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Immediately loaded zygomatic implants vs conventional dental implants in augmented atrophic maxillae: 4 months post-loading results from a multicentre randomised controlled trial

Key words *atrophic maxilla, bone augmentation, bone substitute, immediate loading, zygomatic implants*

Purpose: To compare the clinical outcome of immediately loaded cross-arch maxillary prostheses supported by zygomatic implants vs conventional implants placed in augmented bone.

Materials and methods: A total of 71 edentulous patients with severely atrophic maxillas, who did not have sufficient bone volume to place dental implants or when it was possible to place only two implants in the front area (minimal diameter 3.5 mm and length of 8 mm) and less than 4.0 mm of bone height subantrally, were randomised according to a parallel group design. They (35 patients) received zygomatic implants to be loaded immediately vs grafting with a xenograft, followed, after 6 months of graft consolidation, by the placement of six to eight conventional dental implants, submerged for 4 months (36 patients). To be loaded immediately, zygomatic implants had to be inserted with an insertion torque superior to 40 Ncm. Screw-retained, metal-reinforced, acrylic provisional prostheses were provided to be replaced by definitive Procera Implant Bridge Titanium prostheses (Nobel Biocare, Göteborg, Sweden) with ceramic or acrylic veneer materials 4 months after initial loading. Outcome measures were: prosthesis, implant and augmentation failures, any complications, quality of life (OHIP-14), the number of days that patients experienced total or partial impaired activity, time to function, and number of dental visits, assessed by independent assessors. Patients were followed up to 4 months after loading.

Results: No augmentation procedure failed. Three patients dropped out from the augmentation group. Six prostheses could not be delivered or failed in the augmentation group vs one prosthesis in the zygomatic group, the difference being statistically significant (difference in proportions = 15.32%; $P = 0.04$; 95% CI: 0.23 to 31.7). Eight patients lost 35 implants in the augmentation group vs three implants in one patient from the zygomatic group, the difference being statistically significant (difference in proportions = 21.38%; $P = 0.001$; 95% CI: 3.53 to 39.61). In total, 14 augmented patients were affected by 20 complications vs 26 zygomatic patients (35 complications), the difference being statistically significant (difference in proportions = 31.87%; $P = 0.008$; 95% CI: 6.48 to 53.37). The OHIP-14 score was 3.68 ± 5.41 for augmented patients and 4.97 ± 5.79 for zygomatic patients, with no statistically significant differences between groups (mean difference = 1.29; 95%CI -1.60 to 4.18; $P = 0.439$). Both groups had significantly improved OHIP-14 scores from before rehabilitation ($P < 0.001$ for both augmented and zygomatic patients). The number of days of total infirmity was, on average, 7.42 ± 3.17 for the augmented group and 7.17 ± 1.96 for the zygomatic group, the difference not being statistically significant (mean difference = -0.25; 95% CI: -1.52 to 1.02;

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P = 0.692). Days of partial infirmity were on average 14.24 ± 4.64 for the augmented group and 12.17 ± 3.82 for the zygomatic group, the difference being statistically significant (mean difference = -2.07; 95% CI: -4.12 to -0.02; *P* = 0.048). The mean number of days to have a functional prosthesis was 444.32 ± 207.86 for augmented patients and 1.34 ± 2.27 for zygomatic patients, the difference being statistically significant (mean difference = -442.9; 95% CI: -513.10 to -372.86; *P* < 0.001). The average number of dental visits was 16.79 ± 10.88 for augmented patients and 12.58 ± 5.21 for zygomatic patients, the difference not being statistically significant (mean difference = -4.21; 95% CI -8.48 to 0.06; *P* = 0.053).

Conclusions: Preliminary 4-months post-loading data suggest zygomatic implants were associated with statistically significantly less prosthetic (one vs six patients) and implant failures (one patient lost three implants versus 35 implants in eight patients) as well as time needed to functional loading (1.3 days vs 444.3 days) when compared with augmentation procedures and conventionally loaded dental implants. Even if more complications were reported for zygomatic implants, which were solved spontaneously or could be handled, zygomatic implants proved to be a better rehabilitation modality for severely atrophic maxillae. Long-term data are essential to confirm or dispute these preliminary results.

Conflict of interest statement: *This study was originally supported by Nobel Biocare, the manufacturer of the implants, and the provisional and definitive prosthetic components used in this study, which were provided free for the patients. However, before any results were known, Nobel Biocare withdrew the financial support and recruitment had to be stopped. Tecnoss (Giaveno, Torino, Italy) kindly donated the bone substitutes and the membranes, whereas Global D (Brignais, France) donated the osteosynthesis screws. Data property belonged to the authors and by no means did the manufacturers interfere with the publication of the results.*

■ Introduction

Dental implants are used for replacing missing teeth[1]. The placement of dental implants can be limited by the presence of insufficient bone volume to allow their anchorage. In order to solve this problem, several bone augmentation procedures have been developed. In principle, the missing bone is taken from a donor site (for example the iliac crest), transplanted where needed and then implants are placed. Sometimes, major bone grafting operations have to be undertaken under general anaesthesia meaning patients must be hospitalised for a few days. Some degree of morbidity relating to the donor site must be expected although, more recently, bone substitutes are used to minimise morbidity[2-4], and two to three surgical interventions may be needed before the implants are functional. Sometimes patients have to wait more than 1 year before a prosthesis can be fixed to the implants and the total treatment cost is high. At the start of the 1990s, a long, screw-shaped implant – the zygomatic implant[5] – was developed by Professor P-I Brånemark as an alternative to bone augmentation procedures. Zygomatic implants are generally inserted through the alveolar crest to engage the body of the zygomatic bone[6], either passing or not passing through the maxillary sinus, depending on the individual local anatomic conditions[7]. One to three zygomatic implants can be inserted through the alveolar crest to engage the body of each zygomatic bone. However, more commonly, two zygomatic implants are placed in each zygoma and they can be loaded immediately if inserted with a sufficient torque[8]. This is potentially a major advantage over conventional bone augmentation procedures, since patents could be functionally rehabilitated in a single day instead of undergoing two to three surgical procedures over several months[3,9]. Therefore, zygomatic implants are an alternative to conventional bone augmentation and implant rehabilitation for severely atrophic maxillae[6]. Despite zygomatic implants being in use for almost 20 years[5,6,10-12], reliable comparative trials evaluating the effectiveness and potential risks when

compared with conventional augmentation procedures are still lacking[13].

The aim of this randomised controlled trial (RCT) of parallel group design was to compare the clinical outcome of immediately loaded cross-arch maxillary prostheses supported by zygomatic implants vs conventional implants placed in augmented bone for the rehabilitation of patients with atrophic or severely atrophic maxillae. It was planned to report data up to 15 years after loading and this is the first of the planned publications. This article is reported according to the CONSORT statement for improving the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

Materials and methods

Trial design

This was a three-centre RCT of parallel group design with two arms, balanced randomisation and, when possible, blind outcome assessment. Patients with totally edentulous atrophic maxillae were randomly allocated to bone augmentation with a bone substitute and six to eight conventionally loaded dental implants (augmentation group) or four zygomatic implants, or two zygomatic and two conventional implants to be immediately loaded (zygomatic group). Originally another two centres agreed to participate in this trial and should have treated 20 patients apiece, but neither provided any data.

Eligibility criteria for participants

Any patient with a severely atrophic edentulous maxilla and not having sufficient bone volumes for placing dental implants at all or when it was possible to place only two implants in the anterior area (minimal diameter 3.5 mm and length of 8.0 mm) as evaluated on TC scans and having a residual bone height under the maxillary sinus less than 4.0 mm as measured on cone-beam computer tomography (CBCT) or conventional computer tomography (CT) scans requesting a fixed prosthesis, who was 18 or older and able to understand and sign an informed consent form, was eligible for the trial. Coronal slices were added to conventional CBCT/CT scans to evaluate the osteomeatal complex and the sinus epithelium conditions. Only patients with healthy sinuses were asked to join the trial. Patients were not admitted if any of the following exclusion criteria was present:

- General contraindications to implant surgery;
- Irradiated in the head and neck region with more than 70 Gray;
- Immunosuppressed or immunocompromised;
- Treated or under treatment with intravenous amino-bisphosphonates;
- Untreated periodontal disease;
- Poor oral hygiene and motivation;
- Uncontrolled diabetes;
- Pregnant or lactating;
- Addiction to alcohol or drugs;
- Psychiatric problems;
- Lack of opposite occluding dentition/prosthesis;
- Restricted mouth opening (less than 3.5 cm interarch anteriorly);
- Acute or chronic infection/inflammation in the area intended for implant placement;
- Unable to commit to a 15-year follow-up;
- Patients participating in other studies, if the present protocol could not be properly adhered to;
- Referred only for implant placement.

Patients were categorised according to the degree of maxilla atrophy into: i) atrophic – if there was sufficient bone to place at least two 8.0 mm long and 3.5 mm wide implants in the anterior portion of the maxilla, and ii) severely atrophic – if there was not sufficient bone to place at least two 8.0 mm long and 3.5 mm wide implants in the anterior portion of the maxilla. Patients were also categorised into three groups according to what they declared: i) non-smokers, ii) moderate smokers (up to 10 cigarettes per day), and iii) heavy smokers (more than 10 cigarettes per day).

After the informed consent was signed, patients were randomly allocated to zygomatic implants (depending on the degree of jaw atrophy either to four zygomatic implants Figs 1a to j or two zygomatic and two conventional implants Figs 2a to j) to be immediately loaded, or bone augmentation with a bone substitute, depending on the degree of jaw atrophy either bilateral sinus lift and horizontal augmentation (Figs 3a to m), or bilateral sinus

lift only followed by delayed placement of six to eight conventional implants loaded after 4 months of unloaded healing, according to the indications contained in the sequentially numbered envelope corresponding to the patient's recruitment number.

Setting and locations

Patients were treated at three different centres: i) the Hospital Clinic in Barcelona, Spain, (27 out of 40 planned patients); ii) Policlinico Sant'Orsola Malpighi, in Bologna (10 out of 20 planned patients) and Ospedale San Filippo Neri, in Rome, Italy (34 out of 30 planned patients).

The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were followed. The study was approved by the ethical committees of the Hospital Clinic in Barcelona (HCP/2011/063) on 2 May 2011, the Policlinico Sant'Orsola Malpighi in Bologna (Prot. n 1633/2011) on 19 July, 2011, and the Ospedale San Filippo Neri (prot. n. v.f. 03/2013 and prot n. 50/C.E.F.S.N.) on 27 May, 2013. All patients received thorough explanations, and understood and signed a written informed consent form prior to being enrolled in the trial.

Surgical procedures

Stereolithographic models of the maxillae were created from CBCT/CT scans to better plan the implant insertion angles. Anatomical landmarks to be avoided, such as the infraorbital foramens and the correct implant insertion axes, were marked with a pencil. Diagnostic wax-up and surgical guides were prepared to help clinicians select the most appropriate position and angle of each implant. Efforts were made to plan implant exits at crestal level, rather than palatally.

Patients rinsed with 0.2% chlorhexidine mouthwash for 1 min prior to surgical procedures. Surgeons were free to decide with the patients the preferred type of anaesthesia (general anaesthesia with local anaesthesia, local anaesthesia with sedation, or local anaesthesia alone) to deliver. Articaine with adrenaline 1:100.000 was injected locally to reduce bleeding and increase visibility. Before augmentation and implantation procedures, systemic antibiotic (1750/250 mg of amoxicillin-clavulanic acid or 600 mg of clindamycin for patients allergic to penicillin) were administered orally, or in the case of intravenous sedation/general anaesthesia (850/125 mg of amoxicillin-clavulanic acid or 300 mg of clindamycin for patients allergic to penicillin) intravenously prior to bone augmentation and implant installation. Patients were randomised to two groups: zygomatic implants or bone augmentation. However, according to the degree of bone atrophy of the maxilla, there were two different treatment alternatives in each group:

- For zygomatic implants

1. Four zygomatic implants in severely atrophic maxillae (Figs 1a to j).

   Two zygomatic implants per side were placed and immediately loaded (within 1 week) when they were placed with insertion torque superior to 40 Ncm, otherwise implants were submerged for 4 months. After crestal and release incisions, a mucoperiosteal flap was elevated exposing the maxilla to allow the identification of the infraorbital foramen and of the incisura between the zygomatic arch and the lateral and medial surface of the frontal process of the zygomatic bone. If necessary, a 10 mm× 5 mm window or wider windows extending from the sinus floor to the base of the zygomatic bone, was opened on the lateral wall of the maxillary sinus close to the infrazygomatic crest, and the sinus lining was carefully lifted. As an alternative and, preferably, when anatomical conditions allowed it, zygomatic implants were not inserted through the sinus cavity but into or on to the bone external to the sinus. Surgical templates were used to position the implant exit into the oral cavity at crestal level and not on the palate. A retractor was placed on the incisura between the zygomatic arch and the lateral and medial surface of the frontal process of the zygomatic bone to facilitate the correct three-dimensional orientation of the implant. Initially, a round bur was used. Adequate saline irrigation was provided while drilling. Then a twist drill of 2.9 mm diameter was used until it penetrated the outer cortical layer of the zygomatic bone at the incisura. The length of the zygomatic implant to be used was determined with

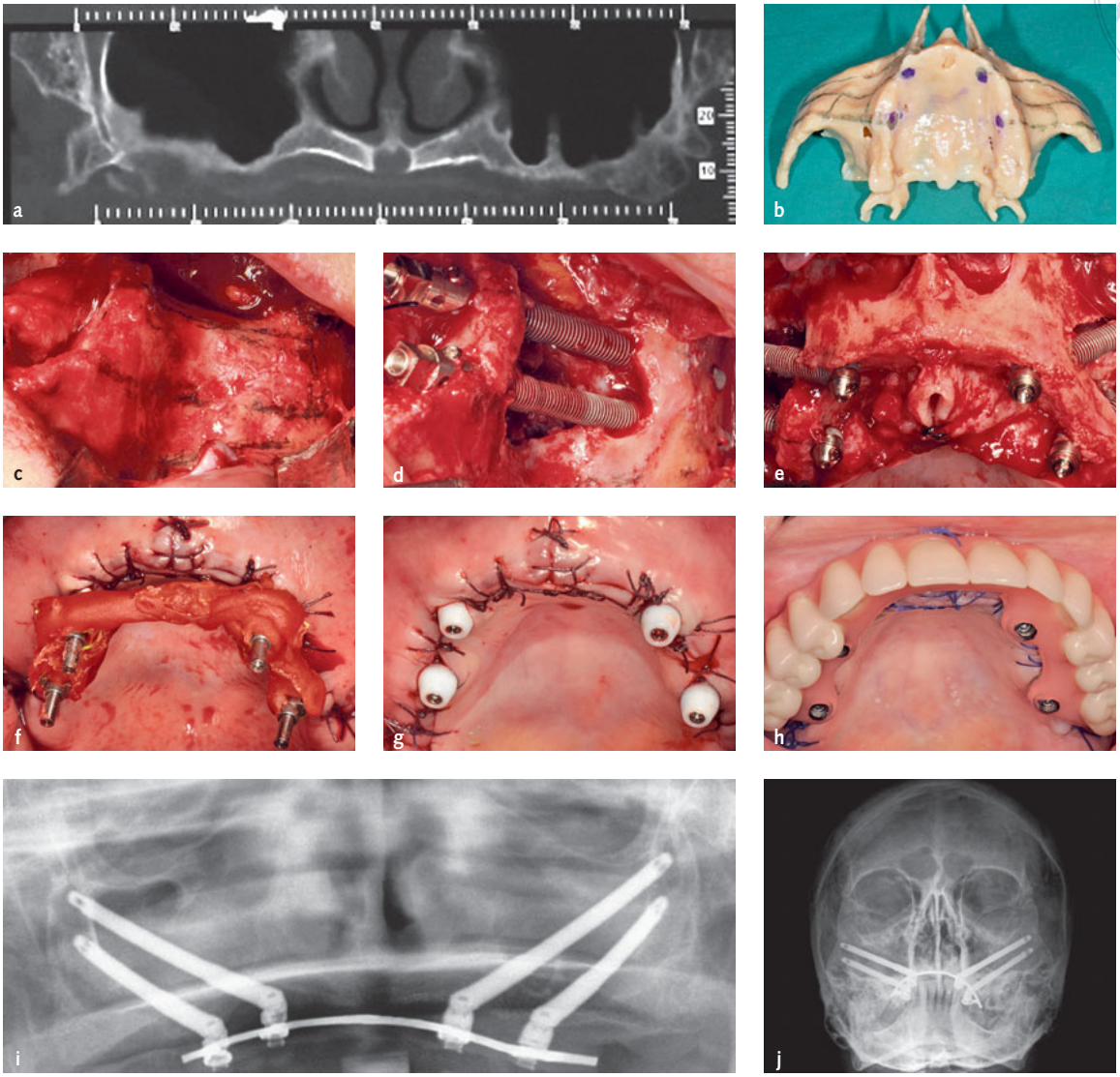

Fig 1a to j a) Preoperative CBCT of a severely atrophic maxilla randomly allocated to receive four immediately loaded zygomatic implants (Dr Pistilli, Rome); b) stereolithographic model used to plan the placement of the zygomatic implants; c) the future position of the zygomatic implants was designed on the bone; d) placement of two zygomatic implants after opening of a lateral sinus window; e) the four zygomatic implants in place; f) impression-taking, a brass wire was used together with self-curing acrylic resin to stabilise the impression copings; g) healing caps are placed while the provisional prosthesis is fabricated; h) delivery of the provisional prosthesis the following day; i) panoramic radiograph at implant loading; j) teleradiography at 4 months post-loading.

a straight depth indicator. A 3.5 mm diameter pilot drill was then used, followed by a 3.5 mm twist drill. Branemark System Zygoma Ti-Unite Implants RP (Nobel Biocare, Gothenburg, Sweden) with the following lengths – 30.0, 35.0, 40.0, 42.5, 45.0, 47.5, 50.0 and 52.5 mm and a diameter of 4.0 mm – were inserted in a bid to achieve an insertion torque of at least 40 Ncm to allow for immediate loading. Bicortical engagement was always obtained, meaning that the tip of the implant protruded for 1.0 mm to 2.0 mm on the other side of the zygoma. After the first implant was placed, the same procedures were repeated to place the second implant. It was attempted to place the implant apexes about 1 cm apart. At their discretion, each centre was allowed to cover exposed implant threads using a paste made of 600 micron to 1000 micron pre-hydrated collagenated cortico-cancellous granules of porcine origin, mixed with OsteoBiol Gel 0 in sterile syringe (OsteoBiol mp3, 1 cc, Tecnoss,

Giaveno, Italy) and resorbable collagen barriers (OsteoBiol Evolution, Tecnoss). As an alternative, the Bichat's fat pads were exposed and gently shifted medially to cover the exposed implant portions in 14 patients from the Italian centres. Flaps were then sutured with simple, interrupted 4-0 resorbable sutures (Vicryl, Ethicon FS-2, Johnson & Johnson, New Brunswick, NJ, USA) around the impression copings.

2. Two zygomatic and two conventional implants in atrophic maxillae (Figs 2a to j)
   One zygomatic and one conventional implant were placed on each side and were immediately loaded (within 1 week), if an insertion torque of at least 40 Ncm was obtained; otherwise they were submerged for 4 months. The same procedure was used to place the zygomatic implants. In addition, one conventional Nobel Active implant (Nobel Biocare) with an internal connection was placed on each side in the anterior zone (canine to canine) following the manufacturer's instructions in an attempt to achieve an insertion torque superior to 40 Ncm to allow immediate loading. Operators were free to choose implant lengths (8.5, 10.0, 11.5, 13.0 and 15.0 mm) and diameters (3.5, 4.3 and 5.0 mm) according to the clinical indications and their preferences.

The following post-surgical instructions were given:

- 850/125 mg of amoxicillin-clavulanic acid or 300 mg of clindamycin for patients allergic to penicillin or Clindamycin 300 mg) three times a day for 1 week;
- Ibuprofen 600 mg prescribed to be taken four times a day during meals for 1 week, but patients were instructed not to take them in the absence of pain;
- Xylometazoline hydrochloride (nasal decongestant) 1 mg, five drops three times a day for 2 weeks;
- A soft diet was recommended for 2 weeks;
- 0.2% chlorhexidine rinses twice a day for 2 weeks;
- Patients were recalled and checked on day 3, day 10 (suture removal) and month 1.

- For augmentation procedure and conventional implants

1. Augmentation procedure and conventional implants in severely atrophic maxillae (Figs 3a to m)
   In the posterior maxilla, bilateral two-stage sinus lift procedures were performed. After crestal and release incisions and mucoperiosteal flap elevation, a window was designed above the maxillary sinus floor using rotating burs or piezosurgery. After internal displacement of the bony window, the maxillary epithelium lining was carefully elevated and the sinus was packed with the mp3 bone substitute. In case of rupture of the sinus lining, resorbable barriers (OsteoBiol Evolution) were used to contain the graft. In the anterior maxilla, collagenated blocks (OsteoBiol, Sp-Block) of equine cancellous bone were used as onlays/veneers. The blocks were hydrated before use for 5 to 10 min with sterile, lukewarm physiological solution or with antibiotics. Afterwards, they were modelled to be adapted to the receiving site, which was accurately decorticated to guarantee maximum contact and high blood perfusion. Blocks were fixed with osteosynthesis self-drilling Ti6Al4V microscrews (Graftek, Global D) with either a 1.5 mm or 2.0 mm diameter and in various lengths from 4.0 mm to 19.0 mm. To fill the gaps between the recipient bone and the bone blocks, mp3 bone substitute granules were used. Small defects could only be grafted with bone substitute granules according to clinical indications and the surgeon's preference. Nasal sinus lift procedures using mp3 bone substitute granules could also be implemented. All the grafted areas and the maxillary windows were covered with OsteoBiol Evolution resorbable barriers from equine pericardium. After 6 months of healing time, six to eight conventional Nobel Active implants were placed and left to heal submerged for a further 4 months. Just prior to implant placement, a second CBCT scan was made to properly evaluate bone anatomy and to plan implant placement.

2. Augmentation procedure and conventional implants in atrophic maxillae
   Operators were free to choose one or two-stage lateral window sinus lift procedures, as previously

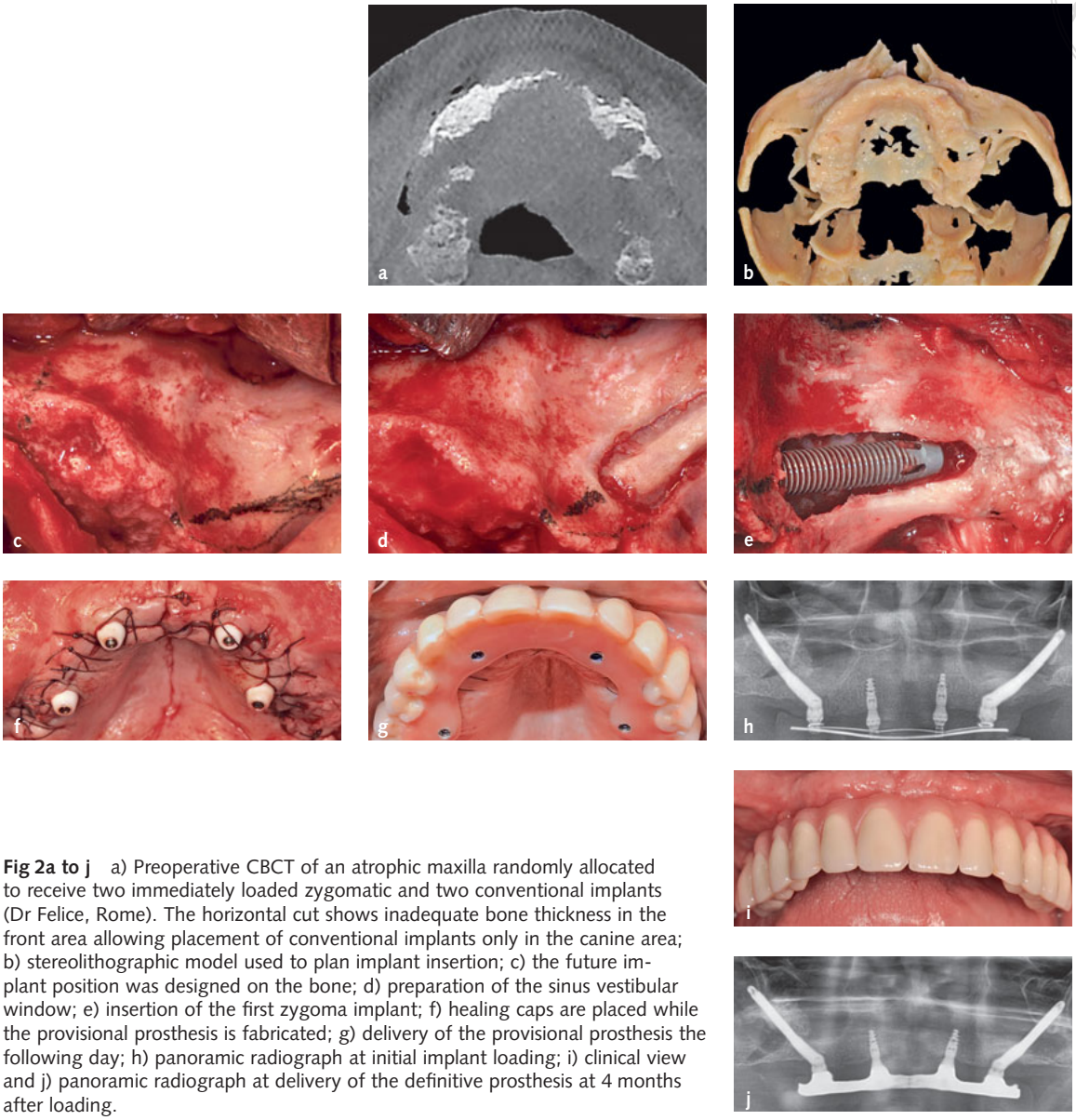

Fig 2a to j a) Preoperative CBCT of an atrophic maxilla randomly allocated to receive two immediately loaded zygomatic and two conventional implants (Dr Felice, Rome). The horizontal cut shows inadequate bone thickness in the front area allowing placement of conventional implants only in the canine area; b) stereolithographic model used to plan implant insertion; c) the future implant position was designed on the bone; d) preparation of the sinus vestibular window; e) insertion of the first zygoma implant; f) healing caps are placed while the provisional prosthesis is fabricated; g) delivery of the provisional prosthesis the following day; h) panoramic radiograph at initial implant loading; i) clinical view and j) panoramic radiograph at delivery of the definitive prosthesis at 4 months after loading.

described, depending whether or not the implants could be stabilised. In the case of the one-stage sinus lift procedure, implants were left to heal submerged for 6 months. In case of a two-stage sinus lift procedure, after 6 months healing, six to eight conventional Nobel Active implants were placed and left to heal submerged for 4 months. The same previously described postoperative instructions were given, and the following were added:

- To avoid blowing the nose or using a straw to drink;
- In the case of sneezing, to try to keep the mouth open in order to decrease intra-sinus pressure;
- Patients with severely atrophic maxillae (subjected to horizontal augmentation procedures) were not allowed to wear any removable denture up to 1 month postoperatively.

Prosthetic procedures

Prosthetic procedures at implants to be immediately loaded were initiated immediately after flap suturing. Panoramic radiographs were taken to verify proper seating of all the impression copings. A self-curing acrylic resin (DuraLay, Reliance Dental Manufacturing, Worth, IL, USA) was positioned on a brass wire, to further stabilise the impression

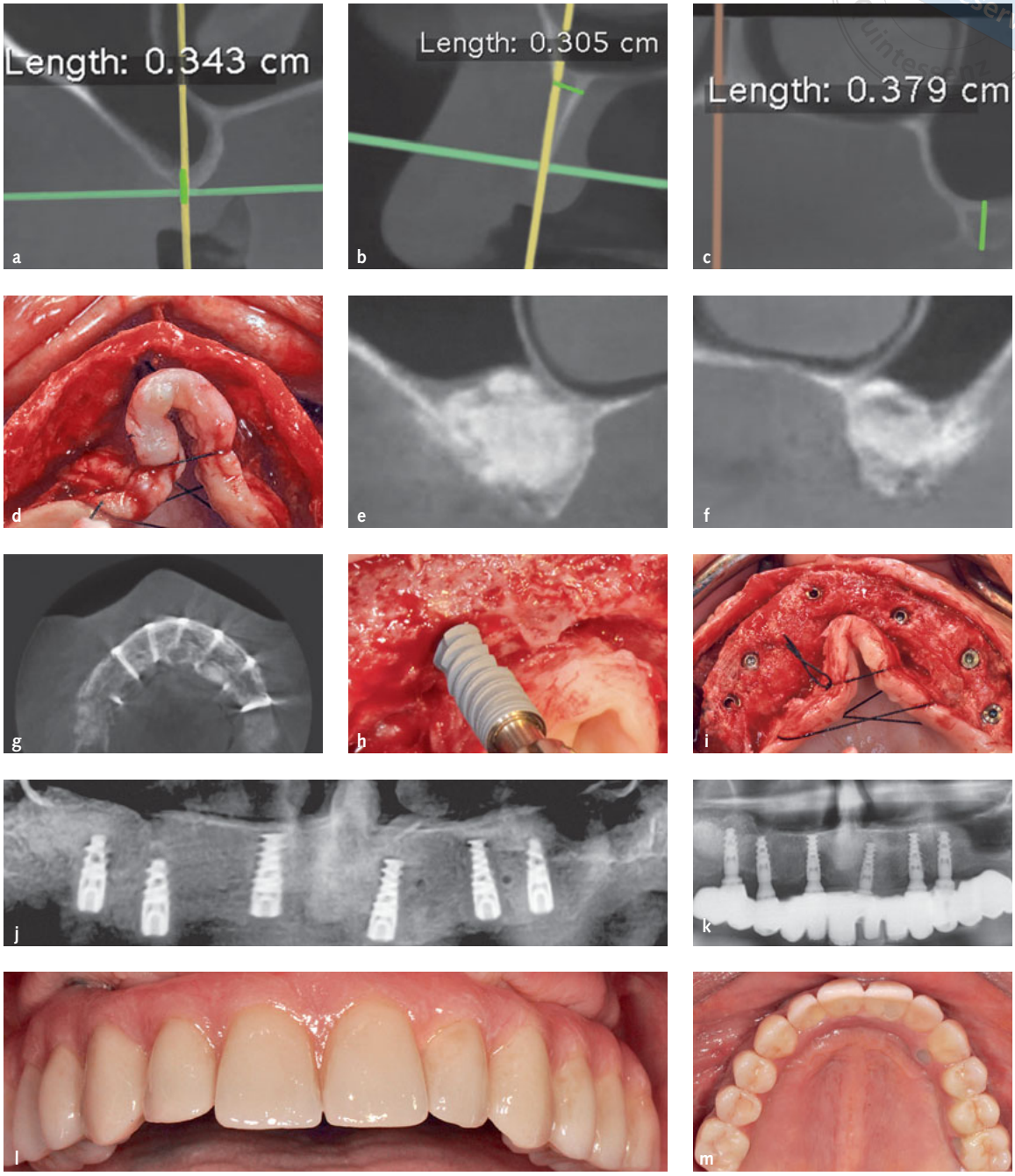

Fig 3a to m a, b and c) preoperative CBCT of a severely atrophic maxilla randomly allocated to receive six to eight implants conventionally loaded (Dr Pistilli, Rome); d) surgical view; e and f) post-augmentation CBCT, both sinuses were grafted and g) the maxilla was reconstructed with horizontal equine bone blocks; h) placement of one of the NobelActive implants after 6 months of graft healing; i) six conventional implants were placed; j) panoramic radiograph after implant placement; k) panoramic radiograph at delivery of the provisional prosthesis about 4 months and half after implant placement; l and m) frontal and occlusal view of the provisional prosthesis 4 months after initial loading (deviation of the protocol).

copings in position. A pick-up impression was taken using a polyether material (Impregum, 3M ESPE, Milan, Italy), and when possible, the patient's denture, with holes in the resin palate, as a customised tray. Healing caps were positioned. A screw-retained, metal-reinforced, acrylic cross-arch provisional prosthesis was delivered within 1 week.

Four months after initial loading, the provisional prostheses were removed, implant stability was checked by tightening the abutment screws with a 15 Ncm torque using a manual torque wrench, and

a definitive impression at abutment level was taken using a rigid impression material and impression copings with an open tray, as previously described. Within 1 month, definitive screw-retained, cross-arch fixed Procera Implant Bridge Titanium (Nobel Biocare) with ceramic or acrylic veneer materials were to be delivered. However, due to a misunderstanding regarding the financial agreements, 35 patients at the Italian centres did not receive the definitive prosthesis 4 months after loading and the remaining patients did not receive Procera Implant Bridge Titanium prostheses.

Patients were enrolled on an oral hygiene programme with recall visits every 6 months. Operators were free to increase maintenance frequency (every 2 to 4 months) based on individual needs. Dental occlusion was evaluated at each maintenance visit. Local independent blind outcome assessors conducted follow-ups.

Outcome measures

- Prosthesis failure defined as no prosthesis delivery or prosthesis replacement because of implant failure or for any other reason.
- Implant failure defined as an implant displaying rotational mobility, any infection dictating implant removal, and/or any mechanical complication rendering the implant unusable (e.g. implant fracture or deformation of the connecting platform). Implant stability assessments were done, with the removed prostheses, at abutment connection (augmented group only) and at delivery of the definitive prostheses, by tightening the abutment screws with a 15 Ncm torque. Rotating implants were considered failures and were removed. It was possible that a few zygomatic implants displayed a slight horizontal mobility due to their lengths and possible lack of alveolar bone at their exits. This was recorded, but if the implants were not rotating, they were considered to be successful and left in place.
- Any biological or prosthetic complications.
- Failure of the augmentation procedure. This was to be considered a failure if, after it had been performed, it was not possible to place the planned implants in the augmented site.
- Peri-implant marginal bone levels on periapical radiograph will be reported at the end of the 1-year post-loading follow-up.
- Oral Health Impact Profile (OHIP-14) that measures people's perceptions of the social impact of oral disorders on their wellbeing[14]. There are 14 questions that can be answered in the following way: never = 0, hardly ever = 1, occasionally = 2, very often = 3, fairly often = 4. The maximum score that can be obtained is 56 and corresponds to the most negative outcome. It was recorded at patient enrolment prior to delivery of any interventions and 1 to 2 weeks after definitive prostheses delivery (about 4-and-a-half months after initial loading).
- The number of days that patients reported total or partially impaired activity: Days of total impaired activity are those days that, in the patient's opinion, he/she could not perform his/her ordinary life activity, including work. Days of partially impaired activity were those days that, according to the patient, he/she could only partially perform his/her ordinary life activity, including work. It should have been assessed at the delivery of the definitive prostheses, but was actually assessed 3 months after loading.
- Time to function: Number of days from the first surgical intervention to the delivery of the implant-supported provisional prosthesis.
- Number of sessions with the clinician: Total number of appointments, including those for maintenance and treatment of complications, required by the patient over the entire follow-up period (up to 4 months post-loading).

Sample size, random sequence, allocation concealment and blinding

The sample size was calculated for the primary outcome measure (patient experiencing at least one implant failure): a two-group continuity corrected chi-square test with a 0.050 two-sided significance level has 80% power to detect the difference between a proportion of 0.100 and a proportion of 0.300 for patients experiencing at least one implant failure (odds ratio of 3.857) when the sample size in each group is 72. It was planned to recruit 65 patients per group over a 3-year recruitment interval period

since this was the maximum number that clinicians committed to treat, but only 35 and 36 patients per group could actually be recruited.

Five computer-generated restricted randomisation lists were created with an equal number of patients in both groups. Only one of the investigators (Dr Esposito), who was not involved in the selection and treatment of the patients, was aware of the randomisation sequence and could have access to the randomisation list stored on his password-protected portable computer. The randomised codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened sequentially after patients were enrolled onto the trial. Therefore, treatment allocation was concealed from the investigators in charge of enrolling and treating the patients.

Practitioners not involved in the patients' treatment, measured the following parameters at each centre: implant failures, quality of life (OHIP-14), patients' number of days of total or partial impaired activity, time to function, and number of dental visits, assessed without knowing group allocation. Complications were registered and treated by the treating surgeons in a non-blinded mode.

Statistical methods

All data analysis was carried out according to a pre-established analysis plan. Dr Ippolito, who has expertise in statistics analysed the data, without knowing the group codes. The patient was the statistical unit of the analyses. An intention-to-treat analysis was applied. Differences in the proportion of prosthetic failures, implant failures, augmentation procedure failures and complications were compared between groups using the Fisher's exact probability test. Differences between the groups in number of days with total or partial impaired activity, time to function, and number of sessions with the dentists were compared by independent-samples *t* tests. A Mann-Whitney U-test was used to compare the OHIP-14 scores between groups. Comparisons between the 4-month post-loading endpoint and the pre-operative measurements were made by Wilcoxon tests, to detect changes in OHIP-14 scores for each study group. Comparisons among the three centres were carried out using a one-way ANOVA for continuous variables (difference for number of days with total or partial inactivity, time to function, and number of sessions with the clinicians), a Pearson's chi-square test for categorical data (difference in proportion for drop-out, prosthetic, implant and augmentation procedure failures and complications) and a Kruskal-Wallis test for ordinal variables (difference in OHIP-14 scores). Finally, the post hoc test used was an independent *t* test with Bonferroni correction of the *P*-value ($P = 0.017$). All statistical analyses were conducted using the Statistical Package for Social Sciences Software (IBM Corp, Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). All statistical comparisons were conducted at the 0.05 level of significance.

Results

In total, 93 patients were screened for eligibility, but 22 patients were not enrolled in the trial: 16 patients did not want to participate in the trial for various reasons, three patients had more bone volume than the inclusions criteria, two were under treatment with biphosphonates, and one because she had recently had breast cancer diagnosed. Seventy-one patients were considered eligible and were consecutively enrolled and treated. All patients were treated according to the allocated interventions. Three patients dropped out from the augmentation group: two who died from lung and gastric cancer and one patient 1 month after the augmentation procedure for depression following her husband's death. The data of all remaining patients was evaluated in the statistical analyses. The following protocol deviations were observed:

- 35 patients from the Italian centres and three from the Spanish centre did not receive the definitive prosthesis during the first 4 months in function.
- The nine patients who were rehabilitated with definitive prostheses in Bologna and Roma did not receive the planned Procera Implant Bridge Titanium prosthesis, but conventional screw-retained cast metal-acrylic or metal-ceramic cross-arch prostheses.
- Patients received different numbers than those attributed by the random list (Spanish centre only).
- The Spanish centre recruited and treated 27 instead of the 40 planned patients. Dr Felice recruited 24

instead of the 20 initially planned patients, but due to organisational reasons only the first 10 patients were treated in Bologna and the remaining 14 patients recruited at the Bologna centre were treated by Dr Felice at the centre in Rome. The Rome centre recruited 20 patients, but 34 patients – 14 from Bologna – were treated in Rome.

- One patient, who should have received only two zygomatic implants (one per side) actually received an additional zygomatic implant since the surgeon at the centre in Rome considered the distance between the conventional implant in position 11 and the zygomatic one to be too far away.
- In one patient, absorbable haemostatic gelatine sponges (Spongostan Special, Ethicon, Johnson & Johnson, New Brunswick, NJ, USA) were used to protect the sinus epithelium after its displacement.

Patients were initially treated from February 2012 to September 2015. The follow-up of all patients was up to 4 months after prosthetic loading.

The main baseline patient characteristics are presented in Table 1. There were no apparent systematic baseline imbalances between the two groups.

An overall comparisons of all outcome measures at 4-month post-loading is presented in Table 2

- Prosthetic failures (Tables 3a and 3b): Six prostheses could not be delivered or failed in the augmentation group vs one prosthesis in the zygomatic group; the difference being statistically significant (difference in proportions = 15.32%; $P = 0.04$; 95% CI: 0.23 to 31.7).
- Implant failures (Tables 3a and 3b): Eight patients lost 35 implants in the augmentation group versus three implants in one patient of the zygomatic group, the difference being statistically significant (difference in proportions = 21.38%;
- $P = 0.001$; 95% CI: 3.53 to 39.61).
- Complications (Tables 3a and 3b): Twenty-six zygomatic patients were affected by 35 complications vs 14 augmented patients (20 complications), the difference being statistically significant (difference in proportions = 31.87%; $P = 0.008$; 95% CI: 6.48 to 53.37).
- Quality of life (OHIP-14): The initial OHIP-14 score was 27.58 ± 8.97 in augmented patients and 29.29 ± 9.40 for zygomatic patients (Table 4a). The initial OHIP-14 did not significantly differ between groups ($P > 0.05$). The OHIP score at 4 months post-loading was 3.68 ± 5.41 in augmented patients and 4.97 ± 5.79 for zygomatic patients, with no statistically significant differences between the groups (mean difference = 1.29; 95%CI -1.60 to 4.18; $P = 0.439$; Table 4b). When looking at the individual items, the only statistically significant difference was observed when asking whether the patient's diet had been unsatisfactory (OH7): patients with zygomatic implants were less satisfied than augmented patients (0.36 ± 0.78 vs 0.07 ± 0.38; $P = 0.028$). Both groups had significantly improved OHIP-14 scores from before rehabilitation ($P < 0.001$ both for augmented and zygomatic patients).
- The number of days patients experienced either total or partially impaired activity: Days of total infirmity were on average 7.42 ± 3.17 for the augmented group and 7.17 ± 1.96 for the zygomatic group; the difference not being statistically significant (mean difference = -0.25; 95% CI: -1.52 to 1.02; $P = 0.692$). Days of partial infirmity were, on average, 14.24 ± 4.64 for the augmented group and 12.17 ± 3.82 for the zygomatic group; the difference being statistically significant (mean difference = -2.07; 95% CI: -4.12 to -0.02; $P = 0.048$).
- Time to function: The mean number of days to have a functional prosthesis were 444.32 ± 207.86 for augmented patients and 1.34 ± 2.27 for zygomatic patients; the difference being statistically significant (mean difference = -442.9; 95% CI: -513.10 to -372.86; $P < 0.001$).
- Number of dental visits: The average number of dental visits was 16.79 ± 10.88 for augmented patients and 12.58 ± 5.21 for zygomatic patients; the difference not being statistically significant (mean difference = -4.21; 95% CI -8.48 to 0.06; $P = 0.053$).

Comparisons of the clinical outcomes between the three surgeons are presented in Table 5. There were differences among the surgeons for days with total impaired activity ($P = 0.010$; with significantly more days of impaired activity in the Spanish group than in Dr Pistilli's group) and number of dental visits ($P = 0.001$; with a higher number of visits in the Spanish group than in both Italian groups).

Table 1 Main patient and intervention characteristics (71 patients).

	Zygomatic implants (35 patients)	Conventional implants (36 patients)
Females (%)	18 (51.4%)	21 (58.3%)
Age (range)	58.31 (43-74)	57.58 (36-71)
Non-smoker	22 (62.9%)	23 (63.9%)
Smoking up to 10 cigarettes/day	3 (8.6%)	8 (22.2%)
Smoking more than 10 cigarettes/day	10 (28.6%)	5 (13.9%)
Severely atrophic maxilla (no possibility to place conventional implants)	29 (82.9%)	23 (63.9%)
Atrophic maxilla (possibility to place two frontal implants)	6 (17.1%)	13 (36.1%)
General + local anaesthesia	35 (100.0%)	33 (91.7%)
Sedation + local anaesthesia	0 (0.0%)	3 (8.3%)
Both sinus lift and augmentation with blocks/granular bone	NA	19 (52.8%)
Only 1-stage sinus lift	NA	2 (5.5%)
Only 2-stage sinus lift	NA	15 (41.7%)
Total number of inserted implants	141 (37.2%)	238 (62.8%)
Implants inserted with a torque superior to 40 Ncm	136 (96.5%)	158 (66.4%)
Implants inserted with a torque up to 40 Ncm	5 (3.5%)	80 (33.6%)
Zygoma implants with the neck fully embedded in crestal bone	102 (77.9%)	NA
Zygoma implants with exposed threads	81 (61.8%)	NA
Zygoma implants with exposed threads which have been grafted	39 (29.8%)	NA
Number of 8.5 mm long implants	2 (1.4%)	38 (16.0%)
Number of 10.0 mm long implants	0 (0.0%)	84 (22.2%)
Number of 11.5 mm long implants	4 (2.8%)	42 (17.6%)
Number of 13 mm long implants	4 (2.8%)	46 (19.3%)
Number of 15 mm long implants	0 (0.0%)	28 (11.8%)
Number of 35 mm long implants	7 (5.0%)	NA
Number of 40 mm long implants	25 (17.7%)	NA
Number of 42.5 mm long implants	13 (9.2%)	NA
Number of 45 mm long implants	28 (19.9%)	NA
Number of 47.5 mm long implants	17 (12.1%)	NA
Number of 50 mm long implants	32 (22.7%)	NA
Number of 52.5 mm long implants	9 (6.4%)	NA
Number of 3.4 mm diameter implants	0 (0.0%)	1 (0.4%)
Number of 3.5 mm diameter implants	6 (4.3%)	151 (63.4%)
Number of 3.75 mm diameter implants	2 (1.4%)	0 (0.0%)
Number of 4.0 mm diameter implants	131 (92.9%)	NA
Number of 4.3 mm diameter implants	1 (0.7%)	86 (36.1%)
Number of 5.0 mm diameter implants	1 (0.7%)	0 (0.0%)

NA = not applicable.

Table 2 Overall comparisons of all outcome measures at 4 months post-loading.

	Zygomatic implants	Augmentation	Difference	95% CI	*P*-value
Patients with prosthetic failures	1 out of 35	6 out of 33	15.32%	0.23 to 31.7	0.04*
Patients with implant failures	1 out of 35	8 out of 33	21.38%	3.53 to 39.61	0.001*
Patients with complications	26 out of 35	14 out of 33	31.87%	6.48 to 53.37	0.008*
OHIP-14	N = 33; 4.97 ± 5.79	N = 28; 3.68 ± 5.41	1.29	-1.60 to 4.18	0.439
Days of total infirmity	N = 35; 7.17 ± 1.96	N = 33; 7.42 ± 3.17	-0.25	-1.52 to 1.02	0.692
Days of partial infirmity	N = 35; 12.17 ± 3.82	N = 33; 14.24 ± 4.64	-2.07	-4.12 to -0.02	0.048*
Days to functional loading	N = 35; 1.34 ± 2.27	N = 33; 444.32 ± 207.86	-442.98	-513.10 to -372.86	0.000*
Number of dental visits	N = 35; 12.58 ± 5.21	N = 33; 16.79 ± 10.88	-4.21	-8.48 to 0.06	0.053

*Statistically significant differences.

Table 3a Description of prosthetic failures, implant failures and complications in the zygomatic group in chronological order.

PROSTHESIS FAILURES			
Patient/Surgeon	**Timing**	**Description**	**Outcome**
Pat 15/Dr Felice	3w pl	Lost 3 zygomatic implants out of 4 with the provisional prosthesis	Back to old denture
IMPLANT FAILURES			
Pat 15/Dr Felice	2-5w pip	Day 12 post-loading the posterior left zygomatic implant was mobile (removed) Prosthesis delivered on the three remaining implants Week 3 post-loading prosthesis mobile: both anterior zygomatic implants were mobile (removed) Posterior right zygomatic implant had 2 mm anterioposterior mobility (kept in place)	Not replaced
COMPLICATIONS			
Pat 11/Dr Felice	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 13/Dr Felice	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 2/Dr Pistilli	Implantation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 3/Dr Pistilli	Implantation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 4/Dr Pistilli	Post-implantation	Mayor swelling involving also the lower lip	Healed spontaneously in 2 weeks
Pat 15/Dr Felice	2-5w pip	Day 12 post-loading the posterior left zygomatic implant was painful and mobile Week 3 post-loading both anterior zygomatic implants were painful and mobile	Three implants removed + antibiotic therapy
Pat 10/Dr Felice	3w pip	Major swelling under the right eye	Amoxicillin + clavulanic acid 875/125 mg every 8 h for 10 days + painkillers –recurrence after 2 weeks exploratory surgery necrotic Bichat's fat pad into the sinus - removed + amoxicillin + clavulanic acid 875/125 mg every 8 h for 10 days + painkillers – solved
Pat 16/Spain	1 m pip	Sinusitis	Improved with amoxicillin-clavulanic acid 875/125 mg every 8 h for 1 month and nasal rinses with isotonic seawater (Rhinomer); persistent cacosmia right nasal fossa that slowly disappeared on its own
Pat 1/Spain	1 m pip 4 m pip	Zygoma and periorbital infection evolving in (see below) chronic fistula	Cutaneous debridement + levofloxacin 500 mg/day for 10 days resection + implant apex resection – solved
Pat 20/Spain	1 m pip	Headache	Solved spontaneously
Pat 25/Spain	1 m pip 4 m pip 4 m pip	Right maxillary sinusitis Right maxillary tumefaction Peri-implant mucosa recessions at front implants	Amoxicillin-clavulanic acid 875/125 mg every 8 h for 7 days Amoxicillin-clavulanic acid 875/125 mg every 8 h for 7 days - solved Not treated
Pat 3/Spain	2 m pip	Right maxillary sinusitis	Amoxicillin-clavulanic acid 875/125 mg every 8 h for 7 days – solved
Pat 4/Dr Felice	3 m pip	Peri-implant mucositis + fistula at anterior left zygoma implant	Prosthesis removal and debridement - healed after 1 week + maintenance every 2 months

w = weeks; m = months; pl = post-loading; pip = post-implant placement. All patients treated at the Italian centres (21 patients) experienced a transient (from 1 week to 3 months) paraesthesia of the infraorbital nerves.

Table 3b Description of prosthetic failures, implant failures and complications for the augmented group in chronological order.

PROSTHESIS FAILURES			
Patient/surgeon	**Timing**	**Description**	**Outcome**
Pat 19/Spain	2 to 34m pip	Three out of eight implants lost 11 migrated to nasal space 2 months after placement 22 mobile 30 months after placement 24 mobile 34 months after placement	Delayed prosthesis placement
Pat 1/Dr Felice	ab	Six out of six implants mobile at abutment connection	Back to old denture
Pat 7/Dr Felice	ab	Seven out of eight implants mobile at abutment connection	Back to old denture
Pat 18/Spain	ab	Three out of eight implants mobile at abutment connection Three implants replaced after 6 months	Delayed prosthesis placement
Pat 7/Spain	13m pip	Six out of eight implants lost for infection	Placement of four zygomatic implants successfully loaded
Pat 11/Spain	14 to 45m pip	Six out of eight implants removed	Placement of four zygomatic implants
IMPLANT FAILURES			
Pat 19/Spain	2 to 34m pip	Three out of eight implants lost 11 migrated to nasal space 2 months after placement 22 mobile 30 months after placement 24 mobile 34 months after placement	Spontaneously came out from the nose New left nasal floor elevation + implant placement 23, 35 months after first implant placement
Pat 1/Dr Felice	ab	Six out of six implants mobile at abutment connection Patient wore denture from day 20 post-implantation	Back to old denture
Pat 7/Dr Felice	ab	Seven out of eight implants mobile at abutment connection Patient wore denture from week 2 post-implantation	Back to old denture
Pat 18/Spain	ab	Three out of eight implants mobile at abutment connection One replaced implant mobile at new abutment connection	3 implants replaced after 6 months
Pat 5/Spain	ab	Three out of eight implants mobile: Implant 23 mobile at abutment connection Implant 11 mobile 3 months after abutment connection Implant 16 mobile 4 months after abutment connection	All three implants replaced 16 months after placement of first implants
Pat 6/Spain	7m pip	Lost implant 16 out of eight implants	None
Pat 7/Spain	13m pip	Six out of eight implants lost to infection	Surgical removal of the infected graft and placement of four zygoma implants
Pat 11/Spain	14m pip	Six out of eight implants removed Implants 11, 23, 24 and 25 lost 14 months after placement Implant 14 lost 39 months after implant placement Implant 13 removed 45 months after implant placement	11 and 26 replaced 22 months after initial placement Placed two zygoma implants in position 22 and 25, 38 months after first implant placement Replaced by two zygoma implants in position 12 and 15, 45 months after loading
COMPLICATIONS			
Pat 5/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 8/Spain	Augmentation 9m pip	Sinus epithelium perforation of right side Exposed vestibular surface of implant 23 at second phase surgery	Placed Evolution membranes Connective tissue graft

COMPLICATIONS			
Patient/surgeon	**Timing**	**Description**	**Outcome**
Pat 11/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 12/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 15/Spain	Augmentation	Bilateral sinus epithelium perforation	Placed Evolution membranes
Pat 18/Spain	Augmentation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 22/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 24/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 26/Spain	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 6/Dr Felice	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 9/Dr Pistilli	Augmentation	Sinus epithelium perforation of right side	Placed Evolution membrane
Pat 18/Dr Pistilli	Augmentation	Sinus epithelium perforation of left side	Placed Evolution membrane
Pat 7/Spain	Implantation - 13m pip	Onlay block fragmentation when placing implant 24 Left maxilla infected The infection progressed to the right side until she lost six implants 13 months after their placement	 Amoxicillin-clavulanic acid 875/125 Bilateral bone graft removal and right maxillary sinus curettage + placement of four zygoma implants
Pat 19/Spain	2m pip	Implant 11 migrated into the nasal space Since the patient lost other two implants a new nasal floor elevation was done but the nasal mucosa was perforated on the right side Peri-implantitis at 23 and at right maxillary implants	Spontaneously came out from the nose Right implants could not be placed Improved after curettage and better hygiene

w = weeks; m = months; pl = post-loading; pip = post-implant placement; ab = abutment connection

Discussion

This trial was designed to understand if it would be preferable to rehabilitate edentulous patients with atrophic maxillae, either performing bone augmentation procedures with bone substitutes and delayed placement of conventionally loaded standard dental implants, or using immediately loaded zygomatic implants. Despite having more complications with zygomatic implants, the interpretation of the overall data suggests a more favourable outcome for zygomatic implants, since less implant and prosthesis failures occurred and patients could be rehabilitated in a couple of days when using zygomatic implant versus an average of 15 months, if augmented. Obviously, these results apply only for a short-term period (4 months after loading). It would be sensible to wait for longer follow-ups (up to 10 years) before drawing definitive conclusions.

The main reason why significantly more complications were reported for zygomatic implants is linked to the presence of post-operative paraesthesiae of both infraorbital nerves, affecting all patients treated at both the Italian centres, but none at the Spanish centre. All paraesthesiae were transient, ranging from 1 week to 3 months, and were solved spontaneously. A plausible explanation for this difference could be possibly linked to different surgical approaches, with the Italian operators opening wider flaps to better visualise the zygomatic bone. The Italian centres were less experienced with zygomatic implants compared with the Spanish centre.

Patient quality of life, measured with the OHIP-14 score, significantly improved with both rehabilitation procedures, with no major difference between the two options. Only on the aspect of the patient's diet having been unsatisfactory, a statistically significant difference was observed in favour of augmented patients. It is difficult to provide a convincing explanation for this difference.

Days with total infirmity were similar for both groups, most likely depending on the major surgical interventions performed under general anaesthesia, whereas an average of two fewer days of partial infirmity were reported by patients rehabilitated with zygomatic implants, the difference being statistically significant. The number of visits required

Table 4a OHIP-14 at baseline, before commencing with the implant-supported prosthesis rehabilitation.

How often in the last year have you had problems with your maxillary prosthesis?		
Question	**Zygoma implants (n = 35)**	**Augmented group (n = 36)**
OH1 Have you had trouble pronouncing any words?	2.26 ± 1.48	2.67 ± 1.10
OH2 Have you felt that your sense of taste has worsened?	2.20 ± 1.18	2.53 ± 1.11
OH3 Have you had painful aching in your mouth?	2.06 ± 1.03	1.64 ± 1.02
OH4 Have you found it uncomfortable to eat any foods?	3.37 ± 1.06	3.17 ± 1.06
OH5 Have you felt self-conscious?	2.80 ± 1.08	2.50 ± 1.11
OH6 Have you felt tense?	2.14 ± 1.00	2.00 ± 1.04
OH7 Has your diet been unsatisfactory?	2.46 ± 1.15	2.69 ± 1.24
OH8 Have you had to interrupt meals?	2.23 ± 1.06	2.17 ± 0.97
OH9 Have you found it difficult to relax?	2.06 ± 1.24	1.64 ± 1.10
OH10 Have you been a bit embarrassed?	2.26 ± 1.20	2.28 ± 1.19
OH11 Have you been a bit irritable with other people?	0.94 ± 0.97	0.83 ± 0.74
OH12 Have you had difficulty doing your usual jobs?	1.57 ± 1.36	1.06 ±1.17
OH13 Have you felt that life in general was less satisfying?	2.06 ± 1.11	1.61 ± 1.15
OH14 Have you been totally unable to function?	0.89 ± 0.76	0.81 ± 0.75
Total score	29.29 ± 9.40	27.58 ± 8.97

Data are presented as mean ± standard deviation. Possible answers: 0 (never), 1 (hardly ever), 2 (occasionally), 3 (very often) to 4 (fairly often).

Table 4b OHIP-14 assessed about 4 months after initial loading, after delivery of the definitive prostheses.

How often in the last four months have you had problems with your maxillary prosthesis?			
Question	Zygoma implants (n = 33)	Augmented group (n = 28)	P-value
OH1 Have you had trouble pronouncing any words?	0.88 ± 1.17	0.64 ± 0.73	0.745
OH2 Have you felt that your sense of taste has worsened?	0.12 ± 0.42	0.07 ± 0.38	0.409
OH3 Have you had painful aching in your mouth?	0.70 ± 0.85	0.50 ± 0.64	0.448
OH4 Have you found it uncomfortable to eat any foods?	0.55 ± 0.90	0.39 ± 0.74	0.489
OH5 Have you felt self-conscious?	0.42 ± 0.71	0.32 ± 0.67	0.562
OH6 Have you felt tense?	0.52 ± 0.71	0.25 ± 0.52	0.115
OH7 Has your diet been unsatisfactory?	0.36 ± 0.78	0.07 ± 0.38	0.028*
OH8 Have you had to interrupt meals?	0.45 ± 0.62	0.54 ± 0.69	0.696
OH9 Have you found it difficult to relax?	0.30 ± 0.47	0.57 ± 0.63	0.087
OH10 Have you been a bit embarrassed?	0.15 ± 0.51	0.07 ± 0.38	0.399
OH11 Have you been a bit irritable with other people?	0.18 ± 0.46	0.04 ± 0.19	0.130
OH12 Have you had difficulty doing your usual jobs?	0.12 ± 0.55	0.07 ± 0.38	0.657
OH13 Have you felt that life in general was less satisfying?	0.18 ± 0.53	0.07 ± 0.38	0.241
OH14 Have you been totally unable to function?	0.03 ± 0.17	0.07 ± 0.38	0.888
Total score	4.97±5.79	3.68±5.41	0.439

Data are presented as mean ± standard deviation. Possible answers: 0 (never), 1 (hardly ever), 2 (occasionally), 3 (very often), 4 (fairly often). * Statistically significant differences.

to rehabilitate the patients was also fewer when zygomatic implants were used. In fact, patients with zygomatic implants required four visits fewer than the augmented patients. Despite the difference not being statistically significant, the *P*-value was very close to significance ($P = 0.053$), suggesting that, also relating to fewer visits, rehabilitation with zygomatic implants proved advantageous.

The reason why at the 4-month post-loading follow-up 35 patients from the Italian centres were not rehabilitated with a definitive prosthesis, as planned at protocol stage, was down to a misunderstanding

Table 5 Comparison of the clinical outcomes between the three treating surgeons at 4 months post-loading.

	Spain	Dr Felice	Dr Pistilli	*P*-value
Number of treated patients	27	24	20	NA
Dropout	2	1	0	0.459
Patients with failed prosthesis	4	3	0	0.210
Patients with failed implants	6 (22 implants)	3 (16 implants)	0	0.077
Patients with failed augmentation procedure	0 out of 13	0 out of 13	0 out of 10	NA
Patients with complications	16 (24 complications)	12 (18 complications)	12 (15 complications)	0.743
OHIP 14	6.10 ± 8.97	2.59 ± 1.99	4.10 ± 2.31	0.129
Mean of total infirmity days	8.44 ± 3.18	7.04 ± 2.27	6.16 ± 1.42	0.010*
Means of partial infirmity days	14.32 ± 5.40	12.61 ± 4.34	12.40 ± 2.21	0.252
Means of days to functional loading	270.09 ± 375.90	157.14 ± 166.76	162.30 ± 165.56	0.281
Average number of patient dental visits	19.86 ± 12.50	12.75 ± 2.97	10.65 ± 2.03	0.001*§

Data are presented as mean ± standard deviation. NA: not applicable; significant comparisons: * Spain vs Dr Pistilli; § Spain vs Dr Felice.

among the Italian centres and Nobel Biocare. The Italian centres did not ask for the definitive abutments and the definitive titanium Procera frameworks, as agreed at protocol level, thinking that patients had to pay for definitive prostheses themselves. As a consequence, 35 patients were unable or unwilling to pay for the definitive prosthesis. As soon as the misunderstanding emerged, patients were called back and offered the definitive prostheses, and were only charged for the dental technician's costs for lining the titanium frameworks with composite-resin or ceramic.

It is not possible to compare the present results with those of similar RCTs, as none are available. The only other published RCT on zygomatic implants compared the use of rotational drills vs piezosurgery using specifically designed inserts to prepare the sites for zygomatic oncology implants[15] in a split-mouth study.

The main limitation of the present investigation was its small number of included patients, however this was still sufficient to provide some useful indications, and able to generate hypotheses for future investigations.

Both procedures were tested in real clinical conditions and patient inclusion criteria were broad, therefore the results of the present trial can be generalised to larger populations with similar characteristics, keeping in mind that placement of zygomatic implants is a complex procedure requiring skilled and experienced operators, as potentially severe complications may occur.

Despite the good clinical performance of zygomatic implants, some unpleasant complications did occur, suggesting that their use should be limited to patients with severely atrophic maxillae. In the presence of less atrophic maxillae allowing the placement of short implants (4 mm to 6 mm long), it could be wiser to use short implants in light of the good results reported so far[9,16-22], even though this hypothesis has not yet been properly tested.

■ Conclusions

Preliminary 4-month post-loading data suggest zygomatic implants were associated with statistically significantly fewer prosthetic (one vs six patients) and implant failures (one patient lost three implants vs 35 implants in eight patients), as well as time needed for functional loading (1.3 days vs 444.3 days) when compared with augmentation procedures and conventionally loaded dental implants. Even if more complications were reported for zygomatic implants, which were solved spontaneously or could be handled, zygomatic implants proved to be a better rehabilitation modality for severely atrophic maxillae. Long-term data are essential to confirm or dispute these preliminary results.

References

1. Brånemark P-I, Hansson BO, Adell R, Breine U, Lindström J, Hallén O, Ohman A. Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Stockholm: Almqvist & Wiksell International, 1977.
2. Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. Interventions for replacing missing teeth: horizontal and vertical bone augmentation techniques for dental implant treatment. Cochrane Database Syst Rev 2009: Chichester, UK: John Wiley & Sons, Ltd.
3. Esposito M, Felice P, Worthington HV. Interventions for replacing missing teeth: augmentation procedures of the maxillary sinus. Cochrane Database Syst Rev 2014: Chichester, UK: John Wiley & Sons, Ltd.
4. Pistilli R, Felice P, Piatelli M, Nisii A, Barausse C, Esposito M. Blocks of autogenous bone versus xenografts for the rehabilitation of atrophic jaws with dental implants: preliminary data from a pilot randomised controlled trial. Eur J Oral Implantol 2014;7:153–171.
5. Stevenson AR, Austin BW. Zygomatic fixtures – the Sydney experience. Ann R Australas Coll Dent Surg 2000;15:337–339.
6. Brånemark PI, Gröndahl K, Öhrnell LO, Nilsson P, Petruson B, Svensson B, Engstrand P, Nannmark U. Zygoma fixture in the management of advanced atrophy of the maxilla: technique and long-term results. Scand J Plast Reconstr Surg Hand Surg 2004;38:70–85.
7. Aparicio C. A proposed classification for zygomatic implant patient based on the zygoma anatomy guided approach (ZAGA): a cross-sectional survey. Eur J Oral Implantol 2011;4:269–275.
8. Davó R, Pons O. Prostheses supported by four immediately loaded zygomatic implants: a 3-year prospective study. Eur J Oral Implantol 2013;6:263–269.
9. Esposito M, Barausse C, Pistilli R, Sammartino G, Grandi G, Felice P. Short implants versus bone augmentation for placing longer implants in atrophic maxillae: One-year post-loading results of a pilot randomised controlled trial. Eur J Oral Implantol 2015;8:257–268.
10. Triplett RG, Schow SR, Laskin DM. Oral and maxillofacial surgery advances in implant dentistry. Int J Oral and Maxillofac Implants 2000;15:47–55.
11. Malevez C, Abarca M, Durdu F, Daelemans P. Clinical outcome of 103 consecutive zygomatic implants: a 6-48 months follow-up study. Clin Oral Implants Res 2004;15:18–22.
12. Hirsch JM, Öhrnell LO, Henry PJ, Andreasson L, Brånemark PI, Chiapasco M, Gynther G, Finne K, Higuchi KW, Isaksson S, Kahnberg KE, Malevez C, Neukam C, Neukam FW, Sevetz E, Urgell JP, Widmark G, Bolind P. A clinical evaluation of the Zygoma fixture: one year of follow-up at 16 clinics. J Oral Maxillofac Surg 2004;62:22–29.
13. Esposito M, Worthington HV. Interventions for replacing missing teeth: dental implants in zygomatic bone for the rehabilitation of the severely deficient edentulous maxilla. Cochrane Database Syst Rev 2013: Chichester, UK: John Wiley & Sons, Ltd.
14. Brennan DS, Spencer AJ. Dimensions of oral health related quality of life measured by EQ-5D+ and OHIP-14. Health Qual Life Outcomes 2004;2:35.
15. Esposito M, Balercia A, Barausse C, Pistilli R, Ippolito DR, Felice P. Conventional drills versus piezoelectric surgery preparation for placement of four immediately loaded zygomatic oncology implants in edentulous maxillae: results from 1-year split-mouth randomised controlled trial. Eur J Oral Implantol 2017;10:147–158.
16. Pistilli R, Felice P, Cannizzaro G, Piatelli M, Corvino V, Barausse C, Buti J, Soardi E, Esposito M. Posterior atrophic jaws rehabilitated with prostheses supported by 6 mm long 4 mm wide implants or by longer implants in augmented bone. One-year post-loading results from a pilot randomised controlled trial. Eur J Oral Implantol 2013;6:359–372.
17. Pistilli R, Felice P, Piattelli M, Gessaroli M, Soardi E, Barausse C, Buti J, Soardi E, Esposito M. Posterior atrophic jaws rehabilitated with prostheses supported by 5 × 5 mm implants with a novel nanostructured calcium-incorporated titanium surface or by longer implants in augmented bone. One-year results from a randomised controlled trial. Eur J Oral Implantol 2013;6:343–357.
18. Esposito M, Pistilli R, Barausse C, Felice P. Three-year results from a randomised controlled trial comparing prostheses supported by 5-mm long implants or by longer implants in augmented bone in posterior atrophic edentulous jaws. Eur J Oral Implantol 2014;7:383–395.
19. Gulje FL, Raghoebar GM, Vissink A, Meijer HJ. Single crowns in the resorbed posterior maxilla supported by either 6-mm implants or by 11-mm implants combined with sinus floor elevation surgery: A 1-year randomised controlled trial. Eur J Oral Implantol 2014;7:247–255.
20. Thoma DS, Haas R, Tutak M, Garcia A, Schincaglia GP, Hammerle CH. Randomized controlled multicentre study comparing short dental implants (6 mm) versus longer dental implants (11-15 mm) in combination with sinus floor elevation procedures. Part 1: demographics and patient-reported outcomes at 1 year of loading. J Clin Periodont 2015;42:72–80.
21. Bolle C, Felice P, Barausse C, Pistilli R, Trullenque-Eriksson A, Esposito M. Four mm-long versus longer implants in augmented bone in posterior atrophic jaws: One year post-loading results from a multicentre randomised controlled trial. Eur J Oral Implantol 2018;10:11:31-47.
22. Gastaldi G, Felice P, Pistilli R, Barausse C, Trullenque-Eriksson A, Esposito M. Short implants as an alternative to crestal sinus lift: a 3-year multicentre randomised controlled trial. Eur J Oral Implantol 2017;10:391-400.