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KEY WORDS
narrow diameter implant, horizontal augmentation, bone substitute, bone lamina

Randomised controlled trial

IMMEDIATE LOADING OF 3 MM-DIAMETER IMPLANTS AS AN ALTERNATIVE TO HORIZONTAL BONE AUGMENTATION FOR PLACING 4 MM-DIAMETER IMPLANTS: ONE-YEAR POST-LOADING RESULTS FROM A MULTICENTRE RANDOMISED CONTROLLED TRIAL

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PURPOSE. To evaluate the effectiveness of immediately loaded 3 mm-diameter implants as an alternative to horizontal bone augmentation procedures to allow placement of implants with a conventional diameter of 4 mm.

MATERIALS AND METHODS. Forty-five partially edentulous patients with between 4 and 5 mm of bone width 3 mm below the crest in areas requiring one to three adjacent implants were randomised, according to a parallel-group design, to receive one to three 3.0 mm-diameter implants to be loaded immediately (23 patients) or horizontal crest augmentation with a granular bone substitute covered with a bone lamina for placing, after 6 months of healing, one to three 4 mm-diameter implants (22 patients) at two centres. Implants at augmented sites were left to heal unloaded for 4 months. Four mm-diameter implants were restored using provisional screw-retained reinforced acrylic prostheses, replaced after 4 months by definitive prostheses. Three mm-diameter implants were loaded immediately with definitive metal-composite prostheses if the insertion torque was ≥ 35 Ncm, or otherwise after 4 months. Patients were followed-up to 1 year post-loading. Outcome measures were: prosthesis and implant failures, any complication, peri-implant marginal bone level changes, and patient satisfaction.

RESULTS. Two patients dropped out of the augmentation group. In three patients, five 3 mm-diameter implants could not be inserted with a torque of 35 Ncm, so they were submerged unloaded for 4 months. Two implants failed in two patients from the augmentation group (P = 0.2333; difference in proportion = -0.09; CI 95% -0.24 to 0.07) and neither patient was fitted with a prosthesis. Five patients with narrow-diameter implants were affected by six complications *versus* 11 augmented patients with 12 complications, the difference being statistically significant (P = 0.0477; difference in proportion = -0.28; CI 95% -0.52 to 0). One year after loading, patients with 3 mm-diameter implants lost on average 0.14 mm of peri-implant bone, while augmentation patients lost 0.52 mm. The difference in bone loss between the two groups was statistically significant (mean difference = 0.38 mm, 95% CI 0.10 to 0.66, P = 0.0112). Five 3-mm group patients *versus* two augmentation group patients (mean difference = 0.12 mm, 95% CI -0.12 to 0.32, P = 0.4205) and one 3-mm group patient *versus* two augmentation group patients (mean difference = -0.06 mm, 95% CI -0.23 to 0.12, P = 0.5900) were partially satisfied with function and aesthetics, respectively, all remaining patients being fully satisfied. All patients would undergo the same procedure again.

CONCLUSIONS. One year after loading, patients treated with 3 mm-diameter implants exhibited better results than those receiving horizontal augmentation for placement of 4 mm-diameter implants. Three mm-diameter implants might therefore be the preferable choice with respect to horizontal bone augmentation, the treatment being less invasive, faster, cheaper, and associated with less morbidity and peri-implant marginal bone loss; however, 5- to 10-year post-loading data will be necessary before reliable recommendations can be made.

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CONFLICT OF INTEREST STATEMENT. Global D (Brignais, France) partially supported this trial and donated the implants and prosthetic components. Osteobiol (Tecnoss, Giaveno, Italy) donated the biomaterials used for bone augmentation. However, the data property belonged to the authors and neither Global D nor Osteobiol interfered in any way with the conduct of the trial or the publication of the results.

INTRODUCTION

Dental implants are used to replace missing teeth in order to rehabilitate function and aesthetics in edentulous patients. However, in many patients it is not possible to place dental implants of "adequate" diameter because there is less than 5 mm of residual bone width due to resorption of the crestal bone. Clinicians, therefore, are faced with the dilemma of whether to attempt a horizontal augmentation procedure, or whether to place narrow implants having a diameter of 3 mm or less.

Various techniques are currently used for horizontal bone augmentation, though only a few of these techniques have been evaluated in randomised controlled trials (RCTs)[1,2]. Augmentation procedures are more technically demanding than simple implant placement, and therefore require skilful operators; moreover, they are expensive, can also be associated with significant postoperative morbidity and complications, and can require a longer period (up to 1 year) before patients are able to chew on their implant-supported prostheses[1,2]. Narrow-diameter implants, on the other hand, could be a simpler, cheaper, less invasive and faster alternative if they could provide similar clinical outcomes to conventional diameter implants placed in augmented bone.

While there have been two randomised controlled trials (RCTs) with 3-year follow-up comparing 3.3-mm narrow-diameter implants with implants having a conventional 4.1 mm diameter placed in sufficient bone volumes[3,4], there have been no RCTs comparing narrow-diameter implants placed in scarce bone volumes with conventional-diameter implants placed in bone volumes created by means of horizontal augmentation. Hence, the aim of this RCT was to compare the effectiveness of immediately loaded 3 mm-diameter implants (In-Kone Universal, Global D, Brignais, France; **FIGS. 1, 2A-H**) as an alternative to placement of identical implants with a conventional diameter of 4 mm following horizontal bone augmentation using a mix of collagenated cortico-cancellous porcine bone (Osteobiol mp3, Tecnoss, Giaveno, Italy) covered with a lamina of cortical porcine bone (OsteoBiol Lamina, 1 mm thick) (**FIGS. 1, 3A-G**).

The study protocol foresees following up patients to the fifth year of function in order to evaluate the outcome of the procedures over time; this report presents the results up to 1 year after loading. A report presenting the results at 4 months after loading has previously been published[5]. The present article has been drafted in line with the CONSORT statement for improving the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

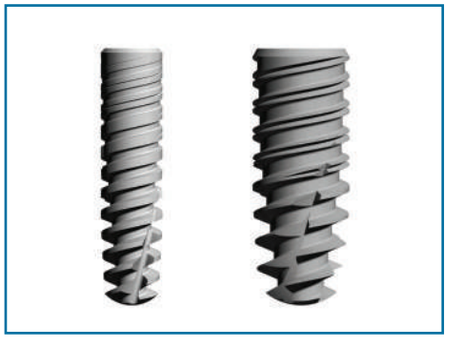
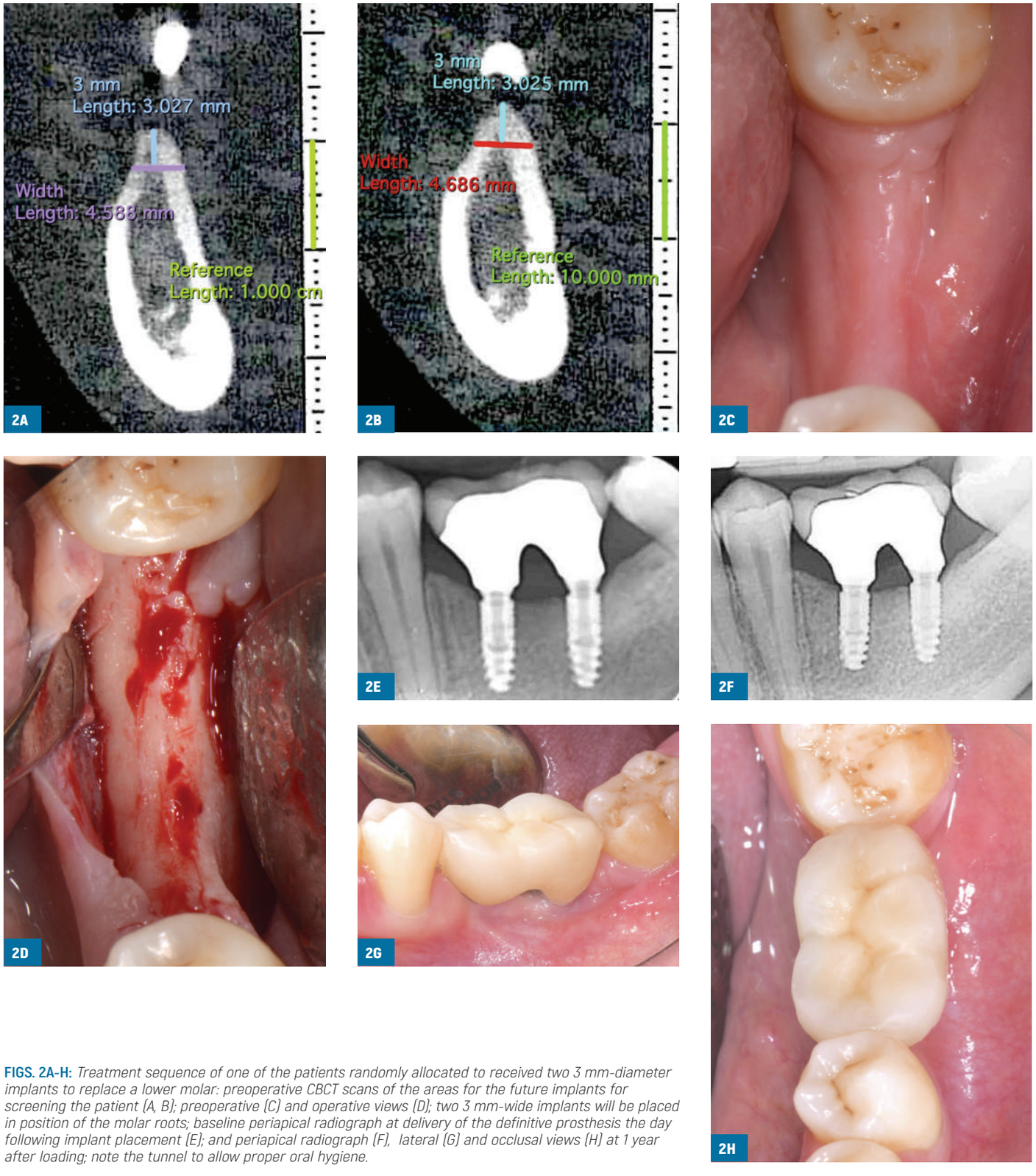


FIG. 1: *Drawings showing the difference in diameters of the implants used in the present study: on the left the 3 mm-diameter and on the right the 4 mm-diameter implant.*

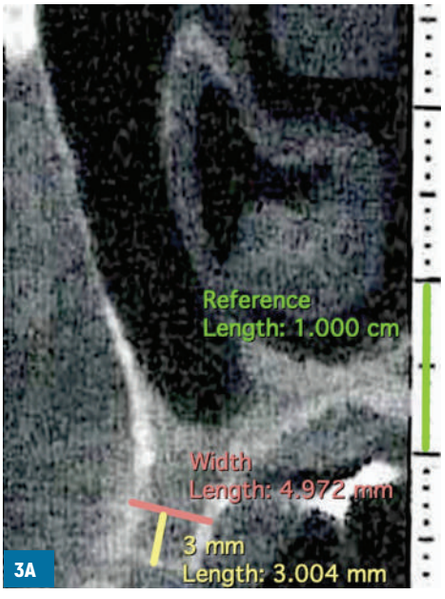
MATERIALS AND METHODS

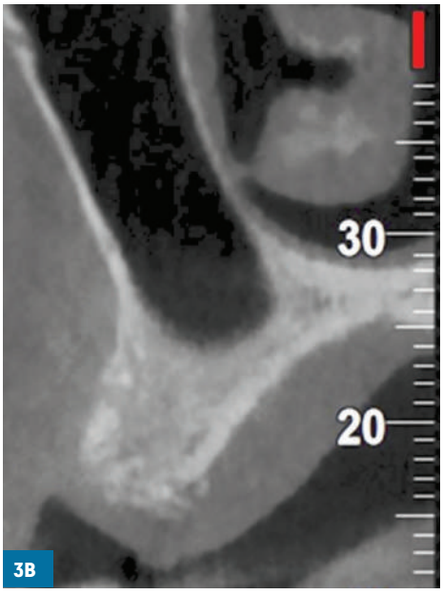
Study design

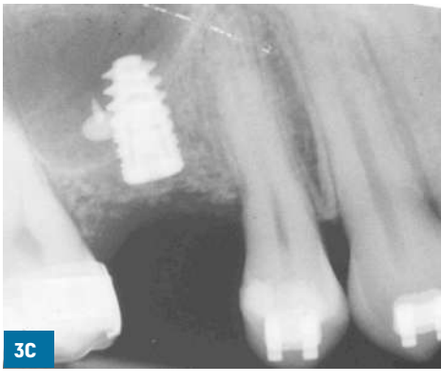
This parallel-group multicentre randomised controlled trial was designed with two arms. One arm received one to three immediately loaded 3 mm-diameter implants (**FIGS. 2A-H**) while the other had crestal bone horizontally augmented and, after 6 months of healing, one to three 4 mm-diameter implants left to heal submerged and unloaded for 4 months (**FIGS. 3A-G**).

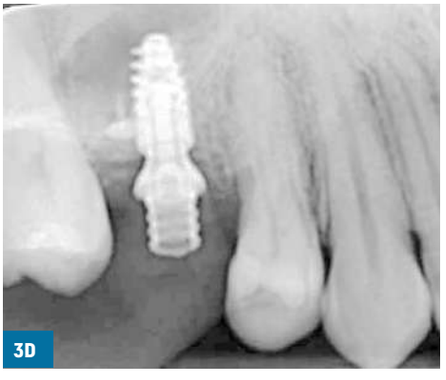


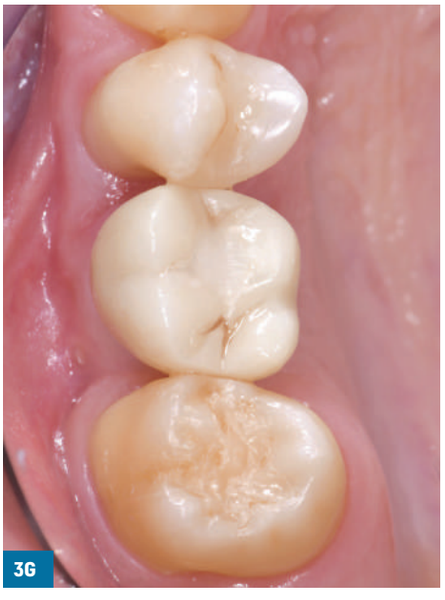
FIGS. 2A-H: *Treatment sequence of one of the patients randomly allocated to received two 3 mm-diameter implants to replace a lower molar: preoperative CBCT scans of the areas for the future implants for screening the patient (A, B); preoperative (C) and operative views (D); two 3 mm-wide implants will be placed in position of the molar roots; baseline periapical radiograph at delivery of the definitive prosthesis the day following implant placement (E); and periapical radiograph (F), lateral (G) and occlusal views (H) at 1 year after loading; note the tunnel to allow proper oral hygiene.*

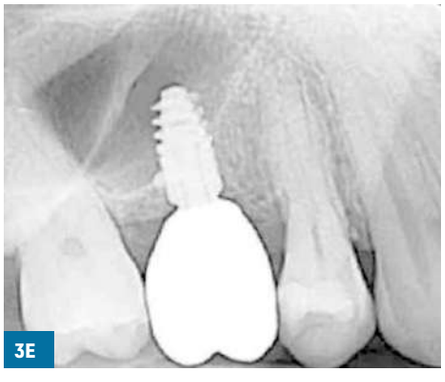


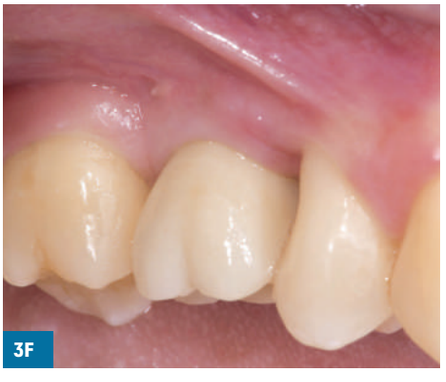












FIGS. 3A-G: *Treatment sequence of one of the patients randomly allocated to receive horizontal bone augmentation to place a 4 mm-diameter implant to replace an upper second premolar: preoperative CBCT scan of the area for the future implant used for screening the patient (A); CBCT taken after 6 months of healing to plan implant insertion (B); periapical radiograph at placement of the 4 mm-diameter implant (C); periapical radiograph at initial loading with the provisional crown (D); and periapical radiograph (E), lateral (F), and occlusal views (G) at 1 year after loading.*

Inclusion and exclusion criteria

Any partially edentulous patient with buccolingual crestal bone width of between 4 and 5 mm 3 mm below the crest at each future implant site, as measured on cone-beam computed tomography (CBCT) scans, in areas requiring one to three dental implants, being 18 years or

older and able to understand and sign an informed consent form, was eligible for inclusion in this trial. The minimal implant length to be used was 8.5 mm. In cases of eligible areas where aesthetics was of concern, for patients to be randomised to small diameter implant(s), a soft tissue connective graft harvested from the palate or the maxillary retromolar area was to be inserted using a pouch technique at implant placement to improve aesthetics. However, no patients needing soft tissue graft for improving aesthetics were actually enrolled. For patients randomly allocated to the 3 mm-diameter group, two implants were used to replace one single molar. In patients having multiple horizontally resorbed areas, only one area was included in the study, specifically that which could be treated using up to three adjacent implants. Each patient could only be treated on one side of the jaw, in accordance with the parallel group design.

Exclusion criteria were:

- General contraindications to implant surgery;
- Irradiation of the head and neck area;
- Immunosuppressed or immunocompromised status;
- Previous or ongoing treatment with intravenous aminobisphosphonates;
- Untreated periodontitis;
- Poor oral hygiene and motivation;
- Uncontrolled diabetes;
- Pregnancy or breast-feeding;
- Substance misuse;
- Psychiatric problems;
- Unrealistic expectations;
- Lack of opposing occluding dentition in the area intended for implant placement;
- Acute or chronic infection/inflammation in the area intended for implant placement;
- Participation in other studies if precluding proper adherence to the present protocol;
- Referral for implant placement alone, i.e., not having the prosthesis or maintenance procedures performed at the study treatment centres;
- Extraction sites with less than 3 months of healing time;
- Inability to participate in 5-year follow-up.

Patients were categorised into three groups according to their declarations: non-smokers, moderate smokers (up to 10 cigarettes per day), and heavy smokers (more than 10 cigarettes per day). Patients were recruited and treated in different centres by two different operators. One operator (Pietro Felice, PF) treated patients at the Bologna university clinic, whereas the other operator (Roberto Pistilli, RP) treated patients in his private practice. Both followed similar standardised procedures.

The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were adhered to. The study was approved by the Comitato Etico Interaziendale Bologna-Imola, Italy, on 9th December 2015 (Cod. CE: 15036). All patients received thorough explanation and signed a written informed consent form prior to being enrolled in the trial.

Augmentation and implant placement procedures

It was decided at the protocol stage to produce surgical templates to guide implant placement for all patients, but this was not actually implemented. Patients received prophylactic antibiotic therapy with 2 g of amoxicillin (or clindamycin 600 mg if allergic to penicillin) one hour prior to augmentation, and rinsed for one minute with chlorhexidine 0.2% just before the procedure. Patients were treated under local anaesthesia (articaine with 1:100,000 epinephri-

ne). After crestal and releasing incisions and flap raising, patients were randomly allocated, by opening a sequentially numbered envelope corresponding to the patient recruitment number, to either the horizontal augmentation procedure to allow placement of one to three implants of 4 mm-diameter (control procedure) or to receive one to three 3.0 mm-diameter implants (test procedure).

In the case of the augmentation procedure, the crestal bone was, when possible, perforated with a bur. In the maxilla, a lamina of cortical porcine bone was then positioned and fixed vestibularly or palatally, depending on the defect location, with one or more 1.2 mm-diameter titanium miniscrews (Minitek-Microtek, Global D). The site was then grafted with mp3 granular bone substitute, and the lamina was bent and fixed palatally or vestibularly with other miniscrews. In mandibles, the lamina was first fixed lingually. The lamina extended for at least 2 mm over the grafted area on sound bone. Incisions were made in the vestibular periosteum to release flaps as coronally as required, and the simple pressure of the fingers (the digitoclastic technique)[6] was used to better release the flaps. Flaps were sutured using horizontal mattress sutures and single simple sutures (Vicryl 4.0 sutures, Ethicon FS-2, St-Stevens-Woluwe, Belgium) until the incisions were perfectly sealed. Ice packs were provided, and 1 g amoxicillin (or 300 mg clindamycin) was prescribed to be taken three times a day for 7 days. Ibuprofen 400 mg (or 1 g paracetamol in the event of allergy to non-steroidal anti-inflammatory drugs) was prescribed 2 to 4 times a day to be taken during meals, as long as required. Patients were instructed to use 0.2% chlorhexidine mouthwash for one minute twice a day for 2 weeks, to eat a soft diet for one week, and to avoid brushing and trauma to the surgical sites. Patients were advised not to wear any removable prostheses. Patients were seen after 3 days, and sutures were removed after 10 days. Patients were recalled for additional postoperative check-ups at 1 and 2 months after the augmentation procedure. Grafted areas were left to heal for 6 months before placing the implants.

In the case of patients randomised to 3 mm-diameter implants, one to three tapered grade 5 titanium-alloy implants (In-Kone Universal, Global D), having a diameter of 3.0 mm, internal connection and a sand-blasted and roughened double acid-etched surface, were inserted. Each missing tooth was replaced by one dental implant. In the event that a single molar had been randomised to be replaced by 3 mm-diameter implants, two implants were placed instead, and three implants were placed to replace two adjacent missing molars. The standard placement procedure was employed, as recommended by the manufacturer. Drills of increasing diameters were used to prepare the implant sites. Bone quality (density) was subjectively assessed at drilling, and classed as "hard", "medium" or "soft". Implant sites were slightly underprepared, and the surgical unit motor was set with a torque of 35 Ncm during implant insertion. Implants inserted with a torque of greater than 35 Ncm were loaded immediately, while those inserted with a torque of less than 35 Ncm were submerged and left to heal for 4 months before being functionally loaded. Implants were placed 2 mm subcrestally. Healing abutments were fitted, and flap closure around the abutments was achieved using single Vicryl 4.0 sutures. In cases where aesthetics was a concern, patients randomised to 3 mm-diameter implants were to be given a connective tissue graft harvested from the maxillary retromolar area or the palate, inserted using the pouch technique at implant placement if necessary to improve aesthetics; however, no graft was actually performed. Baseline periapical radiographs were taken of the study implants. If the peri-implant marginal bone levels were not measurable, a new radiograph was taken. Patients were instructed to take ibuprofen 400 mg (or 1 g paracetamol in the event of allergy) two to four times a day during meals, except in the absence of pain, and to use chlorhexidine mouthwash 0.2% for 1 minute twice a day for 2

weeks. Patients were seen after 1 week for suture removal, occlusion check and oral hygiene instructions.
In the horizontal augmentation group, implants were placed following the same procedures, the differences being that they were 4 mm rather 3 mm in diameter, that only one implant was used to replace one missing tooth (intermediate pontics were allowed), and that they were submerged unloaded for 4 months.

Prosthetic procedures

For the 3 mm-diameter implants that were placed using a torque greater than 35 Ncm, the prosthetic procedures were begun immediately after suturing. All other implants were submerged for 4 months of unloaded healing. Impressions with the pick-up copings were taken using a polyether material (Impregum 3M/ESPE, Neuss, Germany) and customized resin impression trays. Definitive metal-composite prostheses rigidly joining the implants were cemented (Implacem, Dentalica, Milan, Italy at PF's centre or TempBond, Kerr Italia, Scafati, Italy at RP's centre) within 24 hours after impressions. Prostheses were made avoiding cuspid guidance and lateral and protrusive loading, trying to reach a balanced and mutually protected occlusion.
Periapical radiographs were taken using the paralleling technique. If the bone adjacent to the study implant was not properly visible, a second radiograph was taken.
Patients in the 4 mm-diameter group were rehabilitated after 4 months of submerged healing using screw-retained or reinforced cemented provisional prostheses rigidly joining the implants. The occlusal scheme was the same as in the test group.
Four months after loading, implants were manually tested for stability and, in the control group, definitive metal-composite, metal-ceramic or zirconia prostheses rigidly joining the implants were either screw-retained or cemented (using the same provisional cement as in the 3 mm group) onto titanium abutments. Oral hygiene instructions were reinforced, if necessary.
Patients were enrolled in an oral hygiene programme with recall visits every 6 months for the entire duration of the study. Follow-ups were conducted by independent outcome assessors (Dr. Berti at PF's centre and Dr. Cassoni at RP's centre). This report presents data at 1 year after prosthetic loading.

Outcome measures

This study tested the null hypothesis that there would be no differences in clinical outcomes between the two procedures against the alternative hypothesis of a difference. Outcome measures were the following.

- Prosthesis failure: planned prosthesis which could not be placed due to implant failure(s), loss of the prosthesis secondary to implant failure(s), or replacement of a definitive prosthesis for any reason.
- Implant failure: implant mobility, removal of stable implants dictated by progressive marginal bone loss or infection, or any mechanical complications rendering the implant unusable (e.g., implant fracture). The stability of each individual submerged implant was measured at abutment connection (4 months after implant placement) and all implants were tested for stability at 4 months and at 1 year after loading by tightening the abutment screws, with the prosthesis removed, using a manual wrench with 20 Ncm force. Implants supporting single crowns did not have their crowns removed, but instead rocked with the handles of two instruments.
- Any biological or prosthetic complications.
- Peri-implant marginal bone level changes, as evaluated on digital periapical radiographs taken using the paralleling technique at implant placement, and at 4 months and 1 year

after loading. Radiographs were stored on a personal computer in TIFF format with 600 dpi resolution. Peri-implant marginal bone levels were measured using OsiriX (Pixmeo Sarl, Bernex, Switzerland) software. The software was calibrated for each image using the known implant length. Measurements of the mesial and distal bone crest levels adjacent to each implant were made to the nearest 0.01 mm and averaged for implants, patient and groups. The measurements were made parallel to the implant axis. Reference points for the linear measurements were the apical margin of the implant collar and the most coronal point of bone-to-implant contact.

- Aesthetic evaluation of clinical vestibular and occlusal pictures of each individual experimental tooth and its adjacent tooth/implant, taken at 4 months (after delivery of the definitive prostheses in the 4 mm-diameter group) and 1 year after loading, was to be performed on a computer screen by an independent, blinded dentist. The aesthetic evaluation was to be performed using the pink aesthetic score (PES)[7] and the white aesthetic score (WES)[8]. Aesthetic scores were to be evaluated for individual teeth, then averaged for patients and groups. Unfortunately, only pictures of five patients were taken at the 4-month follow-up and only four patients at 1-year follow-up, so no aesthetic evaluation could be performed at these time points.
- Patient satisfaction. Four months and 1 year after loading, the independent outcome assessor at each centre asked patients the following questions:
  1) "Are you satisfied with the function of your implant-supported prosthesis?" Possible answers were: "yes, absolutely", "yes, partly", "not sure", "not really", or "absolutely not";
  2) "Are you satisfied with the aesthetic outcome of your implant-supported prostheses?" Possible answers were: "yes, absolutely", "yes, partly", "not sure", "not really", or "absolutely not";
  3) "Would you undergo the same therapy again?" Possible answers were: "yes" or "no".

Methodological aspects

The study was designed to be conducted at four centres, but only two recruited patients: the University of Bologna dental clinic (PF) and a private practice in Rome (RB). Two dentists (Dr. Berti at PF's centre and Dr. Cassoni at RP's centre) not involved in the treatment of the patients performed the implant stability assessment and took the periapical radiographs without knowing group allocation; however, augmented sites could be easily identified due to their anatomy. Complications were dealt with and reported by the treating clinicians, who were not blinded. One experienced assessor (Dr. Barausse), not involved in the treatment of the patients, performed all radiographic assessments without knowing group allocation; however, augmented sites could be easily identified on radiographs due to the different implant diameters and the presence of a more radiopaque bone substitute.

No sample size calculation was performed since no data on 3.0 mm-diameter implants was available when this trial was conceived. It was agreed to run the trial at four different centres. Each centre had to include 28 patients, 14 having thin ridges in mandibles and 14 in maxillae, to be randomly allocated in equal number to each treatment group. In total, 112 patients were to be recruited, 56 receiving 3 mm-diameter implants and 56 having conventional 4 mm-diameter implants after horizontal bone augmentation. However, two centres did not recruit a single patient, and one centre treated seven patients partially edentulous in mandibles and 10 in maxillae. One computer-generated restricted randomisation list was created for each centre. Only one of the investigators (Dr. Esposito), not involved in the selection and treatment of the patients, was aware of the random sequence and had access to the randomisation list stored on his password-protected laptop computer. The information on how to treat each patient was enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened

sequentially after flap raising. Therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

All data analysis was carried out according to a pre-established analysis plan. A dentist with expertise in statistics (Dr. Buti) analysed the data without knowing the group codes. The patient was the statistical unit of the analyses. Differences in the proportion of patients with prosthesis failure, implant failure and complications (dichotomous outcomes) were compared using the chi-squared test or Fisher's Exact probability test (when 20% of cells with expected count <5). Differences in patient means for continuous outcomes (radiographic bone levels) between groups were compared using a t-test for independent samples. Comparisons between each time point and baseline measurements were made using paired t-tests, to detect any changes in marginal peri-implant bone levels. The chi-squared test or Fisher's Exact probability test were used to compare groups in terms of the number of prosthesis failures, implant failures and complications. The latter tests were also applied to estimate differences between groups in patient satisfaction with aesthetics and function, as the outcomes reported fell into only two (fully vs. partially satisfied) out of the five categories described above, and to answer the question "would you undergo the same treatment again?". A t-test for independent samples was used to compare the marginal bone level changes at the two centres. All statistical comparisons were conducted at the 0.05 level of significance. An intention-to-treat analysis was to be used.

RESULTS

Sixty-one patients were screened for eligibility, but 16 patients were not included in the trial for the following reasons: 13 patients (nine of PF's and four of RP's), requested horizontal bone augmentation in aesthetic areas, and three patients (RP) refused any surgical intervention and asked for an adhesive prosthesis instead. Forty-five patients were considered eligible and were consecutively enrolled in the trial. All patients were treated according to the allocated interventions.

Two patients dropped out before the 1-year post-loading follow-up. Both were from the augmentation group at PF's centre, and both were treated in the lower jaw. One patient (#12 lower), who lost one of the two implants at abutment connection, moved away 3 months after the second implant placement and was unable to complete the rehabilitation. The other patient (#8 lower) was last seen at the 4-month follow-up and become unreachable.

Data pertaining to all remaining patients were evaluated in the statistical analyses, with the exception of the clinical pictures for evaluating aesthetics at 4 months and 1 year after loading, which, as mentioned, were largely absent.

Apart from the reduced number of patients than planned, treated by only two of the four centres involved at the planning stage, the non-production of surgical templates after initial CBCT, and the inconsistencies in taking clinical pictures for aesthetic assessment, the following deviations from the protocol were reported.

- Three mm-diameter implants (test group):
  - in one patient there was insufficient space to place two implants to replace a molar, so only one implant was inserted;
  - in two patients, in whom a torque greater than 35 Ncm was not achieved, healing abutments were placed instead of fully submerging the implants.
  - for one patient no 1-year radiograph was taken since the radiography machine was broken and he was unable to reschedule;
  - in two patients the 1-year radiograph was taken with delays of 3 and 4 months, respectively.

- Augmentation group (control):
  - two patients had one 6 mm-long implant inserted and their implant submerged time prolonged by 2 months due to the augmented bone being too soft;
  - two patients had a connective tissue graft from the palate at their mandibular implants due to total lack of keratinised mucosa and pain on brushing;
  - one patient asked to have the definitive prosthesis fitted directly, eschewing the provisional prosthesis for financial reasons;
  - one patient received the final prosthesis after 1 year, instead of 4 months, for personal reasons.

Patients were recruited and treated from January 2016 to February 2018. The follow-up reported herein was conducted 1 year after initial loading.

The main baseline patient and intervention characteristics, divided by study group and location, are presented in **TABLE 1**. Thirty-five implants were placed in the augmented group (control) and 49 in the 3 mm-wide implant group (test). This difference was due to the fact that two 3 mm-diameter implants were used to replace single molars *versus* only one 4 mm-diameter implant. There were no baseline differences between the two groups, with the exceptions of twice the number of smokers in the 3 mm-diameter group, and the fact that all 3 mm-diameter implants were rehabilitated with cemented metal-resin prostheses. Five implants in three patients from the 3 mm-diameter group were inserted with a torque lower than 35 Ncm, and were loaded after 4 months of unloaded healing. Among the 4 mm-diameter implants, none could be placed with torque of at least 35 Ncm, indicative of a generalised softer bone quality at horizontally augmented sites.

- Prosthetic and implant failures: no patient from the 3 mm-diameter group lost any implant *versus* two patients from the augmentation group who lost one implant each (P = 0.2333 (Fisher's Exact probability test); difference in proportion = -0.09; CI 95% -0.24 to 0.07). One 6 mm-long implant in a lower premolar position was found to be mobile at abutment connection in a non-smoking female whose graft was characterised by poor integration, despite the implant healing having being prolonged by two months. This patient also experienced temporary post-augmentation paraesthesia. Another 8.5 mm-long implant in a lower premolar position was found to be mobile at abutment connection in a female moderate smoker whose graft was characterised by poor integration. Both patients had their failed implants replaced, but one has not received her definitive prosthesis since dropped out.
- Complications: more complications occurred at augmented sites: five patients with narrow-diameter implants were affected by six complications *versus* 11 patients with 12 complications in the augmentation group, the difference being statistically significant (P = 0.0477, chi-squared test); difference in proportion = -0.28; CI 95% -0.52 to 0). A detailed description of the complications and their treatment is presented in **TABLE 2**.
- Peri-implant marginal bone levels: at implant placement, there were no differences in bone levels between 3 and 4 mm-diameter implants (**TABLE 3A**). There were, however, significant differences in bone levels between the two groups at 1 year post-loading (P [t-test] = 0.0142; **TABLE 3A**). Both groups lost a statistically significant amount of bone: 1 year post-loading, 3 mm-diameter implants lost 0.14 mm of bone and 4 mm-diameter implants 0.52 mm; the difference was statistically significant (mean difference = 0.38 mm, 95% CI 0.10 to 0.66, P = 0.0112; **TABLE 3B**).
- Patient satisfaction: five 3-mm group patients *versus* two augmentation group patients (mean difference = 0.12 mm, 95% CI -0.12 to 0.32, P = 0.4205) and one 3-mm group patient *versus* two augmentation group patients (mean difference = -0.06 mm, 95% CI -0.23 to

0.12, P = 0.5900) were partially satisfied with function and aesthetics, respectively; all remaining patients were fully satisfied. All patients declared that they would undergo the same procedure again.

No significant differences were found in outcomes between the two operators (**TABLE 4**).

TABLE 1 PATIENT AND INTERVENTION CHARACTERISTICS

	3 mm-wide implants (n = 23)	Augmented + 4 mm-wide implants (n = 22)
Females	11 (48%)	13 (59%)
Mean age at recruitment (range)	50.26 (27-71)	48.82 (22-72)
Moderate smokers (up to 10 cig/day)	6 (26%)	4 (18%)
Heavy smokers (more than 10 cig/day)	4 (17%)	1 (5%)
Baseline average bone thickness 3 mm below the crest (SD)	4.78 mm (0.13)	4.70 mm (0.23)
Patients treated in mandibles	11 (48%)	10 (45%)
Number of implants	49	35
Number of implants placed in mandibles	22 (45%)	17 (49%)
Number of 6.0 mm-long implants	0 (0%)	2 (6%)
Number of 8.5 mm-long implants	19 (39%)	15 (43%)
Number of 10.0 mm-long implants	7 (14%)	9 (26%)
Number of 11.5 mm-long implants	22 (45%)	6 (17%)
Number of 13.0 mm-long implants	1 (2%)	3 (8%)
Number of implants in upper molar sites	7 (14%)	4 (11%)
Number of implants in lower molar sites	20 (41%)	9 (26%)
Number of implants in upper premolar sites	17 (35%)	12 (34%)
Number of implants in lower premolar sites	2 (4%)	6 (17%)
Number of implants in upper canine sites	3 (6%)	1 (3%)
Number of implants in lower canine sites	0 (0%)	0 (0%)
Number of implants in upper incisor sites	0 (0%)	1 (3%)
Number of implants in lower incisor sites	0 (0%)	2 (6%)
Number of implants placed with at least 35 Ncm torque	44 (90%)	0 (0%)
Number of patients receiving 1 implant	0 (0%)	9 (41%)
Number of patients receiving 2 implants	20 (87%)	13 (59%)
Number of patients receiving 3 implants	3 (13%)	0 (0%)
Number of zirconia screw-retained final prostheses	0 (0%)	5 (23%)
Number of metal/composite screw-retained final prostheses	0 (0%)	9 (41%)
Number of metal-ceramic cemented final prostheses	0 (0%)	4 (18%)
Number of zirconia cemented final prostheses	0 (0%)	2 (9%)
Number of metal-composite cemented final prostheses	23 (100%)	0 (0%)
Number of patients treated with soft tissue grafts	0	2 (9.1%)*

**Soft tissue grafting was only to be allowed to improve the aesthetics at small-diameter implants placed in aesthetic areas, but no procedure was actually implemented, with the exception of two protocol deviations justified by lack of keratinised mucosa*

Only cemented prostheses could be manufactured for 3 mm implants since their abutment is of press-fit type

TABLE 2 DESCRIPTION OF COMPLICATIONS AND THEIR OUTCOMES UP TO 1 YEAR AFTER LOADING

Patient number	Time	Complication	Treatment and outcome
Patients allocated to 3 mm-diameter implants			
2 lower (PF)	4w.pi	Cover screw loosening and inflammation of the peri-implant tissues	Chlorhexidine flushing and gel applications, and retightening of the cover screw. Chlorhexidine gel twice/day for 14 days. Resolved after 2 weeks
1 lower (PF)	2m.pl	Prosthesis de-cementation	Recemented
19 lower (RP)	3m.pl 12m.pl	Prosthesis de-cementation Mucositis at 2 implants replacing 46 **(FIG. 4)**	Recemented Removal and cleaning of the prosthesis, chlorhexidine 0.2% mouthwash twice/day for 14 days and re-instruction. Proposed connective tissue graft refused by the patient. Resolved after 2 weeks
13 upper (PF)	9m.pl	Mucositis at 24 & 25	Removal and cleaning of the prosthesis, chlorhexidine 0.2% mouthwash twice/day for 14 days and re-instruction. Proposed connective tissue graft refused by the patient. Resolved after 2 weeks
13 lower (PF)	12.pl	Mucositis at 2 implants replacing 36 **(FIG. 5)**	Removal and cleaning of the prosthesis, chlorhexidine 0.2% mouthwash twice/day for 14 days and re-instruction. Proposed connective tissue graft refused by the patient. Resolved after 2 weeks
Patients allocated to horizontal augmentation and 4 mm-diameter implants			
5 lower (PF)	0d.pg	Temporary paraesthesia	Resolved after 2 weeks
15 lower (RP)	0d.pg 4m.pl	Temporary paraesthesia Loosening of the prosthesis screw at 36	Resolved after 2 weeks Retightened
8 lower (PF)	0d.pg	Temporary paraesthesia	Resolved after 3 weeks
1 upper (PF)	3d.pg	Large ecchymosis from 13	Resolved after 2 weeks
17 upper (RP)	6d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and applications of chlorhexidine gel twice a day for 3 weeks, and thereafter water and salt mouthwash twice/day until implant placement
18 upper (RP)	7d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and applications of chlorhexidine gel twice a day for 3 weeks, and thereafter water and salt mouthwash twice/day until implant placement
5 upper (PF)	11d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and applications of chlorhexidine gel twice a day for 3 weeks, and thereafter water and salt mouthwash twice/day until implant placement
8 upper (PF)	1m.pg	Small central and occlusal wound dehiscence	Flushing with chlorhexidine and applications of chlorhexidine gel twice a day for 3 weeks, and thereafter water and salt mouthwash twice/day until implant placement
4 lower (PF)	4m.pl	Prosthesis loosening with chipping on 36	Retightened at 20 Ncm and chipping fixed chairside with composite
3 lower (PF)	4m.pl	Pain on brushing	Connective tissue graft. Resolved
11 lower (PF)	4m.pl	Pain on brushing	Connective tissue graft. Resolved

upper = upper arch; lower = lower arch; d.pg = days post-grafting; w.pi = weeks post-implantation; m.pl = months post-loading

TABLE 3A MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVELS

	Implant placement/loading				4 months post-loading				1 year post-loading			
	N	Mean	(SD)	[95% CI]	N	Mean	(SD)	[95% CI]	N	Mean	(SD)	[95% CI]
3 mm implants	23	0.02	(0.03)	[0.01 to 0.03]	23	0.11	(0.10)	[0.07 to 0.15]	22	0.16	(0.13)	[0.10 to 0.22]
4 mm implants	22	0.02	(0.03)	[0.01 to 0.03]	20	0.27	(0.29)	[0.13 to 0.40]	20	0.54	(0.62)	[0.25 to 0.82]
Difference		0		[-0.02 to 0.02]		0.16		[0.01, 0.30]		0.38		[0.08 to 0.67]
P-value			0.8304				0.0319*				0.0142*	

**Statistically significant difference*

TABLE 3B MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVEL CHANGES

	Baseline - 4 months post-loading				Baseline - 1 year post-loading			
	N	Mean	(SE)	[95% CI]	N	Mean	(SE)	[95% CI]
3 mm implants	23	0.09	(0.02)	[0.05 to 0.13]	22	0.14	(0.03)	[0.09 to 0.19]
4 mm implants	20	0.26	(0.07)	[0.12 to 0.39]	20	0.52	(0.13)	[0.24 to 0.80]
Difference		0.17		[0.02 to 0.31]		0.38		[0.10 to 0.66]
P-value		0.0235*				0.0112*		

**Statistically significant difference. All changes from baseline statistically different [P [paired t-test] ≤ 0.001]*

TABLE 4 COMPARISON OF OUTCOMES BETWEEN THE TWO STUDY CENTRES UP TO 1 YEAR AFTER LOADING

	PF 27 patients				PR 17 patients				Difference	95% CI	P-value
Patients with implant failures (# of implants)	2 (2)				0 (0)				0.07	-0.10 to 0.19	0.5192
Patients with complications (# of complications)	12 (12)				4 (6)				0.19	-0.10 to 0.44	0.1891
	N	Mean	(SE)	[95% CI]	N	Mean	(SE)	[95% CI]	Difference	95% CI	P-value
Peri-implant bone loss	25	0.31	(0.43)	[0.14 to 0.49]	17	0.33	(0.51)	[0.07 to 0.59]	0.02	-0.29 to 0.32	0.9196

DISCUSSION

This trial was designed to assess whether 3-mm narrow-diameter implants could be a viable treatment option for rehabilitating thin ridges (4 to 5 mm) with fixed implant-supported partial prostheses. The control procedure was horizontal augmentation using a granular bone substitute covered by a 1-mm thin bone lamina of porcine origin. Both tested interventions provided satisfactory outcomes, but 3 mm-diameter implants were associated with fewer complications and failures, and could be loaded immediately. In contrast, control-group patients had to wait for at least 10 months, and bone augmentation surgeries were more invasive and caused more discomfort.

Although these results come from a limited number of patients, who have been followed up for only 1 year after loading thus far, some interesting observations can be made. First and foremost, it was interesting to note that sometimes horizontal bone augmentation procedures, that had postoperative occlusal dehiscence of the soft tissues, resulted in a bone of poor consistency after a healing period of 6 months. This seems to suggest that these procedures should be improved if possible.

Furthermore, regarding peri-implant marginal bone level changes, using implant placement as baseline, 1 year after loading 3 mm-diameter implants lost on average 0.14 mm, and 4 mm-diameter implants about 0.52 mm. The 0.38 mm difference between groups was statistically significant, though may not be of clinical significance. Such a difference may not be unexpected, since recently augmented and not fully mineralised bone might be, at least initially, more prone to bone loss. These patients will be monitored to see whether more bone loss occurs over time, especially at the augmented sites.

It is difficult to compare the results of the present trial with those of similar studies, as these could not be found in the published literature. That being said, our results do show interesting similarities to those of other RCTs investigating vertical atrophy cases, comparing 4- to 6.6-mm short implants *versus* augmentation procedures to place 10 mm or longer implants[9-14]. Such results, obtained in vertically atrophic mandibles, were also summarised in a recent systematic review[15]; together they suggest that augmentation procedures to create new supporting bone are more technically demanding than placing narrow-diameter or short implants, and are generally associated with higher post-operative morbidity, more complications, longer treatment periods and an increased number of surgeries. Therefore, the less invasive technique could be the preferable choice. Nevertheless, more RCTs with larger sample sizes and longer follow-ups are needed; it would also be interesting to test other horizontal bone augmentation techniques.

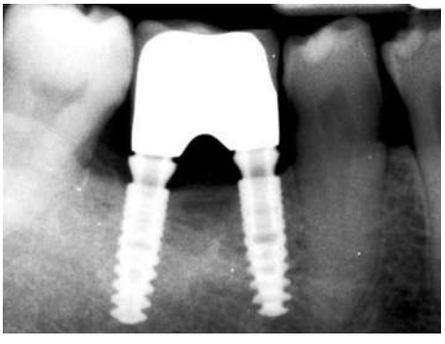


FIG. 4: *Periapical radiograph at 1 year after loading of one of the patients affected by peri-implant mucositis. Notice the abutment-crown gap, which may have favoured submucosal plaque retention.*

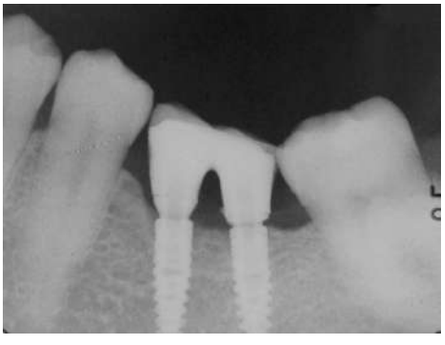


FIG. 5: *Periapical radiograph at 1 year after loading of another of the patients affected by peri-implant mucositis. Note the presence of some cement mesial to the distally placed implant, which may have favoured submucosal plaque retention.*

As regards complications, at 1-year follow-up it was observed that three patients from the narrow implant group developed peri-implant mucositis, and this was attributed to difficulties in oral hygiene procedures due to a lack or insufficiency of keratinised mucosa. After crown removal and local debridement, patients were offered a connective tissue graft to increase the keratinised mucosa, but all of them refused. By looking at the radiographs with a more attentive eye, an abutment-to-implant gap can be discerned (**FIG. 4**), as well as some residual cement (**FIG. 5**), which may have favoured the accumulation of subgingival plaque; therefore, thickening of the local oral mucosa may not necessarily have improved the situation.

There are several limitations to the present investigation, including the small number of patients included in the trial, especially those treated in aesthetic areas. Other features that may affect results are the use of different prosthesis designs in the two groups, the lack of aesthetic evaluation, and the short duration of follow-up.

Regarding the small number of patients included, there were two issues: 1) the trial was originally supposed to include 112 patients at four different centres, but two centres did not recruit a single patient and one centre did not manage to treat their full allotted quota; 2) thirteen potentially eligible patients who were edentulous in "aesthetic" areas refused to participate in the trial, opting instead for the augmentation procedure. Probably the most likely reason for this attitude is that all those patients were referred to the treatment centres for bone augmentation, and had therefore already been convinced by their referring dentists that bone augmentation was the best option for them, even though this might not, in fact, have been the case. In addition, the original protocol allowed for soft tissue grafting at implant placement in those patients whose aesthetics could have been compromised by using 3 mm-diameter implants without horizontal augmentation; however, no soft tissue

augmentation was, in fact, implemented. That being said, in order to understand better how things work in reality, it is important to be open-minded, and to bear in mind that many of the procedures commonly implemented nowadays may not be the best option for a patient's individual treatment.

There was a systematic difference between the two groups in terms of prosthesis design; the immediately loaded narrow-diameter implant group had to be rehabilitated with cemented prostheses because the abutments that could be used were of press-fit type only. As the narrow-diameter implants and the related prosthetic components are structurally weaker than normal diameter implants, the manufacturer elected to minimise the risk of fractures by providing only the cemented option, and we used metal-composite prostheses in all patients. Although the same type of prostheses should have been fitted in the augmentation group, the clinicians elected to use a variety of prosthesis types, the majority being screw-retained. This is an unfortunate protocol deviation that could have been avoided, but it is often difficult to make clinicians follow strict research protocols specifically designed to minimise possible confounding factors. It is also very difficult though to speculate to what extent these differences in prosthesis type may have impacted the results.

The lack of aesthetic assessment at both 4 months and 1 year after loading was due to the fact that, for some reason, both assessors neglected to take clinical photographs in most cases. It is still our intention, however, to take pictures of all patients at 5-year post-loading follow-up, to be reported in due course. Indeed, we consider aesthetics to be of great interest in a proper comparison of the two groups, especially because it could be the only parameter in favour of the augmentation procedure. It is noteworthy, however, that the aesthetics as evaluated by the patients themselves did not reveal any trend in favour of either procedure, bearing in mind that the great majority of the patients were treated in "non-aesthetic" areas. In terms of future research, it would be interesting to run a similar trial focussing on the anterior portion of the mouth, which is actually the area that narrow-diameter implants were designed to be used for.

The present follow-up, at 1 year post-loading, is, of course, short, but we plan to follow these cohorts of patients up to 5 years after loading, so these findings should be considered preliminary.

Both operators were experienced with the bone augmentation procedures evaluated in this trial, and this might limit extrapolations of the present results; however, all interventions were tested under real clinical conditions, and the inclusion criteria were sufficiently broad to allow the results of the present trial to be generalised with confidence to a wider population with similar characteristics.

CONCLUSIONS

Bearing in mind the limitations at this stage of the trial, in particular the lack of aesthetic evaluation, it is apparent that better results were achieved at one year after loading in patients treated with 3 mm-diameter implants than those horizontally augmented to receive 4 mm-diameter implants. As the former treatment is less invasive, faster, cheaper, and associated with less morbidity and marginal peri-implant bone loss, it may be the preferable option, although 5- to 10-year post-loading data will be necessary before reliable conclusions on this issue can be drawn.

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