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ORIGINAL RESEARCH

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Randomized clinical trial comparing PEG-based synthetic to porcine-derived collagen membrane in the preservation of alveolar bone following tooth extraction in anterior maxilla

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Abstract

Objectives: The objective of this randomized controlled trial was to compare alveolar ridge preservation using a bone substitute material and covered with a synthetic or porcine collagen membrane.

Materials and methods: Thirty-two sockets in the aesthetic maxillary region of 30 patients were randomized into two groups. Randomization was stratified according to bone wall defect. Flapless technique was used, and sockets were grafted with bi-phasic calcium phosphate particulate bone substitute and covered by synthetic polyethylene glycol (PEG; test group) or porcine-derived collagen membrane (CM; control group). No primary closure was attempted. A cone beam computed tomography (CBCT) scan was performed immediately after the surgical procedure and repeated 22 weeks later. OnDemand3D was used to superimpose scan images and assess changes. The mean vertical and horizontal percentage bone loss were calculated and implants placed after 6 months with or without additional augmentation.

Results: There were no baseline differences between groups or dropouts. The mean percentage loss at the labial plate and at the coronal part of the sockets was statistically significantly lower in the test group compared with controls (−2.86% [*SD* = 13.48] versus 7.42% [*SD* = 11.95]; 13.45% [*SD* = 11.97] versus 28.59% [*SD* = 16.97]). Implants were placed after 6 months, and there was no difference in need for further augmentation between PEG ($n = 5$) or CM ($n = 4$).

Conclusion: Sites treated with PEG membrane showed less percentage loss in horizontal and vertical measurements in this trial.

KEYWORDS

alveolar ridge preservation, bone implant interactions, bone regeneration, dental implant, guided bone regeneration, imaging, socket grafting

1 | INTRODUCTION

Following extraction of a tooth, a series of structural and dimensional changes occur to the alveolar ridge profile as the buccal and lingual bone crests migrate apically with more resorption reported on the buccal aspect (Araujo & Lindhe, 2005; Cardaropoli, Araujo, & Lindhe, 2003). These results are due to the fact that the buccal bone has proportionally more bundle bone, which is reliant on an existing tooth and its associated function and blood supply whilst the palatal aspect has relatively more lamellar bone with a proportionate increase in non-dental blood supply and is thus less influenced by the loss or removal of a tooth or teeth (Schropp, Wenzel, Kostopoulos, & Karring, 2003; Tan, Wong, Wong, & Lang, 2012).

This reduction in bone can have a significant impact if implant retained prosthesis is considered for replacement of the tooth. A number of techniques, grouped under the term "alveolar ridge preservation" (ARP) have been proposed to counteract this resorption and maintain alveolar ridge volume to allow for simplified implant surgical procedures and optimal aesthetics and function (Darby, Chen, & De Poi, 2008; Horvath, Mardas, Mezzomo, Needleman, & Donos, 2013; Ten Heggeler, Slot, & Van der Weijden, 2011; Vignoletti et al., 2012). Most of these methods make use of various biomaterials, with a selection of purported osteo-genetic, osteo-inductive or osteo-conductive properties. The materials are generally placed in the socket and either left exposed or covered with cell occlusive barrier membranes, soft tissue grafts or combinations of these to allow undisturbed healing and prevent soft tissue ingress (MacBeth, Trullenque-Eriksson, Donos, & Mardas, 2017).

Many studies have compared the various bone substitutes used within the socket (MacBeth et al., 2017). However, there is a dearth of literature that delves into the effects that the cell occlusive membrane plays in the overall success of these techniques. In recent years, synthetic polyethylene glycol (PEG) membrane was introduced as a synthetic biodegradable hydrogel that forms in situ after the two-component PEG solution is mixed and injected into the site. It has been demonstrated in animal and clinical studies that PEG membranes work as successfully as animal-derived collagen membranes in guided bone regeneration (GBR) simultaneous with implant placement, when augmenting bone defects on the buccal aspect of implants (Jung, Benic, Scherrer, & Hammerle, 2015; Jung et al., 2006; Thoma et al., 2009). Higher rates of delayed soft tissue healing or secondary dehiscence were seen in the PEG membrane group than collagen membrane group in one study (Thoma et al., 2009). This, however, had no impact on the eventual bone gain after 6 months. Spontaneous epithelialization of the dehisced membrane was reported; this would offer an obvious advantage when used in open sockets. Furthermore, less time was required for clinical handling and application of PEG membrane in comparison with the collagen membrane.

Although there is evidence to support the application of PEG membrane in simultaneous GBR with implant placement, its usage in ARP has not been reported previously. Therefore, the primary aim of this randomized controlled clinical trial was to compare percentages of vertical and horizontal alveolar ridge changes after 6 months of healing in extraction sockets grafted with bi-phasic calcium phosphate bone substitute and covered with, either porcine-derived collagen membrane (CM) or, synthetic polyethylene glycol (PEG) membrane. The secondary aim was to assess the number of sockets in each group that were suitable for implant placement and whether they required additional augmentation at the time of placement.

2 | MATERIALS AND METHODS

This was a prospective, double-blinded, single-centre randomized controlled clinical trial which complies with the CONSORT guidelines. Participants, CBCT image assessors and the team performing the data analyses were unaware of the membrane placed. The study protocol acquired ethical approval from the National Health Service (NHS) Research Authority (Registration number 12/LO/1014). The trial was conducted under the terms of the Declaration of Helsinki with regards to experimentation involving human subjects as well as the Global Harmonization Task Force Guidelines for Post Market Surveillance Studies and followed the requirements of Good Clinical Practice in the form of ISO 14155:2003.

Patients attending the Barts Health NHS Trust Hospital who required at least one tooth extraction in the aesthetic maxillary region (incisor, canine, first premolar) were invited to participate in the study. All participants were given a verbal and written outline explanation of the study, and they provided informed written consent. An oral examination was subsequently completed, and full medical and dental histories were recorded.

Inclusion criteria were as follows: (a) patients had to be 18 years or over in age; (b) requiring extraction of a single maxillary anterior tooth in the aesthetic zone due to caries, endodontic failure or trauma (including first premolars); (c) the extraction site had to have adjacent teeth present.

Exclusion criteria included (a) systemic disease that can interfere with dental implant therapy (e.g., uncontrolled diabetes); (b) adjacent teeth requiring extraction; (c) greater than one wall of the socket missing—assessed at time of extraction; (d) any contraindications for oral surgical procedures; (e) history of local irradiation therapy in the head-neck region; (f) mucosal diseases (e.g., erosive lichen planus); (g) current untreated periodontitis or gingivitis—in particular, probing depths of >3 mm on one of the teeth immediately adjacent to the extraction site; (h) smokers; (i) non-compliant patients; (j) pregnant or breastfeeding patients; (k) plaque scores >25%; (l) patients involved in current research or who had recently been involved in any research prior to recruitment.

The sample size calculation was based on change in bone width reported in the study conducted by Fiorellini and colleagues (Fiorellini et al., 2005), which demonstrated a mean increase in bone width after treatment with 1.50 mg/ml rhbmp-2/ACS of 3.97 mm ($SD = 2.48$) compared to placebo response of 1.79 mm ($SD = 1.68$). This suggested there could be a difference in means of approximately 2.2 mm. To find a difference of 2.2 mm in bone width between the

two groups with a standard deviation of 2.2, with a power of 80% at the 5% significance level, 32 sites (16 in each group) were needed.

Participants were randomized into a test or control group. The randomization process followed a stratified randomization technique in order to balance the groups for initial bone defects. It included two sets of computer-generated randomization slips created for sockets with no bone wall defect (NBD) or bone defect (BD). Sockets with no bone wall defect meant that they had intact bone walls. Sockets with bone defect meant that the buccal wall was not intact and had either a dehiscence or fenestration without any soft tissues defect. The dehiscence was defined when buccal bone below 3 mm of gingival margin was missing. Fenestration was defined as an isolated area with break of continuity of the buccal wall but where the marginal buccal bone was intact. Randomization

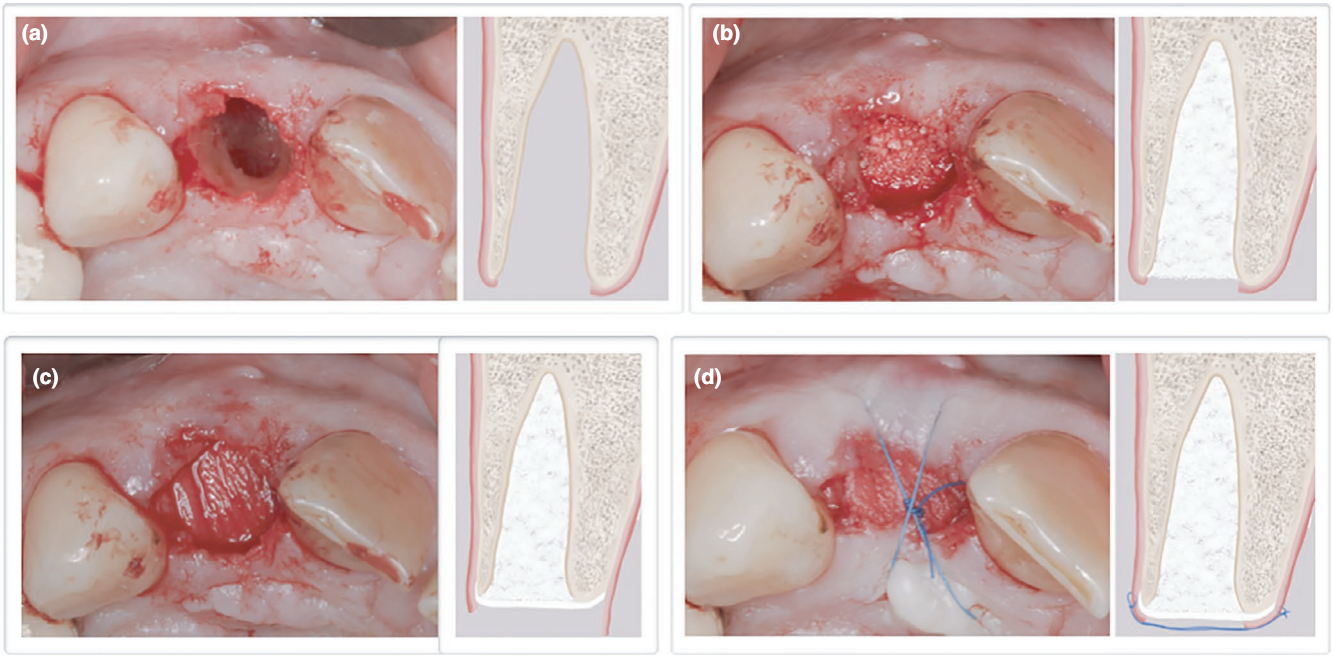

FIGURE 1 Collagen Membrane (CM) in extraction socket with no bone defect (NBD). (a) Alveolus cleaned; (b) Alveolus grafted with bone substitute 3mm below the gingival margin; (c) CM tucked into a pouch between the gingiva and the alveolar bone; (d) Cross suture showing a slight closure of the gingival edges

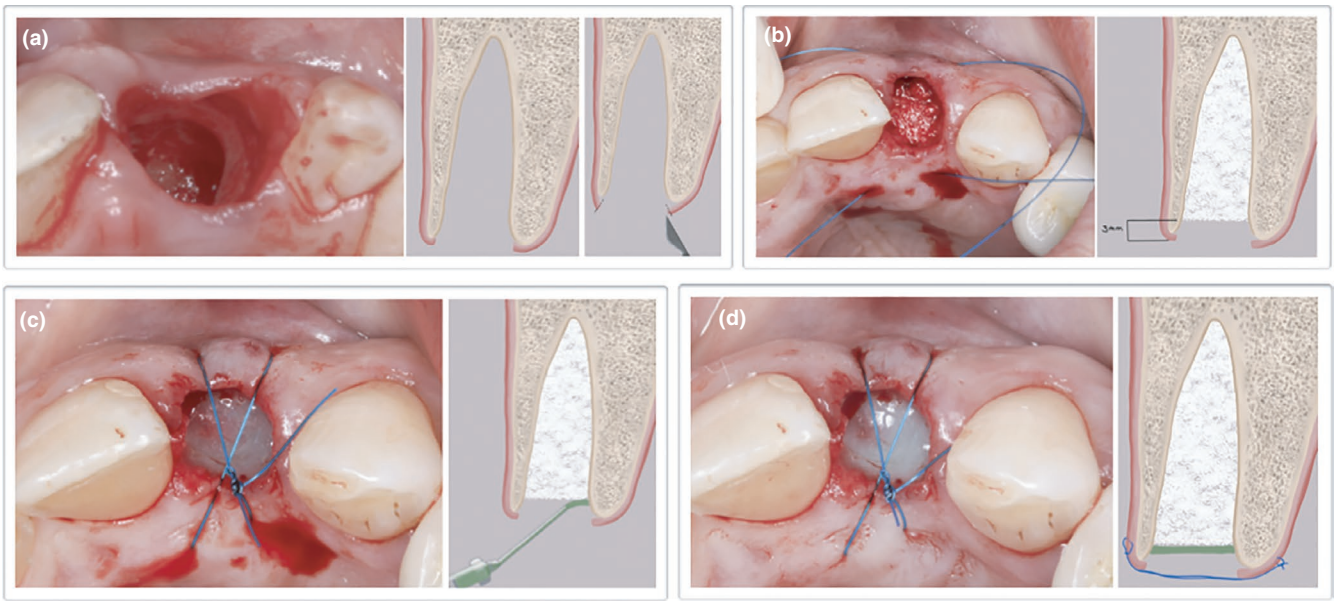

FIGURE 2 Polyethylene Glycol (PEG) membrane in extraction socket with no bone defect (NBD). (a) Alveolus cleaned; De-epithelization of the sulcular epithelium; (b) Alveolus grafted with bone substitute 3 mm below the gingival margin; (c) Application of PEG membrane below the gingival margin; (d) Suture showing a slight closure of the gingival border

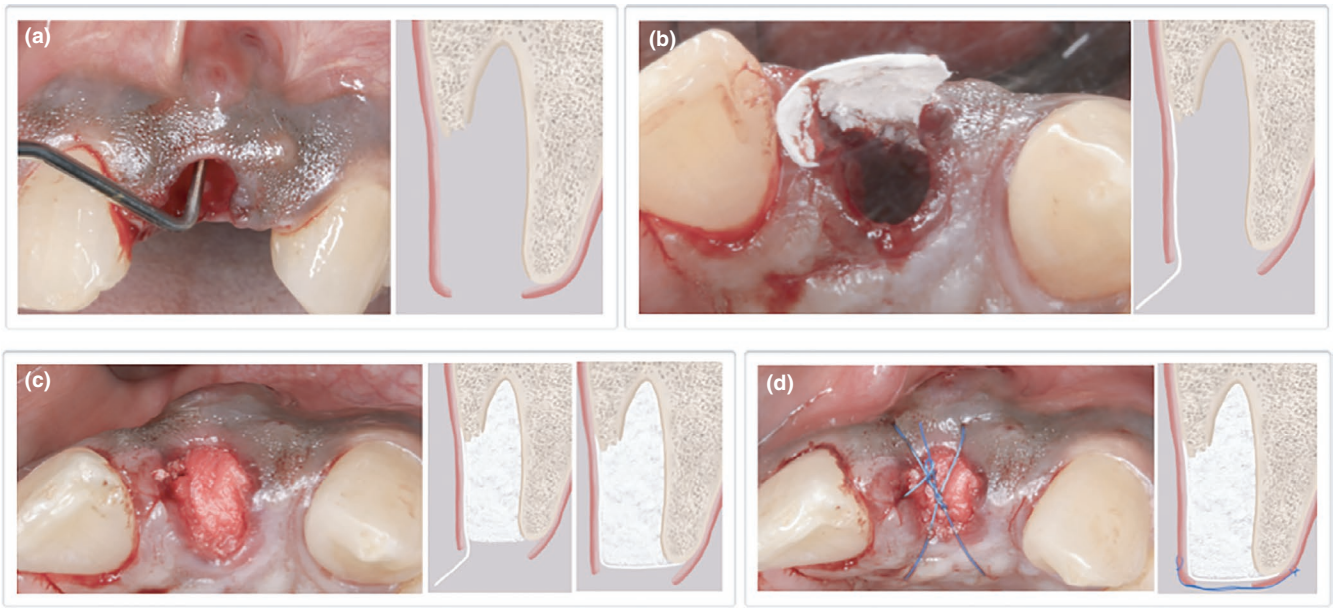

FIGURE 3 Collagen Membrane (CM) in extraction socket with bone defect (BD). (a) Alveolus cleaned and bone defect confirmed; (b) CM tucked into a pouch between the alveolar mucosa and alveolar bone at the point of defect; (c) Alveolus grafted with bone substitute 3 mm below the gingival margin and remaining CM wrapped over and into a pouch between the palatal gingiva and the alveolar bone; (d) Cross suture showing a slight closure of the gingival edges

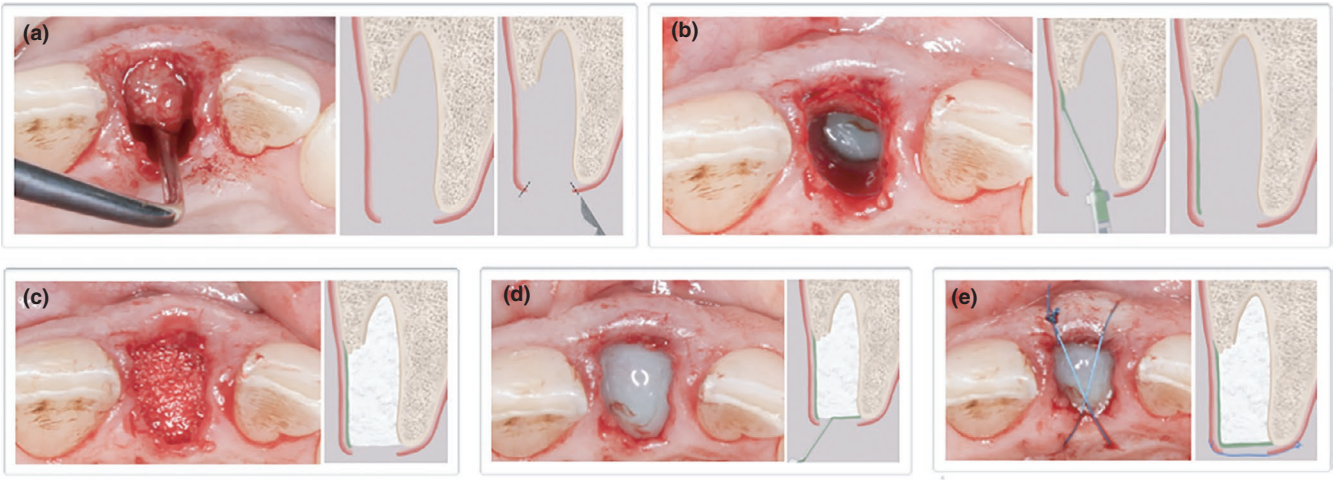

FIGURE 4 Polyethylene Glycol (PEG) membrane in extraction socket with bone defect (BD). (a) Alveolus cleaned; De-epithelization of the sulcular epithelium; (b) Missing bone wall lined with PEG on the inner side of the extraction socket; (c) Alveolus grafted with bone substitute 3 mm below the gingival margin; (d) Application of PEG membrane below the gingival margin; (e) Suture showing a slight closure of the gingival border

was executed by a member of the research team (AG) who otherwise had no contact with the trial's participants. Sequentially numbered opaque sealed envelopes were used to conceal allocation. Two sets of envelops were created by the same research team member (AG) for sockets with NBD or BD and to guarantee they were opaque, sealed and sequentially numbered. They were opened in sequential order by the research nurse after tooth extraction, socket degranulation and prior to material placement. The study nurse was informed whether the patient had any bone defect or not and in turn selected and opened the appropriate envelope to reveal which membrane was to be used.

Once informed of the material to be used, the socket was prepared according to the prescribed protocol and the selected material placed by one operator only (SS). The clinical techniques are illustrated in Figures 1 and 2. Cleaning of the alveolus and a circumferential de-epithelialization of the sulcular epithelium of the extracted tooth with 15c blade was carried out (Figure 1a,b). If no bone defect was present, bi-phasic calcium phosphate particulate bone substitute (Straumann Bone Ceramic; Straumann AG) soaked in saline was placed within the confines of the socket but maintained at least 3 mm below the edge of the marginal epithelium (Figure 2a,b). It was covered with the randomly selected membrane: either a

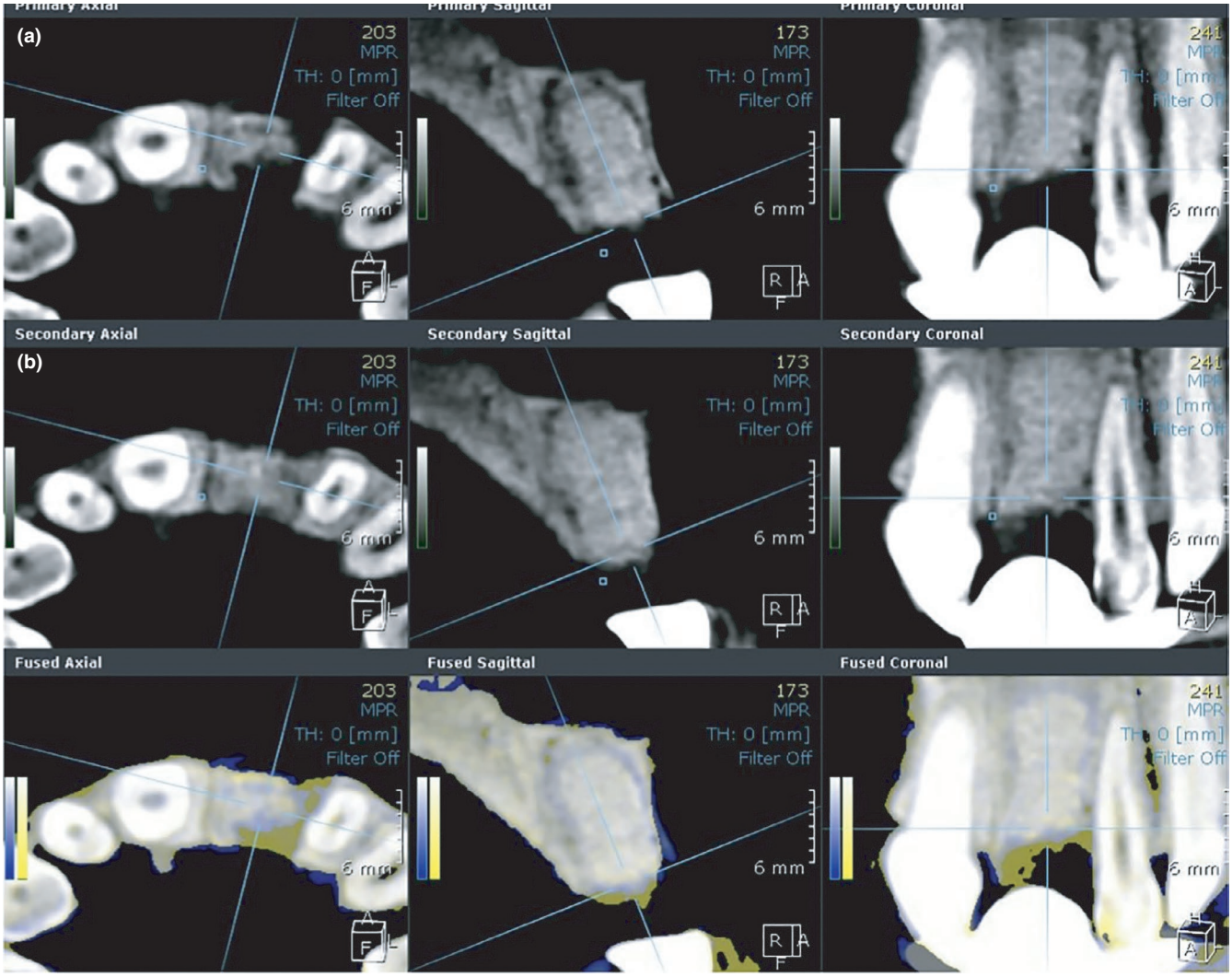

FIGURE 5 Sagittal cross-sectional of cone beam computed tomography (CBCT) images from the dental alveolus immediately after socket grafting procedure (a) and 6 months later (b)

porcine collagen control membrane (Bio-Gide; Geistlich Biomaterials) (Figure 1c), or synthetic PEG test membrane (Figure 2c), (Membragel; Straumann AG). All surgeries were flapless, and there was neither primary closure nor tightening of the edges of the buccal and palatal flap (Figures 1d and 2d).

The injectable PEG membrane was prepared according to the manufacturer's instructions. A thin layer was applied over the socket opening, starting from the buccal side to the palatal following a mesial/distal movement whilst ensuring the surface of the membrane remained below the level of the marginal epithelium. After the membrane set, a tension-free cross suture was placed using a 5–0 mono-filament polyamide suture (Seralon; Serag-Wiessner) with the aim of securing the membrane in place (Figure 2d).

If a defect was present, the randomly selected membrane was placed adjacent to the defect, bone substitute was placed and subsequently covered by the same membrane material (Figures 3 and 4). Patients were prescribed antibiotics (Amoxicillin 250 mg tds); analgesics (Ibuprofen 400 mg tds or paracetamol 500 mg qds); and an antiseptic mouthrinse (Chlorhexidine 0.2% qds).

A cone beam computed tomography (CBCT) scan was performed immediately after the surgical procedure with the patient wearing a radiopaque template. This was a tool reference for bone dimensions comparison. The CBCT unit used was the Vatech Pax Rev3D. The smallest field of view of 5 × 5 cm with the voxel size of 200 mm was used with the exposure time of 12 s under 5 mA and 85 kV.

All patients were reviewed at 1-week post-surgery for suture removal and a removable, tooth-supported, provisional prosthesis was modified, to ensure it did not make contact with the surgical site. A space was maintained to allow for any inflammatory volume increase in the soft tissues. There were further reviews at weeks 2, 4, 6, 10 and 20 for assessing healing and clinical measurements of soft tissue closure. At week 22, a second CBCT scan was taken with the same radiopaque stent that was used for the first scan and with the same parameters as the first CBCT image.

The DICOM (Digital Imaging and Communications in Medicine) data were used to compare the dimensional changes with the baseline, and follow-up scans were superimposed using the OnDemand3D (Ver 1.0.9.3223, CyberMed). Once the two scans

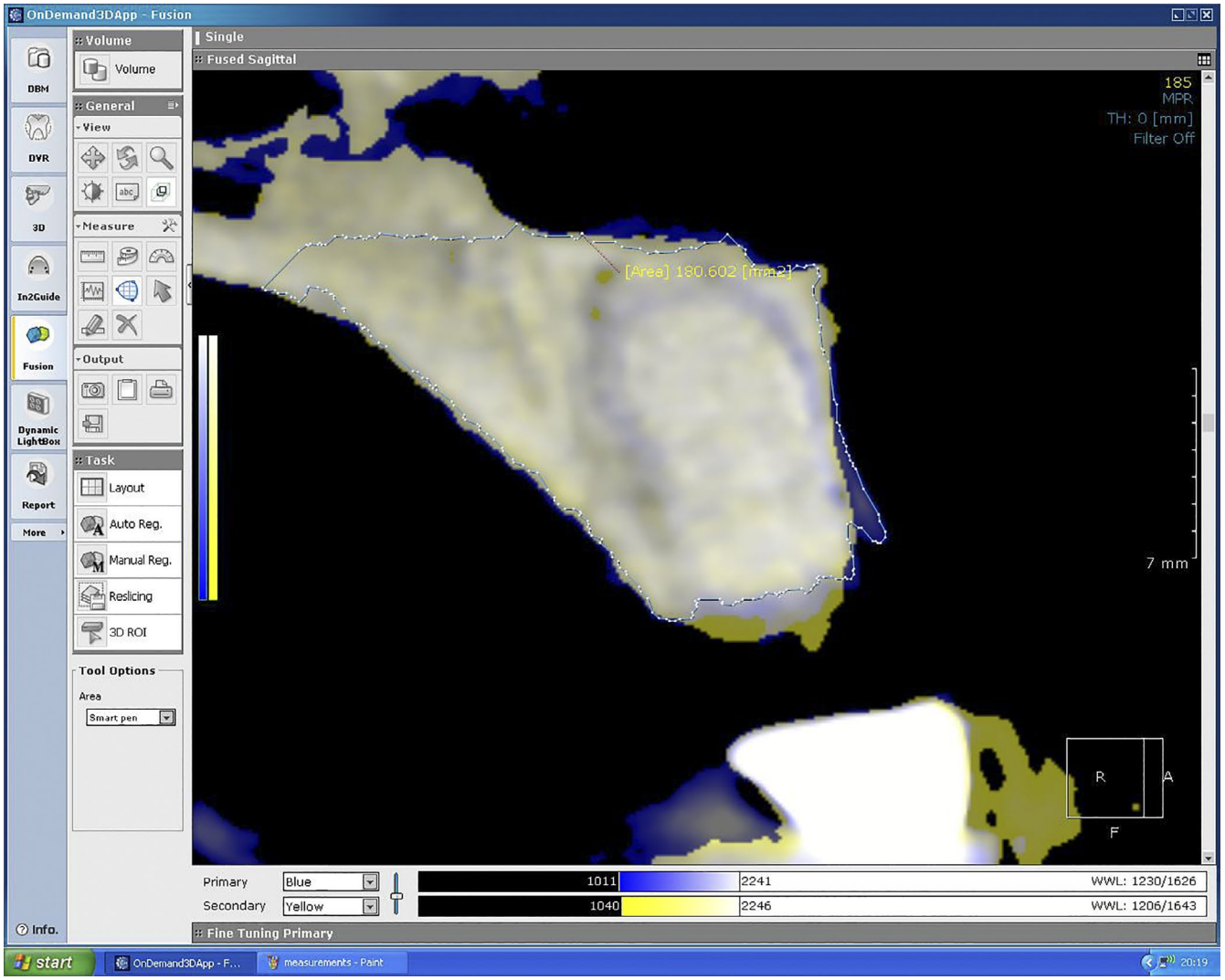

FIGURE 6 Magnitude of bone changes seen through the superimposed cone beam computed tomography (CBCT) images of the dental alveolus immediately after socket grafting procedure (Blue) and 6 months later (Yellow)

were uploaded in the software, the "Fusion" tool was used to superimpose them. The software uses a mathematical algorithm method that calculates the best fit and automatically superimposes the two volumetric images based on voxel-based information. The CBCT image at baseline was chosen for the primary image and the follow-up image as the secondary image. If the automatic superimposition obtained was not a perfect fit, the secondary image was manually aligned to the primary image using the manual registration tool. Finally, to ensure that the axis position matched in the two volumetric images the function "Reslicing" was used. This tool allows the secondary image to be rescaled based on the primary image. In this way, measurements can be performed on the same slice, at the same position, in both the primary and secondary images. The images were resliced twice to provide complete superimposition (Figure 5). The superimposition between the 2 images was presented as coloured images to identify the areas of labial bone resorption (Figure 6). A horizontal reference line was traced connecting the labial and palatal crest of bone on the immediate post-extraction image for standardized measurements. Horizontal socket dimensions were measured at distances of 0 (H0), 2 (H2), 4 (H4), 6 (H6), 8 (H8), 10 (H10) and 12 mm (H12) from the most coronal point of the reference line (Figures 7 and 8). The tooth root axis on the immediate post-extraction scan served as the vertical reference line for the measurements. Vertical measurements using the two reference lines were made at: the middle of the socket (V0); the labial plate (VLP); the palatal plate (VPP); a distance midway from the labial plate to the V0 (VMLP) and; a distance midway from palatal plate to V0 (VMPP) (Figures 9 and 10).

In order to minimize the error in measurement, one investigator (JM) carried out the superimposition whilst both the observers (JM, EG) carried out measurements on the same superimposed images. As a result, any discrepancies were limited to the alveolar ridge width and height measurements at the predetermined points only. This approach eliminated any errors that could have been encountered during superimposition of images. Both examiners were trained by a Consultant Radiologist and carried out numerous independent

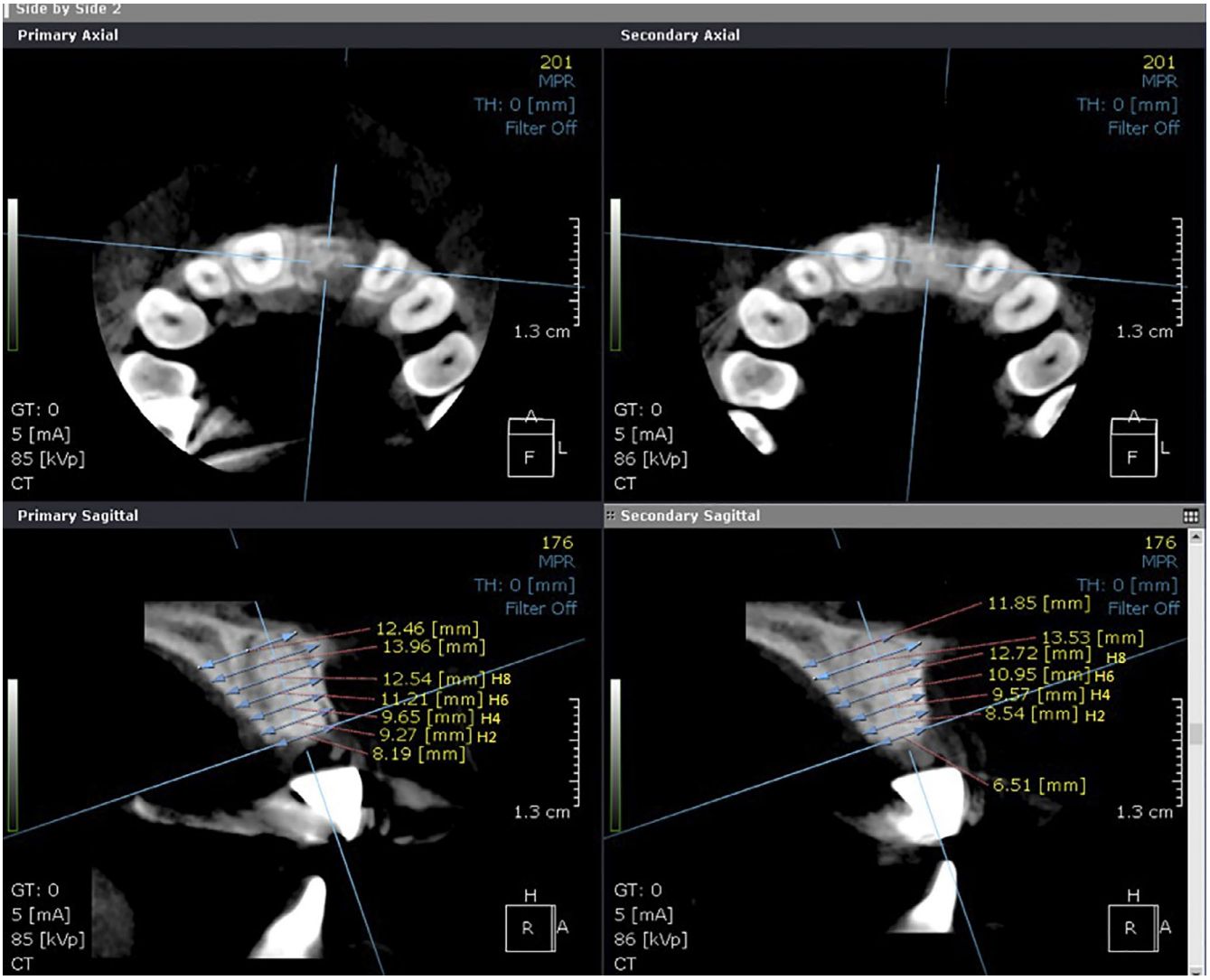

FIGURE 7 Horizontal socket dimensions measured at distances of 0 (H0), 2 (H2), 4 (H4), 6 (H6), 8 (H8), 10 (H10) and 12 mm (H12) from the most coronal point of the reference line

measurements followed by discussions until they had consistent measurements and negligible discrepancies. These discrepancies were primarily due to the observer's perception in grey value, and agreement was sought along with the Consultant Radiologist if the magnitude of the difference was more than twofold.

2.1 | Statistical analysis

Data analysis was computed with SPSS® software (IBM SPSS Statistics, v. 24.0. Armonk, NY: IBM Corp.). Mean percentage bone loss was calculated for H2, H4, H6, H8, V0, VLP, VMLP, VPP and VMPP from CBCT images taken immediately after grafting and after 22 weeks healing. The mean percentage for the whole sample was described, and standard deviations were calculated for each point. Two-way ANOVA analysis was performed to compare alveolar ridge changes in extraction sockets grafted with bi-phasic calcium phosphate and covered with PEG or CM.

The number of sites that needed further GBR at implant placement was counted. Fisher's exact test was used to compare differences between those treated with CM or PEG.

The 95% confidence interval was considered.

3 | RESULTS

Thirty-two non-adjacent sockets present in 30 patients were treated in this study. Twenty patients were male and the mean age was 40 years (Table 1). There was no statistically significant demographic difference between test and control groups ($p = .783$). All participants were non-smokers.

Table 2 describes the total distribution of tooth extraction sites, the reason for extractions and the differences between test and control groups. Test and control groups were comparable in relation to extraction sites and reasons for extraction. There were 5 fenestration and 3 dehiscence defects allocated to the test

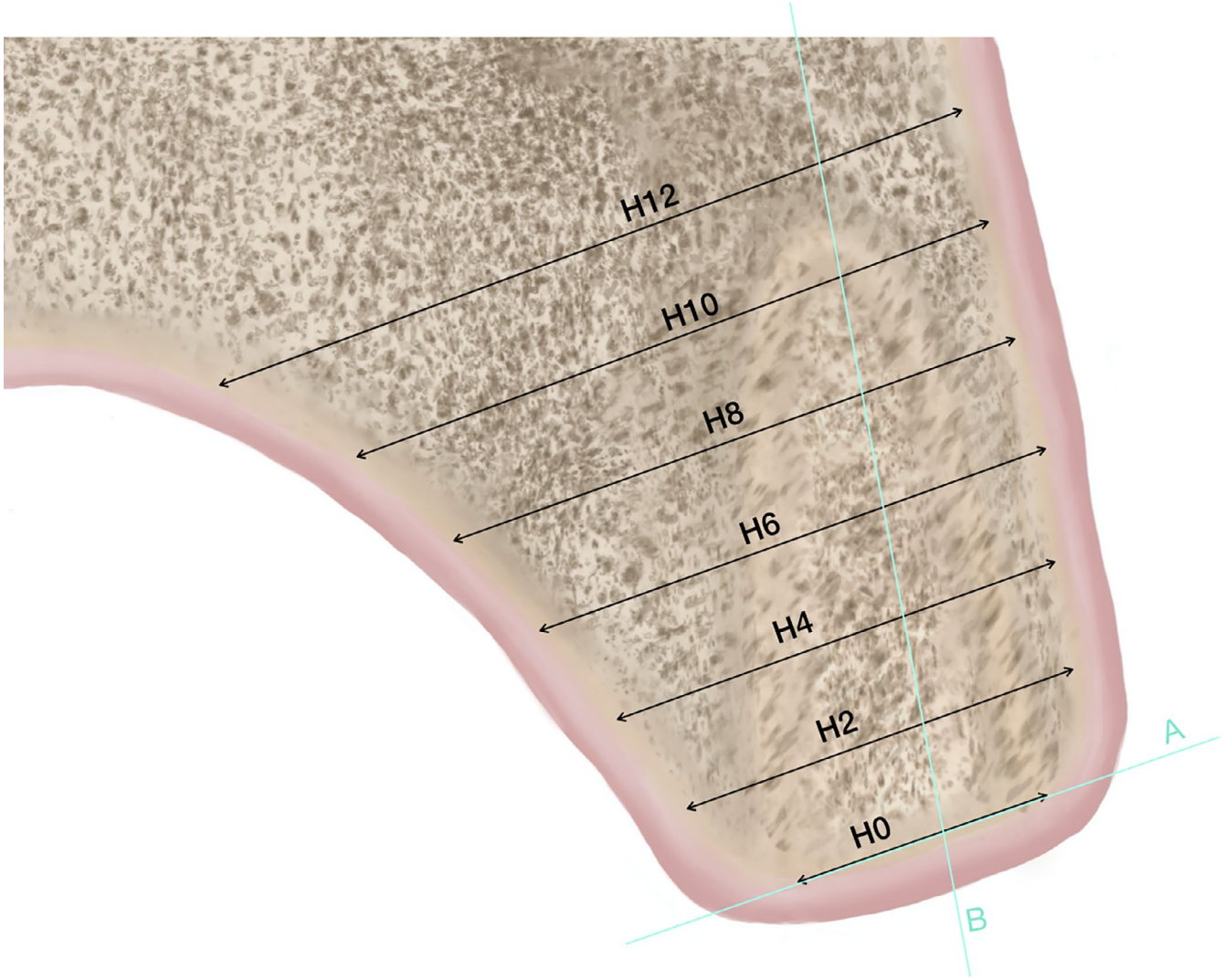

FIGURE 8 Schematic diagram illustrating horizontal measurements. Line "A" represents a horizontal reference line connecting the labial and palatal crest of bone on the immediate post-extraction image. Horizontal socket dimensions were measured at distances of 0 (H0), 2 (H2), 4 (H4), 6 (H6), 8 (H8), 10 (H10) and 12 mm (H12) from line A

group and 3 fenestration, 4 dehiscence and 1 with combined fenestration and dehiscence defect that were allocated to the control group.

The mean alveolar width measurements and mean percentage bone loss for each point is described in Table 3. The greater mean percentage bone loss occurred at VLP and H2 and greater variations occurred at VLP and VPP.

Differences between test and controls are described in Table 4. CM showed a statistically significantly greater percentage bone loss at H2 (Mean 28.59 [*SD* = 16.97]) compared with PEG (Mean 13.45 [*SD* = 11.97] [*p* = .008]); at H4 (Mean 14.84 [*SD* = 9.91] compared with PEG Mean 7.54 [*SD* = 7.17] [*p* = .026]); at VMLP (Mean 7.42 [*SD* = 11.95] compared to PEG Mean −2.86 [*SD* = 13.48] [*p* = .022]). There was no statistically significant difference between membranes at H6, H8, VLP, VPP and VMPP. There were no statistically significant interaction effects for membrane*presence or absence of bone defect.

All sites had an implant placed after 6 months and 9 (28.1%) sites required additional augmentation at implant placement or at least use of a membrane only (*n* = 1; Table 5). Six of the sites (66.7%) had intact bone walls initially at the time of extraction. From these 9 sites, 4 (44.4%) had been treated with CM and there was no statistically significant difference between CM or PEG (*p*-Value = 1.000). Table 5 describe characteristics of these sites in relation to tooth extraction site, type of defect at extraction, presence of any adverse effect during healing and type of defect at implant placement.

4 | DISCUSSION

The results of this randomized controlled trial show that PEG membrane, when used as a socket seal but left exposed over grafted extraction socket, preserves more alveolar ridge dimensions after

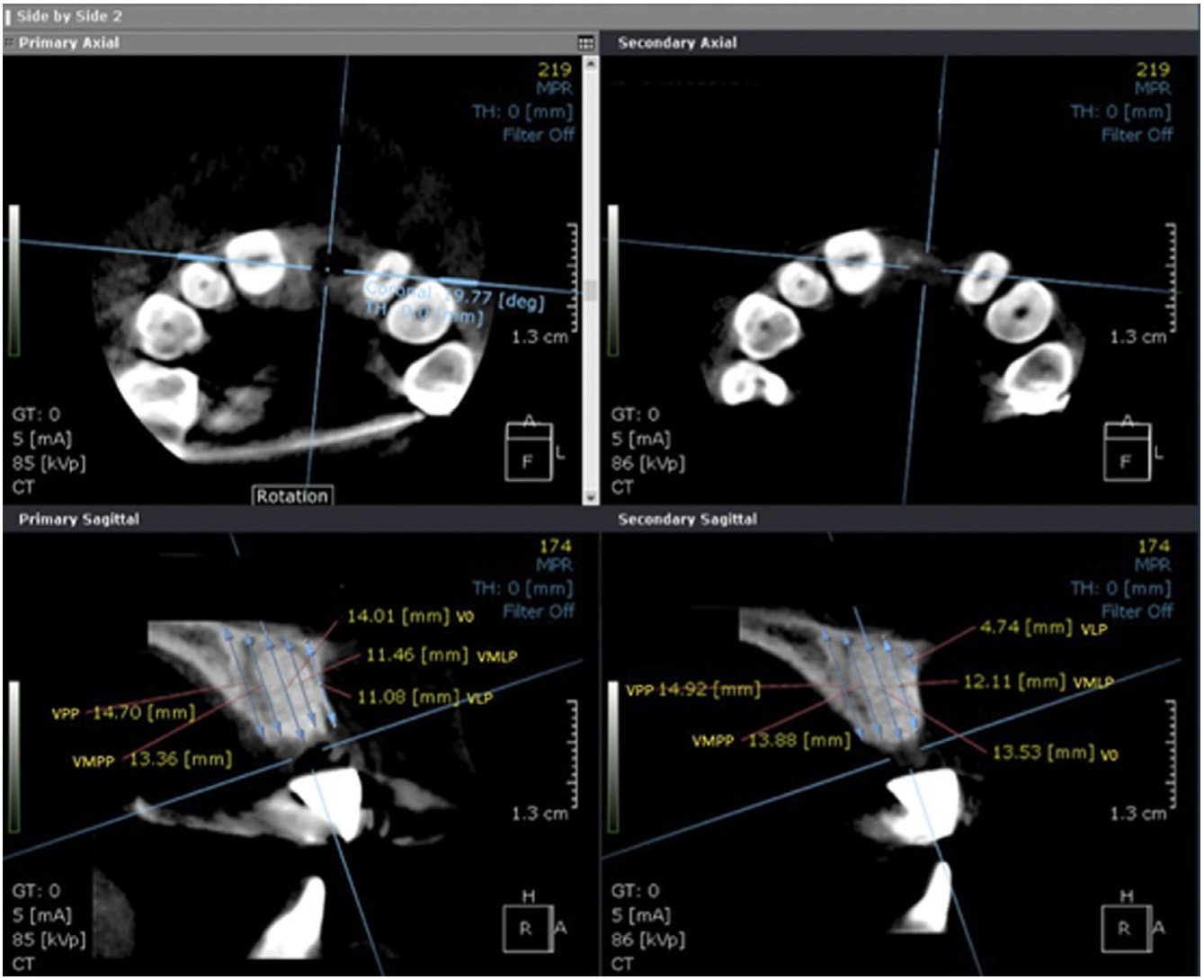

FIGURE 9 Vertical measurements using the two reference lines at the middle of the socket (V0), at the labial plate (VLP), at the palatal plate (VPP), at a distance midway from the labial plate to the V0 (VMLP) and at a distance midway from palatal plate to V0 (VMPP)

six months when compared to collagen membrane. Both the barrier membranes were left exposed in this study, which is in contrast with most of the previously published studies on CM, where a flap was raised and primary closure either achieved or attempted (Mardas, D'Aiuto, Mezzomo, Arzoumanidi, & Donos, 2011).

In the coronal aspects of the socket, PEG showed less horizontal and vertical change in comparison to CM. This could be attributed to the differences in the application technique of the two membranes. For CM, a pouch was created to tuck the membrane between the soft tissues and the bone to stabilize the membrane with an additional cross suture. In contrast, the PEG was injected and stabilized with a cross suture without any need for a pouch. Surprisingly, this difference was statistically significant in NBD groups where the intact crestal bone should have supported the graft and prevented greater loss. It is a possibility that detaching the periosteum from the bone has a detrimental effect on bone healing, even though studies seem to have contradicted this (Engler-Hamm, Cheung, Yen, Stark, & Griffin, 2011).

Polyethylene glycol membrane stiffens once it polymerises, and therefore, it should offer better stability for guided bone regeneration (GBR). Its use as a barrier in sockets with BD is even more interesting for the clinician. Again, in order to line the defect inside with a CM, the overlying flap and bone need to be separated to insert the membrane as a barrier, before packing the bone substitute and folding the remaining length of the membrane over the open socket as a seal and secured with a cross suture (Tan-Chu, Tuminelli, Kurtz, & Tarnow, 2014). Despite careful suturing to avoid any tension, some collapse of the coronal aspect was noted immediately during the procedure. In comparison, PEG was injected along the missing inner socket wall to create a barrier buccally (as all the BD sockets had only buccal wall missing). This did not require any manipulation of the buccal soft tissues. Once set, bone graft was inserted and a second layer of PEG applied over the socket opening and secured with a cross suture. The results confirm that within the coronal 4 mm, PEG preserved more alveolar

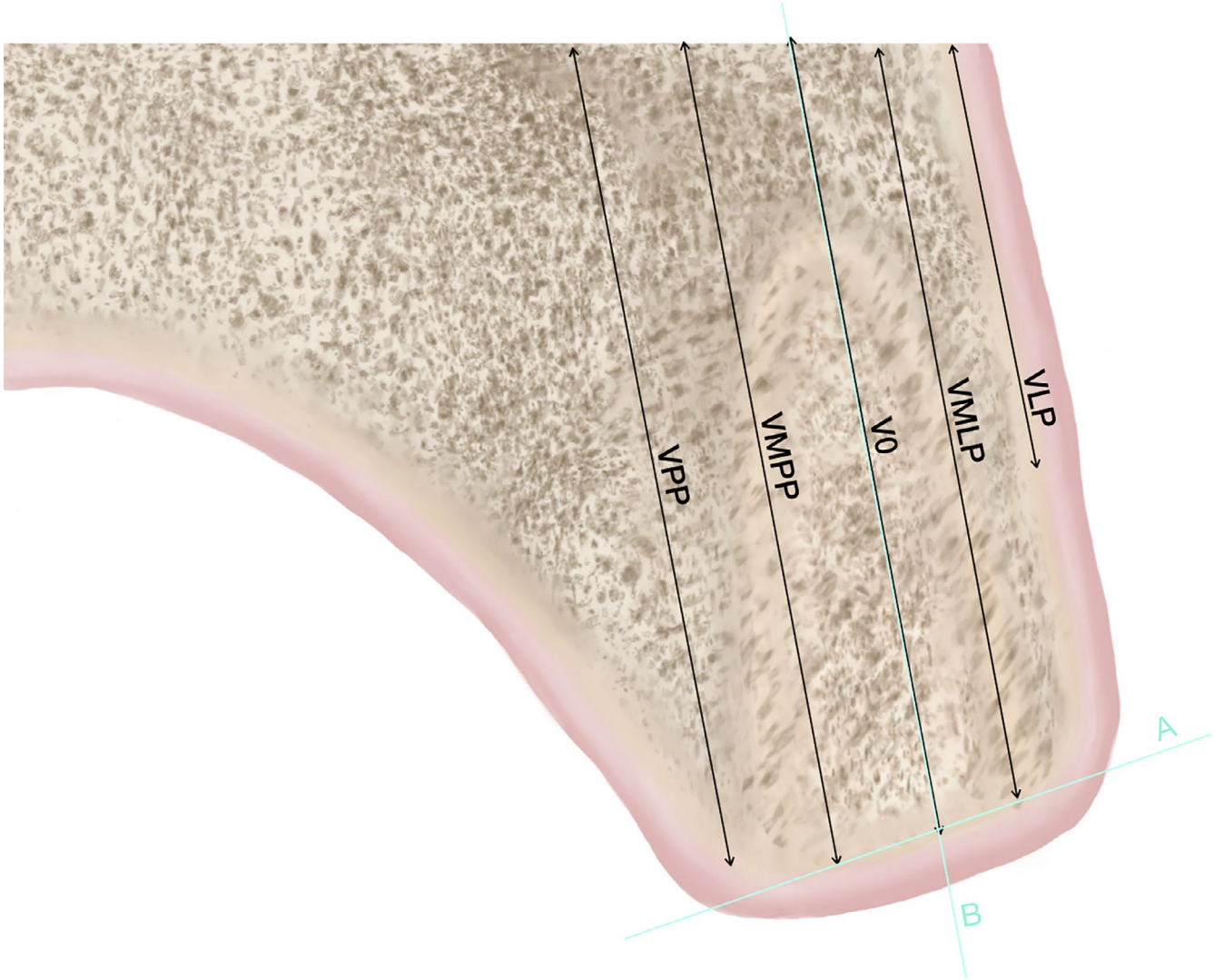

FIGURE 10 Schematic diagram illustrating vertical measurements. Line "B" represents a vertical reference line along the root axis denoting the middle of the socket (V0). VLP and VPP represent the Labial and Palatal plates; and VMLP and VMPP represent the point midway between the VO to VLP; and VO to VMPP, respectively

TABLE 1 Description of demographic distribution between test (PEG) and control (CM) groups

	Test (PEG) $N = 16$	Control (CM) $N = 16$	Total $N = 32$	*p*-Value
Gender	*N* (%)	*N* (%)	*N* (%)	
Male	11 (68.8)	9 (56.3)	20 (62.5)	.716*
Female	5 (31.3)	7 (43.8)	12 (37.5)	
Age (years)				
Mean	43.7	36.4	40.1	.079**
Median	44.0	37.5	42.0	
SD	11.1	11.9	11.9	
Min	21.0	19.0	19.0	
Max	68.0	52.0	68.0	

*p-Values (statistically significant at the level of $p < .05$) with Fisher's exact test.

**p-Value (statistically significant at the level of $p < .05$) with independent-samples t test for differences in means between groups

ridge width. Another important observation to note here is that the CM was applied outside, whereas PEG was applied inside the socket wall. In theory, the socket dimension would be reduced by the thickness of the layer of PEG when set and yet, a greater socket dimension was preserved in the test group.

This study again reinforces the established fact that grafting of extraction sockets fails to fully preserve the dimensions of the alveolar sockets (MacBeth et al., 2017). However, most of the previous studies have been conducted on sockets with intact bone or at least 3 walls of the socket remaining and greater than 50% of the fourth wall remaining after extraction of the tooth (MacBeth et al., 2017). Whilst the benefit of grafting such sockets might not be clinically significant or beneficial, an attempt at preservation of alveolar volume where one socket bone wall is damaged and missing, might prevent the need for staged bone augmentation procedures for future implant placement. Our results showed that 71.9% of the treated sockets did not require further GBR at the

TABLE 2 Distribution of tooth extraction site and reason for extraction between test (PEG) and controls (CM)

	Test (PEG) $N = 16$	Control (CM) $N = 16$	Total $N = 32$	p-Value*
Tooth extraction site	*N* (%)	*N* (%)	*N* (%)	
Anterior sites				
13	0 (0)	2 (12.5)	2 (6.3)	.654
12	3 (18.8)	3 (18.8)	6 (18.8)	
11	3 (18.8)	2 (12.5)	5 (15.6)	
21	3 (18.8)	4 (25.0)	7 (21.9)	
22	2 (12.5)	1 (6.3)	3 (9.4)	
23	1 (6.3)	2 (12.5)	3 (9.4)	
Premolar sites				
14	2 (12.5)	2 (12.5)	4 (12.5)	
24	2 (12.5)	0 (0)	2 (6.3)	
Reason for extraction				
Fractured tooth/Trauma	7 (43.8)	7 (43.8)	14 (43.8)	1.000
Internal resorption/	0 (0)	1 (6.3)	1 (3.1)	
Unsuccessful endodontic treatment/	7 (43.8)	6 (37.5)	13 (40.6)	
Agenesis with persistent deciduous	2 (12.5)	2 (12.5)	4 (12.5)	

*p-Values (statistically significant at the level of $p < .05$) with Fisher's exact test.

TABLE 3 Mean percentage bone loss in millimetres for each measurement point from immediately after graft procedure and after 22 weeks

	Alveolar widths immediately after alveolar ridge preservation (mm)		Alveolar widths after 22 weeks of alveolar ridge preservation (mm)		Mean percentage bone loss	
Measurement point	**Mean**	***SD***	**Mean**	***SD***	**Mean**	***SD***
Horizontal measurements						
H2	7.62	1.25	6.02	1.68	21.02	16.32
H4	8.08	1.34	7.18	1.45	11.19	9.28
H6	8.41	1.68	7.86	1.68	6.61	7.16
H8	8.72	2.03	8.44	2.06	3.26	7.49
Vertical measurements						
VLP	9.59	2.88	5.28	4.09	44.03	42.32
VPP	9.97	3.55	8.23	3.65	18.36	24.37
VMLP	10.31	3.04	10.00	2.90	2.27	13.57
VMPP	10.51	3.46	10.12	3.41	2.75	13.90
V0	11.00	3.32	10.87	3.32	0.29	15.08

time of implant placement. The use of PEG or CM over a grafted extraction socket was equally likely to decrease the need for further augmentation at implant placement.

Most of the previous studies on ARP have included all extraction sites in both maxilla and mandible, thereby subject to a wider interpretation of the results and subsequent application to clinical situations. In this study, the defects were limited to the anterior maxilla extending up to first premolar. Research suggests that the majority of alveolar sockets in anterior maxilla, including first premolar, have less than 1 mm labial bone thickness (Braut, Bornstein, Belser, & Buser, 2011) with a statistically significant decrease in thickness from the first premolars to the central incisors. This observation, in combination with well-established theory of bundle bone resorption after extraction of teeth, explains why NBD group demonstrated greater percentage bone loss at H2 and H4 in comparison with BD group, irrespective of the chosen barrier membrane.

Most of the previous studies have either used plain film radiographs or CBCT imaging for comparing the changes in bone volume. Certainly, plain film before and after grafting would offer a very limited perspective of change, only in vertical dimension. As a result, CBCT images have become a popular method

TABLE 4 Differences in mean percentage bone loss between test (PEG) and controls (CM)

Measurements	Mean percentage bone loss: Controls (±*SD*) *N* = 16	Mean percentage bone loss: Test (±*SD*) *N* = 16	*β*	*SE*	*p*-Value
Horizontal measurements					
H2	28.59 (16.97)	13.45 (11.97)	−15.13	5.26	.008
H4	14.84 (9.91)	7.54 (7.17)	−7.29	3.10	.026
H6	6.59 (7.34)	6.64 (7.23)	0.04	2.59	.986
H8	2.62 (7.98)	3.91 (7.17)	1.29	2.72	.637
Vertical measurements					
VLP	49.54 (44.38)	38.53 (40.84)	−0.78	1.58	.625
VPP	22.78 (27.26)	13.94 (21.04)	−8.84	8.57	.311
VMLP	7.42 (11.95)	−2.86 (13.48)	−12.44	3.81	.003
VMPP	5.51 (15.93)	−0.01 (11.37)	−5.52	4.93	.272
V0	4.86 (11.91)	−4.27 (16.84)	−1.11	0.51	.040

TABLE 5 Distribution of tooth extraction site, type of defect at extraction, reported adverse effect during healing and type of defect at implant placement surgery between test (PEG) and controls (CM) for participants who required further augmentation at implant placement

	Test (PEG) *N* = 5	Control (CM) *N* = 4	Total *N* = 9
Tooth extraction site	*N* (%)	*N* (%)	*N* (%)
14	0 (0)	0 (0)	0 (0)
13	0 (0)	1 (25.00)	1 (11.10)
12	2 (40.00)	1 (25.00)	3 (33.30)
11	1 (20.00)	1 (25.00)	2 (22.20)
21	0 (0)	1 (25.00)	1 (11.10)
22	1 (20.00)	0 (0)	1 (11.10)
23	1 (20.00)	0 (0)	1 (11.10)
24	0 (0)	0 (0)	0 (0)
Type of defect at extraction			
No defect	3 (60.00)	3 (75.00)	6 (66.70)
Dehiscence	0 (0)	1 (25.00)	1 (11.10)
Fenestration	2 (40.00)	0 (0)	2 (22.20)
Both dehiscence and fenestration	0 (0)	0 (0)	0 (0)
Presence of any adverse effect during healing			
No	3 (60.00)	4 (100.00)	7 (77.80)
Yes	2 (40.00)	0 (0)	2 (22.20)
Type of defect at implant placement surgery			
No defect	0 (0)	1 (25.00)	1 (11.10)
Dehiscence	3 (60.00)	0 (0)	3 (33.30)
Fenestration	2 (40.00)	2 (50.00)	4 (44.40)
Both dehiscence and fenestration	0 (0)	1 (25.00)	1 (11.10)

of assessing radiographic change in alveolar ridge dimensions after bone grafting (Jung et al., 2015; Temmerman et al., 2016). However, comparing two CBCT images taken at different time points, poses a major challenge when identifying the same slices (anatomical points) and therefore measuring changes accurately. The methodology used in this study allowed precise superimposition of the pre- and post-graft CBCT images. The majority of the images were automatically aligned by the software used and very few required manual alterations to achieve accurate superimposition to allow for multi-dimensional measurement of ridge width and height change in post-grafting CBCT taken after six months. A previous study has demonstrated that the standard deviation for superimposition using this method was low (0.038 to 0.070 of the root mean square in millimetres) and the method of superimposition using this software was accurate and reproducible (Koerich, Burns, Weissheimer, & Claus, 2016). Nevertheless, it remains a limitation of this study in particular and CBCT related measurements in general.

Whilst this study demonstrated maintenance of alveolar ridge volume in ARP on CBCT images even in sites with missing labial bone plate, this does not necessarily always translate into a site where (a) an implant can be successfully placed; (b) the quality of bone is optimal; (c) successful osseointegration of implant occurs and; (d) the regenerated bone is maintained in the long term (De Coster, Browaeys, & De Bruyn, 2011). In this study, 28.1% of sites required additional augmentation at the time of implant placement. Such sites may have required a block bone graft (staged augmentation) if allowed to fully heal for the same time period of six months without ARP procedure. Therefore, intervention at extraction may have avoided a need for a more invasive surgery later, which carries its own cost implications and patient morbidity. Only 33.3% of the sites requiring secondary augmentation had missing labial bone at the time of extraction. It is plausible that the other 6 sites with intact labial bone had thin bone phenotype and the

inevitable bundle bone resorption accounted for the loss of volume thereby necessitating secondary augmentation. Further research into the effect of bone phenotype on outcomes of ARP would be recommended. Besides, the benefit of ARP is questionable given that all the sites would have been amenable to Type II implant placement with simultaneous GRB after 6–8 weeks of extraction (Buser et al., 2013).

The study included thirty-two non-adjacent sockets in 30 patients, and the analysis did not consider the potential clustering effect. Subsequently, the results were confirmed after repeating the analysis for 30 sites in 30 patients and randomly excluding one site each from the patients who had two grafted sites.

The sample size was calculated based on a previous study reporting changes in millimetres (mm) rather than a percentage (%). In the present study, the results remained unchanged irrespective of whether analysed in mm or %. In the author's opinion, reporting % change allows a more comparable interpretation of the results and excludes the magnitude of the individual ridge dimensions when measuring the change in mm, that is 2 mm loss in a 4 mm and 10 mm ridge equates to 50% and 20%, respectively.

Within the limitations of this study, it can be concluded that PEG membrane can be successfully used as a barrier over an open socket for ARP procedure showing less alteration in horizontal and vertical changes in the coronal third in comparison to the CM. The ARP with PEG membrane is even more advantageous in defects with missing labial bone where an internal barrier can be custom built without the need to elevate a flap.

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APPENDIX 1

CONSORT 2010 checklist of information to include when reporting a randomised trial

Note

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Title page
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Pages 2-4
	2b	Specific objectives or hypotheses	Page 4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	Pages 4-5
	4b	Settings and locations where the data were collected	Pages 4-5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Pages 6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Pages 7-8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	Page 5
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Page 5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Page 5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Page 5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Page 6

(Continues)

APPENDIX 1 (Continued)

Section/Topic	Item No	Checklist item	Reported on page No
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Page 6
	11b	If relevant, description of the similarity of interventions	Page 6-7
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Page 8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n/a
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Consort diagram
	13b	For each group, losses and exclusions after randomisation, together with reasons	Consort diagram
Recruitment	14a	Dates defining the periods of recruitment and follow-up	January 2013 – March 2016
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	In each table
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Pages 8-9
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Pages 9-13
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Pages 9-13
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Pages 9-13
Other information			
Registration	23	Registration number and name of trial registry	n/a
Protocol	24	Where the full trial protocol can be accessed, if available	n/a
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Straumann Institut, Basel, Switzerland

Note: We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.