

## RESEARCH ARTICLE

# MRI for the display of autologous onlay bone grafts during early healing—an experimental study

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**Objectives:** Autologous bone grafts are the gold standard to augment deficient alveolar bone. Dimensional graft alterations during healing are not known as they are not accessible to radiography. Therefore, MRI was used to display autologous onlay bone grafts *in vivo* during early healing.

**Methods and materials:** Ten patients with alveolar bone atrophy and autologous onlay grafts were included. MRI was performed with a clinical MR system and an intraoral coil preoperatively (t0), 1 week (t1), 6 weeks (t2) and 12 weeks (t3) postoperatively, respectively. The graft volumes were assessed in MRI by manual segmentation by three examiners. Graft volumes for each time point were calculated and dimensional alteration was documented. Cortical and cancellous proportions of bone grafts were assessed. The intraobserver and interobserver variability were calculated. Statistical analysis was performed using a mixed linear regression model.

**Results:** Autologous onlay bone grafts with cortical and cancellous properties were displayed *in vivo* in eight patients over 12 weeks. The fixation screws were visible as signal voids with a thin hyperintense fringe. The calculated volumes were between 0.12–0.74 cm<sup>3</sup> (t1), 0.15–0.73 cm<sup>3</sup> (t2), and 0.17–0.64 cm<sup>3</sup> (t3). Median changes of bone graft volumes of –15% were observed. There was no significant difference between the examiners ( $p = 0.3$ ).

**Conclusions:** MRI is eligible for the display and longitudinal observation of autologous onlay bone grafts. Image artifacts caused measurements deviations in some cases and minimized the precise assessment of graft volume. To the knowledge of the authors, this is the first study that used MRI for the longitudinal observation of autologous onlay bone grafts.

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## Introduction

Despite the availability of a wide range of bone grafting techniques and materials that are used in clinical

routine, the radiographic display of bone grafts has not been standardized and a multitude of variables leads to incongruent results for their display.<sup>1–3</sup> Nevertheless, imaging of bone grafts is crucial to assess the success of healing and integration of the graft and to select the

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appropriate dimensions of a subsequently placed dental implant.

Radiographic examinations, especially tomographic imaging such as CT and cone-beam CT (CBCT), may display bone three-dimensionally, however limitations apply. Autologous onlay grafts imaged at an early healing time point are not adequately displayed due to their low degree of mineralization. Furthermore, bone block grafts are fixed to the underlying bone with titanium screws inducing artifacts in the form of streaks and extinctions and potentially mask the graft and surrounding structures.<sup>4,5</sup> The ionizing character of radiographic imaging and the accompanying health risks prohibit its repeated use and therefore exclude longitudinal studies.<sup>6,7</sup>

Dimensional changes of bone grafts may be estimated by the measurement of soft tissue alterations as demonstrated for dimensional changes of the alveolar crest after tooth extraction.<sup>8</sup> Measurement of soft tissue is easy to accomplish clinically or on individually fabricated stone cast.<sup>9</sup> The information, however, on three-dimensional dimensions of bone grafts is limited as the amount or thickness of the soft tissue is unknown. Furthermore, the bone quality during bone graft healing cannot be assessed with either technique.

The diagnostic capabilities of CT and CBCT in dental implantology are restricted to the display of mineralized tissues (bone, teeth) with a deficiency in the display of tissue with a low grade of mineralization (*e.g.*, bone transplants, hard tissue in regeneration/revascularization phase). CBCT has been used in studies evaluating synthetic or xenogenic bone replacement material with mineralized particles of high radio opacity.<sup>10</sup> Furthermore, dimensional changes of bone grafts were observed using CBCT, when high-density bone substitute materials or combinations of bone with bone substitute materials were used.<sup>11–14</sup>

CT has been used to display the dimensional changes of autologous bone grafts over time.<sup>15–17</sup> In CT, the density of tissues corresponds to Hounsfield units (HU), therefore applying a HU-based filter can give information on the tissue (*e.g.*, bone) quality and allow quantitative analysis of images. In CBCT, the displayed gray values vary and do not allow a standardized correlation with HU; therefore, the quantification and qualification of bone grafts using CBCT may not be accomplished.<sup>6,18–20</sup>

The lack of knowledge about the dimensions of bone grafts consequently due to the absence of an appropriate imaging method is addressed in this study.

MRI could be used as an alternative imaging modality for alveolar bone and bone grafts as it has proven successful to display the dento-alveolar complex using intraoral coils and standard MRI equipment for the head and neck region.<sup>21–23</sup> Furthermore, MRI may be used to display soft tissues and hard tissues with low mineralization. These two reasons predestine MRI for the display and longitudinal observation of autologous cortico-cancellous bone grafts.

MRI is increasingly used for imaging of the dento-maxillofacial complex. The indications for MRI include the delineation of the inferior alveolar nerve in healthy subjects and after iatrogenic injury; the detection of caries, pulpitis and periapical lesions; the localization of impacted teeth and dental implant planning.<sup>24–30</sup> High-resolution images, with voxel sizes of approximately 0.5 mm<sup>3</sup> and clinically feasible scanning times, are achieved with specific surface coils or intraoral coils.<sup>22,23,31,32</sup>

MRI has been used to display the maxillary sinus with incorporated bone substitute material and soft tissue swelling as well as blood retention after sinus augmentation procedures using autologous bone and various bone substitute materials.<sup>33–38</sup>

The use of MRI for the display of autologous onlay bone grafts fixed with titanium osteosynthesis screws has not been evaluated yet. A previously introduced intraoral coil was used for MRI to enhance image resolution and contrast.<sup>22,23</sup>

## Methods and materials

### Patient selection

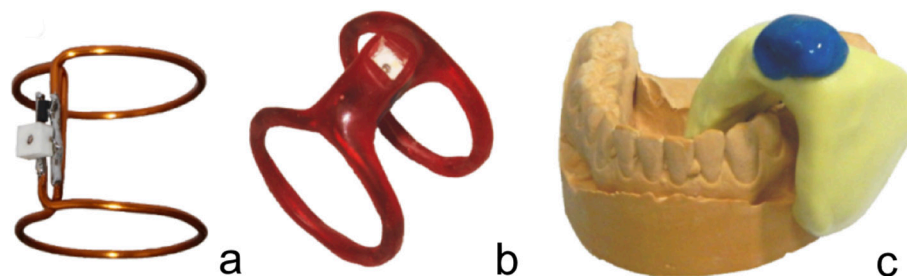
In 10 patients, onlay bone grafting and MRI were performed. The study protocol was approved by the Institutional Review Board of the Medical Center – University of Freiburg, Freiburg, Germany (338/13). Written informed consent for the treatment was obtained from each participant. Patients were aged between 26 and 64 years (mean 52.5 years), three female and seven male patients were included. The bone graft region of each patient is displayed in [Table 1](#).

### Bone grafting

The patients were partially edentulous and presented with an atrophic maxilla ( $n = 6$ ) or mandible ( $n = 4$ ). Out of 10 patients, eight patients received bone grafts from the iliac crest and two patients received bone grafts from the ascending ramus of the mandible. The surgical intervention was performed as previously described.<sup>39</sup>

**Table 1** Patient data and edentulous regions (FDI) that received bone grafts. \*Patients had to be excluded for data analysis

patient	region of bone graft	donor region	age	gender
1	21	iliac crest	59	female
2	21	iliac crest	49	female
3*	46	retromolar	59	male
4*	31–32	retromolar	55	male
5	21–22	iliac crest	27	male
6	15–17	iliac crest	46	male
7	11	iliac crest	61	male
8	35–37	iliac crest	59	female
9	35–36	iliac crest	65	male
10	25–27	iliac crest	52	male



**Figure 1** Inductively coupled intraoral coil with variable capacitor and diodes before (a) and after resin coating (b), and adapted to the individual region of bone augmentation using a silicon coating (c). Figure adapted from previously published work.<sup>23</sup>

Iliac corticocancellous bone grafts were harvested from the medial cortical plate of the anterior superior rim by two horizontal and two vertical osteotomies with an oscillating saw and osteotomes. Bone grafts from the retromolar region of the mandible were harvested with a piezotome and osteotomes and consisted mostly of cortical bone. The bone grafts were adapted to the size of the edentulous alveolar ridges and fixed with the cancellous aspect facing the residual bone and the cortical aspects forming the labial and occlusal contour. Each bone graft was fixed with at least two osteosynthesis screws to avoid rotation. The grafted area was covered with a mobilized mucoperiosteal flap after periosteal releasing incisions and closed with running and interrupted sutures.

#### MR imaging

MRI was performed preoperatively (t0), 1 week (t1), 6 weeks (t2) and 12 weeks (t3) postoperatively, respectively. A clinical whole-body MR system (Magnetom Prisma, Siemens Healthineers, Erlangen, Germany) equipped with a body transmit coil, a 4 cm receive loop coil (LC), and an intraoral inductively coupled coil (ICC) tuned to 123.195 MHz<sup>2</sup> for signal enhancement were used (Figure 1).<sup>23</sup> 2D TurboSPINECH0 (TSE) sequences with 1 mm slice thickness and in plane resolution = 300×300 μm<sup>2</sup> were acquired. Depending on the desired image volume, the number of slices varied from 19 to 32, the matrix sizes were between 128×128 and 320×320 and the FOV was between 39×39 mm<sup>2</sup> and 111×111 mm<sup>2</sup>. The acquisition time therefore varied between 2:38 and 5:03 min. Further image parameters were: TE/TR = 15/1860 ms, two averages, band width = 685 Hz/Px, number of echoes = 3, echo spacing between 7.32 and 7.9 ms. The view angle tilting (VAT) technique was applied to suppress image artifacts from susceptibility changes around titanium osteosynthesis screws.<sup>40</sup> VAT is a technique that is applied during MR image acquisition to compensate for possible distortions within each image plane. However, its application limits image resolution.<sup>41</sup>

#### Data evaluation

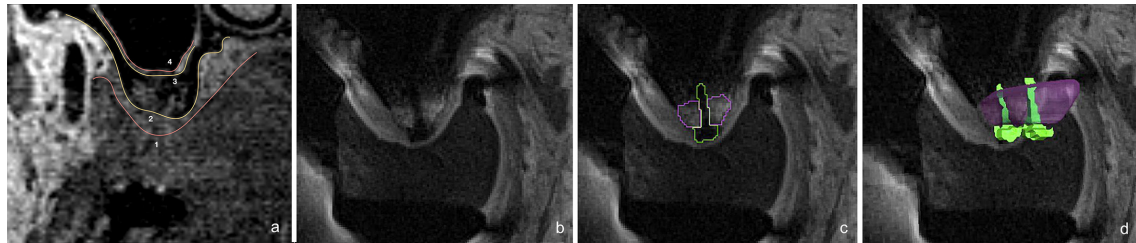
The following protocol was applied for data evaluation. Imaging data were collected and imported to

Amira (V.6.5.0, Thermo Fisher Scientific, Waltham, MA, USA). The displayed range of signal intensity values was adjusted for each imaging sequence and not changed throughout evaluation to avoid bias. Each observer was calibrated using augmented and MRI imaged sheep jaws and introduced to the software to ensure common criteria for the identification of bone transplants and adjacent anatomical structures. The specimens were prepared in a preliminary animal study in which a bone graft harvested from the calvarium of a sheep was fixated with a titanium osteosynthesis screw to the edentulous part of its mandible. The gingival soft tissue was used to cover the bone graft in analogy to the clinical procedure. The specimens were imaged using the intraoral coil and identical MRI protocols. Each examiner received MR images of sheep jaws and after mutual inspection each examiner segmented the bone graft. Results of segmentation were again viewed by all three examiners. After evaluation of sheep specimens, the MR images of bone grafts in the study participants were evaluated.

The bone grafts and neighbouring structures were identified and located in the images. The vestibular and crestal outline of the bone graft consisted of cortical bone and was detected by its hypointense signal, directly adjacent to the hyperintense signal of the surrounding gingiva. In the vestibulo-oral direction, the cortical portion was followed by a hyperintense cancellous portion that was distinguished from the underlying residual bone with cortical properties. For evaluation, bone transplants were delineated in each slice of the imaging sequence. The total volume of each graft was obtained by adding the marked volume in each slice (Figure 2). Three examiners evaluated MR images of bone grafts taken at each interval and repeated measurements three times with a time-lag of two weeks between the measurements.

#### Statistical analysis

Intraobserver and interobserver variability for bone graft volumes were assessed as well as volume changes of bone grafts over time (t1–t3). Statistical analysis was performed using a mixed linear regression model (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).



**Figure 2** Transversal cross-section through region 16 (FDI) preoperatively (t0) (a), with marked gingival outline (1), cortical bone outline (2), sinus floor (3) and Schneiderian membrane (4), postoperatively (t1) (b), with marked volume of bone graft (purple) and osteosynthesis screw (green) (c), and grafted bone volume by adding marked regions in every slice (d).

## Results

MRI of autologous onlay bone grafts was performed with intraoral coils *in vivo* in seven patients. Two patients with mandibular bone grafts were excluded within the course of the study due to claustrophobia during MR examination or due to non-precious-metal-reinforced provisional prostheses masking the augmented region.

In preoperative imaging, cortical bone areas were displayed with hypointense signal, whereas cancellous bone appeared with hyperintense signal. The gingival soft tissues surrounding cortical bone were displayed with hyperintense signal (Figure 3). Autologous bone grafts from the iliac crest ( $n = 7$ ) displayed cortical and cancellous properties that were visible with MRI at every stage (Figure 4). Further images show bone grafts in different regions of the jaw at different healing times (Figure 5).

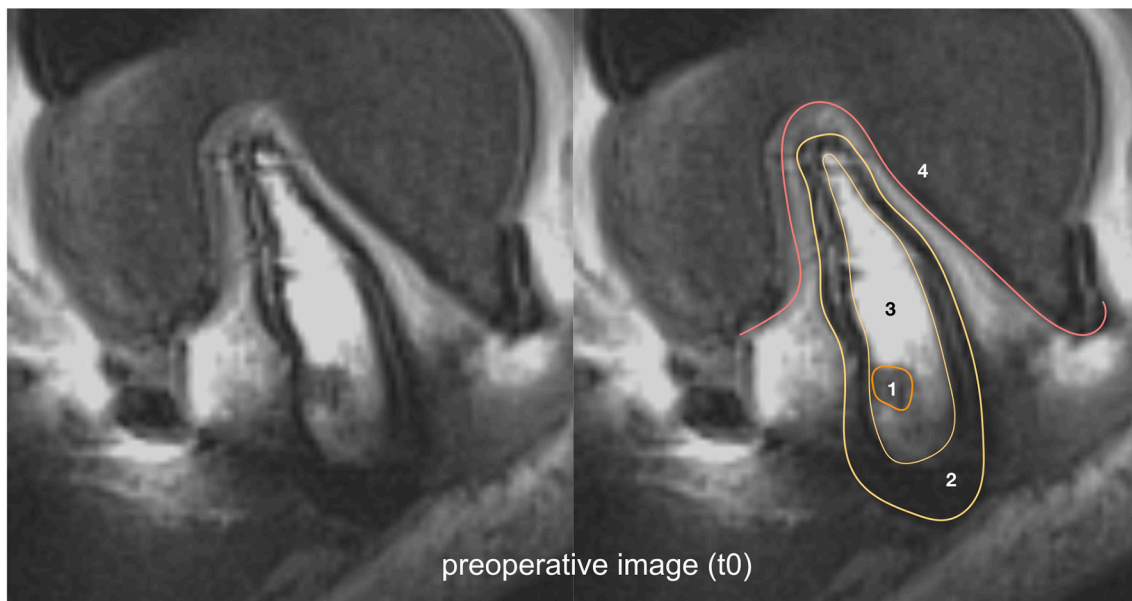
The graft from the ascending ramus of the mandible was mostly cortical. The osteosynthesis screws used to fix the bone grafts were visible as signal voids surrounded by a thin hyperintense fringe.

The calculated volumes of the bone grafts were between  $0.12\text{--}0.74\text{cm}^3$  at t1,  $0.15\text{--}0.73\text{cm}^3$  at t2, and  $0.17\text{--}0.64\text{cm}^3$  at t3. Median dimensional changes of bone graft volumes of  $-15\%$  (Examiner 1),  $-17\%$  (Examiner 2) and  $-9\%$  (Examiner 3) were observed. The overall median dimensional changes of bone grafts were  $-15\%$  (mean  $-5\%$ ). There was no significant difference between the examiners for overall dimensional changes of grafts ( $p = 0.3$ ). Numerical values are displayed in Table 2.

The standard deviation was  $0.090\text{mm}^3$  (confidence interval  $0.051\text{--}0.158$ ) for interexaminer variation and  $0.061$  (confidence interval  $0.041\text{--}0.09$ ) for intraexaminer variation.

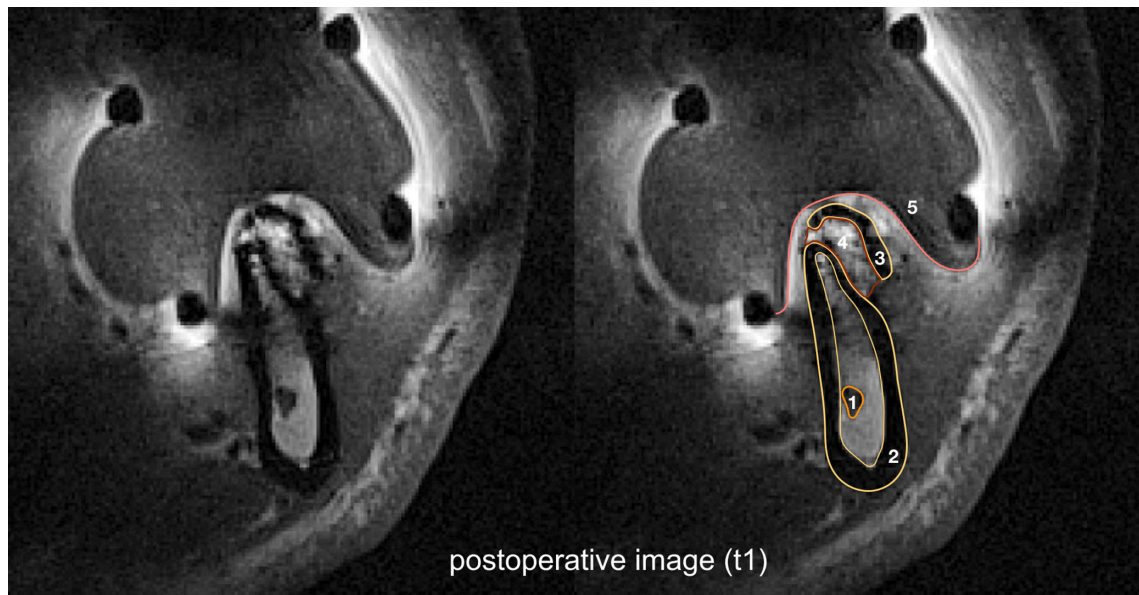
## Discussion

Autologous bone grafts and their dimensional changes during healing were displayed with MRI. Median dimensional changes of  $-15\%$  were observed over 12 weeks.



**Figure 3** Transversal cross-section in preoperative imaging of atrophic mandible (region 36-FDI) displaying the residual bone with inferior alveolar nerve (1), cortical bone (2), cancellous bone (3) and gingiva (4).



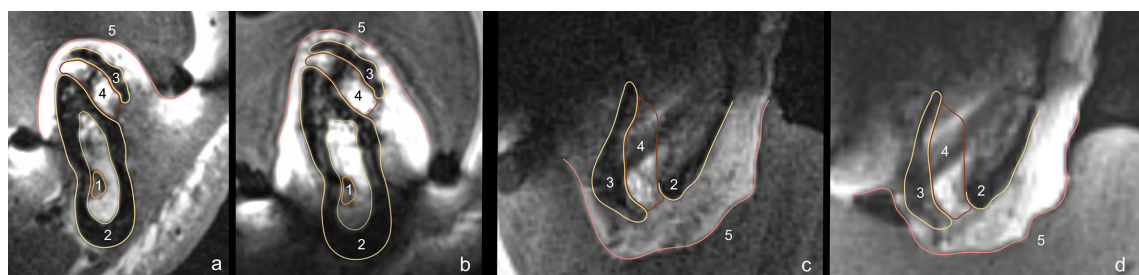


**Figure 4** Transversal cross-section through mandible in region 36 (FDI) displaying the residual bone with inferior alveolar nerve (1), cortical bone (2) and the bone transplant with cortical part (3) and cancellous part (4) covered by the mucoperiosteal flap (5).

Previous studies on the dimensional changes of autologous bone grafts used repeated CT scans for volume assessment.<sup>15-17</sup> Barone et al documented iliac bone grafts with mean volumes of 0.94cm<sup>3</sup> immediately after grafting and 0.69cm<sup>3</sup> after a healing period of 4 months. The mean volume of bone grafts was generally higher, than in the presented study (0.43cm<sup>3</sup> maxilla, 0.74cm<sup>3</sup> mandible). Mean volume change of bone grafts was -29% and therefore also higher than in the presented study (-15%).<sup>17</sup> Sbordone et al examined dimensional changes of autologous iliac bone grafts between 3-5 and 12 months after augmentation surgery. Completely edentulous jaws or partially edentulous jaws, without further specifying the location, the number of missing teeth or the defect size, were treated. Mean bone graft volumes were 1.67cm<sup>3</sup> and 1.96cm<sup>3</sup> in the maxilla and mandible, respectively, and showed a dimensional change of -35% and -51%, respectively, between 3-5 and 12 months.<sup>15</sup> The dimensional changes of bone grafts within the first 3-5 months were not assessed radiographically. Bone graft volumes and

dimensional changes were again significantly higher than in the presented study. In a comparable study, the volume of autologous iliac bone grafts was measured at 3-5 months (1.3 and 1.25cm<sup>3</sup>) and up to 6 years after augmentation surgery. The baseline volume of bone grafts (up to 3-5 months) however was not assessed radiographically and therefore the early healing could not be compared to the data in this study.<sup>16</sup> All three studies using CT for the measurement of dimensional changes of iliac bone grafts reported higher volumes of bone grafts and reported higher volume resorption. Lower resorption rates in the presented study may be caused by a favourable ratio of cortical and cancellous bone portions that was previously reported for a specific augmentation technique using bone grafts from the iliac crest.<sup>42</sup>

Previous studies have observed bone grafts with CT after a minimum healing period of 3 months.<sup>15-17</sup> CT and CBCT might be used to assess mineralized portions of transplanted bone. In contrast, MRI displays soft tissues and tissues with a low grade of mineralization.



**Figure 5** Transversal cross-sections through mandible in region 46 (FDI) at t1 (a) and t2 (b) as well as transversal cross-sections through the maxilla in region 21 (FDI) at t2 (c) and t3 (d) displaying the residual bone with inferior with inferior alveolar nerve (1), cortical bone (2) and the bone transplant with cortical part (3) and cancellous part (4) covered by the mucoperiosteal flap (5).

**Table 2** Median, mean (standard deviation – SD) for volume of bone grafts (in cm<sup>3</sup>) at each time point in each patient. Marked volumes are displayed in Figure 5a–d.

patient	t1		t2		t3	
	mean (SD)	median	mean (SD)	median	mean (SD)	median
1	0.12 (0.03)	0.13	0.154 (0.03)	0.16	0.16 (0.03)	0.15
2	0.22 (0.05)	0.21	0.173 (0.08) <sup>5c</sup>	0.13	0.19 (0.03) <sup>5d</sup>	0.18
4	-	-	0.407 (0.23)	0.37	0.30 (0.08)	0.29
6	0.72 (0.06)	0.72	-	-	0.65 (0.07)	0.63
7	0.20 (0.05)	0.21	0.187 (0.03)	0.18	0.17 (0.03)	0.16
8	0.79 (0.16)	0.75	0.711 (0.08)	0.71	0.64 (0.08)	0.65
9	0.70 (0.11) <sup>5a</sup>	0.66	0.596 (0.09) <sup>5b</sup>	0.60	-	-
10	0.87 (0.27)	0.80	-	-	-	-

MRI might be favourable for the assessment of early bone healing, during which the mineralization of grafts has not taken place.

This is the first study to use MRI for the display of autologous onlay grafts and to measure the dimensional changes of bone grafts *in vivo* over time. In previous MRI studies, measurement of grafted volumes was not performed.<sup>36,38</sup> Only in one postoperative MR scan the augmented area was measured favourable changes over time were not evaluated.<sup>33,35,37</sup> One case report noted stable vertical bone dimensions between 10 days and 10 weeks after maxillary sinus augmentation with particulate iliac bone in one patient.<sup>34</sup>

Most previous studies administered contrasting agent intravenously prior to MR imaging.<sup>33–35,38</sup> The administration of contrasting agent was not necessary in this study, as T2W imaging protocols were used with the intraoral coil and enabled high contrast in the field of view.

MRI acquisition times varied between 5:16 min and 10:00 min in existing studies and were therefore longer than the acquisition time of 2:38 min in this study.<sup>33,34,37,38</sup> Short acquisition times are intended *in vivo*, to minimize discomfort of the patient and artifacts due to patient movement.

An intraoral coil was used to enhance contrast and improve image resolution in the region of interest.<sup>22,23</sup> An unprecedented in-plane image resolution of 300×300 μm and 1 mm slice thickness were achieved which is comparable to CBCT. This is accomplished with an intraoral coil and a small image volume. With the use of standard head and neck coils, a surface coil for dental imaging or smaller surface coils that were adapted to the respective side of the face, the image resolution of MRI is limited to around 0.5 mm.<sup>24,30,43,44</sup> Previous studies of bone augmentation using MRI applied standard MRI equipment and achieved image resolutions over 700×700 μm with slice thicknesses up to 4 mm.<sup>33,34,37</sup>

The bone grafts could be delineated in cortical (hypointense) and cancellous (hyperintense) parts. The surrounding mucosa was displayed with hyperintense signal. One previous study characterized bone as hypointense and bovine bone mineral material in the maxillary sinus was initially as hyperintense and

not clearly distinguished from swollen mucosa in T1W MR images. Bone regeneration was interpreted, when the augmentation material appeared hypointense in T1 images after 104 days.<sup>38</sup> Other studies did not describe appearance of bone grafts in MR images and described mucosal swelling, exudate or blood retention in the maxillary sinus, all presenting with hyperintense signal in MR images.<sup>34,36</sup>

The delineation of bone grafts was performed by three examiners at the three different time points. The results for intraexaminer variation showed a wide confidence interval, which was interpreted as the difficulty to repeatably identify the bone graft outlines, especially in the presence of artifacts originating from osteosynthesis screws, dental restorations of adjacent teeth and in one patient a neighbouring dental implant. Previous studies on bone graft dimensions did not include repeated measurements of bone grafts and multiple examiners, respectively.<sup>15–17</sup> Therefore, no comparison can be made. To date there is a lack of an *in vivo* imaging method and evaluation protocol, which can be considered a validated and reliable standard to quantify the volume of bone grafts.

In one participant (no.1), an increase of bone volume between t1 and t3 was observed. This effect was explained with an imprecise measurement of graft volume due to image artifacts originating from surrounding teeth with metallic restorations. A high standard deviation and deviation between mean and median bone volumes underlines the difficulty to clearly delineate the graft volume in MR images of some participants.

Artifacts originating from titanium osteosynthesis screws were found in preliminary imaging of bone grafts in sheep jaws and were regarded as hindrance to display autologous onlay grafts with MRI (unpublished data). Using the VAT technique, these artifacts could be minimized, and bone grafts could be displayed with MRI. The benefit of artefact suppression with the VAT technique is associated with the compromise of a lower image resolution. It resulted in non-isometric image resolution which is a limitation with regard to multi planar display for subsequent implant planning. However, it did not hinder adequate measurement of bone grafts and was therefore beneficial in this study.

One limitation of this study was that the intraoral coil could not be placed due to postoperative mucosal swelling and mobilization of mucosa and subsequent flattening of the vestibulum. Especially in the first postoperative MR scan (1 week postoperatively), this led to a lower signal in the augmented region. The development of MR protocols producing comparable image quality not using an intraoral coil, but a standard head coil, could help to overcome that limitation, inherent to bone augmentation sites.

MRI is a safe procedure, if contraindications such as cardiac pacemakers, mechanical heart valves, metallic surgical clips and metallic foreign bodies are carefully regarded.<sup>45</sup> Claustrophobia and vast dental restorations are as well contraindications to MR imaging and were the reason for drop-out of three participants in this study.

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## Conclusion

To the knowledge of the authors, this is the first study that used MRI for the longitudinal observation of early healing of autologous onlay bone grafts. MRI is eligible for the display of autologous onlay bone grafts and longitudinal observation of bone graft dimension. In spite of the high image resolution achieved when using intraoral coils, artifacts and postoperative swelling complicate the reproducible delineation of grafts in the early healing period.

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