CLINICAL EFFICACY OF POROUS POLYETHYLENE MEMBRANE FOR ALVEOLAR RIDGE PRESERVATION : A PILOT STUDY

BY

JIRAPA WONGPAIROJPANICH

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE PROGRAM IN DENTAL IMPLANTOLOGY FACULTY OF DENTISTRY

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MS. JIRAPA WONGPAIROJPANICH

ENTITLED

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was approved as partial fulfillment of the requirements for the degree of master of science program in dental implantology on June 30, 2020

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Thesis Title	CLINICAL EFFICACY OF POROUS POLYETHYLENE MEMBRANE FOR ALVEOLAR RIDGE PRESERVATION: A PILOT STUDY
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ABSTRACT

Objective: To evaluate the clinical efficacy of novel porous polyethylene membrane (PPE) in comparison with high-density polytetrafluoroethylene membrane (d-PTFE) in alveolar ridge preservation.

Materials and methods: Thirty patients were randomized into two groups following tooth extraction. All extraction sites were preserved with synthetic bone substitutes and then covered with the assigned membrane, a porous polyethylene membrane (PPE membrane) or dense polytetrafluoroethylene membrane (d-PTFE), then left exposed with a secondary wound healing. All patients were monitored for socket wound healing at day 1,3,7,14,28 and 4 months. Both types of membranes were removed on day 28 following the standard protocol. Dimensional changes of the alveolar ridge were measured immediately after tooth extraction and 4 months using intraoral scan and CBCT. At 4 months all socket bones from both membrane groups were harvested during implant osteotomy for histology and histomorphometry analysis. Implant stability at insertion and prior to prosthesis delivery were recorded.

Results: No statistically significant difference ($p<0.05$) for early socket healing between two membrane groups except on day 14 which had a higher degree of wound closure found in PPE (25.38 ± 31.33%) than d-PTFE (-1.06± 33.89%). Overall for dimensional changes by intraoral scan and CBCT analysis demonstrated higher ridge resorption on buccal side than lingual side while more changes were observed in the coronal part than apical part of the alveolar ridge in both membrane groups. No statistically significant difference ($p<0.05$) in the mean of vertical and horizontal changes were seen in both groups. For histomorphometric analysis, new bone formation was slightly more in d-PTFE than PPE groups (31.03±6.47%) and (27.06±7.91%) respectively. Whereas more residual bone graft was found in PPE group than d-PTFE

(33.22±6.73%) and (30.58±4.66%) however no statistically significant differences were found between two groups. Significant increase in the implant stability was seen in all implants from placement to prosthesis delivery. However, no statistically significant difference ($p<0.05$) was observed between PPE and d-PTFE groups.

Conclusion: Porous polyethylene membrane could be potentially used as an alternative choice for an inexpensive membrane material in alveolar ridge preservation, however further use for tissue regeneration needs to be investigated.

Keywords: Alveolar ridge preservation; Porous polyethylene membrane; Polytetrafluoroethylene; Dimensional changes

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Jirapa Wongpairojpanich

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LIST OF ABBREVIATIONS

Symbols/Abbreviations	Terms
%	Percent
>	Greater-than
<	Lesser-than
±	Plus-minus
®	Registered trademark
e.g.	For example
mm	Millimeter(s)
mm^2	Square millimeter(s)
n	Number of patients
SD	Standard deviation
A	Wound area in Square millimeter(s)
NA	Not available
p	P-value
EDS	Extraction defect sounding
ARP	Alveolar ridge preservation
GTR	Guided tissue regeneration
GBR	Guided bone regeneration
PGA	Poly (glycolic acid)
PLA	Poly (lactic acid)
PLA /PLGA	Polylactic Acid and Polylactic acid/Polyglycolic Acid Copolymer
PEG	Polyethylene Glycol

PCL	Polycaprolactone
PE	Polyethylene
PPE	Porous Polyethylene
HDPE	High-density polyethylene
PTFE	Polytetrafluoroethylene
e-PTFE	Expanded Polytetrafluoroethylene
d-PTFE	High-Density Polytetrafluoroethylene
Ti-e-PTFE	Titanium re enforce expanded Polytetrafluoroethylene
BMPs	Bone morphogenetic proteins
rhBMP-2	Recombinant human bone morphogenetic protein-2
PRF	Platelet-rich fibrin
CEJ	Cementoenamel junction
CBCT	Cone-beam computed tomography
IST	Implant stability values
H&E	Hematoxylin and eosin
MTEC	National Metal and Materials Technology Center

CHAPTER 1

INTRODUCTION

1.1 Background and rationale

Over the last few decades, implant dentistry has gained increasing popularity and became a treatment of choice for replacing teeth. Dental implants can mimic the natural tooth in both physical appearances and functions. However, implant placement may be limited by local conditions of an edentulous alveolar ridge, such as the amount of remaining alveolar bone in both quality and quantity after losing a tooth (1). Extraction is one of the most commonly performed procedures in dentistry which has been well-documented that could cause significant dimensional changes of the alveolar ridge (2, 3). Most of the studies have demonstrated that reduction of the alveolar ridge after a tooth extraction is an unavoidable and irreversible process (3-5). The resorption pattern of alveolar bone was reported in approximately around 40 % of alveolar bone height and 60 % of the width, in which two-thirds of the ridge is lost during the first 3 months after tooth extraction and continues at a mean 0.5-1% a year for life (2, 6-9). Dimensional loss of the alveolar ridge may result in an unfavorable architecture and alveolar bone volume, which affect tooth replacement therapy, especially when implant-supported restorations are planned (10). In case of severe dimensional change of the alveolar process often necessitates for ridge augmentation procedures including guided bone regeneration (GBR) by using particulate bone grafting, block grafting, or

other extensive surgical procedures, which increase morbidity, cost and time of treatment (11).

To eliminate or minimize these extensive regenerative surgical procedures, the alveolar ridge preservation procedure (ARP) is recommended to perform at the time of tooth extraction to preserve the alveolar bone dimensions and architecture to prevent hard and soft tissue collapse (8, 9, 11, 12). Various modalities of ARP have been described and published in recent decades (12). In most cases, extracted sockets were grafted with bone substitutes then occluded with or without barrier membranes before attempting to close to wound by suturing across the alveolar ridge. Properties of the membrane have a significant role in ARP and biological responses. Various natural and synthetic barrier materials, including bioabsorbable (collagen, polylactic acid, chitosan, aliphatic polyesters, and their co-polymers) and nonabsorbable (polytetrafluoroethylene or PTFE), have been widely used and described (8, 9, 12-18). Important properties of these membranes are including epithelial and bacterial cells exclusion while allowing osteogenic cells to migrate and form bone inside the extracted socket. In clinical situations, nonresorbable membrane such as dense PTFE (d-PTFE), may have more advantages due to the porosity of the membrane structure because of d-PTFE membrane allows the clinician to preserve the interdental papilla and the full width of keratinized mucosa without the concerns of bacterial contamination or infection. In addition, when advancement flap is not required for primary closure thus, soft tissue and the position of the mucogingival junction can be preserved without losing vestibular depth. Pertinently, the size of the flap advancement is often related to the amount of patient morbidity (19).

However, the downside of APR procedure is the cost of materials, including bone graft substitutes and especially the barrier membrane. In Thailand, the average cost of imported membrane per sheet is around 3,000-7,000 baht. Hence, this would exclude many patients who cannot afford the cost of the treatment. While, polyethylene (PE), polymeric biomaterial is another potential material that can be used as nonresorbable barrier membrane, which has been successfully used in several medical applications, with good physicochemical, mechanical and biological properties (20-23). For this reason, National Metal and Materials Technology Center (MTEC) has developed a novel bi-layer porous polyethylene membrane (PPE), which has been extensively tested both in vitro and in vivo for its biofunctional, biosafety and biocompatibility. Importantly, satisfying clinical results from more than 20 procedures in cranio- and maxillofacial reconstruction and more than 70 procedures in orbital reconstruction were reported (24-33). However, PPE membrane has not been tested for alveolar ridge preservation in human yet. Therefore, the aim of this research was to extend the application of this porous polyethylene membrane material in dentistry. The clinical efficacy, histological, and histomorphometric analysis of this porous polyethylene membrane were evaluated and compared to commercial-non resorbable membrane material in alveolar ridge preservation (APR) prior to implant placement.

1.2 Research objectives

The aim of this study was to evaluate the clinical efficacy of novel porous polyethylene membrane (PPE) in comparison with high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200) in alveolar ridge preservation prior to implant replacement.

1.3 Research hypothesis

Ho: There are no significant differences in dimensional change of alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There are differences in dimensional change of alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.4 Statistical hypothesis

1.4.1 Degree of wound closure

Ho: There is no significant differences in degree of wound closure after alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There is a significant difference in degree of wound closure after alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.4.2 Dimensional changes of soft tissue

Ho: There is no significant differences in dimensional change of alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There is a significant difference in dimensional change of alveolar ridge after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.4.3 Dimensional changes of hard tissue

Ho: There is no significant differences in dimensional change of alveolar bone after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There is significant differences in dimensional change of alveolar bone after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.4.4 Implant stability values (IST)

Ho: There is no significant differences in implant stability values (IST) after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There is significant differences in implant stability values (IST) after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.4.5 Histomorphometric analysis

Ho: There is no significant difference in percentage of new bone formation, connective tissue, and residual graft particles after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

Ha: There is a significant difference in percentage of new bone formation, connective tissue, and residual graft particles after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200).

1.5 Scope of the research

This prospective randomized, controlled clinical trial in 30 patients who needed tooth extraction and replaced with dental implant at the Faculty of Dentistry, Thammasat University hospital. The effectiveness of porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, CytoplastTM Regentex TXT-200) for alveolar ridge preservation were compared and evaluated.

1.6 Expected benefits

1.To evaluate efficacy of porous polyethylene membrane as a regenerative material as a barrier membrane for GBR in the future.

2.To be material of choice in regenerative dentistry, for economic reasons and affordable oral health care.

CHAPTER 2

REVIEW LITERATURES

2.1 Alveolar process

The alveolar process, periodontal ligament and dental cementum are a tooth-dependent structure, which formed in harmony with the eruption and development of the teeth. The tooth is anchored into the jaws via the bundle bone which is contributed by the periodontal ligament fibers. The shape and volume of the alveolar process are determined by the size and shape of the tooth, the site and inclination of tooth eruption, and the presence or absence of the teeth (7, 34). The “alveolar bone proper” or “bundle bone” in histologically term means to the inner portion of socket walls. The “alveolar bone” is called the remaining hard structure, which included circumferential, concentric and interstitial lamellae bone. Moreover, bundle bone in the circumferential lamellae bone, wide 0.2– 0.4 mm, consists of the Sharpey’s fibers which inserted between dental cementum, periodontal ligament and the alveolar bone create a unit of tooth-dependent structure (34).

Araujo et al. (2005) (13) reported that the coronal aspect of buccal bone was often consisted of only the bundle bone and assumed that major bone resorption of the extraction socket is related to a higher proportion of bundle bone, which undergone resorption due to the loss of its functionality and disappear (13, 35). In addition, the bundle bone and the buccal bone plate frequently exhibit a similar thickness at the anterior tooth region. Another study showed the facial bone thickness in anterior maxilla has been shown to be 90% of cases less than 1 mm and almost 50% of cases

less than 0.5 mm (36-39). Correlate with Januario et al. (2011) (36) which reported the buccal bone thickness in most locations of all anterior teeth was ≤1 mm (average ~0.5 mm) and approximately to 50% of these had a buccal bone thickness was ≤0.5 mm. Besides, the study in bone resorption pattern with cone beam computed tomography (40) showed the thin wall phenotype (thickness ≤ 1 mm) lead to more vertical bone loss when compared with thick wall phenotype (thickness > 1 mm). Therefore, most of the thin buccal bone wall is a tooth-dependent structure and the tooth in the anterior maxilla position with a thin buccal bone plate can lead to bone loss after tooth extraction. Moreover, the separation of the periosteum from the underlying bone from the surgical trauma during extraction procedure leads to vascular damage and an acute inflammatory response, which conduct bone resorption (41, 42).

2.2 Classification of extraction sockets

There are several extraction defect classification systems, which based on the anatomy of both hard and soft tissue in the extraction site, exist in the literature. The benefit of each system aid in the development of a treatment plan to management of established ridge defects. It provides a clinical intervention algorithm, optimizing bone management strategies and creating potential implant sites which lead to predictable restorations.

Although there are multiple variables present in each classification system, the key factor to determine the quality of the socket following extraction is the presence or absence of the buccal hard and soft tissue. Recently, new simplified classifications were proposed to allow easier documentation and better communication between clinicians, researchers, and readers.

Elian N et al, 2007 (43) have classified the extraction sockets into 3 types based on the remaining of buccal plate and labial soft tissue after extraction.

Type I: The facial soft tissue and the buccal plate of bone are at normal levels in relation to the cemento-enamel junction of the pre-extracted tooth and remain intact post extraction. This socket type is the easiest and most predictable to treat with the implant.

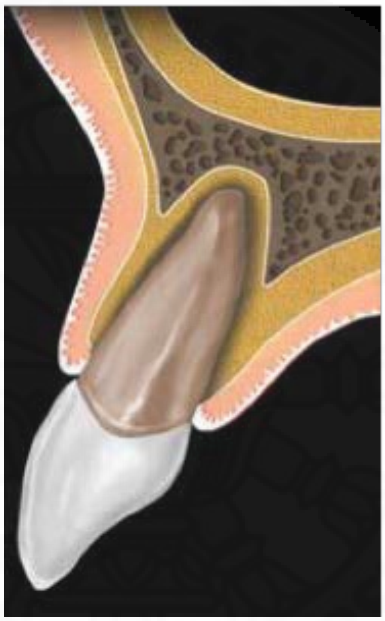

Figure (2.1) Type I socket, the facial soft tissue and the buccal plate of bone are at normal levels in relation to the cemento-enamel junction (Elian N et al, 2007).

Type II: The facial soft tissue is present but the buccal plate is partially missing following extraction. The socket is very difficult to diagnose. This socket can be very deceptive, as the inexperienced clinician may make the mistake of treating it as a type I socket. Improper treatment of type II sockets can cause esthetic problems because the

recession of soft tissue after treatment may occur. Only way to see buccal plate is CT scan.

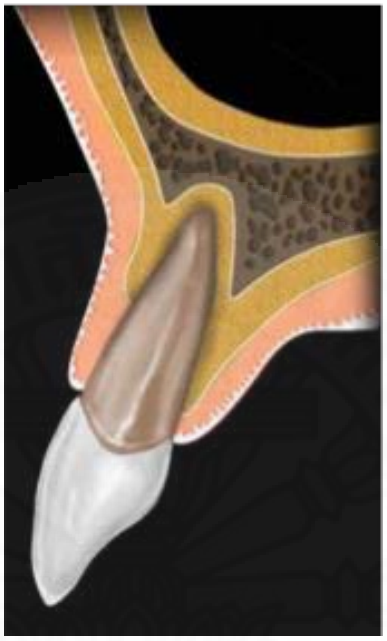

Figure (2.2) Type II Socket; the facial soft tissue is present but the buccal plate is partially missing (Elian N et al, 2007).

Type III: The facial soft tissue and the buccal plate of bone are both markedly reduced after tooth extraction. This socket type is very difficult to treat and requires soft tissue augmentation or bone graft with connective tissue augmentation to re-establish soft tissue. This type is associated with soft tissue recession and loss of the buccal plate on the tooth prior to extraction.

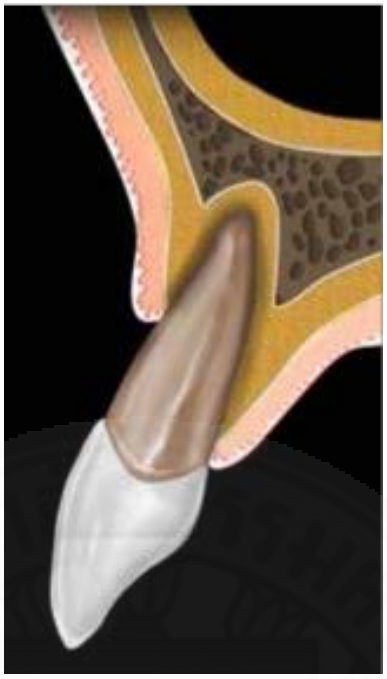

Figure (2.3) Type III Socket. The facial soft tissue and the buccal plate of bone are both reduced after tooth extraction (Elian N et al, 2007).

2.3 Dimensional changes after tooth extraction

Tooth extraction has been well-documented that can cause significant dimensional changes of the alveolar ridge (2, 3, 5, 7, 44-48). The resorption pattern of alveolar bone is reported in approximately around 40 % of alveolar bone height and 60 % of alveolar bone width, which two-thirds of the ridge is lost during the first 3 months after tooth extraction and continues at a mean 0.5-1% a year for life (2, 4, 5, 44, 49). The degree of dimensional changes in alveolar ridge width is greater than alveolar ridge height and the amount of bone resorption is greater at the buccal side than at the lingual side, its related to several factors such as anatomic, prosthetic, metabolic, functional, iatrogenic factors, surgical trauma from flap elevation, lack of functional stimulus on the remaining bone walls, lack of periodontal ligament and genetic information (4, 9,

13, 17, 50). A systematic review in 2009 has reported dimensional changes of sockets after tooth extraction in humans, the resorption of the alveolar ridges is around 3.87 mm in width and 1.67 mm in height (51). While, another systematic review showed average bone resorption after tooth extraction alone is around 29–63% horizontally and 11–22% vertically within the first 6 months (6). In single-tooth extraction, the alveolar ridge may limit the reduction in vertical dimension, but substantial reduction in horizontal dimension (7, 46) (Figure 2.4, 2.5).

However, most of the studies have demonstrated that resorption of the alveolar ridge is an unavoidable and irreversible process (1-3). As a result of tooth loss, a relocation of the alveolar crest margin, specific pattern, is tending to shift lingually/palatally position, the alveolar process will undergo atrophy (52, 53). And resulting in myriad prosthodontic, esthetic, and functional challenges during the replacement of missing teeth, especially when implant-supported restorations are planned (10).

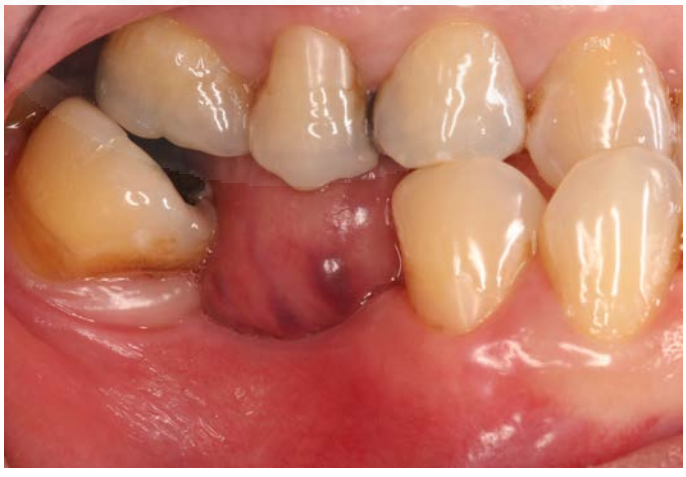

Figure (2.4) Substantial reduction in the vertical dimension of the healed ridge of an alveolar ridge at 12 months after tooth extraction.

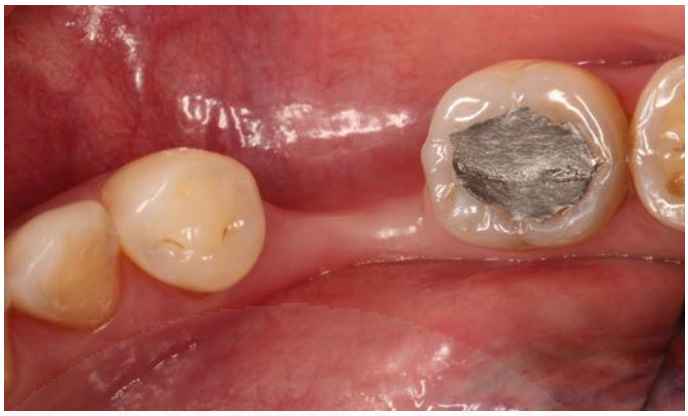

Figure (2.5) Substantial reduction in the horizontal dimension of the healed ridge of an alveolar ridge at 12 months after tooth extraction.

2.4 Guided bone regeneration (GBR)

In the 1950s, Guided tissue regeneration (GTR) was first described by Hurley, who used the barrier membrane to develop a gap between soft and hard tissue in the areas of active bone formation (54). After that, a membrane technique was used to generate new bone around implants based on the principle of GTR was defined as guided bone regeneration (GBR) (55, 56). Nowadays, GBR is one of the most common and promising augmentation techniques to regain adequate width and height of the alveolar bone at implant sites, or to preserve dimension of alveolar sockets after tooth extraction (57-60). Both GTR and GBR techniques, the major key is the barrier membrane which is used to prevent epithelial or undesirable tissues migration into the defective area, whether the graft material is filled or not, and permits adequate time for bone, cementum, and periodontal ligament regeneration (61). The ideal properties of membrane, which used in GTR and GBR, should have biocompatibility, cell

conclusiveness, space maintenance ability, integrated by the host tissues, and clinical manageability (62, 63).

In general, the membranes are mainly divided into two groups, bioabsorbable and non-resorbable membranes. In clinical use, each membrane has been extensively applied. Moreover, the characteristic of membrane, for use as a medical device, must fulfill five main design criteria, as described by Scantlebury (1993) (64)

1. Biocompatibility

Biocompatibility of membranes must be at an acceptable level and not have a negative effect between the material and the surrounding tissue. Moreover, membranes should encourage healing outcomes and safety for the patient.

2. Cell conclusiveness

To prevent fibrous tissue growth into the healing site, which can cause delay or prevent bone formation. The barrier membrane must have an optimal cell selective property. Occlusive property for instance, has a significant effect on the potential for cell invasion and is closely related to porosity of membrane (65). Nevertheless, this property may be at least as important as space-maintaining property. Especially, when membrane was used to create space for new bone in the regenerative areas (66). Although the porosity of membrane encourages the diffusion of oxygen, nutrients and substances for soft and hard tissue regeneration. Small pore size is designed to prevent the ingrowth of epithelial cells or gingival fibroblasts. A larger pore size is allow faster-growing cells such as epithelial cells to overpopulate the defect site and impede the activity and infiltration of bone-regenerating cells (67). However, if the pore size is too

large, this could lead to an easy pathway for bacterial contamination, and complicated to surgical removal of the contaminated membrane due to excess soft tissue ingrowth (68, 69). On the other hand, too small pore size can limit the migration of all cells which results in increased collagen deposition, formation of avascular tissue, and failure of capillary ingrowth and infiltration (70). Consequently, pore size will affect the capacity of the membrane to encourage the regenerating tissue.

3. Space maintenance ability

To create and maintain a suitable space for the intended osseous regeneration, the membrane should have an adequate stiffness. This property is predominantly related to the membrane thickness. Furthermore, a membrane should provide an optimal space that can be maintained for tissue ingrowth but also still provide sufficient support to the tissue, even in large defect sites. Therefore, the membrane material should be appropriately malleable to provide the specific geometry required for functional reconstruction, but be adequately stiff to resist the pressures exerted by external forces such as mastication in jaw reconstructions (67). If the membrane collapses into the defect space, it can result in reduction of the regenerated volume and cannot be accomplished as an optimal clinical outcome.

4. Tissue integration

The key aspect of all tissue regeneration techniques is tissue integration because it is important that it is integrated between host tissue and membrane. Constitute prerequisites for predictable new bone formation composed of the structural integrity of the barrier membrane and the adequate adaptability of its borders to the adjacent

original bone (71). Tissue integration stabilizes the healing wound procedure, and helps to create a seal between the membrane and bone to protect tissue integration of fibrous connective into the defect site. Tissue integration between the membrane and the contours of the adjacent bone is reliable on the space-making ability of the membrane material, if a material is too stiff, it would not be able to mold the shape of the membrane to the defect site.

5. Clinical manageability

The membrane should be easy to use in the clinical situation, especially to apply in narrow space such as in GBR procedures. Difficult clinical management or handling can result in complications or unsatisfied outcome (15). Membrane with high stiffness with some sharp edges can cause perforate of the gingival tissue and subsequent exposure of the membrane (11, 41). K. Ito et al, 1998 has shown that non-resorbable membranes can provide a suitable stiffness over resorbable membranes for optimal bone width and height in GBR procedure (72).

2.5 Alveolar ridge preservation (ARP)

The main objective of ARP is to limit vertical and horizontal dimension changes of alveolar ridge or preserve alveolar ridge volume within the envelope existing at the time of extraction (73, 74). In addition to reduce the volume of alveolar ridge resorption, preserve crestal buccal plate integrity, ARP also improve vital bone fill, decrease the need for future bone augmentation prior to conventional or implant-based prosthetic therapy, and reduce the cost and time of treatment. Current methods of

alveolar ridge preservation based on the principle of guided bone regeneration (GBR) including the use of particulate autografts, allografts, alloplasts, xenografts, and bioabsorbable or non-resorbable membranes materials.

There are several studies in alveolar ridge preservation technique that have been reported that when grafting of extraction sockets with biomaterials and barrier membranes are able to reduce the degree of dimensional changes (4, 16, 75-77). Especially, when alveolar ridge is preserved for dental implant placement to achieve the best bone availability for successful implant prosthesis (78).

Although alveolar ridge preservation helps in reducing the degree of alveolar bone resorption but several studies have found that it cannot completely prevent alveolar bone loss phenomenon (79). In a recent systematic review, Vittorini et al, 2013 (80) concluded that alveolar ridge preservation has a slight advantage over no treatment due to less horizontal and vertical bone loss. Klijn, R. J. et al, 2010 (81) have reported in a meta-analysis study and recommend that alveolar ridge preservation is preferable to perform after tooth extraction in the esthetic areas such as anterior maxillary, which the buccal bone thickness is less than 1.5 to 2 mm, and when several teeth are extracted or when anatomical structures such as the maxillary sinus and mandibular canal are located in immediate proximity.

Darby et al, 2008 (82) have been suggest a specific indication for ridge preservation include the following:

1. If an implant is planned to be placed at the extracted site more than six to eight weeks after tooth extraction.

2. If an implant is to be placed at the time of extraction or within six to eight weeks following extraction, there appears to be little benefit in carrying out ridge preservation procedures at the time of extraction.

3. Even when an implant might not be planned in the near future, ridge preservation should be considered in strategically important sites to retain the possibility of an implant option for the patient in the future.

4. Sites where the buccal plate is less than 1.5-2 mm thick and sites where there has been damage or loss of one or more of the socket walls.

5. In patients where many teeth are to be extracted and preservation of the bone is important for further restoration.

6. Sites where maintaining bone volume is crucial to minimize the risk of involving anatomical structures before implant placement, such as the posterior maxilla or mandible.

7. If the patient with high esthetic demands, such as a high lip line or a thin biotype, which is prone to more recession.

Various systematic reviews in 2009 have been focus on this topic, confirming the efficacy of different alveolar ridge preservation (ARPs) in preventing post-extraction dimensional changes of alveolar ridges (73, 80, 83). The last consensus “Osteology Consensus Report” (73) have been stated the indications for “ARPs” as follows:

1. Implant placement is planned at a time point later than tooth extraction

a) When immediate or early implantation is not recommendable

b) When patients are not available for the immediate or early implant placement (pregnancy, holidays)

c) When primary stability of an implant cannot be obtained

d) In adolescent people.

2. Contouring of the ridge for conventional prosthetic treatment.

3. Provided the cost/benefit ratio is positive.

4. Reducing the need for elevation of the sinus floor.

In addition, based on the systematic review by Vignoletti et al, 2012 (84) the group concluded that the reasons for ridge preservation included:

1. Maintenance of the existing soft and hard tissue envelope.

2. Maintenance of a stable ridge volume for optimizing functional and esthetic outcomes.

3. Simplification of treatment procedures subsequent to the ridge preservation

a. Generation of a good soft tissue volume for the time of implant placement thus simplifying implantation procedures at earlier time points.

b. Generation of a good hard tissue volume for the time of implant placement thus simplifying implantation procedures at later time points.

Contra-indication of ridge preservation

1. General contraindication against oral surgical interventions.

2. Infections at the site planned for ridge preservation, which cannot be taken care of during the ridge preservation surgery.

3. Patients radiated in the area planned for ridge preservation.

4. Patients taking bisphosphonates.

Consequently, alveolar ridge preservation is any procedure which performs at the time of tooth extraction and based on the GBR principle to minimize resorption of alveolar ridge and maximize bone formation within the socket (83). Moreover, many procedures have been suggested including minimally traumatic tooth extraction, soft and hard tissue grafting, concomitant use of barrier membranes and immediate implant placement.

In general, alveolar ridge preservation procedure can be divided into 3 steps composed of 1. Minimally traumatic tooth extraction 2. Socket preparation 3. Coverage of the socket by soft tissue (85).

Minimally traumatic tooth extraction/ atraumatic extraction

Tooth extraction is a traumatic procedure, which can lead to morphological change of the alveolar process. Therefore, appropriate methods and instruments to remove tooth by gentleness are important in attenuating the soft and hard tissue losses that are caused by extraction.

After adequate local anesthesia, to limit the damage, the dentogingival and dentoalveolar connective tissue fibers can be separated by the use of a sharp surgical blade like a #15, #15-c surgical blade or periotomes around the tooth before extracted.

Because the periotomes can be inserted into the sulcus and works by severing the periodontal ligament fibers between the root of the tooth and the bony socket walls. After inserting periotome into the sulcus, progressively driven apically to a depth of 3–5mm, which can be achieved manually or by light tapping with a surgical mallet. Then slowly severed the periodontal ligament fibers all around the tooth, but should not be used on the buccal aspect for the purpose of preventing accidental trauma to the thin labial bony plate. To remove the tooth can be used the periotomes or small elevator.

In case of crown intact, the extraction forceps should be used in action with a gentle and slow rotational pulling force until completely torn the periodontal ligament fibers. To reduce the chance of damage to the thinner buccal plate, the buccolingual movement must be avoided. In the case of multirooted tooth should be sectioned to ensure that all of the alveolar bone walls are preserved. Furthermore, all extraction procedures should be accompanied by thumb support against the buccal aspect of the alveolar process to further preserve the thin labial plate and the integrity of the soft tissue walls (82, 85).

Socket preparation: debridement and decortication of the socket

After atraumatic extraction, all of granulation tissues and residual periodontal ligament fibers must be absolutely debrided from the inner wall of the extraction socket. Because the remaining granulation tissues can perform as a source of cells resulting in regrowth of soft tissue into the extraction area and jeopardize the formation of new bone in the socket. However, extensive debridement of the socket walls may be not required. So that the removal of residual granulation tissue can be accomplished by using hand instruments like curettes or using a round bur with light pressure.

A complete intact socket wall, which has four remaining bony walls, is the preferred site for alveolar ridge preservation. However, good results can be achieved in sockets which have residual bony defects. Besides, the apical part of the bony socket wall can be decorticated by using a 1⁄2 round bur under copious irrigation to increase the participation of bone-forming cells in the socket but except in the labial bone wall.

The bone graft material should be hydrated with sterile normal saline solution or the patient's blood and placed in a sterile stainless-steel dish of appropriate dimensions 3–5 minutes before filling in the socket. The graft material should be a "wet sand" consistency when placed into the socket and condensed by using a graft plugger or similar instrument with the light pressure. Significantly, over condensation of the graft material can inhibit the ingrowth of vascular supply into the graft.

The original alveolar ridge contours are important to preserve for esthetic reasons especially in the anterior maxilla region. Therefore, the graft materials can be used to maintain or slightly augment the original ridge contours by overlaid on the buccal and the coronal portion of the alveolar process. Importantly, the graft material should be covered with the membrane. Some membranes may need to be hydrated prior to use which making them more flexible to adapt to extracted socket. The membrane should be completely covering the graft materials and tuck into the buccal and lingual soft tissues (82, 85, 86).

Coverage of the socket by soft tissue

Soft tissue coverage is recommended to maintain, stabilize and protect grafting materials. To cover the socket, various techniques have been suggested such as coronal advancement of a buccal flap technique, or using free gingival or subepithelial connective tissue grafts (87-89). However, coronally advanced flaps need to be undermined and advanced a relatively great distance to completely cover an extraction socket. This technique may lead to complications such as altering the mucogingival line and creating a shallow vestibule, which may require following surgery to correct these complications (10). These problems can be avoided by using a subepithelial connective tissue graft which is taken from a window or the envelope procedure from the palate. However, subepithelial connective tissue graft is required for an adequate volume of donor site. Therefore, the membrane material can be used for coverage around the extraction socket to prevent necrosis of the graft in the initial phase of healing. Additionally, one of the major keys to success is the primary tension-free closure of the socket wound. The smallest diameter suture, which can provide adequate tensile strength such as 4-0 or 5-0 suture, should be used (85).

2.6 Materials used for socket preservation

A numerous material can be used in alveolar ridge preservation procedure. For optimal results, all of the graft materials required a sufficient blood supply, a type of mechanical support, and osteogenic cells supplied by the host, graft materials, or both (90). So that ideal property of all materials should have osteogenic, osteoinductive, or osteoconductive properties.

According to the GBR principle, there are many factors that contribute to a successful GBR outcome. For instance, the use of a barrier membrane is a major component to facilitate augmentation of alveolar ridge defects, induce new bone formation and increase the success rate of implant osseointegration (91, 92). Owing to the occlusive property of membrane and peripheral sealing between the membrane and host bone can result in stability of bone graft material, adequate vascular supply and access to bone-forming cells (71, 93-97). Furthermore, in the last few years, several membrane materials and designs have been investigated not only to enhance new bone formation, but also stabilize the bone graft below the membrane and minimize the risk of collapse and/or soft tissue ingrowth (51, 98-102).

2.7 Type of barrier membrane

Numerous barrier membranes for GBR have been developed to apply various clinical situations. According to degradability property, membrane material can be divided into 2 major groups, as resorbable or non-resorbable membranes. The physico-chemical properties of membranes ultimately influence their function. Therefore, a wide selection of specific materials were investigated with each material bearing inherent advantages and disadvantages for bone regeneration applications (103).

2.7.1 Resorbable membranes

Based on the original sources, resorbable membranes can be divided into 2 groups, natural or synthetic biomaterials. For instance, a collagen membrane and synthetic aliphatic polyesters are best known and widely used for their medical applicability. Collagen is derived from sources and membrane fabrication. Another

group of resorbable membrane, polyglycolide or polylactide can be tailored, modified their specific properties with different physical, mechanical, and chemical properties also able to be made in large quantities.

The advantage of resorbable materials offer the property of being resorbed by the body. So that, no need for second-stage surgery to remove the membrane material. Therefore, resorbable membranes are attractive to both clinicians and patients because of reducing the risk of patient morbidity, the risk of tissue damage, and a cost-benefit point of view (104, 105).

The disadvantages of resorbable materials are their unpredictable degree and rate of resorption, which can significantly influence the amount of new bone formation (106). If the resorption rates of membranes are too fast, it results in lack of rigidity of the grafted site and may be required additional support (107, 108). The membrane will rapidly degree of resorption especially when the membranes are exposed and/or associated with inflammatory reactions in the adjacent tissue due to the enzymatic activity of macrophages and neutrophils. After the membrane is exposed, its effect the structural integrity of the membrane and causes decreased barrier function and less new bone regeneration or bone fill. Especially when grafting in conjunction with implant placement because it can affect the stability of the implant (109).

Additionally, bone regeneration may fail due to bone defect areas that were not supported by the physical barrier membrane. Even though the membranes are initially able to maintain the space, they generally lose their strength and collapse into the space and lead to a failed reconstruction (110); for instance, resorbable membranes may have a tendency to collapse when used to treat periodontal defects (111).

Resorbable membranes based on natural polymer

Membrane based on collagen

Collagen membranes have more interesting in GTR and GBR research due to several superior properties such as biodegradation without foreign-body reaction, weak immunogenicity, good tissue integration, chemotactic action for fibroblasts, hemostatic property, fast vascularization, osteoblastic cell adhesion and their proven biocompatibility and facility of promoting wound healing process (112-117).

Mostly, collagen membranes are made from collagen types I and III which varies in collagen types, physical or chemical structures. These membranes are resorbed by collagenases/proteases via enzymatic degradation, and macrophage-derived enzymes (118), and bacterial proteases (119, 120) such as Bio-Gide®, Ossix®, Biomend® and BiomendExtend®. Even though collagen membranes have outstanding cell affinity and bio-compatibility (121), and similar bone regeneration capacity when compared to non-resorbable membranes (122). However, disadvantages of this membrane are space-maintaining ability (118, 123) , risk of a disease transmission from animal to human (124), inferior mechanical strength, and too rapid biodegradation (125). Furthermore, poor mechanical properties, rapid degradation or shortened functional period, greater susceptibility to infection, and the regeneration of new tissue are the limitation of membrane (126, 127). So that, various chemical, physical, and biological cross-linking methods have been introduced to cross-link collagen in order to reinforce the mechanical and biodegradable stability. Cross-linking process is used to improve tensile strength of collagen and prolong their degradation time (128). Nevertheless, the residual elements or secondary products during collagen degradation may have toxic effects and limit their applications in GTR/GBR (125).

Physical treatments such as heat treatment, gamma irradiation, ultraviolet irradiation and microwave irradiation, dehydrothermal treatment and biological methods (e.g., transglutaminase) may be used as an alternative method (129-133). Cross-linked collagen membrane can maintain block bone stability in comparison with the use of non-cross-linked collagen in the early healing period of lateral substitutes dimensionally stable in comparison with the use of non-cross-linked collagen in the early on lay graft (131). Though cross-linking of collagen provides it with more advantages. But there are still some problems with cross-linked collagen; for example, cross-linked membranes display prolonged membrane integrity with surrounding tissues and blood vessels compared with the non-cross-linked membrane (134). Additionally, study in rats and dogs demonstrated that chemically and enzymatically cross-linked collagen membranes showed delayed angiogenesis property and insufficient bone regeneration compared to the non-cross-linked collagen membrane (122, 131, 135).

Membrane based on chitosan

Barrier membranes based on chitosan have been attractive to be alternative membrane materials in GTR and GBR procedure. Owing to this membrane shows many advantages such as low cost, excellent biocompatibility, suitable degradation period, non-antigenicity, hemostatic activity, flexibility in hydrated environments, antimicrobial and wound healing capacity (136-139). For example, chitosan membranes cross-linked with genipin show less inflammatory response and result in faster healing times (140). Furthermore, another attractive characteristic is antibacterial property because chitosan is widely used as an antibacterial agent (141). So that

antibacterial property of chitosan could be used to improve regenerative procedures in periapical surgery.

Resorbable membranes based on synthetic polymer

Most of current resorbable synthetic polymer membranes are based on aliphatic polyesters such as poly (lactic acid) (PLA), poly (glycolic acid) (PGA), poly(ε-caprolactone) (PCL), poly (hydroxyl valeric acid), and poly (hydroxyl butyric acid), as well as their copolymers. Some studies found that when applying PLA and PGA membranes as opposed to e-PTFE membranes can reduce the bony defect. However, some inflammatory foreign-body reactions associated with degradation are a drawback of these membranes (142-144). Although, they are generally not as biologically active as natural polymers but these membranes show several excellent properties such as biocompatibility, controllable biodegradability, low rigidity, manageability, process ability, and drug-encapsulating ability (143, 145-148). Therefore, these membranes have been widely considered for orthopedic applications, especially in GBR and GTR procedures.

Polylactic acid (PLA) and polylactic acid/ polyglycolic acid copolymer (PLGA)

Polylactic acid (PLA) is one of the most common and important polymers membranes which has been used in both GTR and GBR procedures. This membrane has biocompatibility and suitable mechanical properties. In order to regulate the degradation rate and hydrophilicity of PLA, copolymers of lactide such as ε-caprolactone, glycolide, etc. have been incorporated. For example, a well-known

alternative for PLA in orthopedic applications is Polylactic acid/polyglycolic acid copolymer (PLGA) membrane. Both PLA and PLGA have been used wildly in GBR and GTR procedures with different resorption periods. For instance, Resolut Adapt® and Resolut Adapt® LT (W.L. Gore and ASSOC, Flagstaff, AZ, USA) membranes can remain substantially integrity for 8–10 weeks and 16–24 weeks, respectively. However, the study has shown that PLGA membrane cannot maintain the horizontal thickness of regenerated bone as well as Ti-e-PTFE membrane and the latter membrane revealed less soft tissue complications (149).

In addition, most of PLA and PLGA membranes are stiff which might impede their medical applications (150). Therefore, softeners such as N-methyl-2-pyrrolidone (NMP) are used to solve this problem. Even though PLA- and PLGA-based membranes are non-cytotoxic and biodegradable however, some studies have reported about the releases of oligomers and acid byproducts during degradation. These may trigger inflammation reactions and foreign body response (150, 151). Moreover, many studies have been carried out to change its properties by blending with hydroxyapatite (150-152).

Polycaprolactone (PCL)

Polycaprolactone (PCL) is an attractive biomedical polymer which has been extensively studied in bone tissue engineering due to its properties such as biocompatibility, low cost and high mechanical strength (153-155). However, only few studies in PCL-based GTR membranes were reported (156, 157). PCL membrane does not create a local acidic environment during the degradation procedure when compared with PLA and PLGA. Additionally, in vivo studies have been reported that complete

bioresorption time of PCL membranes is approximately 2–3 years, which is too long for GTR and GBR procedure (158). Moreover, hydrophobicity of PCL membranes reduces cell adhesion and proliferation. For this reason, PCL is always blended or copolymerized with other polymers before being used in biomedical applications.

Polyethylene glycol (PEG)

Polyethylene glycol (PEG) has several good properties such as biodegradable, cell-occlusive, and biocompatible polymers. So that PEG membrane has also been a candidate for GBR and GTR membranes (159-161). In a randomized controlled clinical trial study, this membrane was as successful as collagen membrane in the treatment of peri-implant bony dehiscence with simplified clinical handling (161). Furthermore, In the recent studies have been found that PEG membranes have potential to be used in lateral alveolar ridge augmentation and preservation of the alveolar ridge contours (117, 162-164).

Resorbable membranes containing functional materials

Polymer membranes loaded with antibacterial agents

Because bacterial infections are considered to be the major reason for the failure of membranes in GTR and GBR applications. Moreover, periodontitis is mainly related to bacteria activities. So that antibacterial properties of the membrane, which represents the broadest group of anti-infective biomaterials, are interesting to be war against implant-related infections. These membranes have been designed for local drug release to overcome the unfavorable outcomes of conventional systemic drug administration. For example, to improve the periodontal and bone regeneration, metronidazole is

loaded into the polymeric membrane. In general, antibiotic drugs are directly blended with membranes, causing a high burst release and short release period that could not effectively inhibit bacterial infections. Therefore, sustained and controlled release of antibacterial agents from membrane material are the key to develop novel membranes to use in GTR/GBR procedure especially when used in specific situation such as patients with diabetes mellitus, smoker (165).

Polymer membranes loaded with growth factors

Critical signaling molecules which instruct cells behavior through binding to specific transmembrane receptors on the target cells in the tissue regeneration process are growth factors (166). These membrane types act as a localized controlled release system. After that growth factors encourage the differentiation of osteogenic progenitor cell types in the separated space under the membrane (167). In the past, controlled drug delivery and releasing systems with several osteogenic factors are widely used clinically to promote bone regeneration procedure, especially bone morphogenetic proteins (BMPs) (168). BMPs have a potential to augment alveolar bone by initiating proliferation of mesenchymal stem cells, differentiation of osteoblasts and chondroblasts and angiogenesis into the regenerative area. However, the safety in use of recombinant human bone morphogenetic protein-2 (rhBMP-2) is still to concern in terms of appropriate methods and optimal doses (169). The study in implantation of rhBMP-2 loaded membranes has shown more new bone formation in the defect sites (170).

Resorbable membranes based on other polymers

Compress of platelet-rich fibrin (PRF) as a membrane-like form has also been used as an alternative for commercially available barrier membranes in GTR treatment (171). PRF membrane acts as a potent source of growth factors to facilitate the tissue regeneration

The main disadvantage of PRF membrane to use in applications like GBR and GTR is insufficient periods of time for tissue regeneration due to degradability of membrane within two weeks or less (172). Therefore, cross-linking treatments may be used to provide resistance against enzyme-dependent degradation of membranes. Kawase et al, 2015 (172) reported the heat treatment technique to prepare PRF membrane, which reduces the rate of biodegradation without sacrificing its biocompatibility.

2.7.2 Non-resorbable membranes

Non-resorbable membranes such as polytetrafluoroethylene (PTFE) and titanium mesh have a biocompatible property and have a unique characteristic (173). These membranes provide an effective barrier function and space maintainer property beneath resorbable membrane because of their structure can be varied in porosity for a more adaptable and tissue-compatible alternative, and multiple designs are commercially available and can be further developed on demand (103). Therefore, based on their performance resulting in a more predictable sufficient period of healing time, reduced risk of long-term complications and simple clinical management (174). The major disadvantage of this membrane is the necessity for a second- stage surgical removal procedure. Nevertheless, this disadvantage may be minimized by the

advantages offered. Non-resorbable membranes can provide an effective barrier function in terms of biocompatibility, give a space maintainer property beneath the membrane for a sufficient period, reduced risk of long-term complications and predictable outcome from their performance. These also offer a unique characteristic. Now, non-resorbable membranes are the expanded and dense forms of PTFE (e- and d-PTFE), Polyethylene membrane and titanium mesh.

Expanded polytetrafluoroethylene membrane: e-PTFE membrane

According to its structure, the e-PTFE membrane, such as Gore-Tex1 membrane (W.L. Gore & Associates, Flagstaff, AZ, USA), has been widely used in clinical treatments and become a first-choice membrane material for tissue/bone regeneration. Owing to its effectiveness in tissue-guided repair, this lead e-PTFE to be used extensively in digestive, cerebral and cardio-vascular surgeries (175). In a recent controlled study demonstrated that a combination of an e-PTFE membrane and autogenous bone graft at edentulous sites may limit graft resorption, while enhancing bone repair (176).

e-PTFE membrane is composed of two different microstructures, the coronal border and the occlusive portion. With the internodal distance of 25 mm in the coronal border has an open microstructure collar to accelerate early clot formation and collagen fiber attachment to stabilize the membrane until it becomes fixed (103, 175). Whereas, the internodal distance of less than 8 mm in the occlusive portion has to allow nutrient inflow while preventing the infiltration of other tissue cell types (103). Numerous small pores in e-PTFE membrane encourage tissue cell attachment that stabilizes the host-tissue interface because these smaller pores also act to restrict the migration of epithelial

cells (177). Furthermore, in the case of inflammation or infection, the exposed membrane must be removed immediately (178). At present, e-PTFE membrane has been discontinued and is not available commercially.

High density polytetrafluoroethylene membrane: d-PTFE membrane

High density PTFE (d-PTFE) membrane (e.g. Cytoplast™ Regentex GBR-200 or TXT-200; Osteogenics Biomedical Inc., Lubbock, Texas, USA) is one alternative to non-resorbable membranes. This membrane was originally developed in 1993 and successfully in bone and tissue regeneration procedure (68, 179). Because of high density and small submicron (0.2 mm) pore size resulting in limited bacterial infiltration into the bone. So that membrane can protect the underlying graft material and/or implant. Furthermore, d-PTFE can completely block the penetration of food and bacteria. For this reason, this membrane can leave exposed in the oral cavity without need of primary soft tissue closure (68, 179). Due to d-PTFE does not have a porous structure so that tissue attachment to membrane is weak. Accordingly, d-PTFE membrane can be removed easily by pulling on the membrane without lifting the mucosal flap and has a low risk of infection though its exposed when compared with e-PTFE membrane (175).

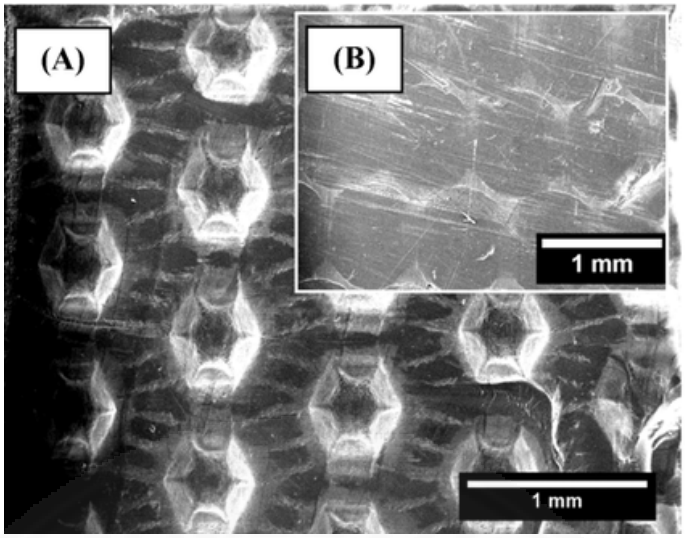

Figure (2.6) SEM images of Cytoplast ® TXT-200, a high-density PTFE membrane. (A) SEM image of the surface designed to interact with the epithelial tissue and (B) SEM image of the surface that will be facing the bone defect (180).

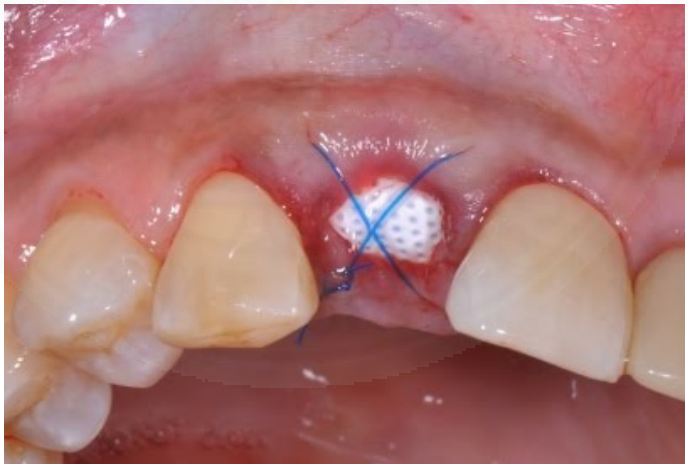

Figure (2.7) d-PTFE membrane (Cytoplast TXT-200) in alveolar ridge preservation procedure.

Polyethylene membrane (PE)

Polyethylene membrane is one of the most commonly used polymers in medicine, and made into many medical implant products (such as orthopedic total hip, knee, shoulder joints and cosmetic implants) with well-documented biocompatibility and safety. A great number of basic and clinical studies have shown that bone- forming cells (i.e., osteoblasts, osteocytes and their precursors) and bone tissue could indeed grow into the pores of original porous polyethylene implants without the presence of inflammation and infection. In order to eliminate or decrease the disadvantages of present nonresorbable and resorbable barrier membranes, a novel bi-layered nonresorbable porous polyethylene (PPE) sheet with differential pore sizes and porosities on both layers, that recently developed by National Metal and Materials Technology Center (MTEC) Bangkok, Thailand, is preliminarily designed as a potential non-retrieval permanent barrier membrane based on its superior biological, mechanical and clinical properties. The formula includes 70% v/v raw material of high-density polyethylene (HDPE) powder with a particle size of approximately 305 μm and 30% v/v adhesive binders (i.e., maltodextrin, polyvinyl alcohol) (29). This specific formula will contribute to a relatively smooth and dense outer layer, and a relatively coarse and porous inner layer. It is hypothesized that, used as a potential non- retrieval permanent barrier membrane, this novel bi-layered porous polyethylene membrane could provide ideal or sufficient biocompatibility, space maintenance, cell-occlusiveness, tissue integrity and intraoperative. Following the superior characteristic, it potential useful for medical and dental application, like bio-inertia and biocompatibility for long-term in-vivo biosafety and stability; interconnecting porous microarchitecture for tissue attachment, bone cell migration, ingrowth, penetration,

integration, nutrient and fluid exchanges; sufficient durability for permanent in-vivo implantation and potentially no need for secondary surgical removal; minimal thickness to balance adequate mechanical strength and least in-vivo residual volume; good thermoplasty for excellent clinical maneuverability; esthetic ivory shade for cosmetic applications, etc. Moreover, there are porous polyethylene implants in more than 20 procedures that have been performed in cranio- and maxillofacial reconstruction and more than 70 procedures in orbital implant reconstruction (24, 26, 28). But this application has not been reported for Alveolar ridge preservation in humans.

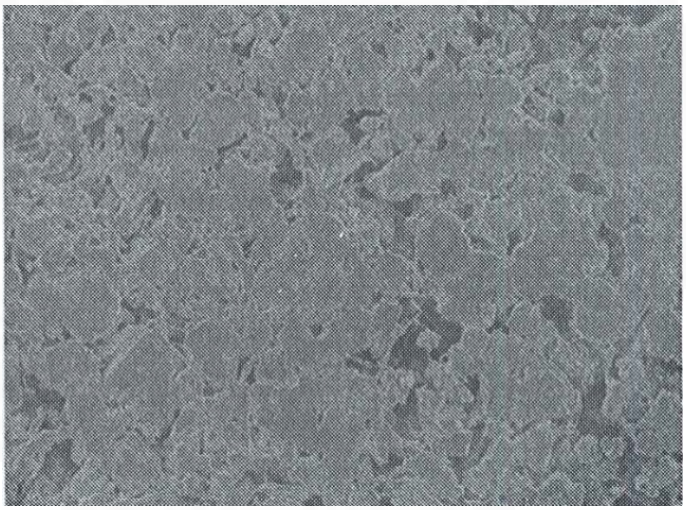

Figure (2.8) Morphology of bilayer porous polyethylene implant (low porosity side) (31).

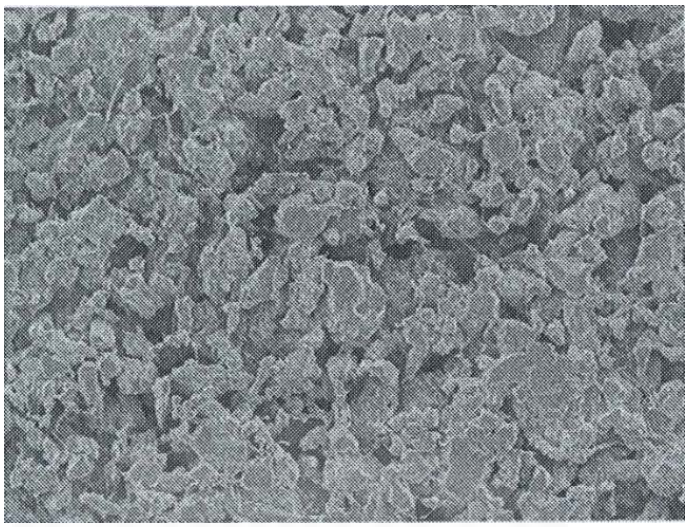

Figure (2.9) Morphology of bilayer porous polyethylene implant (high porosity side) (31).

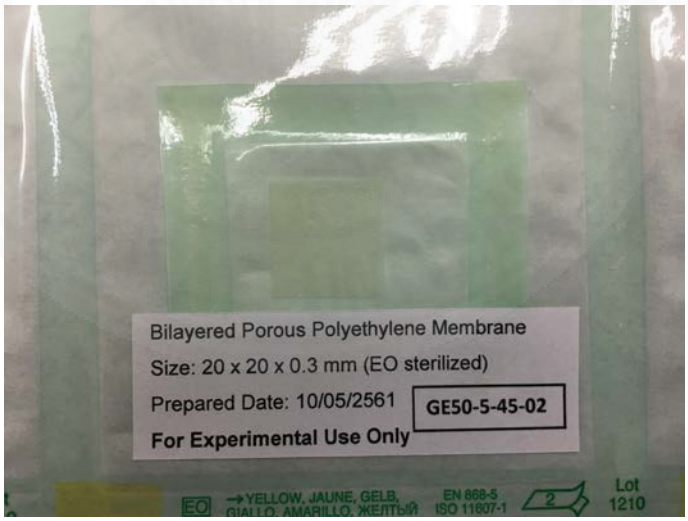

Figure (2.10) Porous polyethylene membrane from MTEC.

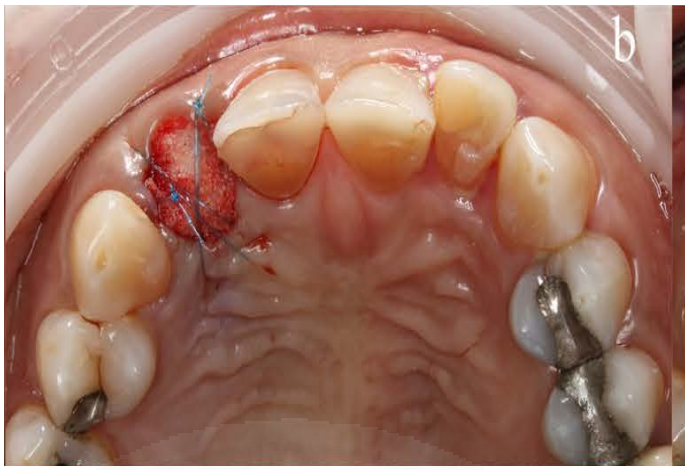

Figure (2.11) Porous polyethylene membrane in alveolar ridge preservation procedure.

CHAPTER 3

RESEARCH METHODOLOGY

3.1 Study design

The study was a single-blinded randomized controlled trial primarily designed to evaluate clinical and histological outcomes of soft and hard tissue dimensional changes after alveolar ridge preservation with porous polyethylene membrane (PPE) or high-density polytetrafluoroethylene membrane (d-PTFE, Cytoplast™ TXT200, Osteogenics, USA) non-resorbable membrane.

3.2 Study population

Thirty patients who needed tooth extraction and were replaced with a dental implant at the Faculty of Dentistry, Thammasat University Hospital during the period March 2018 to January 2020 were enrolled. All patients were informed about the details and purpose of the study, underwent an examination of the potentially eligible teeth, and provided written informed consent prior to study participation (Appendix I). All patients received proper periodontal treatment prior to beginning the study procedures when necessary.

Inclusion criteria:

1. Adult patients (Age > 18 years)
2. Good general health (ASA 1, 2) and no contraindications for tooth extraction
3. The diagnosis and indications for tooth extraction were: endodontic failures or traumatic complications (e.g. root fracture), unrestorable teeth from severe caries or complicated crown/root fracture, hopeless prognosis from periodontal and prosthodontic reasons.
4. Patients with controlled periodontal status.
5. Smoking history <10 cigarettes per day. For subjects, who smoked less than 10 cigarettes per day, were requested to stop smoking two weeks before and after tooth extraction and implant placement.
6. No history of allergy or hypersensitivity to any of the products to be used in the study such as polyethylene.
7. Only tooth with an intact buccal bone plate (>50%) and no signs of acute inflammation or infection/abscess. The condition of the buccal bone plate was evaluated intra-surgically immediately after tooth extraction. All extraction sites were presented with a minimum width of 2 mm of keratinized gingival tissue.
8. Signed informed consent.

Exclusion criteria:

1. Age <18 years.
2. Presence of relevant medical conditions: Patients with bone disease, diabetes mellitus, unstable or life-threatening conditions, or requiring antibiotic prophylaxis. Patients with medication of drugs influencing the bone metabolism or use of bisphosphonates.
3. Smoking status of more than 10 cigarettes/day.
4. Pregnancy or lactation.
5. Patients who cannot take impressions (both conventional and digital) and CBCT.
6. Patients who had socket destruction more than 50% after extraction.
7. History of malignancy, radiotherapy, or chemotherapy for malignancy in the past 5 years.
8. History of autoimmune disease or long-term prescribed steroid drugs.
9. Lack of opposite dentition, which occluded in the area intended to extract and replace with dental implant, and absence of adjacent teeth.
10. Unwillingness to return for the follow-up examination

3.3 Materials

3.3.1 Data collections

Patient examination record form of the Implantology clinic, Faculty of Dentistry, Thammasat University (Appendix II), including:

- General information: patient's demographic information (e.g., name, age, gender, race, occupation, address, telephone number).
- Medical record: past and present medical history and treatment, medication outcomes.
- Dental record: chief complaint, dental history, clinical and radiographic examinations, procedures and outcomes.
- Clinical examinations including:
    - Baseline clinical records: plaque index, gingival index, hard and soft tissues dimensions, etc.
    - Peri-operative clinical measurements: hard and soft tissue dimensions
    - Postoperative clinical measurements: postoperative hard and soft tissue dimensions, wound healing, etc.
    - Follow up clinical record: postoperative wound healing, complications, etc.
- Radiological examination record, including:

- Pre- operative Periapical film record
- Baseline CBCT record immediately after tooth extraction
- Final CBCT record 4 months after surgery for evaluate dimensional change of alveolar bone before and after bone alveolar ridge preservation.

- Conventional and digital impression using intraoral scanner (CEREC AC Omnicam 1.0, Dentsply Sirona, Germany) to evaluate degree of wound healing and dimensional change of soft tissue before and after bone alveolar ridge preservation.
- Histology and Histomorphometry analysis at the time of implant placement to evaluate percentage of new bone formation, residual graft particles and connective tissue.

3.3.2 Control and testing materials:

1. Porous polyethylene membrane (PPE) (MTEC, Thailand)
2. High density PTFE (d-PTFE) membrane (ex. Cytoplast™ TXT200, Osteogenics, USA)

3.3.3 Other material:

1. Instrumentations

    a. UNC-15 probe (Hu Friedy®, USA)

    b. Surgical armamentarium including periotomes for atraumatic extraction and implant placement

    c. Periapical x-ray and plate scanner size 0-2 (Apixia® Digital Sensors imaging system, San Jose Ave, U.S.A.)

2. CBCT x-ray and imaging system (DentiiScan 1.1, NSTDA, Pathumthani, Thailand)

3. Intraoral scan imaging system (CEREC AC Omnicam 1.0, Dentsply Sirona, Germany)

4. Implant system (CMI Implant system, IS-III active®, Neobiotech Co., Ltd., Korea).

5. Bone graft materials (NanoBone®, granule size 0.6 mm, Artoss, Germany).

6. Analysis software:

    a. three-dimensional file processing software (MeshLab v2016.12, ISTI—CNR, Rome Italy).

    b. Image J software (Image J 1.52a, U. S. National Institutes of Health, Bethesda, Maryland, USA).

c. 3D slicer software (3D Slicer version 4.10.1, http://www.slicer.org).

d. Open-source precise industrial 3D metrology software (GOM Inspect 2019, GOM GmbH, Braunschweig, Germany).

7. Chemical and other material for histology in the laboratory.

a. Microtome (Leica RM2235, Leica Biosystems Nussloch GmbH., Germany).

b. Light microscope equipped with a camera (Nikon DS-U3, USA).

3.4 Variables and measurements

3.4.1 Independent variables:

1. Porous polyethylene membrane (PPE) (MTEC, Thailand)

2. High density PTFE (d-PTFE) membrane (Cytoplast™ TXT200, Osteogenics, USA)

3.4.2 Dependent variables:

1. Clinical variable: degree of wound closure (A_1-A_n), complication.

2. Dimensional change of soft tissue:

a. Horizontal dimensional change of alveolar ridge

b. Vertical dimensional change of alveolar ridge

3. Dimensional change of hard tissue:

    a. Horizontal dimensional change of alveolar bone

4. Implant stability values (IST) at implant placement (IST1) and before insert the prosthesis (IST2) in each group

5. Histomorphometric analysis: percentage of new bone formation, connective tissue and residual graft particles.

3.5 Methods

3.5.1 Ethical approval

This study protocol was approved by the research ethical committee of Thammasat University, the Ethical Review Sub-Committee Board for Human Research Involving Sciences, Thammasat University, No. 3. (the ethical approval number 183/2560) (Appendix III). Flowchart of the study design and timeline are shown in Figure 3.1.

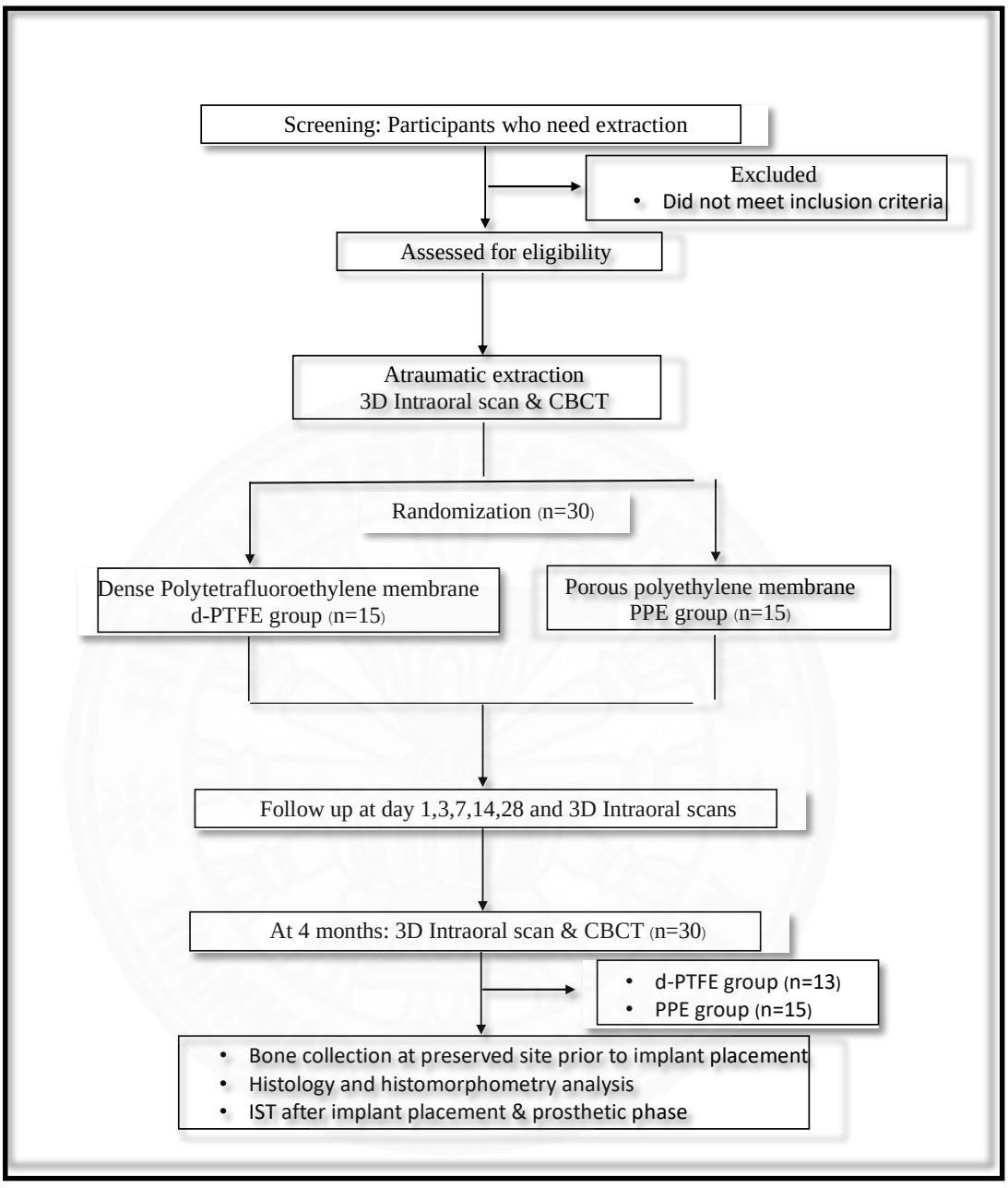

Figure (3.1) Study design and timeline; PPE = porous polyethylene membrane, d-PTFE = high-density polytetrafluoroethylene membrane, CBCT = cone beam computed tomography, IST = implant stability test.

3.5.2 Sample size calculation

The ideal sample size to assure adequate power for this RCT was calculated considering differences of at least 0.5 mm in buccal bone height between groups and assuming a standard deviation of 0.4 mm previously reported (76). Based on these calculations, it was defined that 11 teeth per group were necessary to provide an 80% power with an α of 0.05. Considering an attrition of about 20%, it has been established that at least 13 teeth should be included in each treatment group.

Sample size calculation = 15 patients per group (test and control), total of 30 patients were included in this study.

3.5.3 Sample preparation

Bi-layers porous polyethylene membrane (PPE) was prepared as described previously (Song JC., 2019). A combination of grounded high-density polyethylene particles (Thaizex 7000F, Bangkok Polyethylene Co., Ltd, Bangkok, Thailand), maltodextrin powder (Shandong Duqing, Inc., Shandong, China) and polyvinyl alcohol powder (Sigma-Aldrich Inc., MA, USA), was thoroughly mixed at a ratio of 50:40:10 w/w. The mixture was then put in the mold cavity and compression molded at 145 ℃ for 45 minutes using a wet salt bed technique (30) to produce both low- and high-porosity surfaces in single membrane. One side contains much greater porosity and the pore sizes ranging from 140 to 830 mm while another contains less porosity and lower pore size to facilitate fibroblast proliferation and deter penetration. (Figure 3.2). They were then sonicated in distilled water, dried and sterilized by ethylene oxide gas prior to the clinical study. The control sample in this study was a commercial high-density

polytetrafluoroethylene membrane (d-PTFE, CytoplastTM TXT200, Osteogenics, USA) all were in the same batch.

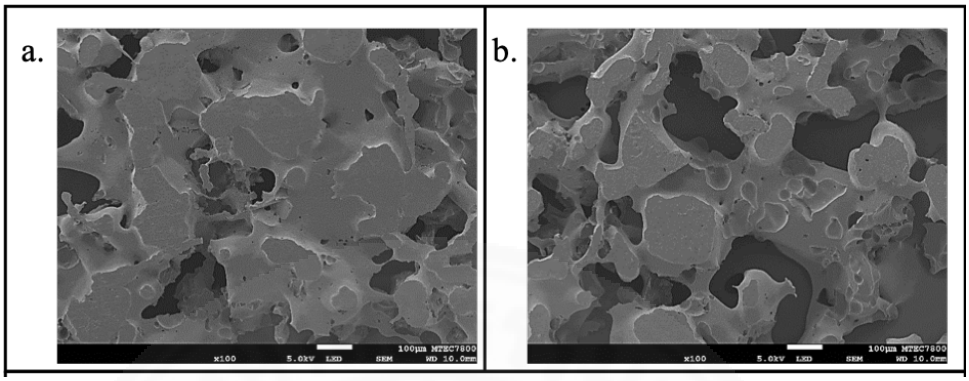

Figure (3.2) A scanning electron microscope (SEM) of bi-layered porous polyethylene membrane (PPE) shown low-porosity sides (a) and high-porosity sides (b) in single membrane.

3.5.4 Surgical procedure

(1) Presurgical procedures

a. Preliminary impressions (upper and lower arch) were taken with alginate to create the study models for treatment planning, diagnostic wax up and fabrication of surgical stent (acrylic jig).

b. Alveolar ridge contours were recorded by an intraoral scan imaging system (CEREC AC Omnicam 1.0, Dentsply Sirona, Germany).

c. Intraoral photographs were taken to indicate any other pathology and being an initial data.

d. Radiographic examination was performed with intra-oral x-ray film #2 (Periapical imaging system) and extension cone paralleling to evaluate the root form of the extracted tooth and the alveolar bone before extraction.

e. Diagnostic wax up and treatment planning.

The full contour wax-up of a designed prosthetic crown was created on a stone cast to determine the location of the final prosthesis. After duplicated waxed up cast, the surgical stent was fabricated by using clear acrylic resin.

(2) Surgical procedure

All the surgical procedures were performed by only one surgeon in all 30 patients under local anesthesia.

- Extraction procedure

- Blood pressure measurement and rinsing with chlorhexidine 0.12% for 1 min. Administration of the local anesthesia with 2% lidocaine with epinephrine 1:100,000 at the extraction site

- Atraumatic extractions were performed by using peritomes and elevators to avoid distortion or other damage of the buccal/lingual bone plate. Then, removed all of granulation tissue by bone curettes and carefully inspected the presence of fenestration or dehiscence of the socket wall. Irrigated the socket

with a saline solution. In case of a severely damaged bony wall or completely loss during the extraction procedure, the patient was excluded from the study.

- Before alveolar ridge preservation

- A baseline Cone-beam computed tomography (CBCT1) scan with surgical stent (acrylic jig) was performed immediately after tooth extraction.

- Intraoral scanning of socket wound area and alveolar ridge contour was performed with intraoral scan imaging system (CEREC AC Omnicam 1.0, Dentsply Sirona, Germany)

- Alveolar ridge preservation

- After socket preparation, the soft tissues around the extraction site were slightly pouched and then the extracted sockets were grafted with a synthetic bone graft material (NanoBone®, granule size 0.6 mm, Artoss, Germany). Bone grafting materials were rehydrated in saline before placing the graft into the socket up to the level of the buccal and lingual/palatal bone plate. Then the patients were divided into two groups including a control group (d-PTFE membrane) (ex. CytoplastTM Regentex TXT-200; Osteogenics Biomedical Inc., Lubbock, Texas, USA) and an experimental group (PPE membrane) (MTEC, Thailand) by randomly assigned to each patient.

- The randomization codes were generated by computer. Then, the sequentially numbers were printed and enclosed in opaque sealed envelopes. The randomization envelope was opened by another researcher who was not

involved in other aspects of this study. Then, the assigned treatment (test or control) was revealed to the surgeon. After that, the assigned membranes were placed over the bone graft and inserted underneath pouched tissue. Cross sutures were performed to secure the preservation area. Both membranes were left intentionally exposed to the oral cavity with a secondary wound healing. After 28 days, both membranes were removed and soft tissue was left to heal spontaneously until the wound closure was completed (Figure 3.3).

- Post-operative instruction and medication with amoxicillin 500 mg. given orally 2 capsules/2 times/day for 5 days, Ibuprofen 400 mg. given orally 1 tablet/3 times/day and chlorhexidine mouthwash rinse 2 times/day.

- After alveolar ridge preservation

- Subjects were monitored at day 1, 3, 7, 14, 28, 120 after alveolar ridge preservation for observing any complications and intraoral scanning of socket wound area and alveolar ridge contour using intraoral scan imaging system (CEREC AC Omnicam 1.0, Dentsply Sirona, Germany). At day 14 all sutures were removed. And at day 28 the membrane was removed. Then, all subjects were recalled at 4 months postoperative.

- After 4 months, before the re-entry, Cone-beam computed tomography (CBCT2) scan with surgical stent (acrylic jig) was performed and then recorded the aforementioned measurements scores of plaques index, bleeding index, gingival recession, and pocket depth.

- Implant placement procedure and histological process

- For implant placement procedure, the position of implant was marked by using a small round surgical bur through the surgical stent (acrylic jig), during the implant site preparation, a trephine bur with a 2-mm inner diameter and 6 mm length were used for harvesting the bone at the preserved site. The bone core, a 2x6 mm cylindrical bone core from the central part of the former socket, was immersed in a fixative (10% formaldehyde).

- The implant osteotomy was continued following the implant's company protocol (CMI Implant system, IS-III active®, Neobiotech Co., Ltd., Korea). Implant stability at insertion (IST1) and prior to prosthesis delivery (IST2) were recorded using a modified damping capacity analysis device (AnyCheck IMT-100, Neobiotech Co., Ltd., Korea).

- Post-operative instruction and medication with amoxicillin 500 mg. given orally 2 capsules/2 times/day for 5 days, Ibuprofen 400 mg. given orally 1 tablet/3 times/day and chlorhexidine mouthwash rinse 2 times/day. Subjects were evaluated at 2 weeks of suture removal.

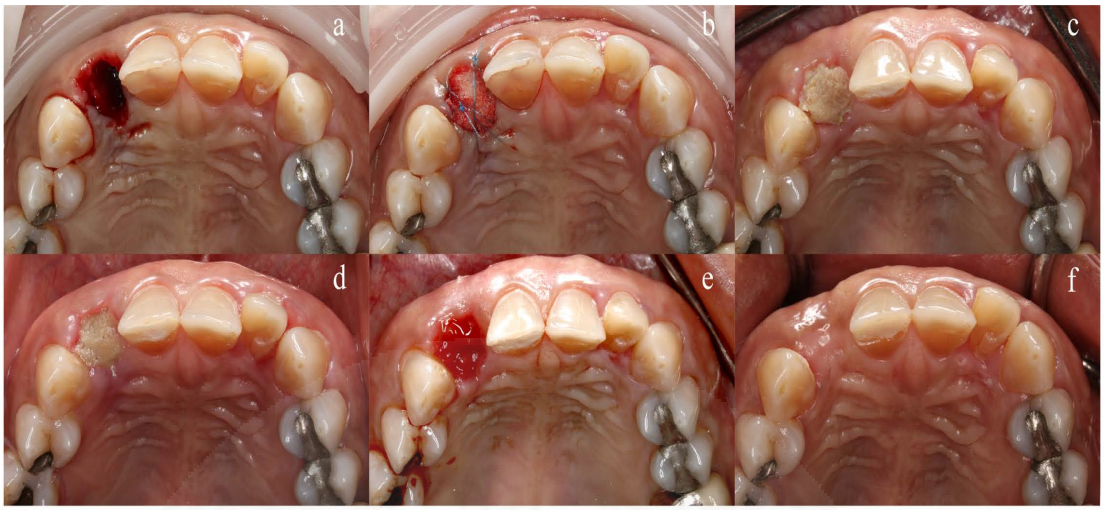

Figure (3.3) Surgical procedures of alveolar ridge preservation and follow up period performed in this study; (a) Atraumatic extraction without flap elevation; (b) Alveolar ridge preservation with bone graft covered with assigned membrane; (c-d) Follow up period after alveolar ridge preservation at day 14 and 28; (a) After membrane removal and (f) At 4 months.

(3) Scan procedures and CBCT measurements

- All measurements were done by one examiner.

- Intraoral scanner and CBCT x-rays (DentiiScan 1.1, NSTDA, Thailand) were performed in all patients. For the degree of wound closure, the 3D model files (STL files) were obtained at different time points (follow up period 1,3,7,14,28 days after extraction) and then imported into the three-dimensional file processing software (MeshLab v2016.12, ISTI—CNR, Rome Italy) to superimpose the STL files based on the adjacent teeth to create the same alignment of the all 3D model files (Figure 3.4), after that area of wound closure was calibrated and analyzed by the software (ImageJ 1.52a, U. S. National Institutes of Health, Bethesda, Maryland, USA).

- Dimensional changes of soft tissue were obtained from data of intraoral scanner. The 3D model files (STL files) were created and occlusal planes at the middle point of the socket were measured and compared as vertical dimensional changes. The perpendicular line at the middle part of the socket was created each 1mm. at differences 6 levels form CEJ, the horizontal dimensional changes were measured in buccal and oral (lingual/palatal) regions (Figure 3.5).

- For dimensional changes of hard tissue, the alveolar bone changes were measured by two consecutive CBCT x-rays DICOM (digital imaging and communication in medicine) files at the baseline and 4 months then processed by using 3D slicer software (3D Slicer version 4.10.1, http://www.slicer.org). After selecting the region of interest (ROI) that included only hard tissues before

converted into 3D models. The horizontal dimensional changes of alveolar bone were analyzed using GOM software as previously described (Figure 3.6).

- Blinded analysis was performed after data superimposed without patient information from the digitized images and all 3D model files.

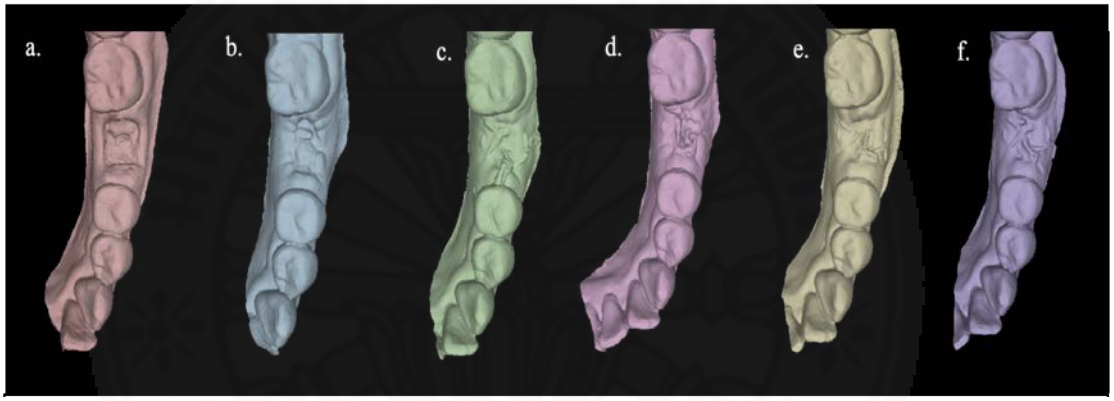

Figure (3.4) STL files from intraoral scanner after superimposition of 3D surface models before wound area measurement;(a) Immediately after tooth extraction and (b-f) follow up periods after alveolar ridge preservation at day 1, 3, 7, 14, 28 respectively.

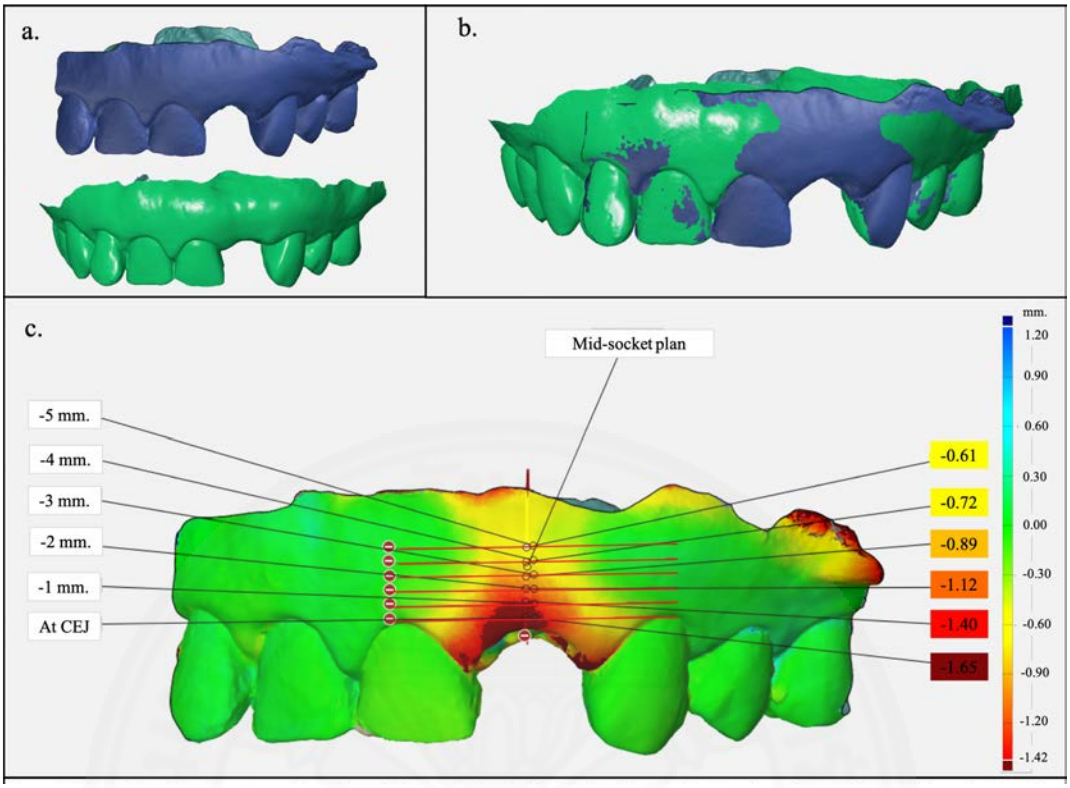

Figure (3.5) STL files from intraoral scanner performed immediately after tooth extraction (blue) and 4 months later (green) were imported into GOM Inspect software (a) and they were superimposed (b). Vertical plan (mid-socket plan) and horizontal plan at 6 different levels form CEJ were created in buccal and lingual regions and the dimensional changes of alveolar ridge were measured (c).

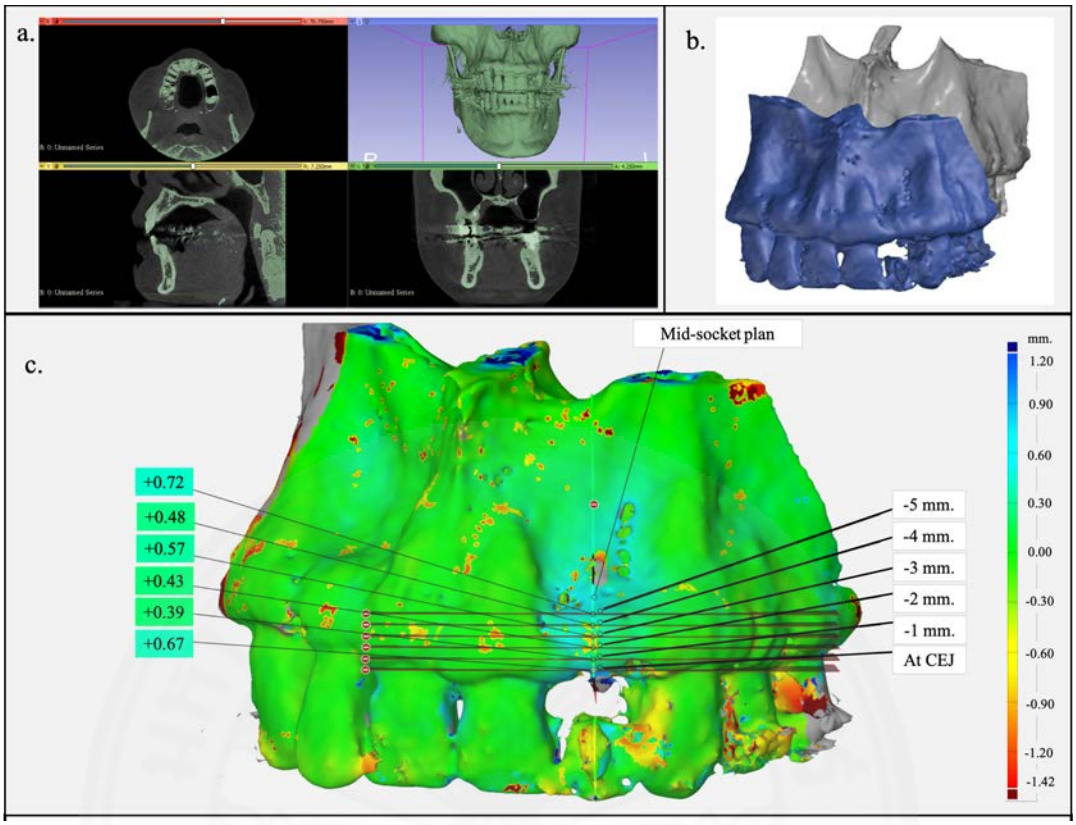

Figure (3.6) Hard tissue region of DICOM files from CBCT were extracted and reconstructed into to 3D STL image file (a). Alveolar bone at immediately after tooth extraction (blue) and 4 months later (gray) were imported into GOM Inspect software (b). After two 3D models were superimposed, vertical plan (mid-socket plan) and horizontal plan at 6 different levels form CEJ were created in buccal and lingual regions and the dimensional changes of alveolar bone were measured (c).

(4) Histological processing

The harvested bone cores were fixed in 10% buffered formalin solution for further histologic processing. The specimens were decalcified by immersing in 10% formic acid for 48 h, dehydrated in serial ethanol and embedded in paraffin blocks. After tissue processing, multiple 3-5 μm slices in apicocoronally axis from the middle part of each sample were cut by a microtome (Leica RM2235, Leica Biosystems Nussloch GmbH., Germany) and stained with hematoxylin and eosin (H&E). At least 8 fields of view per sample were examined and photographed by using a light microscope equipped with a camera (Nikon DS-U3, USA). Sections were examined for cellular activity and any evidence of tissue reaction. Histomorphometry was performed by drawing nine 1 cm square boxes which were equally spaced in the middle of tissue area in each slice and the area of connective tissue, new bone formation and residual grafts within the drawn boxes were then quantified, the percentage of each interested area per total area were then calculated. The histological tissue processing was kindly supported by Mr. Manoch Yawatta; from the Pathology of Thammasat University Hospital. Slides were numerically coded and manually read in a blind fashion by two independent examiners.

3.6 Statistical analysis

A data analysis was performed with descriptive statistics including the mean, standard deviation. All variables were examined with Shapiro-Wilks test to validate the normal distribution of the data. The significance of difference in mean values of measurement between two groups was determined using an independent t-test. Wilcoxon signed rank test was also performed to compare the difference of IST values between treatment periods. A p-value <0.05 was considered statistically significant. All analyses were performed using GraphPad Prism software version 8 (GraphPad software, La Jolla California, USA).

CHAPTER 4

RESULTS AND DISCUSSION

All preserved sites healing was uneventful, without inflammation or infection. Two patients from the d-PTFE group were unable to continue with implant treatment due to personal finance problems. However, all parameters were measured except histomorphometry analysis and implant stability.

4.1 The clinical efficacy of porous polyethylene membrane

4.1.1 Demographic characteristics

Thirty-five volunteers were screened and examined at the clinic. Of these, A total of thirty eligible subjects were consecutively included in this study, consisting of 7 males and 23 females with a mean age of 56.07± 11 and 60.73±7.98 years old in PPE and d-PTFE group, respectively. Their physical conditions were all classified as ASA I and well tolerant of intraoral surgeries. There were 14 extraction sockets in maxilla and 16 in mandible. General demographic data such as age, gender and location and number of the roots were not significantly different in both groups as shown in Table 4.1.

Table 4.1: Demographic data of the control and experimental groups.

Characteristic		d-PTFE (Control group, n=15)	PPE (Experimental group, n= 15)
Age, mean ±SD, (years)		60.73±7.98	56.07± 11
Gender N (%)	Male	3 (20%)	4 (26.67%)
	Female	12 (80%)	11 (73.33%)
Location (%)	Maxillary	5 (33.33%)	9 (60%)
	Mandibular	10 (66.67%)	6 (40%)
No. of root (%)	Single root	6 (40%)	7 (46.67%)
	Multiple root	9 (60%)	8 (53.33%)

4.1.2 Degree of wound closure

For early wound healing, the wound areas were measured at each period after preservation. The degree of wound closure which was the difference between the wound area at 1 day after preservation and the value at each time point afterward (A1-An) was then calculated to determine the progress of wound closure with time and was compared between two groups. The greater the values signified the faster degree of the wound closure. At the same time after preservation, PPE group generally showed greater degree of wound closure than that of d-PTFE group. However, the degree of wound closure between two groups was found to be not statistically different, except at day 14 (p=0.03). Wound area and degree of wound closure in both groups as shown in Table 4.2.

Table 4.2: A comparison of wound area (mm^2) and degree of wound closure (A_1-A_n) at each follow up period after alveolar ridge preservation (Mean ± SD).

Day(s) after extraction or study time	d-PTFE (Control group, n=15)		PPE (Experimental group, n=15)		P-value
	Wound area, A (mm^2)	Degree of wound closure (mm^2)	Wound area, A (mm^2)	Degree of wound closure (mm^2)	
Day 1	29.56±12.28	NA	45.96±8.88	NA	NA
Days 3	30.55±11.46	-4.80±12.19	49.59±10.9	-8.03±12.66	0.48
Days 7	27.53±12.64	6.07±22.48	40.23±9.98	10.94±21.72	0.55
Days 14	30.07±15.86	-1.06±33.89	33.66±14.12	25.38±31.33	0.03*
Days 28	1.91±3.79	95.40±7.45	0.97±1.80	97.97±3.73	0.42

*P-values (statistically significant at the level of $P < 0.05$) with independent-samples t-tests for differences in means between groups of the degree of wound closure (A_1-A_n)

4.1.3 Dimensional change of soft tissue

The comparison of dimensional changes of the alveolar ridge at 4 months after preservation, in the PPE group, the mean vertical and horizontal dimensional changes were: 1.30±0.78 and 1.20±0.63mm. The distribution of mean horizontal dimensional changes subdivided into buccal and oral changes, buccal sites at level 0-5 mm from CEJ were 1.43±0.72, 1.43±0.64, 1.44±0.49, 1.40±0.56, 1.38±0.65 and 1.33±0.74 mm. Lingual sites at level 0-5 mm from CEJ were 1.25±0.64, 1.13±0.64, 0.97±0.65, 0.93±0.50, 0.85±0.41 and 0.79±0.38 mm.

While, in the d-PTFE group, the mean vertical and horizontal dimensional changes were: 1.21±0.77 and 1.12±0.77mm. The distribution of mean horizontal dimensional changes subdivided into buccal and oral changes, buccal sites at level 0-5 mm from CEJ were 1.37±0.85, 1.30±0.78, 1.13±0.80, 1.11±0.81, 1.04±0.85 and 0.94±0.85 mm. Lingual sites at level 0-5 mm from CEJ were 1.48±0.84, 1.38±0.82, 1.20±0.78, 0.88±0.60, 0.80±0.55 and 0.75±0.51mm.

The total dimensional changes in vertical direction of both groups were greater than that of the horizontal direction. In contrast, when compared at the CEJ level, the resorption in horizontal direction was contrary greater than that of vertical direction. Additionally, the changes at the coronal part and the buccal side of alveolar ridge were greater than those of the apical part and lingual side. However, the mean vertical and horizontal dimensional changes in all locations of alveolar ridge contour were not significantly different between two groups ($P > 0.05$) as shown in Table 4.3.

Table 4.3: Dimensional changes of alveolar ridge in vertical and horizontal directions at 4 months after preservation in each group (Mean ± SD).

Location		Dimensional changes of alveolar ridge (mm.)				P-value
		d-PTFE (Control group, n=15)		PPE (Experimental group, n=15)		
		Buccal	Lingual	Buccal	Lingual	
Horizontal	At CEJ	-1.37±0.85	-1.48±0.84	-1.43±0.72	-1.25±0.64	0.66
	1 mm	-1.30±0.78	-1.38±0.82	-1.43±0.64	-1.13±0.64	0.76
	2 mm	-1.13±0.80	-1.20±0.78	-1.44±0.49	-0.97±0.65	0.83
	3 mm	-1.11±0.81	-0.88±0.60	-1.40±0.56	-0.93±0.50	0.32
	4 mm	-1.04±0.85	-0.80±0.55	-1.38±0.65	-0.85±0.41	0.21
	5 mm	-0.94±0.85	-0.75±0.51	-1.33±0.74	-0.79±0.38	0.15
	Total Horizontal	-1.12±0.77 mm.		-1.20±0.63 mm.		0.09
Total Vertical		-1.21±0.77 mm.		-1.30±0.78 mm.		0.74

4.1.4 Dimensional changes of hard tissue

The comparison of dimensional changes of the alveolar bone at 4 months after preservation, in the PPE group, the mean horizontal dimensional changes were: -0.11±0.59 mm. The distribution of mean horizontal dimensional changes subdivided into buccal and oral changes, buccal sites at level 0-5 mm from CEJ were -0.23±1.06, -0.33±0.98, -0.31±0.68, -0.21±0.66, -0.18±0.46 and 1.33±0.74 mm. Lingual sites at level 0-5 mm from CEJ were 0.00±0.53, -0.01±0.38, 0.00±0.35, 0.02±0.36, 0.00±0.27 and 0.79±0.38 mm.

While, in the d-PTFE group, the mean horizontal dimensional changes were: -0.14±0.69 mm. The distribution of mean horizontal dimensional changes subdivided into buccal and oral changes, buccal sites at level 0-5 mm from CEJ were -0.39±0.90, -0.23±0.73, -0.22±0.46, -0.11±0.58, -0.01±0.51 and 0.00±0.32 mm. Lingual sites at level 0-5 mm from CEJ were -0.60±1.09, -0.25±0.79, 0.05±0.72, 0.12±0.68, -0.03±0.33 and 0.00±0.32 mm.

The result in the dimensional changes of the alveolar bone in both groups were similar to the total alveolar ridge dimensional changes, the dimensional changes of alveolar bone at the coronal part and buccal side was greater than those at the apical part and lingual side especially when measuring at greater than 3 mm from CEJ. In general, PPE group showed comparable alveolar bone preservation to those of d-PTFE at buccal side, but exhibited greater alveolar bone preservation at lingual side than those of the d-PTFE group at all levels of measurement. At 5 mm, the changes in dimension of alveolar bone in PPE group at both lingual and buccal side was evidently greater than those of the d-PTFE group. However, the mean horizontal dimensional changes

in all locations of alveolar bone contour were not significantly different between two groups (P > 0.05) as shown in Table 4.4.

Table 4.4: Dimensional changes of alveolar bone in horizontal direction at different location of measurement at 4 months after preservation (Mean ± SD).

Location	Dimensional change of alveolar bone (mm.)				P-value*
	d-PTFE (Control group, n=15)		PPE (Experimental group, n=15)		
Horizontal	Buccal	Lingual	Buccal	Lingual	
At CEJ	-0.39±0.90	-0.60±1.09	-0.23±1.06	0.00±0.53	0.11
1mm	-0.23±0.73	-0.25±0.79	-0.33±0.98	-0.01±0.38	0.41
2mm	-0.22±0.46	0.05±0.72	-0.31±0.68	0.00±0.35	0.98
3mm	-0.11±0.58	0.12±0.68	-0.21±0.66	0.02±0.36	0.32
4mm	-0.01±0.51	-0.03±0.33	-0.18±0.46	0.00±0.27	0.52
5mm	0.00±0.32	0.00±0.32	1.33±0.74	0.79±0.38	0.37
Total Horizontal	-0.14±0.69 mm.		-0.11±0.59 mm.		0.24

*P-values (statistically significant at the level of P < 0.05) with the independent-samples t-tests for the difference in the bucco-lingual width of the alveolar ridge between d-PTFE and PPE groups.

4.1.5 Implant stability values (IST)

Implant stability at implant placement and before prosthesis delivery were similar in both groups. High average stability (IST>75) were found in both membrane groups. Implant stability prior to prosthesis delivery (IST2) was found to have a statistically significant increase in both groups when compared to Implant stability at the time of implant placement (IST1). However, there was no statistically difference for IST1 or IST2 between d-PTFE and PPE groups (P>0.05) as shown in Table 4.5.

Table 4.5: Implant stability values (IST) at implant placement (IST1) and before insert the prosthesis (IST2) in each group (Mean ± SD).

Implant stability	d-PTFE (Control group, n=13)	PPE (Experimental group, n=15)	P-value*
IST1	75.14±10.86	76±6.15	0.77
IST2	80.67±5.61	83.32±3.49	0.13
P-value**	0.0011**	<0.0001**	

*P-values (statistically significant at the level of P < 0.05) with the independent-samples t-tests for the difference in IST values between d-PTFE and PPE groups.

**P-values (statistically significant at the level of P < 0.05) with the Wilcoxon signed rank test for the differences within each group between IST1 and IST2.

4.1.6 Histologic and histomorphometric

At 4 months after preservation, the H&E stained sections from all harvested bone core samples from both membrane groups revealed histologically normal features (Figure 4.1). New bone formation was seen in all samples without any signs of inflammatory response, necrosis, or foreign body reaction. The infiltration of connective tissue and the remaining residual bone graft were also observed. The bone graft particles were surrounded by or in contact with the newly formed bone matrix. From histomorphometric analysis, new bone formation, residual bone and connective tissue were 27.06±7.91%, 33.22±6.73% and 39.78±4.03%, respectively in PPE group and 31.03±6.47%, 30.58±4.66% and 38.08±8.62%, respectively in the d-PTFE group. However, all histomorphometric data did not show statistically significant differences between two groups as shown in Table 4.6.

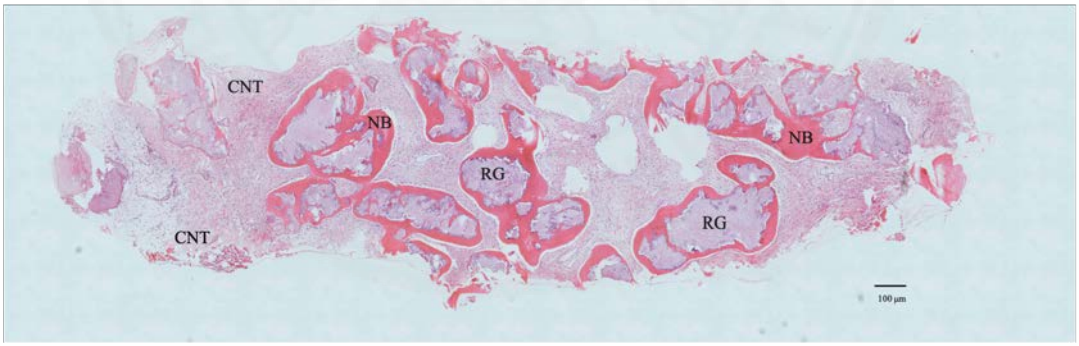

Figure (4.1) The histological section of bone core specimen at 4 months from PPE group revealed residual bone graft (RG) surrounded with newly formed bone (NB) and connective tissue (CT). Hematoxylin and eosin [H&E]; original magnification, 20X).

Table 4.6: Histomorphometric data in d-PTFE group and PPE groups at 4 months after preservation (Mean ± SD).

Measurement	d-PTFE (Control group, n=13)	PPE (Experimental group, n=15)	P-value
Connective tissue (%)	38.08±8.62	39.78±4.03	0.85
Residual bone graft (%)	30.58±4.66	33.22±6.73	0.24
New bone formation (%)	31.03±6.47	27.06±7.91	0.16

4.2 Discussion

In general, bone resorption after loss of the teeth is an inevitable phenomenon and may adversely affect both oral health and social complications. An edentulous site can be replaced with dentures, bridges or dental implants; however, the quantity and quality of soft and hard tissue are essentially needed. Two-thirds of the alveolar ridge resorption were reported within the first 3 months after extraction (5) while the resorption occurred approximately 29 – 63% in the horizontal direction and 11 – 22% in the vertical direction within 3 - 6 months after extraction (6). A systematic review by Van der Weijden F et al. demonstrated that horizontal and vertical alveolar ridge resorption were found around 3.87 and 1.67 mm respectively at 3 months when ARP was not performed (51). Therefore, many efforts have been made to reduce and maintain the structure of extracted alveolar ridge. At least 3 systematic reviews and meta-analyses demonstrate significantly less vertical and horizontal dimensional changes of the alveolar bone when ARP was performed. Although, the data were insufficient to quantify the influence of other contributing factors, such as the type of surgery, the membrane materials and coverage and the filling materials (80, 84, 181).

For dental implant therapy, ARP is frequently recommended as it could simplify the surgical procedures and reduce the need of additional bone graft surgery. By the use of membrane, the extracted socket is covered to maintain the graft materials while preventing soft ingrowth and promoting maximum bone healing. Resorbable and non-resorbable membranes have been developed for decades for mainly used in guided bone regeneration (GBR) which also applied to ARP procedure (17). When considering the material properties, non-resorbable membranes may be more suitable for ARP than the

resorbable one. For resorbable membrane primary closure is mostly needed, an exposure of resorbable membranes with presence of periodontal pathogens at the preservation site can lead to faster degradation or unpredictable resorption which compromise the final outcome (115). Unlike the most of resorbable membranes, a non-resorbable membrane such as d-PTFE membrane can be left exposed in the oral cavity without the risk of infection of the grafted area (19). Since the primary closure is not necessary, only minimal flap reflection or dissection is required to place and stabilize the d-PTFE membranes. Consequently, the vascularization to the bone graft material and surgical site is not compromised, as occurred with large flap reflections (57, 68, 179, 182-184). Compromised or decreased vascularization to the surgical site can lead to decreased healing process and decreased bone regeneration (19). Moreover, the absence of internal tissue integration into the structure of membranes result in membranes can remove easily and no need for a second surgery to remove the d-PTFE membranes (19, 185). In addition, without the need of an advancement flap for primary closure as a result in the position of the mucogingival junction, the interdental papilla and the full width of keratinized mucosa can be preserved (19, 68, 179, 182). Previous study by Arbab H et al. demonstrated the mean dimensional changes of alveolar ridge were −2.2 ± 1.5 mm. in horizontally and −0.5 ± 1.6 mm. in vertically in PTFE group (186). d-PTFE are a stable polymer with chemically and biologically inert, resistance to degraded through enzymatic reactions and bacterial penetration. Although, important characteristic of the d-PTFE membrane is the capacity of cellular occlusion, which allows epithelial and bacterial cells exclusion from the healing sites and show well-vascularized bone free of fibrosis or chronic inflammation in the socket (183, 187, 188). However, some studies demonstrated that due to the limited porosity of the d-PTFE

membranes can lead to limited blood supply to the grafted area, while the successful bone regeneration relies on adequate blood supply (14, 183). Alternative membrane materials are being developed to improve their properties at a lower cost. Novel PPE used in this study contained two layers with different pore sizes and porosity which were suitable for both rapid fibrovascularization and facilitate new bone formation (25-27, 189).

To compare the clinical efficiency of novel PE membranes with PTFE, clinical response such as rate of socket wound closure is necessary. Recently, intraoral scanner has been widely used in implant dentistry (190), this high accuracy and precision scanner allow to measure or monitor the wound healing process without any pressing or disruption to the wound especially in the early stage, resulting in less distortion compare with conventional impression technique. (191, 192). For long term follow up, digital scanned image data also makes it possible to see the dimensional changes at different time points. For this study, monitoring of the early wound healing after ARP with exposed membrane is an important concern, regarding a higher risk of inflammation and infection from migration of bacteria (193). After tooth extraction, the socket is filled with blood clot and then completely replaced by granulation tissue within 2-7 days (193). By 24 hours, epithelialization from the peripheral gingival margins starts and becomes complete wound closure after 1-5 weeks depending on factors such as socket width, tooth location and concomitant extraction of adjacent teeth (193, 194).

As the result from table 2, both membranes demonstrate good biocompatibility without causing a delay to socket wound healing. No sign of inflammation indicates

conclusive property of membranes which protect the penetration of food and bacteria into the preserved area. Efficacy of ARP after 4 months was calculated using linear measurement technique, which provides a high level of accuracy of the dimensional changes of alveolar ridges without anatomical limitation and produces less error by using same reference structures (195). Similar results with previous studies were observed including higher degree of resorption on buccal side than lingual side and coronal part than apical one (5, 77, 196-198). Flu¨gge T et al, 2015 (199), demonstrated that the mean dimensional changes after 4 months for non-augmented sockets were 1.0 mm (min 0.0 – max 2.2 mm) and the augmented sockets were 0.8 mm (min 0.1 – max 2.9 mm). These results were consistent with our study whereas resorptions were found 1.12±0.77 mm. in the d-PTFE group and 1.20±0.63 mm. in the PPE group. Moreover, results from CBCT analysis showed that mean horizontal bone resorption was 0.14±0.69 mm. d-PTFE group versus -0.11±0.59 mm. for the PPE group.

In this study, minimal dimensional changes of alveolar bone were achieved by ARP using both membrane materials. Hence, after 4 months all preserved socket sites were allowed to place implants without the need of major bone augmentations. In addition to the amount of ridge, bone quality of preserved socket is also revealed by implant stability and histomorphotometric analysis. Pang et al. 2016 showed mean primary stability was 63.40 ±2.47 in the ARP group and 62.60±1.88 in the extraction alone after six months (200). Interestingly, in this study high levels of IST were found in both groups, 75.14±10.86 in PPE and 76±6.15 in d-PTFE, and showed a progressive increase in stability over time.

Histomorphometric analysis from this study showed similar results in both membrane groups. For d-PTFE group, Gustavo Avila-Ortiz et al, 2014 (201) demonstrated similar results of the mean area of new bone 28.88%, remaining graft particle 47% and the fibrous tissue 33.66% in bone samples 4 months after ARP these were corresponded with reported from Cheon et al, 2017 (202) and Fotek et al, 2009 (203). A recent systematic review in 2019 comparing ARP techniques with and without coverage membrane demonstrated superior results when membrane was applied (204). For longer preservation time, Perelman-Karmon et al, 2012 (205) showed higher % bone area fractions in the ARP with membrane group compared to APR without membrane group after 9 months. The importance of membrane in ARP was also emphasized by Perelman-Karmon et al, 2012, since the membrane confines the grafted particles during the first period of healing and stabilizes the entire site, in addition to its biologic contributions (205). In unprotected sites, some particulate biomaterial would be lost or reside in the overlying soft tissue. It should be considered that with membrane-protected socket site greater newly formed bone can be anticipated.

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusion

Porous polyethylene membrane could be potentially used as an alternative choice for an inexpensive membrane material in alveolar ridge preservation, however further tissue regeneration needs to be investigated.

5.2 Recommendations

The limitations of the study may be any error generated by inaccuracy of the intraoral scanning technique is the hand-made production in clinical situation, Number of participants in each group, skill of handling material and surgical technique may be affecting the measurement of true effectiveness of membrane in ARP.

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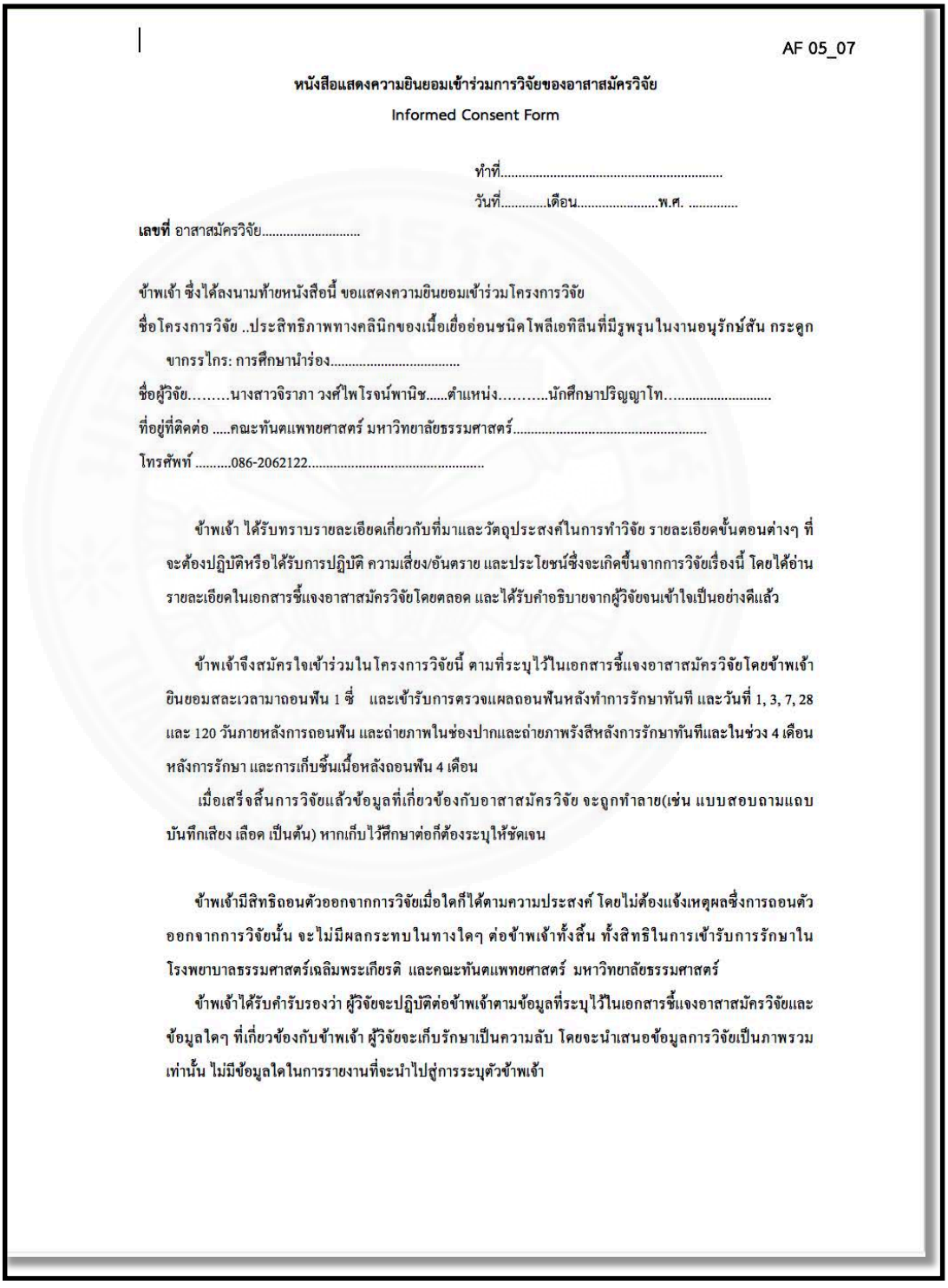
APPENDICES

Appendix I: Informed consent form.



AF 05_07

หนังสือแสดงความยินยอมเข้าร่วมการวิจัยของอาสาสมัครวิจัย

Informed Consent Form

ทำที่.....

วันที่.....เดือน.....พ.ศ. .....

เลขที่ อาสาสมัครวิจัย.....

ข้าพเจ้า ซึ่งได้ลงนามท้ายหนังสือนี้ ขอแสดงความยินยอมเข้าร่วมโครงการวิจัย

ชื่อโครงการวิจัย ..ประสิทธิภาพทางคลินิกของเนื้อเยื่ออ่อนชนิดโพลีเอทิลีนที่มีรูพรุนในงานอนุรักษ์สัน กระดูกขากรรไกร: การศึกษานำร่อง.....

ชื่อผู้วิจัย.....นางสาวจิราภา วงศ์ไพโรจน์พานิช.....ตำแหน่ง.....นักศึกษาปริญญาโท.....

ที่อยู่ที่ติดต่อ .....คณะทันตแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์.....

โทรศัพท์ .....086-2062122.....

ข้าพเจ้า ได้รับทราบรายละเอียดเกี่ยวกับที่มาและวัตถุประสงค์ในการทำวิจัย รายละเอียดขั้นตอนต่างๆ ที่จะต้องปฏิบัติหรือได้รับการปฏิบัติ ความเสี่ยง/อันตราย และประโยชน์ซึ่งจะเกิดขึ้นจากการวิจัยเรื่องนี้ โดยได้อ่านรายละเอียดในเอกสารชี้แจงอาสาสมัครวิจัยโดยตลอด และได้รับคำอธิบายจากผู้วิจัยจนเข้าใจเป็นอย่างดีแล้ว

ข้าพเจ้าจึงสมัครใจเข้าร่วมในโครงการวิจัยนี้ ตามที่ระบุไว้ในเอกสารชี้แจงอาสาสมัครวิจัยโดยข้าพเจ้ายินยอมสละเวลามาถอนฟัน 1 ซี่ และเข้ารับการตรวจแผลถอนฟันหลังทำการรักษาทันที และวันที่ 1, 3, 7, 28 และ 120 วันภายหลังการถอนฟัน และถ่ายภาพในช่องปากและถ่ายภาพรังสีหลังการรักษาทันทีและในช่วง 4 เดือนหลังการรักษา และการเก็บชิ้นเนื้อหลังถอนฟัน 4 เดือน

เมื่อเสร็จสิ้นการวิจัยแล้วข้อมูลที่เกี่ยวข้องกับอาสาสมัครวิจัย จะถูกทำลาย(เช่น แบบสอบถามแถบบันทึกเสียง เลือด เป็นต้น) หากเก็บไว้ศึกษาต่อก็ต้องระบุให้ชัดเจน

ข้าพเจ้ามีสิทธิถอนตัวออกจากการวิจัยเมื่อใดก็ได้ตามความประสงค์ โดยไม่ต้องแจ้งเหตุผลซึ่งการถอนตัวออกจากการวิจัยนั้น จะไม่มีผลกระทบในทางใดๆ ต่อข้าพเจ้าทั้งสิ้น ทั้งสิทธิในการเข้ารับการรักษาในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ และคณะทันตแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

ข้าพเจ้าได้รับคำรับรองว่า ผู้วิจัยจะปฏิบัติต่อข้าพเจ้าตามข้อมูลที่ระบุไว้ในเอกสารชี้แจงอาสาสมัครวิจัยและข้อมูลใดๆ ที่เกี่ยวข้องกับข้าพเจ้า ผู้วิจัยจะเก็บรักษาเป็นความลับ โดยจะนำเสนอข้อมูลการวิจัยเป็นภาพรวมเท่านั้น ไม่มีข้อมูลใดในการรายงานที่จะนำไปสู่การระบุตัวข้าพเจ้า

AF 05_07

หากข้าพเจ้าไม่ได้รับการปฏิบัติตรงตามที่ได้ระบุไว้ในเอกสารชี้แจงอาสาสมัครวิจัย ข้าพเจ้าสามารถร้องเรียนได้ที่: คณะอนุกรรมการจริยธรรมการวิจัยในคน มหาวิทยาลัยธรรมศาสตร์ ชุดที่ 3 อาคารราชสุดา ชั้น 1 ศูนย์ส่งเสริมสุขภาพ คณะพยาบาลศาสตร์ มหาวิทยาลัยธรรมศาสตร์ ศูนย์รังสิต โทรศัพท์ 02-986-9213 ต่อ 7373 โทรสาร 02-5165381

ข้าพเจ้าได้ลงลายมือชื่อไว้เป็นสำคัญต่อหน้าพยาน ทั้งนี้ข้าพเจ้าได้รับสำเนาเอกสารข้อมูลสำหรับ อาสาสมัครวิจัย และสำเนาหนังสือแสดงความยินยอมเข้าร่วมการวิจัยของอาสาสมัครวิจัยไว้แล้ว

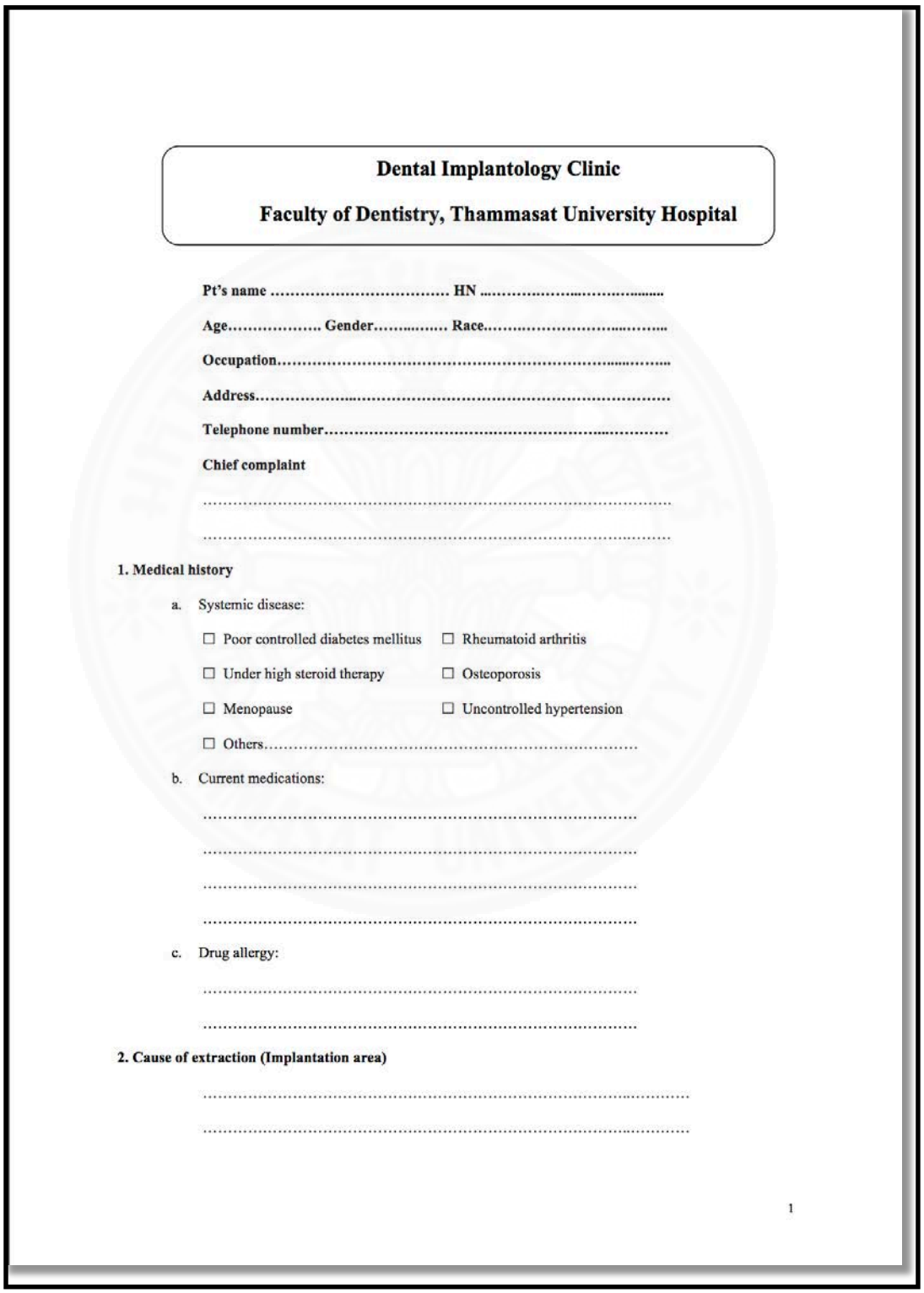
ลงชื่อ.....
(นางสาวจิราภา วงศ์ไพโรจน์พานิช)
ผู้วิจัยหลัก
วันที่...../...../.....

ลงชื่อ.....
(.....)
อาสาสมัครวิจัย
วันที่...../...../.....

ลงชื่อ.....
(.....)
พยาน
วันที่...../...../.....

ลงชื่อ.....
(.....)
พยาน
วันที่...../...../.....

Appendix II: Patient examination record form of the Implantology clinic, Faculty of Dentistry, Thammasat University.



Dental Implantology Clinic

Faculty of Dentistry, Thammasat University Hospital

Pt's name ..... HN .....

Age..... Gender..... Race.....

Occupation.....

Address.....

Telephone number.....

Chief complaint

.....

.....

1. Medical history

a. Systemic disease:

☐ Poor controlled diabetes mellitus ☐ Rheumatoid arthritis

☐ Under high steroid therapy ☐ Osteoporosis

☐ Menopause ☐ Uncontrolled hypertension

☐ Others.....

b. Current medications:

.....

.....

.....

.....

c. Drug allergy:

.....

.....

2. Cause of extraction (Implantation area)

.....

.....

1

3. Habit

☐ Bruxism ☐ Clenching ☐ Non-smoking

☐ Smoking……. cig. /day

4. Extraoral examination

☐ Head ……

……..

☐ Face ……

……

☐ Nose ……

……..

☐ Lip ……

……..

☐ High lip line ☐ Gummy smile ☐ Low lip line

5. Intraoral examination

Tooth number (plan extraction): ……

Alveolar ridge width:

B-L …… mm

M-D …….. mm (at gingival margin)

Approximate tissue thickness ……..…… mm

Keratinized tissue (AGW1) .....……mm

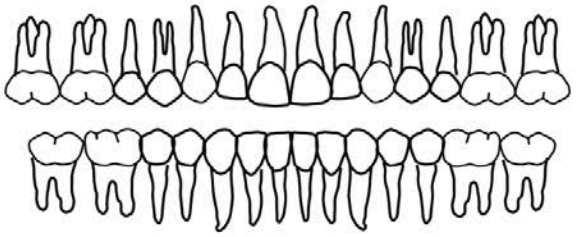
Angle's classification: ☐ Class I ☐ Class II ☐ Class III

Interocclusal space ……..……mm

Lateral movement: ☐ Canine guidance ☐ Group function

Type of antagonist tooth: ☐ natural tooth ☐ Prosthesis

……



6. Oral hygiene status

Last visit to the dentist ……for……..……..

Plaque index (O'Leary)

☐ good (<20%) ☐ fair (20 – 50 %) ☐ Poor (>50%)

Bleeding index ……..……

Periodontal Diagnosis: ……..

History of Periodontal treatment:

☐ when ……..……

☐ how ……..……..……..……

7. Radiographic finding

Technique: ☐ Parallel ☐ Bisecting ☐ OPG ☐ CT/CBCT

Bone available: From sinus floor to alv. crest ……mm

From inf. alv. canal to alv. crest ……mm

M-D width of neighboring tooth at CEJ ……..……mm

CEJ – alv. crest……..…… mm

8. Cerec scanner result: ……..……

……..…..

……..…..

3

9. Operation (Extracted time)

a. Preparation & Operative finding:

Local anesthesia with...……..……

b. Pre-medication

……..…

……..…

c. Complication

☐ Intra – operation (Extraction time)

……..…

……..…

☐ Post – extraction

……..…

……..…

d. Measurements:

Alveolar ridge width: B-L ……..…….mm

M-D ……..…….mm

Buccal bone plate thickness ……..……..……..mm

Lingual/Palatal bone plate thickness ……..……..mm

Keratinized tissue ……..……mm

e. Post-medication

……..

……..

f. Radiographic finding (CT/CBCT after extraction)

Vertical buccal bone height (VBBH1) ……..……mm

Horizontal bone width (HBW1) ……..mm

Thickness of the buccal bone plate ……..……..mm

Thickness of the lingual/palatal bone plate ……..…….mm

4

10. Follow up time

Follow up day1:

☐ infection ☐ swelling ☐ pus / exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

Follow up day3:

☐ infection ☐ swelling ☐ pus / exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

Follow up day7:

☐ infection ☐ swelling ☐ pus / exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

Follow up day28: (Stitches off):

☐ infection ☐ swelling ☐ pus / exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

Follow up day120: (Implant placement):

☐ infection ☐ swelling ☐ pus / exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

11. Re-entry time and implant placement (4 months after extraction)

a. Before surgery:

Plaque index (O'Leary)

☐ good (<20%) ☐ fair (20 – 50 %) ☐ Poor (>50%)

Bleeding index ……

Alveolar ridge width: B-L ……..……..….mm

M-D ……..…….....mm

Buccal bone plate thickness ……..……..mm

Lingual/Palatal bone plate thickness ……..……...mm

Keratinized tissue ……..……mm

6

Cerec scanner result……..

……..

……..

Radiographic finding (CT/CBCT 4 month before re-entry time)

Vertical buccal bone height (VBBH1) ……..….mm

Horizontal bone width (HBWRe-1)…… ……..mm

Thickness of the buccal bone plate ……..……..mm

Thickness of the lingual/palatal bone plate ……...…..….mm

b. Preparation & Operative finding:

Pre-medication

……..

……..

Local anesthesia with...……

Tissue thickness.…….mm

Alveolar ridge width: B-L ……...……...….mm

M-D ……..…….....mm

Bone support:☐ sufficiency ☐ insufficiency

☐ horizontal bone defect ☐ vertical bone defect

Bone shape: ☐ knife edge ☐ round ☐ other……

c. Bone augmentation: ☐ yes (simultaneously with implant placement) ☐ no

☐ Primary augmentation needed before implant placement

How……

d. Implant placement procedures:

Bone quality Type: ☐ 1 ☐ 2 ☐ 3 ☐ 4

Implant system: ……

Configuration:☐ Bone level ☐ Straight ☐ Conical

Implant location …#...……..

Implant size: ☐ Ø…… mm. ☐ length …….. mm

☐Cover screw ☐Healing abutment (Height ..…. mm Ø….mm.)

Drilling speed ……..…….. rpm

7

Irrigation system internal / external

Implant insertion speed and torque……..…Ncm

Primary stability obtains……

Defect bone ☐ no bony defect ☐ dehiscence ☐ fenestration

GBR simultaneously with implant placement

How……

Augmentation material

☐ Autogenous ☐ Xenograft ☐ Synthetics

☐ others……

Membrane: ☐Bio-Gide ☐ Biomend ☐ others……

Pin:……

Stage: ☐ one (transmucosal) ☐ two (submerged)

Loading: ☐ immediate ☐ early ☐ delayed

Post-medication:

……

……

……

Complication (intra-operation)

☐ no primary stability ☐ wrong direction

☐ others……

e. Follow up time

Follow up 1 week:

☐ infection ☐ swelling ☐ pus exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

8

Follow up 1 month:

☐ infection ☐ swelling ☐ pus exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

Follow up 3 months:

☐ infection ☐ swelling ☐ pus exudates

☐ others……

☐ VAS Score

ไม่ปวด ปวดรุนแรงมากที่สุด

f. ISQ measurement

At implant placement ……

At 1 month follow up……

At 3 month follow up (prosthetic loading) ……

g. Histology and Histomorphology analysis

Percentage of connective tissue……

Percentage of new bone formation……

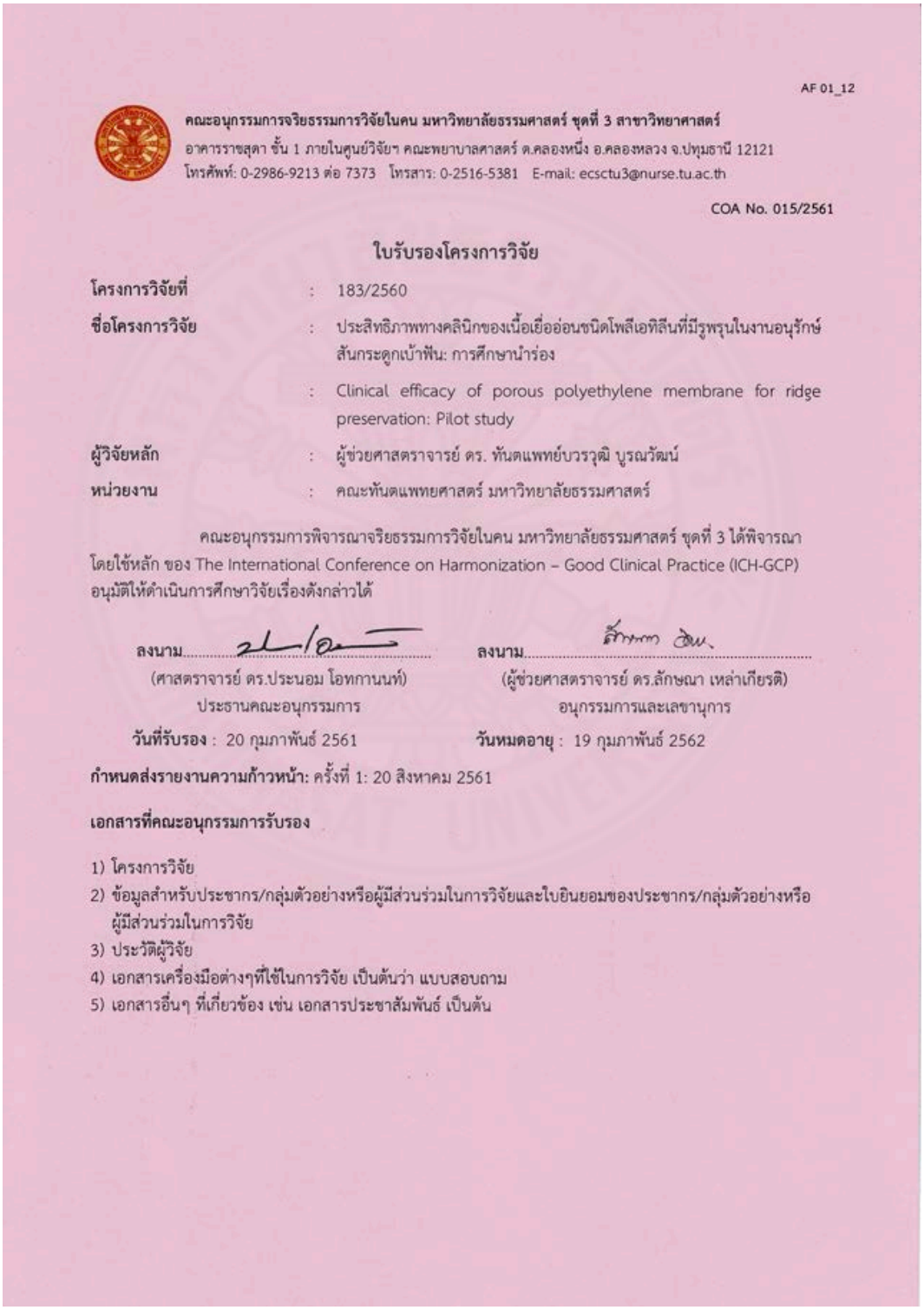
Percentage of residual graft particle……..

Others ……

……

9

Appendix III: The ethical approval letter from the Ethical Review Sub-Committee Board for Human Research Involving Sciences, Thammasat University, No. 3. (the ethical approval number 183/2560).



AF 01_12

คณะอนุกรรมการจริยธรรมการวิจัยในคน มหาวิทยาลัยธรรมศาสตร์ ชุดที่ 3 สาขาวิทยาศาสตร์
อาคารราชสุดา ชั้น 1 ภายในศูนย์วิจัยฯ คณะพยาบาลศาสตร์ ต.คลองหนึ่ง อ.คลองหลวง จ.ปทุมธานี 12121
โทรศัพท์: 0-2986-9213 ต่อ 7373 โทรสาร: 0-2516-5381 E-mail: ecsctu3@nurse.tu.ac.th

COA No. 015/2561

ใบรับรองโครงการวิจัย

โครงการวิจัยที่ : 183/2560

ชื่อโครงการวิจัย : ประสิทธิภาพทางคลินิกของเนื้อเยื่ออ่อนชนิดโพลีเอทิลีนที่มีรูพรุนในงานอนุรักษ์สันกระดูกเบ้าฟัน: การศึกษานำร่อง

: Clinical efficacy of porous polyethylene membrane for ridge preservation: Pilot study

ผู้วิจัยหลัก : ผู้ช่วยศาสตราจารย์ ดร. ทันตแพทย์บวรวุฒิ บูรณวัฒน์

หน่วยงาน : คณะทันตแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

คณะอนุกรรมการพิจารณาจริยธรรมการวิจัยในคน มหาวิทยาลัยธรรมศาสตร์ ชุดที่ 3 ได้พิจารณาโดยใช้หลัก ของ The International Conference on Harmonization – Good Clinical Practice (ICH-GCP) อนุมัติให้ดำเนินการศึกษาวิจัยเรื่องดังกล่าวได้

ลงนาม.....
(ศาสตราจารย์ ดร.ประนอม โอทกานนท์)
ประธานคณะอนุกรรมการ

ลงนาม.....
(ผู้ช่วยศาสตราจารย์ ดร.ลักษณา เหล่าเกียรติ)
อนุกรรมการและเลขานุการ

วันที่รับรอง : 20 กุมภาพันธ์ 2561 **วันหมดอายุ** : 19 กุมภาพันธ์ 2562

กำหนดส่งรายงานความก้าวหน้า: ครั้งที่ 1: 20 สิงหาคม 2561

เอกสารที่คณะอนุกรรมการรับรอง

1) โครงการวิจัย
2) ข้อมูลสำหรับประชากร/กลุ่มตัวอย่างหรือผู้มีส่วนร่วมในการวิจัยและใบยินยอมของประชากร/กลุ่มตัวอย่างหรือผู้มีส่วนร่วมในการวิจัย
3) ประวัติผู้วิจัย
4) เอกสารเครื่องมือต่างๆที่ใช้ในการวิจัย เป็นต้นว่า แบบสอบถาม
5) เอกสารอื่นๆ ที่เกี่ยวข้อง เช่น เอกสารประชาสัมพันธ์ เป็นต้น

คณะอนุกรรมการจริยธรรมการวิจัยในคน มหาวิทยาลัยธรรมศาสตร์ ชุดที่ 3 สาขาวิทยาศาสตร์ ScF 03_01
ห้อง 110 ชั้น 1 อาคารปิยชาติ มหาวิทยาลัยธรรมศาสตร์ ศูนย์รังสิต ต.คลองหนึ่ง อ.คลองหลวง
จ.ปทุมธานี 12121 โทรศัพท์: 0-2986-9213 ต่อ 7358 E-mail: ecsctu3@nurse.tu.ac.th

COA No. 015/2561

ใบรับรองโครงการวิจัย

โครงการวิจัยที่ : 183/2560

ชื่อโครงการวิจัย : ประสิทธิภาพทางคลินิกของเนื้อเยื่ออ่อนชนิดโพลีเอทิลีนที่มีรูพรุนในงานอนุรักษ์สันกระดูกเบ้าฟัน: การศึกษานำร่อง

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หน่วยงาน : คณะทันตแพทยศาสตร์ มหาวิทยาลัยธรรมศาสตร์

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ลงนาม.....
(ศาสตราจารย์ ดร.ประนอม โอทกานนท์)
ประธานคณะอนุกรรมการ

ลงนาม.....
(ผู้ช่วยศาสตราจารย์ ดร.ลักษณา เหล่าเกียรติ)
อนุกรรมการและเลขานุการ

วันที่รับรอง : 20 กุมภาพันธ์ 2562

วันหมดอายุ : 19 กุมภาพันธ์ 2563

กำหนดส่งรายงานความก้าวหน้า: ครั้งที่ 3: 20 สิงหาคม 2562

เอกสารที่คณะอนุกรรมการรับรอง

1) โครงการวิจัย
2) ข้อมูลสำหรับประชากร/กลุ่มตัวอย่างหรือผู้มีส่วนร่วมในการวิจัยและใบยินยอมของประชากร/กลุ่มตัวอย่างหรือผู้มีส่วนร่วมในการวิจัย
3) ประวัติผู้วิจัย
4) เอกสารเครื่องมือต่างๆที่ใช้ในการวิจัย เป็นต้นว่า แบบสอบถาม
5) เอกสารอื่นๆ ที่เกี่ยวข้อง เช่น เอกสารประชาสัมพันธ์ เป็นต้น