Journal of Oral Science, Vol. 62, No. 3, 308-313, 2020

Original article

Clinical and histological evaluations of alveolar ridge augmentation using a novel bi-layered porous polyethylene barrier membrane

Ji-Chuan Song[1,2], Jintamai Suwanprateeb[3], Daraporn Sae-Lee[2,4], Teerapan Sosakul[4], Suwadee Kositbowornchai[5], Poramaporn Klanrit[5,6], Waranuch Pitiphat[6,7], and Saengsome Prajaneh[5,6]

[1] Graduate School of Dentistry, Khon Kaen University, Khon Kaen, Thailand
[2] Neuroscience Research and Development Group, Khon Kaen University, Khon Kaen, Thailand
[3] Biofunctional Materials and Devices Research Group, National Metal and Materials Technology Center, Pathumthani, Thailand
[4] Department of Prosthodontics, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand
[5] Department of Oral Biomedical Science, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand
[6] Research Group of Chronic Inflammatory Oral Diseases and Systemic Diseases Associated with Oral Health, Khon Kaen University, Khon Kaen, Thailand
[7] Department of Preventive Dentistry, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand

(Received May 23, 2019; Accepted October 8, 2019)

Abstract: Guided bone regeneration (GBR) is an effective alveolar ridge reconstruction technique used before or at implant placement. The combination of various barrier membranes and bone substitutes has been employed. This study aimed to perform a preliminarily evaluation of the safety and performance of a new nonabsorbable bi-layered porous polyethylene (PPE) membrane, in combination with a freeze-dried cortical bone allograft in posterior mandibular ridge augmentation. Fifteen adults who had combined posterior mandibular defects were included for ridge augmentation via GBR using PPE membrane and allograft before implant placement. The keratinized mucosa width (KW), ridge width (RW), ridge height (RH), distance from measurement matrix to bone (DMB), and horizontal alveolar width at 14.0 mm apical to the occlusal plane (HAW) were clinically measured at 15 intended implant sites before and after the augmentation. Fifteen biopsy specimens were harvested at the implant sites for histological analysis. All the subjects completed the whole study. The KW and RH showed minor gains by 0.2 ± 1.4 mm and 0.9 ± 2.3 mm respectively; however, no statistically significant differences were found between, before, and after the augmentation ($P > 0.05$). In contrast, the RW and HAW significantly increased by 4.8 ± 1.6 mm and 2.3 ± 1.7 mm, respectively, ($P \leq 0.001$), while DMB significantly decreased by 1.0 ± 0.8 mm after treatment ($P < 0.001$). Histological analysis revealed that allograft underwent active bone remodeling. The PPE membrane was adequately safe and efficient to use with allograft in GBR for the reconstruction of combined ridge defects. Although some complications were observed, these were manageable and subsequently lead to successful implant placement for all the subjects. However, further randomized controlled trials are still needed to confirm these findings.

Keywords; alveolar ridge augmentation, barrier membrane, bi-layered porous polyethylene membrane, guided bone regeneration

Introduction

Tooth loss leads to irreversible alveolar ridge atrophy owing to the absence of internal loading [1]. Without effective interventions, the concomitant horizontal and vertical bone resorptions occur, especially within the first 3-6 months [2,3]. If implant restorations are required, the atrophic alveolar ridges will make ideal implant placement challenging.

In order to repair alveolar ridge defects for optimal implant rehabilitation, multiple bone reconstruction techniques, including guided bone regeneration (GBR), inlay/onlay bone grafting, ridge splitting, sinus lift, and distraction osteogenesis, have been utilized. Although currently, there is no consensus about which technique is the most efficient, GBR is reported as an effective and predictable bone augmentation technique with the synergistic application of barrier membranes and bone substitutes [4]. This technique has been widely used to repair various ridge defects, including implant fenestration, dehiscence, and even segmental bone defects [5-7].

Barrier membrane is crucial for the success of the GBR procedure. In addition to providing good biocompatibility, it should preserve blood clots, stabilize bone substitutes, create and maintain space for new bone formation within defects, and provide biological isolation for the fast-growing fibroblasts and connective tissue to prevent premature penetration [8]. Various natural and synthetic barrier membranes, including bioabsorbable (e.g. collagen, polylactic acid) and nonabsorbable (e.g. polytetrafluoroethylene, titanium mesh) membranes have been employed [9-11]. Bioabsorbable membranes are widely used because there was no need for secondary surgical removal and because they caused fewer morbidities, revisits, and impairments. However, they usually cannot provide sufficient space maintenance. In contrast, nonabsorbable membranes can provide better space maintenance for predictable bone regeneration; however, they usually cause more healing complications (e.g. wound dehiscence, premature exposure, and local infection), necessitating secondary surgical removal. Therefore, they are mainly used for the reconstruction of the challenging large and vertical ridge defects. Among these nonabsorbable membranes, expanded polytetrafluoroethylene (e-PTFE) membrane has been considered as the gold standard in previous decades because of its superior space maintenance and bone regeneration potential [12]. Currently, multilayered barrier membrane has gained interest because it can be intentionally designed to contain differential pore microstructures, simulate different types of tissues, and possess proper biomechanical properties for different functions on each side [10,12-14].

Polyethylene is a polymeric biomaterial with good physicochemical, mechanical, and biological properties [15-17]. Porous polyethylene has been employed in orthopedics, ophthalmosurgery, as well as craniomaxillofacial and plastic surgeries for tissue repair and augmentation due to its fibrovascularization and bone ingrowth capacity [15-19]. For dental application, it has been investigated as a graft containment for ridge preservation [20]. Based on these studies, a new bi-layered porous polyethylene (PPE) that contained both low- and high-porosity layers in a single sheet was developed using a wet salt bed technique, as reported [21]. Its pore microstructure, material properties, and preclinical performance were already characterized [22]. It was postulated that PPE could be utilized as a barrier membrane in GBR procedure for ridge augmentation. The purpose of this clinical study was to perform a preliminarily investigation about the safety and performance of PPE membrane in the reconstruction of combined ridge defects in posterior mandible prior for implant placement.

Materials and Methods

Subject population

This clinical trial was carried out at the Dental Hospital, Faculty of Dentistry, Khon Kaen University, Thailand between April 2017 and February

Correspondence to Dr. Daraporn Sae-Lee, Department of Prosthodontics, Faculty of Dentistry, Khon Kaen University, 123 Mittraphap Rd, Tambon Nai Mueang, Mueang Khon Kaen District, Khon Kaen 40002, Thailand
E-mail: darsae@yahoo.com

J-STAGE Advance Publication: June 10, 2020
Color figures can be viewed in the online issue at J-STAGE.
doi.org/10.2334/josnusd.19-0218
DN/JST.JSTAGE/josnusd/19-0218

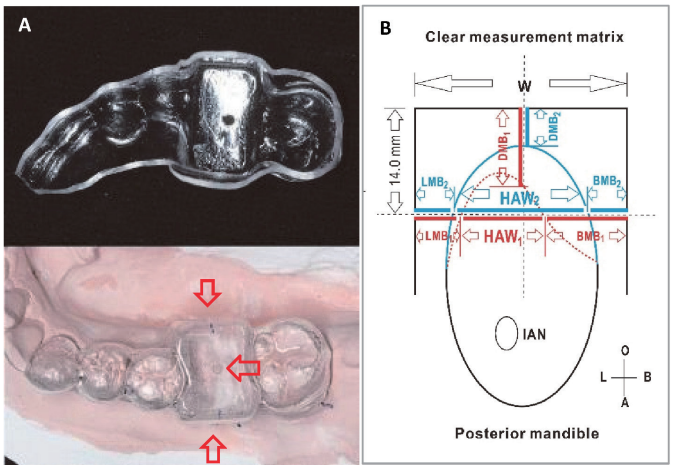

Fig. 1 A clear matrix for intraoperative ridge dimension assessment at the middle cross-section of the edentulous area. (A) Intaglio and occlusal views. (B) Schematic diagram for horizontal and vertical ridge dimension measurements. IAN, inferior alveolar nerve; DMB, distance from matrix to bone; HAW, horizontal alveolar width; BMB, buccal distance from matrix to bone; LMB, lingual distance from matrix to bone; W, matrix width; B, buccal; L, lingual; A, apical; O, occlusal

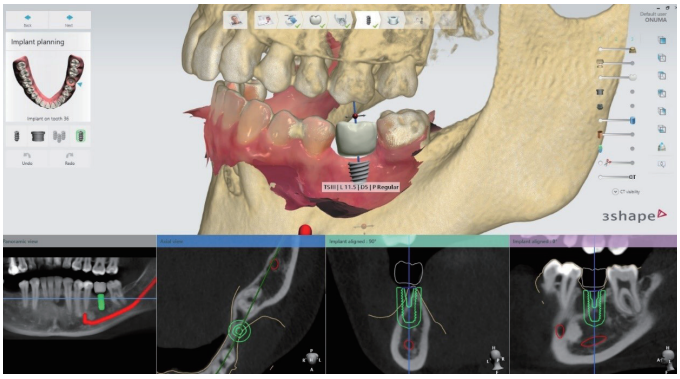

Fig. 2 Initial diagnosis of ridge defect and treatment planning through virtual crown wax-up and implant placement before augmentation

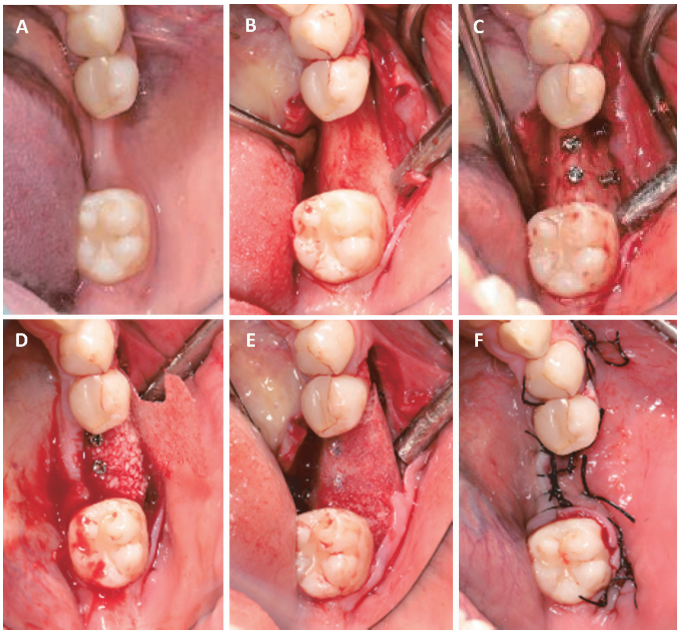

Fig. 3 Surgical procedure of alveolar ridge augmentation at site # 36

2019. It was approved by the Khon Kaen University Ethics Committee for Human Research (HE592276). The inclusion criteria were as follows: (1) Adults (ASA I-II) aged 20-70 years old, (2) one-/two-tooth combined ridge defects at the posterior mandible, (3) edentulous ridge width (RW) <6.0 mm, (4) ridge height defect ranging from 2.0 to 4.0 mm on cone beam computed tomography (CBCT), (5) sufficient three-dimensional space for screw-retained implant restoration, and (6) good periodontal conditions and oral hygiene. Individuals with a health condition or an unhealthy life style for bone healing or metabolism, including head/neck malignancy and related chemoradiotherapy, long-term immune diseases and therapies, severe osteoporosis (≥2 fragility fractures), intravenous bisphosphonate therapy (≥5 years), and heavy smoking (≥10 cigarettes/day), were excluded. For those with two-tooth ridge defect, only the mesial defect site was considered for assessing bone augmentation and implant placement. All the eligible subjects were required to sign a written informed consent before study participation.

PPE membrane preparation

The PPE membrane was prepared as described previously [21,22]. Briefly, the mixture of high-density polyethylene (Thaizex 7000F, Bangkok Polyethylene Co., Ltd., Bangkok, Thailand), maltodextrin (Shandong Duqing, Inc., Heze, P. R. China), and polyvinyl alcohol (Sigma-Aldrich Inc., Natick, MA, USA), was prepared at a ratio of 70:20:10 w/w. The mixture was loaded in the mold and heated at 145°C for 45 min using a wet salt bed technique to produce both low- and high-porosity surfaces in single membrane with a dimension of 60 × 40 × 0.3 mm^3. All the membrane samples were sterilized with ethylene oxide gas prior to usage.

Alveolar ridge dimension evaluation

Alveolar ridge dimensions were measured by an experienced surgeon (J. C. S) with a calibrated periodontal probe UNC 15 (Hu-Friedy, Chicago, IL, USA) before and after ridge augmentation. The keratinized mucosa width (KW) was measured as the distance from the mid-crest to buccal mucogingival junction. The ridge width (RW) was measured as the buccolingual ridge width at the crest. The ridge height (RH) was measured as the vertical distance from the vestibular sulcus to the crest. All three variables were measured at the mesiodistal midpoint before incision.

In order to ensure the same anatomical locations for intraoperative ridge dimension measurements before and after augmentation, a clear measurement matrix was preoperatively fabricated with two parallel buccolingual walls perpendicular to an occlusal wall. A hole at the geometric center of the occlusal wall and two buccolingual coaxial holes at 14.0 mm apical to the occlusal wall were prepared with a diameter of 1.0 mm on the middle cross-section of the edentulous area (Fig. 1A). The occlusal hole was used to measure the vertical distance from the matrix to the bony crest (DMB), while two buccolingual holes were utilized to measure the horizontal distances between the buccolingual walls to the bone plates (BMB, LMB). Then, the horizontal alveolar width (HAW) was calculated by subtracting the BMB and LMB from the predetermined matrix width (W), HAW = W − BMB − LMB. The horizontal and vertical bone gains (ΔHAW, ΔDMB) were calculated as the differences of the ridge dimensions before and after augmentation, $\Delta HAW = HAW_2 - HAW_1$ or, $\Delta DMB = DMB_2 - DMB_1$ (Fig. 1B).

Alveolar ridge augmentation

Prior to augmentation surgery, the initial digital impression data acquired using a 3D intraoral scanner (3Shape A/S, Copenhagen, Denmark) and the CBCT data (Acteon, Mérignac, France) were aligned in an implant-planning program (3Shape A/S). A virtual diagnosis wax-up of the crown was fabricated, and a virtual implant was inserted within the edentulous area following the prosthesis-driven principle. Thus, the ridge defect was identified and diagnosed (Fig. 2), and a primary treatment plan of alveolar ridge augmentation and staged implant placement was developed.

All the surgeries were executed and managed by a panel of two surgeons. Subjects were given a prophylaxis antibiotic (amoxicillin, 1 g; those who were allergic were given clindamycin, 450 mg) and an analgesic (ibuprofen, 400 mg) 30 min before the surgery. The procedure was conducted under local anesthesia. The KW_1, RW_1, and RH_1 were recorded. A mid-crestal and intra-sulcus incision was made and extended beyond one or two teeth at both the ends as necessary. The intact buccolingual full-thickness flaps were gently elevated to access the augmentation site. The soft tissue remnants on the crest were thoroughly curetted. The measurement matrix was then positioned, and the HAW_1 and DMB_1 were recorded. The augmentation bed was decorticated with a small high-speed round bur under

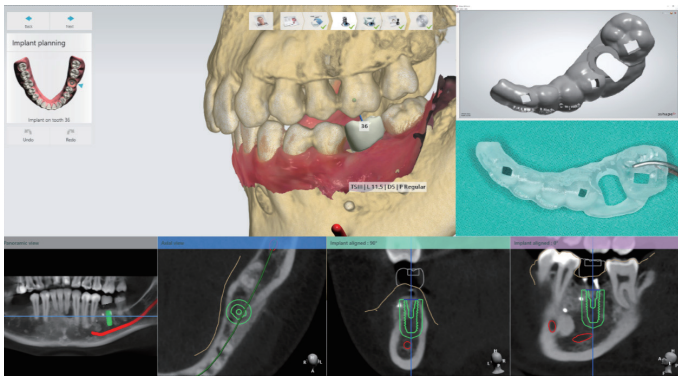

Fig. 4 Virtual implant planning and surgical stent preparation after ridge augmentation

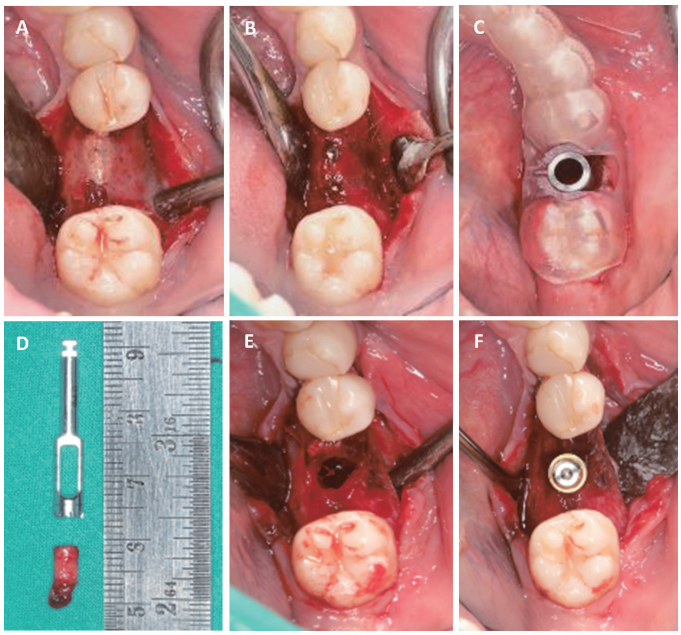

Fig. 5 Surgical procedure of staged implant placement at site # 36

copious saline irrigation. The PPE membrane was tailored with a plastic template to ensure a distance of at least 1.0 mm from the adjacent roots and placed with low-porosity side outwards. The membrane was first fixed with 4.0-mm titanium miniscrews (Jeil Medical Corp., Seoul, Republic of Korea) at the buccoapical site and gently shaped to contain the bone substitute within the augmentation site. In some cases, two to four miniscrews were used for tenting beneath the membrane. Freeze-dried cortical bone allograft granules (HansBiomed Corp., Daejeon, Republic of Korea) with a particle size ranging 200-850 μm were appropriately packed into the augmentation bed after saline rehydration. The membrane was then overlaid into the lingual site and fixed with miniscrews. The buccal flap was subtly managed by making an L-shaped mucoperiosteal incision and full subperiosteal release with a sharp scalpel to get primary tension-free closure. The incision was firmly closed with sequential horizontal mattress and interrupted sutures (Fig. 3). The subjects were prescribed oral antimicrobial prophylaxis (amoxicillin, 1 g, bid; or if allergic, clindamycin, 300 mg, qid; and metronidazole, 600 mg, bid) for 10-14 days and painkiller (ibuprofen, 400 mg) as needed. They were instructed to maintain good oral hygiene using 0.12% chlorhexidine mouthwash twice daily for at least two weeks. They were called again for clinical evaluation of wound healing and suture removal at two weeks.

Implant placement

Bone regeneration was assessed using repeat CBCT scanning after a consolidation stage. A second digital intraoral impression was also taken and aligned with current CBCT in the implant-planning program. An implant treatment plan was thus developed by the team, and the implant dimensions were determined. Based on current implant planning, a tooth-borne surgical stent was virtually designed, and printed using a 3D printer with a clear resin (Detax GmbH & Co. KG, Ettlingen, Germany) (Fig. 4).

The implant surgery was conducted under local anesthesia. The KW_2, RW_2, and RH_2 were measured before the incision. The same incision was made, and the flaps were reflected as in the augmentation surgery. All the miniscrews and PPE membranes were gently removed. The clear matrix was seated to measure the HAW_2 and DMB_2. The surgical stent was then positioned in place. A metal sleeve adaptor was inserted onto the guide hole of the surgical stent to collimate a trephine for biopsy bone core harvesting before osteotomy preparation. The bone core was immersed in 10% neutral buffered formalin. The implant osteotomy was further prepared with a guided surgery kit (Hiossen Implant Co., Ltd, Englewood Cliffs, NJ, USA), as instructed. The implant fixture (Osstem Implant Co., Ltd, Seoul, Republic of Korea) was then fully guided for proper installation with the aid of a surgical stent (Fig. 5). The initial implant stability quotient (ISQ) was measured with a resonance frequency device (Osstell AB, Gothenburg, Sweden). Thereafter, a cover screw was immediately connected, and the flaps were closed using simple suturing. These subjects were given the same regimen of postoperative medication and wound care as that for augmentation surgery.

Histological examination

Fourteen cylindrical bone cores were harvested at re-entry for implant placement, while only a block mass within the augmentation site was curetted for histological analysis at debridement for one subject who was diagnosed to have GBR failure. All the specimens were decalcified in 10% nitric acid. Then, they were buccolingually hemi-sectioned and embedded in paraffin. Three consecutive sections were prepared and stained with haematoxylin and eosin (H&E). The histological slices were analyzed using an optical microscopy (Nikon Corp., Tokyo, Japan).

Statistical analyses

Statistical analyses were performed with SPSS Statistics version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). Shapiro-Wilk test revealed that all the outcome measured variables were normally distributed except RW. Thus, Wilcoxon signed rank test was used to compare the RW, while paired *t*-test was applied to compare other variables (KW, RH, HAW and DMB) between, before, and after ridge augmentation. Significance level (α) was set at 0.05.

Results

Table 1 summarizes the demographic and clinical data of the subjects. Fifteen eligible subjects, including 10 men and 5 women, with a mean age of 52 ± 11 years (range 32-66 years) were enrolled. They were all classified as ASA I and were well tolerant of intraoral surgeries. The ridge defects included 13 single-tooth and 2 two-tooth defects in the posterior mandible. They were all diagnosed with combined ridge defects. No subjects dropped out during the study.

Clinical assessment

Allograft with a mean volume of 0.5 ± 0.1 mL (range 0.3-0.7 mL) was intraoperatively used, depending on defect size. After augmentation, all the ridge defects turned to normal ridges, except in Case 2, wherein it remained a combined defect due to GBR failure and in Case 12, wherein it became a vertical defect.

The alveolar ridge dimensions before and after augmentation were summarized in Table 2. Although the mean KW and RH increased by 0.2 mm and 0.9 mm, respectively, there were no significant differences in both the values between before and after augmentation ($P > 0.05$). In contrast, the mean RW and HAW significantly increased by 4.8 mm and 2.3 mm, respectively ($P \leq 0.001$). The mean DMB significantly decreased by 1.0 mm, indicating a vertical bone gain after augmentation ($P < 0.001$).

Endosseous implants with diameter 4.5 ± 0.5 mm (range 3.5-5.0 mm) and 10.4 ± 1.2 mm in length (range 8.5-11.5 mm) were successfully placed with a mean initial ISQ value of 75.1 ± 7.8 (range 60-86) (Table 1).

The complications encountered after augmentation included early wound dehiscence (3/15), membrane exposure/extrusion (9/15), miniscrew loosening/extrusion (7/15), minor local infection (10/15), mild mental nerve paresthesia (3/15), and wound hemorrhage (1/15). In case of

Table 1 Demographic and clinical data of all 15 subjects

Patient No.	Age (years)	Sex	Defect site	Pre-augmentation defect type	Post-augmentation defect type	Allograft use (mL)	Membrane action period (month)	Consolidation period (month)	Implant diameter (mm)	Implant length (mm)	Initial ISQ
1	48	F	# 36	combined	normal	0.4	2.7	8.0	3.5	11.5	65
2	62	M	# 46	combined	combined	0.4	6.0	8.0	4.5	8.5	85
3	59	F	# 46	combined	normal	0.5	9.0	9.0	5.0	11.5	79
4	59	M	# 46	combined	normal	0.4	1.0	7.0	4.5	10.0	69
5	56	F	# 36	combined	normal	0.3	4.4	6.0	5.0	8.5	86
6	65	F	# 36, 37	combined	normal	0.7	2.5	7.5	4.0	10.0	82
7	61	M	# 46	combined	normal	0.7	4.6	7.0	5.0	10.0	80
8	34	M	# 36	combined	normal	0.3	2.4	9.0	4.0	11.5	75
9	66	M	# 36, 37	combined	normal	0.5	7.0	7.0	5.0	11.5	75
10	52	M	# 36	combined	normal	0.7	7.0	7.0	4.0	10.0	66
11	54	M	# 36	combined	normal	0.5	3.0	7.0	4.0	10.0	70
12	47	M	# 46	combined	vertical	0.7	6.0	6.7	5.0	8.5	60
13	35	M	# 34	combined	normal	0.4	4.3	4.3	4.0	11.5	73
14	50	M	# 46	combined	normal	0.5	4.0	4.0	5.0	11.5	80
15	32	F	# 36	combined	normal	0.5	4.5	4.5	5.0	11.5	82
	52 ± 11					0.5 ± 0.1	4.6 ± 2.1	6.8 ± 1.5	4.5 ± 0.5	10.4 ± 1.2	75.1 ± 7.8

F, female; M, male; cc, cubic centimeter; ISQ, implant stability quotient

Table 2 Comparisons of alveolar ridge dimensions before and after augmentation (n = 15)

Variable	Stage	Min	Max	Median	Mean (SD)	Mean difference (SD)	P value
KW	KW_1	1.5	5.0	3.0	3.3 (1.1)	0.2 (1.4)	0.517
	KW_2	1.0	6.0	3.5	3.5 (1.5)		
RW*	RW_1	2.0	5.0	3.0	3.1 (0.9)	4.8 (1.6)	0.001
	RW_2	6.0	11.0	7.0	7.9 (1.8)		
RH	RH_1	2.0	12.0	7.0	7.4 (3.0)	0.9 (2.3)	0.160
	RH_2	4.0	15.0	8.0	8.3 (2.8)		
HAW*	HAW_1	0	7.0	3.0	2.9 (2.0)	2.3 (1.7)	<0.001
	HAW_2	0	11.5	5.5	5.2 (3.1)		
DMB*	DMB_1	9.0	14.0	13.0	12.6 (1.4)	−1.0 (0.8)	<0.001
	DMB_2	8.0	14.0	12.0	11.6 (1.7)		

SD, standard deviation; KW, keratinized mucosa width; RW, ridge width; RH, ridge height; HAW, horizontal alveolar width; DMB, distance between matrix to bone. The subscripts 1 and 2 indicate before and after augmentation, respectively. *Statistically significant difference between before and after ridge augmentation. The units for all variables were millimeter (mm).

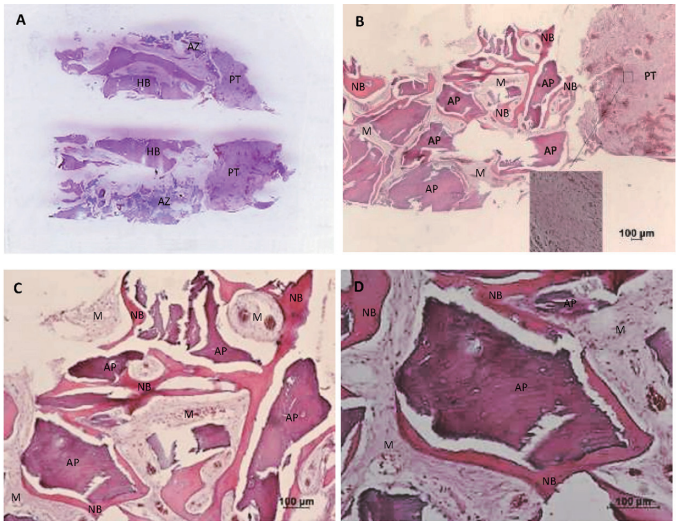

Fig. 6 Typical histological sections from mature subgroup. (A) Slice overview showing the host bone (HB), periosteum-like tissue (PT), and augmentation zone (AZ). (B) Magnified view showing a thick layer of periosteum-like tissue (PT) consisting of collagenized fibrous tissue with slight inflammatory infiltration (inserted image), fibrovascular marrow (M), allograft particles (AP), and new bone (NB). (C) Magnified view of augmentation zone. (D) High-magnification view demonstrating the peripheral resorption of allograft particles (AP) and subsequent apposition of new bone (NB). (H&E stain, original magnification: B, ×40; C, ×100; D, ×200)

infection, the miniscrews and membranes were removed in one or multiple steps, depending on the infection scope and severity. In a stepwise strategy, the occlusal and buccolingual membrane fragments were sequentially removed to retain the noninfected allografts. The augmentation sites were properly debrided followed by local and systemic anti-infection therapies according to current guidelines, and all subjects achieved secondary healing. Subject 2 experienced uneventful soft tissue healing within postoperative 6 months. However, no new bone was seen; however, only a block mass of inflammatory granulation tissue was found within the augmentation site beneath membrane. The subject was thus diagnosed with GBR failure. The site was properly debrided for uneventful secondary healing, and a short regular implant was placed 2 months thereafter. After active treatment, the nerve paresthesia in 3 subjects disappeared at the time of implant placement. The wound hemorrhage was properly managed at an emergent recall.

PPE membranes in 9 cases had to be prematurely removed before re-entry for implant placement (premature subgroup) owing to complications and GBR failure. This premature subgroup had a mean membrane action period of 3.6 ± 1.7 months (range 1.0-6.0 months) and a mean consolidation period of 7.4 ± 0.9 months (range 6.0-9.0 months). In contrast, the PPE membranes in the remaining 6 cases were retained until re-entry (mature subgroup) with a mean action period of 6.0 ± 2.0 months (range 4.0-9.0 months) and a mean consolidation period of 6.0 ± 2.0 months (range 4.0-9.0 months). Uneventful wound healing after implant surgery was achieved in all the subjects.

Histological analyses

Residual allograft particles were observed in 9 of the 14 bone cores, including 6 from the mature subgroup and 3 from the premature subgroup. They were usually found at the buccal and/or occlusal sides of the slices. For those from the mature subgroup, the specimens mainly consisted of host bone, fibrovascular marrow, allograft, and surrounding new viable bone, and a thick overlying layer of periosteum-like tissue. This periosteum-like tissue consisted of a large amount of compact collagenized fibrous tissue with a slight inflammatory infiltrate of plasma cells, lymphocytes, and histiocytes (Fig. 6A, B). For those from the premature subgroup, the specimens mainly consisted of host bone, fibrovascular marrow, allograft, and a thin overlying layer of trabecular bone that was newly developed from the periosteum-like tissue instead. Under high magnification, the allograft particles in the augmentation zone of both the subgroups demonstrated non-vital, darkly stained bone spicules, some peripheral areas of which showed resorption with simultaneous apposition of layers of newly formed, viable

trabecular bone. This active bone remodeling was characterized with the presence of newly regenerated bone tissue surrounding the allograft, varying amounts of multi-nucleated osteoclasts within Howship's lacunae at the jagged interface, and large young osteocytes with prominent nuclei within the new bone (Fig. 6C, D).

For the remaining 5 bone cores from the premature subgroup, only host bone tissue was observed under both low and high magnifications. Neither residual allograft nor periosteum-like tissue was observed.

For the GBR failure subject, the specimen consisted of inflammatory granulation tissue only. No residual allograft, new bone, or host bone was observed. Under high magnification, large numbers of newborn capillaries and chronic inflammatory infiltrates of the plasma cells and lymphocytes were found to diffusely distribute.

Discussion

GBR is an efficient and predictable procedure for alveolar ridge augmentation. Its success relies considerably upon the correct selection and application of an appropriate barrier membrane. Absorbable membranes are widely used because there is no need for secondary surgical removal; however, they degrade rapidly, lack stiffness, and may cause osteolysis for acidic products during degradation. In contrast, nonabsorbable membranes can provide better space maintenance for sufficient duration owing to its greater stiffness and nonabsorbable nature that would help predictable bone regeneration, especially in clinically challenging vertical and large ridge defects. From the clinical perspective, in this study, the tight soft tissue adhesion and attachment to PPE membrane observed at re-entry indicate its good biocompatibility and tissue integration that in turn enhance postoperative membrane stability. This feature may be attributed to the specific 2D and 3D pore microstructures characterized previously [22]. These pores not only facilitate transmembrane transport of blood supply, nutrients, oxygen, and thus bone regeneration, but also enable cell occlusiveness. In addition, PPE membrane provided easy intraoperative tailoring and shaping, indicating its good clinical manageability.

For ridge augmentation using barrier membranes, especially the rigid non-absorbable membranes, sufficient subperiosteal tissue release and crestal advancement were usually needed for tension-free wound closure due to the increased ridge volume, leading to a decrease of keratinized mucosa width [23]. Out of 15 subjects in this study, 5 exhibited reduction in KW to various degrees, ranging from 0.5-2.5 mm, with one subject showing 1.0-mm KW after augmentation. These could be due to the insufficient keratinized mucosa at baseline and/or surgical intervention, as mentioned [23]. However, the mean KW generally increased slightly (0.2 mm) in this study; this might be attributed to the proliferation of scar tissue during wound healing and/or the expansion of the augmented ridge. Although the efficacy of adequate KW (>2.0 mm) on implant success is controversial, it is generally believed to be beneficial for maintaining long-term peri-implant tissue health and oral hygiene following rehabilitation [24-26]. Wound/flap design modifications and/or peri-implant soft tissue augmentation were reported to be efficient for increasing the KW in such subjects [27-29].

Although no significant difference was found in RH, the mean RH increased by 0.9 mm after augmentation, comparable to a normal vestibular depth. The increase might be attributed to the joint effect of intraoperative subperiosteal tissue release, crestal flap advancement, and vertical bone gain and would be helpful for improving vestibular morphology, oral hygiene, cosmetics, prosthetic functionality, and peri-implant tissue health [30]. In contrast, the mean RW significantly increased from 3.1 mm to 7.9 mm. The mean width gain (4.8 mm) at crest in this study was much higher than that in two similar clinical trials using e-PTFE and polyglycolic acid/trimethylene carbonate (PGA/TMC) membranes, 2.7 mm and 2.8 mm respectively [31,32]. When comparing the RW at an approximate alveolar level (14.0 mm apical to the occlusal plane in this study vs. 4.0 mm apical to the alveolar crest in other study [32]), the mean ΔHAW was comparatively close (2.3 ± 1.7 mm vs. 3.1 ± 1.9 mm).

Considering the preoperative knife-edge crest shape, remodeling of the allograft was mostly visible at the buccal slice margin. The standard implants with diameter 4.5 ± 0.5 mm were successfully placed into augmented ridges with good initial stability (mean ISQ = 75.1). Previously, at least 1.5 mm buccolingual bone was recommended for single implant placement [33]. The mean 4.8-mm RW increase at crest and 2.3-mm HAW increase at 14.0 mm apical to the occlusal plane were thus sufficient, and both were mainly attributed to bone augmentation. In addition, the significant vertical bone gain (ΔDMB = −1.0 mm) enabled safe placement of the standard implants of 10.4 ± 1.2 mm in length without any morbidities. These findings indicated that the GBR procedure using PPE membrane and allograft had achieved the primary objective of ridge augmentation for staged implant placement.

It is noteworthy that the GBR procedure using a nonabsorbable barrier membrane is technically-challenging for the lateral, and especially vertical or combined ridge augmentations [34]. Compared with other studies on vertical GBR using nonabsorbable membranes, the PPE membrane caused a higher rate of healing complications. However, the incidences of other complications (i.e. early wound dehiscence, sensory and vascular disorders) were comparable to those in previous reports [35]. Multiple factors, such as defect type and size, mucogingival biotype, surgical protocol and technique, surgeon skill, habituation, soft tissue management, membrane stiffness and patient compliance, might be associated with the occurrence of complications and GBR failure.

When the membrane rescues did not work, the PPE membranes were removed in a stepwise manner to avoid complete augmentation failure. This management strategy was slightly different from the routine complete membrane removal as recommended [12]. This stepwise manner might have contributed to the significant increases of both RW and HAW for maximal allograft preservation at buccocclual sites. Then, a mean ΔHAW of 2.3 mm was obtained that was comparable to the use of an autograft and a resorbable collagen barrier plus osteosynthesis plate (2.2 mm) or a titanium-reinforced e-PTFE membrane (2.5 mm) [36]. However, most subjects (6/9) with allograft and new bone visible in histological slices came from the mature subgroup. They usually had uneventful wound healing with no or fewer complications. In contrast, the remaining six subjects with only host bone or granulation tissue visible, usually had eventful healing and premature membrane removal for various severe complications or GBR failure. Furthermore, when considering the bone gains between two subgroups, the premature subgroup showed much less horizontal and vertical bone gains (premature vs. mature: ΔHAW 1.6 ± 1.7 mm vs. 3.4 ± 1.0 mm; ΔDMB −0.5 ± 0.6 mm vs. −1.8 ± 0.5 mm; not reported above). These coincident clinical and histological findings could be correlated to the different mean membrane action periods (3.6 vs. 6.0 months) and action/consolidation ratios (3.6/7.4 vs. 6.0/6.0) between the two subgroups. It revealed the importance of sufficient uneventful tissue healing and consolidation under the effective protection of barrier membrane for the success of ridge augmentation.

The dominant buccal ridge atrophy in combined ridge defect, the corresponding ridge augmentation at buccocclusal site, and the earlier occlusal membrane removal and graft debridement in a stepwise manner might partially explain why the allograft was observed mainly at the buccal side of the histological slices in 9 subjects. The later buccolingual membrane removal might have rescued the corresponding allograft and new bone, leading to significant increases in RW and HAW. A thick layer of periosteum-like tissue was usually observed beneath the PPE membrane in the mature subjects similar to that in other studies that used nonabsorbable membranes [37,38]. This tissue was found to transform into a thin layer of developing trabeculae over allograft after membrane removal in some premature subjects. In addition, some allograft particles were observed to be surrounded by a thin layer of active remodeling trabeculae. This periosteum-like tissue was speculated to develop due to membrane micromotion, air encapsulation, anoxia, graft shrinkage, and collapse during consolidation, and potentially transform into normal bone tissue if the consolidation period was adequate [37,38]. In contrast, allograft invisibility in the remaining 5 subjects might be attributed to less severe buccal ridge defect at baseline and corresponding augmentation, and/or aggressive allograft removal during debridement.

In this study, the tenting screws were used to support and stabilize the PPE membranes only in the last few cases that achieved better bone regeneration with fewer complications. This indicated that the PPE membrane could not provide sufficient stiffness to maintain the space for predictable bone regeneration. This could lead to early wound dehiscence, membrane micromotion, extrusion, exposure, and collapse during mastication that could lead to local infection or even GBR failure, as observed. Therefore,

further PPE membrane modifications, additional use of tenting screws/osteosynthesis plates, and simultaneous implant placement, could be considered when PPE membrane is used in challenging situations, such as intractable large and vertical bone defects.

Within the limitations of this study, it was found that the alveolar ridge augmentation via GBR using PPE membrane and allograft could significantly increase the horizontal and vertical ridge dimensions in the posterior mandible for staged implant placement. The PPE membrane could possibly be employed as a viable alternative to current barrier membranes for GBR if efficient actions are taken to reduce the potential complications. However, further randomized controlled trials are needed to establish a definitive conclusion.

Acknowledgments

This research was jointly supported by the 30th Anniversary of Faculty of Dentistry Khon Kaen University Research Funding (DTR6001), the Khon Kaen University Graduate School Thesis Support Scholarship (No.59212101), and the Neuroscience Research and Development Group, Khon Kaen University, Thailand.

Conflict of interest

Jintamai Suwanprateeb was the principal investigator for the research and development of the PPE membrane, and had a patent (No.1601002490) pending. There was no any conflict of interest with all commercial products mentioned and among all the authors.

References

1. Hansson S, Halldin A (2012) Alveolar ridge resorption after tooth extraction: a consequence of a fundamental principle of bone physiology. J Dent Biomech 3, 1-8.
2. Van der Weijden F, Dell'Acqua F, Slot DE (2009) Alveolar bone dimensional changes of post-extraction sockets in humans: a systematic review. J Clin Periodontol 36, 1048-1058.
3. Tan WL, Wong TL, Wong MC, Lang NP (2012) A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clin Oral Implants Res 23, 1-21.
4. Esposito M, Grusovin MG, Coulthard P, Worthington HV (2006) The efficacy of various bone augmentation procedures for dental implants: a Cochrane systematic review of randomized controlled clinical trials. Int J Oral Maxillofac Implants 21, 696-710.
5. Rosen PS, Reynolds MA (2001) Guided bone regeneration for dehiscence and fenestration defects on implants using an absorbable polymer barrier. J Periodontol 72, 250-256.
6. Sverzut CE, Faria PE, Magdalena CM, Trivellato AE, Mello-Filho FV, Paccola CA et al. (2008) Reconstruction of mandibular segmental defects using the guided-bone regeneration technique with polylactide membranes and/or autogenous bone graft: a preliminary study on the influence of membrane permeability. J Oral Maxillofac Surg 66, 647-656.
7. Binsalah MA, Ramalingam S, Alkindi M, Nooh N, Al-Hezaimi K (2018) Guided bone regeneration of femoral segmental defects using equine bone graft: an in-vivo micro-computed tomographic study in rats. J Invest Surg 5, 1-11.
8. Scantlebury TV (1993) 1982-1992: a decade of technology development for guided tissue regeneration. J Periodontol 64, 1129-1137.
9. Di Stefano DA, Greco GB, Cinci L, Pieri L (2015) Horizontal-guided bone regeneration using a titanium mesh and an equine bone graft. J Contemp Dent Pract 16, 154-162.
10. Elgali I, Omar O, Dahlin C, Thomsen P (2017) Guided bone regeneration: materials and biological mechanisms revisited. Eur J Oral Sci 125, 315-337.
11. Wessing B, Lettner S, Zechner W (2018) Guided bone regeneration with collagen membranes and particulate graft materials: a systematic review and meta-analysis. Int J Oral Maxillofac Implants 33, 87-100.
12. Dimitriou R, Mataliotakis GI, Calori GM, Giannoudis PV (2012) The role of barrier membranes for guided bone regeneration and restoration of large bone defects: current experimental and clinical evidence. BMC Med 10, 81.
13. Ku Y, Shim IK, Lee JY, Park YJ, Rhee SH, Nam SH et al. (2009) Chitosan/poly(L-lactic acid) multilayered membrane for guided tissue regeneration. J Biomed Mater Res A 90, 766-772.
14. Lu J, Cheng C, He YS, Lyu C, Wang Y, Yu J et al. (2016) Multilayered graphene hydrogel membranes for guided bone regeneration. Adv Mater 28, 4025-4031.
15. Klawitter JJ, Bagwell JG, Weinstein AM, Sauer BW (1976) An evaluation of bone growth into porous high density polyethylene. J Biomed Mater Res 10, 311-323.
16. Spector M, Flemming WR, Kreutner A (1976) Bone growth into porous high-density polyethylene. J Biomed Mater Res 10, 595-603.
17. Li S, Burstein AH (1994) Ultra-high molecular weight polyethylene. The material and its use in total joint implants. J Bone Joint Surg Am 76, 1080-1090.
18. Rai A, Datarkar A, Arora A, Adwani DG (2014) Utility of high density porous polyethylene implants in maxillofacial surgery. J Maxillofac Oral Surg 13, 42-46.
19. Fernandez-Bueno I, Di Lauro S, Alvarez I, Lopez JC, Garcia-Gutierrez MT, Fernandez I et al. (2015) Safety and biocompatibility of a new high-density polyethylene-based spherical integrated porous orbital implant: an experimental study in rabbits. J Ophthalmol 2015, doi: 10.1155/2015/904096.
20. Swords GA, Spagnoli DB (2016) Bone graft material containment structures. US Patent 9433707 B2, Sep 6.
21. Suwanprateeb J, Thammarakcharoen F, Suvannapruk W (2013) Preparation and characterization of 3D printed porous polyethylene for medical applications by novel wet salt bed technique. Chiang Mai J Sci 41, 200-212.
22. Song JC, Suwanprateeb J, Sae-Lee D, Sosakul T, Pitiphat W, Prajaneh S et al. (2019) 2D and 3D pore structure characterization of bi-layered porous polyethylene barrier membrane using SEM and Micro-CT. ScienceAsia 45, 159-171.
23. Frisch E, Ratka-Krüger P, Ziebolz D (2015) Increasing the width of keratinized mucosa in maxillary implant areas using a split palatal bridge flap: surgical technique and 1-year follow-up. J Oral Implantol 41, e195-e201.
24. Lin GH, Chan HL, Wang HL (2013) The significance of keratinized mucosa on implant health: a systematic review. J Periodontol 84, 1755-1767.
25. Pranskunas M, Poskevicius L, Juodzbalys G, Kubilius R, Jimbo R (2016) Influence of peri-implant soft tissue condition and plaque accumulation on peri-implantitis: a systematic review. J Oral Maxillofac Res 7, e2.
26. Araujo MG, Lindhe J (2018) Peri-implant health. J Clin Periodontol 45 Suppl 20, S230-S236.
27. Reddy VK, Parthasarathy H, Lochana P (2013) Evaluating the clinical and esthetic outcome of apically positioned flap technique in augmentation of keratinized gingiva around dental implants. Contemp Clin Dent 4, 319-324.
28. Bruschi GB, Crespi R, Capparé P, Gherlone E (2014) Clinical study of flap design to increase the keratinized gingiva around implants: 4-year follow-up. J Oral Implantol 40, 459-464.
29. Thoma DS, Naenni N, Figuero E, Hämmerle CHF, Schwarz F, Jung RE et al. (2018) Effects of soft tissue augmentation procedures on peri-implant health or disease: a systematic review and meta-analysis. Clin Oral Implants Res 29 Suppl 15, 32-49.
30. Kao SY, Lui MT, Fong J, Wu DC, Wu CH, Tu HF et al. (2005) A method using vestibulosulcoplasty combining a split-thickness skin graft and a palatal keratinized mucosa graft for peri-implant tissue secondary to oral cancer surgery. J Oral Implantol 31, 186-191.
31. Chiapasco M, Abati S, Romeo E, Vogel G (1999) Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. Clin Oral Implants Res 10, 278-288.
32. Geurs NC, Korostoff JM, Vassilopoulos PJ, Kang TH, Jeffcoat M, Kellar R et al. (2008) Clinical and histologic assessment of lateral alveolar ridge augmentation using a synthetic long-term bioabsorbable membrane and an allograft. J Periodontol 79, 1133-1140.
33. Shenoy VK (2012) Single tooth implants: pretreatment considerations and pretreatment evaluation. J Interdiscip Dentistry 2, 149-157.
34. Fontana F, Maschera E, Rocchietta I, Simion M (2011) Clinical classification of complications in guided bone regeneration procedures by means of a nonresorbable membrane. Int J Periodontics Restorative Dent 31, 265-273.
35. Elnayef B, Monje A, Gargallo-Albiol J, Galindo-Moreno P, Wang HL, Hernández-Alfaro F (2017) Vertical ridge augmentation in the atrophic mandible: a systematic review and meta-analysis. Int J Oral Maxillofac Implants 32, 291-312.
36. Merli M, Migani M, Esposito M (2007) Vertical ridge augmentation with autogenous bone grafts: resorbable barriers supported by ostheosynthesis plates versus titanium-reinforced barriers. A preliminary report of a blinded, randomized controlled clinical trial. Int J Oral Maxillofac Implants 22, 373-382.
37. Simion M, Jovanovic SA, Tinti C, Benfenati SP (2001) Long-term evaluation of osseointegrated implants inserted at the time or after vertical ridge augmentation. A retrospective study on 123 implants with 1-5 year follow-up. Clin Oral Implants Res 12, 35-45.
38. Gutta R, Baker RA, Bartolucci AA, Louis PJ (2009) Barrier membranes used for ridge augmentation: is there an optimal pore size? J Oral Maxillofac Surg 67, 1218-1225.