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MR visible localization device for radiographic-pathologic correlation of surgical specimens

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Abstract

Purpose—The detection of small parenchymal hepatic lesions identified by preoperative imaging remains a challenge for traditional pathologic methods in large specimens. We developed a magnetic resonance imaging (MRI) compatible localization device for imaging of surgical specimens aimed to improve identification and localization of hepatic lesions ex vivo.

Materials and methods—The device consists of two stationary and one removable MR-visible grids lined with silicone gel, creating an orthogonal 3D matrix for lesion localization. To test the device, five specimens of swine liver with a random number of lesions created by microwave ablation were imaged on a 3T MR scanner. Two readers independently evaluated lesion coordinates and size, which were then correlated with sectioning guided by MR imaging.

Results—All lesions ($n = 38$) were detected at/very close to the expected localization. Inter-reader agreement of lesion localization was almost perfect (0.92). The lesion size estimated by MRI matched macroscopic lesion size in cut specimen (± 2 mm) in 34 and 35, respectively, out of 38 lesions.

Conclusion—Use of this MR compatible device for ex vivo imaging proved feasible for detection and three-dimensional localization of liver lesions, and has potential to play an important role in the ex vivo examination of surgical specimens in which pathologic correlation is clinically important.

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Keywords

Small lesions; Detection; Characterization; Ex vivo

1. Introduction

Accurate identification and anatomic localization of small parenchymal lesions during pathologic sectioning of surgical specimens remains a challenging task. Ex vivo identification of lesions found on in vivo imaging can be particularly demanding due to deformation and altered orientation of the resected specimen. Furthermore, even if there were standardized methods of pathologic evaluation, especially with hepatic resection [1], it is difficult to discriminate lesions from adjacent parenchyma, leading to missed lesions.

In an explanted liver or hemi-specimen pathologists will generally perform 5–6 representative sections of the liver parenchyma including a cut at the resection margin, a cut at the hilum and a representative cut of the gall bladder. If hepatocellular carcinoma (HCC) lesions are known to be present clinically, additional sections of these regions are performed and a special silver staining is performed. In explanted livers that might carry additional lesions, each cut is searched grossly for additional lesions. Other pathologists cut the entire specimen in 5 mm slices and or even smaller intervals when needed. Unfortunately, pathologists do not routinely review the information about additional lesions that are suspected radiologically. In view of the clinical importance of the detection of all lesions [2–5], it is of significant interest to understand whether all radiographically identified “lesions” are indeed malignant. Similarly, it would be of clinical importance to know if all lesions detected pathologically are identified by preoperative imaging [6].

In order to facilitate lesion detection and improve direct comparison of histopathologic specimens with prior in vivo imaging, we developed an MRI compatible localization device, with MR-visible fiducial marks for ex vivo imaging to facilitate radiographic-pathologic correlation. The primary purpose of the present study was to first develop and then to test the feasibility of this device. Our secondary aim was to evaluate the sensitivity and specificity of its use in localizing simulated lesions in animal livers.

2. Materials and methods

2.1. Imaging device description

The device was constructed from Plexiglas and designed to consist of two stationary MR grids (along x, y-axis) and one removable grid (along z-axis) that together create a 3D matrix (Fig. 1). Total size of the device is $27 \times 14 \times 14 \text{ cm}^3$. Along the bottom and two sides, laser-etched grid lines and labels were filled with silicone gel (Dow-Corning, Midland, Michigan, US) to facilitate MR-visible fiducial landmarks. A small amount of red dye was added to the silicone to improve visibility of the edges and labels by eye. Laser etched numbers (1–11) were oriented along the width, upper case letters (A–W) along the length and lower case letters (a–l) along the height. All grid lines were spaced 1 cm apart (Fig. 2). This design facilitated three-dimensional localization and labeling within a 1.0 cm^3

volumes, with the combined lettering/numbering coding, for example “3, D, f” would be the code for a lesion located within that volume identified by the 3D grid.

When examining ex vivo tissue specimen, alginate is used to externally stabilize the tissue (e.g. liver) during imaging and to facilitate sectioning. The alginate used was Accu-Cast 880-B (Accu-Cast, Bend, Orgeon, US). After preparation as described in the manual, the bottom of the box is covered when the Accu-Cast starts to set (1–5 min, depending on the amount of Accu-Cast). Thereafter, the liver specimen is placed in the box and the remainder of the alginate is poured over the specimen casting it from all sides. Afterwards, the top piece (also imprinted with upper case letters and numbers, is placed, and gently imprinted onto the top surface of the alginate, marking a grid pattern. Once the alginate hardens to a soft solid within several minutes, MR examination of the device containing the tissue specimen is performed. Accurate localization of lesions in three dimensions is determined by referencing the lesions in space relative to the three dimensions of the MR-visible grid.

After lesion identification radiographically, the top piece and the vertically oriented grid along the length of the box are removed. Slicing of the specimen within the box is now enabled in a guided fashion through prefabricated grooves spaced 1 cm apart (Figs. 2 and 3) along the y-direction (width of the box). The slice positions correspond to the grid lines of the device. The grooves accommodate any commercially available sectioning knives.

2.2. Imaged specimen

To test the device, five separate specimens of swine liver were used for radiographic-pathologic correlation. In each specimen, lesions were created using a random number (0–15) of ultrasound-guided microwave ablation zones by an interventional radiologist. The number and location of the ablations were blinded to the two MR-readers. Ablations were carried out in different sizes between 5 and 15 mm, based on previous calibration of the time-energy deposition relationship [7].

2.3. MR-protocol

MR imaging was performed directly after embedding the liver in the box and setting of the alginate. A clinical 3T MR scanner (Discovery MR750 v25.0, GE Healthcare, Waukesha, WI) with a single channel head coil was used. Acquisition parameters of the high-resolution 3D spoiled gradient echo T1 weighted acquisition included: TR/TE = 9.8/4.1 ms, flip angle = 20°, BW = ±162 kHz, FOV = 280 × 252 × 180 mm³, 450 × 420 × 225 matrix, for true spatial resolution of 0.6 × 0.6 × 0.8 mm³ interpolated to 0.5 × 0.5 × 0.4 mm³ through zero-filling. Total scan time was 21:16 min.

2.4. Imaging analysis

Two radiologists blinded to number and localization of lesions independently analyzed the MR images using multiplanar reconstruction (MPR) images, maximum intensity projections (MIP) and the original acquired data sets. The total numbers and 3-dimensional coordinates of the lesions as well as lesion diameter (measured on MR images) were reported on a provided spreadsheet.

2.5. Pathological analysis and correlation

After analysis of MR data, the specimens were sliced according to the MR-analysis spreadsheet and lesions were measured within each slice using a ruler with 1mm spaced etching (Fig. 3B). If lesions were identified within the coordinate-slice and not on the cut planes between the coordinate slices, the cut section was cut again longitudinally to produce 5 mm thick sections. Pathologic findings were reported on the same spreadsheet as the radiographic data. For lesion verification, a 3-point Likert scale was used: If lesions were found exactly at the expected location, lesion verification was rated 2, if lesions were found in very close proximity (<1 cm), verification was rated 1 and the distance was measured. If the lesion was found >1 cm distant to the expected location, verification was rated 0.

2.6. Statistical analysis

Mean sizes of lesions as well as mean values of distances from lesions predicted on MRI to those seen at sectioning were reported. Sensitivity and specificity values for lesion detection for both readers were reported.

Inter-reader agreement was measured using Cohen's Kappa analysis. A κ value of 0–0.2 indicates slight, 0.21–0.4 fair, 0.41–0.6 moderate, 0.61–0.8 substantial and 0.81–1 almost perfect agreement after Landis and Koch [8].

3. Results

MR Imaging with the proposed device was feasible and all images were of high diagnostic image quality. In total, in five liver specimens, 38 lesions were created with ultrasound guided microwave ablation. Lesions measured between 5 and 12 mm (mean 8.2 mm $\pm$ 1.7). Three lesions showed a size of 5 mm, 27 lesions a size between 6 and 9 mm (mean 7.8 mm), while 8 lesions were 10–12 mm in size (mean 10.8 mm).

In one liver a total of 11 lesions was created, in a second liver 10 lesions, in 2 livers 6 lesions and in one liver 5 lesions. Both readers correctly identified the number and location all lesions in all specimens using MR images. No false positive lesion identification occurred. Reader 1 correctly located all lesions with MR imaging according to the macroscopic localization in specimen cuts for all 38 lesions (Likert scale 2). The second reader visualized one lesion 5 mm away from the location seen (Likert scale 1) in the cut specimen, all others at the exact localization (score 2). Inter-reader agreement of lesion localization was almost perfect (0.92).

Measured lesion sizes in MR Imaging compared to specimen cuts for both readers can be found in Table 1. There was no difference concerning the size of the lesion and trending towards over- or underestimation.

4. Discussion

In this work we have reported the design, and preliminary feasibility testing and evaluation of an MR-compatible device with visible 3D grid intended for radiographic-pathologic correlation in ex vivo hepatic specimens with parenchymal lesions. Use of the device proved

feasible with 100% accuracy for both readers on a per specimen and per lesion basis. Only 4 respectively 3 lesions were under- or overestimated in size (± 3 or 4 mm) when compared to gross pathological evaluation.

Comparison between MR Imaging and ex vivo pathologic assessment is important for many fields of medicine. In 2005, Eriksson et al. demonstrated a tool to cut and correlate brain specimen after temporal lobe resections in patients with epilepsy [9]. They showed that preoperative MRI datasets matched confidently with histopathology using uniform slice thickness and slice angles. Furthermore, different devices have been developed for sectioning prostatectomy specimen, that facilitate comparison between histology and in vivo MRI [10,11]. The device present in this work, allows for a similar comparison between MR Images and gross pathologic assessment.

In contrast to the referenced papers, our device allows for cutting the specimen into 1 cm parallel cuts of tissue. Those slices may further be cut in narrower intervals if no lesion is found on the initial cut surface. Assuming that a comparably high sensitivity can be achieved in clinical specimens from patients, our device may enable guided and focused pathologic analysis in contrast to analyzing specimens blindly, with a greater chance to miss small lesions. This could result in a higher sensitivity of pathologic examinations especially of larger surgical specimens (e.g. hemi-liver specimens).

Furthermore, pathologic examination time could potentially be reduced as analyses can be performed with guidance of the ultrahigh resolution ex vivo MR-scan. To the best of our knowledge, the device we present in this work is the first one to use for ex vivo liver imaging. As alginate is used for casting and preserved orientation once the specimen has been placed, the device may have important applications other specimen types, such as the pancreas or kidneys, where the orientation and pathological analysis of the specimen presents challenges, particularly when multiple lesions are present. It is unlikely that the alginate changes the specimen, as it does not enter the tissue. In principle, the device can be used for fixed and non-fixed specimens.

In this work we demonstrated the feasibility of our device in swine livers with lesions created with ultrasound guided radiofrequency ablations. Therefore, the sizes of the lesions ranged between 5 and 12 mm and had a very uniform, simply to detect pattern in the T1 weighted sequence with the high resolution we used for imaging acquisition. In this study, only T1 weighted MR imaging was performed. To optimize image contrast in clinical studies, acquisition of MR-sequences with different contrast mechanisms such as T2- and diffusion-weighting. MR- scanning parameters will likely require further optimization for specific tissue types and diseases. Opportunities to optimize imaging include administration of intravenous MR-contrast agents (e.g. gadoxetic acid) immediately before or during surgical resection.

Further evaluation of the device will include evaluation of human hepatic specimens, examining ex vivo imaging for lesion identification and localization in patients with HCC or metastatic disease. In these settings, the use of gadoxetic acid enhanced imaging, will be of interest to ensure detection of small lesions [12–14]. Preoperative MR Imaging using

gadoxetic acid will be an additional target for comparison in that setting. Future studies must also demonstrate the feasibility of this approach to evaluate its generalizability in the clinical setting.

5. Conclusions

We have developed and tested an MRI compatible device for ex vivo specimen imaging and 3D localization. The MR-visible 3D grid proved feasible for detection and three-dimensional localization of liver lesions with 100% sensitivity and specificity. Use of this device in the clinical setting has the potential to play an important role in improving radiographic-pathologic correlation.

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Fig. 1.
Box components shown how they appear on MR Imaging. All engraved letters and numbers can clearly be seen on MRI. The schematic three-dimensional coordinate system shows how width, length and heights are labeled.

Fig. 2. Multiplanar reconstruction (MPR) of the MR Images of the box with loaded liver (A, axial view). Note that the alginate (blue component in B) is not showing up in MR Imaging. Multiple microwave ablations in different sizes can be seen (arrowheads) in the liver specimen as well as the upper cases on the bottom piece of the box. Arrows in B point to the slicing channels every 1 cm.

Fig. 3.

View of the cut tissue specimen in the box (A), outside the box for lesion measurements and localization (B) and as appearing on MR Imaging (C). Note the correlation of the liver lesion (arrow) ex vivo and on MR Imaging. On MR Imaging the grid can be seen as marked lines and dots (arrowheads in C), depending on the orientation.

Table 1
Lesion size evaluation and its deviation in mm in MR Imaging compared to pathology for both readers.

		MR size deviation compared to pathology (in mm)						
		-3/-4	-2	-1	0	+1	+2	+3/+4
Reader 1	3	7	6	10	11	0	1	
Reader 2	1	6	11	13	2	3	2	