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Randomized controlled trial

0.5 MM *VERSUS* 1.5 MM SUBCRESTAL PLACEMENT OF DENTAL IMPLANTS WITH INTERNAL CONICAL CONNECTION: EIGHT-YEAR POST-LOADING RESULTS FROM A MULTICENTRE WITHIN-PERSON RANDOMIZED CONTROLLED TRIAL

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PURPOSE. To determine whether there are clinical advantages to placing single dental implants 0.5 *versus* 1.5 mm subcrestally in healed bone crests.

MATERIALS AND METHODS. Sixty partially edentulous patients requiring two single implant-supported crowns had both sites randomly allocated to either 0.5 mm or 1.5 mm subcrestal implant placement according to a split-mouth design at six centres; implant sites were left to heal for 3 months either submerged in aesthetic areas or not in non-aesthetic areas. Provisional acrylic crowns were fitted and after 2 months replaced by definitive metal-ceramic crowns. Patients were followed up to 8 years after loading. Outcome measures were: crown or implant failures; complications; aesthetics, assessed using the pink esthetic score (PES); peri-implant marginal bone level changes; and patient preference, recorded by blinded assessors.

RESULTS. Out of the 54 patients, 7 dropped out. There were no statistically significant differences between groups in failure rates (seven implants failed in the 0.5mm group *versus* three in the 1.5-mm group; difference = 0.07; P = 0.125) or complications (in the 0.5-mm group ten complications occurred in nine patients *versus* seven complications in seven patients in the 1.5-mm group; difference = 0.04; 95% CI 0.37 to 10.92; P = 0.688). At 8 years after loading, the mean pink aesthetic score was 11.04±2.27 and 10.6±2.46 for the 0.5 and 1.5 mm group, respectively. There were no statistically significant differences between the two groups at 8 years (P = 0.367). Eight years after loading, patients of the 0.5 mm lost on average 0.17±0.45 mm and those of the 1.5 mm group 0.15±0.50 mm, the difference not being statistically significant (difference = -0.10 mm; 95% CI -0.22 to 0.02; P = 0.091). Patients did not prefer any depth of the implant placement over the other.
There were no differences in outcomes among centres, except for the number of patients with no preferences (P = 0.047). However, patients were equally satisfied with both implant placement sites.

CONCLUSIONS. Eight years after loading, no statistically significant differences were found between 0.5 mm *vs.* 1.5 mm subcrestal placement when implant were surrounded by at least 1 mm of bone, and clinicians are therefore free to choose which depth they prefer.

CONFLICT OF INTEREST STATEMENT. Anthogyr (Sallanches, France), the manufacturer of the implants used in this investigation, partially funded this trial and donated the implants and the prosthetic components. However, all data belonged to the authors and the sponsor did not interfere with the conduct of the trial or the publication of its results in any way.

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INTRODUCTION

Among the legends circulating in implant dentistry, there is the belief that aesthetics can be improved by placing implants in a subcrestal position. The origins of this myth are difficult to trace, but some authors attribute this to Buser[1]. However, his original statement actually referred to ITI transmucosal implants with a polished collar, recommending that the transition portion between the rough section and the polished collar be placed 1 mm below the bone crest in vertically augmented bone. A dedicated randomized controlled trial (RCT) tested whether the hypothesis would hold true in non-augmented bone[2]. Although no statistically significant differences in peri-implant marginal bone levels and other secondary parameters were observed one year after loading, the authors concluded that, 'From a biological point of view, the placement of the border between the rough and the smooth surfaces into a subcrestal location should not be recommended'.

A more recent RCT[3] evaluated the influence of the placement level of implants with a laser-microtextured collar design on the bone and soft tissue levels twelve months after immediate placement (8 months post-loading) of crestal *versus* 1-mm subcrestal implants following extraction. No statistically significant differences were observed at 8 months post-loading, and the authors concluded that 'the level of placement did not influence horizontal and vertical bone and soft tissue changes'.

Another RCT[4] evaluated platform-switched implants with a conical connection, placed at either crestal level or 1 or 2 mm subcrestally. One year after loading, there was statistically significantly more bone loss (0.27 mm) at implants positioned at crestal level than those positioned 1 and 2 mm below, but no difference between the latter. However, another RCT[5], in which platform-switched implants were placed at crestal level or 1 mm below the crest, found the opposite. Specifically, three years after loading significantly more bone loss (0.65 mm) was observed at implants placed 1 mm subcrestally as compared to those placed crestally; no other differences were noted in any of the remaining parameters. Another RCT[6], involving two different implant types, found no significant differences in bone levels or other parameters between implants placed crestally *versus* 1.5 to 2 mm subcrestally. However, implants were not loaded and follow-up was only 3 months, so no meaningful conclusions could be drawn. Similarly, an RCT comparing single transmucosal implants placed crestally *versus* 1.5 mm subcrestally in 80 patients found no statistically significant differences; however, only 4-month post-loading outcomes were recorded[7].

Therefore, it would be interesting to know whether better aesthetic outcomes can be achieved by placing implants 1.5 mm or 0.5 mm subcrestally. Hence, the aim of this pragmatic multicentre RCT was to compare clinical outcomes of single dental implants placed either 0.5 or 1.5 mm subcrestally in healed bone crests. This report, presenting data obtained 8 years after loading, is the fourth in a series; previous publications presented 1-[8], 3-[9] and 5-year data[10]. This article has been drafted in line with the CONSORT statement (http://www.consort-statement.org/) and its extension checklist for improving the quality of reporting of within-person randomized trials (http://www.consort-statement.org/extensions/overview/withinperson).

MATERIALS AND METHODS

Trial design

This was a multicentre randomized controlled superiority trial (RCT) of within-subject design and blind assessment. Each patient received two identical implants (one test and one control implant): the test implant was placed 1.5 mm below the crest and the control implant 0.5 mm subcrestally.

The original protocol was to terminate the study at 5-year post-loading follow-up, but it was then decided to extend the trial for another 5 years. Ethical approval was obtained from the Calabria Region Area Centre Section Ethics Committee, Italy (protocol number 462 of 17th December 2020).

Patient selection

Any patient requiring at least two single implant-supported crowns in any jaw location, being at least 18 years old and able to understand and sign an informed consent form was eligible for inclusion. The two sites could be adjacent, but had to allow the placement of two implants of length at least 6.5 mm and width at least 3.4 mm, leaving at least 1 mm of bone around the implant. For patients with more than two suitable implant sites, the operator could choose the two sites with most similar characteristics at the screening appointment. The operator coded the selected sites as implant site number 1 and implant site number 2.

Exclusion criteria were:

- general contraindications to implant surgery;
- immunosuppression or immunocompromise;
- irradiation to the head and/or neck area;
- uncontrolled diabetes;
- pregnancy or lactation;
- untreated periodontitis;
- poor oral hygiene and motivation;
- substance abuse;
- psychiatric disorders;
- unrealistic expectations;
- acute infection or suppuration at any of the sites intended for implant placement;
- need for any type of bone augmentation at implant placement;
- post-extraction sites (implants could, however, be inserted after at least 5 months of healing);
- inability to commit to 5-year post-loading follow-up;
- ongoing or previous treatment with intravenous aminobisphosphonates;
- referral for implant placement alone (no follow-up at the treatment centre possible);
- participation in other clinical studies precluding full adherence to the study protocol.

Patients were divided into three groups based on the number of cigarettes they declared smoking per day: i) non-smokers, ii) moderate smokers (up to 10 cigarettes per day) and ii) heavy smokers (more than 10 cigarettes per day).

Equal numbers of patients were recruited and treated by six different doctors using similar, standardized procedures at private practices located in Northern Italy (Milan, Lovere/Bergamo, Verona, Preganziol, Campagna Lupia and Noventa Padovana). Each clinician treated ten patients. Prior to enrolment, all patients were asked to read an information sheet and sign an informed consent form to document that they understood the scope of the study (including procedures, follow-up evaluations and any potential risks involved); they were given opportunities to ask questions pertaining to this study, and were apprised of treatment alternatives. The study was open to any qualifying patients, without regard to sex or race.

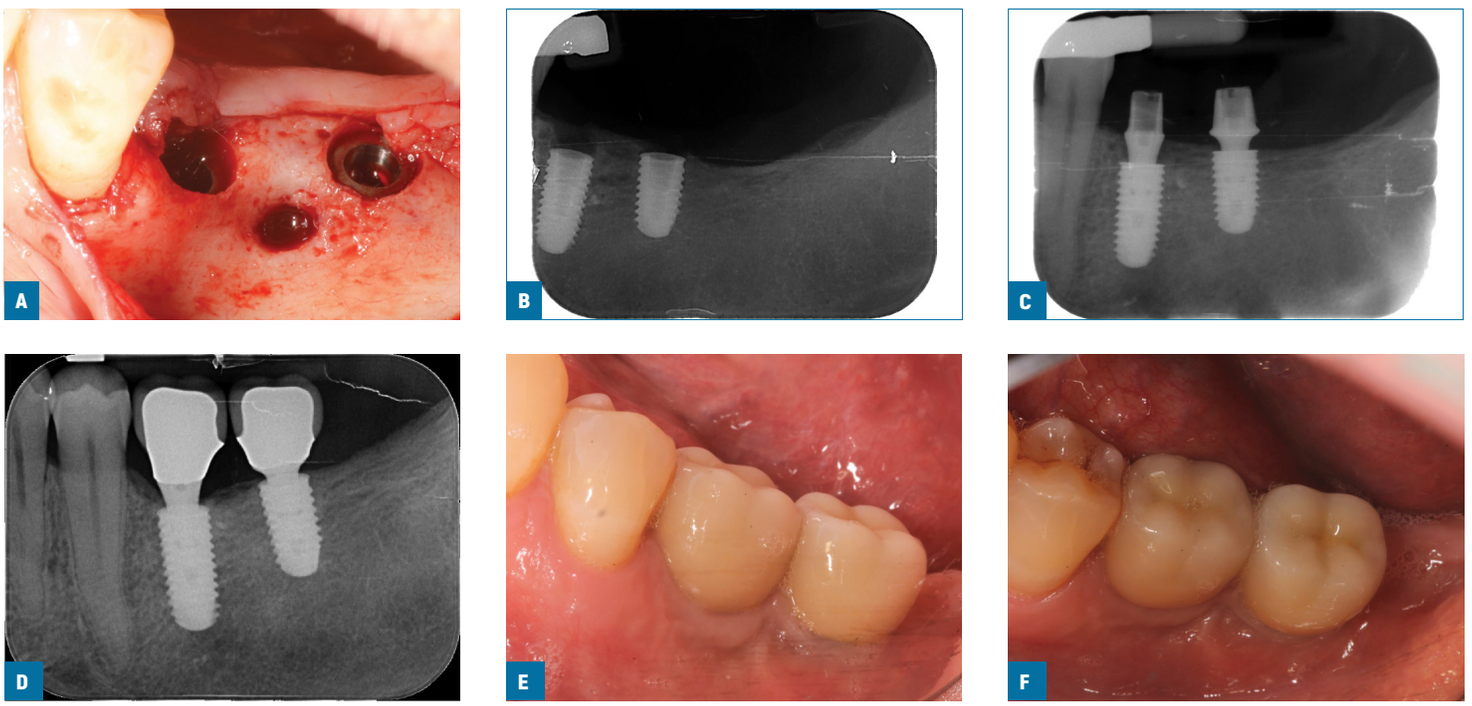
Clinical procedures

Preoperative radiographs were taken; investigators were free to choose the most appropriate examination according to the clinical case, whether periapical or panoramic radiography

or cone-beam computed tomography (CBCT). All patients underwent at least one oral hygiene session within the 10 days prior to the implantation procedure.

Patients received a single dose of prophylactic antibiotic 1 hour prior to the intervention: 2 g of amoxicillin, or 500 mg of clarithromycin if allergic to penicillin. Patients rinsed with 0.2% chlorhexidine mouthwash for 1 minute prior to the intervention. Patients were treated under local anaesthesia using 1:100,000 articaine with adrenaline. No intravenous sedation was given. After crestal incision and flap elevation, the sequentially numbered sealed envelope corresponding to the patient recruitment number was opened and implant site number 1 was treated as instructed in the envelope. Consequently, the other intervention was performed at implant site number 2, according to a within-patient design (**FIGS. 1A-F**).

The two study implants were placed using similar procedures during the same surgical session and were restored simultaneously with similar single crowns. Bone quality was subjectively quantified at drilling as: "hard", "medium" or "soft". Implant sites were prepared using drills of increasing diameters as suggested by the implant manufacturer, using burs to different depths according to the random allocation and tapping in hard bone. Tapered Axiom REG (Anthogyr, Sallanches, France) implants with internal conical connection and platform switching were placed; they are made of titanium alloy (Ti6Al4V-ELI acc. to ISO5832-3) and have a surface sand-blasted with BCP bioceramics, consisting of a mixture of hydroxyapatite (HA) and β-TCP (beta-tricalcium phosphate), and then subjected to mild acid treatment. Operators were free to use implants of diameters 3.4 mm (8.0, 10.0, 12.0 and 14.0 mm long), 4.0 mm, 4.6 mm or 5.2 mm (6.5, 8.0, 10.0, 12.0 and 14.0 mm long), according to the clinical indications and their preferences.



FIGS. 1A-F: *Treatment sequence of a representative patient treated by Dr Salina: site 36 was randomly allocated to receive an implant with the neck 1.5 below the crest and site 37 at 0.5 mm (A); post-operative baseline periapical radiograph clearly showing the difference in depth positioning (B); periapical radiograph at initial loading (C); periapical radiograph (D); vestibular (E) and occlusal views at 8 years after loading (F). Typically bone levels repositioned at the implant-abutment connection.*

In line with the random allocation, the neck of the implant was sunk either 0.5 mm or 1.5 mm subcrestally using the most apical peak of the surrounding bone as a reference point. Periapical radiographs were taken, and repeated if the peri-implant marginal bone levels were difficult to assess on the first. Implants in aesthetic areas were submerged, and implants in non-aesthetic areas received transmucosal healing abutments (Anthogyr). Ibuprofen 400 mg was prescribed, to be taken 2 to 4 times a day at mealtimes, for as long as required. In cases of stomach issues or allergy to non-steroidal anti-inflammatory drugs, 1 g of paracetamol was recommended instead. Patients were instructed to rinse with 0.2% chlorhexidine mouthwash for one minute twice a day for 2 weeks, and to avoid brushing and possible trauma to the surgical sites. A soft diet was recommended for 2 weeks.

After 1 week, patients were checked, and sutures were removed. Implants were left to heal unloaded for three months, after which submerged implants were exposed; the stability of individual implants was assessed by torquing the abutment screws at 25 N.cm, and then impressions were taken at implant level.

Provisional crowns were fitted on provisional titanium abutments, periapical radiographs were taken, and oral hygiene instructions were delivered. Exactly the same procedures were implemented at both implants. After two months, 1.5-, 2.5-, 3.5- or 4.5-mm (OPST abutments, Anthogyr) definitive standard straight titanium abutments lengths were fitted, selecting the abutment shoulder to be 0.5 to 1 mm shorter than the buccal gingival margin. The diameters of healing caps and definitive abutments used were 5 mm for implants replacing molars, and 3.4 or 4.0 mm for implants replacing other teeth, based on clinician assessment. The provisional restorations were replaced by definitive metal-ceramic crowns, cemented on definitive standard straight titanium abutments using provisional cement. Implant stability was assessed and vestibular and occlusal pictures were taken of the study implants, including one adjacent tooth per side. Standardized periapical radiographs of the study implants were to be taken using a customized stent, and oral hygiene motivation reinforced. Patients were recalled every 6 months for maintenance for the entire duration of the study. Dental occlusion was assessed at each visit.

Outcome measures

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

Outcome measures were the following.

Implant/crown failures: implant mobility, removal of stable implants dictated by progressive marginal bone loss or infection, and any mechanical complications rendering the implant unusable (e.g., implant fracture) were considered implant failures. If a definitive crown had to be replaced for any reason, it was counted as a crown failure. Stability of individual implants was measured two months after implant placement at the fitting of definitive crowns, applying a reverse torque of 20 N.cm with a dedicated wrench. Implant stability was re-assessed at 1, 3, 5 and 8 years after loading using the metal handles of two dental instruments.

Any biological or biomechanical complications: examples of biological complications were fistula and peri-implantitis, while examples of biomechanical complications were loosening or abutment screw fracture.

Peri-implant marginal bone level changes: these were evaluated on periapical radiographs taken with the paralleling technique at implant placement, initial loading, and 1, 3, 5 and 8 years after loading. In the event of measurement difficulties, a second radiograph was taken. Non-digital radiographs were scanned into TIFF format with 600-dpi resolution, and stored on a desktop computer. Peri-implant marginal bone levels were measured using ImageJ softwa-

re, version 1.48 (NIH, Bethesda, MD, USA). The software was calibrated for every single image using the known distance between the two most coronal consecutive threads and/or the implant diameter. Measurements of the mesial and distal bone crest levels adjacent to each implant were made to the nearest 0.01 mm. Reference points for the linear measurements were the coronal margin of the implant collar and the most coronal point of visible bone-to-implant contact. When the bone was coronal to the implant collar, a zero value was assigned. The measurements at the mesial and distal sides of each implant were averaged at implant level and then at group level. All radiographic measurements were made by a single blinded dentist (LS).

Aesthetics: the vestibular and occlusal clinical pictures, including one adjacent tooth per side, taken at definitive crown fitting (2 months after initial loading), and at 1, 3, 5, and 8 years after loading were assessed on a computer screen by a blinded dentist (LS). The aesthetic evaluation was performed using the pink esthetic score (PES)[11]. In brief, seven variables were evaluated: mesial papilla, distal papilla, soft tissue level, soft tissue contour, alveolar process deficiencies, and soft tissue colour and texture. A 0/1/2 scoring system was used, 0 being the lowest and 2 being the highest score, with a maximum achievable score of 14 per implant.

Patient preference: 1, 3, 5, and 8 years after loading, local blind outcome assessors provided a mirror to patients, indicated both implant-supported crowns, and asked them which crown they preferred. Possible patient responses were: i) the crown at implant site number 1; ii) the crown at implant site number 2; iii) I am equally pleased with both crowns; iv) I am equally displeased with both crowns. Patients could also express comments if they so desired.

At each centre there was one local blind outcome assessor who assessed implant stability and recorded patient preference. One blinded dentist (LS), not involved in the treatment of the patients, evaluated both aesthetic and marginal bone levels, without knowing group allocation. Complications were handled and reported directly by the treating clinicians, who were not blinded.

Sample size, randomization and allocation concealment

No sample size calculation was performed, but it was agreed to recruit 60 patients, 10 at each of the six centres participating in this trial. Six computer-generated restricted randomisation lists were created. Only one investigator (ME), who was not involved in the selection and treatment of patients, knew the random sequence and had access to the randomization list, stored on a password-protected laptop computer.

The randomization codes were enclosed in sequentially numbered identical, opaque, sealed envelopes. After flaps were raised, the envelope corresponding to the patient recruitment number was opened, and implant site number 1 was allocated to the group as per the instruction in the envelope, with the other site receiving the other treatment. Therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

Statistical analysis

All data analysis was performed according to a pre-established analysis plan by a dentist with expertise in statistics (JB), who analysed the data without knowing group codes. The implant sites were the statistical unit of the analyses. Between-group differences in crown/implant failures and complications (dichotomous outcomes) were compared using the McNemar test, while between-group differences in continuous outcomes (mean marginal bone-level changes and aesthetics scores) were compared using a paired t-test. Comparisons between baseline measurements and the various follow-up endpoints were made using paired t-tests.

Differences among centres in continuous outcomes were analysed using the ANOVA test, followed by Tukey's HSD post-hoc test. For categorical outcomes, the chi-squared test or Fisher's Exact test were used, depending on the count per cell (small cell sizes with values less than 5). Zero-count cells were handled by adding 0.5 to each of the cells, and then the odds ratio over these adjusted cell counts (Haldane–Anscombe correction) was calculated. All statistical comparisons were conducted at a 0.05 level of significance.

RESULTS

Sixty-three patients were screened at the six centres, but 60 patients were consecutively enrolled in the trial as three patients declined to participate. All patients were treated according to the allocated interventions. Patients were recruited and received the implants from June 2013 to April 2015. The follow-up of all patients remaining in the study was to 8 years after implant loading. There were 34 females and 26 males, with a mean age of 53.4 years (range 28 to 81). There were 47 non-smokers, six moderate smokers and seven patients smoking more than 10 cigarettes per day. Implant characteristics are described by study group in **TABLE 1**. There were no apparent significant baseline imbalances between the two groups.

Seven patients dropped out:

- one patient refused to come back after fitting of the provisional crowns (Campagna Lupia);
- one patient was last seen at the 3-year follow-up and failed to come back, most likely because she had changed dentists (Noventa Padovana);
- one patient was last seen at the 5-year follow-up, and refused further appointments (Verona);
- one patient was last seen at the 5-year follow-up and then became unreachable (Preganziol);
- one patient moved to another country and was last seen at the 5-year follow-up (Campagna Lupia);
- one patient was last seen at the 5-year follow-up. She did not attend due to her husband's terminal illness (Campagna Lupia);
- one patient was last seen at the check-up at 7 years and 6 months, but did not attend the 8-year follow-up due to health problems (Preganziol).

Periapical radiographs could not be taken of either implant in one patient at either 2 months or 1 year after loading because she was pregnant at both timepoints (Verona); however, bone levels were assessed 3 years after loading and no bone loss had occurred, so the missing data was imputed (as 0). The data of all patients were evaluated in the statistical analyses.

The main deviations from the protocol were the following.

- Standardized periapical radiographs were to be taken with customized stents. However, the use of radiographic stents was discontinued after the first cases were treated, and totally abandoned at the 5-year follow-up due to difficulties in repositioning them over time. As per the protocol, radiographs which were not of adequate quality were taken again, and all radiographs were measurable by the outcome assessor.
- In eight patients (two from Verona, four from Campagna Lupia, and two from Noventa Padovana), implants which were supposed to support individual crowns were actually joined under the same partial fixed prosthesis. These protocol deviations were not reported previously.
- In one patient, both definitive crowns were placed eleven months after loading, because the patient had health problems and did not return for check-up (Milan).

TABLE 1 INTERVENTION CHARACTERISTICS

	0.5 mm N = 60	1.5 mm N = 60
Implants in central incisor position	0	0
Implants in lateral incisor position	0	0
Implants in canine position	1 (1.7%)	0
Implants in first premolar position	7 (11.7%)	9 (15%)
Implants in second premolar position	15 (25%)	16 (26.7%)
Implants in first molar position	31 (51.7%)	30 (50%)
Implants in second molar position	5 (8.3%)	5 (8.3%)
Implants in third molar position	1 (1.7%)	0
Implants in maxillae	17 (28.3%)	15 (25%)
Implants in mandibles	43 (71.7%)	45 (75%)
Implants with 3.4 mm diameter	21 (35%)	21 (35%)
Implants with 4.0 mm diameter	35 (58.3%)	35 (58.3%)
Implants of diameter 4.6 mm	2 (3.3%)	3 (5%)
Implants of diameter 5.2 mm	2 (3.3%)	1 (1.7%)
Implants of length 6.5 mm	6 (10%)	8 (13.3%)
Implants of length 8.0 mm	24 (40%)	30 (50%)
Implants of length 10.0 mm	28 (46.7%)	22 (36.7%)
Implants of length 12.0 mm	2 (3.3%)	0
Implants of length 14.0 mm	0	0
Abutments of length 1.5 mm	33 (55%)	19 (31.7%)
Abutments of length 2.5 mm	20 (33.3%)	31 (51.7%)
Abutments of length 3.5 mm	7 (11.7%)	10 (16.7%)
Abutments of length 4.5 mm	0	0
Abutments of diameter 3.4 mm	4 (6.7%)	1 (1.7%)
Abutments of diameter 4.0 mm	31 (51.7%)	37 (61.7%)
Abutments of diameter 5.0 mm	23 (38.3%)	21 (35%)
Abutments of diameter 6.0 mm	2 (3.3%)	1 (1.7%)
Soft bone quality	8 (13.3%)	6 (13.3%)
Medium bone quality	31 (51.7%)	34 (56.7%)
Hard bone quality	21 (35%)	20 (33.3%)

- In another patient, both definitive crowns were placed nine months after provisional crowns; data was considered as the 1-year post-loading follow-up (Verona).
- In a further patient, a customized mono-block abutment (OPRM100, Anthogyr) was used instead of standard abutment at the implant placed 1.5 mm below the crest (Milan); at 4 and a half years after loading, this implant (46) was used as pilaster for a partial fixed implant-supported prosthesis (46-44) when the implant from the 0.5-mm group in position 45 failed.
- One patient was seen with a 6-month delay with respect to the 5-year follow-up because of the COVID-19 lockdown (Lovere/Bergamo).

Outcome measures were as follows.

- Crowns and implant failures: out of 54 patients, 7 implants failed in the 0.5-mm group *versus* 3 in the 1.5 mm group. The between-group difference in proportions of implant failures was not statistically significant (difference = 0.07; 95% CI NaN to infinity; P = 0.125). Three patients lost both implants at around the same time. One patient developed a fistula and lost both implants, which had initially been loaded with provisional crowns, and were found to be mobile and removed at definitive impression taking. Both failed implants were successfully replaced, but the data pertaining to the replacements was not recorded, being beyond the scope of the present study. The other six implant failures in the 0.5-mm group were caused by peri-implantitis, which occurred at 3 years and 1 month; 4 years and 6 months; 5 years; 5 years and 3 months; 6 years and 5 months; and 7 years and 9 months after loading, respectively. The other two implant failures in 1.5 subcrestally placed implants were also caused by chronic peri-implantitis, and implants were removed at 5 years and 3 months and at 6 years and 5 months after loading, respectively. One additional crown in the 1.5-mm group had to be remade as a partial fixed prosthesis because of the failure of the adjacent mesial implant from the 0.5-mm group.
- Complications: out of 54 patients, ten complications in nine patients occurred in the 0.5-mm group *versus* seven complications in seven patients at implants from the 1.5-mm group. There was no statistically significant between-group difference in number of patients experiencing complications (difference = 0.04; 95% CI 0.37 to 10.92; P = 0.688). Four patients had both implants affected by the same complications. Specifically, one patient (ID = 33) presented with a fistula and mobile implant in position 14 at the time of definitive impression-taking. It was removed and successfully replaced. Exactly the same problem occurred at the other implant in the same patient (both implants failed). Another patient (ID = 17) was affected by peri-implantitis at both implants, which were adjacent to each other, at 1 year and 6 months after loading. Both implants were surgically debrided, and the frequency of maintenance recalls was increased. Marginal peri-implant bone at both implants stabilized for some years, but at the 5-year follow-up the peri-implantitis reoccurred and both implants were lost. Another patient (ID = 46) had both implants affected by peri-implantitis at 5 years and 3 months after loading, and both failed. In the 1.5-mm group, one patient (ID = 17) was affected by peri-implantitis at both study implants at 1 year 6 months after loading, and this was treated with ultrasound debridement, laser, H_2O_2 irrigation, and local application of doxycycline (140 mg Ligosan, Heraeus Kulzer, Milan, Italy), but eventually both implants failed. Further complications resulting in the loss of one implant in the 0.5-mm group included one patient (ID = 10) who was affected by peri-implantitis at both implants 2 years after loading; this was treated as previously described, and the situation seemed to stabilize, but the peri-implant soft tissue remained inflamed, and eventually the implant failed. Another patient (ID = 13) had permanent post-operative paraesthesia at the implant in position 36, and one (ID = 27) presented with inflammation around the implant in position 46 at time of abutment connection, which resulted in bone loss at 1 year after loading (peri-implantitis). She was treated with light-scaling using the piezoelectric device (Mectron, Carasco, Italy) with a polytetrafluoroethylene (PTFE) tip, and curettage, irrigation with saline, and injection of a solution of tetracycline hydrochloride (Ambramicina, 250 mg, Scharper, Milan, Italy). This treatment was repeated after 2 weeks, but the implant could not be saved. In another patient (ID = 8,) peri-implant bone resorption was observed 2 years after loading. No inflammation was evident, so no treatment was delivered, but at 4 years and 6 months after loading, bone loss had increased (peri-implantitis) and the implant was removed. One patient (ID

= 40) had a small ceramic fracture at implant 35, 43 months after loading, which was repaired by a dental technician. The same implant was affected by peri-implantitis at 6 and a half years after loading. It was treated with non-surgical debridement, but it failed. Another complication in this group, which did not result in implant loss, was an episode of peri-implant mucositis, which occurred at the implant in position 27 (pocket depth = 4.5 mm palatally) in one patient (ID = 5), who was immediately given light ultrasonic treatment using polytetrafluoroethylene (PTFE) tips and one application of 810 nm diode laser (1.2 watts for 1 min x 3 times) with simultaneous irrigation of 3% H_2O_2. The peri-implant sulcus was then filled with 0.5% chlorhexidine gel (Oralsan, IDS, Genoa, Italy), and 500 mg azithromycin (Zitromax, Pfizer, Latina, Italy) was prescribed (one tablet per day for 3 days). The situation returned to normal in 20 days, and the patient was recalled monthly for 6 months.

Other complications reported for implants in the 1.5 mm group included one patient (ID = 29) who lost the cover screw at implant 36 one week after its placement; the soft tissues covered the implant, and no treatment was necessary. However, a fistula and mobility were present at the implant in position 15 in the same patient (ID = 33), who lost this and the adjacent implant, as noted above. Another patient (ID = 10) was by affected peri-implantitis at both implants, which was treated as previously described, with the implant from the 1.5 mm subcrestal group surviving. One patient (ID = 39) was affected by peri-implant mucositis at implant 47, 45 months after loading; it healed after abutment/crown replacement with a healing abutment for 3 weeks. Finally, one patient (ID = 27) had peri-implantitis at implant site 45, noticed at 4 years and 8 months, but this was successfully treated with open flap debridement and a solution of 250 mg tetracycline hydrochloride (Ambramicina, Scharper, Milan, Italy).

Aesthetics: overall, there were no statistically significant differences between the two groups in either average total PES score or at the individual aesthetic domains, as assessed a blind assessor with the aid of a paired t-test (**TABLE 2**). At fitting of the definitive prostheses, two months after loading the average total PES score was 11.22±1.91 in the 0.5-mm group and 11.12±1.59 in the 1.5-mm group (P = 0.626); five years after loading, the average PES score was 10.89 ± 2.30 in the 0.5-mm group and 10.79±2.41 in the 1.5-mm group (P = 0.943), and 8 years after loading, the average PES score was 11.04±2.27 in the 0.5-mm group and 10.60±2.46 in the 1.5-mm group (P = 0.367; **TABLE 2**).

TABLE 2 PES SCORES AT 8 YEARS AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAINS (SD IN BRACKETS)

Group	Mesial papilla	Distal papilla	Soft tissue level	Soft tissue contour	Alveolar process deficiencies	Soft tissue colour	Soft tissue texture	Total PES score
0.5 mm N = 47	1.60 (0.58)	1.11 (0.60)	1.60 (0.54)	1.68 (0.56)	1.70 (0.46)	1.68 (0.52)	1.68 (0.52)	11.04 (2.27)
1.5 mm N = 50	1.52 (0.68)	1.1 (0.61)	1.54 (0.58)	1.6 (0.61)	1.54 (0.50)	1.64 (0.56)	1.66 (0.52)	10.60 (2.46)
Difference [95% CI]	-0.04 [-0.31 to 0.22]	0.02 [-0.18 to 0.22]	-0.02 [-0.16 to 0.12]	-0.04 [-0.16 to 0.08]	-0.13 [-0.27 to 0.02]	-0.02 [-0.14 to 0.09]	0 [-0.14 to 0.14]	-0.23 [-0.75 to 0.28]
P-value (paired t-test)	0.749	0.829	0.767	0.485	0.083	0.709	1.000	0.367

- Patient preference was assessed at definitive crown delivery (2 months after initial loading), and at 1, 3, 5 and 8 years after initial loading, only in those patients who did not experience any implant failure. At definitive crown fitting, 57 patients had no preference (pleased with both crowns to the same extent), but one patient preferred the crown at the implant positioned 1.5 mm subcrestally. At 5 years after loading, 53 patients had no preference (pleased with both crowns to the same extent), while one patient preferred the crown on the implant placed 0.5 mm subcrestally. At 8 years after loading, 43 patients had no preference, whereas two patients preferred the crown on the implant placed 0.5 mm and two the crown on that placed 1.5 mm subcrestally.
- Peri-implant marginal bone level differences between groups were not statistically significant (**TABLE 3**). At baseline, all bone level measures equalled 0 in both groups. At 8 years post-loading, peri-implant marginal bone level/loss was 0.17±0.45 mm at 0.5-mm implants and 0.15±0.50 mm at 1.5-mm implants (difference = -0.1 mm; 95% CI -0.22 to 0.02; paired t-test P = 0.091).

The comparison among the six centres is presented in **TABLE 4**. At 8 years post-loading there were no statistically significant differences among centres, except for the number of patients having no preference (P = 0.047).

DISCUSSION

This within-patient trial was designed to determine whether it would be more advantageous to place implants 0.5 mm or 1.5 mm subcrestally. Eight years after loading, no statistically significant differences of any kind were noted, suggesting that clinicians can choose to place implants at the depth (0.5 or 1.5 mm) they prefer. Simply put, the subcrestal positioning of implants 0.5 or 1.5 mm in healed sites leads to no clinically appreciable consequences for the patient. That being said, logic dictates that it might be more sensible to place implants at a depth of 0.5 mm in order to be able to make full use of 1 mm more of bone support, especially where limited bone height is available. Our current findings are in agreement with those of other similar RCTs[2-4,7] testing the same hypothesis, even though implants with different design were used, such as transmucosal implants[2,7].

TABLE 3 MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVELS AND LEVEL CHANGES UP TO 8 YEARS AFTER LOADING

Time point	Implant placement	Loading	2 months post loading	1 year post-loading	3 years post-loading	5 years post-loading	8 years post-loading
Group	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]	N Mean (SD) [95% CI]
0.5 mm	60 All implants = 0	59 0.07 (0.21) [0.01, 0.12]	58 0.16 (0.39) [0.06, 0.26]	58 0.21 (0.51) [0.07, 0.34]	58 0.34 (0.87) [0.12, 0.57]	55 0.53 (1.43) [0.14; 0.91]	47 0.17 (0.45) [0.04; 0.31]
1.5 mm	60 All implants = 0	59 0.04 (0.13) [0.01, 0.07]	58 0.10 (0.38) [-0.01, 0.20]	58 0.11 (0.36) [0.02, 0.21]	58 0.19 (0.54) [0.05, 0.33]	57 0.31 (0.98) [0.05; 0.57]	50 0.15 (0.50) [0.01; 0.30]
Difference [95% CI]	0	0.03 [-0.02, 0.07]	0.06 [-0.02, 0.15]	0.10 [-0.01, 0.20]	0.15 [0.00, 0.30]	0.26 [0.05; 0.47]	-0.10 [-0.22; 0.02]
P-value	1.000	0.209	0.152	0.078	0.046*	0.016*	0.091

**Statistically significant difference. All changes from baseline statistically different (P <0.05). When available, radiographs of failed implants were also measured, with the exception of year 8*

TABLE 4 COMPARISON OF CLINICAL OUTCOMES AMONG THE SIX CENTRES AT 8 YEARS AFTER LOADING

	Milan	Lovere/ Bergamo	Verona	Preganziol	Campagna Lupia	Noventa Padovana	P-value
Drop-outs	0/10	0/10	1/10	2/10	3/10	1/10	0.381
Crown failures	3/20	2/20	1/20	3/16	2/16	0/18	0.445
Implant failures	2/20	2/20	1/20	3/16	2/16	0/18	0.509
Complications	4/20	3/20	3/20	4/16	2/16	0/18	0.331
PES score 0.5 mm group	10.88 ± 1.81	11.89 ± 1.76	12.11 ± 0.78	10.50 ± 2.35	10.5 ± 4.37	10.00 ± 2.00	0.329
PES score 1.5 mm group	10.00 ± 2.11	10.78 ± 2.49	11.78 ± 0.97	10.57 ± 2.64	11.17 ± 4.54	9.56 ± 1.81	0.475
Peri-implant bone loss 0.5 mm group	0.05 ± 0.14	0.30 ± 0.50	0.29 ± 0.62	0 ± 0	0.30 ± 0.73	0.08 ± 0.23	0.606
Peri-implant bone loss 1.5 mm group	0.57 ± 0.95	0.04 ± 0.13	0.14 ± 0.43	0 ± 0	0 ± 0	0.03 ± 0.10	0.093
Patients with no preference	8/8	6/9	9/9	5/6	6/6	9/9	0.047*

**Statistically significant difference*

However, ideally, in the same trial, we should also have tested the placement of identical implants at crestal level or even slightly supracrestally to have a complete overview of the relationships between implant positioning depth and aesthetic outcome, as well other potentially clinically relevant parameters. Indeed, in the other RCTs, when implants were crestally placed, some statistically significant differences in bone loss were reported. For instance one RCT[4], evaluating platform-switched implants with a conical connection, placed at crestal level, 1 and 2 mm subcrestally reported 0.27 mm more bone loss for implants positioned at crestal level 1 year after loading. Surprisingly, another RCT[5], which compared platform-switched implants placed at crestal level or 1 mm below, showed 0.65 mm more bone loss at subcrestally placed implants 3 years after loading.

In this trial, bone loss at 8 years was less than that measured at previous time points in both groups. Nevertheless, this can be easily explained by the fact that some implants were affected by peri-implantitis, and once they failed they were removed; hence, as in other, similar studies, their negative bone loss values were removed from the calculations, leading to apparently less bone loss overall. To get a better idea of the actual bone loss, it might be better to include the bone loss at failed implants in the calculations.

As regards complications, no statistically significant differences were noted between the two groups. Nonetheless, it is interesting to observe that most of complications were linked to infections, and that only two, very minor, biomechanical complications occurred (the loosening of a cover screw and chipping of a ceramic crown), which is indicative of the good quality of the implant system used in the present trial.

Similarly, no statistically significant differences between implants positioned 0.5 or 1.5 mm subcrestally nor trends were observed in aesthetics (PES score) up to 8 years after loading. This could be interpreted as both procedures achieving similar aesthetic outcomes. That being said, it should be noted that aesthetics improved slightly between month 2 and month 12 post-loading, especially mesial and distal papillae scores. This suggests that some sort of creeping attachment phenomenon occurred after the delivery of the definitive crowns, indicating that the peri-implant soft tissues gradually grew around the crowns[8]. This improvement remained stable up to the third year after loading, and regressed to the baseline values at 5 years post-loading[10], remaining largely unchanged at 8 years.

Comparing clinical outcomes among the different centres revealed no statistically significant differences in crown/implant failures, complications, or peri-implant marginal bone level

changes. However, the sample might have been too small to detect differences between operators. Nonetheless, there was a statistically significant difference among centres in terms of patient preference, with one centre (Lovere/Bergamo) having fewer patients with no preference (6/9) than the others.

Periapical radiographs were initially taken in a standardized way using customized stents. The decision to use stents was taken by the centres and was incorporated in the research protocol. This request was not considered necessary by the study coordinator since by experience it is known that after some years stents will not fit any longer and they do not provide more accurate measurements at least at implants, when the implant length is known. Stents are more useful at teeth, since the actual length of teeth is unknown and therefore it is otherwise not possible to calibrate the measurements.

Nevertheless, in the present investigation both procedures were tested under real clinical conditions and patient inclusion criteria were broad. Therefore, results may be generalized with confidence to a wider population with similar characteristics.

CONCLUSIONS

Up to 8 years after loading, no statistically significant differences were found between implants placed 0.5 mm or 1.5 mm subcrestally when surrounded by at least 1 mm of bone, and clinicians are therefore free to choose which depth they prefer.

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