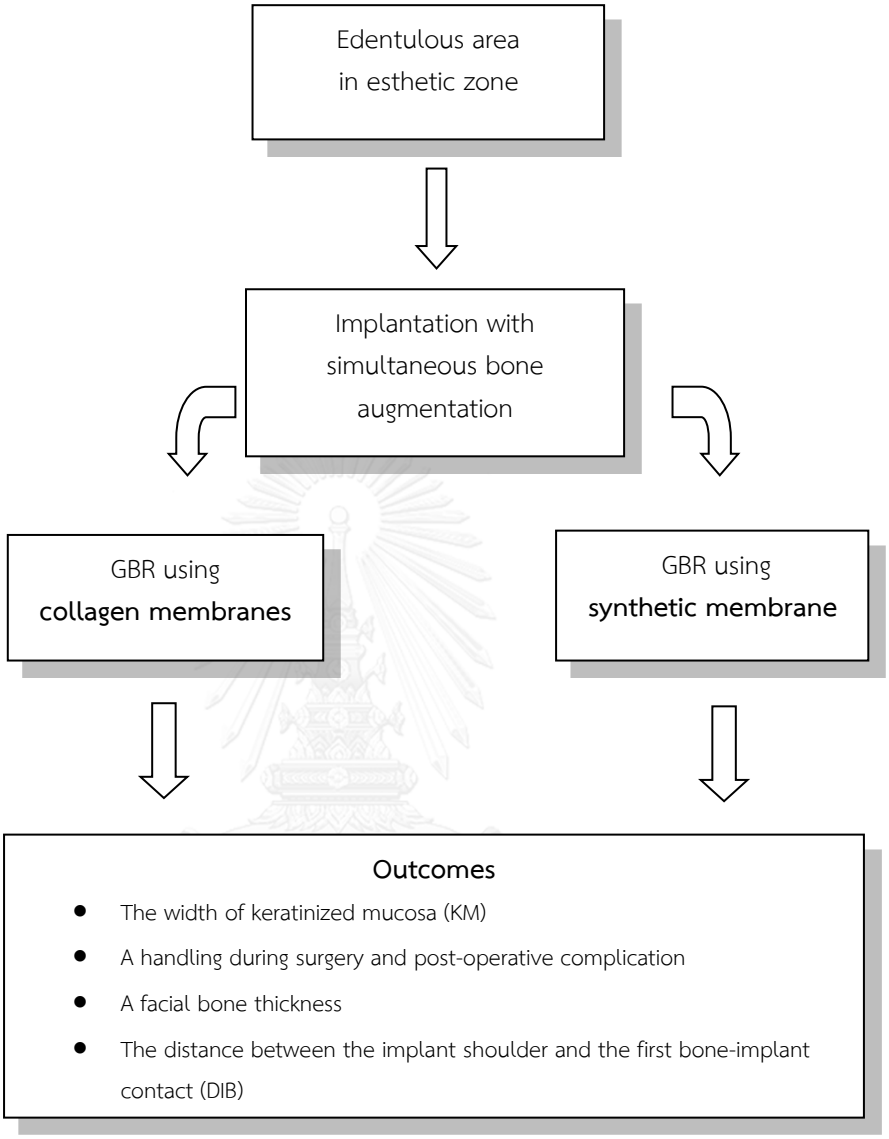

Figure 1 Conceptual Framework

CHAPTER II

REVIEW OF BASIC KNOWLEDGE AND LITERATURE

Implant placement in esthetic zone

Anterior maxillary sites are most likely linked to esthetic expectations and often considered a challenge to oral surgeons and dental clinicians. This esthetic challenge is based on a variety of local risk factors that are frequently presented in the anterior teeth area and possible to endangering the predictability of treatment outcomes.[5, 34] To placed dental implants in the esthetic zone, clinicians need a concept of treatment that offers a pleasing result with a great predictability and a least complications. There is very important to analyze various factors prior to implantation including level of the smile line, dental midline, inter-arch relationship, size of edentulous area, status of adjacent teeth, gingival biotype, gingival morphology and anatomy of alveolar crest. There are two anatomical bony structures that are extremely important to the construction of soft tissue in the anterior sites. First is the interproximal crest height and the second one is the bone thickness and the bone height of facial wall. In the anterior region, most extracted socket has a thin of facial bone wall because these teeth generally located in the facial position. Moreover, the facial bone wall can often be damaged and disappeared following tooth extraction. Having a sufficient facial bone wall is essential for stability of concordant gingiva surrounding implants and adjacent teeth.[5, 35] To achieve the esthetic outcome in anterior site requires bone augmentation at implant placement for obtain favorable the facial bone wall. Various bone augmentation procedures have been proposed to establish the bone structure for facilitate a dental implant placement such as bone expansion, distraction osteogenesis, block grafting and GBR. Those techniques can performed prior to, simultaneous or post implantation. Nowadays, bone augmentation procedures are routinely accomplished simultaneously with implant placement for avoidance of multiple surgeries, less patient morbidities and shorten treatment time.

The timing of implant placement was one of critical factors influenced on success outcomes.[36] The concept of immediate implant placement in an extracted socket simultaneous with bone augmentation has been offered for minimize the amount of surgical procedures. Although this concept is well

evidenced with high survival rate, clinical studies [37-39] clearly reported about esthetic complications with immediate implant especially in risk for mucosal recession at the facial aspect with a frequency of around 35% to 40%. Several studies [40, 41] confirmed that the recession of the facial mucosa is the major complication observed with immediate implants. The potential risk factors indicated to cause such complications are facial malpositioning of the implant[37, 38] and the facial bone defect at implant placement.[39] In addition, less predictable of facial bone augmentation with immediate implants was one potential cause of gingival recession. Consequently, the early implant placement following 4-8 weeks of tooth extraction has been suggested as alternative approach. This approach comprised a healed soft tissue of post-extraction site prior to implant placement to permit a predictable contour augmentation.[42]

Guided bone regeneration

Guided bone regeneration (GBR) technique is a one of the most frequently used and scientifically well documented procedures that have been suggested for contour augmentation simultaneous with implant placement. The GBR is a regenerative technique using membranes and developed from the guided tissue regeneration (GTR) that was earliest described by Nyman *et al* [43] in 1980. The GTR principle is based on the perivascular cells from both the periodontal ligament (PDL) and alveolar bone conduce to the formation of new bone, cementum, and PDL. The GTR was indicated as a periodontal apparatus formative procedure and evolved from a series of studies. [44, 45] To achieve the reconstruction of an osseous defect, the rate of bone regeneration growing inside from surrounding boundary must overcome the rate of fibrous formation spreading from enclosing gingival tissue. Therefore, the objectives of GTR are an obstruction of the fibroblast cell's migration with using a barrier membrane for isolation of epithelium and connective tissue and allow the PDL cells populate on the root surface. Currently, there are very plentiful of publication with animal researches and clinical studies in regard to GTR for correction of bone defects in both natural teeth and dental implants.

GBR concept manipulated the similar rationale of particular tissue blockage had an objective for regeneration of bone only. Dahlin and colleagues [46] preceded initially research of GBR in an effort to treat an bony defects of jaws including the reconstructing of the atrophic ridge and continued to sustain

for the principle of GBR in the bone regeneration for clinical used in further studies.

The depletion of alveolar bone may exist prior to tooth extraction due to bone destruction suffering from periapical pathology, trauma, or periodontal disease. Traumatic tooth extraction may cause bone loss of the alveolar bone. Moreover, alveolar bone resorption post-extraction is a common occurred phenomenon. All of these can lead to alveolar ridge alteration and inadequate bone for dental implant placement. The GBR was proposed as a surgical procedure for increasing the bone volume quantity of bone and became a popularly used technique for alveolar ridge augmentation to facilitate the implant surgery. GBR procedures can be performed prior to dental implant placement when there had a large osseous defect, no primary stability of implants or less predictable outcomes. Furthermore, GBR can be accomplished in conjunction with dental implantation to increase the quantity of bone where defect would endanger the esthetics or function of dental implants.[47]

Grunder *et al.*[48] declared that the great number of esthetic implant cases required GBR to abstain from gingival recession caused by alveolar bone resorption. Alveolar ridge resorption and alterations in the marginal gingival position may occur unless the facial alveolar bone thickness is approximately 2.0 mm at the time of implantation. Thus, the GBR should be performed in many cases to achieve sufficient facial alveolar bone thickness and the proper marginal gingival position.

Principles of GBR

To improve clinical outcomes, GBR barrier should occupy the following five main criteria by Scantlebury [49]: biocompatibility, space-making, cell-occlusiveness, tissue integration and clinical manageability.

Biocompatibility: The barrier membrane should not provide harmful effect to the surrounding tissue and the healing result. The interaction between the material and tissue must be overall safe for the patient.

Space-making: The barrier membrane should create an optimal space for osseous regeneration and provide adequate support to the tissue. Moreover, the membrane should have the sufficient stiffness to withstand the external forces because the quantity of regeneration was reduced due to the collapse of membrane into the defect space.

Cell-occlusiveness: The optimal barrier membrane should isolate surrounding fast-growing epithelium and connective tissue, and provide slower growing bone-forming cells accessed for bone regeneration. Therefore, the membrane porosity has a crucial influence on the capability for cell occlusion.

Tissue integration: Tissue integration is the essential aspect for the structural integrity of the barrier membrane and the adequate adaptability of its borders to the adjacent original bone constitute prerequisites for creates a completely to prevent fibrogenesis. The membrane border should be extended 2-3 mm far away from all margins of the defect. In addition, the corners membrane should be carefully trimmed and not be sharp to prevent accidental flap perforation.

Clinical manageability: The barrier membrane should be practical for clinical use. A membrane that is difficult to use, such as one that is too flexible, can be collapse and will often lead to complications and frustrating outcomes. In the other hand, a membrane that is too stiff cannot be contoured easily and could perforate the gingival tissue and following exposure of the membrane.

Factors influencing the success of GBR

A numerous factors that have been associated with adversely influence the outcome of GBR include [50]:

Smoking: A clinical study to define the influence of smoking on regeneration results by Tonetti *et al.*[51] reported that patients who were smokers had a 4.3 times increased risk for an undesirable outcome to nonsmokers. Approximately 43.8% to 62.5% of sites had an undesirable response in smoker while only 8.7% of sites in nonsmoker patients had undesirable result after 1 year.

Diabetes: Although there are no direct information to determine an effect of diabetes on the success of bone regeneration, Kornman and Robertson [52] stated that the risk for a failure of regenerative therapy was theoretically increased in diabetics with poor glucose control. A delayed wound healing response may be one determinant of the increased risk. This late healing and inflammatory process were the probable result of disable control of glucose level. To reduce this risk factor, the only practical management is improved the glucose metabolic control.

Defect morphology: The success of regenerative procedure has been associated with the defect depth and number of defect walls. The alveolar ridge width between 2.5 to 5.0 mm was a suitable indication for GBR treatment.

Bacterial contamination: Plaque control is well documented to be a critical component part for success outcomes of surgical procedures.[52] Some study [53] reported a important role of bacteria in decreased bone regeneration. The local area that has a dental plaque was related to statistical significance of lower bone formation and clinical attachment level. The colonization of bacterial colonization of various species was not associated with the type of membranes used in bone regenerative procedures.[54] However, the comparatively high degree of bacterial contamination was found in e-PTFE membranes.[55]

Membrane Exposure: This is the most common postoperative complication of GBR. The exposed membrane also leads to supplementary complications that impact on wound healing such as infection from bacterial contamination. A covered thin flap may become necrosis and resulted in postoperative soft tissue dehiscence and early membrane exposure. Nowadays, it is still controversy that the early membrane exposure affected the bone regeneration. The frequency of membrane exposure of GBR procedures was reported approximately 60% and significantly jeopardized the outcome in GBR with dental implant when compared to GTR around tooth. Simion *et al.* [56] investigated the influence of membrane exposure on osseointegrated implants with GBR. They stated the bone regeneration about 48.6% where early membrane exposure occurred while the bone regeneration was gained 99.6% in bony defects with no membrane exposure. They concluded that bone formation is noticeably reduced with the membrane exposure. Becker *et al.* [57] examined bone formation around immediate implant placements and reported 41.6% bone regeneration when membranes exposed compared to 96.6% bone regeneration for implants with non-exposed membrane. They concluded that the membrane exposure was significantly less bone regeneration. To prevent this complication, complete primary wound closure is necessary. However, Mellonig and Triplett [58] stated that the result of GBR was not affected by early membrane exposure, it was depended on other conditions so frequent appointment for close follow-up and proper management were still necessary in these patients. Shanaman [59] concluded that no significance of membrane exposure in case of adequate postoperative oral hygiene management.

Because an attentive oral hygiene can decreases the possibility of infection resulting from membrane exposure.

Gingival thickness: a study of Anderegg *et al.* [60] to assess the correlation of the flap thickness covering the membrane with postsurgical gingival recession at six month. The authors found that the flap thickness was importance to be considerate. In the group of less than 1 mm flap thickness had a gingival recession with a mean of 2.1 mm while as a gingival recession in the group of more flap thickness was found with a mean of 0.6 mm. A thickness of gingiva more than 1.5 mm is required to retain blood supply for preclude the flap from necrosis and accomplish the desirable outcomes. The gingival recession and loss of interdental papillary were prone to occurred in the event of GBR with deep bony defects and thin gingival biotype in the anterior maxilla.

Success of GBR

The success of GBR is a one of the essential considerations in dental implant surgery. Mellonig and Triplet [58] described the first definition of success of GBR in 1993 as the capability of complete covering of a regenerated hard tissue on a dehiscence or fenestration of implant surface. In 2009, the second definition of success was proposed by Fugazzotto. [61] This second definition was the regenerate an adequate volume of bone for resist functional forces over time. However, any previous definition is not enough for success of GBR in the esthetic zone. Because the definition of success must include regeneration of alveolar ridge dimension to ultimately sustain the soft tissues covering and help to possible excellent treatment outcomes, such an explanation of the third definition of success of GBR.[61]

The implants placed into augmented bone and barrier membranes mostly reported more than 90% survival rate with at least 1 year after loading and comparable outcome with conventional implants placement in native bone.[62, 63] The study of Zitzmann *et al.*[20] evaluated implants placed into regenerated bone compared to native bone. The cumulative implant survival rates were not reached the significant differences among three groups: 95.4% implant survival rates in regenerated bone with a collagen membrane, 92.6% implant survival rates in regenerated bone with an e-PTFE membrane and 97.3% implant survival rates in native bone without GBR.

A prospective controlled study [63] evaluated the survival rate of thirty-

eight implants in seven patients with an average of 25 months follow-up. Twenty-one implants were placed in GBR with a polylactic, polyglycolic acid membrane as a test group and seventeen implants were placed in the pristine bone with no additional bone regeneration procedure as a control group. The survival rate was reported 100% for all implants at a mean of 25 months follow-up and there was no significant difference of the marginal bone levels between two groups.

Today, the GBR procedures are routinely used by using barrier membranes in conjugation with autogenous bone grafts and other bone substitutes. The goal of long-term stability of contour augmentation by GBR is institution of a facial bone thickness at least 2 to 3 mm to accomplish adequate and durable bone for sustain the facial soft tissues.[13, 35]

Buser *et al.*[13] analyzed a long-term stability of treatment outcome following single-tooth early implant placed simultaneous with contour augmentation by GBR in the anterior maxilla for six years. In their prospective study, twenty patients were followed and assessed at 1, 3 and 6 year follow-up with clinical, radiologic, and esthetic parameters. Furthermore, a cone beam computed tomography (CBCT) was used for investigated a facial bone wall at 6 year follow-up. Over time of the study period, all twenty implants were prosperously integrated and had steadiness of the clinical parameters. Esthetic outcomes were evaluated with the pink esthetic scores (PES) and presented satisfying results. No any implants were recorded of one millimeter or more of mucosal recession. The peri-implant bone levels were stable by periapical radiographs and the facial bone wall thickness was detected in all implants at six years with a mean of 1.9 mm. The authors concluded that contour augmentation with GBR was suitable for construct a sustained facial bone wall with stable peri-implant tissues in all twenty patients.

Type of bone grafts

Numerous methods have been used to maintain and support the space for against membrane collapse. Several bone graft materials were suggested to place under the membrane for mechanical support and promote bone formation. Bone grafts can collected from many sources and are generally named according to their origin as autograft, allograft, xenograft, and alloplasts.

Autogenous bone grafts

Autogenous bone is acquired from the personal for which the graft is purposed. It has long been accepted the gold standard among the bone graft materials used. Autogenous bone grafts build up bone by the three processes of bone formation: osteogenesis, osteoinduction, and osteoconduction and can be harvested from both extraoral and intraoral sites. Moreover, it has no risk of disease transmission.[17]

However, there are many disadvantages of using autogenous bone such as the requirement of a second operative area, the limited availability of bone grafts especially from intraoral sites, the patient morbidity, and complications including neurosensory disturbance, wound dehiscence, and infection.[18, 19] These disadvantages led to development of alternative bone substitute material including allografts and alloplasts. A systematic review of Chiapasco and Zaniboni [64] analyzed clinical outcomes of GBR to repair the peri-implant dehiscence and fenestrations and reported no superiority of bone regeneration of autogenous bone compared with other bone grafting materials.

Fiorellini *et al.*[23] reported the percentage of bone-to-implant contact (BIC) following GBR in an animal model with a randomized various bone fillers. An e-PTFE membrane was used for covering all defects for ridge augmentation and removed at 8 months later with implant placement procedures. All beagle dogs were sacrificed after 3 months of implant surgery. All implant sites exhibited high percentages of BIC; however there were no significant differences among treatment groups. No sign of peri-implantitis was occurred with the osseointegrated implants. In addition, this study demonstrated that all implants placed in wholly augmented bone can accomplish osseointegration with not related to type of the bone grafting used.

Allografts

Allografts have been proposed as optional bone grafting from another individual of the same species or cadavers. The advantages include ready available, osteoinductive property, osteoconductive property and elimination of the need for a patient donor site. However, the main disadvantage of allografts is the probable transmission of antigenicity and disease.[65] The most commonly used for reconstructing osseous defects are mineralized freeze-dried bone allografts and demineralized freeze-dried bone allografts (FDBA or DFDBA). Allografts have no osteogenesis property, so they takes longer time for

bone regeneration and results in lesser amount of new bone compared with autogenous grafts. FDBA may form bone by osteoinduction and osteoconduction and hardens faster than DFDBA. FDBA has approximately resorption time 6-15 months whereas DFDBA has resorption time about 2-4 months and usually used for periodontal defect only.

Meffert [66] compared the use of FDBA and DFDBA for sinus grafting procedure. After 6 months, FDBA revealed a new bone formation while as DFDBA presented a dense connective tissue. Another study[67] evaluated the alveolar ridges augmented with FDBA and an e-PTFE barrier prior to the placement of implants. The clinical outcome and histologic analysis of this study demonstrated predictable results.

The use of DFDBA has been suspected because it has reported with regard to unpredictable of new bone regeneration. Brugnami F *et al.* [68] studied the use of DFDBA for induction of new bone in humans. They found the DFDBA particles be surrounded by connective tissue. A later study[69] has shown that the osteoinductive activity of DFDBA may considerably alter among bone banks as well as among different samples from the same bone bank.

These are no vastly approved certifies to secure that DFDBA material converges the minimum standards for osteoinduction. Because this graft material has dropped out of appreciation with numerous surgeons, there has limited reports to assess the osteoconductive properties of DFDBA. [70]

Xenografts

Xenografts are taken from other species that mostly were animals such as cow, pig and horse.[71] These bone grafting are used to repair osseous defects and atrophy alveolar ridges by served as a scaffold for new bone formation. Similar advantages to allografts, using xenografts eliminated secondary surgical site and patient morbidity. Nevertheless, xenografts has been demonstrated only osteoconductive property and possible transmission of prion-related diseases from bovine products. [22]

Bovine bone-derived substitute

Bio-Oss® (Geistlich Pharma AG, Wolhusen, Switzerland) is anorganic, deproteinized bovine bone-derived substitute that has been remove organic part with chemical method. This material is one of the most popular and well-

studied bone substitutes that considered as the gold standard. The scaffold of this material had a specific three-dimensional surface structure that relevant to a natural bone mineral. The dental implant placed in combination with Bio-Oss® and collagen membranes was reported a high survival rate ranging from 95.4 to 100%. [20, 21]

Dahlin *et al*.[72] evaluated the GBR technique for bone augmentation with bovine hydroxyapatite (BHA) in regard to the stability of soft and hard tissue over time. The Implant survival rate, marginal bone level (MBL), and marginal soft tissue level (MSTL) were recorded for 5 years following implant placement in 20 patients with 41 implants. The defect area was corrected with BioOss® in a combination with 20% autogenous bone chips assembled during the implant placement. They stated the cumulative implant survival rate about 97.5% during the duration of the study with one mobile implant at visit of abutment connection. Although the reduction in MBL and MSTL were reached the statistical significance over the five-year observation, all patients exhibited a stable bone level above the implant platform with favorable papillae appearance.

During the last decade, the bovine hydroxyapatite has been vastly used in many clinical situations due to its osteoconduction and resemblance to human bone.[73] This material was originally regarded a slow resorbing bone substitute. However, a several studies are supported that no signs of resorption of the bovine hydroxyapatite particles was found after 6 years.[74, 75]

Alloplasts

Alloplasts or synthetic bone grafts are introduced as alternative scaffold in bone regeneration. These materials have no need of second operative site and no transmissible disease. A few recent studies [23-26] reported that no significant differences between synthetic bone and deproteinized bovine bone mineral. Based on the histologic and histometric results, the regeneration of bone among two different materials resulted in similar and comparable proportions of direct contact between bone and the implant surface. Alloplasts are available in various sizes, textures, shapes, porosity and composition resulted in varying rate of bioresorbability.

Bioactive glass ceramics

Two characteristics of bioactive glass ceramics that conduce to the successful outcomes are a fast rate of reaction with host cells and the capabillity of bonding to a collagen. The high level of bioactivity may induce osteogenesis and encourage the repair process.[76] The reaction layers were developed immediately after implantation. The osteogenic cells in the site of implant placement migrated to the particles and generated a collagen on these surfaces of the particles. However, the superior biological important properties of bioactive glass abide to be studied.

Tricalcium phosphate

Tricalcium phosphate (TCP) is not a natural composition of bone. TCP is similar to hydroxyapatite and changed to crystalline hydroxyapatite in the body.[77] The resorption rate of TCP was varied and considerably depended on the chemical structure, particle size and porosity of material. Similar to other bone substitute materials, TCP had an osteoconductive property and was purposed to provide a suitable physical scaffold for new bone formation.[65] It was often used for correction nonpathologic sites where might be predicted for resorption of the graft and coexisting bone replacement.[78] TCP was safe and well tolerated.[76] Moreover, it can used with other grafting materials for the better handling property during operation.[65]

Hydroxyapatite

The properties of a hydroxyapatite (HA) define the resorption rate and the clinical utilities of this bone grafts.[65] For example, smaller particles take faster resorption and shorter remaining at the site of augmentation.[79] The immense porosity of the material provides more scaffolding for new bone formation and quick resorption of the graft. The more crystalline graft influences slower resorption rate. Consequently, crystalline grafts resorb more slowly than amorphous grafts. Solid, dense blocks of HA have a greater compressive strength but are also more fragile; hence, they are not determined appropriate for load-bearing circumstance. A general weakness of ceramics is that their strength exponentially reduces as their porosity increases. Using particles in place of solid, dense blocks decreases the problem of fragileness. Particulate HA is often utilized for ridge augmentation and well adapt to the underlying bone structure.

Biphasic calcium phosphate

The HA/TCP is a new wholly synthetic bone substitute available as particle and also called biphasic calcium phosphate. It is composed of insoluble crystalline hydroxyapatite (HA) and soluble beta-tricalcium phosphate (β-TCP) sintered in vary ratio at temperatures of 1100–1500°C. It is 90% porous with diameter of interconnected pores ranged 100–500 microns. [80] HA provided a scaffold function for maintain the space, whereas the bone regeneration was promoted by the resorbed β-TCP at the same time. A limited literature can be found on the use of HA/TP in socket preservation or crestal bone defects. [24]

Straumann Bone Ceramic® (Institut Straumann AG, Basel, Switzerland) is a one of synthetic bone substitute. It is a composite of 60% HA and 40% β-TCP that might yield a better scaffolding function for new bone gain more than using either HA or TCP alone. [81] All batches are consistent and homogenous. It is recommended for 6 months in order to allow bone to form and mature at augmented sites. Schwarz F *et al.* [26] studied the GBR treatment at dehiscence-type defects using Straumann Bone Ceramic and Bio-Oss in dogs. Immunohistologic analysis revealed no difference of new BIC, bone fill, and the percentage of osseointegration between groups at four and nine weeks of healing. The authors indicated that both grafting materials can serve as an osteoconductive scaffold for supporting GBR at dehiscent defects. This property has been proved by other studies of randomized controlled clinical trial in humans by histology after augmentation with sinus floor elevation [82, 83] and healing of alveolar ridge preservation in extracted sockets. [24]

Assche *et al.* [25] exhibited split-mouth prospective randomized study that compared the ability of Straumann Bone Ceramic® and Bio-Oss® covering dehiscence peri-implant in 14 patients. The implant was covered with autogenous bone and followed with different bone substitutes either Bio-Oss® or Straumann Bone Ceramic®. All defects were covered by a collagen membrane (Bio-Gide®). All patients were observed up to 1 year after prosthesis placement for clinical and radiological evaluations. The result showed 100% survival rate for all implants and no significant difference was found between two substitutes for any of the parameter. The authors concluded that these bone substitutes were equally capable of cover dehiscence with implant placement.

Antunes *et al.* [84] compared the deproteinized bovine bone mineral

(DMMB; Bio-Oss®) and hydroxyapatite/tricalcium phosphate (HA/TP; Straumann Bone Ceramic®) as grafting materials for promotion of osseointegration and stability of implant in dog mandible bone defects with two different procedures of implant placement. The better stability of implant placement in healed socket was a consequence of higher bone area and BIC. They reported that DBBM, and HA/TP groups provided similar bone area and bone-to-implant contact. Considering with the different procedures, the staged approach presented higher stability results compare with immediate approach. The least stability of implant placement was found in defects filled with DBBM in immediate approach.

Type of membranes

Barrier membranes are used for the objective to guide different tissues and for facilitate selective cell repopulation and proliferation based during wound healing. [85] Many early studies were involved with the correction of periodontal defects, augmentation of alveolar ridge, enhancement of bone regeneration, and repairing the defect around dental implants.[86, 87]

The five considerable conditions that had to achieve for produce the barrier membranes including cell occlusiveness, biocompatibility, space making, tissue integration and clinical manageableness.[88, 89] Barrier membrane materials have been developed in different type concomitant with the extension of time and clinical applications. Generally, barrier membranes can be divided into two groups, non-resorbable and resorbable membranes.

Non-resorbable membranes

The earliest nonresorbable membrane in the market was generated from an expended polytetrafluoroethylene (e-PTFE; Gore-Tex®). This membrane was popularly used in many experimental and clinical studies; moreover it has been affirmed as the gold standard. [27, 28, 90] An e-PTFE membrane barrier consists of two portions. The first one is a part for unmoved membrane by early clot formation and the penetration of collagen fiber. The second is a part for cell occlusiveness that prevents gingival tissues ingression and permits the complete healing at the defect side.[27]

Buser *et al*.[29] studied the GBR using an e-PTFE membrane with tenting pins for ridge augmentation before dental implant procedure in 12 patients. Six to ten months of the healing period, the new bone formation was gained about 1.5 to 5.5 mm and nine patients demonstrated an increased sufficient bone volume for place the dental implants. The authors stated the favorable healing and high predictable regeneration without complication.

In 1995, Buser *et al*.[91] studied the bone regeneration with membrane in the mandible of five adult foxhounds. The fifteen implants were bilaterally non-submerged placement and the histologic analysis was done at 9 months later. The result showed direct BIC of all implants and ability of new regenerated bone for supporting loading. It may be inferred that bone regeneration in a barrier membrane-protected defects similar to bone remodeling of innate bone.

Becker *et al.*[57] examined 49 immediate implants that were placed concurrently with augmentation by using e-PTFE barrier membranes and followed up for 1 year after loading. This study expressed the adequate bone formation and confirmed the predictability of an e-PTFE membrane protection over a dental implant.

Space creation and continuation of adequate space beneath the barrier membrane are essential factors for accomplished outcome. Consequently, titanium-reinforced e-PTFE membranes were designed for more stabilization of membranes and increasing of tenting property that is needed for complete regeneration.[92, 93] Several studies[94, 95] demonstrated a greater biological capability for the alveolar bone and periodontal tissues regeneration of the titanium-reinforced e-PTFE membranes. Moreover, the greater resistance to collapse into the space was obtained in titanium-reinforced e-PTFE membranes when compared with non-reinforced membranes.

The substantial advantage of this membrane is it is stable in place and sustains the functional roles for satisfactory healing as long enough until it was removed, so clinicians can manage a healing time and delay the membrane removal for a process of maturing of the regenerated tissues in case of large bony.[28]

However, the main disadvantage of using e-PTFE membrane is a requirement of second surgery for removal of membrane that can increases the cost and patient morbidity.[27] A bacterial adhesion and colonization were easy to occur due to the surface roughness of e-PTFE membranes. Therefore, a

primary closure over the membrane is necessary for prevent the membrane exposure to the oral cavity.

Resorbable membranes

There are two categories of biologically resorbable membranes: collagen membrane and synthetic polymers: polylactic acid, polyglactide and polylactide, polyglactin.

Collagen membrane

A collagen membrane has been introduced and used in oral surgery since the mid-1990s with similar criteria to nonresorbable membranes. The resorbability of collagen membrane was related with either biodegradation by enzymatic activity or bioabsorption by. The inflammatory response should be minimum and reversibility, in addition, the regenerative outcome should not effect from these processes.[27]

The unique property of all resorbable membranes included collagen membranes is no need of second surgical procedure for take membrane out that can shorten the treatment time, save cost and more appreciated to patients. A collagen is the main important component that provides structural support for connective tissue.[49] Properties of collagen membranes are hemostasis, chemotaxis, and ease of manipulation, well tolerated, bio-resorbable and slow absorption. A large number of collagen membrane exits, some more popular than others. Notwithstanding, all collagen membranes originate from animal sources, which can cause difficulties for patient acceptance, immune responses, and a transmission of infectious agents. Furthermore, another potential drawback of collagen membranes is the fast biodegradation, resulting in a reduced ability to maintain space, thus compromising the isolated wound area.[33]

Bio-Gide® membrane

Bio-Gide® (Geistlich Biomaterials, Wolhusen, Switzerland) is one of the most popular collagen membranes that used in many studies. Bio-Gide® has a slow bio-resorption rate with at least 4 months of resorbability. Bio-Gide® is no additional chemicals and no organic residue. A bilayer collagen membrane of Bio-Gide® composed of type I and type III porcine dermal collagen under the

procedure of an alkaline treatment for eradicate the possible contamination. Bio-Gide® is designed for two different surfaces of membrane; a smoother side faced with gingiva for prevent intrusion of fibroblast and rougher side and faced with the bone for provide bone regeneration.[96]

Bio-Gide® was mostly used combining with a porous bovine bone mineral and yielded an effective bone formation in many studies [30-32, 97] and various procedures including ridge augmentation prior to or/and simultaneous with implants placement, GBR, sinus augmentation and filling in the bone defect after root resection or cystectomy. Currently, this membrane was accepted as the gold standard.

Zitzmann *et al*. [31] studied the implant placement with GBR between a collagen membrane (Bio-Gide®) and a conventional e-PTFE (Gore-Tex®) in 25 patients with split-mouth design. All defects were filled with Bio-Oss® and covered with the two different membranes randomly, one defect site with Bio-Gide® and the other site with Gore-Tex®. Changes in defect surface for both types of membranes were statistically significant. Bio-Gide® sites showed the mean percentage of bone fill about 92%, whereas Gore-Tex® sites presented 78% of that. These were statistically significant between two membranes. In addition, wound dehiscences and/or premature membrane removal occurred 44% for Gore-Tex® sites. The authors concluded that Bio-Gide can be a useful alternative membrane to the e-PTFE membranes in combination with a bone graft.

Carpio *et al*. [30] compared the effectiveness of GBR between bioabsorbable collagen membrane (Bio-Gide®) with non-resorbable membrane (Gore-Tex®) combined with xenograft and autograft bone to the defects around dental implants in 48 subjects. The reduction in defect size was no statistically significant difference between two membranes. However, at six-month healing, the e-PTFE barriers yielded 4.1% of wound dehiscence of overlying soft tissue and 12.5 % of membrane exposures higher than the collagen membranes (0% and 8.7%, respectively) with statistical significances for both. With respect to the failure rate of implant, there was no statistical significant difference between two membranes, similar to the length or width exposure of the failed implants. They concluded that the efficacy of both collagen and e-PTFE barriers were attested for the success of GBR.

Taguchi *et al*. [98] examined the histological changes and cellular events in GBR with a collagenous membrane (Bio-Gide®). They reported that this

membrane exhibits osteoconductivity and result in a well-augmented alveolar ridge. This study concluded that Bio-Gide® is suitable for GBR following dental implant procedure and excellent increasing of osteoblastic activity.

Dahlin *et al*. [72] evaluated the GBR technique between two membranes combined with a xenografts of twenty patients for 5 years. An e-PTFE membrane (Gore-Tex®) was used in twelve patients and a resorbable membrane (Bio-Gide®) was used in the remaining eight patients. No implant losses were founded over this study, hence, they concluded that the GBR technique is a predictable treatment for localized defects surrounding dental implant either with Bio-Gide® or Gore-Tex® membranes.

Jung *et al*. [99] studied the long-term outcome of dental implants placement concurrent with GBR between resorbable collagen membranes (Bio-Gide®) and non-resorbable membranes (e-PTFE; Gore-Tex®) with demineralized bovine bone mineral of 265 implants in 72 patients after 12–14 years of follow-up. 112 implants were covered with Bio-Gide® membrane, 41 implants were applied with e-PTFE membranes, and the rest of 112 implants that fully encircled with bone and no need of GBR were considered as a control group. There was no statistical significance of the cumulative implant survival rate among the groups at the follow-up period. Moreover, the marginal bone level was not reached the statistical different over time among three groups with radiographic analysis. Therefore, there was concluded that implants placement simultaneous with GBR both resorbable and non-resorbable membranes showed a high survival rate, safe and predictability over time.

As the membrane is a collagen product obtained from pigs, allergic reaction may occur. Due to the special physical properties and the prolonged absorption time, an inflammatory reaction may happen. Possible other complications which may occur including local inflammation, swelling, bleeding, bone loss, flap sloughing, infection and pain same as any surgery.

Synthetic polymers

Synthetic polymers that can be reproduced in unlimited quantities under strictly controlled conditions are clear preference over collagen membrane. Another advantage is the ability of complete biodegradation to carbon dioxide and water. However, these membranes may elicit tissue reactions that could influence wound healing as well as their overall effectiveness.[100, 101] Nowadays, synthetic barrier membrane materials are made

from polymers including polyglycolics acid (PGAs), polylactic acid (PLAs), Polydioxanones, trimethylene carbonates and copolymers.

Guidor® membrane

Guidor® (Sunstar, Foster Ave, Chicago, USA) was the first synthetic barrier membrane that be approved by the Food and Drug Administration (FDA) in 1993. This bioresorbable membrane is consisted of a blend of polylactides (PLA) that become softer to facilitate for a clinical adaptation by a citric acid. This membrane was designed for a multilayered matrix not only to allow a gingival connective tissue growing in, but also for prevent a growth of gingival epithelium moving apical downward.[27] The inner layer which faced up to the bone had small circular perforations with a several space for the new attachment formation. While the outer layer which is contacted with a gingival tissue had larger rectangular perforations for permit a gingival tissue growing into. Between two layers had a interspace to minimize or obstruct a growing=down epithelium.[102, 103] The resorption rate was prescribed at least 6 weeks for secure a barrier property. Generally, a complete resorption was mostly occurred at approximately 12 months.[103, 104]

Several studies have presented the capability of PLA barrier membranes for produce a new attachment and bone formation to correct an interproximal and infrabony defects, gingival recession, and Class II furcation defects.[105-107] These studies showed the results of using this matrix barrier around teeth that diminished a probing depths; increased a clinical attachment; reduced an incidence of gingival recession and pathologic disease.[104]

Hugoson *et al*.[108] compared the effectiveness of Class II furcation defects between bioresorbable PLA membranes and e-PTFE membranes. The result showed less gingival recession and a clinical attachment was a significantly gained with using both barrier membranes especially in clinical horizontal attachment. However, postoperative complications including a swelling and pain were more frequently occurred during the first month of healing with the use of e-PTFE membrane.

Roccuzzo *et al*.[102] compared the reliability of resorbable PLA barriers and non-resorbable e-PTFE membranes for root coverage and clinical attachment gain in the treatment of gingival recession and reported no differences for any clinical variables assessed. However, the advantages of the bioresorbable barrier included reduced discomfort, stress, and expense

because of the single-step procedures. Others showed significantly more new attachment formation and less gingival inflammation and device exposure with using of PLA membranes when compared with e-PTFE membranes.

Clinical outcomes of implant or success criteria of implant

There are many examinations that were used to assess the success of GBR with implantation at follow-up period. Basically, the clinical outcomes of implant can be examined into two methods; clinical parameters and radiographic parameters. Indeed, histological analysis provides for the evaluation of new bone formation, resorption patterns, remaining graft material and soft tissue presence. Generally, biopsy of the augmented bone was collected by using a trephine bur to the bone surface. This analysis needs a bloc resection unfortunately; ethical concerns disallow this examination in clinical studies.

Clinical parameters

Standard soft tissue parameters were most clinical parameters that were routinely used in long-term prospective studies for more than 20 years [3, 109, 110] including modified plaque index (mPLI), [109] modified sulcus bleeding index (mSBI), [109, 110] probing depth (PD), [3, 35, 110] width of keratinized mucosa (KM) [110] and the distance between the implant shoulder and the mucosal margin (DIM).[3, 35, 110] Soft tissue parameters are the key indicators for peri-implant mucositis. Early detection of peri-implant mucosal change will helps patients manage their oral health care for adequate good oral hygiene that consequently effect to long-term success of GBR and survival rate of implant.

Currently, the main focus of the study of implants therapy with GBR takes an interest directly to the long-term stability of the esthetic outcomes. Belser *et al.* [111] was the first to define a novel comprehensive esthetic indices termed the pink esthetic score (PES) and white esthetic score (WES) to assess the esthetic outcomes for single-tooth implants of anterior maxilla. The WES index is particularly concentrates on the restorative part of the implant such as crown prosthesis that comes out from mucosa. The WES index is composing of the five parameters including tooth form, outline/ volume of the clinical crown, color (hue and value), surface texture, and translucency/ characterization; hence this index is mainly dependent on the quality and experience of the

dental technician. The PES index was modified from previous published peri-implant soft tissue index [112] to evaluated from soft tissue esthetics and consists of following five parameters: the height of mesial and distal papillae, the level and curvature of the facial mucosa, the root convexity, soft tissue color and texture.

Radiographic parameters

Conventional radiography

Traditionally, periapical and panoramic images were the most of conventional radiography that have been applied to support clinicians for both planning implant treatment and routine follow-up period due to readily available and relatively inexpensive. Panoramic images are vastly available and very useful for a screening. [113] It is commonly used to assess the overall of jaws including the vital structures for example inferior alveolar nerve and maxillary sinus, the status of all remaining teeth, the relationship to opposing teeth including the space and of the site of implantation. However, panoramic radiographs are low image sharpness and resolution. Anatomical structures are superimposed and distorted often leads to inaccurate interpretation and measurements. [113] To solve this problem, periapical image has been used to provide more accuracy in interested area for assess the adjacent teeth and alveolar bone. Furthermore, it has been used for deciding vertical height, structure and bone quality of local bone such as bone density and amount of cortical bone or trabecular bone. Nevertheless, periapical images still had geometric limitation. If a paralleling technique was not used, the foreshortening or elongation will be occurred. Therefore, the standardized periapical images should be performed with bite-blocks for a minimal distortion.

The distance between the implant shoulder and the first bone-implant contact (DIB) was introduced in 1992 by Weber *et al*. [114] It was the one of standard clinical parameters that were routinely used in the studies of GBR with implant placement to examine the crestal bone-level changes and indicate crestal bone loss after implantation. The DIB value was measured on periapical radiographs for proximal aspects of the implant both mesial and distal sites; therefore the facial bone thickness cannot be examined by this parameter. Changes in facial bone thickness following implant placement is

essential to monitor because it can create esthetic problems consequently such as gingival recession or changes in the contour of the gingiva.[115]

Computed Tomography (CT)

Although periapical and panoramic images were used to evaluate bone anatomy for many decades, this two dimensional conventional radiographs have some limitations because of intrinsic distortion, low sharpness and resolution. With the development of technology, CT has recommended to achieve better implant imaging. Clinicians enable the evaluation of diagnosis, treatment planning for dental implants by using CT that provides more information than other imaging techniques. The numerous advantages of using CT overcome a conventional radiography. First, CT image erases the superimposition of anatomical structures outside the interested area. Next, CT has a high contrast resolution. A different physical density between tissues less than 1% can be discriminated whereas conventional radiography demands a 10% difference of physical density for discrimination. In addition, CT consists of multiple contiguous images that can be inspected in any desirable plane including axial, coronal and sagittal planes with the tool setting. Then, it is referred to as multiplanar reformatted imaging.

Due to the fact that CT exhibited a higher of radiation exposure, cost, area, and difficulty in accessibility, the cone beam computed tomography (CBCT) scan was developed and has becomes a commonly accepted diagnostic implement for dental imaging.[113, 116] This equipment provides extremely accurate a three-dimensional view of the hard tissue and adds benefit of decreased x-ray exposure for small Fields of View (FOV) with good image quality.[14, 117]

The accuracy between CT and CBCT for measured implant site dimensions was compared. The CBCT showed more accurate than CT images.[118, 119] Furthermore, The CBCT was recommended for the assessment of dental implant sites as the imaging of choice by the American Academy of Oral and Maxillofacial Radiology (AAOMR).[116]

In accordance with problem in examination of facial bone thickness, this can only be easily performed by CBCT. The CBCT is non-invasive application that can be sequentially used and resulted in reasonably low levels of radiation dosage (20.02 μSv) comparing with multi-slice CT (474-1160 μSv).[120] The radiation doses of CBCT are approximate 3 to 7 times more than

panoramic image and about 40% lower than conventional CT.[121, 122] Loubele *et al.*[122] studied the effective doses among three different CBCT scanners; Accuitomo 3D®, i–CAT®, and NewTom 3G® with multi-slice computed tomography (MSCT) for maxillofacial applications. They reported that the effective dose levels of CBCT imaging which ranged from 13 to 82 μSv were less than those of MSCT (474 to 1160 μSv). The least CBCT dose levels were obtained from Accuitomo 3D® (13 to 44 μSv), and highest for the i-CAT® (34 and 82 μSv). The radiation dose of CBCT scanners was between 2 times (for the Accuitomo 3D®) and about 15 times (for the i-CAT®) higher as that of a panoramic scanners.

According to National Council on Radiation Protection and Measurements (NCRP)[123], the daily naturally occurring background radiation in the USA was 8.5 μSv and US population average exposure (including medical, occupational and consumer product exposures) was 17 μSv per day. As a comparison, the lowest effective doses estimated for CBCT examination were about 2-9 days of US daily natural background radiation whereas an optimized (digital, rectangle collimation) bite-wing doses range from 18 to 42 % of daily natural background radiation.[124] The International Commission on Radiological Protection (ICRP)[125, 126] recommended dose limits for occupational exposure of workers over the age of 18 years for an effective dose of 100 mSv over 5 year periods, and should not greater than 50 mSv in any single year. In addition, the lens of the eye had an equivalent dose of 150 mSv per year and 500 mSv per year for the extremities or the skin. Diagnostic reference levels for comforters and careers, and volunteers in biomedical research have not relate to the numeric values of the Commission's dose limits. However, the radiation exposure of persons should only be undertaken in standardization of medical radiological equipment on the radiological protection of patients.

Recently, the CBCT was used to examine a facial bone in the esthetic zone for investigated three dimensional alterations by Chappuis *et al.* [10] Thirty-nine patients were obtained two consecutive CBCT, first immediate post-extraction and the second at 8 weeks later following flapless tooth extraction. They reported that the vertical bone loss in sites was statistically significant different between thin or thick phenotype. A thin-wall phenotype reported 62.3% of median vertical bone loss and 10.5% of median horizontal bone loss whereas the thick-wall phenotype demonstrated 9.1% of median vertical bone loss and 0% of median horizontal bone loss. This study provided a better

understanding of characteristic bone resorption patterns and clearly presented that a resorption of facial bone also occurs post-extracted at the anterior maxilla especially in central areas. This study reported a facial bone alteration 2 to 3.5 times in the esthetic zone that is more severe when compare to the finding established in a previous study in dogs. [7, 9] In addition, patterns of a facial bone wall resorption were typical, and displayed significantly different between mid-facial and proximal areas. Mid-facial area was a risk zone that more influenced to bone loss and had a correlation with thin-wall phenotypes (facial bone wall thickness ≤ 1 mm).

CHAPTER III

MATERIAL AND METHODS

Population and Samples

Target Population

The patients who were evaluated during an initial screening visit at Faculty of Dentistry, Chulalongkorn University and required surgical implant placement simultaneously with GBR procedures for the replacement in partially edentulous area.

Sample Population

The patients who had a requirement and eligibility for surgical implant placement simultaneously with GBR procedures for the replacement in partially edentulous area at Department of Oral and Maxillofacial Surgery, Special Clinic, Esthetic and Implant Clinic of Faculty of Dentistry, Chulalongkorn University from April 2014 - Oct 2015

Inclusion criteria

- The patients with age above 20 years old
- The patients with good general health or well-controlled disease (ASA I or II)
- The patients with the presence at least one of the hopeless tooth in the incisor, canine or first premolar area of maxilla that had to extracted and would be appropriate for dental implant replacement in conjunction with GBR
- Primary stability of the implant must have been achieved during single-stage procedure
- The residual facial wall height was at least half of implant length
- The patient was willing and able to comply with all study-related procedures
- The patient was able to fully understand the proposed study and signed an informed consent for participation in this study

Exclusion criteria

- The patients with uncontrolled diabetes, immunodeficiency or systemic diseases that affect the alveolar bone, heavy smokers, severe periodontal diseases, and unwillingness to undergo dental surgery
- General contraindications for dental and/or surgical treatments were present
- The patients with allergy to any material and/or medication used in the study.
- The patients with physical and/or psychological disability that have a problem in communication such as deafness, blindness, dumbness, mental retardation etc.
- The patient had a history of malignancy, radiotherapy and/or chemotherapy for malignancy within the past 5 years.
- The patients who are either pregnant or breastfeeding.
- The patients who unable to continue for all follow-up periods.

All patients who met the above inclusion and exclusion criteria were consecutively enrolled in this study. Each patient was clearly explained the process of research protocol and risk or benefit by researcher. Each patient was obtained a chance to ask for more information about this research. Patients who voluntarily to participate in this study signed the informed consent prior to the beginning. However, patients could leave the study at any time they desire. The patients assigned to the study or the comparison group by block randomization. Moreover, if the patient was presented with more than one site for implant placement with GBR, the split mouth technique will be used.

Sample grouping

- *Study group:* The patients who require surgical implant placement simultaneously with GBR procedures using a synthetic bone graft in combination with a synthetic resorbable membrane
- *Comparison group:* The patients who require surgical implant placement simultaneously with GBR procedures using a synthetic bone graft in combination with a collagen resorbable membrane

Sample size calculation

$$n = \frac{(\sigma_1^2 + \sigma_2^2)(Z_\alpha + Z_\beta)^2}{(\mu_1 - \mu_2)^2}$$

n = the amount of samples in one group

σ_1 = the standard deviation of group 1

σ_2 = the standard deviation of group 2

Z_α = Z-score derived from Z-score table at α level

Z_β = Z-score derived from Z-score table at β level

μ_1 = the mean of the facial bone thickness of group 1

μ_2 = the mean of the facial bone thickness of group 2

In order to achieve the statistical significant answers of the question in this study, the sample size was calculated from the formula showed above with data of the variables arisen from related previous study. Typically, α is set at 0.05 and β is set at 0.2 for significance level.

Nevertheless, there was lack of previous related study that examined the clinical outcomes of different membranes using for implant placement with GBR in esthetic zone by assessment of the facial bone thickness from CBCT as a parameter. The only study of Buser *et al.*[13] measured the thickness of the facial bone wall at 3 different levels: 2 mm, 4 mm, and 6 mm apical to the implant shoulder in 20 patients after six years of early implants placed with simultaneous contour augmentation. Unfortunately, no comparison of different membrane using and no baseline data of facial bone thickness at time of implant placement reported in that study, thus μ_1 and μ_2 were lack of data to use for calculating the sample size for our study.

Generally, the data should collect from enough samples for normal distribution which is beneficial to parametric statistic testing. According to The Central Limit Theorem,[127, 128] more than 30 samples could be considered for normal distribution. Therefore this study collected at least 30 samples of each group that could enough represented statistically significant difference of clinical outcomes in contour augmentation with simultaneous implantation.

Materials

Dental implant and regeneration material

Bone level Straumann® dental implants (Institut Straumann AG, Basel, Switzerland) were used in this study for all samples with a surgical stent in a correct 3-dimensional position. Different implant lengths and diameter were used according to each patient's alveolar ridge dimension.

All implants were placed simultaneously with GBR using synthetic bone graft (Straumann Bone Ceramic®, Institut Straumann AG, Basel, Switzerland) and covered with synthetic resorbable membrane (Guidor®, Sunstar, Foster Ave, Chicago, USA) in study group whereas collagen resorbable membrane (Bio-Gide®, Geistlich Biomaterials, Wolhusen, Switzerland) were used to cover the grafting materials in comparison group.

Methods

Ethical consideration

After the approval of research proposal by the ethical committee of Faculty of Dentistry, Chulalongkorn University (HREC-DCU 2014-034), the samples were selected in accordance with the above inclusion and exclusion criteria. All patients planned to reconstruct partial edentulous area with implant placement simultaneously with GBR procedures were invited to enroll in this study. Patients who fulfill all of criteria and volunteer to participate in this study had to sign the informed consent before the beginning of the study.

Surgical procedure

After planning of implantation and patient examination, dental impressions were taken for making surgical template and Cone Beam Computer Tomograpic (CBCT) Scan (Accuitomo 3D®, J. Morita Corporation, Kyoto, Japan) was used for pre-operative evaluation prior to surgical procedure of dental implant placement by only one experienced staff or post-graduate students under supervision of that staff. Each patient underwent implant surgery with different timing after tooth extraction that can classified as immediate, early and delay implant placement[129] depend on each patient's condition for proper treatment. The guided bone regeneration was planned for contour

augmentation simultaneous with implantation, but alveolar bone defect could be re-evaluation during the operation that actually shown true defect.

Operation

The implant site was prepared under local anesthesia for adequate pain control during implant surgery according to standard protocol and manufacturing recommendation for dental implant and biomaterial used. After getting numb, incision was extended to the neighboring teeth with an elevation of a full-thickness mucoperiosteal flap. Dental implant was placed with the use of surgical template to correct 3-dimensional position for ideal emergence profile and peri-implant soft tissue. 3 to 4 mm healing abutment was used in order to obtain the single-stage procedure. The exposed implant surface was covered with locally harvested autogenous bone first and then follow with a superficial layer of synthetic bone graft (Straumann Bone Ceramic®, Institut Straumann AG, Basel, Switzerland) on the facial aspect for contour augmentation. The augmented material was covered with the randomized membrane; synthetic resorbable membrane (Guidor®) in study group or collagen resorbable membrane (Bio-Gide®) in comparison group. The barrier membranes were trimmed and adapted to the shape of the individual defect so that the membrane overlapped the defect circularly by a minimum of 2 mm. The flaps were coronally replaced in order to cover the biomaterials and secured by tension-free primary wound closure.

Post-operative medication

The post-operative protocol included systemic antibiotic (1 g amoxicillin, twice a day) and analgesic (500 mg mefenamic acid, three times a day) were administered for 5 days, in case of allergy to penicillin, 300 mg clindamycin were administered. All patients were advised to withhold from tooth brushing at the operated area and use a 0.2% chlorhexidine mouthwash twice daily for the first week of post-operation. A removable prosthesis was not applied before the adjustment for relieve any pressure to the operative area. The sutures were removed after two weeks and all clinical and radiographic parameters were collected as a baseline data in this visit.

Follow-up examination

All patients were routinely arranged an appointment for clinical assessment at 1, 3 and 6 months follow-up periods. A radiographic examination was taken at 6 months after implantation with the same CBCT machine as baseline (Accuitomo 3D®, J. Morita Corporation, Kyoto, Japan).

Clinical parameters

The width of keratinized mucosa (KM)

The width of keratinized mucosa was measured in mm from mucogingival junction to gingival crevice at mid-facial aspect.

The complications

The complications were observed over this study in both groups (e.g. membrane exposure, healing screw loosening or delayed wound healing) for assess of clinical manageability.

Radiographic parameters

The distance between the implant shoulder and the first bone-implant contact (DIB)

The distance between the implant shoulder and the first bone-implant contact[114] from digital 2D periapical film was measured in mm both mesial and distal aspects of each implant using the distance measurement tool of INFINITT PACS Viewer software (INFINITT Healthcare Co., Ltd.). (Figure 2)

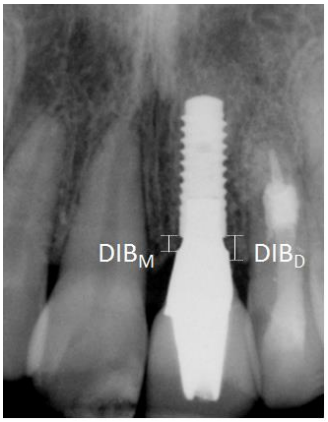

Figure 2 The measurement of DIB both mesial and distal aspects of implant.

Facial bone thickness

According to a study of Chappuis *et al.* [10], ridge alterations of facial bone wall post-extraction in the esthetic area were investigated in thirty-nine patients. The central area of the facial bone wall was a risk zone that displayed a significant bone resorption pattern and more susceptible to bone loss compared with the proximal areas. Moreover, correlation analysis presented a risk zone likely to proclaimed bone resorption of thin-wall phenotypes with a facial bone wall thickness ≤ 1 mm. Therefore, this study would analyze the bone resorption after augmentation in central site of the implant axis at various levels using CBCT with small FOV for decrease x-ray exposure. Each implant was set to measurement for evaluate the facial bone thickness along implant axis and measured in mm on the CBCT image using the distance measurement tool of One Volume Viewer software (J. Morita Corporation, Kyoto, Japan) at mid-facial aspect of 4 different levels: implant platform and 2 mm, 4 mm, and 6 mm apical to the implant shoulder as a previous studies.[13, 111] (Figure 3)

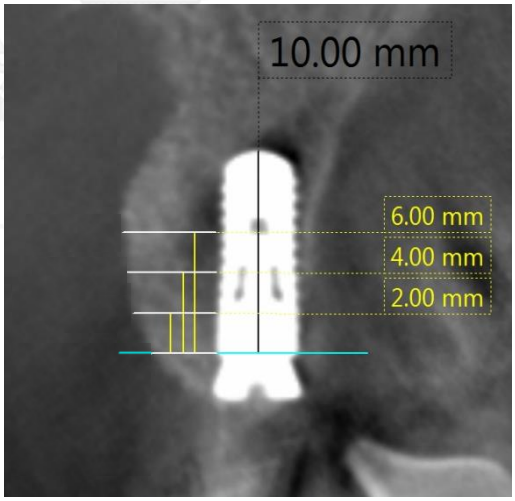

Figure 3 The measurement of facial bone thickness along implant axis at mid-facial aspect of 4 different levels; implant platform and 2 mm, 4 mm, and 6 mm apical to the implant shoulder.

Data collection

All parameters were planned to collect by one examiner whom trained with experienced radiologist and performed intra-examiner calibration to ensure the reliability. First follow up was scheduled within 14 days after completion of implant placement, clinical and radiographic examinations were assessed in this visit for a baseline data as previously mentioned. Assessment of all clinical outcomes was taken again at 1, 3 and 6 months post-operation and radiographic parameters were evaluated at 6 months after implantation with the same CBCT machine as baseline.

Data analysis

Both descriptive and inferential statistic was applied to analyze all data collected in this study. Nominal or ordinal data was reported by the descriptive statistic for a countable number and percent, whereas data presented in interval scale or ratio scale was presented in the form of mean with standard deviation. Statistical Package for Social Science version 22.0 (SPSS Inc., Chicago, US) was used for inferential statistics to infer the result of all samples in this study to the target population. Statistical significance is considered at p-value less than 0.05 to represent the confidence interval of 95%

The test of normality distribution of all data was done via Kolmogorov-Smirnov test and equal variance was tested via Levene's test before hypothesis statistical test in order to apply the parametric statistic because of the greater power of test than non-parametric statistic.

To compare clinical outcomes and stability of contour augmentation of guided bone regeneration at 6 months between synthetic and collagen membrane in guided bone regeneration with a synthetic bone graft, all parameters are tested for difference of mean by Independent-samples t test for parametric test. Moreover, the correlation between keratinized mucosa and facial bone wall thickness is tested by Pearson's correlation for parametric test.

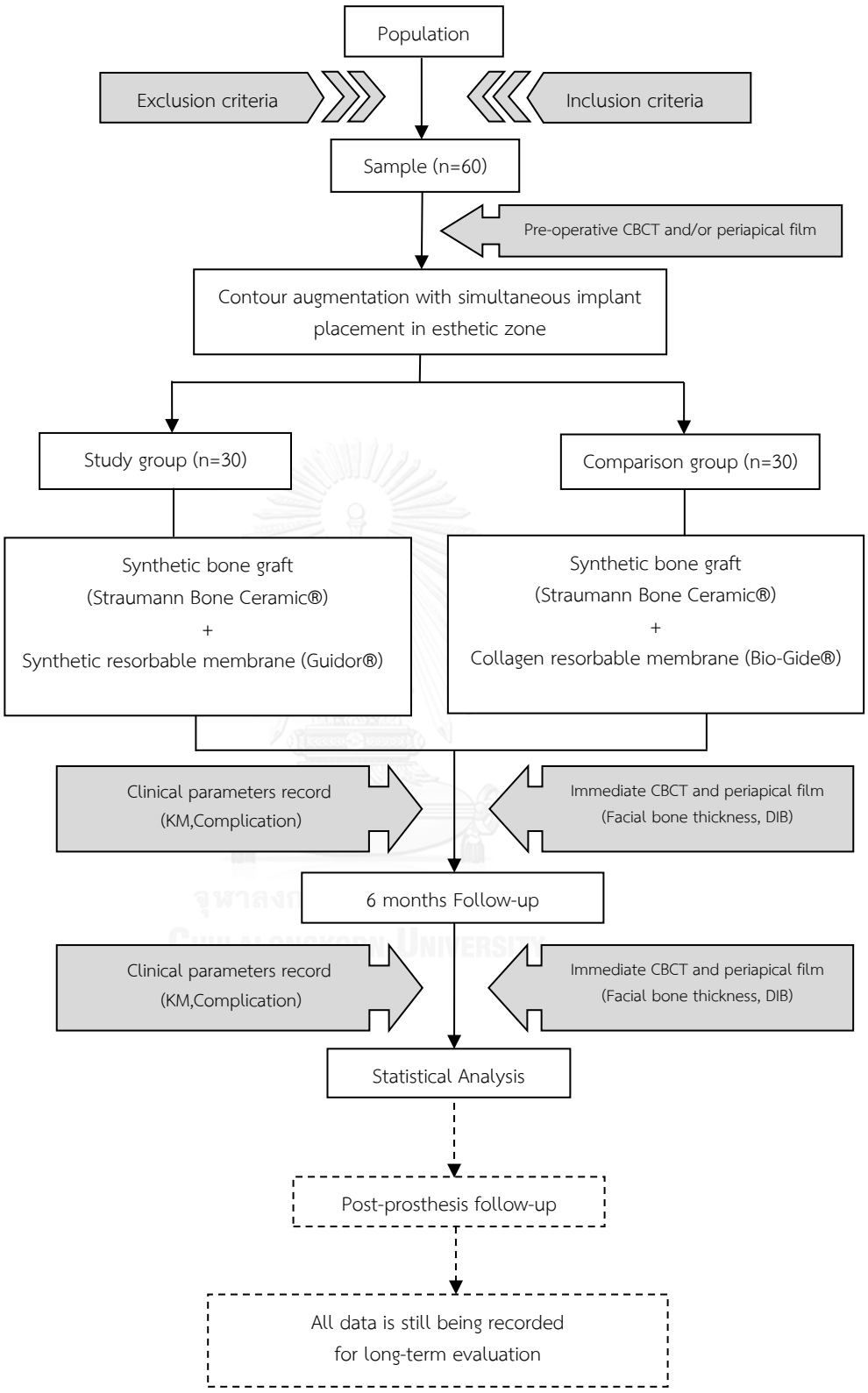

Figure 4 Method flowchart

The conflict of interest

The author declares no support from manufacturers of any materials used in this thesis and no potential conflicts of interest with respect to the process of this thesis.

CHAPTER IV
RESULTS

Patient information and Demographic data

A total 60 implants were placed with simultaneously GBR in the anterior esthetic zone of maxilla in forty-eight patients whom fulfill the inclusion and exclusion criteria were consecutively enrolled in this study. 30 implants were allocated to the study group that using a synthetic resorbable membrane (Guidor®) while as 30 implants were allocated to the comparison group that using a collagen resorbable membrane (Bio-Gide®) by block randomization. Seventeen patients were male and thirty-one female with similar in gender distribution both two groups. The Patients ranged in age of 21 to 78 years old and have the average of age 51.22±16.19 years with no significant different between two groups (48.80±15.58 years in study group and 53.63±16.69 years in comparison group)

The diameter and length of implants used in this study were 3.3NC10, 4.1RC8, 4.1RC10 and 4.1RC12 depend on each patient's alveolar ridge dimension. Implants were placed with GBR in 25 central incisors, 17 lateral incisors, 8 canines and 10 first premolars. About the timing of implant placement, 21 implants were placed as immediate, 9 implants were placed as early and the others were placed as delay which was the most of implants in this study. The surgical procedure was done by one experienced staff for 33 implants and post-graduate student under supervision of that staff for 27 implants. (Table 1)

Variables	Study (n=30)	Comparison (n=30)	Total (n=60)	*p*-value[a]
SEX				
Male	10	11	21	.020*
Female	20	19	39	
AGE				
≤40 years	9	6	15	
41-60 years	13	13	26	.212
≥61 years	8	11	19	
IMPLANT AREA				
Central Incisor	13	12	25	
Lateral Incisor	6	11	17	.008*
Canine	6	2	8	
First Premolar	5	5	10	
IMPLANT SIZE				
3.3NC10	12	13	25	
4.1RC8	1	0	1	.000*
4.1RC10	17	16	33	
4.1RC12	0	1	1	
TIMING OF IMPLANT PLACEMENT				
Immediate	9	12	21	
Early	6	3	9	.004*
Delay	15	15	30	
Operator				
Staff	15	18	33	.439
Student and Staff	15	12	27	

Table 1 Patient information and demographic data.

a: The patient demographic and clinical variables according to the study and comparison group by Chi-Square test

*: Statistical significant at 95% confident interval

The Clinical Outcomes

The width of keratinized mucosa (KM)

The width of keratinized mucosa was measured in mm at mid-facial aspect of implant immediately and 6 months later. In the study group, the mean of KM at immediate post-operation and the 6-month follow-up were 5.02 mm and 4.29 mm, respectively. Similar to the control group, the mean of KM at immediate post-operation and the 6-month follow-up were 4.77 mm and 4.02 mm, respectively. The KM over 6 months had the same tendency of significant recession within each groups (p-value<0.05), nevertheless there was no significant differences of the change of KM between two groups (p-value=0.961). (Figure 5)

The complications

The minor complications were observed in both groups with greater proportion in the study group. The gingival inflammation was the most common post-operative complications existed in 4 cases (two cases equally in both groups) and the membrane exposure was the second common post-operative complications which founded in 3 cases only in study group. All complications were recovered uneventfully.

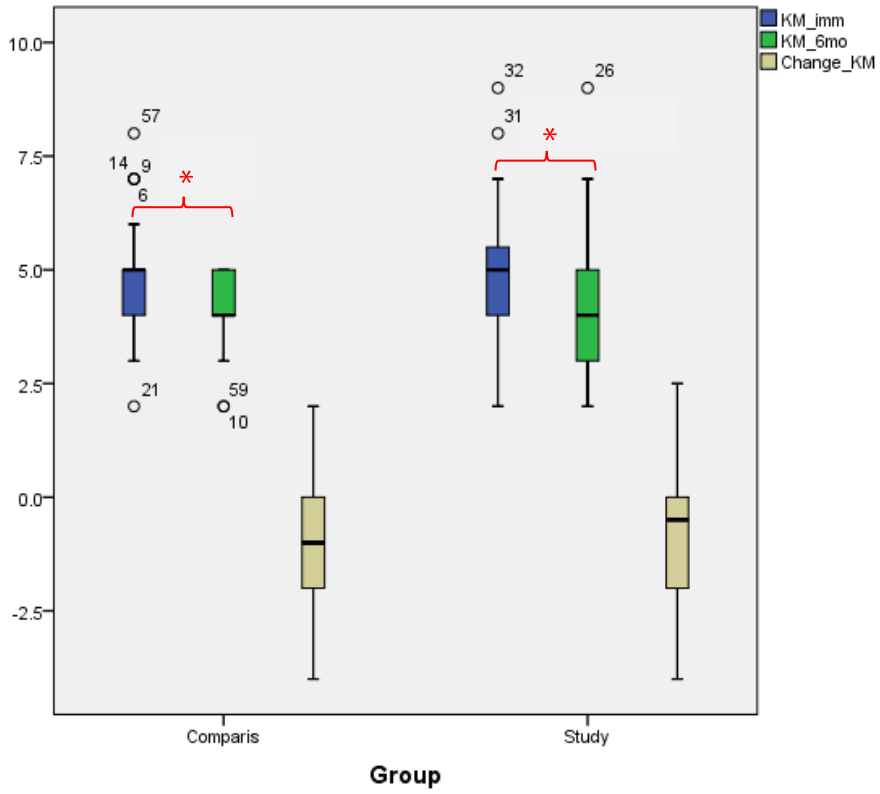

Figure 5 The Box plot of the width of keratinized mucosa of comparison group and study group.

KM_imm: the width of keratinized mucosa at immediate post-operation

KM_6mo: the width of keratinized mucosa at 6-month follow up

Change_KM: the change of the width of keratinized mucosa between immediate post-operation and 6 months later

* There were statistically significant of the change of the width of keratinized mucosa over 6 months in the Paired-Samples T Test within each group (*p*-value<0.05), but no significant difference was found in the Independent-Samples T Test between two groups (p-value>0.05).

The Stability of Contour augmentation

The facial bone thickness

When patients came back for sutures removal, the immediate post-implantation CBCT were obtained. Patients were also recalled for CBCT at 6 months later for evaluate the stability of contour augmentation by facial bone thickness along implant axis at mid-facial aspect of 4 different levels: implant platform and 2 mm, 4 mm and 6 mm apical to the implant shoulder. All implants were stable with existing facial bone and no implant loss was found over two consecutive CBCT. (Figure 6-9)

The mean thickness of facial bone at immediate post-operative implant placement with GBR were 3.22, 3.55, 3.69 and 3.62 mm in study group and 3.42, 3.90, 4.00 and 3.82 mm in comparison group at the level of implant platform and 2 mm, 4 mm and 6 mm apical to the implant shoulder respectively. After 6 months of GBR, the mean facial bone thickness were significantly decreased in both groups (p-value<0.001). The study group reported the mean facial bone thickness 2.07, 2.53, 2.82 and 2.92 mm similar to the comparison group that had the mean facial bone thickness 2.30, 3.00, 3.24 and 3.04 mm with a same level of measurement. This facial bone resorption was analyzed in a percentage of change between baseline and the 6-month follow-up. In the study group, the percentage of facial bone thickness change were -34.30%, -27.94%, -24.25% and -19.81% while the percentage of facial bone thickness change in comparison group were -34.80%, -24.06%, -19.52% and -20.45% at four level of measurement. Notwithstanding, these percentages of change were not reached the statistical significant difference between two groups (p-value>0.05). (Table 2 and 3)

The distance between the implant shoulder and the first bone-implant contact (DIB)

After implantation with GBR, the distance between the implant shoulder and the first bone-implant contact (DIB) was analyzed both mesial and distal aspects of each implant from the immediate periapical film for baseline data and re-assessed at 6 months later.

All implants in this study group presented the average of DIB value of 3.13 and 2.96 mm at mesial and distal aspects at baseline and significantly

reduced to 1.40 and 1.56 mm after 6 months (*p*-value<0.001). While the average of DIB value in the comparison group was 3.10 and 3.06 mm at mesial and distal aspects at baseline and showed less reduction with DIB value of 2.03, 1.90 mm at 6 months later. However, these reductions were also reached statistical significant difference (*p*-value<0.001). Change in DIB values were calculated between baseline and the 6-month follow-up in term of percentage for both aspects. Interestingly, the study group had a greater proximal bone reduction and revealed the percentage of DIB value change -57.81% for mesial aspect and -47.23% for distal aspect. Contrast to the comparison group that showed the percentage of DIB value change -33.82% for mesial aspect and -32.25% for distal aspect. Moreover, the statistical significant difference was found between groups for only mesial aspects (*p*-value=0.017). (Table 4 and 5)

Levels of measurement	Facial bone thickness (mm)					
	Study Group			Comparison Group		
	immediate	6 months	*p*-value	immediate	6 months	*p*-value
platform	3.22 ± 1.00	2.07 ± 0.94	.000*	3.42 ± 0.85	2.30 ± 1.10	.000*
2 mm apical	3.55 ± 0.98	2.53 ± 0.93	.000*	3.90 ± 0.88	3.00 ± 1.01	.000*
4 mm apical	3.69 ± 1.13	2.82 ± 1.18	.000*	4.00 ± 0.91	3.24 ± 0.97	.000*
6 mm apical	3.62 ± 1.18	2.92 ± 1.26	.000*	3.82 ± 0.99	3.04 ± 1.00	.000*

Table 2 The facial bone thickness immediate post-operative implant placement with GBR and 6 months later of both groups (mean ± standard deviation).

* There were statistically significant of the facial bone thickness between immediate GBR and the 6-month later in the Paired-Samples T Test of all levels of measurement within each group (*p*-value≤0.001).

Levels of measurement	The change of facial bone thickness (%)		
	Study Group	Comparison Group	*p*-value
platform	-34.30 **± 23.85**	-34.80 **± 23.68**	.935
2 mm apical	-27.94 **± 17.88**	-24.06 **± 13.73**	.350
4 mm apical	-24.25 **± 17.59**	-19.52 **± 12.39**	.233
6 mm apical	-19.81 **± 18.06**	-20.45 **± 14.14**	.880

Table 3 The percentage of facial bone thickness change immediate post-operative implant placement with GBR and 6 months later of both groups (mean ± standard deviation).

There were no significant differences of percentage of facial bone thickness change over 6 months in the Independent-Samples T Test of all levels of measurement between two groups (*p*-value>0.05).

Group	The DIB value (mm)					
	Mesial aspect			Distal aspect		
	immediate	6 months	*p*-value	immediate	6 months	*p*-value
Study	3.13 ± 0.96	1.40 ± 1.24	.000*	2.96 ± 0.94	1.56 ± 1.19	.000*
Comparison	3.10 ± 1.21	2.03 ± 1.30	.000*	3.06 ± 1.11	1.90 **± 1.27**	.000*

Table 4 The distance between the implant shoulder and the first bone-implant contact (DIB) immediate post-operative and 6 months later for mesial and distal aspects of both groups (mean ± standard deviation).

* There were statistically significant of the DIB values between immediate GBR and the 6-month later in the Paired-Samples T Test of mesial and distal aspects within each group (*p*-value≤0.001).

Group	The change of DIB value (%)	
	Mesial aspect	**Distal aspect**
Study	-57.81 **±** 39.85	-47.23 **±** 31.84
Comparison	-33.82 **± 35.60**	-32.25 **±** 55.41
***p*-value**	.017*	.204

Table 5 The percentage of the distance between the implant shoulder and the first bone-implant contact (DIB) change immediate post-operative and 6 months later for mesial and distal aspects of both groups (mean ± standard deviation).

* There was significant difference of percentage of change in the DIB values over 6 months in the Independent-Samples T Test between two groups for mesial aspect (*p*-value<0.05) but no significant difference was found for distal aspect (*p*-value>0.05).

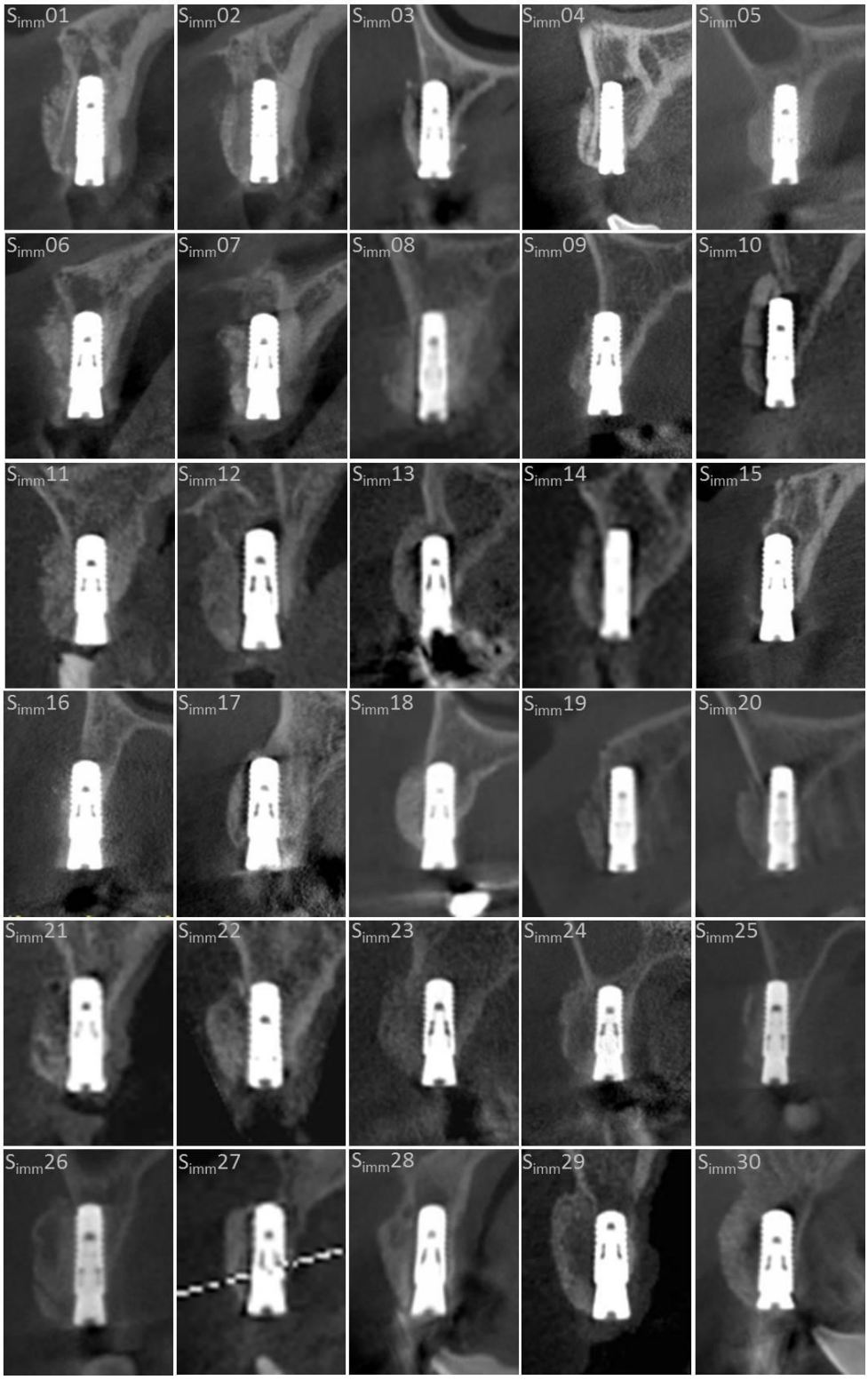

Figure 6 The CBCT images of all implants of study group at baseline.

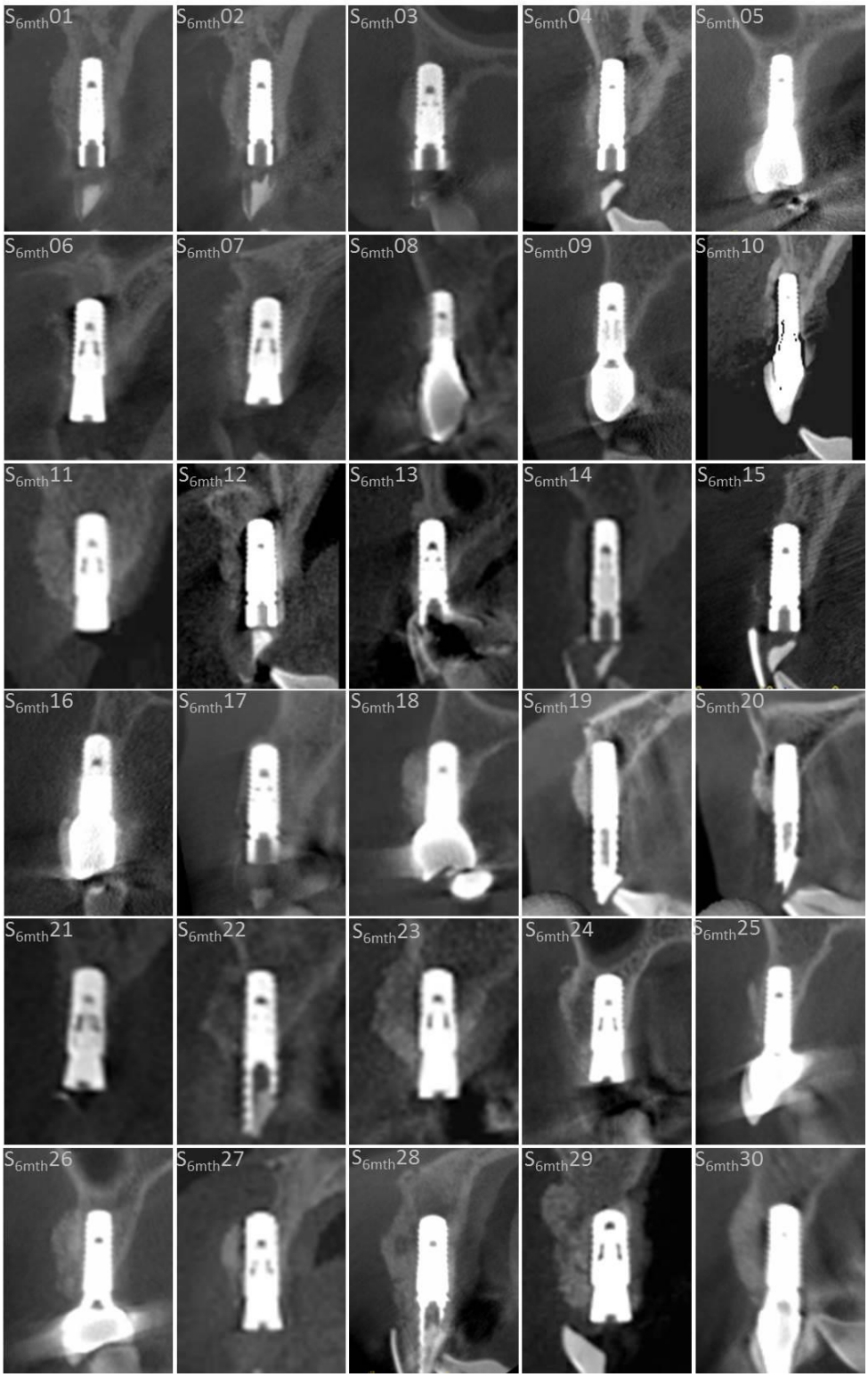

Figure 7 The CBCT images of all implants of study group at 6-month follow-up.

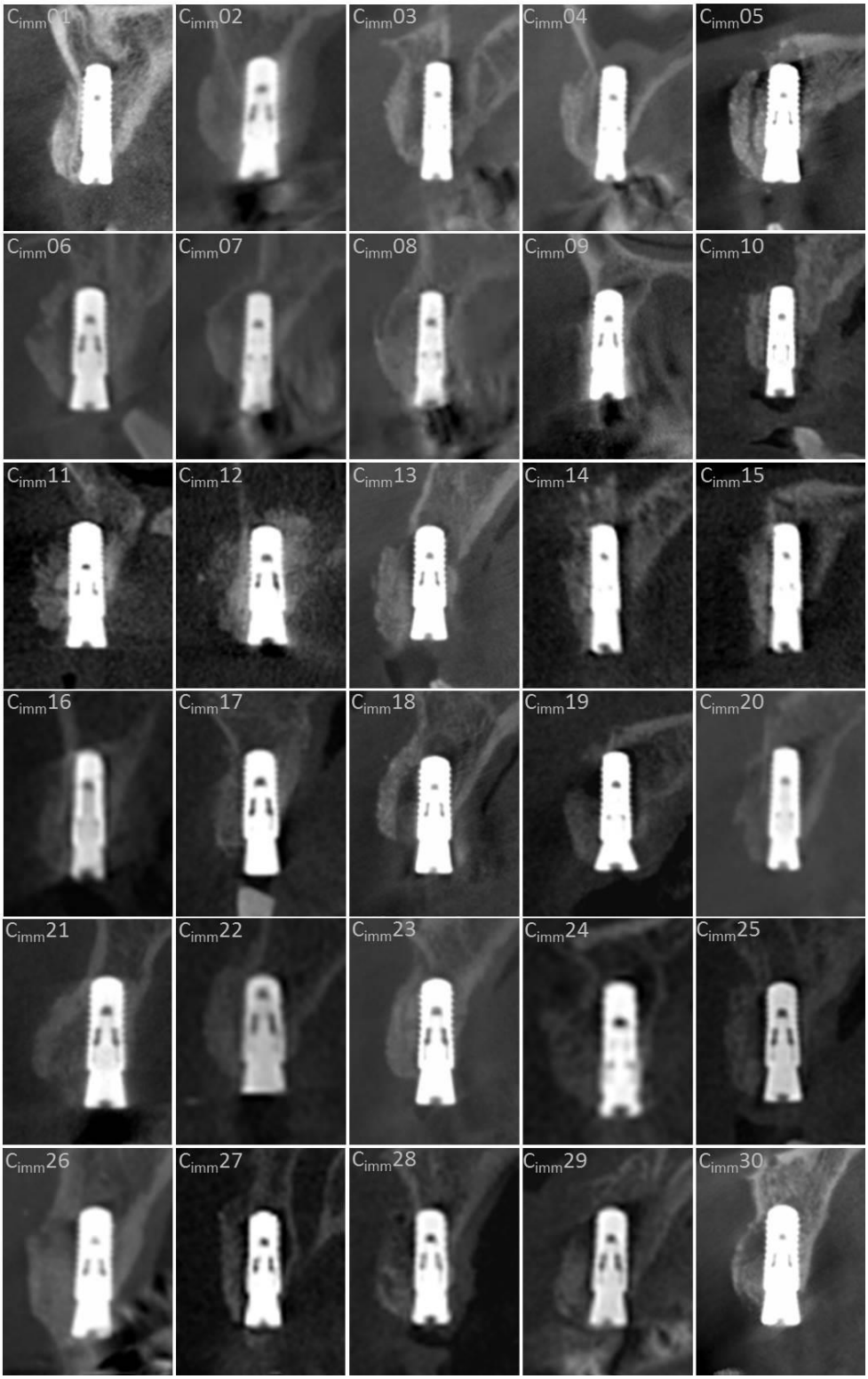

Figure 8 The CBCT images of all implants of comparison group at baseline.

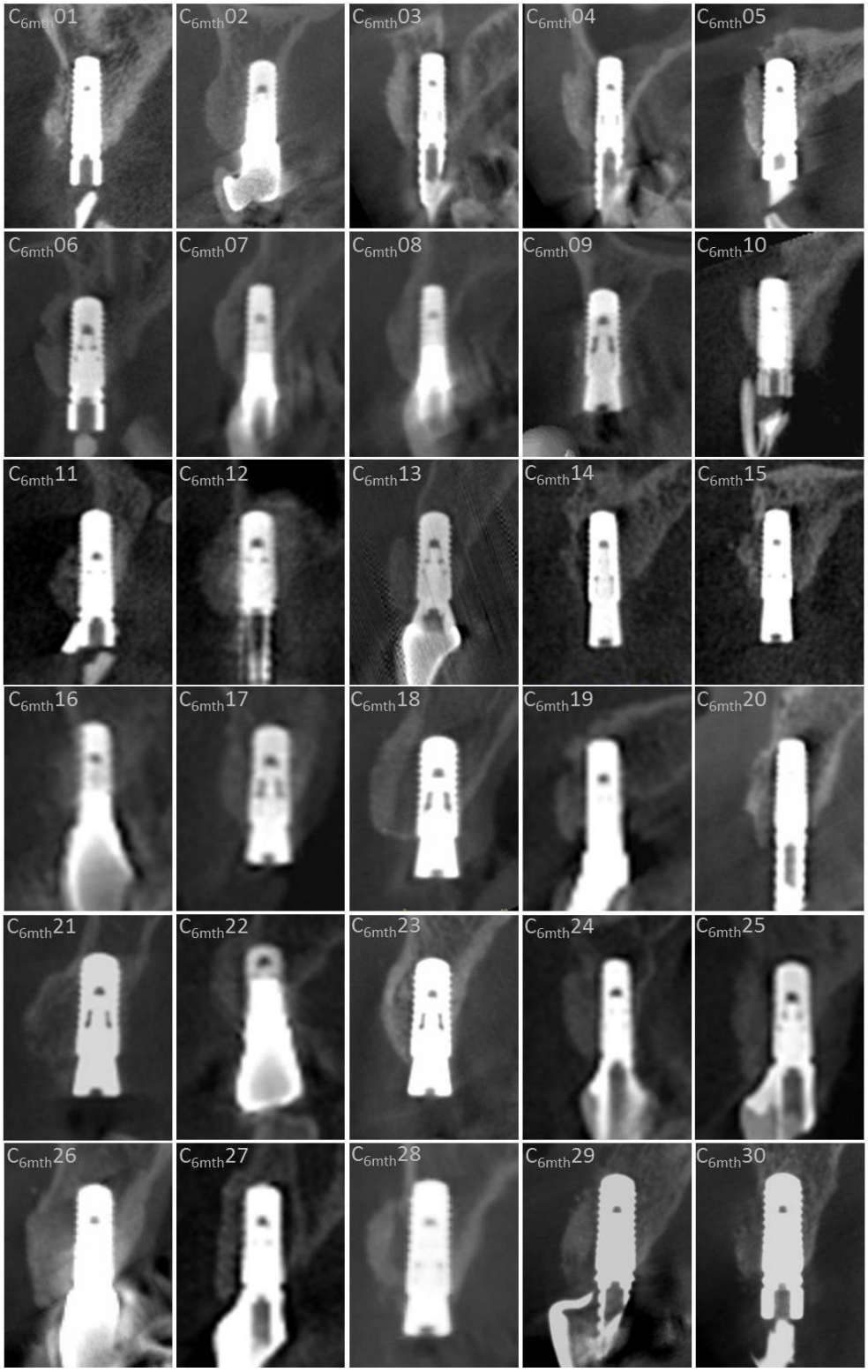

Figure 9 The CBCT images of all implants of comparison group at 6-month follow-up.

CHAPTER V
DISCUSSION

There were two important factors for success in GBR; the quality of surgery and the properties of the utilized biomaterials for contour augmentation. All surgical procedures in our study were performed and supervised by only one experienced surgeon, thus the quality of surgery can be controlled in standard and permit the result influenced only by the biomaterials used. The purpose of contour augmentation by GBR is to establish a sufficient facial bone thickness to support soft tissues for esthetic outcomes. The thickness of facial bone can be measured only by 3D radiography. Nowadays, the CBCT was proposed and has become a commonly accepted diagnostic implement for dental imaging in many studies [113, 116].

In this randomized controlled clinical study, the CBCT was used to evaluate the facial bone thickness for dental implant placement in esthetic zone, simultaneously GBR using different membranes; a synthetic resorbable membrane and a collagen resorbable membrane. The CBCT results indicated that a resorbable synthetic membrane combined with autogenous bone and synthetic bone particles is able to provide successful contour augmentation as well as a resorbable collagen membrane. In addition, the CBCT images demonstrated facial bone thickness more than 2 mm after 6 months of contour augmentation for all implants in both groups and showed a favorable clinical outcome. This result was similar to recently study by Buser et al.[13], in 2013 that analyzed the stability of esthetic outcomes in twenty patients with single-tooth of early implant placement simultaneous with contour augmentation in the anterior maxilla at six years. The CBCT scan was used to investigate facial bone wall at platform, 2mm, 4mm, and 6 mm apical to the implant shoulder. A detectable facial bone wall was exhibited of all twenty implants with a mean thickness of 1.9 mm at six years. The authors concluded that contour augmentation with GBR was able to institute and sustain a facial bone in all twenty patients. However, data of facial bone wall at the baseline had not been recorded; therefore the volume of facial bone change was not able to evaluate.

This facial bone resorption also been supported in another recent prospective studies [10, 13, 15, 16, 130, 131] by consecutive CBCT images. Among

these, recent paper of Chappuis et al.[15] in 2015 compared the facial bone crest dimensions following implantation with GBR of two different implant neck designs at 5-9 years in the esthetic zone using the CBCT. They measured the bone crest at various levels; implant shoulder, 2 mm, 4mm, and 6 mm below the shoulder level. The authors reported that a facial crest thickness had a statistical significant between the bone level neck design (1.2 mm) and the soft tissue level neck design (0 mm) at implant shoulder level while the other levels was not exhibited the significant differences. Unfortunately, this report had no data of facial bone wall immediate post-operation likewise; the alteration of facial bone wall dimension could not be analyzed.

Although GBR technique simultaneous with dental implant placement offered high predictability of the contour augmentation in order to obtain the successful esthetic outcomes, the facial bone wall resorption has also been arisen and continuously driven to dimensional change of alveolar ridge following tooth extraction particularly the immediate and early implant placement according to the bundle bone resorption theory.[7, 9, 13, 130, 132] A recent systematic review[133] stated that the most alteration of alveolar ridge was occurred during the first 6 months post-extraction. This study showed the facial bone resorption at 6 months after contour augmentation in both study and comparison group. In the study groups, the decrease of facial bone thickness was 34.30% at platform level, 27.94% at 2 mm apical, 24.25% at 4 mm apical, 19.81% at 6 mm apical to implant shoulder while as there has 34.80%, 24.06%, 19.52% and 20.45% facial bone resorption in the comparison group at level of implant platform, 2 mm, 4 mm, 6 mm apical to the implant shoulder respectively. This reduction was slightly higher in the study group compared with the comparison group. Notwithstanding, these change did not reach the statistically significant difference between two groups. These bone resorptions were resulted from their manipulation and mechanical properties, the synthetic membranes were stiff and difficult in adaptation of membrane to the site of GBR. For this reason, the completely seal off was not achieved. On the contrary, the collagen membranes were soft and fast degraded so it was collapsed and unable to fully maintain the horizontal bone contour.

Previous clinical study of Schneider et al. [134] in 2011 evaluated the stability of peri-implant tissue following bone and soft tissue augmentation using different technique from our study. They used the cast models obtained from the alginate impressions to assess the dimensional changes of peri-

implant tissue. Casts were optically scanned and digitally superimposed to compare dimensions of peri-implant tissue at different time points. The authors concluded that augmented peri-implant tissue was remained stable within 1 year after crown insertion with a mean loss of 0.04 mm in labial direction and a mean gingival recession of 0.2 mm.

Miyamoto and Obama[14] in 2011 compared the labial bone thickness and postoperative gingival recession around dental implants with GBR in anterior maxillary region comparing between delayed two-stage and immediate placement techniques by using CBCT scan. They reported that an occurred gingival recession was negatively related to labial bone resorption after implant placement. They found the minimal gingival recession in sites where the labial bone thickness was approximately 1.2 mm or more at the cervical of the implant and suggested the criterion of labial bone thickness for 2.0 mm in order to accomplish satisfied outcomes and compensated to average bone resorption approximate to 0.7 mm from opened-flap operation. They concluded that a gingival recession was significantly higher using immediate placement compared to a delayed placement method and decreasing recession in the case of labial bone thickness ≥ 2 mm for both methods.

The dimensional ridge alteration was not prominently occurred only in horizontal direction but also in vertical direction. In addition, the bone reduction was reported that a greatest diminution had taken place in the marginal portion more than 60% whilst the middle and apical portions showed mild resorption[130]. The change of DIB values demonstrated crestal bone loss after implant placement that can be attributed to the insertion depth and the implant neck design. In recent years, some studies [135-137] have demonstrated a good stability of crestal bone for the platform-switching design of the bone level implants due to the less micro-leakage at implant-abutment interface and the reduced maximum biomechanical stress at the crestal bone. The advantage of preservation crestal bone of bone level implants is supported by direct comparison to soft tissue level implants with a recent publication[15]. They informed that soft tissue level implants showed a significant difference of a proximal bone loss with DIB values of -2.18 mm whilst the bone level implants revealed a lesser proximal bone loss with DIB values of -0.44 mm. In this study, all used implants were bone level implant with platform-switching design and the results yielded a favorable DIB values for both groups. The study group displayed the mean of DIB value 1.40 mm for mesial aspect and

1.56 mm for distal aspect contrary to the comparison group that exhibited a higher mean of DIB value 2.03mm for mesial aspect and 1.90 mm for distal aspect after 6 months of implantation with GBR. The decreased DIB values at mesial aspect was 57.81% in the study group and 33.82% in the comparison group whereas the DIB values was diminished at distal aspect with a mean value of 47.23% in the study group and 32.25% in the comparison group. These reductions reached the significant difference for only mesial aspect. It is difficult to establish the reason that why mesial aspect demonstrated more marginal bone resorption compared to distal aspect the insertion depth, adjacent teeth or implants may influence on the proximal bone level then these factors should be further analyzed.

The stability of the underneath facial bone wall had an effect on the steadiness of the keratinized mucosa. This study showed the width of keratinized mucosa with a mean recession of 0.73 mm in the study groups and 0.75 mm in the control group. There was no statistical difference between two groups. In this study, the width of keratinized mucosa was measured from mucogingival junction to mid-facial ginigival crevice immediate post-operation and 6 months follow-up. The ginigival crevice can differ between sample who already be inserted final crown and not yet. In the case of incomplete installation of prosthesis, the width of keratinized mucosa was measured from mucogingival junction to mid-facial aspect of healing abutment or provisional crown. Aside from prosthesis, timing of implant placement had an influence on gingival recession. In a recent systematic review[138] reported increased mucosal recession rate between 20-40% in immediate implant surgery. Unfortunately, samples of immediate case in our study were not enough to analyze the influence of timing of implant placement. Further long-term study with larger sample sizes was suggested.

The minor complications were observed in both groups with greater proportion in the study group. The most common complication in our study was the mild gingival inflammation that existed in 4 cases (two cases of study group and others of comparison group) due to excess bone ceramic particles in thin gingival biotype. This complication was showed at 4-6 months post-operative that the resorbable membrane was already completely degraded, therefore the spiky and shape particles of bone graft material could irritate thin buccal gingiva. Consequently, these excess bone particles were removed by curettage and patient were appointed for follow up until normal wound

recovery. The membrane exposure was the second common post-operative complications which founded in 3 cases of study group but all sites recovered uneventfully. This clarified the benefit of the structure of synthetic membranes for promote soft tissue healing. About manipulation of two different membranes, the surgeon was stated that the synthetic membrane was more difficulty to use than collagen membrane because of the rigidity so this membrane should to pre-shape for suitable adaptation to site of GBR. Then, this synthetic membrane was suggested for experienced users. Furthermore, the synthetic membrane was required to keep in cold storage.

Others clinical parameters should be recorded for evaluate the result of different membranes such as modified plaque index (mPLI), modified sulcus bleeding index (mSBI), pocket depth (PD), and the distance between the implant shoulder and the mucosal margin (DIM). These parameters mostly measured after prosthetic insertion that peri-implant soft tissue was stable. However, our study analyzed the outcomes at 6 month post-implantation with GBR that some cases did not get prosthesis so long term follow up was recommended.

CHAPTER VI

CONCLUSION

A synthetic resorbable membrane revealed a favorable clinical outcome and effective contour augmentation similar to resorbable collagen membrane and suitable used for GBR simultaneous with dental implants. However, this study reported the stability of contour augmentation with GBR between two different membranes with respect to facial bone thickness in a short term period. A long term follow-up with greater number of samples is required for evaluation of the stability of contour augmentation. Moreover, a various factors such as type of implant placement, type of prosthesis, duration of function should be analyzed for correlation to facial bone resorption.

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APPENDICES

Appendix A Data recorded form

No. .....

Name..... **HN.** .....

Sex ..... **Age**..... **Tel** ..... **Placement Date** .....

BoneCeramic ☐ **0.25 g** ☐ **0.5 g**

Membrane type ☐ **Guidor®** ☐ **Bio-Gide®** size ○13x25 mm ○25x25 mm

Parameter	Operation				2 wk F/U				3 month F/U				6 month F/U			
	B	M	L	D	B	M	L	D	B	M	L	D	B	M	D	L
KM																
RFA																
DIB					M		D						M		D	
Facial bone thickness					PF	2 mm	4 mm	6 mm					PF	2 mm	4 mm	6 mm

Complications:

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Appendix B The width of keratinized mucosa (KM) at immediate post-operation, the 6-month follow-up and the change of KM in study group and comparison group

ID	KM_{imm} (mm)	KM_{6mo} (mm)	Change of KM (mm)	ID	KM_{imm} (mm)	KM_{6mo} (mm)	Change of KM (mm)
S01	5.0	5.0	0.0	**C01**	5.0	5.0	0.0
S02	5.0	5.0	0.0	**C02**	7.0	5.0	-2.0
S03	6.0	6.0	0.0	**C03**	3.0	5.0	2.0
S04	5.0	5.0	0.0	**C04**	5.0	5.0	0.0
S05	7.0	4.0	-3.0	**C05**	7.0	5.0	-2.0
S06	4.5	5.0	0.5	**C06**	3.0	2.0	-1.0
S07	4.5	4.0	-0.5	**C07**	5.0	5.0	0.0
S08	6.0	4.0	-2.0	**C08**	6.0	4.5	-1.5
S09	5.5	3.5	-2.0	**C09**	7.0	3.0	-4.0
S10	6.5	9.0	2.5	**C10**	5.0	3.0	-2.0
S11	5.0	3.0	-2.0	**C11**	5.0	4.0	-1.0
S12	4.0	4.0	0.0	**C12**	6.0	4.0	-2.0
S13	5.5	5.0	-0.5	**C13**	5.0	4.0	-1.0
S14	8.0	7.0	-1.0	**C14**	2.0	3.0	1.0
S15	9.0	5.0	-4.0	**C15**	3.0	4.0	1.0
S16	2.0	2.0	0.0	**C16**	4.0	5.0	1.0
S17	5.0	3.0	-2.0	**C17**	5.0	4.0	-1.0
S18	5.0	4.0	-1.0	**C18**	5.0	4.0	-1.0
S19	4.0	3.0	-1.0	**C19**	4.5	4.0	-0.5
S20	4.0	3.0	-1.0	**C20**	4.0	3.0	-1.0
S21	4.0	5.0	1.0	**C21**	4.0	4.0	0.0
S22	4.0	4.0	0.0	**C22**	4.0	3.0	-1.0
S23	7.0	5.0	-2.0	**C23**	4.0	4.0	0.0
S24	5.0	5.0	0.0	**C24**	4.0	4.0	0.0
S25	4.0	3.0	-1.0	**C25**	4.0	5.0	1.0
S26	5.0	3.0	-2.0	**C26**	5.0	4.0	-1.0
S27	4.0	4.0	0.0	**C27**	8.0	5.0	-3.0
S28	3.0	3.0	0.0	**C28**	3.5	4.0	0.5
S29	5.0	3.0	-2.0	**C29**	4.0	2.0	-2.0
S30	3.0	4.0	1.0	**C30**	6.0	4.0	-2.0

Appendix C The facial bone thickness (FBT) along implant axis at mid-facial aspect of 4 different levels: implant platform (PF) and 2 mm, 4 mm and 6 mm apical to the implant shoulder at immediate post-operation and the 6-month follow-up in study group

ID	Immediate post-operation				6-month follow-up			
	FBT_PF (mm)	FBT_2mm (mm)	FBT_4mm (mm)	FBT_6mm (mm)	FBT_PF (mm)	FBT_2mm (mm)	FBT_4mm (mm)	FBT_6mm (mm)
S01	3.41	4.13	4.59	4.35	3.06	3.47	4.25	3.75
S02	3.63	3.97	4.03	3.63	2.72	3.53	3.78	3.56
S03	1.13	2.06	2.62	2.50	0.81	1.38	2.03	1.59
S04	3.41	3.38	3.03	2.88	1.44	1.84	1.84	1.56
S05	2.92	3.44	3.54	2.96	2.00	2.84	3.16	2.78
S06	2.53	2.53	2.38	3.78	1.92	1.56	1.52	2.96
S07	1.87	1.91	2.81	3.84	1.76	1.88	2.68	3.16
S08	3.75	4.50	4.25	3.50	2.00	2.50	2.25	2.00
S09	2.79	2.63	2.29	1.67	0.16	1.25	1.66	1.59
S10	3.00	3.00	3.00	2.75	2.88	2.38	2.25	2.63
S11	4.25	4.00	4.75	4.50	3.50	3.75	4.50	4.50
S12	4.75	4.50	4.75	4.75	3.75	3.25	3.63	3.50
S13	3.75	4.00	3.75	3.50	1.75	1.50	1.25	1.00
S14	3.25	3.75	4.00	3.50	2.50	2.75	3.25	3.00
S15	2.38	2.31	0.87	0.44	2.31	2.25	0.63	0.41
S16	1.42	1.75	1.48	2.03	1.20	1.60	1.44	1.88
S17	2.38	2.67	2.62	2.42	1.22	1.50	1.19	1.03
S18	2.81	3.75	4.00	3.81	2.31	2.94	3.12	3.44
S19	2.81	3.50	4.00	2.94	1.50	2.37	2.56	2.31
S20	3.25	4.00	4.19	4.06	1.69	2.81	3.19	3.00
S21	4.75	4.50	4.25	3.75	0.75	1.00	1.25	1.75
S22	1.88	3.25	4.13	4.50	1.75	3.00	4.00	3.75
S23	5.00	5.50	5.75	5.63	3.50	4.75	5.25	5.25
S24	4.68	4.92	4.64	5.20	1.71	3.09	3.68	4.48
S25	2.60	2.08	2.48	2.56	0.88	1.44	1.92	2.20
S26	4.52	4.48	4.60	4.52	3.36	3.20	3.68	4.16
S27	2.75	3.00	3.25	3.25	1.00	1.75	2.50	2.75
S28	3.36	4.04	4.76	5.16	2.67	3.39	4.19	4.93
S29	4.25	4.75	5.13	5.25	3.50	3.50	3.75	4.25
S30	3.40	4.24	4.64	4.88	2.44	3.56	4.06	4.56

Appendix D The facial bone thickness (FBT) along implant axis at mid-facial aspect of 4 different levels: implant platform (PF) and 2 mm, 4 mm and 6 mm apical to the implant shoulder at immediate post-operation and the 6-month follow-up in comparison group

ID	Immediate post-operation				6-month follow-up			
	FBT_PF (mm)	FBT_2mm (mm)	FBT_4mm (mm)	FBT_6mm (mm)	FBT_PF (mm)	FBT_2mm (mm)	FBT_4mm (mm)	FBT_6mm (mm)
C01	3.63	3.31	2.81	1.94	1.91	3.09	2.50	1.34
C02	4.37	5.19	5.44	5.31	4.25	5.06	5.38	5.16
C03	3.16	3.88	4.40	4.12	2.80	3.56	4.04	3.80
C04	3.44	4.08	4.44	4.52	2.72	3.60	4.08	4.36
C05	4.00	4.34	4.53	4.50	1.91	2.22	2.50	2.84
C06	3.25	4.69	5.19	3.50	2.32	3.36	3.84	2.60
C07	2.38	3.13	4.19	4.06	1.75	2.63	2.94	3.25
C08	3.38	4.31	4.88	4.81	2.81	3.50	3.81	3.50
C09	1.84	1.75	1.75	1.25	1.31	1.19	1.22	1.03
C10	2.00	2.25	2.75	2.25	0.00	1.25	1.88	2.25
C11	3.50	4.50	3.50	4.50	2.50	3.25	2.50	2.00
C12	3.75	4.25	4.50	4.50	3.50	4.00	3.75	3.00
C13	4.78	5.06	4.53	4.03	3.19	3.03	3.00	2.78
C14	2.50	2.75	3.00	3.75	1.25	1.75	2.50	3.50
C15	2.50	2.75	3.25	3.75	1.50	1.50	2.25	2.75
C16	3.25	3.50	3.25	3.25	2.25	2.75	2.75	2.25
C17	3.25	3.25	3.00	3.25	1.50	2.50	3.00	2.75
C18	3.37	4.81	4.97	4.67	2.58	4.58	4.71	4.44
C19	3.25	3.63	4.00	3.50	1.75	2.75	2.75	2.50
C20	2.62	3.81	3.31	2.56	2.25	3.06	2.81	2.44
C21	5.68	5.68	5.40	4.28	4.59	4.91	5.12	4.11
C22	2.75	3.50	3.75	3.25	0.25	2.50	3.50	3.25
C23	3.20	3.32	3.36	3.04	1.32	2.28	3.08	3.04
C24	3.00	4.00	4.50	5.00	1.75	2.75	3.50	3.75
C25	4.00	4.50	5.00	4.75	3.25	3.50	4.00	3.75
C26	5.00	5.13	5.19	5.50	4.25	4.75	4.88	5.19
C27	2.75	3.00	3.25	3.50	2.50	2.25	2.25	2.00
C28	3.75	4.25	4.50	4.75	0.94	2.19	2.94	3.19
C29	4.50	4.00	3.50	3.00	3.60	3.44	3.25	2.35
C30	3.56	4.00	3.72	3.00	2.37	2.88	2.51	2.03

Appendix E The percentage of facial bone thickness change between immediate post-operation and the 6-month follow-up at 4 different levels: implant platform (PF) and 2 mm, 4 mm and 6 mm apical to the implant shoulder of both study group and comparison group

ID	The change of facial bone thickness				ID	The change of facial bone thickness			
	PF (%)	2mm (%)	4mm (%)	6mm (%)		PF (%)	2mm (%)	4mm (%)	6mm (%)
S01	-10.26	-15.98	-7.41	-13.79	**C01**	-47.38	-6.65	-11.03	-30.93
S02	-25.07	-11.08	-6.20	-1.93	**C02**	-2.75	-2.50	-1.10	-2.82
S03	-28.32	-33.01	-22.52	-36.40	**C03**	-11.39	-8.25	-8.18	-7.77
S04	-57.77	-45.56	-39.27	-45.83	**C04**	-20.93	-11.76	-8.11	-3.54
S05	-31.51	-17.44	-10.73	-6.08	**C05**	-52.25	-48.85	-44.81	-36.89
S06	-24.11	-38.34	-36.13	-21.69	**C06**	-28.62	-28.36	-26.01	-25.71
S07	-5.88	-1.57	-4.63	-17.71	**C07**	-26.47	-15.97	-29.83	-19.95
S08	-46.67	-44.44	-47.06	-42.86	**C08**	-16.86	-18.79	-21.93	-27.23
S09	-94.27	-52.47	-27.51	-4.79	**C09**	-28.80	-32.00	-30.29	-17.60
S10	-4.00	-20.67	-25.00	-4.36	**C10**	-100.00	-44.44	-31.64	0.00
S11	-17.65	-6.25	-5.26	0.00	**C11**	-28.57	-27.78	-28.57	-55.56
S12	-21.05	-27.78	-23.58	-26.32	**C12**	-6.67	-5.88	-16.67	-33.33
S13	-53.33	-62.50	-66.67	-71.43	**C13**	-33.26	-40.12	-33.77	-31.02
S14	-23.08	-26.67	-18.75	-14.29	**C14**	-50.00	-36.36	-16.67	-6.67
S15	-2.94	-2.60	-27.59	-6.82	**C15**	-40.00	-45.45	-30.77	-26.67
S16	-15.49	-8.57	-2.70	-7.39	**C16**	-30.77	-21.43	-15.38	-30.77
S17	-48.74	-43.82	-54.58	-57.44	**C17**	-53.85	-23.08	0.00	-15.38
S18	-17.79	-21.60	-22.00	-9.71	**C18**	-23.44	-4.78	-5.23	-4.93
S19	-46.62	-32.29	-36.00	-21.43	**C19**	-46.15	-24.24	-31.25	-28.57
S20	-48.00	-29.75	-23.87	-26.11	**C20**	-14.12	-19.69	-15.11	-4.69
S21	-84.21	-77.78	-70.59	-53.33	**C21**	-19.19	-13.56	-5.19	-3.97
S22	-6.91	-7.69	-3.15	-16.67	**C22**	-90.91	-28.57	-6.67	0.00
S23	-30.00	-13.64	-8.70	-6.75	**C23**	-58.75	-31.33	-8.33	0.00
S24	-63.46	-37.20	-20.69	-13.85	**C24**	-41.67	-31.25	-22.22	-25.00
S25	-66.15	-30.77	-22.58	-14.06	**C25**	-18.75	-22.22	-20.00	-21.05
S26	-25.66	-28.57	-20.00	-7.96	**C26**	-15.00	-7.41	-5.97	-5.64
S27	-63.64	-41.67	-23.08	-15.38	**C27**	-9.09	-25.00	-30.77	-42.86
S28	-20.54	-16.09	-11.97	-4.46	**C28**	-74.93	-48.47	-34.67	-32.84
S29	-17.65	-26.32	-26.90	-19.05	**C29**	-20.00	-14.00	-7.14	-21.67
S30	-28.24	-16.04	-12.50	-6.56	**C30**	-33.43	-28.00	-32.53	-32.33

Appendix F The distance between the implant shoulder and the first bone-implant contact (DIB) of both mesial and distal aspects at immediate post-operation and the 6-month follow-up in comparison group

ID	Immediate post-operation		6-month follow-up	
	DIB_Mesial (mm)	DIB_Distal (mm)	DIB_Mesial (mm)	DIB_Distal (mm)
C01	3.80	3.46	3.07	3.12
C02	1.34	3.15	0.81	1.30
C03	3.20	1.75	3.06	2.83
C04	2.40	2.73	1.79	2.35
C05	4.34	4.39	2.73	2.61
C06	2.59	2.65	0.68	0.90
C07	0.75	1.08	1.16	2.88
C08	2.77	2.47	3.11	1.89
C09	1.50	2.24	1.35	1.90
C10	3.75	3.75	0.88	1.50
C11	4.60	2.90	1.70	1.60
C12	3.80	4.30	1.40	2.50
C13	4.47	4.37	1.96	1.76
C14	5.00	5.00	4.50	2.75
C15	5.00	5.00	4.50	2.50
C16	3.75	1.25	1.25	1.00
C17	3.00	2.25	2.40	-1.10
C18	1.36	1.06	1.33	0.83
C19	3.20	2.10	1.00	-1.10
C20	3.13	3.32	2.48	-0.34
C21	4.42	4.75	4.05	4.37
C22	1.10	1.90	0.10	1.70
C23	1.99	2.06	1.50	1.31
C24	2.70	3.00	-0.20	0.90
C25	4.00	3.75	2.70	3.20
C26	4.38	4.42	4.13	3.84
C27	3.40	2.70	1.20	2.29
C28	3.10	3.30	1.93	2.16
C29	3.20	3.30	3.80	2.90
C30	1.32	3.48	0.46	2.76

Appendix G The distance between the implant shoulder and the first bone-implant contact (DIB) of both mesial and distal aspects at immediate post-operation and the 6-month follow-up in study group

ID	Immediate post-operation		6-month follow-up	
	DIB_Mesial (mm)	DIB_Distal (mm)	DIB_Mesial (mm)	DIB_Distal (mm)
S01	3.70	3.63	2.24	2.86
S02	3.78	3.61	2.75	3.53
S03	1.94	1.85	1.16	0.53
S04	3.74	3.97	2.06	2.56
S05	2.58	2.95	2.19	2.36
S06	3.45	4.39	2.78	2.69
S07	4.48	4.56	2.60	3.94
S08	3.00	2.00	3.00	1.75
S09	2.58	2.69	0.10	0.85
S10	2.70	2.90	1.50	1.60
S11	4.00	3.75	2.20	1.80
S12	3.75	4.00	1.63	2.13
S13	1.75	2.50	-0.75	1.00
S14	3.70	3.00	1.40	1.10
S15	3.57	3.57	-1.05	-0.97
S16	1.43	1.36	-0.93	0.63
S17	3.74	2.15	0.68	1.03
S18	1.32	2.77	1.21	1.88
S19	4.13	3.26	-0.51	1.08
S20	3.72	4.05	2.22	-0.71
S21	3.60	3.60	3.20	2.20
S22	2.10	1.20	0.80	1.00
S23	4.13	3.40	2.40	2.80
S24	3.81	3.93	3.52	3.61
S25	1.33	3.50	0.58	0.58
S26	3.84	1.96	1.48	1.42
S27	3.40	2.80	2.80	2.00
S28	4.13	2.18	0.19	0.13
S29	2.80	1.60	1.80	1.50
S30	1.69	1.69	0.44	0.28

Appendix H The percentage of the distance between the implant shoulder and the first bone-implant contact (DIB) change between immediate post-operation and the 6-month follow-up of mesial and distal aspects of both study group and comparison group

ID	The change of DIB values		ID	The change of DIB values	
	Mesial (%)	Distal (%)		Mesial (%)	Distal (%)
S01	-39.46	-21.21	**C01**	-19.21	-9.83
S02	-27.25	-2.22	**C02**	-39.55	-58.73
S03	-40.21	-71.35	**C03**	-4.38	61.71
S04	-44.92	-35.52	**C04**	-25.42	-13.92
S05	-15.12	-20.00	**C05**	-37.10	-40.55
S06	-19.42	-38.72	**C06**	-73.75	-66.04
S07	-41.96	-13.60	**C07**	54.67	166.67
S08	0.00	-12.50	**C08**	12.27	-23.48
S09	-96.12	-68.40	**C09**	-10.00	-15.18
S10	-44.44	-44.83	**C10**	-76.53	-60.00
S11	-45.00	-52.00	**C11**	-63.04	-44.83
S12	-56.53	-46.75	**C12**	-63.16	-41.86
S13	-142.86	-60.00	**C13**	-56.15	-59.73
S14	-62.16	-63.33	**C14**	-10.00	-45.00
S15	-129.41	-127.17	**C15**	-10.00	-50.00
S16	-165.03	-53.68	**C16**	-66.67	-20.00
S17	-81.82	-52.09	**C17**	-20.00	-148.89
S18	-8.33	-32.13	**C18**	-2.21	-21.70
S19	-112.35	-66.87	**C19**	-68.75	-152.38
S20	-40.32	-117.53	**C20**	-20.77	-110.24
S21	-11.11	-38.89	**C21**	-8.37	-8.00
S22	-61.90	-16.67	**C22**	-90.91	-10.53
S23	-41.89	-17.65	**C23**	-24.62	-36.41
S24	-7.61	-8.14	**C24**	-107.41	-70.00
S25	-56.39	-83.43	**C25**	-32.50	-14.67
S26	-61.46	-27.55	**C26**	-5.71	-13.12
S27	-17.65	-28.57	**C27**	-64.71	-15.19
S28	-95.40	-94.04	**C28**	-37.74	-34.55
S29	-35.71	-6.25	**C29**	18.75	-12.12
S30	-73.96	-83.43	**C30**	-65.15	-20.69

Appendix I The *p*-value of within study group for the width of KM, FBT, DIB values between immediate post-operation and the 6-month follow-up

Paired Samples Test

		Paired Differences						
					95% Confidence Interval of the Difference			
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	n	*p*-value
1	KM_imm - KM_6mo	.7333	1.3244	.2418	.2388	1.2279	30	.005*
2	FBT_PF_imm - FBT_PF_6mo	1.15467	.91912	.16781	.81146	1.49787	30	.000*
3	FBT_2mm_imm - FBT_2mm_6mo	1.01700	.74106	.13530	.74028	1.29372	30	.000*
4	FBT_4mm_imm - FBT_4mm_6mo	.87067	.68529	.12512	.61478	1.12656	30	.000*
5	FBT_6mm_imm - FBT_6mm_6mo	.69267	.60301	.11009	.46750	.91783	30	.000*
6	DIB_M_imm - DIB_M_6mo	1.73167	1.17884	.21523	1.29148	2.17185	30	.000*
7	DIB_D_imm - DIB_D_6mo	1.39700	1.12359	.20514	.97745	1.81655	30	.000*

* : Statistical significant at 95% confident interval by the Paired-Samples T Test.

Appendix J The *p*-value of within comparison group for the width of KM, FBT, DIB values between immediate post-operation and the 6-month follow-up

Paired Samples Test

		Paired Differences						
					95% Confidence Interval of the Difference			
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper	n	*p*-value
1	KM_imm - KM_6mo	.7500	1.3245	.2418	.2554	1.2446	30	.004*
2	FBT_PF_imm - FBT_PF_6mo	1.12633	.69311	.12654	.86752	1.38514	30	.000*
3	FBT_2mm_imm - FBT_2mm_6mo	.89300	.52846	.09648	.69567	1.09033	30	.000*
4	FBT_4mm_imm - FBT_4mm_6mo	.76233	.51426	.09389	.57030	.95436	30	.000*
5	FBT_6mm_imm - FBT_6mm_6mo	.77967	.60706	.11083	.55299	1.00635	30	.000*
6	DIB_M_imm - DIB_M_6mo	1.06767	1.03162	.18835	.68245	1.45288	30	.000*
7	DIB_D_imm - DIB_D_6mo	1.15400	1.27631	.23302	.67742	1.63058	30	.000*

* : Statistical significant at 95% confident interval by the Paired-Samples T Test.

Appendix K The Statistical Analysis for comparison between groups of within comparison group of the percentage of change in the width of KM, FBT, DIB values

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means			
		F	Sig.	n	Mean Difference	Std. Error Difference	*p*-value
Change_KM	Equal variances assumed	.000	.996	60	.0167	.3420	.961
	Equal variances not assumed			60	.0167	.3420	.961
Change_FBT_PF	Equal variances assumed	.175	.677	60	.49994	6.13586	.935
	Equal variances not assumed			60	.49994	6.13586	.935
Change_FBT_2mm	Equal variances assumed	1.271	.264	60	-3.87963	4.11593	.350
	Equal variances not assumed			60	-3.87963	4.11593	.350
Change_FBT_4mm	Equal variances assumed	.619	.435	60	-4.73612	3.92786	.233
	Equal variances not assumed			60	-4.73612	3.92786	.233
Change_FBT_6mm	Equal variances assumed	.603	.441	60	.63753	4.18750	.880
	Equal variances not assumed			60	.63753	4.18750	.880
Change_DIB_M	Equal variances assumed	.023	.880	60	-23.98869	9.75622	.017*
	Equal variances not assumed			60	-23.98869	9.75622	.017*
Change_DIB_D	Equal variances assumed	1.091	.301	60	-14.98099	11.66838	.204
	Equal variances not assumed			60	-14.98099	11.66838	.206

* : Statistical significant at 95% confident interval by the Independent-Samples T Test.

Appendix L Thai consent form

เอกสารยินยอมเข้าร่วมการวิจัย (Consent Form)

การวิจัยเรื่อง การเปรียบเทียบผลของการใช้แผ่นเยื่อกีดขวางสองชนิดที่แตกต่างกันในการฝังรากเทียมร่วมกับการชักนำให้เกิดการสร้างใหม่ของกระดูกในบริเวณที่ต้องการความสวยงาม

ข้าพเจ้า (นาย, นาง, นางสาว).....

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

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

ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้

1. ข้าพเจ้าได้รับทราบรายละเอียดข้อมูลคำอธิบายสำหรับอาสาสมัครที่เข้าร่วมในการวิจัย รวมทั้งได้รับการอธิบายจากผู้วิจัยถึงวัตถุประสงค์ของการวิจัย วิธีการทำวิจัย อันตรายหรืออาการที่อาจเกิดขึ้นจากการทำวิจัยหรือจากยาที่ใช้ รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการวิจัยอย่างละเอียดและมีความเข้าใจดีแล้ว
2. ผู้วิจัยรับรองว่าจะตอบคำถามต่างๆ ที่ข้าพเจ้าสงสัยด้วยความเต็มใจไม่ปิดบังซ่อนเร้นจนข้าพเจ้าพอใจ
3. ผู้วิจัยรับรองว่าจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพเจ้าเป็นความลับและจะเปิดเผยได้เฉพาะในรูปที่เป็นสรุปผลการวิจัย การเปิดเผยข้อมูลเกี่ยวกับตัวข้าพเจ้าต่อหน่วยงานต่างๆ ที่เกี่ยวข้องกระทำได้เฉพาะกรณีจำเป็นด้วยเหตุผลทางวิชาการเท่านั้น และผู้วิจัยรับรองว่าหากเกิดอันตรายใดๆ จากการวิจัยดังกล่าว ข้าพเจ้าจะได้รับการรักษาพยาบาลโดยไม่คิดมูลค่า
4. ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยนี้เมื่อใดก็ได้และการบอกเลิกการเข้าร่วมการวิจัยนี้จะไม่มีผลต่อการรักษาโรคที่ข้าพเจ้าจะพึงได้รับต่อไป

ข้าพเจ้าจึงสมัครใจเข้าร่วมโครงการวิจัยนี้ตามที่ระบุในเอกสารข้อมูลคำอธิบายสำหรับอาสาสมัครและได้ลง นามในใบยินยอมนี้ด้วยความเต็มใจ และได้รับสำเนาเอกสารใบยินยอมที่ข้าพเจ้าลงนามและลงวันที่ และเอกสารยกเลิกการเข้าร่วมวิจัย อย่างละ 1 ฉบับ เป็นที่เรียบร้อยแล้ว

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

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

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

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ข้าพเจ้าไม่สามารถอ่านหนังสือได้ แต่ผู้วิจัยได้อ่านข้อความในใบยินยอมนี้ให้แก่ข้าพเจ้าฟังจนเข้าใจดีแล้ว ข้าพเจ้าจึงลงนาม หรือประทับลายนิ้วหัวแม่มือขวาของข้าพเจ้าในใบยินยอมนี้ด้วยความเต็มใจ

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

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

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

ในกรณีที่ผู้ถูกทดลองยังไม่บรรลุนิติภาวะ จะต้องได้รับการยินยอมจากผู้ปกครองหรือผู้อุปการะโดยชอบด้วยกฎหมาย

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

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

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

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