KEY WORDS
small 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 NORMAL DIAMETER IMPLANTS: FOUR-MONTH 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 in 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 a bone width of between 4 and 5 mm 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-wide 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 implants at least 4 mm wide (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 (if the insertion torque was ≥ 35 Ncm) or after 4 months with definitive metal-composite prostheses. Patients were followed-up to 4-month post-loading. Outcome measures were: prosthesis and implant failures, any complication, peri-implant marginal bone level changes, and patient satisfaction.

RESULTS. No patient dropped out. In three patients, five 3 mm-diameter implants could not be inserted with a torque of 35 Ncm, so were submerged unloaded for 4 months. Two implants failed in two patients from the augmented group (P [Fisher's exact probability test] = 0.2333; difference in proportion = -0.09; CI 95% -0.24 to 0.07) and neither patient was fitted with a definitive prosthesis. Three patients with small diameter implants were affected by three complications *versus* nine augmented patients with 10 complications, the difference being statistically significant (P [chi-square test] = 0.0346; difference in proportion = -0.28; CI 95% -0.50 to -0.01). Patients with 3 mm-diameter implants lost on average 0.09 mm of peri-implant bone at 4 months, while augmented patients lost 0.26 mm, a statistically significant difference (mean difference = 0.17 mm, 95% CI 0.02 to 0.31, P = 0.0235). All patients were fully satisfied with both function and aesthetics, with two exceptions: one patient from the 3-mm group was only partially satisfied with both aesthetics and function, and one patient from the augmentation group was only partially satisfied with the aesthetics. However, all patients would undergo the same procedure again.

CONCLUSIONS. Four months after loading, patients treated using 3 mm-wide implants displayed better results than those horizontally augmented to receive 4 mm-wide implants. Three mm-wide implants might therefore be a preferable choice with respect to bone horizontal bone augmentation, the treatment being less invasive, faster, cheaper, and associated with less morbidity; however, 5- to 10-year post-loading data will be necessary before reliable recommendations can be made.

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.

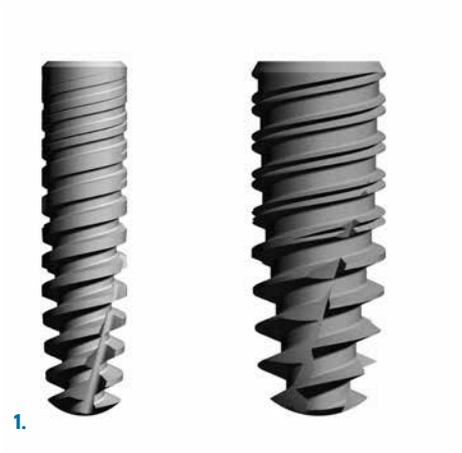
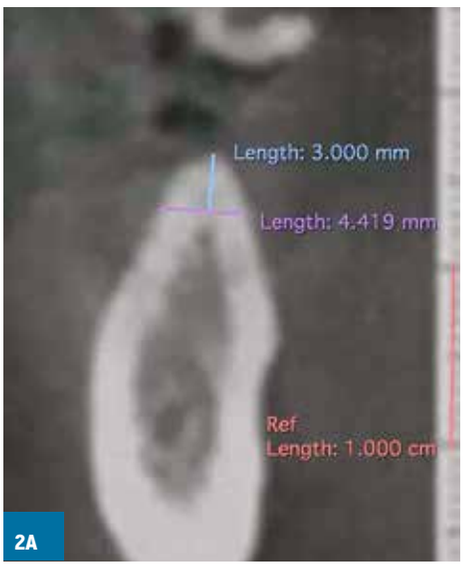
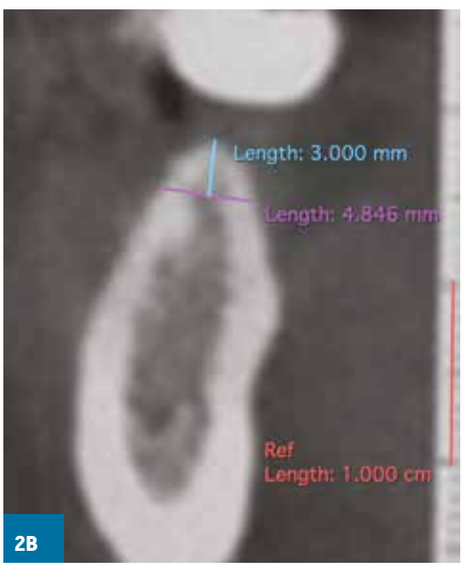


Fig. 1: *Drawings showing the difference in diameters of the implants used in the present study: on the left the 3 mm-diameter and on the right the 4 mm-diameter implant.*





INTRODUCTION

Dental implants are used to replace missing teeth for rehabilitating 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 small 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]. 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 may require a longer period (up to 1 year) before patients are able to chew on their implant-supported prostheses[1]. Small 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) comparing 3.3-mm small-diameter implants with implants having a conventional 4.1 mm diameter placed in sufficient bone volumes with 3-year follow-up [2,3], there have been no RCTs comparing small-diameter implants placed in scarce bone volumes with conventional-diameter implants placed in similar 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) **(FIG. 1)** as an alternative to the placement of identical implants with a conventional diameter of 4 mm following horizontal bone augmentation using a mix of collagenated corticocancellous porcine bone (OsteoBiol mp3, Tecnoss, Giaveno, Italy) covered with lamina of cortical porcine bone (OsteoBiol Lamina, 1 mm thick) **(FIGS. 2A-K)**.

The study protocol foresees following-up patients to the fifth year of function in order to evaluate the success of the procedures over time; this preliminary report presents the clinical outcomes at 4 months after loading. 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/).

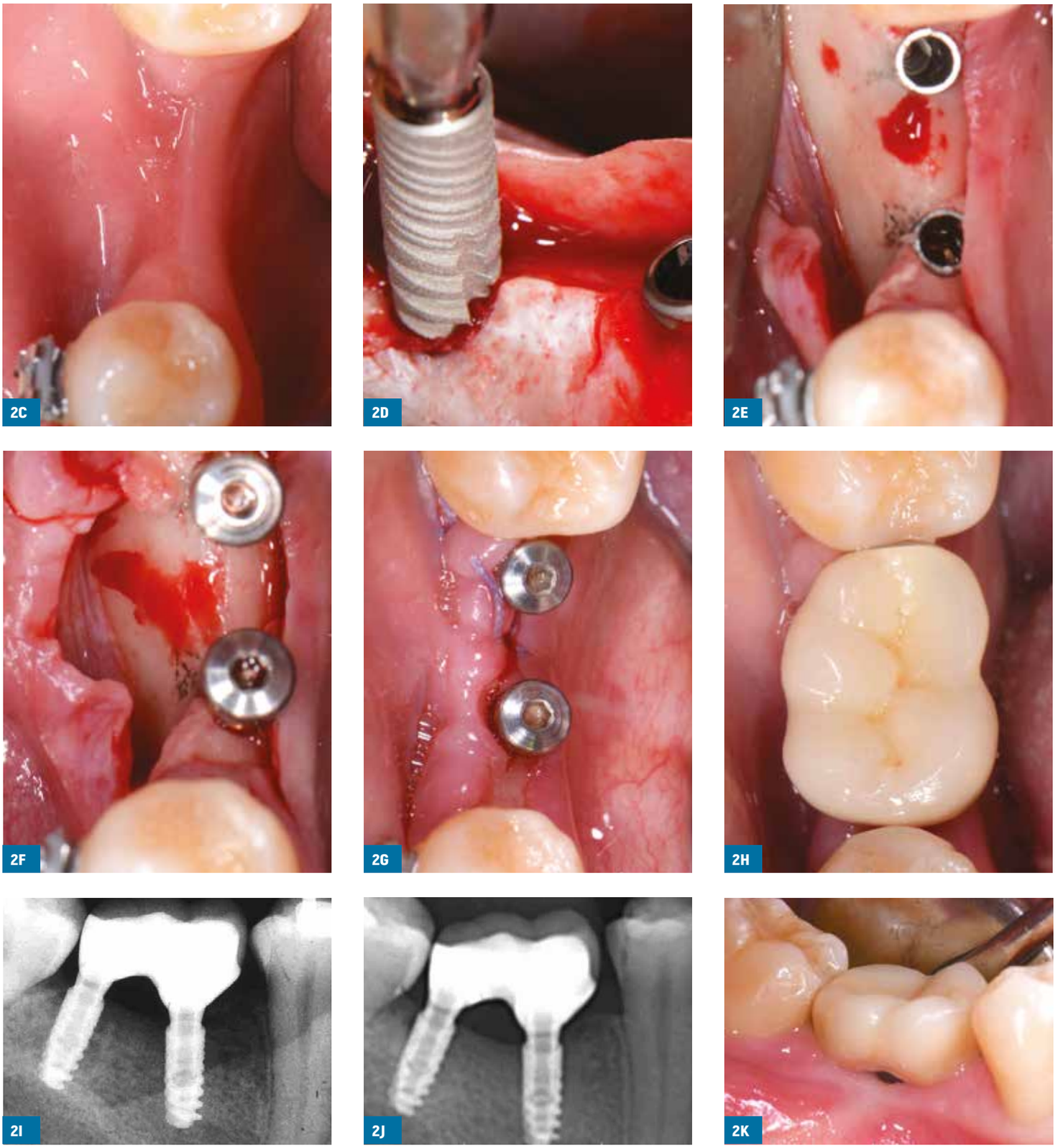
MATERIALS AND METHODS

Study design

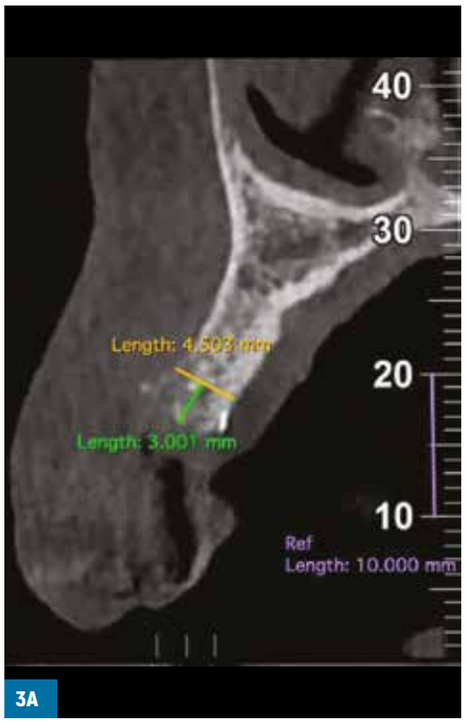
This parallel-group randomised controlled multicentre trial was designed with two arms. One arm received one to three immediately loaded 3 mm-diameter implants **(FIGS. 2A-K)**, while the other had crestal bone horizontally augmented and, after 6 months of healing, one to three 4 mm-diameter implants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

Inclusion and exclusion criteria

Any partially edentulous patient with crestal bone of buccolingual 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 of 8.5 mm. In case of an eligible area



Figs. 2A-K: *Sequence of treatment of one of the patients randomly allocated to receive two 3 mm-diameter implants to replace a lower molar: A) and B) preoperative CBCT scans of the areas of the future implants for screening the patient; C) preoperative clinical view; D) two 3 mm-wide implants were placed in position of the molar roots; E) occlusal view; F) healing abutments in position; G) clinical view with sutures just before immediate loading; H) immediate loading with a definitive metal-composite crown; I) periapical radiograph at implant placement/immediate loading; J) periapical radiograph and K) clinical view 4 months after loading; note the tunnel to allow proper oral hygiene.*



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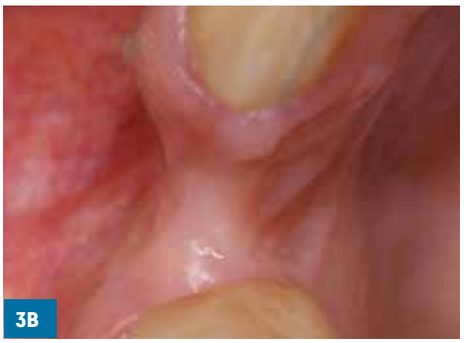
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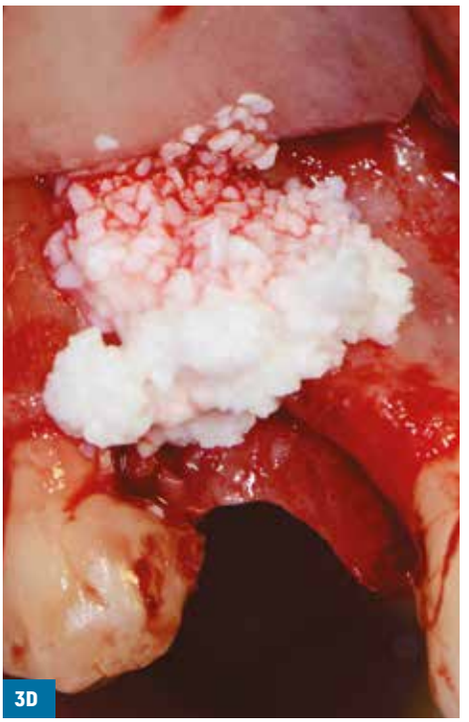
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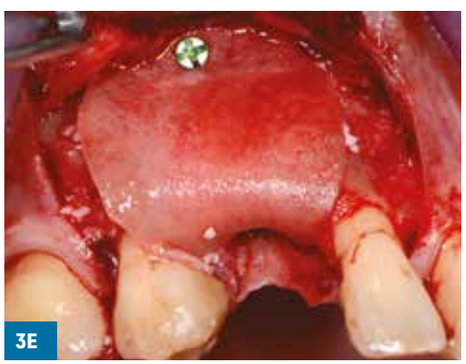
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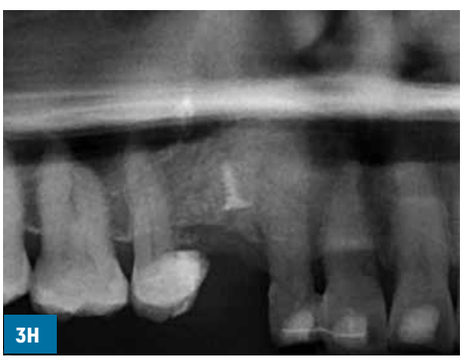
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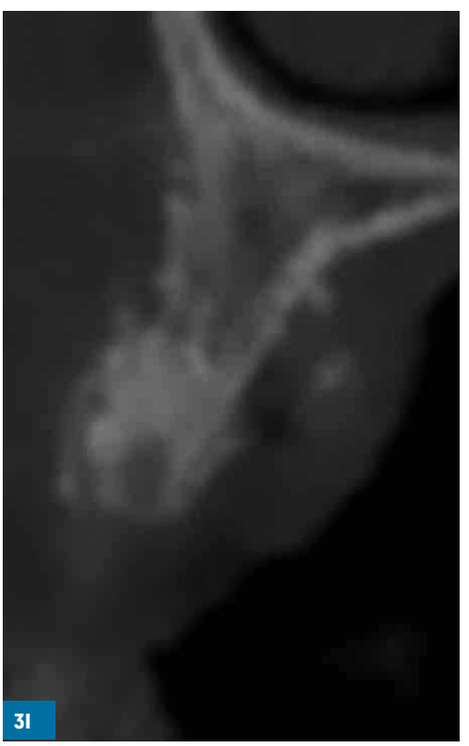
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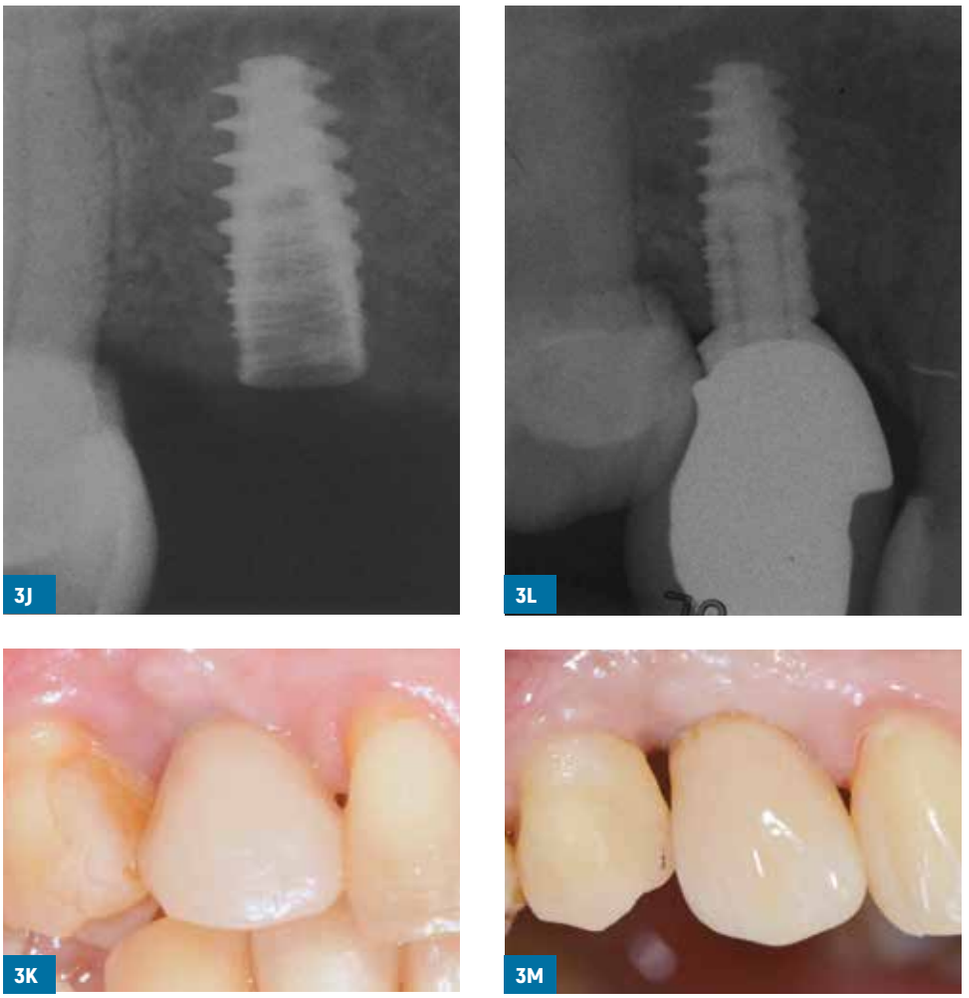

Figs. 3A-M: *Sequence of treatment of one of the patients randomly allocated to receive horizontal bone augmentation to place a 4 mm-diameter implant to replace an upper canine: A) preoperative CBCT scan of the area of the future implant used for screening the patient; B) preoperative clinical view; C) after flap raising the area was randomly allocated to horizontal augmentation; D) positioning the bone substitute; E) final fixation of the bone lamina; F) clinical evaluation of the horizontally augmented portion; G) sutures; H); postoperative control panoramic radiograph; I) CBCT scan after 6 months of healing to plan implant insertion; J) periapical radiograph at placement of the 4 mm-diameter implant; K) clinical view of the provisional resin crown placed after 4 months of submerged healing; L) periapical radiograph at delivery of the definitive crown, 4 months after initial loading; M) clinical view of the definitive crown at its delivery.*

where aesthetics was of concern, for patients randomised to small diameter implant(s), a soft tissue connective tissue 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 to improve aesthetics were actually enrolled. To replace one single molar, two small diameter implants were used.

In patients having multiple horizontally resorbed areas, only one area was included in the study—the area 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 in the Bologna University clinic, whereas the other operator (Roberto Pistilli, RP) treated patients in his private practice. Both followed similar standardised protocols.

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, ethics committee on 9th December 2015 (Cod. CE: 15036). All patients received thorough explanation and signed an informed written consent form prior to being enrolled in the trial.

Augmentation and implant placement procedures

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% before the procedure. Patients were treated under local anaesthesia (articaine with 1:100,000 adrenaline). 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-wide implants (test procedure).

In the case of augmentation procedure, the crestal bone was, when possible, perforated with a bur. In the maxilla, a lamina of cortical bone was then positioned and fixed vestibularly or palatally, depending on the defect location, with one or more titanium miniscrews of width 1.2 mm (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)[4] was used to better release the flaps. Flaps were sutured with horizontal mattress sutures and single simple sutures, using 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 case 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 chlorhexidine mouthwash 0.2% for 1 minute twice a day for 2 weeks, to eat a soft diet for one week, and to avoid brushing or 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 receive the 3 mm-wide implants, one to three titanium-alloy grade 5 tapered implants (In-Kone Universal, Global D), having a diameter of 3.0 mm, internal connection and a sand-blasted and double acid-etched roughened surface, were inserted under guidance of surgical stents to optimise implant positioning. Each missing tooth was replaced by one dental implant. In the case that a single molar had been randomised to be replaced by 3 mm-diameter implants, two implants were used instead, and three implants were used to replace two adjacent missing molars. The standard placement procedure was used, 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 divided into "hard", "medium" and "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 up to 35 Ncm were submerged and left to heal for 4 months before being functionally loaded. Implants were placed 2 mm subcrestally. Healing abutments were placed, and flap closure around the abutments was achieved using single Vicryl 4.0 sutures. In the case of aesthetic concerns, patients randomised to receive 3-mm diameter implants were to be given a soft tissue connective tissue graft harvested from the maxillary retromolar area or the palate, inserted using the pouch technique, at implant placement to improve aesthetics. 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 case 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 horizontally augmented group, implants were placed following the same procedures, the differences being that they were 4 mm rather than 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-wide 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 customised resin impression trays. Definitive metal-composite cemented crowns rigidly joining the implants were delivered within the 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 made.

Patients from the 4 mm-diameter group were rehabilitated after 4 months of submerged healing using reinforced provisional screw-retained or cemented 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 with provisional cement (Implacem, Dentalica, Milan, Italy, at PF's centre, or TempBond, Kerr Italia, Scafati, Italy, at RP's centre) on titanium abutments, and 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 preliminary outcome data at 4 months 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 reasons.
- 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 4 months after loading by tightening the abutment screws with the removed prostheses using a manual wrench with a force of 20 Ncm.
- Any biological or prosthetic complications.
- Peri-implant marginal bone levels changes, as evaluated on digital periapical radiographs taken using the paralleling technique at implant placement, and 4 months after loading. Radiographs were stored in TIFF format with a 600 dpi resolution on a personal computer. Peri-implant marginal bone levels were measured using OsiriX (Pixmeo Sarl, Bernex, Switzerland) software. The software was calibrated for each single 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, patients 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 loading (after delivery of the definitive prostheses in the 4 mm-diameter group), on a computer screen by a blinded independent dentist. The aesthetic evaluation was to be performed using the pink aesthetics score (PES)[5] and the white aesthetics score (WES)[6]. Aesthetics scores were to be evaluated at single teeth, and then averaged for patients and groups. Unfortunately only pictures of five patients were taken, so no aesthetic evaluation could be performed.
- Patient satisfaction: four months after loading, the independent outcome assessor at each centre asked to the patient the following questions:
  1) "Are you satisfied with the function of your implant-supported prostheses?" Possible answers were: "yes, absolutely", "yes, partially", "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, partially", "not sure", "not really", or "absolutely not";
  3) "Would you undergo the same treatment 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 of (RP). 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 directly 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 radio-opaque 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 numbers to each treatment group. In total, 112 patients were to be recruited, 56 receiving 3 mm-wide implants and 56 having conventional 4 mm-diameter implants after horizontal bone augmentation. However, two centres did not recruit one single patient, and one centre treated seven partially edentulous patients 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 patients, was aware of the random sequence and could have 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) were compared between groups using a t-test for independent samples. Comparisons between each time point and the 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 the number of prosthesis failures, implant failures and complications, and a t-test for independent samples was used to compare the marginal bone level changes in at the two centres. All statistical comparisons were conducted at the 0.05 level of significance.

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. No patient dropped-out before 4-month post-loading follow-up, and data from

all patients could be evaluated in the statistical analyses, with the exception of the clinical photographs to be used for evaluating aesthetics 4 months after loading.

Apart from the reduced number of patients than planned, treated by only two of the four planned centres, and the inconsistencies in taking clinical photographs for the aesthetic evaluation at 4 months after loading, 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 which a torque superior 35 Ncm was not achieved, healing abutments were placed instead of fully submerging the implants.
- 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 soft 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 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 was 4 months 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 augmentation group (control) and 49 in the 3 mm-wide implant group (test). This difference was due to the fact that two 3 mm-wide 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 exception of twice the number of smokers in the 3 mm-diameter group, and 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 (Fisher's exact probability test) = 0.2333; difference in proportion = -0.09; CI 95% -0.24 to 0.07). One mandibular 6 mm-long implant in a premolar position was found to be mobile at abutment connection in a non-smoking female whose graft was characterized by poor integration, despite the implant healing having been prolonged by two months. This patient also experienced temporary post-augmentation paraesthesia. Another mandibular 8.5 mm-long implant in a premolar position was found to be mobile at abutment connection in a female moderate smoker whose graft was characterized by poor integration. Both patients had their failed implants replaced, but have not yet received their definitive prostheses.
- Complications: significantly more complications occurred at augmented sites: three patients from the 3 mm-diameter group were affected by three complications *versus* 10 complications in nine patients from the augmented group (P (chi-square test) = 0.0346; difference in proportion = -0.28; CI 95% -0.50 to -0.01). A detailed description of the complications and treatment is presented in **TABLE 2**.

TABLE 1 PATIENT AND INTERVENTION CHARACTERISTICS

	3 mm-wide implants (n = 23)	Augmentation + 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 screw-retained zirconia definitive prostheses	0 (0%)	5 (23%)
Number of screw-retained metal/composite definitive prostheses	0 (0%)	9 (41%)
Number of cemented metal-ceramic definitive prostheses	0 (0%)	4 (18%)
Number of cemented zirconia definitive prostheses	0 (0%)	2 (9%)
Number of cemented metal-composite definitive prostheses	23 (100%)	0 (0%)
Number of patients treated with soft tissue grafts	0	2 (9.1%)*

** Soft tissue grafting was only allowed to improve the aesthetics at small-diameter implants placed in aesthetic areas, but no procedure was actually implemented with the exception of 2 protocol deviations, justified by lack of keratinised mucosa. On 3-mm implants only cemented prostheses could be manufactured since the abutment is of press-fit type.*

— Peri-implant marginal bone levels: at implant placement, there were no differences in bone levels between 3 and 4 mm-diameter implants **(TABLE 3)**. There were, however, significant differences in bone levels between the two groups at 4 months post-loading (P [t-test] = 0.0319; **TABLE 3**). Both groups lost a statistically significant amount of bone: at 4

TABLE 2 DESCRIPTION OF COMPLICATIONS AND THEIR OUTCOMES UP TO 4 MONTHS

Patient number	Time	Complications	Treatment and outcome
Patients allocated to 3 mm-diameter implants			
2 Mand (PF)	4w.pi	Cover screw loosening and inflammation of the peri-implant tissues	Chlorhexidine flushing and gel application, and retightening of the cover screw. Chlorhexidine gel twice/day for 14 days. Problem solved
1 Mand (PF)	2m.pl	Prosthesis de-cementation	Recemented
19 Mand (RP)	3m.pl	Prosthesis de-cementation	Recemented
Patients allocated horizontal augmentation and 4 mm-diameter Implants			
5 Mand (PF)	0d.pg	Temporary paraesthesia	Resolved after 2 weeks
15 Mand (RP)	0d.pg 4m.pl	Temporary paraesthesia Loosening of the prosthesis screw at 36	Resolved after 2 weeks Retightened
8 Mand (PF)	0d.pg	Temporary paraesthesia	Resolved after 3 weeks
1 Max (PF)	3d.pg	Large ecchymosis from 13 **(Fig. 4)**	Totally resorbed after 14 days
17 Max (RP)	6d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and applications of chlorhexidine gel twice a day for 21 days, and thereafter water and salt mouthwash twice/day until implant placement
18 Max (RP)	7d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and application of chlorhexidine gel twice a day for 21 days, and thereafter water and salt mouthwash twice/day until implant placement
5 Max (PF)	11d.pg	Central and occlusal wound dehiscence	Flushing with chlorhexidine and application of chlorhexidine gel twice a day for 21 days, and thereafter water and salt mouthwash twice/day until implant placement
8 Max (PF)	30d.pg	Small central and occlusal wound dehiscence	Flushing with chlorhexidine and application of chlorhexidine gel twice a day for 21 days, and thereafter water and salt mouthwash twice/day until implant placement
4 Mand (PF)	4m.pl	Prosthesis loosening with chipping on 36	Retightened at 20 Ncm and chipping fixed chairside using composite

Max = maxilla; Mand = mandible; d.pg = days post-grafting; w.pi = weeks post-implantation; m.pl = months post-loading; (PF) = Dr. Pietro Felice; (RP) = Dr. Roberto Pistilli.

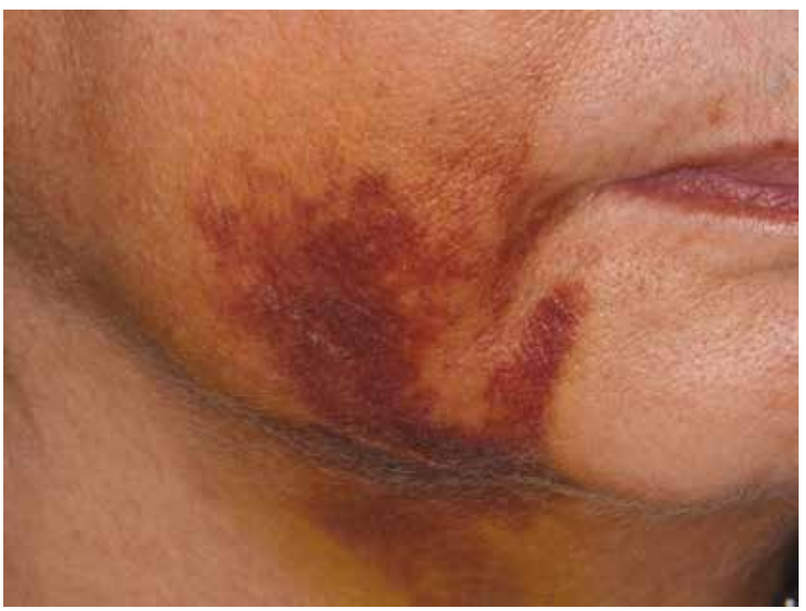

Fig. 4: *Picture taken 8 days post-operatively of a large ecchymosis that occurred in one of the patients treated with horizontal augmentation at the upper canine. It totally resorbed spontaneously 14 days after augmentation.*

months post-loading, 3 mm-diameter implants were associated with 0.09 mm bone loss, and 4 mm-diameter implants with 0.26 mm. The difference was statistically significant (mean difference 0.17 mm, 95% CI 0.02 to 0.31, P = 0.0235; **TABLE 3**).

- Patient satisfaction: almost all patients were fully satisfied with both function and aesthetics, with two exceptions: one patient from the 3-mm group was only partially satisfied with both aesthetics and function, and one patient from the augmentation group was only partially satisfied with the aesthetics. That being said, all patients declared that they would undergo the same procedure again.

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

DISCUSSION

This trial was designed to evaluate whether or not 3-mm narrow-diameter implants could be a treatment option for the rehabilitation of 4 to 5-mm thin ridges with implant-supported partial fixed 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.

TABLE 3 MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVELS AND CHANGES BY GROUP AND TIME PERIOD

	Implant placement/loading	4 months post-loading	Baseline – 4 months post-loading
	N Mean (SD) [95% CI]	**N Mean (SD) [95% CI]**	**N Mean (SE) [95% CI]**
3-mm implants	23 0.02 (0.03) [0.01, 0.03]	23 0.11 (0.10) [0.07, 0.15]	23 0.09 (0.02) [0.05, 0.13]
4-mm implants	22 0.02 (0.03) [0.01, 0.03]	20 0.27 (0.29) [0.13, 0.40]	20 0.26 (0.07) [0.12, 0.39]
Difference	0 [-0.02, 0.02]	0.16 [0.01, 0.30]	0.17 [0.02, 0.31]
P-value	0.8304	0.0319*	0.0235*

**Statistically significant difference. All changes from baseline were statistically different (P [paired t-test] < 0.001).*

TABLE 4 COMPARISON OF THE OUTCOMES AT THE TWO STUDY CENTRES UP TO 4 MONTHS AFTER LOADING

	Dr. Felice 28 patients	Dr. Pistilli 17 patients	Difference	95% CI	P-value
Patients with implant failures (# of implants)	2 (2)	0 (0)	0.07	-0.10, 0.19	0.5192
Patients with complications (# of complications)	8 (8)	4 (5)	0.05	-0.22, 0.29	0.7108
	N Mean (SE) [95% CI]	**N Mean (SE) [95% CI]**	**Difference**	**95% CI**	**P-value**
Peri-implant bone loss	26 0.16 (0.04) [0.07, 0.24]	17 0.19 (0.06) [0.05, 0.32]	0.03	-0.12, 0.18	0.6792

Although these results come from a limited number of patients, who were followed for only 4 months after loading, some important observations can be made. First and foremost, it was interesting to note that sometimes horizontal bone augmentation procedures, after a healing period of 6 months, were associated with occlusal dehiscence of the soft tissues, and resulted in bone of poor consistency. This seems to suggest that such procedures should be improved if possible.

Furthermore, regarding peri-implant marginal bone level changes, using implant placement as baseline, four months after loading 3 mm-diameter implants lost on average 0.09 mm bone, and 4 mm-diameter implants about 0.26 mm. The 0.17 mm difference between groups was statistically significant, thought may not be of clinical significance. Such a minor difference may not be unexpected since recently augmented and not fully mineralised bone might be, at least initially, more prone to bone loss.

It is difficult to compare the results of the present trial with those from similar trials, 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[7-12]. Such results, obtained in vertically atrophic mandibles, were also summarised in a recent systematic review[13]; together they suggest that augmentation procedures to create new supporting bone are more technically demanding than placing small-diameter or short implants, and are generally associated with higher post-operative morbidity, 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; in it would also be interesting to test other horizontal bone augmentation techniques.

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

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 allocated 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 to explain 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 for 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 better understand 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 options for a patient's individual treatment.

There was a systematic difference between the two groups in prosthesis design; the immediately loaded small-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 small-diameter implants and the related prosthetic components are structurally weaker

than normal-diameter implants, we elected to minimise the risk of fractures by making all prostheses out of cemented metal composite. Although the same type of prostheses should have been used in the augmentation group, 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 to speculate to what extent these differences in prosthesis type may have impacted the results.

The lack of aesthetic evaluation 4 months after loading (i.e., at delivery of the definitive prostheses in the control group) was due to the fact that both assessors neglected to take the clinical photographs, except for of the first five patients treated. It is our intention, however, to take pictures of all patients at the 1-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 has the potential to shift the findings in favour of the augmentation procedure. It is interesting to observe, however, that the aesthetic assessment performed by the patients themselves did not reveal any trend in favour of either procedure, bearing in mind, however, that the great majority of 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 small-diameter implants were actually designed for to be used.

The present 4-month post-loading follow-up is, of course, short, but it was planned to follow these cohorts of patients up to 5 years after loading, so these findings should be considered as 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 in real clinical conditions and the inclusion criteria were sufficiently broad, therefore the results of the present trial can be generalised with confidence to a wider population with similar characteristics.

In terms of future research it would be interesting to run another similar trial focussing on the anterior portion of the mouth, which actually is the area for which small-diameter implants were actually designed to be used for.

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 4 months after loading in patients treated with 3 mm-wide implants than those horizontally augmented to receive 4 mm-wide implants. As the former treatment is less invasive, faster, cheaper, and associated with less morbidity, 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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