Ex-vivo MR imaging of excised human livers as a new method to reliably co-localize nodules and nodule components on imaging and pathology: preliminary 6-month experience

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Background: MR imaging plays a pivotal role in assessing liver nodules (1), and is used to detect and stage hepatic malignancies (2), guide surgical and non-surgical management, and differentiate benign from malignant nodules. However, MR has limited sensitivity and specificity for small nodules and relative inability to predict histological grade of tumors. One important obstacle to improving MR diagnosis of nodules is that currently there is no reliable method to spatially co-localize nodules and nodule components at MR imaging and at pathology. Several strategies to spatially co-localize small nodules and nodule components on pre-operative *in-vivo* imaging and pathology (3,4) have been employed in the past, including detailed pathological descriptions, schematics, and overlay grids. However, such approaches are flawed because the liver's shape and orientation are altered after excision, and sectioning the specimen in the *in-vivo* imaging plane to ensure spatial co-localization of small nodules and nodule components is not possible. To address these problems, we recently implemented a system in which the liver specimen is imaged *ex-vivo* after resection or explantation. *Ex-vivo* imaging serves as a link to spatially co-localize *in-vivo* imaging and *ex-vivo* pathology findings. The purpose of this abstract is to describe our technique and our preliminary six-month experience.

Materials and Methods: Fixation. After specimen procurement, the portal veins, hepatic veins and hepatic arteries of the specimen are cannulated and 10% formalin is infused by manual pressure. This rapidly and uniformly distributes the fixative throughout the specimen. Fixation firms the liver, facilitating subsequent thin sectioning in the *ex-vivo* imaging plane.

Ex-vivo imaging. Fixed specimens are placed in non-ferromagnetic containers and imaged *ex-vivo* at 3T. (Initially, the specimens were sectioned by the pathologist and then imaged *ex-vivo*. However, in the first two cases done in this manner, *ex-vivo* imaging identified a total of 25 sub-cm nodules missed by the pathologist; these nodules were sampled histologically after imaging-directed re-sectioning and were confirmed to be malignant. Since then, specimens have been imaged *ex-vivo* prior to sectioning). High-resolution SE, FSE, and GRE sequences are obtained in different planes with fixed FOV (**Table**). ^{1}H MRS is performed in selected voxels using the STEAM sequence. Whole livers are imaged using a cardiac-phased array coil. Smaller specimens are imaged with a 3-inch coil.

Table. Ex-vivo Imaging Parameters for Scanning Whole Liver Explants

Sequence	TR	TE	ST	Resolution
ME SE	3000+	13-109msec	2-4 mm	384 x 224
T2w FSE	3000+	30-60msec	2-4 mm	448 x 320
DW SE (b=0, 600)	3000+	45msec	2-4 mm	384 x 192
T1w GRE (3D)	6.0	2.0msec	1 mm	280 x 280
ME GRE	15	1.2-7.7msec	2-4 mm	192 x 192
MRS (STEAM)	3500	10msec	15mm^3 voxel	

ME SE = multi-echo spin echo (generates T2 map), FSE = fast spin echo, DW = diffusion weighted, SE = spin echo, GRE = fast gradient recalled echo, ME GRE = multi-echo GRE (generates fat fraction and T2* maps), MRS = magnetic resonance spectroscopy, STEAM = stimulated echo acquisition mode, ST = slice thickness, TR = Repetition time, TE = echo time

Sectioning. Post *ex-vivo* imaging, livers are sectioned into 3-mm slices in the *ex-vivo* imaging plane by the pathologist and radiologist working in conjunction. Sectioning the liver is straightforward because the liver is firm post fixation. Occasionally a section is reimaged to localize small nodules (<5mm) and nodule components not visible on cut surfaces of specimens. Co-localization. Using landmarks (architectural, vascular, etc), nodules and nodule components are located on pre-operative *in-vivo* imaging studies (using 3D reformation of *ex-vivo* or *in-vivo* images on a workstation) and also on pathology sections. Once located on pathology sections, nodules and nodule components are submitted for histology.

Results and Discussion: In six months, we performed *ex-vivo* imaging on 46 livers (27 cirrhotic and 19 non-cirrhotic). Spectrum of cases included HCC (n=26 patients), regenerative nodules (n=7), metastases (n=5), peribiliary cysts (n=1), hepatic adenoma (n=1), hemangioma (n=1), focal nodular hyperplasia (n=1), embryonal sarcoma (n=1) and other (n=3). Images with high signal- and contrast-to-noise ratios were consistently obtained without physiological or other artifacts. Using the *ex-vivo* images as a key link between the *in-vivo* images and pathology, we successfully co-localized each nodule seen at *in-vivo* imaging, permitting reliable histological sampling of nodules. The combined use of *ex-vivo* imaging and pathology detected 32 nodules (2 – 8 mm in size; 29 malignant, 3 benign) in three patients not visualized at *in-vivo* imaging (**Fig 1**) even on retrospective review. In the other 43 patients, no additional nodules were detected by the combined use of *ex-vivo* imaging and pathology. However, in these patients, *ex-vivo* imaging helped to co-localize nodule components (e.g., tumor septa and capsules; capsular disruption; perilesional nodules, infiltration, and vascular invasion; intralesional necrosis and hemorrhage) (**Fig 2**). Intrahepatic venous gas may produce susceptibility artifacts but these were negligible with appropriate selection of bandwidth, sequence and spatial resolution.

Conclusion: We implemented a system in which liver specimens are imaged *ex-vivo* prior to pathology sectioning. In our six-month preliminary experience, *ex-vivo* MR liver imaging permits accurate image-guided tissue sampling and reliable radio-pathological correlation of small nodules and nodule components. It helps identify small nodules that may be missed by routine pathology sectioning. It serves as a link between *in-vivo* imaging and pathology and helps to locate on pathology sections small nodules and nodule components identified at *in-vivo* imaging. With further refinement, this approach may develop as a versatile research tool leading to a better understanding of the imaging and histological features of liver nodules.

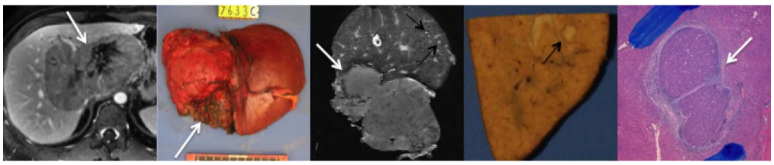

Fig 1: 54-year-old male with large HCC on *in-vivo* (A) and gross pathology (B) images (arrows). *Ex-vivo* images (C) show 2 nodules 2 mm in size (black arrows) not seen on *in-vivo* images. Pathology section (D) and H & E image (E) show a co-localized 2 mm nodule, which was a pathologically proven HCC (white arrow).

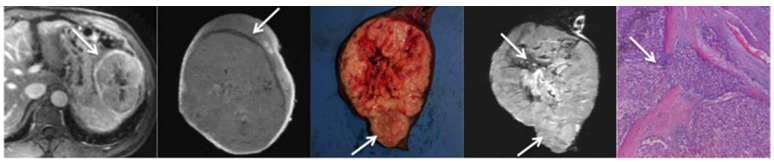

Fig 2: 60-year-old male with HCC. *In-vivo* image (A) showing left lobe exophytic HCC with *ex-vivo* (B) image of specimen (arrows). Pathologic section (C) of mass and ex-vivo axial image (D) (black arrows) co-localizes nodule components like hemorrhage, scars, capsule and extracapsular extension (inferior arrow) seen on H & E image (E).

References

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