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Role of apparent diffusion coefficient values for the differentiation of viable and necrotic areas of breast cancer and its potential utility to guide voxel positioning for MRS in the absence of dynamic contrast-enhanced MRI data

Uma Sharma[a], Rani G. Sah[a], Rajinder Parshad[b], Raju Sharma[c], Vurthaluru Seenu[b], Naranamangalam R. Jagannathan[a,*]

[a]Department of Nuclear Magnetic Resonance, All India Institute of Medical Sciences, New Delhi-110029, India
[b]Department of Surgery, All India Institute of Medical Sciences, New Delhi-110029, India
[c]Department of Radio-diagnosis, All India Institute of Medical Sciences, New Delhi-110029, India

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Abstract

We carried out retrospective analysis of apparent diffusion coefficient (ADC) values in 48 infiltrating ductal breast cancer patients who had dynamic contrast-enhanced magnetic resonance imaging (DCEMRI; Group I) and in 53 patients (Group II) for whom DCEMRI data were not available. Twenty-three patients of Group I showed no necrosis (Group Ia), while in 25 patients, both viable (nonnecrotic) and necrotic tumor areas (Group Ib) were observed on DCEMRI. T1-weighted, fat-suppressed and short inversion recovery images were used to identify the viable and necrotic tumor areas in Group II patients, and necrosis was not seen in 11 patients (Group IIa), while 42 (Group IIb) showed both viable and necrotic tumor areas. The ADCs of the necrotic area of Group Ib ($1.79 \pm 0.30 \times 10^{-3}$ mm^2/s) and Group IIb ($1.83 \pm 0.40 \times 10^{-3}$ mm^2/s) patients were similar and significantly higher ($P<.01$) compared to the ADCs of the viable tumor area of Group Ia ($0.96 \pm 0.21 \times 10^{-3}$ mm^2/s) and Group IIa ($0.90 \pm 0.17 \times 10^{-3}$ mm^2/s) patients. Proton MR spectroscopy (MRS) data were also available in these patients, and the ADC values were retrospectively determined from the voxel from which MR spectrum was obtained. These values were compared with the ADC obtained for the viable and necrotic areas of the tumor. ADC of the MRS voxel was similar to that obtained for the viable tumor area in patients of both groups. This interesting observation reveals the potential utility of using ADC values to identify viable tumor area for positioning of voxel for MRS in the absence of DCEMRI data.

Keywords: Dynamic contrast-enhanced magnetic resonance imaging (DCEMRI); Magnetic resonance spectroscopy (MRS); Diffusion-weighted imaging (DWI); Apparent diffusion coefficient (ADC); Breast cancer; Necrosis

1. Introduction

In India, more than 70% of the breast cancers are locally advanced breast cancers (LABCs) that are treated with neoadjuvant chemotherapy (NACT) due to inoperable tumor size. Malignant breast tissues exhibit total choline (tCho) resonance at 3.2 ppm in the in vivo proton magnetic resonance spectroscopy (^{1}H MRS), which has been used as a potential biomarker for diagnosis and for assessment of early response of breast tumors to NACT [1–5]. Large-sized tumors like LABCs tend to undergo central necrosis or fibrosis and may have nests of necrotic regions. Therefore, it is crucial to identify the viable tumor regions for optimal detection of tCho signal in ^{1}H MRS. Dynamic contrast-enhanced magnetic resonance imaging (DCEMRI) is a useful method for the differentiation of viable (nonnecrotic) and necrotic areas of the tumor [6,7] and has been used to localize the voxel position in the viable areas of the tumor for MRS [8]. However, in patients with poor socioeconomic status who are unable to afford the cost of contrast, it is

* Corresponding author. Tel.: +91 11 2659 3253; fax: +91 11 2658 8663.
E-mail addresses: jagan1954@hotmail.com, nrjgj@yahoo.co.in (N.R. Jagannathan).

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essential to explore alternative methods to identify the necrotic parts of the tumor, so that voxel may be appropriately positioned in viable tumor area for MRS studies.

Diffusion-weighted imaging (DWI) measures the Brownian motion (diffusion) of water molecules in tissues, and the DWI-derivable apparent diffusion coefficient (ADC) values are lower in tissues than the ADC of free water due to restrictions imposed by the tissue structure [9]. Factors like molecular viscosity, permeability, transport of molecules, directionality of structures and cellularity have an effect on the diffusion of water in tissues. Previous studies have established a relationship between ADC values and the tumor cell density [10,11]. Due to the sensitivity of ADC to tissue structure, DWI has been evaluated in grading of brain tumors like gliomas and astrocytomas [12,13]. The DWI technique has also been documented as an important method for the differentiation of malignant, benign and normal breast tissues [10,14–16]. In addition, the potential of DWI in monitoring the treatment response of breast tumors has been reported [17–20]. Recently, Matsubayashi et al. investigated the correlation of ADC values in invasive ductal carcinomas with the histological features and enhancement ratios on DCEMRI [21]. They reported that enhancement ratios of breast carcinomas on DCEMRI and ADC can provide detailed histological or biological information about the tumors. DWI reflected the growth patterns of carcinomas, including cellular density and architectural features of the stroma [21].

Several studies have documented the use of ADC values in the differentiation of viable and necrotic part of the brain tumors [6,7] and hepatic lesions [22]. However, no systematic study is available in the literature evaluating the use of ADC in the characterization of viable and necrotic tumor regions in breast cancer patients. Therefore, in the present investigation, our objectives were (a) to carry out retrospective analysis of ADC values of viable and necrotic regions of the breast tumor in 48 infiltrating ductal carcinoma (IDC) patients who had DCEMRI (Group I) and in 53 patients for whom DCEMRI data were not available (Group II), (b) to determine retrospectively the ADC values from the voxel from which the MR spectrum was obtained in all these patients and (c) to compare the ADC values of the MRS voxel with the values obtained for the viable and necrotic areas of the tumor in patients of both groups. We envisage that the ADC values of viable and necrotic regions obtained through DWI may be useful in planning the voxel position for MRS acquisition that may help increase the sensitivity of detection of tCho signal.

2. Patients and methods

2.1. Patients

The ADC values of a total of 101 women with cytologically proven IDC attending the breast cancer clinic of our Institute during the period 2007–2011 were analyzed. The following inclusion criteria were adopted for the recruitment of patients. Only patients with IDC were included. None of the patients had undergone any hormonal, chemotherapy or radiotherapy prior to the MR scan. Written informed consent was obtained from each patient, and the study was approved by the institutional ethical committee.

The American Joint Committee on Cancer TNM staging criteria based on the investigation of the primary tumor size (T), the regional lymph nodes status (N) and the distant metastases (M) were followed for the clinical staging of the breast cancer patients. There were 18 patients (mean age 47.2±11.4 years; 7 premenopausal and 11 postmenopausal) in stage IIA, 17 in stage IIB (mean age 44.2±9.9 years; nine premenopausal and eight postmenopausal) and IIIA (mean age 43.2±10.2 years; nine premenopausal and eight postmenopausal) and 49 patients in stage III (B+C) (mean age 47.0±9.9 years; 22 premenopausal and 27 postmenopausal).

Breast cancer patients with metastasis, claustrophobia, prior treatment, metallic implants or pacemaker; those who were pregnant or were using contraceptive pills; and those not willing to take part in the study were excluded.

2.2. MR examination

All MR investigations were performed using a four-channel phased array breast matrix coil at 1.5 T (Magnetom AVANTO, Siemens Healthcare Sector, Germany). Subjects were positioned prone with each breast fitting into the cup of the coil. Following the scout image, short inversion recovery (STIR) coronal images were acquired [repetition time/echo time (TR/TE)=6940/58 ms, slice thickness=3 mm, matrix size=320×256]. Also, fat-suppressed MR images were acquired in the transverse and sagittal planes with the following parameters: TR/TE=6270/102 ms, slice thickness 3 mm with no gap, matrix size=512×440. DCEMRI was carried out in 48 patients in the axial plane using a fat-saturated three-dimensional fast low angle shot magnetic resonance imaging with the following parameters: TR/TE=5.46/2.53 ms, flip angle 12°, matrix size=305×448, slice thickness=1.4 mm with no gap. The dosage of the gadodiamide (GdDTPA-BMA) contrast given to each patient depended on the weight of the patient (0.1 mmol/kg) at a rate of 2 ml/s followed by saline flush using an automatic injector. One pregadolinium image series followed by five postgadolinium image series was acquired with a total acquisition time of 5.5 min (6×55 s).

2.3. Diffusion-weighted MRI

DWI was carried out in all 101 patients in the axial plane covering both the breasts using a single shot echo planar imaging (EPI) sequence with the diffusion gradients applied along the orthogonal direction concurrently to reduce motion artifacts. The parameters used were b=0, 500 and 1000 s/mm^2; TR=5000 ms; TE=87 ms; field of view=250–350 mm; number of scans=1, EPI factor=128;