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Original Research Article

Comparison of two graft procedures in a bilateral sinus lift by MRI and histomorphometric analysis: a case report

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Abstract – Magnetic resonance imaging (MRI) was shown to be a viable method for graft healing evaluation. Platelet-rich fibrin (PRF) was found to speed up bone graft healing process. Sinus lift surgery outcomes after healing period are usually performed with computerized tomography that is not capable to describe graft vascularization and exposes patient to ionizing radiation. The objective of this study is to propose contrast-enhanced magnetic resonance imaging (CE-MRI) as a promising method for the in vivo assessment of sinus lift grafting procedures. A bilateral sinus augmentation surgery was performed. Left sinus was grafted only with bovine deproteinized bone mixed in a 1:1 ratio with autologous bone, in the right sinus, the same biomaterials with the addition of platelet-rich fibrin (PRF) were applied. CE-MRI was performed to evaluate angiogenesis before surgery and at 11, 25, 53, and 104 days after surgery. At 6 months (T0) and after 10 years (T1), before dental implants insertion, bone biopsies were performed and analysed quantitatively. Left sinus graft showed a centripetal pattern of angiogenesis, with the central region remaining unvascularized at 104 days post-surgery. Right side showed a wider and homogeneous vascularization from 25 days after surgery. At T0 new bone formation was only peripheral in the left sinus, whereas it developed both peripherally and through biomaterial in the right sinus. At T1 particles of biomaterial were still present in left sinus, while in right sinus they were not. CE-MRI offers quantitative parameters to evaluate vascularization of biomaterials. The addition of PRF promotes an early development of a widespread vascular system.

Introduction

Maxillary sinus floor augmentation is an effective treatment option in case of severe maxilla atrophy [1].

Different biomaterials have been evaluated with the objective to improve newly formed bone quality and density to perform dental implant placement as early as possible including autologous bone, xenogeneic bone, demineralized or mineralized allogeneic bone, and alloplasts [2].

The use of deproteinized bovine bone mineral (DBBM) mixed with autologous bone particles appears to be one of the most efficient types of grafts currently available as DBBM act as a scaffold, while autologous bone has both osteogenic and osteoinductive properties [3].

Platelet-rich fibrin (PRF) is an autologous biomaterial that promotes the development of a microvascularization and has been shown to accelerate bone regeneration when combined with freeze-dried bone allograft [4].

Several authors have demonstrated no advantages other than reduction of healing time in the application of PRF in combination with DBBM when compared with DBBM graft alone [5–9]. PRF's role in hard tissues regeneration remains still controversial due to the lack of clinical studies [10].

X-rays investigations are not appropriate tools for repetitive in vivo evaluation due to the ionizing radiation. Magnetic resonance imaging was successfully used to assess in vivo angiogenesis in bilateral sinus lift graft, permitting repetitive monitoring of healing tissues processes as a non-invasive survey method [11].

The primary aim of this study is to evaluate maturation and angiogenesis of two different sinus lift grafts by means of contrast-enhanced magnetic resonance imaging (CE-MRI) to propose it as a method for the in vivo assessment of sinus lift grafting procedures. The hypothesis is that CE-MRI can clearly describe whether the addition of PRF promotes early vascularization and a faster healing process of sinus graft.

Materials and methods

Approval was obtained from the local ethics committee (number 051_2021H, 01/04/2021).

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Surgical informed consent was obtained to perform bilateral sinus augmentation surgery in an edentulous 50-years old patient with severe maxilla atrophy. No general health contraindications to surgery were found.

PRF was produced following the Choukroun method [12], blood sampling was performed at the beginning of the operation. Immediately after blood sample collection, 9-mL silica-coated plastic tubes (IntraLock, Boca Raton, FL, USA) were centrifuged at about 700 g (2700 rpm) for 12 min (IntraSpin Device, IntraLock, Boca Raton, FL, USA). After the centrifugation process, PRF obtained was prepared and utilized in membrane form.

After local anaesthesia with mepivacaine hydrochloride with adrenaline (Optocain, Molteni Dental S.r.l.), a full-thickness flap was raised to perform osteotomy of the lateral wall of both maxillary sinuses to reach the Schneiderian membrane to be carefully elevated. No perforations of the membrane were noticed, autologous bone chips were harvested from the nearby zygomatic bone region of both sides using a bone scraper mounted on a piezoelectric device (Esacrom Srl, Imola, Italy). The volume between the sinus floor and the Schneiderian membrane was filled with a 1:1 mixture of deproteinised bovine bone mineral (Bio-Oss, Geistlich Pharma AG, Wolhusen, Switzerland) and autologous bone in the left sinus (control). The right sinus was grafted using the same 1:1 mixture of DBBM and autologous bone with the addition of PRF (test).

After the graft was sufficiently stabilized by gently compression of biomaterials, the flap was sutured with single stitches to achieve primary closure.

Six months after the sinus lift operations (T0), a full thickness flap was raised to place 6 implants 11 mm of length and 3.8 mm of diameter (Camlog Screw-line Promote, Camlog, Basel, Switzerland), 3 implants each side. Before implants insertion, cylindrical bone biopsies of both grafting sites were performed using a 4 mm diameter trephine bur (Meisinger, Dussendorf, Germany). The bone obtained was fixed in formalin and prepared with the Schenk's method [13]. Implants were then positioned where the biopsies had been carried out. Due to implants failure occurred after 10-years from the first surgery (T1), after the bone healing period of 4 months, control bone biopsies of both grafting sites were repeated in the identical position of T0 immediately before implant placement. Bone samples obtained at T1 were prepared and analyzed with the same procedure of T0. All surgery steps were performed by the same expert clinician (MM).

Histology

Histomorphometric examination of bone biopsies obtained at T0 and T1 was performed by means of a Axio Imager M1 microscope equipped with a digital AxioCam HRc (Carl Zeiss, Göttingen, Germany). In the samples were marked and distinguished: older bone (OB), newly formed bone (NB), Bio-Oss® (DBBM) and mature bone (MB). Data were measured quantitatively with a computer software (AnalySIS FIVE — software, Soft Imaging System, Münster, Germany).

In vivo evaluation of new angiogenesis

MRI evaluations were obtained before sinus lift operations, and 11, 25, 53, and 104 days after surgery [11].

Analysis were performed by means of short inversion time-inversion recovery (STIR) sequences on the axial plane and conventional spin-echo sequences T1-weighted (T1w-TSE) on the axial, coronal and sagittal plane. Secondary, after obtaining patient's informed consent, a contrast media was injected (Dotarem 20 ml, Guerbet SpA, Genova, Italy) and investigations were executed by means of dynamic scans on the cross-section plane on the maxillary sinus and successively with spectral presaturation with inversion recovery (SPIR) sequences on the axial, coronal and sagittal plane. Images were analysed and reported by a specialized radiologist to evaluate angiogenesis by the enhancement of the contrast media (CM) in tissues.

Results

The patient exhibited overall good wound healing after surgery.

Histomorphometric analysis

The histomorphometric results are presented in Figure 1.

From biopsies performed at T0 were obtained two samples for the left sinus (control) and three for the right sinus (test) of 4×3 mm dimensions. No quantitative differences were obtained in new bone and residual biomaterial in both sites. New bone formation was found only peripherical in control sinus, whereas it developed both peripherally and both through particles of biomaterial in test sinus.

At T1 three samples for the control and two for the test sinus were obtained from bone biopsies. Histomorphometric analysis showed an equal new bone formation from a quantitative point of view. However, particles of biomaterial were still present in control, while in test sinus they were not. Therefore, in test sinus an histomorphometric analysis was not possible at T1.

In vivo evaluation of new angiogenesis

CE-MRI before sinus lift operation and during follow up are shown in Figure 2.

After surgery, augmented material showed maximum axial dimensions of $20 \times 19 \times 25$ mm for control sinus and of $18 \times 17 \times 30$ mm for the test sinus. After 11 days from the surgical time a peripherical enhancement was visible in both left and right maxillary sinus grafts. This finding is compatible

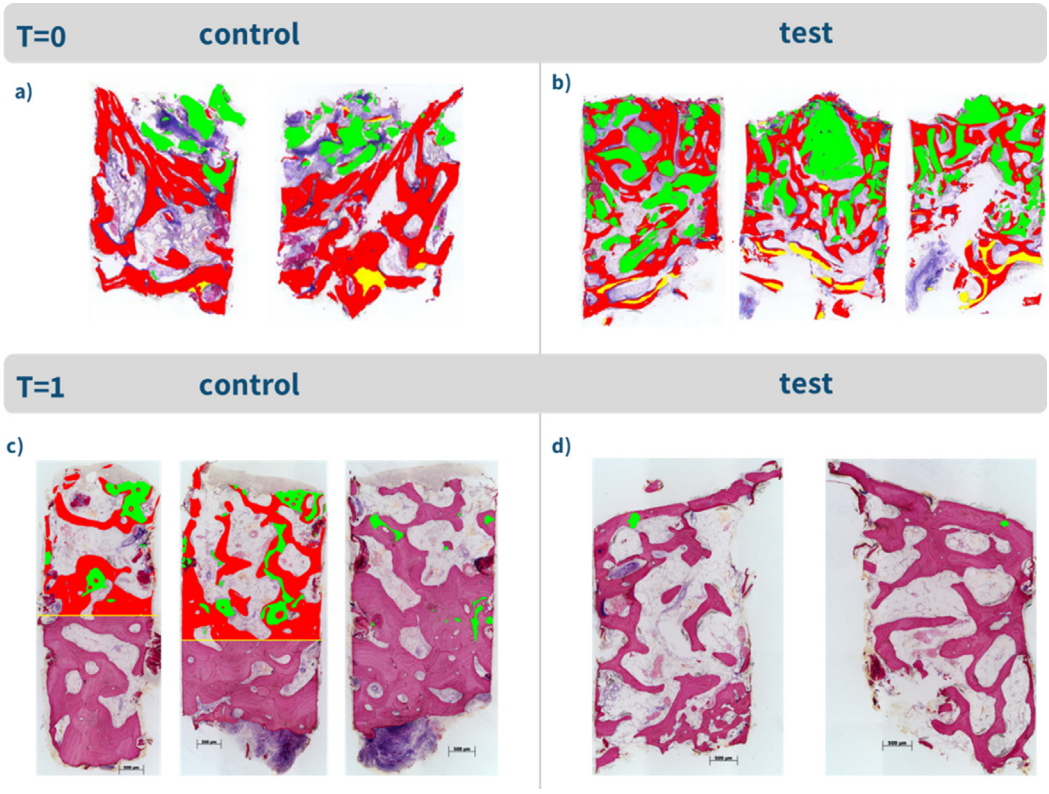

Fig. 1. Saw cuts from the biopsy and their histomorphometric analysis with digital labeling. Soft tissue is stained blue (undecalcified ground section, stained with azure II and pararosaniline, original magnification x50). Digital labeling of Bio-Oss granules (green), newly formed bone (red) and older bone (yellow). a) control sinus at T0, characterized by a peripheral new bone formation around Bio-oss particles; b) test sinus at T0, new bone formation was found through Bio-oss particles; c) control sinus at T1, Bio-oss particles were still present; d) test sinus at T1, no Bio-oss particles were found, only a micrometer fragment of Bio-oss particle was visible.

with the inflammation of sinus mucosa in a normal post-operatory course. After 25 a small volume reduction of both grafts was noticed, probably attributable to the post operatory reduction of the inflammatory component, with maximum axial diameters of $19 \times 15 \times 21$ mm for the control sinus and $17 \times 12 \times 21$ mm for the test one. Regarding the absorption of CM, on the left side a circumferential enhancement was visible only in the most peripherical area of the biomaterial, in the most central area an enhancement was not visible, describing a centripetal vascularization of the graft. As opposite the test sinus showed a widespread and diffuse enhancement of the whole graft.

At 53 days no volumetric variations of the grafts were noticed. In the control sinus the circumferential pattern of the absorption of CM was more evident and a little area with no enhancement was still present in the most central area of the graft. The test sinus showed an unchanged absorption of CM with a homogeneous enhancement of the whole graft as noticed in the previous analysis.

After 104 days on the control sinus there was still a little area in the most central portion of the graft with no enhancement waiting to be revascularized. As opposite, the test side showed a huge and wider enhancement of the whole graft as observed from 25 days after the surgery.

Discussion

The aim of this pilot study was to assess sinus lift graft maturation and angiogenesis of two different sinus bone grafts performed in a single patient by means of histomorphometric analysis and CE-MRI.

Control left maxillary sinus was grafted with a 1:1 mixture of DBBM and autologous bone. Test right sinus was grafted using the same 1:1 mixture of DBBM and autologous bone with the addition of PRF.

The role of PRF in bone wound healing has been investigated by several studies [14].

The addition to PRF in maxillary sinus augmentation surgery provides a more reliable post-operative course [15]. In agreement with other studies, in the present study the addition of PRF to maxillary sinus bone graft showed no increase in new bone formation [6,7,16,17]. Moreover, it was noticed that addition of PRF to maxillary sinus bone graft produced an earlier and widespread graft vascularization, accelerating of the healing process. This result is in accordance with that found in other studies where the addition of PRF led to an acceleration of the healing process and bone regeneration [12,16,18,19].

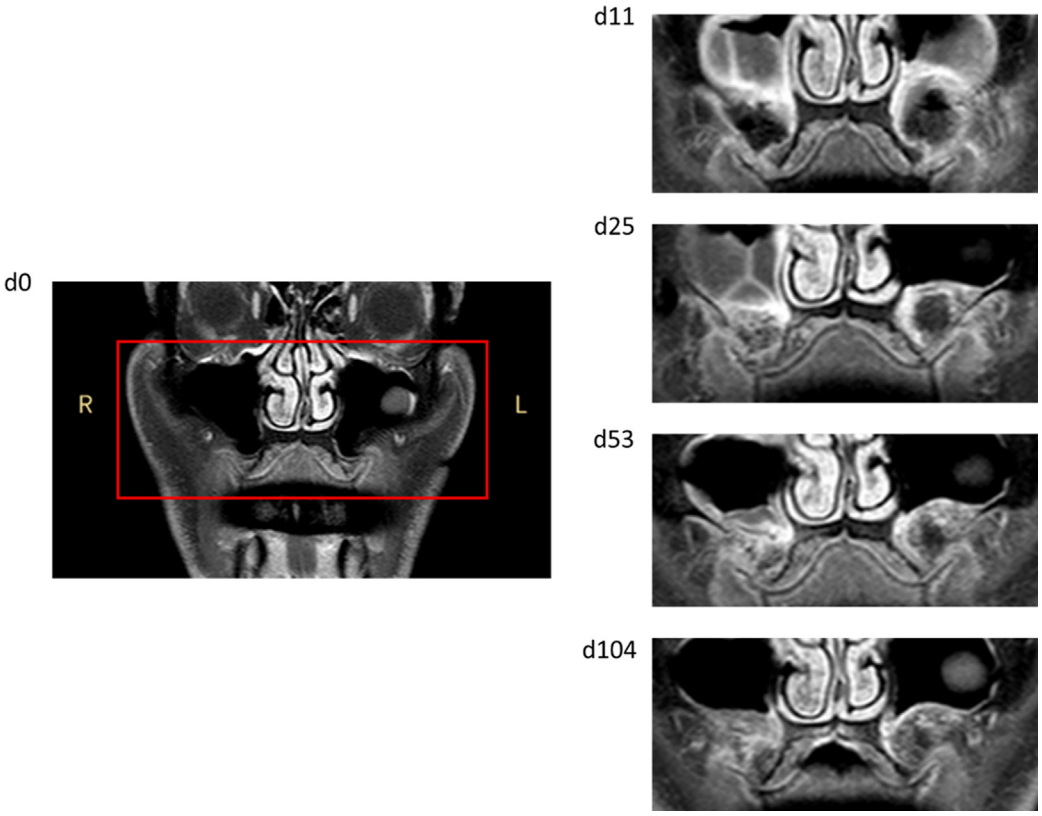

Fig. 2. Coronal SPIR with CM acquisition of left sinus (control) and right sinus (test): d0) before sinus lift operation; d11) 11 days from sinus lift operation; d25) 25 days from sinus lift operation; d53) 53 days from sinus lift operation; d104) 104 days from sinus lift operation.

After 6 months from surgery control sinus graft showed a peripheral new bone formation, whereas in test sinus the osteogenic process was more homogeneous. To the best of our knowledge, this is the first study presenting a 10-year follow-up histomorphometric analysis in a split mouth study design of maxillary sinus augmentation surgery. After 10 years, both sinuses showed an equal new bone formation, in test sinus graft no DBBM particles were found while in control were still present.

CE-MRI revealed a more widespread and homogeneous graft vascularization in test sinus starting from the 25th day after surgery, while it developed with a slower circumferential pattern in control sinus, with the most central portion of the graft still waiting to be vascularized at the 104th day.

Conventional in vivo methods to assess the outcome of a bone regeneration surgery as sinus lift augmentation are histomorphometric analysis and volume tomography. Histomorphometric analysis needs to perform a bone biopsy, therefore is suitable when implant placement is required. Volume tomography well describes hard tissues, however, uses ionizing radiation. Therefore, is not recommended to employ it several times during the bone healing process to monitor post operative bone regeneration or for research purposes. MRI has been successfully used to assess postoperative results of sinus lift augmentation [20]. MRI has a variety of possible contrasts with the potential to demonstrate dynamic function without using ionizing radiation. Moreover, MRI has been employed to measure dimensional changes of autologous onlay grafts giving equivalent results to volume tomography [21]. Another study concluded that MRI is as reliable as volume tomography for sinus graft measurements [22]. Therefore, with MRI is possible to repeat imaging assessments several times monitoring maturation of bone grafts, even for research purposes, without the risk of radiation. Furthermore, with volume tomography, it is almost impossible to evaluate bone graft integration or failure after the healing period. As opposite, CE-MRI offers the possibility to assess angiogenesis of bone grafts during the healing period, an important marker to ensure graft integration.

In the present study, CE-MRI was used to assess graft vascularization during time in two different graft procedure with follow up equivalent to another study [11] that presented a similar design as ours. According to Sauerbier's study, CE-MRI analysis showed that strong absorption of CM was noticed on the swollen mucosa surrounding both sinuses' grafts 11 and 25 days after surgery, while no vascular system was noticed in the most central portion of both sinuses graft. As described in Sauerbier's study, graft vascularization proceeded circumferentially and progressively in sinus lift graft, as it happened in control sinus graft of the present study. The author described that the pattern of CM uptake indicates that vessel development into the biomaterial originates from the peripherical vital tissues surrounding the graft: the Schneiderian membrane cranially and residual bone crest caudally. Interestingly, in the present study, test sinus showed a widespread CM uptake of the graft 25 days after surgery, even in the most central area. This finding

suggests that the addition of PRF promoted an early development of a vascular system in the most central portion of the graft, accelerating the healing process. A limitation to this study is that these findings are shown on a single patient with a split mouth design. To increase the force of evidence, further studies are needed to confirm that MRI can be utilized to assess bone graft vascularization, predicting their integration before surgical re-entry. Finally, further studies are needed to prove that MRI is an effective and non-invasive method to assess which is the most effective type of bone graft in terms of vascularization, and to confirm that the addition of PRF to DBBM provides an early vascularization shortening the healing period.

Conclusions

MRI is a non-invasive method for repetitive imaging assessment of bone grafts maturation, and it can be used safely to monitor bone grafts healing and angiogenesis for clinical or research purposes. The addition of PRF to DBBM mixed with autologous bone graft promotes an early development of a widespread vascular system, accelerating the sinus lift graft healing process.

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Conflicts of interest

All the authors declare to have no conflict of interest.

Data availability statement

Data associated with this article cannot be disclosed due to legal reason.

Author contribution statement

M. Maglione, contributed to Conceptualization (equal); Formal analysis (equal); Writing-review & editing (equal). F. Michelon, contributed to Writing-original draft (equal); Writing-review & editing (equal). L. Bevilacqua contributed to Writing-review & editing (equal). M. Bertolotto contributed to Formal analysis (equal); Writing-review & editing (equal). R. Rothweiler contributed to Writing-review & editing (equal). All authors gave final approval and agreed to be accountable for all aspects of the work.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the University of Trieste (protocol code 051_2021H, 01/04/2021).

Informed consent

Patient consent was obtained for surgery, contrast media injection and magnetic resonance imaging.

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