Nicola De Angelis, Pietro Felice, Gerardo Pellegrino, Andrea Camurati, Paolo Gambino, Marco Esposito

Guided bone regeneration with and without a bone substitute at single post-extractive implants: 1-year post-loading results from a pragmatic multicentre randomised controlled trial

Key words   *guided bone regeneration, post-extractive implants*

Objectives: To evaluate whether the adjunctive use of a bone substitute at immediate single implants placed in fresh extraction sockets with a residual buccal bone-to-implant gap of at least 1 mm could improve the aesthetic outcome of guided bone regeneration (GBR).

Materials and methods: Eighty patients requiring bone augmentation at a single immediate post-extractive implant to improve the aesthetic outcome were randomly allocated to an augmentation procedure using a resorbable barrier alone (GBR group; 40 patients) or a bone substitute plus a resorbable barrier (GBR + BS group; 40 patients) according to a parallel group design at four different centres. Three to 4 months after implant placement/augmentation, implants were loaded with provisional or definitive single crowns. Outcome measures were implant failures, complications, aesthetics assessed using the pink esthetic score (PES), patient satisfaction and peri-implant marginal bone levels, recorded by blinded assessors. All patients were followed up to 1 year after loading.

Results: One patient dropped out from the GBR group. Seven (9%) implants failed: 2 (5%) in the GBR + BS group and 5 (12.5%) in the GBR group. Six minor complications occurred in the GBR + BS group versus 2 in the GBR group. These differences were not statistically significant. Just after implant placement/augmentation, mean bone levels were -0.21 mm at GBR + BS implants and -1.92 mm at GBR implants whereas at 1 year after loading they were -1.04 and -1.76, respectively. When comparing the two groups, GBR + BS implants had 0.70 mm more peri-implant marginal bone than GBR implants. Aesthetics was scored by a blinded assessor as statistically significantly better for the GBR + BS group. Patients were equally satisfied. There were no differences between centres regarding the clinical outcomes.

Conclusions: The use of additional anorganic bovine bone substitute (Endobon) with resorbable collagen barriers (OsseoGuard) in defects around post-extractive implant improves the aesthetic outcome, though single post-extractive implants might be at a higher risk for implant failures.

Conflict-of-interest statement: *Biomet 3i, manufacturer of the implants, membranes and bone substitutes used in this investigation, partially supported this trial. However, the data belonged to the authors and Biomet 3i by no means interfered with the conduct of the trial or the publication of the results.*

Nicola De Angelis, DDS, MSc
Assistant Professor, Department of Periodontology, University of Genoa, Genoa, Italy and private practice, Acqui Terme (AL), Italy

Pietro Felice, MD, DDS, PhD
Resident, Department of Periodontology and Implantology, University of Bologna, Bologna, Italy

Gerardo Pellegrino, DDS
Fellow, Department of Oral and Maxillofacial Surgery, University of Bologna, Bologna, Italy

Andrea Camurati, DDS
Private practice, Genoa, Italy

Paolo Gambino, DDS
Private practice, Turin, Italy

Marco Esposito, DDS, PhD
Freelance researcher and Associate Professor, Department of Biomaterials, The Sahlgrenska Academy at Göteborg University, Sweden

Correspondence to:
Marco Esposito
Casella Postale 34, 20862 Arcore (MB), Italy
Email: espositomarco@ hotmail.com

■ Introduction

Immediate post-extractive implants are currently widely used. With this procedure a dental implant is placed just after tooth extraction in a fresh socket without waiting for any bone or soft tissue healing. While this procedure shortens the treatment periods, it might be at a higher risk of complications and/or failures[1]. It is uncertain whether post-extractive implants decrease the bone resorption that occurs after tooth extraction or not, nevertheless several approaches for augmenting post-extractive sites are currently used and some of these have been evaluated in randomised controlled trials (RCTs)[2-7]. However, it is still unclear if these approaches are needed and which could be the best augmentation technique[1].

In a trial[6] comparing five different procedures in 62 individuals (non-resorbable barrier alone, resorbable barrier alone, autogenous bone chips with a resorbable barrier, autogenous bone chips alone and a non-augmented control), no differences were found, though all problems (2 implant failures and 6 complications) occurred at bone augmented sites versus none in the non-treated control group. The study was underpowered to come to any proper conclusion. A subsequent trial by the same group[7], including 30 patients, compared an anorganic bovine bone substitute with or without a non-resorbable barrier with non-augmented control sites. The sample size was again insufficient to reach any valid conclusions, and once more all 3 complications occurred at augmented sites. In at least one-third of the augmented sites, aesthetics was judged to be unsatisfactory by the operator over a 3-year period in function. Finally, another small RCT[4] of parallel group design, including 20 patients, compared post-extractive implants augmented using a resorbable barrier with or without anorganic bovine bone. No failures, complications or drop-outs occurred up to abutment connection. A statistically significantly higher position of the soft tissue margins in relation to the implant shoulder was found at the buccal aspects of implants treated with barrier plus the bone substitute (2.1 mm versus 0.9 mm; mean difference = -1.2 m) which may suggest a better aesthetic outcome. Unfortunately, data with implants in function were not provided nor will ever be provided due to the premature death of the main author. Therefore there is no reliable published evidence suggesting which could be the most effective procedure for augmenting a post-extractive site at implant placement.

The aim of this randomised clinical trial was to compare the aesthetic outcome at single post-extractive sites augmented at implant placement with a resorbable barrier with or without a bone substitute. At protocol stage, it was planned to follow the patients up to 5 years after loading. The present article is reported according to the CONSORT statement to improve the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

■ Materials and methods

■ Patient selection

Any patient requiring at least one single immediate post-extractive implant between two natural teeth, being at least 18 years old and able to sign an informed consent form was eligible for inclusion (Figs 1a and 1b; Figs 2a and 2b). To be definitively included in the trial, patients had to have a residual buccal bone-to-implant gap of at least 1 mm.
Exclusion criteria were:
- general contraindications to implant surgery
- immunosuppressed or immunocompromised patients
- irradiation in the head or neck area
- uncontrolled diabetes
- pregnant or lactating
- untreated periodontitis
- poor oral hygiene and motivation
- substance abuse
- psychiatric disorders or unrealistic expectations
- acute infection (abscess) in the site intended for implant placement
- necessity to lift the maxillary sinus epithelium
- unable to commit to 5-year follow-up post-loading
- under treatment or had previous treatment with intravenous amino-bisphosphonates
- participation in other clinical trials interfering with the present protocol
- a site judged by the investigator, just after tooth extraction prior to implant placement, to be missing buccal bone sufficient to compromise the aesthetic outcome.
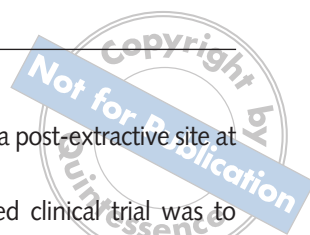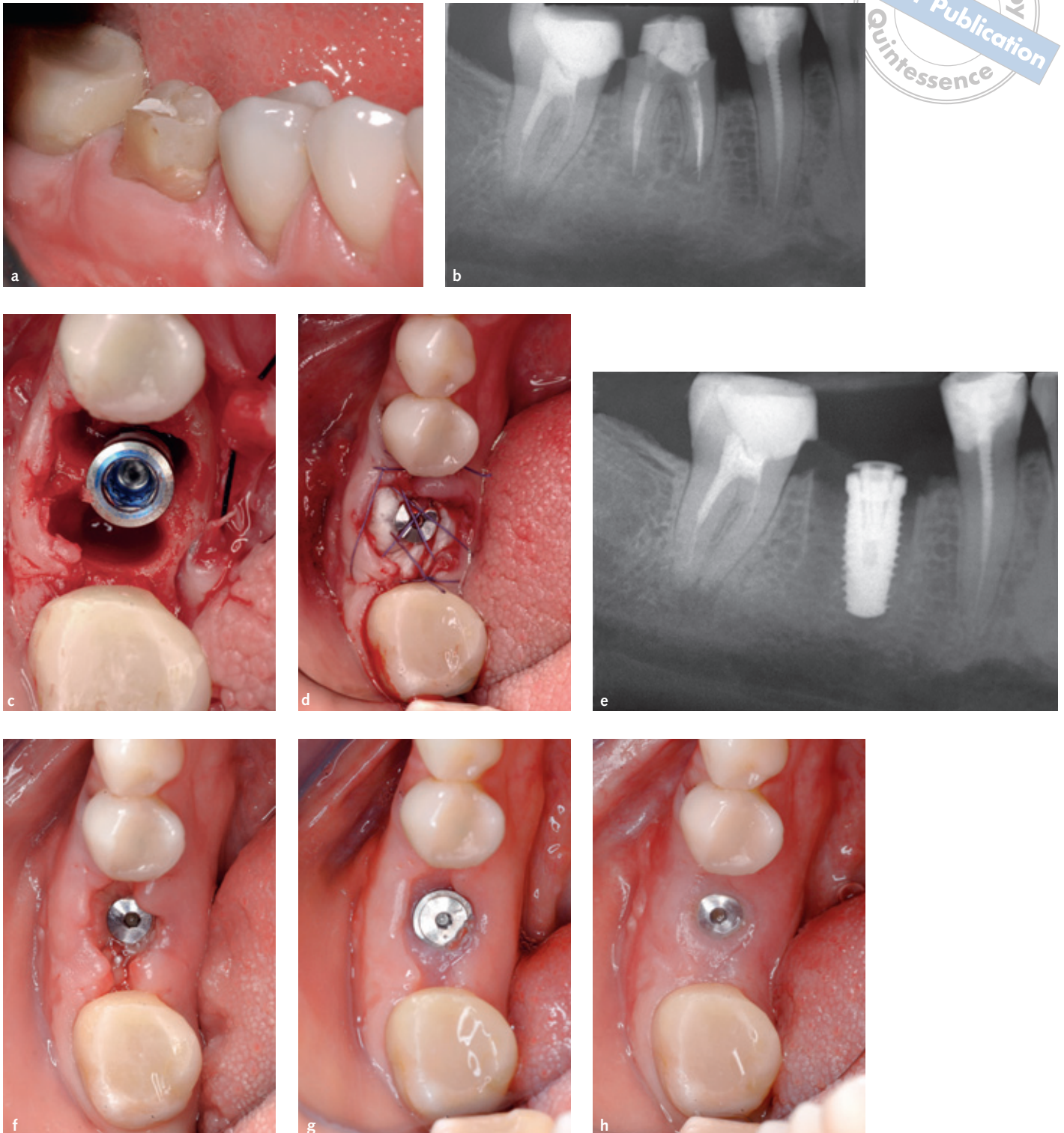
Fig 1   *(continued next page)* Treatment sequence of a mandibular right first molar (46) randomised to the GBR group:
a) initial picture showing tooth 46 to be extracted; b) radiograph showing periapical pathologies around tooth 46; c) after extraction, the implant was placed in the residual septa and then randomised to the GBR group; d) the resorbable barrier was adapted and fixed with the implant cover screw and a crossed suture remaining partially exposed; e) post-implantation baseline radiograph, the implant was placed at the level of the crestal bone; f) occlusal view 1 week after placement showing complete coverage of the barrier; g) occlusal view 1 month after placement; h) occlusal view at abutment connection, 4 months after placement, it appears that the buccal side has resorbed to some degree.
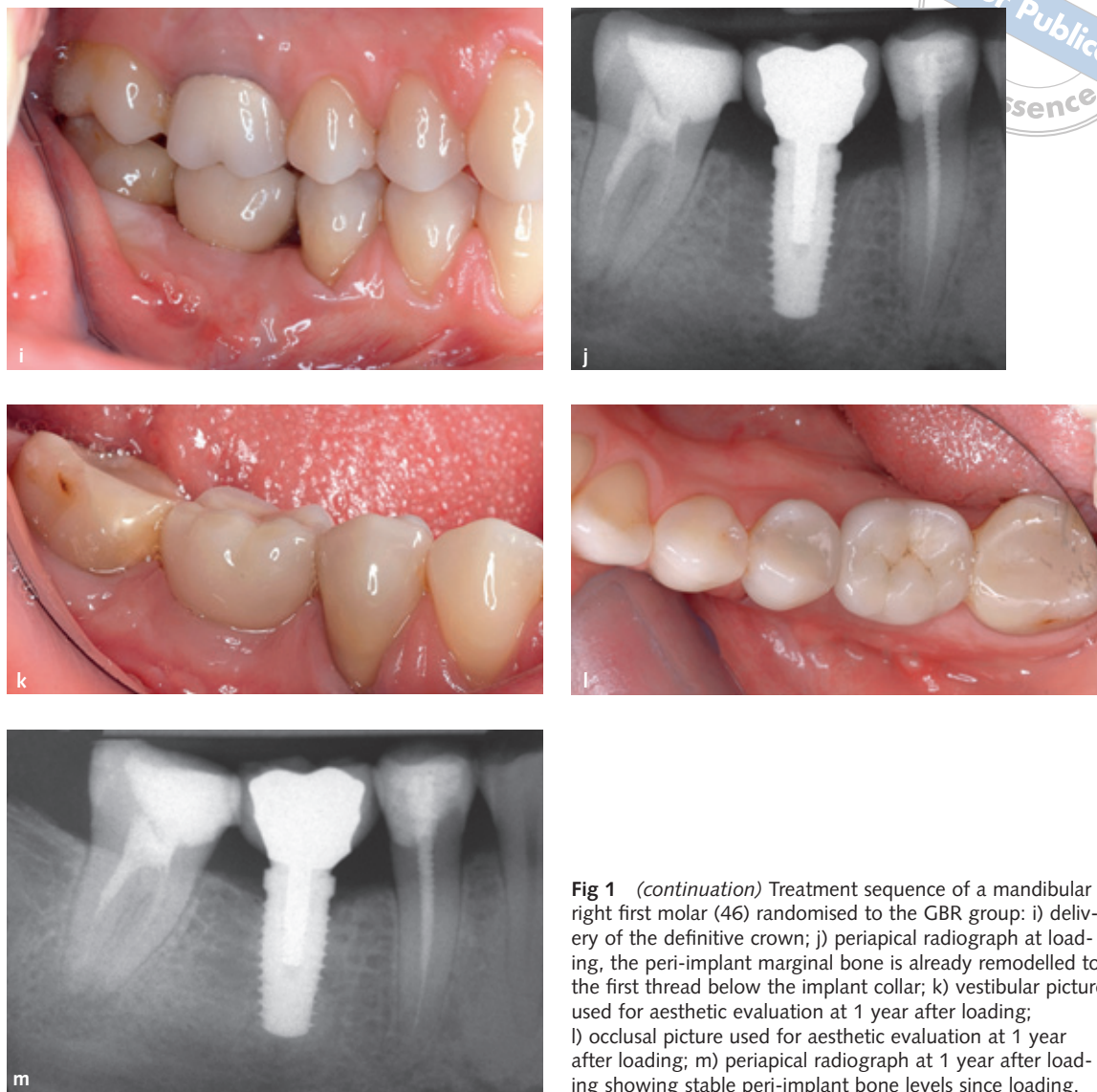
Fig 1 *(continuation)* Treatment sequence of a mandibular right first molar (46) randomised to the GBR group: i) delivery of the definitive crown; j) periapical radiograph at loading, the peri-implant marginal bone is already remodelled to the first thread below the implant collar; k) vestibular picture used for aesthetic evaluation at 1 year after loading; l) occlusal picture used for aesthetic evaluation at 1 year after loading; m) periapical radiograph at 1 year after loading showing stable peri-implant bone levels since loading.

Patients were divided into three groups based on the number of cigarettes they declared to consume per day: non-smokers, light smokers (≤10 cigarettes per day) and heavy smokers (>10 cigarettes per day).

Patients were recruited and treated by four different clinicians: De Angelis, Felice, Camurati and Gambino, using similar and standardised procedures in private practices. Each clinician/centre treated 20 patients (10 in each group). The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were followed. All patients received thorough explanations and signed a written informed consent form prior to being enrolled in the trial. After implant placement, patients were randomised to receive or not a bone substitute under a resorbable barrier.

■ **Clinical procedures**

Patients received a single dose of prophylactic antibiotic 1 hour prior to the intervention: 2 g of amoxicillin or 600 mg of clindamycin, if allergic to penicillin. Patients rinsed with chlorhexidine mouthwash 0.2% for 1 minute prior to the intervention. Patients were treated under local anaesthesia using articaine with adrenaline 1:100,000. No intravenous sedation was used. After crestal incision and flap elevation, teeth were extracted as atraumatically as possible, attempting to preserve the buccal alveolar bone. Sockets were carefully cleaned from any remains of granulation tissue. Drills with increasing diameters were used to prepare the implant site as suggested by the implant manufacturer. NanoTite™ Tapered
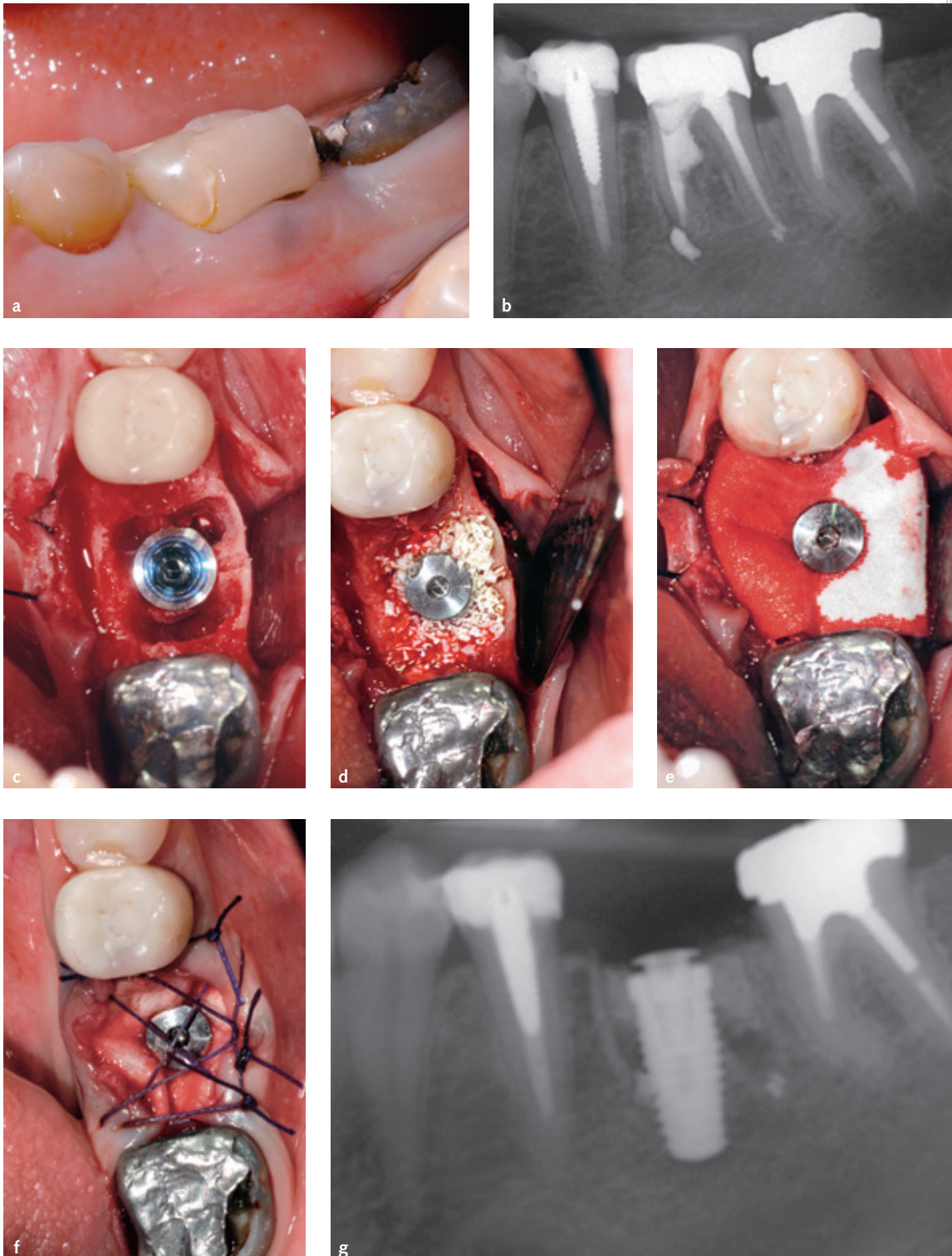
Fig 2 *(continued next page)* Treatment sequence of a mandibular left first molar (36) randomised to the GBR + BS group: a) initial picture showing tooth 36 to be extracted; b) radiograph showing an endodontic root perforation at the mesial root of tooth 36; c) after extraction, the implant was placed in the residual septa and then randomised to the GBR + BS group; d) the gap around the implant was loosely packed with Endobon particles; e) the barrier was trimmed and fixed with the implant cover screw; f) cross sutures were used to fix the flaps, though portions of the resorbable collagen membrane remained exposed to the oral cavity; g) post-implantation baseline radiograph showing the bone substitute in the coronal portion of the defect.
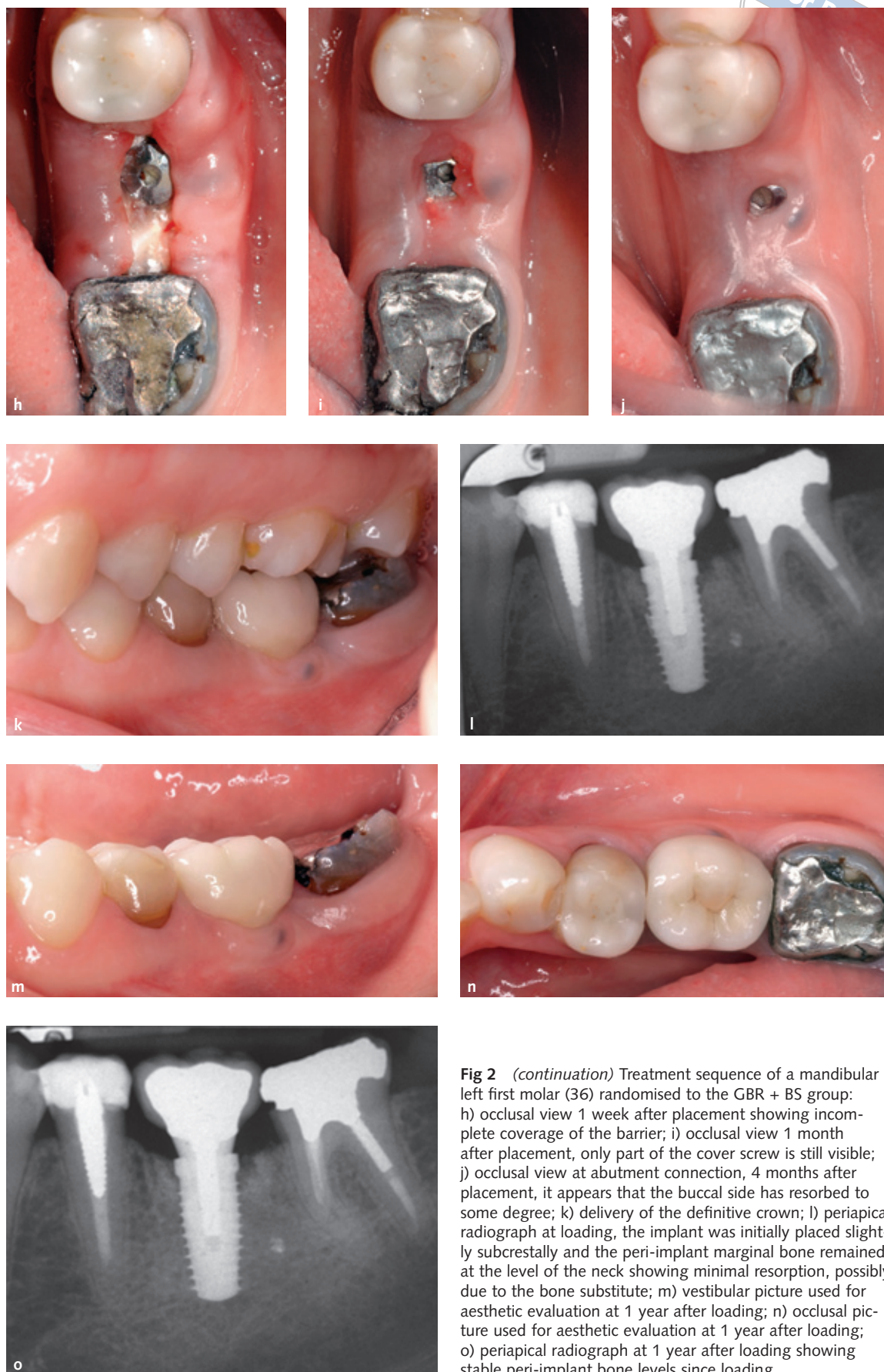
Fig 2 *(continuation)* Treatment sequence of a mandibular left first molar (36) randomised to the GBR + BS group: h) occlusal view 1 week after placement showing incomplete coverage of the barrier; i) occlusal view 1 month after placement, only part of the cover screw is still visible; j) occlusal view at abutment connection, 4 months after placement, it appears that the buccal side has resorbed to some degree; k) delivery of the definitive crown; l) periapical radiograph at loading, the implant was initially placed slightly subcrestally and the peri-implant marginal bone remained at the level of the neck showing minimal resorption, possibly due to the bone substitute; m) vestibular picture used for aesthetic evaluation at 1 year after loading; n) occlusal picture used for aesthetic evaluation at 1 year after loading; o) periapical radiograph at 1 year after loading showing stable peri-implant bone levels since loading.

Certain® Prevail® titanium alloy (Ti6Al4V) implants (Biomet 3i, Palm Beach, FL, USA) with internal connection were used. NanoTite implants are dual acid etched and then partially covered (about 50% of the surface) with nanoscale calcium phosphate crystals; this surface modification procedure is termed DCD (discrete crystalline deposition). Operators were free to choose implant lengths (8.5, 10, 11.5, 13 and 15 mm) and diameters (4 or 5 mm) according to clinical indications and their preferences.

The head of the implants was placed crestally to the adjacent mesiodistal bone, however in aesthetic areas, operators placed them about 1 to 2 mm below the most apical bone peak, and slightly palatally. Implant insertion torque was assessed with a 3i manual wrench and reported as >20 Ncm or <20 Ncm.

In the presence of a residual gap between the implant surface and the buccal bone wall >1 mm, the patient was then included in the study and randomised to one of the intervention groups. Clinical pictures of the vestibular and occlusal (Figs 1c and 2c) aspects were also taken, and the horizontal gap between the buccal bone and the implant was measured and reported in mm.

Only after having placed the implant did the operator know whether the site was to be filled with a bone substitute or not, by opening a sealed envelope. When indicated by the random allocation, the gap between the implant and the bone was loosely packed with the bone substitute granules (Endobon®; Biomet 3i; Fig 2d). Endobon is a bovine-derived, deproteinised, osteoconductive hydroxyapatite ceramic. It is manufactured in a two-stage high-temperature process: pyrolysis at a temperature above 900°C and sintering at a temperature above 1200°C. This leads to the combustion of all organic material in the bone, thus ensuring complete deproteinisation and hence destruction and elimination of all bacteria, viruses, and prions from the original bone. Then a resorbable collagen barrier (OsseoGuard®, Biomet 3i) was trimmed and adapted around the implant to extend for 2 mm on the surrounding bone. Osseoguard barriers are made of type I bovine Achilles tendon collagen derived from closed herds. The material consists of a fibrillar matrix structure to provide strength for tacking or suturing the membrane. Barriers were fixed with the implant cover screws (Fig 2e). Operators were free to leave the barrier partially exposed (Figs 1d and 2f) or to completely close the flaps onto the barrier with sutures after flap mobilisation. Periapical radiographs of the implants were taken according to the paralleling technique (Figs 1e and 2g).

Ibuprofen 400 mg was prescribed to be taken 2 to 4 times a day during meals, as long as required. Patients were instructed to use 0.2% chlorhexidine mouthwash for 1 minute twice a day for 2 weeks, and to avoid brushing and trauma on the surgical sites. Postoperative antibiotics were prescribed: amoxicillin 1 g twice a day for 6 days. Patients allergic to penicillin were prescribed clindamycin 300 mg twice a day for 6 days. After 1 week, patients were recalled and checked. Sutures were removed and occlusal clinical pictures of the implant sites were taken (Figs 1f and 2h). After 1 month, patients were recalled again and occlusal clinical pictures of the implant sites were made (Figs 1g and 2i).

After 3 to 4 months of submerged healing (Figs 1h and 2j) small flaps, if needed, were elevated after local anaesthesia and the implants were tested for stability by reverse torque with a 20 Ncm force with the dedicated wrench. Impressions with the pick-up impression copings were made using a polyether material. Provisional crowns in acrylic resin or definitive metal-ceramic or metal-resin crowns were cemented with provisional cement or screwed on temporary or definitive Biomet 3i platform-switched abutments (Figs 1i and 2k) within 1 week. Peri-apical radiographs of the implants were taken according to the paralleling technique (Figs 1j and 2l). All definitive crowns were delivered within 2 months. Patients were recalled every 6 months for professional maintenance. One year after loading, crowns were manually tested for stability using the metallic handles of two mirrors by the local blinded outcome assessors. Pictures of the vestibular and occlusal aspects including the two adjacent teeth (Figs 1k, 1l, 2m and 2n) were taken with a 1:4 magnification and the satisfaction questionnaire was filled in by the local blinded outcome assessors. Peri-apical radiographs of the implants were taken (Figs 1m and 2o).

■ Outcome measures

This study tested the null hypothesis that there were no aesthetic differences between the two procedures against the alternative hypothesis of a difference.

Outcome measures were:

- Implant failures: implant mobility or removal of stable implants dictated by progressive marginal bone loss or infection. Stability of individual implants was measured at abutment connection with a reverse torque of 20 Ncm with the Biomet 3i wrench, and 1 year after loading by testing the stability of the crowns with the handles of two metallic instruments.

- Any biological or biomechanical complications. Examples of biological complications are nerve injury, fistula and peri-implantitis. Examples of biomechanical complications are loosening or fracture of the abutment screws and fracture of ceramic.

- Peri-implant marginal bone levels evaluated on intraoral radiographs taken with the paralleling technique at implant placement (Figs 1e and 2g), at implant loading (Figs 1j and 2l), and 1 year after loading (Figs 1m and 2o). In cases where the bone levels around the study implants were hidden or difficult to be estimated, a second radiograph was made. Radiographs were scanned, digitised in JPG, converted to TIFF format with a 600 dpi resolution and stored in a personal computer. Peri-implant marginal bone levels were measured using the UTHSCSA Image Tool 3.0 (The University of Texas Health Science Center, San Antonio, TX, USA) software. The software was calibrated for every single image using the known implant length. Measurements of the mesial and distal bone crest level adjacent to each implant were made to the nearest 0.01 mm and averaged at implant level and then at group level. The measurements were taken parallel to the implant axis. Reference points for the linear measurements were the most coronal margin of the implant collar and the most coronal point of bone-to-implant contact.

- Aesthetic evaluation of the vestibular and occlusal clinical pictures, taken with a magnification of 1:4 and including the two adjacent teeth at 1 year after loading, on a computer screen by an independent blinded clinician (GP). The aesthetic evaluation was performed following the pink esthetic score (PES)[8]. In brief, seven domains were evaluated: mesial papilla, distal papilla, soft tissue level, soft tissue contour, alveolar proc- ess deficiencies, soft tissue colour and texture. A 0-1-2 scoring system was used, 0 being the lowest and 2 being the highest value, with a maximum achievable score of 14.

- Patient satisfaction. At 1 year after loading, the local blinded outcome assessors provided a mirror to the patients showing the implant-supported crown on which patients had to express their opinions and were asked 'are you satisfied with the function of your implant-supported tooth?' Possible answers were 'yes absolutely', 'yes partly', 'not sure', 'not really' and 'absolutely not'. Then patients were asked 'are you satisfied with the aesthetic outcome of the gums surrounding this implant?' Possible answers were 'yes absolutely', 'yes partly', 'not sure', 'not really' and 'absolutely not'. Finally, patients were asked whether they would undergo the same therapy again. Possible answers were: 'yes' or 'no'. The questions were always posed with exactly the same wording.

At each centre, there was a local blinded outcome assessor who recorded all outcome measures. One blinded dentist (GP) with extensive experience in reading periapical radiographs and scoring aesthetics using the PES score, and not involved in the treatment of the patients, evaluated marginal bone levels and scored aesthetics without knowing group allocation, therefore the outcome assessor was blind. However, Endobon augmented sites could be identified, particularly on baseline radiographs (Fig 2g), but in some cases even after 16 months because they appeared slightly more radiopaque (Fig 2o).

■ Statistical analysis

No sample size calculation was performed since the present authors had no previous experience with the use of the PES score in this situation. This trial will help to establish PES values that could be used for future sample size calculations. It was decided to recruit 40 patients in each group, 20 patients at each of the four participating centres. Each centre randomised 10 patients to each group. Four computer-generated restricted random lists were created. Only one investigator (ME), who was not involved in the selection and treatment of the patients, knew the random sequence and had access to the random

list stored in a password-protected portable computer. The random codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. After the implants were placed and a buccal bone implant gap of at least 1 mm was measured, the envelopes were opened sequentially. Therefore, treatment allocations were concealed to the investigators in charge of enrolling and treating the patients.

All data analysis was performed according to a pre-established analysis plan by a biostatistician with expertise in dentistry who analysed the data without knowledge of the group codes. The patient was the statistical unit of the analyses. An intention-to-treat (ITT) analysis was used. Differences in the proportion of patients with implant failures and complications (dichotomous outcomes) were compared between the groups using the Fisher exact probability test. Differences of means at patient level for continuous outcomes (bone levels and PES) between groups were compared by *t* tests. The Mann–Whitney U test was used to compare the medians of the two groups for patient satisfaction. Differences in the proportion of patients with implant failures and complications (dichotomous outcomes) and of PES (continuous outcome) were compared among the four centres using the chi-square test and one-way analysis of variance, respectively. All statistical comparisons were conducted at the 0.05 level of significance.

■ Results

During initial monitoring it was noticed that one of the original four centres did not follow the protocol at all and was immediately replaced by another centre (Dr Felice). The data of the 5 patients treated by the excluded centre were not considered. Due to an error in the research protocol design, initial radiographs after implant placement were not requested, however clinicians routinely took them at the end of the augmentation procedure. Ninety-five patients were screened at the four centres and 80 patients were consecutively enrolled in the trial. Fifteen patients were not included for the following reasons: 6 patients refused to participate in the trial, 5 patients had an acute abscess and were treated with delayed implants, 2 patients would have had the implant inserted near another implant and 2 patients required a sinus lift procedure because the residual bone height was judged to be insufficient. All patients were treated according to the allocated interventions. One patient from the GBR group dropped out just after definitive crown delivery. She moved away and could not be contacted any longer. Eleven radiographs from 5 patients were lost at one centre (Dr Gambino) and more precisely: 2 at initial loading and 1 at 1 year for the GBR group; and 3 at baseline, 3 at initial loading, and 2 at 1 year for the GBR + BS group. The data of all remaining patients were evaluated in the statistical analyses. The main deviations from the protocol occurred in one centre (De Angelis) and were: one patient randomised to the GBR + BS group received a 'straight' 3.25 mm diameter implant and did not receive the resorbable barrier because it was judged to be useless; another patient from the GBR group received a 'straight' 3.25 mm diameter implant instead of a 4 mm tapered implant as decided at protocol level. Both these implants were placed in lateral incisor sockets.

Patients were recruited and received the post-extractive implants from September 2008 to June 2009. The follow-up of all patients was up to 1 year after implant loading. Patient demographics are presented in Table 1. Forty implants were placed in the GBR group and 40 in the GBR + BS group and there were no apparent significant baseline imbalances between the two groups.

Seven (9%) implants failed: 5 in the GBR group and 2 in the GBR + BS group (Table 2). The differences in proportions of implant failures was not statistically significant (Fisher's exact test $P = 0.43$; difference = 0.075; 95% CI -0.05 to 0.20). All but one failure was discovered at abutment connection (mobile implants). One implant of the GBR + BS group failed 3 months after loading. There were no clinical signs of infection, though in 6 cases implants were slightly painful at percussion. All failed implants were successfully replaced.

Three minor complications occurred in 2 patients of the GBR group versus 6 complications in 6 patients of the GBR + BS group (Table 3). The difference in proportions is not statistically significant (Fisher's exact test $P = 0.26$; difference = 0.10; 95% CI -0.03 to 0.23). All complications resolved spontaneously or were successfully treated.

Table 1 Patient and intervention characteristics.

	GBR (%) [n = 40]	GBR + BS (%) [n = 40]
Females	19 (47.5)	19 (47.5)
Males	21 (52.5)	21 (52.5)
Mean age at implant insertion (range)	46.4 (20-77)	47.7 (24-75)
Smoking up to 10 cigarettes/day	9 (22.5)	10 (25.0)
Smoking more than 10 cigarettes/day	1 (2.5)	4 (10.0)
Implants in maxilla	25 (62.5)	25 (62.5)
Implants in mandible	15 (37.5)	15 (37.5)
Implants in central incisor position	1 (2.5)	1 (2.5)
Implants in lateral incisor position	5 (12.5)	4 (10.0)
Implants in canine position	4 (10.0)	2 (5.0)
Implants in first premolar position	10 (25.0)	7 (17.5)
Implants in second premolar position	5 (12.5)	11 (27.5)
Implants in first molar position	9 (22.5)	12 (30.0)
Implants in second molar position	6 (15.0)	3 (7.5)
Implants with 3.25 mm diameter	1 (2.5)	1 (2.5)
Implants with 4 mm diameter	23 (57.5)	22 (55.0)
Implants with 5 mm diameter	16 (40.0)	17 (42.5)
Implants 8.5 mm long	5 (12.5)	8 (20.0)
Implants 10 mm long	11 (27.5)	15 (37.5)
Implants 11.5 mm long	12 (30.0)	7 (17.5)
Implants 13 mm long	12 (30.0)	9 (22.5)
Implants 15 mm long	0 (0.0)	1 (2.5)
Implants placed with less than 20 Ncm torque	4 (10.0)	2 (5.0)
Mean horizontal gap implant-buccal bone in mm (SD)	2.96 (1.37)	3.15 (1.27)
Sites left with exposed barriers	40 (100)	38 (95.0)
Sites with barriers completely submerged under the flaps	0 (0.0)	2 (5.0)

The complications in the GBR group were:
- loosening of the cover screw at 4 to 6 weeks postoperatively and de-cementation of the final crown of an implant in position 25
- postoperative pain for 1 week treated with antibiotics for an additional 4 days (implant 24).

Complications in the GBR+BS group were:
- loosening of the provisional abutment (implant 26)
- small lesions in the peri-implant mucosa during healing due to Endobon granules (implant 25)
- peri-implant mucositis around the exposed cover screw during healing (implant 36) treated with the application of chlorhexidine gel

- loosening of the cover screw at 4/6 weeks post-operatively (implant 36)
- pain at loading for approximately 2 months (implant 46)
- pain at loading for approximately 2 months (implant 36).

Just after implant placement/augmentation, mean bone levels were -0.21 mm at GBR + BS implants and -1.92 mm at GBR implants (Table 4). When comparing the two groups, there was a statistically significant difference of 0.91 mm in favour of GBR + BS implants ($P < 0.0001$; CI 95% 0.54 to 1.27) at loading, and of 0.72 mm (CI 95% 0.42 to 1.02, $P < 0.0001$) 1 year after loading.

After 1 year, the average PES score, assessed by a blinded assessor, was significantly higher in the GBR + BS group (8.94 versus 11.29; $P < 0.001$, Table 5). This means that sites treated with the addition of an anorganic bone substitute achieved better aesthetics than sites treated only with a resorbable barrier. Aesthetics scored higher for the GBR + BS group in all of the seven domains (Table 5), but in particular for soft tissue contour, alveolar process deficiencies and soft tissue texture.

Patient satisfaction was assessed 1 year after loading only for those patients who did not experience the implant failure. Regarding function, 32 patients of the GBR group declared to be completely satisfied, compared with 37 patients in the GBR + BS group. One patient per group declared to be partially satisfied and one patient per group not satisfied. For aesthetics, 32 patients of the GBR group declared to be completely satisfied, compared with all 39 patients in the GBR + BS group. One patient treated with the barrier alone was uncertain about the aesthetic outcome and another was not satisfied. Both groups of patients were equally satisfied by function (Mann–Whitney U test $P = 0.88$) and the aesthetics of their implant-supported crowns (Mann–Whitney U test $P = 0.13$). All patients declared that they would undergo the same procedure again.

The comparison between the four centres is presented for the dichotomous data in Tables 2 and 3, however there were insufficient failures or complications to undertake statistical tests. There were no statistically significant differences among PES scores between centres ($P = 0.75$).
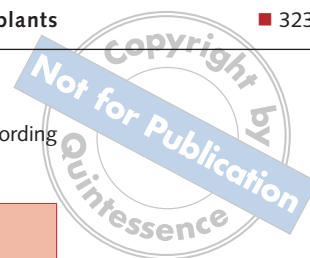
Table 2 Summary of implant failures up to 1 year after loading by study centre. The failed implants are described according to their position.

	De Angelis [n = 18]	Camurati [n = 18]	Gambino [n = 20]	Felice [n = 18)	Total [n = 74]
GBR	22 & 46	47	0	14 & 36	5
GBR + BS	0	44	0	46	2
Total	2	2	0	3	7

Table 3 Summary of patients experiencing complications up to 1 year after loading by study centre.

	De Angelis	Camurati	Gambino	Felice	Total
GBR	1	0	0	1	2
GBR + BS	4	0	0	2	6
Total	5	0	0	3	8

Table 4 Mean radiographic peri-implant marginal bone levels between groups and time periods (for patients with data at implant placement, loading and at 1 year).

	Implant placement			Loading			1 year after loading		
	N	Mean	(SD)	N	Mean	(SD)	N	Mean	(SD)
GBR	40	1.92	(1.86)	33	1.57	(0.88)	33	1.76	(0.67)
GBR + BS	37	0.21	(0.47)	37	0.66	(0.60)	36	1.04	(0.58)

Table 5 PES scores (SD) at 1 year after loading by groups and by different aesthetic domains.

	Mesial papilla	Distal papilla	Soft tissue level	Soft tissue contour	Alveolar process deficiencies	Soft tissue colour	Soft tissue texture	Total PES score
GBR [n = 34]	1.50 (0.66)	1.38 (0.60	1.56 (0.75)	1.32 (1.79)	1.20 (0.77)	1.09 (0.71)	0.91 (0.67)	8.94 (2.85)
GBR + BS [n = 38]	1.54 (0.60	1.58 (0.60)	1.74 (0.50)	1.79 (0.41)	1.68 (0.53)	1.44 (0.55)	1.50 (0.60)	11.29 (2.15)
Difference								-2.35 [95% CI -3.53, -1.17]
P value								<0.001

■ Discussion

This trial was designed to assess which of two techniques would achieve the best aesthetic results for treating buccal gaps between the bone and a single immediate post-extractive implant. One year after loading, the aesthetic outcome and peri-implant marginal bone levels were better at implants subjected to additional grafting with an anorganic bovine bone (Endobon) as an adjunct to resorbable collagen barriers.

Baseline periapical radiographs were taken at the end of the bone augmentation procedures. This explains why the radiographic marginal peri-implant bone levels just after the augmentation procedure were recorded on average more coronal (approximately 1.7 mm) in the GBR + BS group. The bone substitute accounted for this difference and it is plausible to speculate that the loosely packed bone granules remodelled over time, explaining the greater bone loss recorded 1 year after loading. Nevertheless, marginal bone levels at sites treated with Endobon were on average 0.7 mm more coronal than sites in the GBR group 16 months after augmentation, suggesting a benefit of the bone substitute on marginal bone level.

Endobon is only slightly resorbable and therefore stays where it is placed, decreasing the physiologic bone resorption after tooth extraction as demonstrated indirectly by the higher aesthetic score. It is

possible that the bone substitute should be packed more densely and in excess to further improve aesthetics. It would be interesting to compare the aesthetic outcome at immediate post-extractive bone-to-implant gaps filled with non- or slightly resorbable bone substitutes with autogenous bone. Of particular interest would be to test some bone substitutes in putty formulations. Also the exact role of the membrane in the augmentation process should be better understood. Actually, it is unclear whether the membrane added any benefits when used in conjunction with a non-resorbable bone substitute.

When evaluating the aesthetic outcome it is clear that sites treated with Endobon resulted in a better aesthetic outcome. This occurred for all seven domains measured with the PES score (mesial papilla, distal papilla, soft tissue level, soft tissue contour, alveolar process deficiencies, soft tissue colour and texture), however the difference was more evident for soft tissue contour, alveolar process deficiencies and soft tissue texture. This suggests that the highest aesthetic benefit was obtained where it was actually needed, at the buccal aspect of the teeth. The PES score obtained by the two groups was 8.9 and 11.3 out of a maximum possible score of 14. The difference between the two groups of 2.4 corresponded to a 17% aesthetic improvement in favour of GBR + BS, which is clinically relevant. It should be noted that a score of 11.3 out of 14 should be considered as a good aesthetic result for the group augmented with Endobon.

Seven implants (9%) failed. This failure rate for single implants is a bit higher than what is considered the normal failure rate for delayed single-implant placement[9]. The present study supports the notion that post-extractive implants could be at a higher risk for failures than delayed implants, though not all centres had similar failure rates. Similar trends were also observed in a recent systematic review comparing immediate with delayed implant placement[1].

Only one small short-term RCT previously tested the hypothesis of the present study[4]. In this study of parallel group design, including 10 patients per group, a statistically significantly higher position of the soft tissue margins was found in relation to the implant shoulder at the buccal aspects of implants treated with barrier plus the bone substitute (2.1 mm versus 0.9 mm; mean difference = -1.2 mm), which may be suggestive of a better aesthetic outcome. Unfortunately, data with implants in function were not provided. Nevertheless, the results of the present and the previous study are in substantial agreement, suggesting that the use of a non-resorbable bone substitute could be a preferable solution over barriers alone at post-extractive implants in order to improve the aesthetic outcome.

Clinicians preferred to leave the collagen resorbable barriers partially exposed to direct bacterial contamination in the oral cavity. This was done also with the intention to preserve as much keratinised mucosa as possible[10].

One of the main limitations of the present trial is the lack of a requirement in the initial protocol design to include initial periapical radiographs. Clinicians took them anyway routinely at the end of the procedure (after suturing). In this way the presence of the bone substitute could have confounded the assessor, making him initially score the marginal bone levels higher than what they actually were. Ideally, radiographs should have been taken just after implant placement prior to randomly allocating patients to the treatment groups, to see whether the two groups were comparable at baseline. The second limitation is that one of the centres lost 11 radiographs of 5 patients, which means that radiographic data were incomplete for 6% of the patient population. However, the sample size was sufficient to allow the finding of a statistically significant difference in aesthetics between the procedures, which has relevant clinical implications for everyday clinical practice. In fact, it might be convenient to graft gaps around post-extractive implants to improve the final aesthetic outcome of the peri-implant tissues.

There were no statistically significant differences for the aesthetic outcomes between the four different centres. This strengthens the finding that a slightly resorbable bone substitute is effective in improving the aesthetic outcome in the presence of a buccal gap at least 1 mm wide at immediate post-extractive implants. Because the present multi-centre investigation tested both augmentation procedures in real clinical conditions, and patient inclusion criteria were broad, results can be generalised with confidence to a wider population with similar characteristics.

■ Conclusions

The additional use of a bovine anorganic bone substitute (Endobon) with resorbable collagen barriers (OsseoGuard) in defects around single immediate post-extractive implants improves aesthetics and radiographic peri-implant marginal bone levels. Immediate single post-extractive implants might be at an increased risk for failure.

■ References

1. Esposito M, Grusovin MG, Polyzos IP, Felice P, Worthington HV. Interventions for replacing missing teeth: dental implants in fresh extraction sockets (immediate, immediate-delayed and delayed implants). Cochrane Database Syst Rev 2010;(9):CD005968.
2. Gher ME, Quintero G, Assad D, Monaco E, Richardson AC. Bone grafting and guided bone regeneration for immediate dental implants in humans. J Periodontol 1994;65:881-891.
3. Prosper L, Gherlone EF, Redaelli S, Quaranta M. Four-year follow-up of larger-diameter implants placed in fresh extraction sockets using a resorbable membrane or a resorbable alloplastic material. Int J Oral Maxillofac Implants 2003;18:856-864.
4. Cornelini R, Cangini F, Martuscelli G, Wennström J. Deproteinized bovine bone and biodegradable barrier membranes to support healing following immediate placement of transmucosal implants: a short-term controlled clinical trial. Int J Periodontics Restorative Dent 2004;24:555-563.
5. Fiorellini JP, Howell TH, Cochran D, Malmquist J, Lilly LC, Spagnoli D, Toljanic J, Jones A, Nevins M. Randomized study evaluating recombinant human bone morphogenetic protein-2 for extraction socket augmentation. J Periodontol 2005;76:605-613.
6. Chen ST, Darby IB, Adams GG, Reynolds EC. A prospective clinical study of bone augmentation techniques at immediate implants. Clin Oral Implants Res 2005;16:176-184.
7. Chen ST, Darby IB, Reynolds EC. A prospective clinical study of non-submerged immediate implants: clinical outcomes and esthetic results. Clin Oral Implants Res 2007;18:552-562.
8. Fürhauser R, Florescu D, Benesch T, Haas R, Mailath G, Watzek G. Evaluation of soft tissue around single-tooth implant crowns: the pink esthetic score. Clin Oral Implants Res 2005;16:639-644.
9. Esposito M, Hirsch J-M, Lekholm U, Thomsen P. Biological factors contributing to failures of osseointegrated oral implants. (I) Success criteria and epidemiology. Eur J Oral Sci 1998;106:527-551.
10. Cordaro L, Torsello F, Roccuzzo M. Clinical outcome of submerged versus non-submerged implants placed in fesh extraction sockets. Clin Oral Implants Res 2009;20:1307-1313.