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ORIGINAL ARTICLE

Influence of the position of the antrostomy in sinus floor elevation on the healing of mini-implants: a randomized clinical trial

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Abstract

Aim To evaluate histologically the healing of mini-implants installed after sinus floor elevation using a lateral approach and placing the antrostomy at different level from the sinus floor.

Material and methods Sinus floor elevation using a lateral approach was performed in 24 healthy volunteers. The antrostomy was randomly placed either close to the base of the sinus floor (group base) or at about 3–4 mm cranially to it (group standard).

After 6 months of healing, mini-implants were installed within the grafted region, through the alveolar crest. Three months later, biopsies were collected.

Results Sixteen biopsies from 16 patients were available for histological analyses. The new bone reached fractions of 40.9 ± 11.9% and 48.5 ± 20.1% at the base and standard groups, respectively ($p = 0.208$). Xenograft particles were found in contact with the implant surface at percentages of 12.1 ± 11.0% in the base group, and 15.9 ± 23.7% in the standard group ($p = 0.674$).

Conclusions Based on the present study, the choice of one or the other position of antrostomy did not influence significantly the outcome and, therefore, should be left to the preference of the surgeon.

Keywords Maxillary sinus augmentation · Histomorphometric analysis · Biomaterial · Antrostomy · Microimplants

Introduction

The loss of teeth in the posterior segments of the maxilla creates edentulisms that can be restored with fixed prostheses supported by implants. However, due to the alveolar crest resorption that occurs before and after tooth extraction and to the extension of the pneumatization of the maxillary sinus, bone height might result to be insufficient to install implants. In this case, sinus floor elevation represents a solution for bone volume augmentation to allow implant installation [1].

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Aiming to maintain elevated the sinus mucosa, the use of different biomaterials [2], devices [3–5], or implants alone without grafting material [6–9] have been proposed. Nevertheless, a reduction of the dimensions of the grafted region after time is a well-documented occurrence in experimental [10–15] and in clinical studies [16–19].

A systematic review evaluated the loss in dimensions of the grafted sinus both on computerized tomographies and cone beam computerized tomographies [20]. It was shown that autogenous bone was the most resorbed over time, resulting in a loss of about 45% of the augmented volume, while bone substitutes presented a reduction of approximately 18–22%.

A collagenated cortico-cancellous porcine bone was used for sinus floor elevation in clinical studies [18, 19, 21]. In two clinical studies [18, 19], CBCTs were taken after 1 week and 9 months from sinus floor elevation. A reduction of the height of the elevated region ranged between 17 and 25%. Higher resorptions were reported in experimental studies in rabbits, ranged between 25 and 49% [13–15].

It has been shown that bone is formed from the bone walls and the floor of the sinus [7, 13, 22–24]. The preparation of the antrostomy will remove bone from the lateral wall of the sinus. This, in turn, means that position and dimensions of the antrostomy might affect the amount of the lateral bone walls exposed at the base of the elevated region, directly affecting the source of new bone from the parent bone. Considering that the region of higher importance for sinus floor augmentation is that close to the base of the sinus, it might be important to place the lower edge of the antrostomy as far as possible from the floor. This would provide an adjunctive source for new bone formation from the lateral wall.

The effect of the position of the antrostomy on dimensional variations after sinus floor elevation has been already studied on CBCTs and reported in the first part of the present study already published [18]. It was shown that the more cranial was placed the antrostomy, the higher augmentation was obtained. However, histological data were still missing.

Hence, the aim of the present study was to evaluate histologically the healing of mini-implants installed after sinus floor elevation using a lateral approach and placing the antrostomy at different level from the sinus floor.

Material and methods

This randomized controlled trial (RCT) reports histological data while the different aspects regarding the dimensional variations over time of the elevated sinus floor, as evaluated on the cone beam computerized tomographies (CBCTs), have been reported elsewhere [18].

The study adhered to the Declaration of Helsinki on medical protocols and ethics. The protocol was approved by the Ethical Committee of the University Corporation Rafael Núñez, Cartagena de Indias, Colombia (protocol #01-2015; 19 May 2015). The study was carried out at the same university. Informed consent was obtained from all participants. The CONSORT checklist was followed (http://www.consort-statement.org/).

Study population

Twenty-four healthy participants with no contraindications for oral surgery procedures, and in need of sinus floor elevation for oral rehabilitation were recruited.

The inclusion criteria were the following: (i) presence of an edentulous zone in the posterior segment of the maxilla presenting a height of the sinus floor ≤ 4 mm; (ii) need of fix prosthetic rehabilitation on implants in that region; (iii) ≥ 21 years of age. Moreover, participants had to be (iv) in good general health with no contraindication for oral surgical procedures and not pregnant. The following excluding criteria were adopted: (i) presence of systemic disorders; (ii) under chemotherapeutic or radiotherapeutic treatment; (iii) presence of an acute or a chronic sinusitis; (iv) previous bone augmentation procedures in the region. Smokers of > 10 cigarettes per day and patients under bisphosphonates treatment were also excluded.

Due to the absence of previous studies that evaluated the differences in bone formation and bone-to-implant contact percentages (BIC%) on the base of the different position of the antrostomy, an $n = 10$ was calculated to be sufficient to show a differences of at least 10% in BIC%.

The position of the antrostomy was randomly assigned and opaque envelopes were prepared and then opened at the time of the surgery. The randomization was made at the randomization.com website by an author that did not perform the sinus floor elevation procedures (MF). The surgeon was blinded about the allocation until the surgery. The participants were blinded about the allocation treatment. The histological slides were coded so that the outcome assessor (KAAA) was blinded about allocation treatments.

Clinical procedures

Antrostomies of similar dimensions (about 6 mm in height and 12 mm wide; Fig. 1) were randomly prepared either close to the base of the sinus floor (group base) or at about 3–4 mm cranially to it (group standard). A sonic-air surgical instrument (Sonosurgery® TKD, Calenzano, Fi—Italy) was used for antrostomy preparation. A collagenated cortico-cancellous porcine bone (OsteoBiol Gen-Os®, 250–1000 μm, Tecnoss, Giaveno, Italy) was used to fill the elevated space subjacent the elevated sinus mucosa and a collagen membrane (OsteoBiol® Evolution, 0.3 mm, Tecnoss, Giaveno, Italy) was placed to cover the antrostomy. Single silk sutures were used to close the wounds. Antibiotics and analgesic drugs

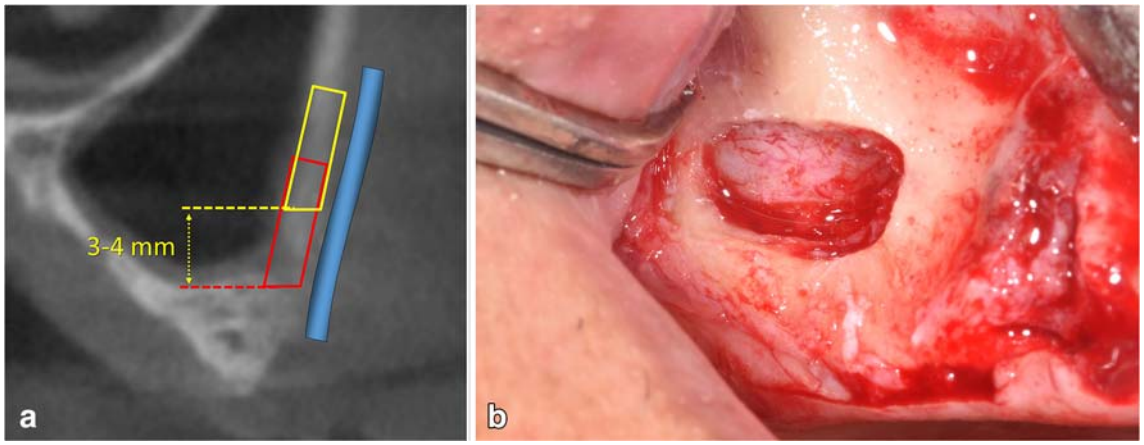

Fig. 1 **a** Schematic drawings showing the different antrostomies location: Standard (in yellow) and Base (in red). **b** Clinical view of the antrostomy

were prescribed as well as mouth rinses with 0.12% chlorhexidine, three times a day for 10 days. Six months after, a crestal incision was performed in the position of a definitive implant. A recipient site was prepared and a mini-implant, 2.4 mm of diameter and 8 mm of length (Sweden & Martina, Due Carrare, Padua, Italy), with a moderately rough surface (ZirTi, Sweden & Martina, Due Carrare, Padua, Italy) [25, 26] was installed in a submerged fashion. After 3 months of healing, the mini-implant was retrieved with a custom-made trephine (GA33M, Bontempi Strumenti Chirurgici, San Giovanni in Marignano, RN, Italy), 3.5 mm and 4 mm of internal and external diameter, respectively. A definitive implant was subsequently installed in the same position.

Histological preparation of the biopsies

The biopsies were kept within the trephines, fixed in 10% buffered formalin and then dehydrated in an ascending series of alcohol. Subsequently, the biopsies were included in a glycol-methacrylate resin (Technovit® 7200 VLC; Kulzer, Wehrheim, Germany) and polymerized. The biopsies were sectioned according to the longitudinal axis of the mini-implant, obtaining specimens of about 150 μm of width that were ground to about 30 μm of width. The specimens were stained with acid fuchsine and toluidine blue.

Histomorphometric evaluation

The histomorphometric evaluation were performed twice by a well-trained author (KAAA), blinded about allocations of the mini-implants. Mean values of the two measurements were used. Measurements were performed after a calibration with another author (DB) and $K > 0.90$ was achieved. High definition photographs (objective × 10) of each histological slide were taken at the facilities of ARDEC Academy (Rimini, Italy) using an Eclipse Ci microscope (Nikon Corporation, Tokyo, Japan) connected to a digital video camera (Digital Sight DS-2Mv, Nikon Corporation, Tokyo, Japan). The microscope was equipped with a motorized stage (EK14 Nikon Corporation, Tokyo, Japan). All measurements were performed using the software NIS-Elements D 5.11 (Laboratory Imaging, Nikon Corporation, Tokyo, Japan). The analyses were performed at × 100 magnification from the most coronal to the most apical contact of the bone to the implant surface.

As linear measurements, the following tissues in contact to the implant surfaces were evaluated: new mineralized bone, old bone (pre-existing bone), marrow spaces, and residues of xenograft particles. The total mineralized bone was calculated as sum of new and old bone. Morphometric measurements were also performed around the implant up to 400 μm from the implant surface. A point counting procedure was [27] using a lattice with squares of 75 μm superposed over the histological photographs. The following tissues were evaluated: new mineralized bone, old bone, marrow spaces, residues of xenograft particles, and vessels.

Data analysis

Mean values and standard deviation (SD) as well as 25th, 50th (median), and 75th percentiles were calculated for each outcome variable.

The primary variable was new bone for both linear and morphometric evaluations. The other parameters were considered as secondary variables. A Mann-Whitney test was used to analyze differences between the base and the standard groups. The level of significance was set at α 0.05.

The hypothesis was that more newly formed bone was found at the standard compared to the base group.

Results

Twenty-four patients were included in the present study (Fig. 2). Two patients of the standard and one of the base

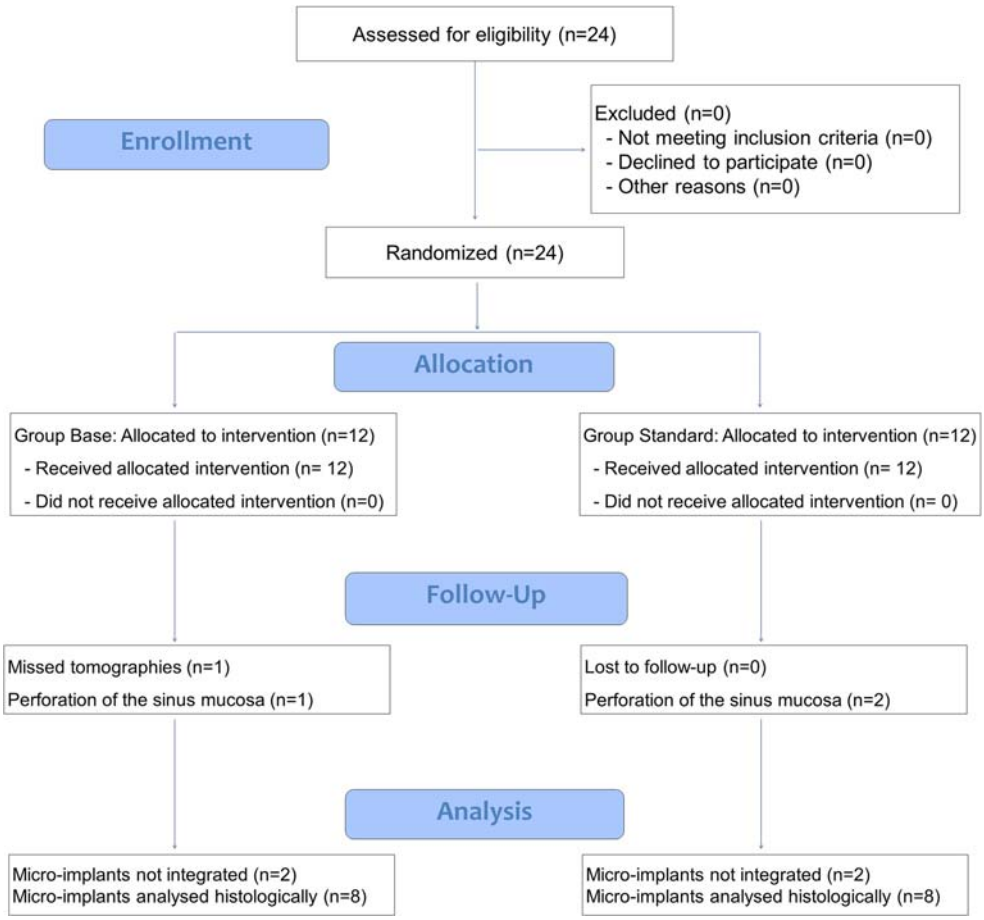

Fig. 2 CONSORT 2010 flow diagram

groups were excluded because of sinus mucosa perforations. Another patient of the base group was excluded for not having complied with the timetable of the CBCTs planning within the limits provided. At the time of biopsies retrieval, three mini-implants were not integrated, two from the base group and one from the standard group. One mini-implant of the standard group was found not integrated at the histological analyses so that a total of 16 mini-implants from 16 patients were analyzed, reaching an $n = 8$.

The biopsies were collected using the trephine in an eccentric mode as shown in Figs. 3a, b [28]. At the histological analysis, the mini-implants were surrounded by new mineralized bone and marrow spaces (Figs. 4a–c). In the coronal region, residues of old bone were found around the implant and, in some instances, also in contact with its surface Fig. 4d). Remnants of xenograft granules were observed, enclosed into new bone and marrow spaces (Figs. 4a–c). Some granules of the xenograft were in close contact with

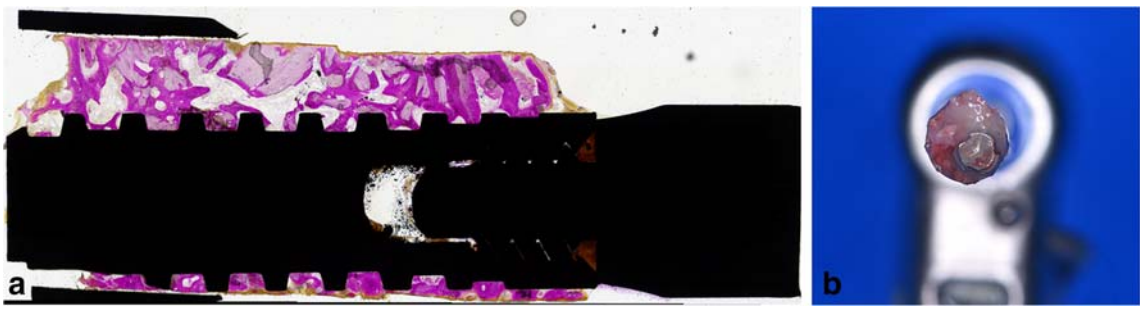

Fig. 3 **a** Ground section illustrating a biopsy still contained within the trephine. Note the excellent integration of the newly formed bone to the implant surface and the eccentric position of the microimplant in respect of the trephine. Image grabbed at × 100 magnification. Acid fuchsine and toluidine blue stain. **b** Clinical view of a biopsy. Note the eccentric position of the microimplant

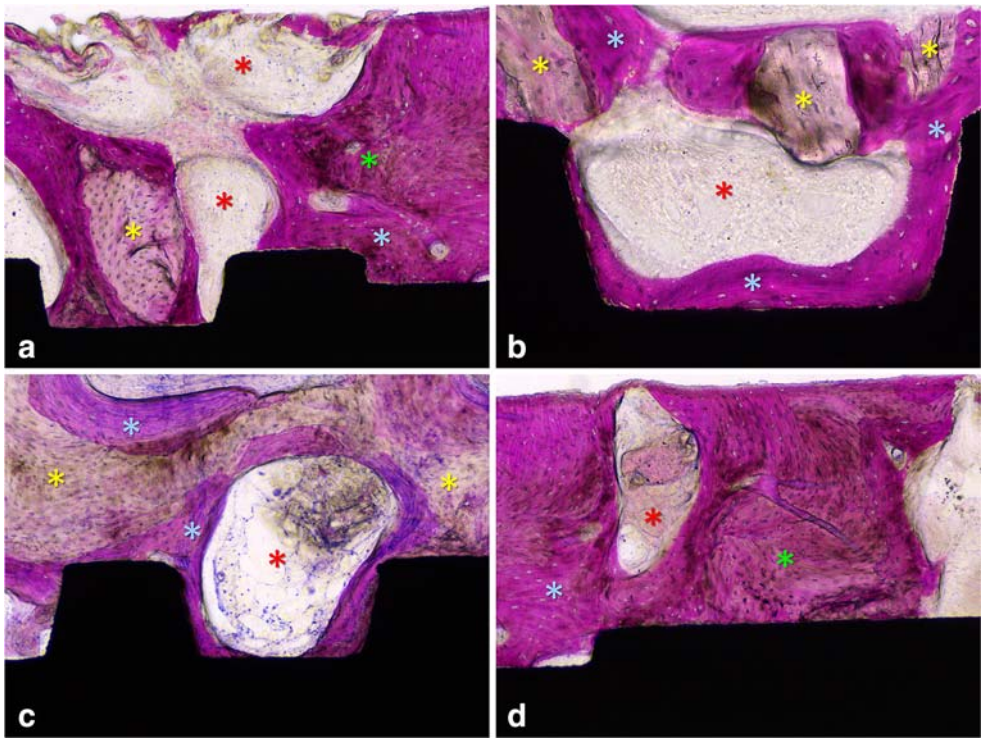

Fig. 4 Photomicrographs of ground sections illustrating the healing at the microimplants after 3 months from installation**. a**–**c** Newly formed bone and marrow spaces surround the implants and are in close contact with the implant surface (a). The xenograft was embedded into new bone and marrow spaces and in close vicinity to the implant surface (a). **d** Old pre-existing bone in contact with the implant surface, located in the coronal regions of the microimplants. Asterisks: light blue, newly formed bone; red, marrow spaces; yellow, xenograft; green, old pre-existing bone. Magnification a, c, d × 100; b × 200. Acid fuchsine and toluidine blue stain

the implant surface without the interposition of soft or mineralized tissues (Fig. 5a), while other granules appeared to be separated by newly formed bone (Fig. 5b).

At the histometric analysis (Table 1; Fig. 6), the new mineralized bone in contact with the implant surface reached fractions of 40.9 ± 11.9% and 48.5 ± 20.1% at the base and standard groups, respectively ($p = 0.208$). The marrow spaces were represented by 42.9 ± 13.2% in the base group, and 34.7 ± 17.1% in the standard group ($p = 0.172$). Pre-existing (old) bone was still present in contact with the implant surface in low percentages, being 4.0 ± 5.4% and 0.9 ± 1.2% ($p = 0.247$) in the base and standard groups, respectively.

Xenograft particles were found in contact with the implant surface at percentages of 12.1 ± 11.0% in the base group, and 15.9 ± 23.7% in the standard group ($p = 0.674$). No osteoclasts cells or inflammatory cells were seen around the xenograft particles.

At the morphometric analysis (Table 2; Fig. 7), new mineralized bone around the implants was found at percentages of 34.1 ± 8.7% and 39.4 ± 9.4% in the base and standard group, respectively ($p = 0.270$). Marrow spaces occupied area proportions of 45.5 ± 8.9% in the base group, and 47.9 ± 15.8% in the standard group ($p = 0.529$). Pre-existing bone was found in low percentages located in the coronal aspect, being 5.4 ±

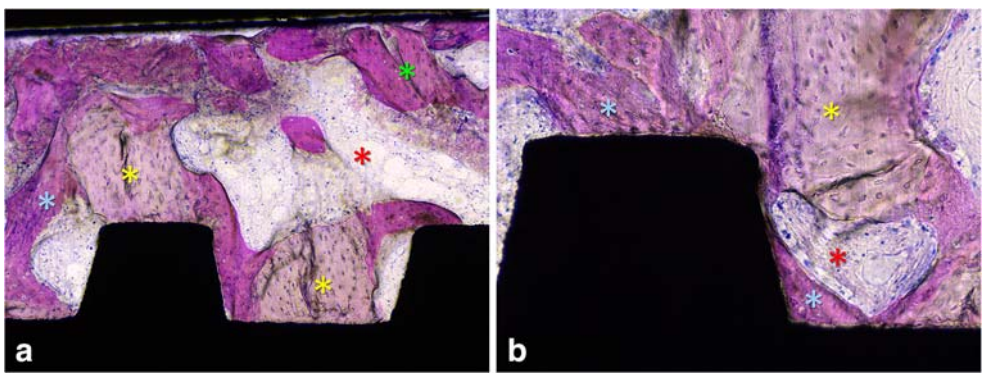

Fig. 5 Photomicrographs of ground sections illustrating the healing at the microimplants after 3 months from installation. **a** Xenograft particles in close contact with the implant surface. The contact resulted perhaps at the time of implant installation and no resorptive process occurred to separate the implant surface from the xenograft. **b** xenograft granule separated from the implant surface by newly formed bone. Asterisks: light blue, newly formed bone; red, marrow spaces; yellow, xenograft; green, old pre-existing bone. Magnification a × 100; b × 200. Acid fuchsine and toluidine blue stain

Table 1 Histometric measurements. Mean percentages ± standard deviations (SD), medians and 25th and 75th percentiles (25th; 75th) of tissues components on the implant surface; ($n = 8$)

		New mineralized bone	Pre-existing (old) bone	Total mineralized bone	Marrow spaces	Xenograft
Base	Mean ± SD	40.9 ± 11.9	4.0 ± 5.4	44.9 ± 14.0	42.9 ± 13.2	12.1 ± 11.0
	Median (25th; 75th)	40.1 (34.0; 43.3)	2.0 (0.0; 5.5)	43.0 (37.5; 51.7)	39.6 (36.4; 46.3)	6.2 (5.5; 20.2)
Standard	Mean ± SD	48.5 ± 20.1	0.9 ± 1.2	49.4 ± 19.7	34.7 ± 17.1	15.9 ± 23.7
	Median (25th; 75th)	51.1 (41.0; 60.5)	0.0 (0.0; 2.0)	53.6 (41.0; 60.5)	30.3 (24.1; 42.2)	6.3 (2.1; 16.8)
Mann-Whitney		0.208	0.247	0.431	0.172	0.674

None of the differences was statistically significant ($p < 0.05$)

5.6% in the base group, and 1.9 ± 2.9% in the standard group ($p = 0.145$). The xenograft was found in fractions of 12.1 ± 8.2% in the base group, and 8.3 ± 6.8% in the standard group ($p = 0.294$). The percentages of vessel were 3.0 ± 2.1% and 2.5 ± 1.8% in the base and standard groups, respectively ($p = 0.598$).

Discussion

The mini-implants analyzed in the present study presented a good integration into the newly formed bone in both groups. A trend of greater bone-to-implant contact and bone density was found at the mini-implants of the standard compared to the base group. However, the difference did not reach a statistical difference for both bone-to-implant contact ($p = 0.208$) and bone density ($p = 0.623$). The difference in bone formation and osseointegration might be ascribed to the fact that in the standard group, the antrostomy was placed 3–4 mm above the floor of the sinus so that part of the lateral bone wall was left as protection of the sinus floor region. Instead, in the base group, a very little portion of the lateral bone wall was left at the sinus floor. The sinus bone walls are the main source for new bone formation, as shown in several experimental studies

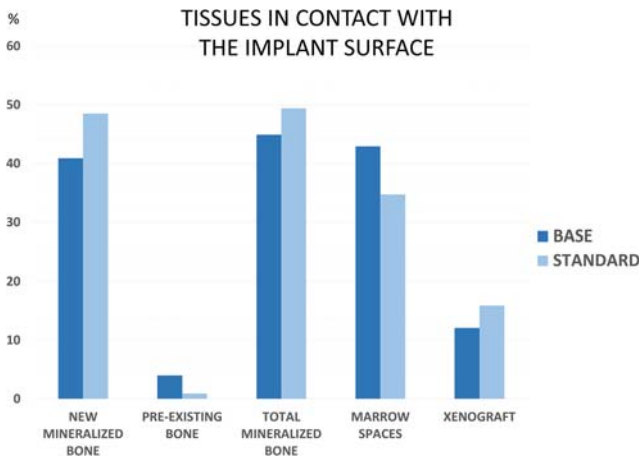

Fig. 6 Graph reporting the percentages of tissues in contact with the implant surface

[7, 11–15, 22–24]. This, in turn, means that the preservation of part of the lateral bone wall in the standard group might have contributed to the formation of higher amounts of new bone in the most important zone of the augmented regions into which the mini-implant was installed.

The amounts of osseointegration observed in the present study (40.9% in the base group, 48.5% in the standard group) were similar to those reported in other articles.

In a clinical study [29], deproteinized bovine bone matrix (DBBM) alone, autogenous bone alone, or 80% of autogenous bone mixed to 20% of DBBM were used as filler material for sinus floor elevation. After 6–9 months of healing, 25 mini-implants with a machined surface were installed in the lateral wall of the sinus into the grafted region. After further 6 months, the mini-implants were retrieved and analyzed. Bone-to-implant contact was 34.6%, 54.3%, and 31.6% for autogenous, mixed, and DBBM groups, respectively. However, no statistically significant differences were found among groups. Bone densities around the mini-implants ranged between 38 and 42%.

Other studies evaluated osseointegration at mini-implants installed simultaneously to the sinus floor elevation.

In a clinical study [30], sinus floor elevation was performed in 13 patients using either a biphasic calcium phosphate (BCP), composed of 70% of hydroxyapatite coated with 30% of beta-tricalcium phosphate, or a DBBM. In each patient, four mini-implants (2 × 10 mm) with a sand-blasted acid etched (SLA) surface were installed simultaneously, and biopsies were retrieved after 6–8 months of healing. Bone-to-implant contact was 38.4% at mini-implants installed in the synthetic graft group, and 34.6% in the DBBM graft group.

Similarly, in another clinical study [31], sinus floor elevation was performed bilaterally in 11 patients, using either a BCP, composed of 60% of hydroxyapatite and 40% of tricalcium phosphate, or a DBBM. Mini-implants with an SLA surface were placed simultaneously through the alveolar crest. After 8 months of healing, the mini-implants were retrieved and analyzed histologically. An osseointegration of 64.6% for the BCP group, and 55.0% for the DBB group was found. The corresponding bone density was 41.1% and 41.6%, respectively.

Table 2 Morphometric measurements. Mean percentages ± standard deviations (SD), medians and 25th and 75th percentiles (25th; 75th) of tissues components around the implant surface; ($n = 8$)

		New mineralized bone	Pre-existing (old) bone	Total mineralized bone	Marrow spaces	Xenograft	Vessels
Base	Mean ± SD	34.1 ± 8.7	5.4 ± 5.6	39.5 ± 11.1	45.5 ± 8.9	12.1 ± 8.2	3.0 ± 2.1
	Median (25th; 75th)	34.1 (27.1; 40.2)	4.1 (1.6; 7.9)	40.9 (31.3; 48.4)	45.7 (39.8; 48.7)	9.9 (6.5; 13.7)	2.8 (1.3; 3.6)
Standard	Mean ± SD	39.4 ± 9.4	1.9 ± 2.9	41.3 ± 10.2	47.9 ± 15.8	8.3 ± 6.8	2.5 ± 1.8
	Median (25th; 75th)	39.2 (36.4; 43.8)	0.6 (0.0; 2.6)	39.8 (36.4; 50.8)	54.8 (34.1; 56.6)	5.7 (4.6; 12.8)	1.8 (1.1; 3.3)
Mann-Whitney		0.270	0.145	0.674	0.529	0.294	0.598

None of the differences was statistically significant ($p < 0.05$)

In case of simultaneous implant installation after sinus floor elevation, the characteristics of the implant surface play an important role. When an implant is installed in a standard edentulous alveolar crest, the entire surface of the implant is in primary contact with mineralized bone tissue and bone marrow. The bone formation will start from multiple regions around the implant body [32]. This is the ideal condition that an implant should find when is installed into a grafted sinus after a period of healing [29]. However, when the implants are installed simultaneously to a sinus floor elevation, they protrude within the elevated space, surrounded by biomaterial and clot. New bone will be formed from the bone walls and the base of the sinus. However, the osseointegration will proceed slowly from the floor of the sinus towards the coronal regions of the implants [7]. Experimental studies in dogs have shown that a moderately rough surface of implants installed in sites presenting self-contained marginal defects provided the conditions for optimal osseointegration [33, 34]. However, when turned surfaces were used in a similar model, residual defects were found interposed between the implant surface and the newly formed bone so that a compromised healing was achieved [35, 36].

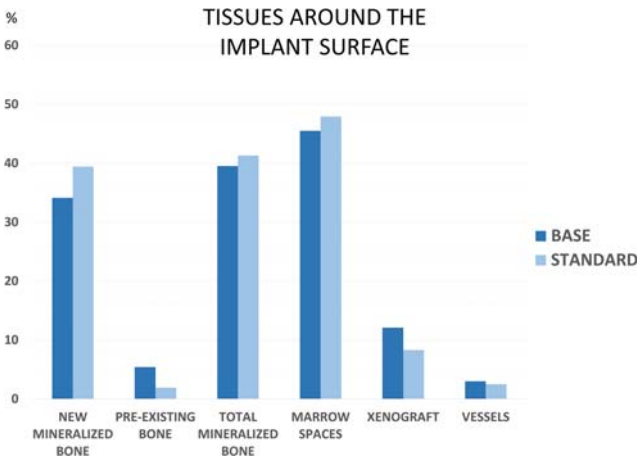

Fig. 7 Graph reporting the percentages of tissues around the implant surface, measured in a region up to 400 μm from the microimplant surface

These outcomes might explain the results reported in a clinical study [37] in which sinus floor elevation was performed in nine patients. Either radiated mineralized cancellous allograft or autogenous bone were used as filler materials. Mini-implants with a turned surface were installed simultaneously through the lateral wall of the sinus, protruding into the grafted regions and retrieved after 6 or 12–14 months. The osseointegration of the portion of the implant protruding within the grafted sinus was 2% and 10% at the allograft and autograft sites, respectively. It should be noted that the osseointegration found at the autologous sites did not benefit from the presence of a high proportion of mineralized bone around the implant (37%).

In the present study, in the region of the bone crest, the pre-existing bone was mostly substituted by new bone in contact with the implant surface. Also in this region, a trend of lower amounts of pre-existing bone was found in the standard compared to the base group, deposing for a higher remodeling trend at the standard compared to the base group. The presence of pre-existing bone in contact with and in close vicinity to the implant surface after few months of healing has been already described in previous animal [38–45] and human studies. [46–50] The timing of the substitution of old with new bone have been discussed in another report [51] that showed that the speed of osseointegration formation is higher in animals compared humans and depends on bone quality.

In a previous report, it was shown that, after 9 months from sinus floor elevation performed with a collagenated cortico-cancellous porcine bone, the grafted region contained ~ 40% of mineralized bone and ~ 15% of residues of xenograft [52]. In the present study, ~ 12–16% of residual xenograft was found in contact with the implant surface installed after 6 months from sinus floor elevation and retrieved after further 3 months of healing. This, in turn, means that the mini-implants intercepted the xenograft particles at the installation, resulting in close contact with the biomaterial. Moreover, in these regions of contact, no integration of newly formed bone

was found interposed between the graft and the implant surface after further 3 months of healing, as instead occurred to the pre-existing bone in the cortical region. This, in turn, means that 12–16% of the implant surface was not integrated into newly formed bone but it was only in contact with the biomaterial. No osteoclast cells were seen on the surface of the xenograft, meaning that no resorptive processes were still in progress.

In the present study, the trephine was used eccentrically to allow to reduce the dimensions of the residual defect, being 4 mm in diameter and 8 mm of depth, but still maintaining a dimension of the biopsies sufficient for histological examination [28].

The main limitation of this study was the low number of the sample, complicated by the loss of for patients for different reasons, and the loss of mini-implants. Further studies with a higher number of participants should be performed that may support with statistically significant differences the trend showed in the present study.

In conclusion, based on the present study, the choice of one or the other position of antrostomy did not influence significantly the outcome and, therefore, should be left to the preference of the surgeon.

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Authors' contributions Atsuya Hirota participated to the concept/design, data analysis/interpretation, drafting article, approval of the article

Giovanna Iezzi participated to histological preparation and evaluation, critical revision of article, approval of the article

Adriano Piattelli participated to the concept/design, drafting article, approval of the article.

Mauro Ferri participated to clinical procedures, clinical management, critical revision of article, approval of the article

Kazushige Tanaka participated to the concept/design, drafting article, approval of the article

Karol Alí Apaza Alccayhuaman participated to the histological measurements, data analysis/interpretation, drafting article, approval of the article

Daniele Botticelli participated to concept/design, clinical procedures, data analysis/interpretation, drafting article, approval of the article

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study adhered to the Declaration of Helsinki on medical protocols and ethics. The protocol was approved by the Ethical Committee of the University Corporation Rafael Núñez, Cartagena de Indias, Colombia (protocol #01-2015; 19 May 2015).

Informed consent Informed consent was obtained from all participants.

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