Clinically Practical MRI/MRS Protocol for Improved Specificity in Breast Cancer Diagnosis

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Synopsis The goal of this study was to determine if a combined MRI/MRS protocol of dynamic contrast enhancement (DCE) T_1-weighted MRI, ^{1}H MRS, and perfusion MRI improves specificity in detection of breast malignancy. 61 patients with positive mammography findings were studied. After DCE MRI showed fast contrast enhancement, single-voxel ^{1}H MRS and perfusion MRI examinations were performed. DCE MRI showed 100% sensitivity and 76% specificity in detection of breast cancer. The specificity improved to 89% with the addition of ^{1}H MRS, and to 96% with the further addition of perfusion MRI.

Introduction Conventional mammography is known to have high false positive rate (60-80%) in detection of breast malignancy, resulting in unnecessary biopsies. In recent years, DCE T_1-weighted MRI demonstrated high sensitivity (88-100%), but rather variable specificity (37-97%) in diagnosis of breast cancer (1). *In vivo* ^{1}H MRS showed excellent specificity in detection of malignant breast tumor (2), using the resonance of choline-containing compounds (Cho) as the marker of viable tumor. Perfusion MRI was used to distinguish benign from malignant breast tumors based on high vascularity of the latter (3).

In this study, an MRI/MRS protocol including DCE MRI, ^{1}H MRS, and perfusion MRI was used to examine patients with suspicious breast lesions. By correlating MR data with pathology results, we sought to determine if this clinically practical MRI/MRS protocol improves the specificity in detection of breast malignancy.

Methods 61 patients with positive mammography findings were recruited to participate in this MR study thus far. Biopsy was performed after but usually within a week of the MR examination.

The MRI/MRS protocol was conducted with a 1.5 T Marconi Edge whole-body scanner with the body coil as the transmitter and a dedicated phased array breast coil as the receiver. For DCE T_1-weighted MRI, a 3D SPGR sequence was employed to acquire 8 frames of sagittal volumetric images of the whole breast with suspicious lesions, with 30^o flip angle, TE = 3.8 ms, TR = 9 ms, 3-5 mm slice thickness, 24 cm FOV and 64x256 matrix size. Usually each frame included 18-26 slices and the acquisition time for each frame was less than 16 sec. Gd contrast agent (0.1 mmol/kg dose) was delivered at 2 cc/sec by IV injection at the start of the second frame acquisition. The images of the first frame were subtracted from images of every frame. Rapid contrast enhancement in lesions with signal intensity reaching plateau by the fourth frame was defined as positive finding. Any enhancement with continuous rising of signal intensity through eight frames or no enhancement was defined as negative finding. The study was discontinued for patients with negative findings. Patients with positive findings, with further consent, continued to undergo ^{1}H MRS and perfusion MRI examinations.

Single-voxel proton spectrum was collected from the enhanced lesion with a PRESS sequence, TE = 135 ms, TR = 2 s, and 128 scan averages. Perfusion MRI was performed on a 5-mm single sagittal slice containing the enhanced lesion with a T_2*-weighted FLASH sequence, 10^o flip angle, TE = 35 ms, TR = 54 ms, 24 cm FOV, 92x256 matrix size, and 40 frames. IV injection of Gd contrast agent (0.1 mmol/kg) was carried out at 4 cc/sec during perfusion MRI acquisition. The detection of an apparent Cho peak (S/N > 2) at 3.23 ppm was defined as positive finding for the MRS study. The relative blood volume map was generated from the perfusion imaging data. The striking enhancement in the lesion area on the map compared to normal tissue area was defined as positive finding for the perfusion MRI study.

Results Fig. 1a shows a image obtained from the DCE MRI experiment. This image was the result of subtraction of the first frame image from the third frame image, revealing an enhanced lesion. The placement of a spectroscopic voxel, encompassing the enhanced area, is also shown in the figure. Fig. 1b shows the time course of image signal intensity from an enhanced lesion of another patient. The intensity reached plateau by the fourth frame, implying positive findings of DCE MRI for this patient. Fig. 2 shows a representative magnified proton spectrum collected from an enhanced lesion of a patient with positive DCE MRI findings. An apparent Cho peak was detected, indicating positive MRS findings. Fig. 3 shows the relative blood volume map of the patient whose DCE MRI image is shown in Fig. 1a and the findings were positive. The strong ring enhancement was seen in the lesion area, revealing high vascularity of the tumor and positive findings for the perfusion MRI study. The MR and pathology results of the 61 patients are summarized in the Table.

Based on the pathology results, there were no false negative findings from DCE MRI studies, showing 100% sensitivity of this method. 10 out of 41 patients with positive DCE MRI findings turned out to have benign lesions, resulting in 76% specificity of this method. With the addition of ^{1}H MRS data, the specificity in detection of breast malignancy improves to 89%. With further addition of perfusion MRI results, the specificity improves to 96%.

Discussion This study shows that while DCE MRI has very high sensitivity in diagnosis of breast cancer, its specificity is unsatisfactory. The MRI/MRS protocol of combined use of DCE MRI, ^{1}H MRS and perfusion MRI techniques substantially improves specificity in detection of breast malignancy and may help to reduce unnecessary biopsies following positive mammograms. It appeared that the false positive findings of ^{1}H MRS studies, which were mostly from fibroadenomas, could be corrected by taking into account the perfusion MRI data. With its technology easy for implementation and its data easy for interpretation by physicians, this MRI/MRS protocol may have the potential for large-scale clinical applications in breast cancer diagnosis.

References 1. Padhani, A.R. *JMRI* **16**, 407 (2002). 2. Yeung, D.K.W. *et al.*, *Radiology* **220**, 40 (2001). 3. Kvistad, K.A. *et al.*, *Acta Radiol.* **40**, 45 (1999).

Table MRI/MRS and Pathology Findings of Patients with Breast Lesions

Patient No.	DCE MRI	MRS	Per. MRI	Path.
13	+	*	*	mag.
20	-	*	*	ben.
18	+	+	+	mag.
6	+	-	-	ben.
1	+	-	+	ben.
1	+	+	-	ben.
2	+	+	*	ben.

Per. = perfusion; Path. = pathology; + = positive findings; - = negative findings; * = MR scans discontinued due to negative DCE MRI findings or at patient's request; mag. = malignant; ben. = benign