



**ORIGINAL REPORT**

**MAXILLARY SINUS LIFT ASSOCIATED WITH FUNCTIONAL ENDOSCOPIC SINUS SURGERY (FESS): A HISTOLOGICAL STUDY**

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**ABSTRACT**

**Objective:** to evaluate on histological preparations the outcome of the maxillary sinus lift surgery associated with the Functional Endoscopic Sinus Surgery (FESS) in patients with a pathological maxillary sinus.

**Materials and methods:** 17 patients with reversible contraindications for maxillary sinus elevation were recruited. Patients had insufficient bone volume in the posterior maxillary (<5 mm). FESS and sinus lift surgery were performed in a single session. Patients have been re-evaluated 7 days, 14 days, 30 days and 3 months after surgery. After 6 months a Trephine bur with a 3 mm diameter was used to prepare the implant site and harvest the biopsy to analyse histologically.

**Results and conclusions:** the histological data of our samples were highly homogeneous and showed the presence of wide marrow spaces and mature bone undergoing mineralization. No signs of inflammation were found. Therefore, the previous sinus pathology did not adversely affect the outcome of maxillary sinus lift.

**Keywords:** osteonecrosis of the jaw, oral bisphosphonates, extraction socket, histological analysis, socket preservation; bone graft.

**INTRODUCTION**

Bone resorption of the maxillary alveolar process is an irreversible consequence of tooth loss <sup>1,2</sup>. The consequent risks of maxillary sinus pneumatization <sup>3</sup> and alveolar bone atrophy<sup>4</sup> significantly reduce the amount of bone volume available for dental implant placement<sup>5,6</sup>. It is well known that implants in the maxillary region show poor clinical outcomes due to low bone quality and lack of residual bone height. For this reason, various surgical techniques have been developed to compensate for the bone quality and quantity in the maxillary region<sup>7,8</sup>. Among these, maxillary sinus lift through elevation of the sinus membrane and grafting was described by Tatum<sup>9</sup>. This surgical technique allows for vertical bone augmentation by creating a space between the sinus membrane and the maxillary floor, which is then filled with grafting materials (autografts, xenografts, allografts, or alloplastic materials). The goal is to increase bone volume by promoting osteoconduction and/or osteoinduction, in order to place adequately

sized osseointegrated implants<sup>10</sup>. Although the procedure is safe and implant success rates exceed 90% <sup>10-13</sup>, several factors may influence the outcome. It has been reported that patients with sinus membranes thicker than 5 mm undergoing sinus lift are at substantial risk of obstruction of the ostiomeatal unit and consequent sinusitis<sup>14</sup>. Regional anatomical alterations such as ostium obstruction, hypertrophy of the sinus membrane, acute or chronic infectious-inflammatory processes, sinus mucocele, and rhinonasal neoplasms<sup>15</sup>. Therefore, accurate identification and assessment of reversible contraindications to the maxillary sinus lift procedure appear to be crucial, as by otorhinolaryngological-affected patients need to resolve the pathological process or anatomical alteration<sup>15</sup>. After 3–4 weeks from the resolution of inflammatory processes, it is possible to perform the oral surgical procedure for maxillary sinus floor elevation. This procedure typically requires two surgical stages, causing considerable discomfort for the patient. Sinus lift procedures are often necessary to increase bone volume in the posterior maxilla for the

placement of dental implants.

When combined with Functional Endoscopic Sinus Surgery (FESS), these procedures can treat nasosinusual pathologies and improve surgical outcomes. Recently, a one-stage surgical procedure has been introduced and reported, which includes maxillary sinus floor elevation in association with FESS for the treatment of inflammatory processes, showing encouraging results in patients with reversible contraindications to sinus lift<sup>16,17</sup>. In fact, a clinical study was conducted to determine whether this surgical approach could be considered for treating minor reversible contraindications to maxillary sinus floor elevation and for simultaneously performing bone augmentation<sup>18</sup>. Lateral maxillary sinus lift associated with FESS has shown good clinical and radiological outcomes in patients with reversible ENT contraindications, such as sinus pathology related to lack of ventilation. Sinus lift combined with FESS allows recovery from rhinosinusual diseases and enables sinus grafting in a single surgical procedure, with the advantage of reduced morbidity for the patient<sup>18</sup>. The aim of the present study was to histologically evaluate bone regeneration obtained when performing lateral sinus elevation using the FESS approach.

## MATERIALS AND METHODS

### Patients

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the local Ethics Committee for Biomedical Research. To perform the study, 16 patients were enrolled (10 female, 6 males, mean age  $52.4 \pm 9.8$ ). They presented reversible contraindications for sinus lift elevation and required bone regeneration for the next implant insertion. All the patients were recruited at “Casa di Cura Stella Maris” and “Centro Salute e Benessere Forum” (San Benedetto del Tronto, Ascoli Piceno, Italy). All patients were examined with a nasal endoscopy associated with Orthopantomography (OPT) radiographs and with maxillo-facial computed tomography (CT) scans. The inclusion criteria were: i) insufficient bone volume ( $<5$  mm) in the posterior maxilla to receive dental implants associated with inflammatory diseases or ii) anatomical alterations in the rhino-sinusual region (chronic hyperplastic sinusitis, mucocoele, ostium obstruction, anatomical alterations of nasal septum).

### Surgical procedure

The Functional Endoscopic Sinus Surgery (FESS or ESS) aims at recreating sinuses proper ventilation by widening the meatal ostium and removing any obstruction to sinus drainage. The sinus lift was performed by lateral trapezoidal flap with horizontal incision on the edentulous ridge and vertical incisions

divergent at least 1 cm from the edge of the mesial and distal antrostomy<sup>19</sup>. The bone window was created using a diamond bur 3 mm in diameter at high speed under abundant cold sterile saline solution irrigation. The window shape was ellipsoidal, with the horizontal longest margin parallel to the crestal margin. The Schneiderian membrane was elevated using periosteal instruments of rounded edges and different length, size and angle. Enzyme deantigenated equine cancellous-cortical bone granules 0.25-1 mm (Osteoxenon, Bioteck S.p.A., Arcugnano, Italy) were used as xenograft and inserted after Schneiderian membrane elevation. Osteoxenon granules are produced and deantigenated through a patented process named Zymo-Teck. This process allows the enzymes to work at low temperature in an aqueous environment to remove all the components that may trigger an immunogenic response. Such method allows the preservation of both the mineral component and the bone collagen in a native conformation<sup>20</sup>. The resulting bone substitute is recognized physiologically by osteoclasts allowing its complete integration in patient's bone in a physiological time<sup>21</sup>. The grafting material was gently compacted to stabilize it between the bone walls and the sinus membrane. Hermetic and passive suture was applied. Follow-up medical examinations and nasal endoscopies were performed at 7 days, 14 days, 30 days and 3 months. Six months after surgery, the fixture was inserted. A 3 mm trephine bur was used to drill the bone for implant site preparation and to collect bone samples.

### Histological analysis

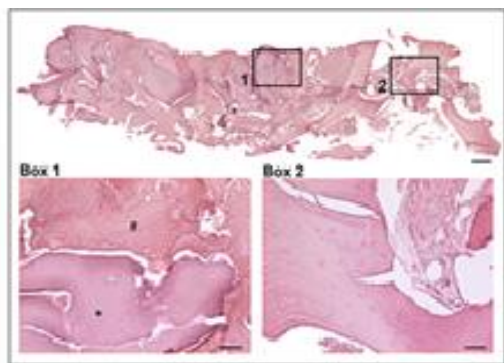
All the samples were immediately fixed in 4% formaldehyde and then decalcified using Biodec-R solution (Bio-Optica, Milan, Italy), according to the manufacturer's instructions. After these treatments, the sample was dehydrated with a series of alcohol rinses and embedded in paraffin for light microscope observations. The samples were cut longitudinally along the major axis using a microtome (Leica Microsystems Srl, Milan, Italy). Three slides of 6  $\mu$ m were stained with Hematoxylin & Eosin (H&E) and Mallory Trichrome staining solutions to identify newly formed bone undergoing mineralization. Histomorphometric analysis was performed using a Zeiss Axioscope optical microscope (Carl Zeiss AG, Oberkochen, Germany) connected to a CoolSNAP camera (Photometrics, Tucson, AZ, USA). The acquired images were analyzed using the dedicated software MetaMorph Image Analysis (Universal Imaging Corp, Downingtown, PA, USA), which offers advanced image acquisition and processing capabilities.

Three histological sections were prepared for each sample to ensure a more accurate evaluation. The examined area was assessed by quantifying the presence of bone marrow spaces, mineralized bone, and residual biomaterial. The surfaces occupied by marrow spaces, bone tissue, and biomaterial were used for histomorphometric analysis,

calculating the ratio between the total examined area and the area occupied by each tissue component. The mean value for each section was then calculated as previously described <sup>22</sup>.

## RESULTS

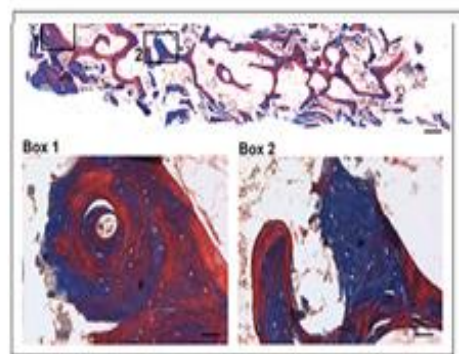
No post-operative complications were clinically found in any of the sites where the procedure was performed and six months after surgery all maxillary sinus surgeries were successful. All the histological samples obtained from the 16 patients appeared homogeneous when observed in light microscopy: bone tissue resulted vital, no evidence of empty lacunae or morphological alterations to osteocytes was found neither signs of inflammation and/or fibrosis were noted. Bone tissue from all the specimens showed features of mature lamellar bone although the presence of woven bone was also found. As shown in Figure 1, the presence of newly formed bone is highlighted by means of H&E staining.



**Figure 1** Two-dimensional (2D) reconstruction of a representative bone sample (H&E staining) (upper panel; magnification 25×, scale bar 400 μm). Bone trabeculae are dark-pink colored (#), whereas graft material appears light-pink colored (\*) (Box 1-2; magnification 200×, scale bar: 100 μm)

The trabeculae appear dense and the amount of bone marrow is minimal (upper panel). The presence of residual biomaterial is appreciated in about half of the samples and, in particular, in the apical portion. The residual graft material is in close contact with the newly formed trabecular bone, highlighting an excellent osseointegration (Box 1-2).

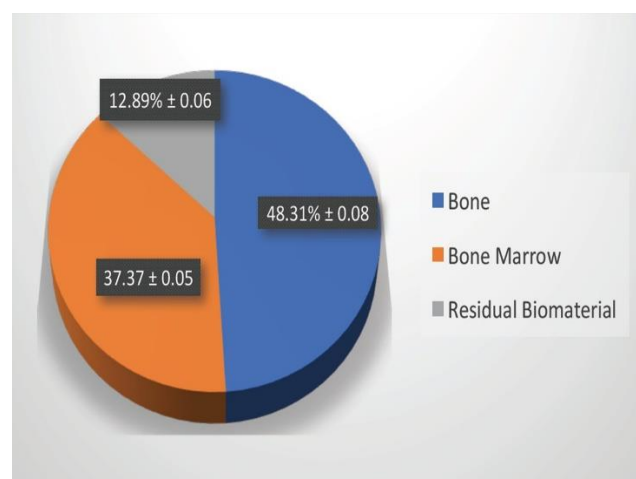
Mature bone tissue already mineralized or in the process of mineralization is shown in Figure 2 by means of Masson Trichrome staining (upper panel). Parallel and concentric bone lamellae together with small osteocyte lacunae can be observed; loose connective tissue rich in fat and blood vessels can be also appreciated (Box 1-2).



**Figure 2** Two-dimensional (2D) reconstruction of a representative bone sample (Mallory Trichrome staining) (upper panel; magnification 25×, scale bar 400 μm). Bone samples show the presence of lamellar bone undergoing mineralization (#) and indicating complete bone remodeling (Box 1-2; magnification 200×, scale bar: 100 μm)

Three serial sections of each sample were analyzed, taken in the coronal part, in the middle part, and in the apical part of the sample. The average percentage of bone tissue, bone marrow and residual biomaterial respectively was calculated for each individual sample as summarized in Table 1.

In 7 out of 16 samples residual biomaterial was found, while in the remaining 9 samples no residual biomaterial was detected. On average, the samples analyzed showed an average percentage of newly formed bone of 48.31 with respect to the total area, a percentage of bone marrow of 37.37 and a residual biomaterial percentage of 12.89 (Figure 3).



**Figure 3** Average percentages of newly formed bone, bone marrow, and residual biomaterial with respect to the total area of the analyzed sample



Table. 1 Average percentage of bone tissue, bone marrow and residual biomaterial for individual samples

Sample	Bone	Bone Marrow	Residual Biomaterial
#1	39.08 ± 0.223%	56.16 ± 0.207%	4.66 ± 0.032%
#2	50.74 ± 0.103%	49.26 ± 0.103%	0.00 %
#3	52.44 ± 0.151%	16.37 ± 0.019%	31.19 ± 0.159%
#4	76.55 ± 0.107%	23.45 ± 0.102%	0.00%
#5	56.91 ± 0.112%	3.42 ± 0.030%	39.67 ± 0.114%
#6	42.19 ± 0.086%	57.81 ± 0.083%	0.00%
#7	73.21 ± 0.080%	26.79 ± 0.043%	0.00%
#8	55.56 ± 0.057%	44.44 ± 0.056%	0.00%
#9	7.74 ± 0.008%	26.84 ± 0.005%	65.42 ± 0.002%
#10	61.18 ± 0.030%	38.82 ± 0.024%	0.00%
#11	48.98 ± 0.097%	51.02 ± 0.099%	0.00%
#12	43.23 ± 0.067%	41.44 ± 0.060%	4.52 ± 0.015%
#13	41.06 ± 0.077%	47.15 ± 0.082%	0.00%
#14	66.41 ± 0.034%	33.59 ± 0.034%	0.00%
#15	39.21 ± 0.067%	13.25 ± 0.022%	47.54 ± 0.033%
#16	18.48 ± 0.033%	68.24 ± 0.019%	13.28 ± 0.012%

## DISCUSSION

Edentulous patient's rehabilitation with implant-supported prostheses currently represents a gold standard practice with reliable long-term results<sup>23</sup>. However, local conditions of the alveolar ridge may be unfavorable for implant placement procedure. In particular, the alveolar bone resorption is one of the main biological consequences connected to tooth loss<sup>24</sup>. Maxillary sinus pneumatization<sup>25</sup> and alveolar bone atrophy<sup>26</sup> represent the main risks connected to bone resorption, leading to a reduction in the long-term outcome of implants placed in this area due to insufficient maxillary bone height and quality<sup>27</sup>.

In recent years, several surgical techniques have been developed to solve the problem of bone quality and quantity of the maxillary region<sup>7</sup>. Above these, maxillary sinus floor elevation and grafting via either a crestal or a lateral approach have become a very common procedure with predictable results and a generally low post-operative complication rates<sup>28</sup>. Complications such as maxillary sinusitis and/or infection of the grafting material are rare<sup>5,29</sup>. It has been demonstrated that patients with history of sinusitis, antral mucosa hyperplasia, anatomic alterations in the nasal cavities may present a higher risk of complications<sup>28</sup>. Such complications are well known and documented and are defined "reversible":

it is therefore mandatory to treat them as soon as possible following safe and reliable treatment protocols<sup>15</sup>. FESS is now considered the gold standard in reversible ENT contraindications treatment. In this scenario, a two-step procedure of FESS followed by the sinus lift after a healing period has already been reported with encouraging results in patients with reversible contraindications<sup>15</sup>. However, the entire procedure requires from one to at least six months before the final implant placement, with a serious discomfort for patients. Combining maxillary sinus floor elevation with FESS in a single-step procedure has proven effective and safe. This approach addresses local contraindications to sinus augmentation and avoids the need for a second surgical procedure, facilitating quicker prosthetic rehabilitation<sup>16</sup>. The authors demonstrated that a one-step approach can be considered as a safe and cheap option for the treatment of minor reversible contraindications avoiding a second surgical procedure and enhancing patients' compliance in completing the prosthetic rehabilitation<sup>16</sup>. Falco et al. demonstrated a positive clinical and radiologic outcome of 69 consecutive maxillary sinus augmentations associated with FESS (2015). Currently, considerable progress has been made regarding this topic, but there are still not many research in the literature that provide histological data supporting clinical outcomes. In the present study, we evaluated histological samples from 16

patients with reversible contraindications who underwent a single session FESS and maxillary sinus lift procedure before implant placement. Patients did not show any clinical complication associated with the intervention and, most importantly, histological analysis indicated a physiological healing of the site. The average percentage of residual biomaterial observed in the analyzed samples was very low as compared with the average percentage of the newly formed bone, indicating that 6 months after sinus elevation, almost all the biomaterial had undergone remodeling, and was substituted by new trabecular bone. The histological data are consistent with previous studies that used enzyme deantigenated equine bone as bone substitute (Osteoxenon, Biotech S.p.A., Arcugnano, Italy)<sup>30,31</sup> in sinus lift surgery. In comparison with other studies using biomaterial grafting, we have not found anomalies or alterations due to the pre-existing sinus pathology.

## CONCLUSIONS

In conclusion, the histological results coming from the analysis of our samples show that there are no histological differences due to sinus pathology. Therefore, we can affirm that it is possible to successfully perform the technique of maxillary sinus lift and the Functional Sinus Surgery Endoscopy (FESS) in a single step.

## DECLARATION

### Competing interest

The authors declare that there are no competing interest.

### Funding

The work was not funded.

### Ethical Approval

"Not applicable"

### Consent for publication

"Not applicable"

### Acknowledgments

"Not applicable"

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