

**Radiographic outcomes of transcrestal and lateral sinus floor elevation: one-year results of a bi-center, parallel-arm randomized trial**

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# Radiographic outcomes of transcrestal and lateral sinus floor elevation: one-year results of a bi-center, parallel-arm randomized trial

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For *Clinical Oral Implants Research***ABSTRACT**

**Objectives:** to comparatively evaluate the radiographic outcomes of transcrestal and lateral sinus floor elevation (tSFE and ISFE, respectively) when applied concomitantly with implant placement.

**Materials and Methods:** Patients with at least 1 edentulous site with residual bone height of 3-6 mm were enrolled in a bi-center, parallel-arm, randomized trial. Both tSFE and ISFE were associated with a bovine-derived xenograft, and implants were inserted concomitantly. In ISFE group, the antrostomy was covered with a resorbable collagen membrane. Marginal bone loss and the maturation of the grafted area were evaluated on periapical radiographs at 6 and 12 months. Twelve-month CT/CBCT was used to assess the effect of grafting procedures circumferentially around the implant. A *per-protocol* analysis analysis was performed.

**Results:** The *per-protocol* study population consisted of 26 patients in the tSFE group and 28 patients in the ISFE group. At 12 months, the median proportion of the implant surface in contact with the peri-implant radiopaque area was 100% in both groups, with no significant inter-group difference. Sub-optimal bone-to-implant contact was observed in 13% and 3.6% of tSFE and ISFE cases, respectively. In both groups, marginal bone loss was minimal ( $\leq 1$  mm) and infrequent, and the radiographic aspect was suggestive of an advanced stage of maturation.

**Conclusions:** At sites with residual bone height of 3-6 mm, tSFE and ISFE can similarly result in a substantial increase in peri-implant bone support at 12 months.

(ClinicalTrials.gov ID: NCT02415946)

## INTRODUCTION

At maxillary posterior sites where post-extraction pneumatization of the maxillary sinus has contributed the dimensional reduction of the residual bone crest following tooth loss (Eufinger et al. 1997, 1999, Farina et al. 2011, Pramstraller et al. 2011), maxillary sinus floor elevation with a lateral (ISFE) or transcrestal (tSFE) approach represent two options to enhance the available bone and restore the local conditions compatible with the placement and long-term survival of dental implants (Pjetursson et al. 2008, Tan et al. 2008, Listl & Faggion 2010, Tetsch et al. 2010, Esposito et al. 2014).

Indications to apply tSFE or ISFE should be determined primarily on the basis of their potential to enhance the peri-implant bony support. Due to the possibility to visualize directly the sinus cavity through the lateral antrostomy and extend the elevation of the sinus membrane according to individual needs and local anatomy, ISFE has several technical premises for achieving substantial augmentation. Confirmatory data come from studies reporting a mean vertical extent of sinus lift varying from about 8 mm to more than 14 mm when ISFE was obtained with a bovine-derived xenograft (Felice et al. 2009, Chackartchi et al. 2011, Merli et al. 2013). On the other hand, tSFE has limitations related to its closed approach to the sinus, including the difficulty in determining the extent of sinus lift achievable in relation to the presumed tensile resistance of the sinus membrane. Consistently, several clinical trials reported a vertical extent of sinus lift lower than that reported for ISFE, with mean values ranging between 1.7 mm (Pjetursson et al. 2009) and more than 8 mm (Kfir et al. 2007, Sisti et al. 2012).

To date, studies that comparatively evaluated tSFE and ISFE either lack of a randomized design or refer to different surgical conditions between treatments (Zitzmann & Schärer 1998, Rodoni et al. 2005, Krenmair et al. 2007, Jurisic et al. 2008, Cannizzaro et al. 2009, Tetsch et al. 2010, Kim et al. 2011, Al-Almaie et al. 2013, Yu et al. 2017, Temmerman et al. 2017). Most of them included a radiographic assessment based on bi-dimensional radiographic exams such as ortopantomography and/or periapical radiographs (Rodoni et al. 2005, Krenmair et al. 2007, Jurisic et al. 2008, Cannizzaro et al. 2009, Tetsch et al. 2010, Kim et al. 2011, Al-

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Almaie et al. 2013, Yu et al. 2017), with the impossibility to evaluate the extent of peri-implant bone augmentation circumferentially around the implant. Tridimensional radiographic exams such as conventional or cone-beam computed tomography (CT or CBCT, respectively) were used in a limited number of studies, only in a subsample of consenting patients (Zitzmann & Schärer 1998) or at very short post-surgery intervals (Temmerman et al. 2017).

Recently, we performed a bi-center, parallel-arm, randomized trial comparatively evaluating tSFE and ISFE when applied concomitantly with implant placement at sites with limited (3-6 mm) residual bone. The results of the study have been partly published, and allowed for the identification of differences in the morbidity following the two interventions (Farina et al. 2018). Based on bi- and tri-dimensional radiographic assessments conducted by Farina et al. (2018), the purpose of the present study is to comparatively evaluate the extent of bone augmentation (with particular emphasis to the contribution of each intervention to the peri-implant bony support) obtained at 1 year following either tSFE or ISFE and concomitant implant placement.

## **MATERIALS AND METHODS**

### **Experimental design**

The study is a bi-center, parallel-arm, single-blind, randomized controlled clinical trial, and is part of a larger project which comparatively evaluated tSFE and ISFE under several perspectives. Information on ethical approval and trial registration, the methodological aspects of the study and the surgical aspects of the procedures have been reported in a recent publication on the morbidity of tSFE and ISFE (Farina et al. 2018). The present study reports only methodological aspects and data functional to evaluate the radiographic outcomes of the two investigated interventions.

### **Study population**

Patients were recruited at two University-Hospitals (Ferrara and Modena, Italy) according to selection criteria reported by Farina et al. (2018). Briefly, each patient contributed the study with one maxillary quadrant

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(identified as “experimental”) with  $\geq 1$  maxillary posterior site edentulous for at least 6 months and showing a residual bone height (RBH) of 3–6 mm. RBH was measured on CT or CBCT performed while wearing a radiological stent with 4-mm thick radiopaque indicators.

### **Surgical and post-surgical procedures**

The surgical aspects of tSFE and ISFE and the post-surgical procedures are described briefly in the following paragraphs. Additional details have been reported in a previous publication (Farina et al. 2018).

tSFE was performed according to the *Smart Lift* technique (Trombelli et al. 2008, 2010a,b). After placing a plug of collagen matrix (Mucograft Seal®; Geistlich Pharma, AG, Wolhusen, Switzerland), the trephined bone core was condensed and malleted with a calibrated osteotome (*Smart Lift Elevator*) to fracture the sinus floor. Membrane perforation was assessed by the Valsalva maneuver. If no perforation was detected, a pre-determined amount of deproteinized bovine bone mineral (DBBM; Bio-Oss® spongiosa granules, particle size 0.25-1.0 mm; Geistlich Pharma, AG, Wolhusen, Switzerland), which was related to the programmed extent of implant penetration into the sinus (Supplemental Table 1), was pushed through each implant site by gradual increments with the *Smart Lift Elevator*. When membrane perforation was detected, it was treated with repeated insertions of plugs trimmed from a collagen matrix (Mucograft Seal®; Geistlich Pharma AG, Wolhusen, Switzerland) in the apical portion of the crestal access. The Valsalva maneuver was then re-assessed: if negative, the grafting procedure was completed and the implant was inserted; if positive, the patient exited the study, and tSFE and concomitant implant placement were postponed at 4 months following first surgery.

In patients assigned to ISFE, lateral access to the maxillary sinus was obtained with rotating and/or manual instruments. The grafting procedure was performed with DBBM (Bio-Oss® spongiosa granules, particle size 0.25-1.0 mm or 1-2 mm; Geistlich Pharma, AG, Wolhusen, Switzerland) immediately after the elevation of the sinus membrane with manual instruments (Hu-Friedy, Chicago, US). The particle size and amount of graft

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1  
2 material were left at operator discretion. Implant bed preparation was, then, performed according to the  
3  
4 sequence of burs recommended by the implant manufacturer (Thommen Medical AG; Grenchen, Switzerland).  
5  
6 The window in the lateral wall was covered with a resorbable collagen membrane (Bio-Gide; Geistlich Pharma,  
7  
8 AG, Wolhusen, Switzerland). When membrane perforation (as visually detected) occurred, it was treated  
9  
10 according to Fugazzotto & Vlassis (2003), and the grafting procedure was completed.  
11  
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15  
16 In both tSFE and ISFE groups, implants (SPI Inicell Element<sup>®</sup>; Thommen Medical AG, Grenchen, Switzerland)  
17  
18 were inserted immediately after the completion of the grafting procedure with the 1.0 mm polished collar above  
19  
20 the bone crest. The healing protocol (submerged or transmucosal) was left at the operator's discretion.  
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26 Implants placed with a submerged healing protocol at day 0 were surgically exposed at 20 weeks post-  
27  
28 surgery, and a healing abutment was positioned. Implants were loaded with a provisional or definitive  
29  
30 restoration (according to their treatment plan) between week +24 and week +32. The patient exited the study  
31  
32 at week +48.  
33  
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35

### 36 **Radiographic exams and measurements**

37  
38 At the time of implant loading with a provisional or definitive restoration (performed between week +24 and  
39  
40 week +32) and at week +48  $\pm$  4 weeks (identified as 6- and 12-month follow-up visits, respectively), peri-apical  
41  
42 radiographs were obtained with a paralleling technique using a Rinn film holder with a rigid film-object X-ray  
43  
44 source, and were then scanned, digitized, and stored at a resolution of 600 dpi. Also, a CT or a CBCT of the  
45  
46 implant areas was performed at 12-month visit, and data were saved in Digital Imaging and Communications  
47  
48 in Medicine (DICOM) file format.  
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55 Measurements on digitized periapical radiographs were performed using an image-processing software (NIS  
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57 Elements<sup>®</sup> v4.2; Nikon Instruments, Campi Bisenzio, Firenze, Italy), while a software for implant planning was  
58  
59 used for measurements on CT and CBCT scans (Nobel clinician<sup>®</sup> v2.6.3.2; Nobel Biocare Services AG,  
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1  
2 Kloten, Switzerland). All radiographic measurements were performed by a single trained examiner (G.F.) who  
3  
4 had previously undergone a calibration session for linear measurements on periapical radiographs on a  
5  
6 sample of 15 patients not included in the study (Cohen's k-coefficient for intra-examiner agreement: 0.981)  
7  
8 and had participated as clinical examiner in previous clinical trials on sinus lift procedures (Trombelli et al.  
9  
10 2008, 2010a,b, 2012, 2014, 2015, Franceschetti et al. 2014, 2015, 2017, Farina et al. 2018). The examiner  
11  
12 was kept blinded as to treatment group and observation interval.  
13  
14  
15  
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17 On digitized periapical radiographs taken at 6- and 12-month visit, the following measurements were  
18  
19 performed using a digital caliper:  
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21

- 22 ▶ radiographic implant length (rIL): distance (in mm) from the apical margin of the implant shoulder to the  
23  
24 implant apex as assessed at the mesial or distal aspect of the implant;  
25  
26
- 27 ▶ peri-implant bone level at the mesial (mPBL) and distal (dPBL) aspects of the implant: distance (in mm) from  
28  
29 the apical margin of the implant shoulder to the first bone-to-implant contact at the mesial and distal aspect of  
30  
31 the implant, respectively. To account for radiographic distortion, mPBL and dPBL were adjusted for a  
32  
33 coefficient derived from the ratio: true length of the implant / radiographic implant length (rIL);  
34  
35
- 36 ▶ maturation of the grafted space: assessed using the sinus grafting remodeling index (SGRI) (Brägger et al.  
37  
38 2004).  
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46 On CT and CBCT scans performed at 12-month visit, the following parameters were assessed:

- 47 ▶ percentage ratio between the linear length (in mm) of the implant surface in direct contact with the peri-  
48  
49 implant radiopaque area (native bone + newly formed bone) and the linear length (in mm) of implant surface  
50  
51 (CON%). CON% measurements were performed on each of 180 CT/CBCT sections (with a 1° difference in  
52  
53 angle between adjacent sections) parallel to the long axis of the implant and passing through the mid portion  
54  
55 of the implant. CON% measurements from the 180 CT/CBCT sections were averaged (totCON%). Also,  
56  
57 CON% were reported separately for the mesial, distal and apical aspect of the implant as assessed on the  
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1 CT/CBCT mesio-distal section (mCON%, dCON%, and aCON%<sub>m-d</sub>, respectively) and for the buccal, palatal  
2 and apical aspect of the implant as assessed on bucco-lingual CT/CBCT section (bCON%, pCON%, and  
3 aCON%<sub>b-p</sub>, respectively);

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8  
9 ▶ height of the radiopaque area apical to the implant apex (aGH): distance (in mm) occupied by a radiopaque  
10 area between the implant apex and the most apical position of the radiopaque area as assessed at the mid  
11 portion of the implant on the CT/CBCT section passing through the mid portion of the implant apex.  
12  
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## 16 17 18 19 **STATISTICAL ANALYSIS**

### 20 21 **Sample size calculation**

22  
23 totCON% was the primary outcome variable of the study. Since no data on totCON% related to the  
24 investigated interventions could be derived from previous comparative studies, sample size calculation was  
25 based on aGH. Assuming a standard deviation in sinus lift of 2.0 mm for both tSFE, as derived from an internal  
26 analysis of data from the studies by Trombelli et al. (2012, 2014) and Franceschetti et al. (2014), and ISFE  
27 (Chackartchi et al. 2011, Merli et al. 2013), and an expected inter-group difference in sinus lift of 3.0 mm  
28 (Zitzmann & Schärer 1998), a *per protocol* study population of at least 48 patients (24 treated with tSFE, 24  
29 treated with ISFE) was needed for a two-tailed test to detect an inter-group difference in aGH with a power  
30 higher than 95% and a p-level of 0.05.  
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### 46 47 **Descriptive and inferential statistics**

48 A *per-protocol* (PP) analysis was performed. The patient was regarded as the statistical unit. Therefore, for  
49 patients receiving two implants concomitantly with sinus floor elevation in the experimental quadrant, only the  
50 implant showing the lowest totCON% was included for analysis. If multiple implants within the experimental  
51 quadrant had the same totCON%, only the implant with the lowest aGH was included for analysis. Since all  
52 numerical variables showed a non-normal and non-symmetric distribution, they were expressed as median  
53 and interquartile range (IR). Within-group comparisons for mPBL, dPBL and SGRI were performed between 6-  
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1  
2 and 12-month visits using Wilcoxon test. Treatment groups were compared using  $\chi^2$  test or Fisher's exact test  
3  
4 for categorical variables and Mann-Whitney U-test for numerical and ordinal variables. The level of statistical  
5  
6 significance was fixed at 0.05, and the analysis was done using Stata 13 for Windows (StataCorp, College  
7  
8 Station, TX).  
9

## 10 11 12 13 **RESULTS**

### 14 15 **Study population**

16  
17 Twenty-nine patients and 28 patients were randomly allocated to tSFE and ISFE group, respectively (Figure  
18  
19 1). In tSFE group, 1 implant was immediately removed after placement due to the lack of primary stability,  
20  
21 while 1 implant in another patient failed to osseointegrate and was removed at 2 months after insertion. Both  
22  
23 patients were excluded from the present analysis, and received an implant of same dimensions 6 months later  
24  
25 without additional bone augmentation. Another patient in tSFE group suffered acute myocardial infarction after  
26  
27 the 6-month visit, postponed all the 12-month radiographic exams and was therefore excluded from the study.  
28  
29 The PP study population consisted of 26 patients in the tSFE group and 28 patients in the ISFE group (Figure  
30  
31 1). Patient and implant characteristics in tSFE and ISFE groups are reported in Table 1.  
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### 40 41 **Radiographic outcomes**

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43 In tSFE group, DICOM files of three 12-month CT/CBCT exams could not be analyzed due to technical issues.  
44  
45 Therefore, totCON% and aGH measurements in tSFE group were performed on 23 patients. Radiographic  
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47 outcomes are reported in Table 2 and Figures 2-5. Each patient is consistently identified with the same  
48  
49 numeric code through Figures 2-5.  
50  
51

52  
53 No center effect on totCON% and aGH was found. Data on CON% are reported in Table 2 and Figure 2.  
54  
55 totCON% was 100% in both groups, with no significant inter-group difference ( $p= 0.580$ ) (Table 2). Three  
56  
57 patients (13.0%) in the tSFE group showed totCON% lower than 100%, with totCON% values ranging  
58  
59 between 71.1% and 86.3%. In tSFE group, toCON% lower than 100% was mainly due to the absence of a  
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1  
2 peri-implant radiopaque area in the apical part of the implant (i.e.,  $aCON\%_{b-p}$  and  $aCON\%_{m-d} = 0$ ) (Figure 2).

3  
4 One patient (3.6%) in ISFE group showed  $totCON\%$  lower than 100% ( $totCON\% = 77.6\%$ ) due to the partial  
5  
6 absence of a peri-implant radiopaque area at the palatal aspect (i.e.,  $pCON\% = 60\%$ ) (Figure 2).  
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11 aGH was significantly higher in ISFE group (6.2 mm; IR: 3.3 – 8.3) compared to tSFE group (0.6 mm; IR: 0.5 –  
12  
13 1.6) ( $p < 0.0001$ ). aGH was positive in 20 patients (87.0%) and 27 patients (96.4%) in tSFE and ISFE groups,  
14  
15 respectively, and was 0 in the other patients (Figure 3).  
16  
17

18  
19  
20 At 6 months, mPBL and dPBL were 0 mm (IR: 0 - 0) in both groups ( $p = 0.637$  and  $p = 0.790$ , respectively). Two  
21  
22 patients (7.7%) in the tSFE group and 1 patient (3.6%) in the ISFE group showed mPBL and/or dPBL > 0 mm.  
23  
24 At 12 months, mPBL and dPBL were 0 mm (IR: 0 – 0) in both groups ( $p = 0.600$  and  $p = 0.553$ , respectively).  
25  
26 Four (15.4%) patients in the tSFE group and 5 (17.9%) patients in the ISFE group showed mPBL and/or  
27  
28 dPBL > 0 mm (Figure 4). No significant changes in mPBL and dPBL were observed between the 6-month and  
29  
30 12-month visit.  
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36 SGRI values as observed at 6 and 12 months in each patient are reported in Figure 5. At 6 months, SGRI was  
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38 significantly higher in ISFE group (3.0; IR: 2.0 - 3.0) compared to tSFE group (2.0; IR: 2.0 – 3.0) ( $p = 0.006$ ).  
39  
40 The score was 3 at 20 sites, and 2 at 8 sites in ISFE group, whereas 3 at 9 sites, 2 at 11 sites, 1 at 4 sites, and  
41  
42 0 at 2 sites in the tSFE group. At 12 months, SGRI was significantly higher in ISFE group (3.0; IR: 3.0 - 3.0)  
43  
44 compared to tSFE group (3.0; IR: 2.0 – 3.0) ( $p = 0.026$ ). The score was 3 at 24 sites, and 2 at 4 sites in ISFE  
45  
46 group, whereas 3 at 14 sites, 2 at 6 sites, 1 at 4 sites, and 0 at 2 sites in the tSFE group. The variation in SGRI  
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48 as observed between 6 and 12-month visit was significant only in tSFE group ( $p = 0.043$ ).  
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54 Radiographic outcomes as recorded separately in tSFE and ISFE cases with and without membrane  
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56 perforation are reported in Supplemental Table 2.  
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**DISCUSSION**

In the present study, implants with a median length of 9.5 mm were placed at sites with a residual bone height of 3-6 mm. Therefore, at placement, implants were supported by native bone for 31.6% to 63.2% of their length, on average, in both treatment groups. At 1 year after surgery, median totCON% was 100% in both groups, thus indicating that both tSFE (when performed according to the *Smart Lift* technique) and ISFE can similarly contribute to increase substantially the peri-implant bone support at sites where the severity of bone atrophy would have otherwise prevented the implant-supported rehabilitation. Suboptimal implant coverage (i.e., totCON% < 100%) was found with a low prevalence in both groups, and was mainly due to the absence of a peri-implant radiopaque area in the apical (tSFE group) or palatal (ISFE group) aspect of the implant. Some surgical aspects of the two investigated approaches may explain, at least in part, this difference. When implant placement is performed concomitantly with a tSFE procedure, implant insertion unavoidably results in a compressive/displacing effect exerted by the implant apex on the graft material that has been placed into the sinus. Differently, when performing a sinus floor elevation with a lateral approach, the medial portion of the sinus membrane may occasionally be elevated to an insufficient extent to place an adequate amount of graft material to ensure complete coverage of the palatal implant aspect.

In the present material, aGH was significantly higher in ISFE group than in tSFE group (6.5 mm vs 0.9 mm, respectively). This finding is consistent with previous studies indicating that substantially greater volumes of grafted space can be obtained with ISFE (2.84 cm<sup>3</sup>) compared to tSFE (0.63 cm<sup>3</sup>) (Temmerman et al. 2017), and can be explained, at least in part, by the greater average amount of DBBM that was positioned during the two interventions (ISFE: 1975 mg; tSFE: 420 mg) (Farina et al. 2018). When considering that there is substantial agreement on the fact that the space augmented with a sinus floor elevation procedure undergoes progressive reduction over time (Bragger et al. 2004, Pjetursson et al. 2009, Jung et al. 2010, Mardinger et al. 2011, Abdulkarim et al. 2013, Nishida et al. 2013, Mazzocco et al. 2014, Umanjec-Korac et al. 2014, Marković et al. 2016, Tallarico et al. 2017, Temmerman et al. 2017), it is reasonable to hypothesize that the presence of a wide radiopaque area extending beyond the implant surface for several mm may preserve the newly formed

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1  
2 peri-implant bone support from further remodeling on the long-term. A recent study reported that the  
3  
4 percentage reduction of the grafted volume from 1 to 6 weeks post-surgery did not significantly differ between  
5  
6 sites where substantially different grafted volumes (2.84 cm<sup>3</sup> and 0.63 cm<sup>3</sup>) had been obtained at 1 week  
7  
8 (Temmerman et al. 2017), thus supporting the hypothesis that greater amount of grafted space beyond the  
9  
10 implant surface may provide better conditions for the persistence of positive aGH on the long-term. It must be  
11  
12 considered, however, that in tSFE group (where low amounts of graft materials were used compared to ISFE)  
13  
14 aGH was positive in 87.0% at 12 months post-surgery, thus questioning the need to overfill the sinus cavity  
15  
16 with large amounts of graft material beyond those used here for tSFE. Long-term follow-up of the treated  
17  
18 cases will allow for clarifying further the relevance of aGH for implant prognosis following sinus floor elevation.  
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25 At both 6- and 12-month visits, median values of SGRI (Bragger et al. 2004) were significantly higher in ISFE  
26  
27 group than tSFE group. In particular, all ISFE cases showed a score 3 or 2 (suggestive of an advanced stage  
28  
29 of maturation), while some patients in the tSFE group showed a SGRI of 0 or 1, persisting even at 12 months  
30  
31 post-surgery. While the presence of some cases with low SGRI scores at 6 months is consistent with previous  
32  
33 studies on the same tSFE technique associated with DBBM (Trombelli et al. 2012, 2014), no data on SGRI  
34  
35 from previous studies are currently available for ISFE. Therefore, inter-group differences in the level of  
36  
37 maturation of the grafted area remain unexplained. Our data, however, showed that tSFE cases showed a  
38  
39 significant maturation from 6 months to 12 months, thus suggesting that time tends to mitigate these  
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41 differences between tSFE and ISFE.  
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48 In both treatment groups, implants were placed with the polished collar above the bone crest. At both 6- and  
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50 12-month observations intervals, median values of mPBL and dPBL were 0 mm in both groups. Our findings  
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52 confirm the results of previous studies reporting minimal to none peri-implant marginal bone loss in the first  
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54 months following sinus lift and concomitant implant placement, irrespective of the approach used to access the  
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56 sinus (Rodoni et al. 2005, Krenmair et al. 2007, Jurisic et al. 2008, Fornell et al. 2012).  
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2 In conclusion, the results of the present study demonstrated that tSFE (when performed according to the  
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4 *Smart Lift* technique) and ISFE similarly contribute to increase substantially the peri-implant bone support at  
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6 sites with residual bone height of 3-6 mm at 12 months post-surgery.  
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**CONFLICT OF INTERESTS**

The Authors declare they have no conflict of interest related to the present study.

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**TABLE**

**Table 1.** Patient and implant characteristics in tSFE and ISFE groups.

**Table 2.** Proportion of the implant surface in direct contact with the radiopaque area (CON%) as assessed at 12 months post-surgery on the CT/CBCT. CON% measurements were performed on the CT/CBCT mesio-distal section assessing CON% on mesial, distal and apical aspect of the implant (mCON%, dCON%, and aCON%<sub>m-d</sub>, respectively) and on bucco-lingual CT/CBCT section assessing CON% on buccal, palatal and apical aspect of the implant (bCON%, pCON%, and aCON%<sub>b-p</sub>, respectively). totCON% expresses the proportion of the implant surface in direct contact with the radiopaque area obtained by averaging CON% measurements of all 180 CT/CBCT sections parallel to the long axis of the implant and passing through the mid portion of the implant.

**FIGURE LEGEND**

**Figure 1.** Flow chart of patient inclusion and follow-up.

**Figure 2.** CON% (percentage proportion of the implant surface in direct contact with the radiopaque area) values as assessed on the 12-month CT/CBCT of each patient in tSFE and ISFE groups.

**Figure 3.** Height of the radiopaque area apical to the implant apex (aGH) as assessed in mm on the 12-month CT/CBCT of each patient in the tSFE group (a) and ISFE group (b).

**Figure 4.** Peri-implant bone level (as assessed in mm on the 12-month periapical radiograph) at the mesial and distal aspects of the implant (mPBL and dPBL, respectively): **a)** mPBL in each patient of the tSFE group; **b)** dPBL in each patient of the tSFE group; **c)** mPBL in each patient of the ISFE group; **d)** dPBL in each patient of the ISFE group.

**Figure 5.** Sinus graft remodeling index (SGRI, Bragger et al. 2004) values as assessed on periapical radiograph in each patient of the tSFE group at **a)** 6 months and **b)** 12 months, and in each patient of the ISFE group at **c)** 6 months and **d)** 12 months.

**SUPPLEMENTAL APPENDIX (only online)**

**Supplemental Table 1.** Amount of DBBM (expressed in mg as well as in number of 500 mg packages) used in tSFE procedures in relation to the extent of implant penetration into the sinus. (Reprinted from: "Farina, R., et al. *Morbidity following transcresal and lateral sinus floor elevation: A randomized trial. J Clin Periodontol.* 2018; 45:1128–1139.).

**Supplemental Table 2.** Radiographic outcomes in tSFE and ISFE groups according to the occurrence of membrane perforation.

**Table 1.** Patient and implant characteristics in tSFE and ISFE groups.

	n° patients/i mplants	age (years)	gender	smoking status	RBH (mm)	implant diameter (mm)	implant length (mm)
	n	median (IR)	n° males / n° females	n° current smokers / former smokers/never smoked	median (IR)	median (IR)	median (IR)
tSFE group	26	51.6 (47.0 – 58.5)	15 / 11	4 / 2 / 20	5.0 (4.1 – 5.4)	4.0 (4.0 – 4.0)	9.5 (9.5 – 11.0)
ISFE group	28	53.0 (48.5 – 59.0)	11 / 17	3 / 2 / 23	4.1 (4.0 – 5.1)	4.0 (4.0 – 4.0)	9.5 (9.5 – 11.0)
<i>p</i> value		0.461	0.176	0.882	0.123	0.146	0.485

**Table legend**

IR: inter-quartile range; RBH: residual bone height; tSFE: transcrestal sinus floor elevation (*Smart Lift* technique); ISFE: lateral sinus floor elevation.

**Table 2. Proportion of the implant surface in direct contact with the radiopaque area (CON%) as assessed at 12 months post-surgery on the CT/CBCT. CON% measurements were performed on the CT/CBCT mesio-distal section assessing CON% on mesial, distal and apical aspect of the implant (mCON%, dCON%, and aCON%<sub>m-d</sub>, respectively) and on bucco-lingual CT/CBCT section assessing CON% on buccal, palatal and apical aspect of the implant (bCON%, pCON%, and aCON%<sub>b-p</sub>, respectively). totCON% expresses the proportion of the implant surface in direct contact with the radiopaque area obtained by averaging CON% measurements of all 180 CT/CBCT sections parallel to the long axis of the implant and passing through the mid portion of the implant.**

	<b>totCON%</b>	<b>bCON%</b>	<b>aCON%<sub>b-p</sub></b>	<b>pCON%</b>	<b>mCON%</b>	<b>aCON%<sub>m-d</sub></b>	<b>dCON%</b>
<b>tSFE group *</b>	100 (IR: 100 - 100; min: 71.1 - max: 100)	100 (IR: 100 - 100; min: 72.6 - max: 100)	100 (IR: 100 - 100; min: 0 - max: 100)	100 (IR: 100 - 100; min: 60.0 - 100)	100 (IR: 100 - 100; min: 73.6 - max: 100)	100 (IR: 100 - 100; min: 0 - max: 100)	100 (IR: 100 - 100; min: 100 - max: 100)
<b>ISFE group</b>	100 (IR: 100 - 100; min: 77.6 - max: 100)	100 (IR: 100 - 100; min: 100 - max: 100)	100 (IR: 100 - 100; min: 60.0 - max: 100)	100 (IR: 100 - 100; min: 60.0 - max: 100)	100 (IR: 100 - 100; min: 100 - max: 100)	100 (IR: 100 - 100; min: 100 - max: 100)	100 (IR: 100 - 100; min: 100 - max: 100)
<b>p value</b>	0.580	0.606	0.554	0.963	0.800	0.435	0.992

**Table legend**

IR: inter-quartile range; ISFE: lateral sinus floor elevation; min: minimum value; max: maximum value; tSFE: transcrestal sinus floor elevation.

\* In tSFE group, DICOM files of three 12-month CT/CBCT exams could not be analyzed due to technical issues. Therefore, CON% measurements in tSFE group were performed on 23, and not 26, patients.

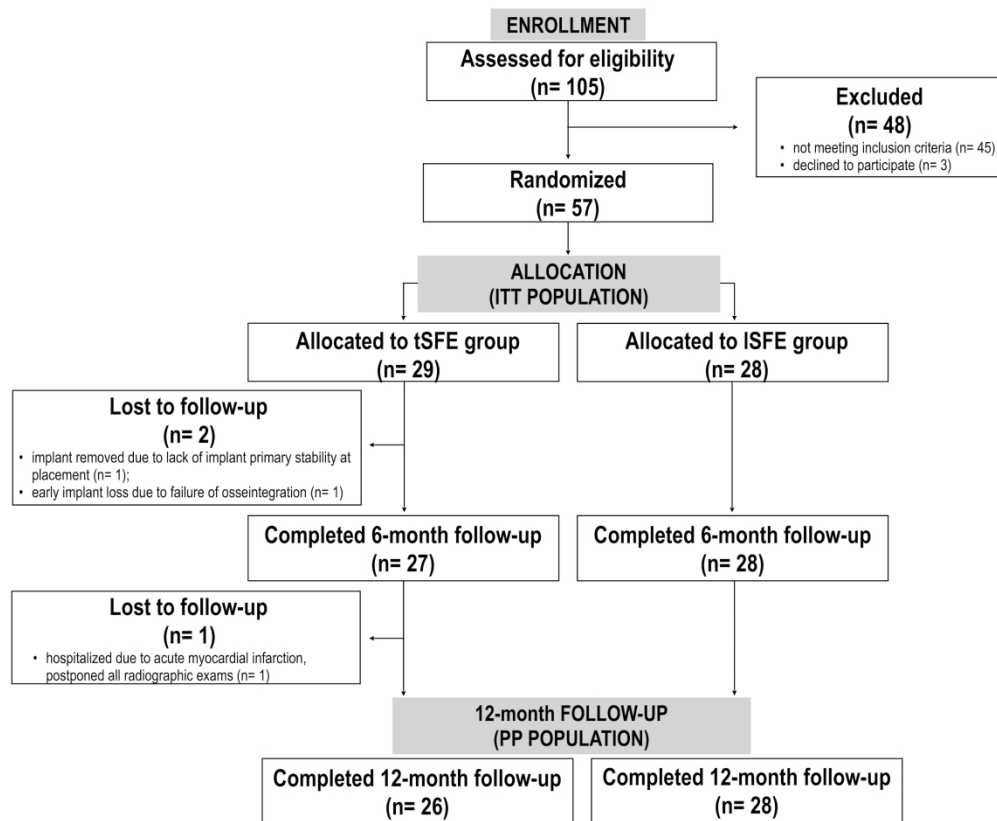


Figure 1. Flow chart of patient inclusion and follow-up.

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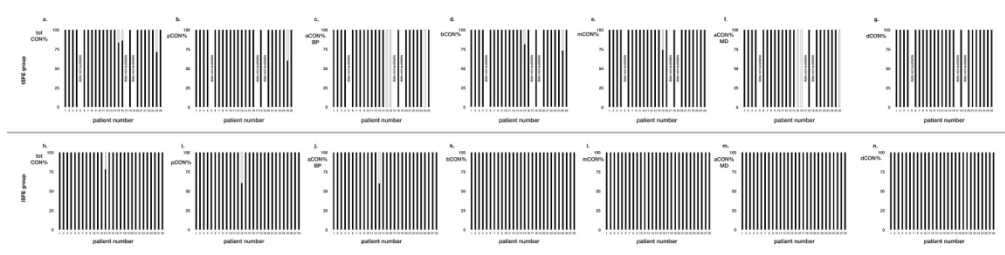


Figure 2. CON% (percentage proportion of the implant surface in direct contact with the radiopaque area) values as assessed on the 12-month CT/CBCT of each patient in tSFE and ISFE groups.

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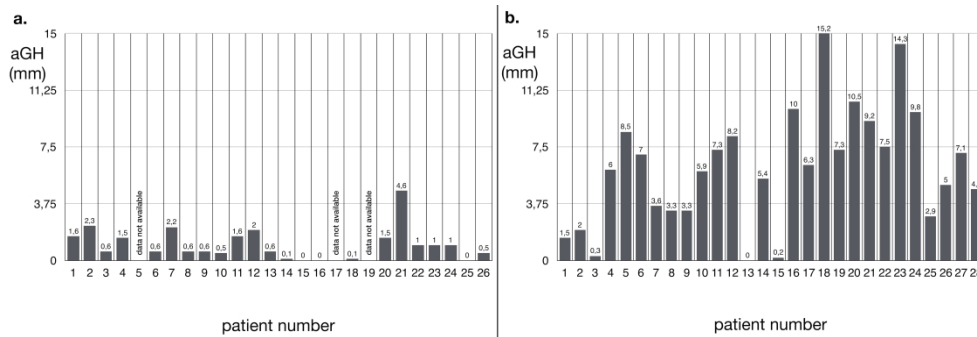


Figure 3. Height of the radiopaque area apical to the implant apex (aGH) as assessed in mm on the 12-month CT/CBCT of each patient in the tSFE group (a) and ISFE group (b).

675x229mm (300 x 300 DPI)

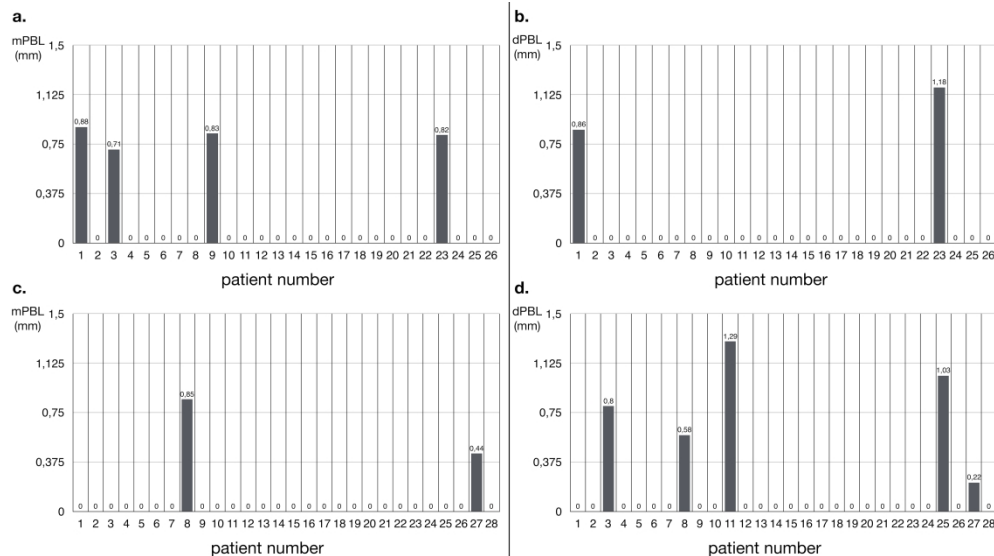


Figure 4. Peri-implant bone level (as assessed in mm on the 12-month periapical radiograph) at the mesial and distal aspects of the implant (mPBL and dPBL, respectively): a) mPBL in each patient of the tSFE group; b) dPBL in each patient of the tSFE group; c) mPBL in each patient of the ISFE group; d) dPBL in each patient of the ISFE group.

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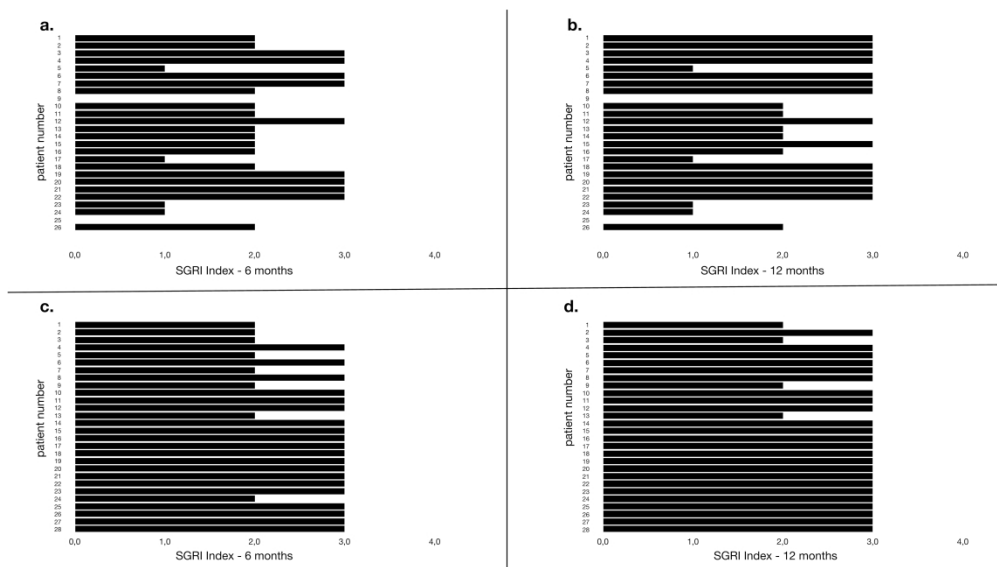


Figure 5. Sinus graft remodeling index (SGRI, Bragger et al. 2004) values as assessed on periapical radiograph in each patient of the tSFE group at a) 6 months and b) 12 months, and in each patient of the ISFE group at c) 6 months and d) 12 months.

677x381mm (300 x 300 DPI)

**Supplemental Table 1.** Amount of DBBM (expressed in mg as well as in number of 500 mg packages) used in tSFE procedures in relation to the extent of implant penetration into the sinus. *Reprinted from: Farina R, Franceschetti G, Travaglini D, et al. Morbidity following transcrestal and lateral sinus floor elevation: A randomized trial. J Clin Periodontol. 2018;45:1128–1139.*

Implant penetration into the sinus (mm)	Amount of DBBM (∅ 0.25-1 mm) (mg)	Amount of DBBM (∅ 0.25-1 mm) (n° of 500 mg packages)
5	330	2/3 of a package
6	500	1 package
7	750	1 package + 1/2 package

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For *Clinical Oral Implants Research***Supplemental Table 2. Radiographic outcomes in tSFE and ISFE groups according to occurrence of membrane perforation.**

Within the limits related to the low incidence of membrane perforation (2 in the tSFE group and 5 in the ISFE group), in tSFE group cases with membrane perforation seemed to be characterized by similarly high totCON% values but lower SGRI (1.5 vs 3.0) when compared to cases without membrane perforation. In ISFE group, no differences in totCON% and SGRI were observed between perforated and non-perforated cases, but a substantial difference in aGH values was evident between perforated (3.6 mm) and non-perforated cases (6.3 mm).

	tSFE group * (n= 26)		ISFE group (n= 28)	
	without membrane perforation (n= 24)	with membrane perforation (n= 2)	without membrane perforation (n= 23)	with membrane perforation (n= 5)
<b>totCON%</b> (%)	100 (IR: 100 - 100; min: 71.1 - max: 100)	100	100 (IR: 100 - 100; min: 100 - max: 100)	100 (IR: 100 - 100; min: 77.6 - max: 100)
<b>aGH</b> (mm)	0.8 (IR: 0.5 - 1.6; min: 0 - max: 4.6)	0.6	6.3 (IR: 4.0 - 8.9; min: 0.2 - max: 15.2)	3.6 (IR: 2.9 - 7.0; min: 0 - max: 7.3)
<b>mPBL</b> (mm)	0 (IR: 0 - 0; min: 0 - max: 0.9)	0 (IR: 0 - 0; min: 0 - max: 0)	0 (IR: 0 - 0; min: 0 - max: 0.9)	0 (IR: 0 - 0; min: 0 - max: 0)
<b>dPBL</b> (mm)	0 (IR: 0 - 0; min: 0 - max: 1.2)	0 (IR: 0 - 0; min: 0 - max: 0)	0 (IR: 0 - 0; min: 0 - max: 0.8)	0 (IR: 0 - 1.0; min: 0 - max: 1.3)
<b>SGRI</b>	3.0 (IR: 2.0 - 3.0; min: 0 - max: 3.0)	1.5 (IR: 1.3 - 1.8; min: 1.0 - max: 2.0)	3.0 (IR: 3.0 - 3.0; min: 2.0 - max: 3.0)	3.0 (IR: 3.0 - 3.0; min: 2.0 - max: 3.0)

**Table legend**

aGH: height of the radiopaque area apical to the implant apex; IR: inter-quartile range; ISFE: lateral sinus floor elevation; min: minimum value; max: maximum value; PBL: peri-implant bone level at the mesial (mPBL) and distal (dPBL) aspects of the implant; SGRI: sinus graft remodeling index (Bragger et al. 2005); totCON: percentage proportion of the implant surfaces in direct contact with the radiopaque area; tSFE: transcresal sinus floor elevation.

Farina et al.

For *Clinical Oral Implants Research*

\* In tSFE group, DICOM files of three 12-month CT/CBCT exams (1 related to a patient experiencing membrane perforation, 2 related to a patient without membrane perforation) could not be analyzed due to technical issues.

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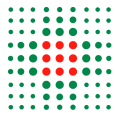
## CONSORT 2010 checklist of information to include when reporting a randomised trial\*

Section/Topic	Item No	Checklist item	Reported on page No
<b>Title and abstract</b>			
	1a	Identification as a randomised trial in the title	<u>1</u>
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	<u>2</u>
<b>Introduction</b>			
Background and objectives	2a	Scientific background and explanation of rationale	<u>4</u>
	2b	Specific objectives or hypotheses	<u>5</u>
<b>Methods</b>			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	<u>5</u>
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	<u>No changes</u>
Participants	4a	Eligibility criteria for participants	<u>4,5</u>
	4b	Settings and locations where the data were collected	<u>5</u>
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	<u>6,7</u>
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	<u>7-9</u>
	6b	Any changes to trial outcomes after the trial commenced, with reasons	<u>No changes</u>
Sample size	7a	How sample size was determined	<u>9</u>
	7b	When applicable, explanation of any interim analyses and stopping guidelines	<u>No interim analyses performed</u>
<b>Randomisation:</b>			
Sequence generation	8a	Method used to generate the random allocation sequence	<u>5</u>
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	<u>5</u>
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	<u>5</u>
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	<u>5</u>

1			interventions	
2	Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	8
3				
4		11b	If relevant, description of the similarity of interventions	Not relevant
5	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9,10
6		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	No additional analyses performed
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11	<b>Results</b>			
12	Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	10, Figure 1
13		13b	For each group, losses and exclusions after randomisation, together with reasons	Figure 1
14	Recruitment	14a	Dates defining the periods of recruitment and follow-up	-
15		14b	Why the trial ended or was stopped	-
16	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
17	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Figure 1
18				
19	Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	10,11
20		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	-
21	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	No additional analyses performed
22				
23	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	10
24				
25	<b>Discussion</b>			
26	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	12,13
27	Generalisability	21	Generalisability (external validity, applicability) of the trial findings	12,13
28	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	12,13
29				
30	<b>Other information</b>			
31	Registration	23	Registration number and name of trial registry	2,5
32	Protocol	24	Where the full trial protocol can be accessed, if available	Not available
33	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	15

1 \*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also  
2 recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials.  
3 Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see [www.consort-statement.org](http://www.consort-statement.org).  
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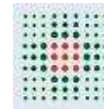
Clinical Oral Implants Research



SERVIZIO SANITARIO REGIONALE  
EMILIA-ROMAGNA  
Azienda Ospedaliero - Universitaria di Ferrara



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DA SEICENTO ANNI GUARDIAMO AVANTI.



SERVIZIO SANITARIO REGIONALE  
EMILIA-ROMAGNA  
Azienda Unità Sanitaria Locale di Ferrara

## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

# VERBALE DELLA SEDUTA DEL 15 MAGGIO 2014

***Aula Arlotti, Direzione Generale – Nuovo Polo Ospedaliero di Cona  
c/o AOU Ferrara – Via Aldo Moro, 8 – 44124 Ferrara***

### Presenti n. 16

<b>AVATO</b>	<b>Francesco Maria</b>	<b>(dalle ore 14.00)</b>
<b>BIANCHI</b>	<b>Stefano</b>	<b>(dalle ore 11.45)</b>
<b>BURNELLI</b>	<b>Roberta</b>	
<b>CAPUZZO</b>	<b>Maurizia</b>	
<b>CAVICCHI</b>	<b>Angelo</b>	<b>(dalle ore 14.00)</b>
<b>FILIPPINI</b>	<b>Graziella</b>	
<b>GOVONI</b>	<b>Marcello</b>	
<b>ORLANDINI</b>	<b>Danilo</b>	
<b>PASTORE</b>	<b>Antonio</b>	
<b>PASTORE</b>	<b>Baldassare</b>	
<b>PATONE</b>	<b>Maurizio</b>	
<b>PAVANELLI</b>	<b>Lina</b>	<b>(dalle ore 14.00)</b>
<b>RIGOLIN</b>	<b>Gian Matteo</b>	
<b>SIMONATO</b>	<b>Michele</b>	<b>(dalle ore 12.00)</b>
<b>TOLA</b>	<b>Maria Rosaria</b>	
<b>WIENAND</b>	<b>Ulrich</b>	

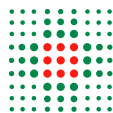
### Assenti n. 4

<b>FERLINI</b>	<b>Alessandra</b>
<b>FERRARESI</b>	<b>Annamaria</b>
<b>PIRINI</b>	<b>Giampiero</b>
<b>SESSA</b>	<b>Giovanni</b>

**Verbalizzante:** **Giulia BERTELLI, Segreteria Amministrativa Comitato Etico  
Ufficio Ricerca e Innovazione – AOU Ferrara**

*Inizio seduta* ore 10.00  
*Termine seduta* ore 17.30

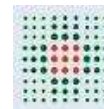




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SERVIZIO SANITARIO REGIONALE  
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Azienda Unità Sanitaria Locale di Ferrara

## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

**STUDIO 140386 "EFFICACY OF A NOVEL SIMPLIFIED, MINIMALLY-INVASIVE PROCEDURE FOR SINUS FLOOR ELEVATION IN THE ATROPHIC POSTERIOR MAXILLA: A MULTICENTER, RANDOMIZED STUDY."**

**Proponente responsabile:** Dott. R. FARINA, Unità Operativa Odontoiatria, Azienda Ospedaliero-Universitaria di Ferrara

**Staff operativo:**

- Unità Operativa di Odontoiatria, Azienda-Ospedaliero-Universitaria di Ferrara (referente: Prof. Leonardo TROMBELLI);
- Unità Operativa di Chirurgia Orale e Maxillo-Facciale, Azienda-Ospedaliero-Universitaria di Bologna (referente: Prof. Claudio MARCHETTI);
- Unità Operativa di Odontoiatria e Chirurgia Maxillo-Facciale, Azienda-Ospedaliero-Universitaria di Modena e Reggio Emilia (referente: Prof. Ugo CONSOLO)
- Unità Operativa di Odontostomatologia, Azienda Ospedaliero-Universitaria di Parma (referente: Prof. Guido Maria MACALUSO).

**Ditta/sponsor:** Regione Emilia-Romagna, Programma di ricerca Regione-Università, Area 1 - Bando Giovani ricercatori "Alessandro Liberati" 2013

**Codice identificativo del piano clinico generale:** PRUA1GR-2013-00000168

**Specialità medicinale (nome o sigla):** //

**Principio/i attivo/i:** //

**Codice CAS (ove disponibile):** //

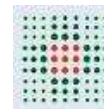
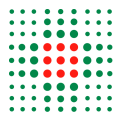
**Classe farmacologica di appartenenza:** //

**Codice ATC proposto (secondo codifica OMS):** //

**Codice ICD:** //

**Fase della sperimentazione clinica:** //

**Indicazione proposta:** Si tratta di uno studio clinico, multicentrico (quattro centri), randomizzato, controllato volto a validare la tecnica Smart Lift come procedura semplificata per la riabilitazione orale di pazienti con sestanti mascellari posteriori edentuli e atrofici. Il centro coordinatore è l'Azienda Ospedaliero-Universitaria di Ferrara.



## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

<b>Forma farmaceutica:</b>	//
<b>Via di somministrazione:</b>	//
<b>Durata dello studio:</b>	24 mesi (estendibile a 36 mesi in caso di necessità)

### Schema dello studio:

L'uso di impianti dentali osteointegrati può migliorare la qualità di vita dei pazienti con gravi deficienze ossee, in quanto estrazioni dentarie multiple possono causare gravi alterazioni dimensionali della cresta ossea. Questo può essere frequentemente osservata nei pazienti affetti da parodontite avanzata. Il deficit con conseguente perdita del supporto osseo può complicare il piano di trattamento protesico convenzionale, spesso limitando il successo funzionale della riabilitazione protesica, con compromissione della funzione masticatoria, fonetica, ed estetica. Di conseguenza la qualità di vita del paziente edentulo è spesso compromessa. L'uso di impianti dentali osteointegrati può migliorare la stabilità della protesi (quando viene utilizzato per supportare una protesi rimovibile) o fornire ancoraggio fisso per corone/ponti. È stato riportato che le protesi supportate da impianti osteointegrati possono migliorare significativamente la qualità della vita dei pazienti edentuli rispetto alle tradizionali protesi totali rimovibili.

Due opzioni chirurgiche per aumentare le dimensioni delle ossa dei sestanti posteriori mascellari consistono nell'elevazione del pavimento del seno mascellare con approccio laterale o transcrestale.

Nei sestanti mascellari posteriori, le alterazioni dimensionali della cresta residua nonché la pneumatizzazione del seno mascellare possono limitare notevolmente l'inserimento di impianti di lunghezza e diametro desiderati.

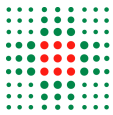
L'approccio chirurgico laterale (ISFE), prevede l'apertura di una finestra nella parete laterale del seno; l'approccio chirurgico transcrestale (tSFE), prevede l'accesso attraverso la cresta ossea edentula. Revisioni sistematiche hanno dimostrato che entrambe le tecniche di potenziamento sono clinicamente efficaci per ottenere un aumento verticale di dimensione cresta e sono associati ad alti tassi di sopravvivenza degli impianti.

Tuttavia, la tecnica che prevede l'accesso laterale (ISFE) è caratterizzata da maggiore invasività chirurgica, rilevante disagio postoperatorio e costi elevati, pertanto si ritiene necessario l'affidamento a tecniche meno traumatiche (come tSFE), che presentano efficacia clinica simile e ridotta morbilità.

La tecnica Smart Lift è una procedura minimamente invasiva, caratterizzata da un accesso transcrestale alla cavità del seno mascellare. Studi recenti hanno dimostrato che la tecnica Smart Lift è facile da usare, può fornire un prevedibile aumento verticale sostanziale della cresta residua, può essere combinato con il posizionamento dell'impianto simultanea, ed è associata a basso rischio di morbilità postoperatoria e poco disagio del paziente. Ad oggi, un numero limitato di studi ha valutato comparativamente l'efficacia e la sicurezza di tSFE e ISFE nella riabilitazione di pazienti con atrofia ossea verticale di grado moderato nei sestanti mascellari posteriori.

L'obiettivo generale del progetto è validare la tecnica *Smart Lift* come procedura semplificata per la riabilitazione orale di pazienti con sestanti mascellari posteriori edentuli e atrofici. A tal fine, gli esiti clinici (ricostruttivi) e i parametri relativi al percepito del paziente del rialzo di seno mascellare con accesso transcrestale (eseguito con tecnica *Smart Lift*) verranno confrontati con quelli del rialzo di seno mascellare eseguito con un approccio convenzionale laterale (ISFE).

I pazienti saranno arruolati consecutivamente e trattati presso i centri ospedaliero-universitari di Ferrara, Bologna, Modena-Reggio Emilia e presso studi privati; l'Azienda Ospedaliero-Universitaria di Ferrara sarà il centro coordinatore dello studio. Ogni centro sarà



## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

completamente attrezzato con materiali necessari per completare le procedure chirurgiche sperimentali nel campione del paziente programmato.

In generale, lo screening punterà a identificare i pazienti con almeno un edentulia posteriore mascellare con moderata atrofia ossea (cioè, altezza residua della cresta edentula compresa tra 3 e 6 mm) e per i quali è previsto il posizionamento di un impianto di 3,5 ÷ 5 mm di larghezza, di almeno 8 mm di lunghezza e di almeno 5 mm più lungo l'altezza ossea residua.

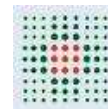
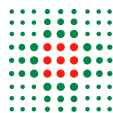
Tutti i pazienti eleggibili saranno assegnati in modo casuale a ricevere tSFE (tecnica Smart Lift) o ISFE.

Il protocollo sperimentale prevede cinque visite:

- Visita di screening: i pazienti saranno selezionati per lo studio secondo i seguenti criteri di inclusione ed esclusione. Tutti i pazienti inclusi siano sottoposti a uno screening completo della bocca, e trattamenti di restauro, endodonzia e/o parodontali, se necessari, saranno eseguiti. Uno stent radiologico sarà realizzato sul modello mascellare utilizzando resina acrilica; successivamente il paziente sarà sottoposto ad una tomografia computerizzata convenzionale o cone-beam (CT e CBCT, rispettivamente) mentre indossa lo stent radiologico.
- Giorno 0: trattamento chirurgico, con tecnica che prevede ingresso transcrestale oppure con tecnica che prevede un ingresso laterale;
- Settimana +2: rimozione delle suture, rilevazione dei parametri di interesse sperimentale;
- Settimana +24 - +32: rilevazione dei parametri di interesse sperimentale, posizionamento della protesi implanto-supportata. Una radiografia periapicale sarà ottenuta per ciascuna area di impianto prima e subito dopo l'inserimento della riabilitazione protesica. Saranno eseguiti ad esempio una ortopantomografia o esami radiografici a tre dimensioni come CT o CBCT solo quando ritenuto necessario dal clinico;
- Settimana +48: rilevazione dei parametri di interesse sperimentale.

I parametri sperimentali sono i seguenti:

- Sopravvivenza degli impianti: ad ogni intervallo di osservazione, la sopravvivenza dell'impianto sarà registrata come la persistenza dell'impianto nella cavità orale con assenza di mobilità (definita come assenza di movimenti verticali, laterali e rotazionali dell'impianto);
- Tempi operatori:
  - Durata della procedura chirurgica: per entrambi tSFE e ISFE, la durata della procedura chirurgica viene registrato come il tempo (in minuti) trascorso dalla incisione al completamento della fase di sutura.
  - Durata della procedura di sollevamento del pavimento del seno: la durata del tSFE sarà registrato come il tempo (in minuti) trascorso dalla perforazione corticale con la fresa Locator per il posizionamento dell'impianto. La durata di ISFE viene registrato come il tempo (in minuti) trascorsi dalla creazione dell'osteotomia sulla parete laterale del seno al posizionamento della membrana riassorbibile a coprire il seno innestato (includendo quindi la procedura di innesto e posizionamento dell'impianto).
- Costi: derivanti dalla realizzazione della procedura chirurgica (ad esempio, esami pre-operatori, materiali), e dovuti al periodo post-operatorio (per esempio, il monitoraggio del paziente post-chirurgica, gestione delle complicanze post-chirurgiche, e le limitazioni in attività quotidiane causate da intervento chirurgico) saranno valutati per ogni paziente.
- Complicanze chirurgiche e post-chirurgiche: l'incidenza di perforazione della membrana sarà valutata la manovra di Valsalva (per tSFE) o visivamente (per ISFE). Altre complicazioni chirurgiche o post-chirurgiche associate alla procedura di



## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

rialzo del seno, tra cui: vertigine parossistica posizionale benigna, infezione post-operatoria, emorragia post-operatoria, sanguinamento nasale, naso chiuso.

- Esiti riferiti dai pazienti: decorso postoperatorio (in termini di dolore, il disagio, la limitazione nelle attività quotidiane e assunzione di farmaci) e l'impatto della chirurgia del seno mascellare e la riabilitazione a supporto implantare sulla salute orale e salute generale - qualità della vita correlata (OHRQoL e GHRQoL, rispettivamente,) saranno valutati attraverso questionari auto-somministrati. Ogni questionario sarà somministrato con dettagliate istruzioni.
- Misurazioni radiografiche: saranno eseguiti tramite CT o CBCT e radiografie periapicali. Tutte le misure saranno effettuate da un unico esaminatore esperto che aveva già subito una sessione di calibrazione su un campione di pazienti non inclusi nello studio e aveva partecipato come esaminatore clinico negli studi clinici precedenti, compresa la valutazione radiografica degli esiti delle procedure di rialzo del seno.

Sono attualmente disponibili dati provenienti da studi precedenti che confrontano l'efficacia/efficienza e la sicurezza di ISFE contro tSFE. Gli studi precedenti hanno indicato una misura medio verticale di rialzo del seno (valutata radiograficamente) di circa 6 a 7 mm per siti trattati con la tecnica Smart Lift mentre un rialzo del seno variabile da circa 8 mm fino a più di 14 mm è stato segnalato per ISFE con DBBM. Assumendo una deviazione standard di rialzo del seno di 2,0 mm per entrambi e una differenza inter-gruppo atteso in rialzo del seno di 3,0 mm (Zitzmann & Schäfer 1998), uno per ogni popolazione di studio del protocollo i 24 ÷ 32 pazienti trattati con tSFE e i 24 ÷ 32 pazienti trattati con ISFE avranno una potenza superiore al 95 % nel rilevare una differenza significativa tra i gruppi, a un livello di p pari a 0,05. Pertanto, per completare lo studio, ogni centro (Ferrara, Bologna, Parma e Modena -Reggio Emilia) tratterà 6 ÷ 8 pazienti con tSFE e 6 ÷ 8 pazienti con ISFE.

### Eventuale terapia concomitante:

Verrà somministrata una premedicazione antibiotica a tutti i soggetti che verranno sottoposti alla procedura chirurgica. Al termine della procedura, inoltre, ciascun soggetto riceverà una prescrizione per un anti-infiammatorio e proseguirà la terapia antibiotica per una settimana.

**AIC in Italia:**  
**all'estero:**

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**Indicazioni all'AIC, posologia, vie di somministrazione e forme farmaceutiche autorizzate: //**

**Precedenti approvazioni/autorizzazioni alla sperimentazione per la stessa indicazione proposta: //**

### Obiettivo/i dello/degli studio/i

**Obiettivo Primario:** l'obiettivo generale del progetto è validare la tecnica *Smart Lift* come procedura semplificata per la riabilitazione orale di pazienti con sestanti mascellari posteriori edentuli e atrofici. A tal fine, gli esiti clinici (ricostruttivi) e i parametri relativi al percepito del paziente del rialzo di seno mascellare con accesso transcrestale (eseguito con tecnica *Smart Lift*) verranno confrontati con quelli del rialzo di seno mascellare eseguito con un approccio convenzionale laterale.

## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

### Obiettivi co-primari:

confrontare il rialzo di seno con accesso transcrestale (tecnica *Smart Lift*) e il rialzo di seno con accesso laterale in termini di parametri centrati sul paziente (complicanze intra- e post-operatorie, dolore e discomfort post-operatorio, assunzione di farmaci nel periodo post-chirurgico, compliance), sopravvivenza implantare a 12 mesi e costi della procedura.

### Secondari:

confrontare il rialzo di seno con accesso transcrestale (tecnica *Smart Lift*) e il rialzo di seno con accesso laterale in termini di entità (radiograficamente determinata a 12 mesi) del rialzo.

**Variabili primarie:** parametri centrati sul paziente (complicanze intra- e post-operatorie, dolore e discomfort post-operatorio, assunzione di farmaci nel periodo post-chirurgico, compliance), sopravvivenza implantare a 12 mesi e costi

### Variabili secondarie:

#### - di efficacia

entità (radiograficamente determinata a 12 mesi) del rialzo

#### - di sicurezza

complicanze intra- e post-operatorie  
dolore e discomfort post-operatorio  
assunzione di farmaci nel periodo post-chirurgico  
compliance  
eventi avversi

### Tipologia dei soggetti da arruolare

**(specificare se pazienti o volontari sani):** In generale, lo screening mirerà ad identificare pazienti con almeno un sito mascellare posteriore edentulo caratterizzato da atrofia ossea moderata e candidato alla riabilitazione impianto-supportata.

### Numero dei soggetti da arruolare:

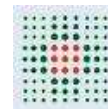
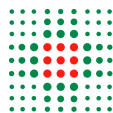
24-32 pazienti per ciascun trattamento (rialzo con tecnica *Smart Lift* o rialzo con accesso laterale). Ciascun centro clinico, quindi, recluterà e tratterà 6-8 pazienti per ciascun trattamento. In totale i pazienti arruolati saranno 48-64.

### Informazione al candidato:

mediante scheda informativa nella quale si riporteranno notizie sulla natura, i metodi e scopo dello studio, nonché il rapporto rischio/beneficio.

Relativamente al modulo denominato "Foglio di informazione per il candidato allo studio sperimentale", si richiede di:

- Per gli studi sperimentali (non osservazionali) stilare una lettera per il medico curante e inserire nel foglio informativo la frase "Il medico della ricerca Le consegnerà una lettera rivolta al Suo medico di base, per informarlo della Sua partecipazione allo studio, per la migliore conduzione clinica dello stesso";
- Inserire la frase "lei deve impegnarsi, sotto la Sua personale responsabilità, ad evitare il verificarsi di una gravidanza per l'intero periodo dello studio e nei successivi ... mesi (specificare il numero di mesi), non potendosi a priori escludere malformazioni del nascituro. Lei potrà ricevere informazioni e discutere con il Medico Sperimentatore le modalità con cui evitare una gravidanza";



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- In merito al trasferimento dei dati personali al di fuori dell'UE inserire la frase: "Sarà cura dello Sponsor garantire la tutela della riservatezza dei dati personali, in conformità a tutte le leggi applicabili in materia di riservatezza dei dati personali, incluso il Safe Harbor Act (2000/520/CE) ed European Union Data Protection Directive, (95/46/EC 24 ottobre 1995)". Esplicitare i titolari ed i responsabili del trattamento dei dati.
- Eliminare la dicitura "Medico che ha informato" sostituendola con "Medico Sperimentatore";
- Aggiungere la data in corrispondenza dello spazio che prevede l'apposizione delle firme.

**Recepimento del consenso:** mediante apposito modulo adeguato

Relativamente al modulo denominato "Foglio di consenso per il candidato" si richiede di:

- Inserire la frase "Sono altresì consapevole che sarà cura dello Sponsor garantire la tutela della riservatezza dei dati personali, in conformità a tutte le leggi applicabili in materia di riservatezza dei dati personali, incluso il Safe Harbor Act (2000/520/CE) ed European Union Data Protection Directive, (95/46/EC 24 ottobre 1995)".
- Eliminare la frase "I suoi dati", sostituendola con "Sono consapevole che i miei dati ...omissis...".
- Eliminare tutte le formule che prevedono l'apposizione di firme, lasciando unicamente quelle poste in calce al presente modulo;
- Sostituire la formula "Medico che ha informato", con "Medico Sperimentatore";
- Aggiungere la data in corrispondenza dello spazio che prevede l'apposizione delle firme.

Nel modulo denominato "Lettera informativa di partecipazione a sperimentazione clinica" si richiede di:

descrivere il trattamento in modo esaustivo;

informare il medico di base circa eventuali trattamenti farmacologici che potrebbero essere dannosi per la salute del paziente che si è sottoposto alla procedura chirurgica prevista dal protocollo di studio;

elenicare tutti i possibili effetti collaterali che potrebbero verificarsi in seguito alla procedura chirurgica cui verrà sottoposto il paziente.

### Criteri di inclusione/esclusione

#### criteri di inclusione:

##### **Patiente-specifici**

- età  $\geq$  21 anni;
- buona salute sistemica (ASA1 o ASA2 in accordo al Physical Status Classification System (American Society of Anesthesiologists));
- condizioni sistemiche e locali compatibili con il posizionamento implantare e con procedure di rialzo di seno mascellare;
- indicazione ad una riabilitazione protesica fissa impianto-supportata che includa, nel piano riabilitativo, una procedura di rialzo del seno mascellare;
- paziente in grado di fornire un adeguato livello di collaborazione allo studio.

##### **Sito-specifici**

Perché un sito possa essere considerato come sperimentale (e, come tale, incluso nell'analisi), i seguenti criteri devono essere soddisfatti:

- almeno 6 mesi trascorsi dalla perdita dentaria;
- altezza ossea residua (determinata radiograficamente)  $\geq$  4 mm and  $\leq$  6 mm;
- programmato per il posizionamento di lunghezza  $\geq$  8 mm.

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### criteri di esclusione:

#### **Paziente-specifici**

- forte fumatore ( $\geq 20$  sigarette/die per  $\geq 6$  prima o al momento della procedura chirurgica);
- malattia parodontale non trattata prima del posizionamento implantare;
- storia di radioterapia nella regione testa-collo;
- storia di chemioterapia;
- patologie o condizioni sistemiche con un effetto documentato sul metabolismo osseo e/o la guarigione ossea;
- passata (entro 6 mesi dall'arruolamento nello studio) o corrente trattamento con farmaci che abbiano un effetto documentato sul metabolismo osseo e/o la guarigione ossea;
- handicap fisico o mentale che possa interferire con la aderenza alle procedure dello studio e con una adeguata compliance igienica domiciliare;
- allergia documentata ai materiali utilizzati per le procedure indicate nel protocollo sperimentale;
- stato di gravidanza o allattamento;
- storia di abuso di alcool e/o droghe.

I partecipanti, inoltre, verranno esclusi dallo studio immediatamente sulla base dei seguenti criteri:

- richiesta di interrompere la partecipazione;
- sviluppo di condizioni dentali, peri-implantari o orali acute che richiedano trattamento;
- sviluppo di condizioni che confliggano con i criteri di esclusione elencati;
- incapacità di collaborare sufficientemente con le procedure richieste dal protocollo.

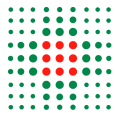
#### **Sito-specifici**

- presenza di lesioni endodontiche a carico dei denti adiacenti al sito implantare;
- precedenti procedure di aumento/preservazione della cresta alveolare nelle aree candidate al posizionamento implantare;
- necessità di procedure ricostruttive di aumento laterale/verticale di cresta in concomitanza alla procedura di rialzo del seno mascellare.

### **Sorveglianza clinica:** //

*Si dà atto che il Comitato Etico ha preso visione della seguente documentazione:*

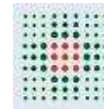
- n.1 copia di protocollo sperimentale in originale (Appendice 1), che include l'individuazione del Centro Coordinatore, l'elenco dei centri partecipanti allo studio, l'elenco degli accertamenti di laboratorio o strumentali da eseguirsi e la flow-chart riassuntiva del disegno sperimentale;
- n.1 copia di sinossi riassuntiva delle caratteristiche dello studio (MOD-702-AZ) (Appendice 2)
- n.1 copia di foglio di informazione per il candidato allo studio sperimentale (Appendice 3);
- n.1 copia di foglio di consenso (Appendice 4);
- n.1 copia di informativa, per il candidato allo studio sperimentale, relativa alla tutela della riservatezza ("privacy") (Appendice 5);
- n.1 copia di informativa per il medico di fiducia (in particolare: medico di medicina generale / pediatra di libera scelta) (Appendice 6);
- n.1 copia di modulistica per la segnalazione di eventi avversi (Appendice 7);
- n.1 copia di modulistica per l'osservazione delle persone in sperimentazione ("diario", "scale", "questionari", "schede") (Appendice 8);
- n.1 copia di autorizzazione allo svolgimento dello studio da parte del direttore dell'U.O. coinvolta (ove non coincida con lo sperimentatore) (Appendice 11);



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- n.1 copia di dichiarazione sul conflitto di interessi del gruppo di sperimentatori coinvolto (Appendice 12);
- n.1 copia di modulo di analisi dell'impatto economico ed organizzativo per studi clinici (MOD-704-AZ) (Appendice 13).

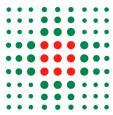
### **Decisione del Comitato Etico**

Si propone allo sperimentatore, in merito al coinvolgimento nello studio di due studi odontoiatrici privati, di arruolare i pazienti nei centri e trattarli nelle strutture ospedaliere.

### **Parere favorevole**

  
Il Presidente del Comitato Etico  
Prof.ssa Graziella Filippini





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## COMITATO ETICO UNICO DELLA PROVINCIA DI FERRARA

### Comunicazione n. 88

**Protocollo:** "Efficacy of a novel simplified, minimally-invasive procedure for sinus floor elevation in the atrophic posterior maxilla: a multicenter, randomized study."

**Codice EudraCT:** //

**Codice:** //

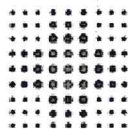
**Data approvazione:** 15 maggio 2014

**Responsabile:** Dott. R. FARINA, Unità Operativa Odontoiatria, Azienda Ospedaliero-Universitaria di Ferrara

**Sponsor:** Regione Emilia-Romagna, Programma di ricerca Regione-Università, Area 1 - Bando Giovani ricercatori "Alessandro Liberati" 2013

**Oggetto:** in data 13 maggio 2014 si invia la modulistica correttamente modificata secondo le richieste del Comitato Etico.

*Il Presidente del Comitato Etico*  
*Prof.ssa Graziella Filippini*



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Comitato Etico Provinciale

Prot. n. 91 / C.E.



UNIVERSITÀ DEGLI STUDI  
DI MODENA E REGGIO EMILIA  
Ateneo fondato nel 1175

Modena, li 13 GEN 2015

Chiar.mo Prof.  
**Ugo Consolo**  
Odontoiatria e Chir. Maxillo Facciale  
Azienda Ospedaliero-Universitaria  
ugo.consolo@unimore.it

Gent.ma Dr.ssa  
**Kyriakoula Petropulacos**  
Direttore Generale  
Azienda Ospedaliero-Universitaria

**OGGETTO: Pratica 144/14 PRUA1GR-2013-00000168** "Efficacia di una nuova procedura minimamente invasiva per il rialzo di seno nei settori mascellari posteriori atrofici: studio randomizzato multicentrico"

NO Sponsor (Azienda Ospedaliero Universitaria di Ferrara - Regione Emilia-Romagna, Programma di ricerca Regione-Università 2013, Area 1)

<b>Co-SPERIMENTATORI</b>	Dr. Carlo Maria Soardi e Dr. Alberto Bandieri
<b>OBIETTIVO PRIMARIO</b>	Confrontare il rialzo di seno con accesso transcrestale (tecnica <i>Smart Lift</i> ) e il rialzo di seno con accesso laterale in termini di parametri centrati sul paziente, sopravvivenza implantare a 12 mesi e costi della procedura
<b>DISEGNO DELLO STUDIO</b>	Interventistico non farmacologico, multicentrico randomizzato in doppio cieco
<b>N° PAZIENTI PER CENTRO</b>	16
<b>DURATA PRESUNTA DELLO STUDIO</b>	Dalla data di autorizzazione - 14/07/2016

Il Comitato Etico per la valutazione dei protocolli di sperimentazione dei farmaci e di ricerca riunitosi il giorno 09/09/14, esaminato il protocollo di studio di cui all'oggetto, aveva sospeso lo studio in attesa che fossero forniti alcuni chiarimenti (prot. 3448 del 16/09/2014).

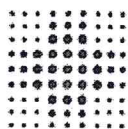
Alla luce della documentazione fornita (prot. 4585 del 21/11/2014) comprensiva di

- 1\_Lettera trasmissione\_versione 2 del 29.09.2014 TF.doc
- 2\_Foglio di informazione per il candidato allo studio sperimentale\_versione 2 del 20.11.2014.docx
- 3\_Lettera al medico di medicina generale\_versione 2 del 29.09.2014.docx
- 5\_Sinossi riassuntiva delle caratteristiche dello studio\_versione 2 del 20.11.2014 TF CLEAN.doc
- 6\_Griglia studi sperimentali senza farmaci\_versione 2 del 20.11.2014 TF.doc
- 7\_Centri partecipanti allo studio\_3 centri\_versione 2 del 20.11.2014.doc
- 9\_Referenti dello studio\_versione 2 del 24.11.2014\_cell 3385000850 TF.doc
- 12.1\_Dichiarazione sostitutiva alla convenzione economica - versione 2 del 20.11.2014 TF.doc
- 12.2\_Scheda materiale\_Bio\_Gide\_Bio\_Oss\_Product\_\_Information\_it.pdf
- 12.3\_Scheda materiale\_element\_mc\_en\_Fo\_02d189.00 01.12.pdf
- 12.4\_Scheda materiale\_Geistlich\_Mucograft\_Seal\_Bio\_Oss\_Collagen\_flyer 601194.1312.it.pdf
- 12.5\_Scheda materiale\_SMARTLIFT Rev. 00.pdf
- 14\_Dichiarazione conflitto di interessi\_versione 2 del 26.09.2014 TF.doc
- 15\_Scheda clinica di raccolta dati CRF\_versione 2 del 29.09.2014.docx
- 18\_Dichiarazione conflitto di interessi Trombelli 20 novembre 2014 TF.pdf

il Comitato Etico, riesaminato lo studio nella seduta del 2/12/14 e sentito il Prof. Consolo e il Dr. Farina in occasione di tale seduta, aveva approvato lo studio a condizione che fossero forniti alcuni chiarimenti (prot. 4855 del 04/12/2014).

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**Comitato Etico Provinciale**

Il Comitato Etico, alla luce della documentazione fornita (prot. 5164 del 22/12/2014) comprensiva di:

- 1.2\_Risposta alle obiezioni sollevate dal Comitato Etico Provinciale di Modena seduta 2.12.2014 \_prot. 4855 del 4.12.2014.pdf
- 2\_Foglio di informazione per il candidato allo studio sperimentale\_versione 3 del 21.12.2014.docx
- 4\_Smart Lift RER - 20 dic 2014.pdf

**ESPRIME PARERE POSITIVO** alla conduzione dello studio di cui all'oggetto,  
**si segnala alla Direzione Generale che, per ricevere l'Autorizzazione, lo Sperimentatore dovrà presentare il Certificato assicurativo stipulato dal Centro Coordinatore per tutti i centri partecipanti nella sua forma definitiva, detto Certificato dovrà essere presentato anche al Comitato Etico.**

*Si ricorda che, prima di iniziare lo studio, lo Sperimentatore che ha ottenuto il parere favorevole del Comitato Etico deve ricevere l'autorizzazione da parte della Direzione Generale competente.  
(Referente amministrativo Sig. Mirella Villani tel. 059 422 4758 - e-mail [dirgen.autorizzaz@policlinico.mo.it](mailto:dirgen.autorizzaz@policlinico.mo.it)).*

Si ricorda inoltre che in riferimento ai rapporti sullo stato di avanzamento dello studio (D.M. 18/03/1998), lo Sperimentatore deve comunicare al Comitato Etico la data di arruolamento del primo paziente, la data di fine arruolamento e data di conclusione dello studio ed inviare annualmente per studi di durata superiore all'anno o semestralmente per studi di durata inferiore all'anno, o più di frequente se richiesto dallo stesso, i riassunti scritti della situazione dello studio. Deve inoltre fornire tempestivamente rapporti scritti in merito ad eventuali cambiamenti che influenzino la conduzione dello studio e/o che aumentino il rischio per i soggetti. Per l'invio delle suddette comunicazioni è possibile fare riferimento al modello disponibile sul sito web del Comitato Etico.

Il Comitato Etico rilascia questo documento in conformità ai propri regolamenti costitutivi e dichiara che il Comitato Etico è organizzato ed opera nel rispetto delle norme di buona pratica clinica (GCP-ICH) e degli adempimenti previsti dall'allegato al Decreto Ministeriale del 15/07/97 (Recepimento delle linee guida dell'Unione Europea di buona pratica clinica per l'esecuzione delle sperimentazioni cliniche dei medicinali) e DL n. 211 del 24/06/03 recante l'attuazione della direttiva 2001/20/CE e successivi decreti applicativi.

Prof. Giuseppe Torelli

Approv. con segn. 144/14.doc

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