Preliminary study of early response to neoadjuvant chemotherapy after the first cycle in breast cancer: comparison of $^1$H magnetic resonance spectroscopy with diffusion magnetic resonance imaging

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Abstract

Purpose. The aim of this study was to assess the efficacy of single-voxel $^1$H magnetic resonance spectroscopy (MRS) at 1.5 T to evaluate early responses to neoadjuvant chemotherapy after the first treatment in breast cancer patients and to compare it to measurements of apparent diffusion coefficient (ADC) values derived from diffusion-weighted magnetic resonance imaging (MRI).

Materials and methods. Nine patients with breast cancer who were scheduled to receive neoadjuvant chemotherapy were recruited. MR examination after the first cycle was scheduled for a few days before the administration of the second dose.

Results. Two patients were excluded from the study because their regimen was changed after the first cycle. MRS before chemotherapy demonstrated the presence of choline (Cho) at 3.22–3.23 ppm in six cases and at 3.27 ppm in one case. Diffusion-weighted MRI before chemotherapy demonstrated a localized high-signal lesion in all cases. The change of the integral value of Cho after the first cycle of chemotherapy showed a positive correlation with the change in lesion size ($r = 0.91$, $P = 0.01$), whereas no correlation was observed between the change of ADC values after the first cycle and the change in lesion size ($r = 0.45$, $P = 0.32$).

Conclusion. MRS after the first cycle may be more sensitive to diffusion-weighted MRI to predict the pathological response.

Key words Breast cancer · Proton MRS · Diffusion-weighted imaging · Neoadjuvant chemotherapy · Therapeutic response

Introduction

Neoadjuvant chemotherapy has been one of the standard therapies for the treatment of stage II and III breast cancer.1–3 The current purposes of imaging during and after neoadjuvant chemotherapy are to evaluate the extent of residual disease and try to predict the pathological response early after the initiation of treatment.

Conventional monitoring of patients with breast cancer during chemotherapy is achieved with physical examination, mammography, and ultrasonography. However, these techniques suffer from low sensitivity to changes in tumor size.4 Recent studies have shown magnetic resonance imaging (MRI) to be superior to physical examination, ultrasonography, and mammography for revealing breast cancer extent and for assessing residual disease after chemotherapy.5–7 Furthermore, kinetic information obtained with dynamic MR protocols has been shown to be suitable for monitoring.8,9

Recently, in vivo proton MR spectroscopy (hydrogen $^1$H MRS) of the breast is demonstrating great promise in the early evaluation of the effects of chemotherapeutic agents.10–12 Meisamy et al.12 reported tumor response to neoadjuvant chemotherapy was evaluated using single-voxel $^1$H MRS at 4 T. In this study, 13 patients with locally advanced cancer were evaluated before and
within 24 h after the first dose and after the fourth dose. The change in the choline (Cho) concentration from baseline to within 24 h after the first dose showed a significant positive correlation with the change in lesion size.

In contrast, diffusion-weighted MRI can be used to detect changes in the apparent diffusion coefficient (ADC) for tissue water associated with changes in tissue and intracellular structure.13,14 Galons et al.15 reported that the ADC in breast cancer increased early in response to successful therapies. Sharma et al.16 reported that the ADC was more useful for predicting early tumor response to chemotherapy than morphological variables. Treatments that caused cells to shrink led to early increases in ADC that were predictive of the ultimate tumor response.

The purpose of this study was to assess the efficacy of 1H MRS at 1.5 T to evaluate early responses to neoadjuvant chemotherapy after the first treatment in breast cancer patients and to compare it to measurements of ADC values derived from diffusion-weighted MRI.

Materials and methods

Patients

Between April 2007 and January 2008, nine patients (age range 27–61 years, mean 49 years) with biopsy-confirmed operable breast cancer who were scheduled to receive anthracycline- or taxane-based neoadjuvant chemotherapy after the first treatment in breast cancer patients and to compare it to measurements of ADC values derived from diffusion-weighted MRI.

Materials and Methods

Patients

Between April 2007 and January 2008, nine patients (age range 27–61 years, mean 49 years) with biopsy-confirmed operable breast cancer who were scheduled to receive anthracycline- or taxane-based neoadjuvant chemotherapy after the first treatment. In this study, two MRI examinations were performed with the use of contrast material, one before chemotherapy and one before surgery. One more MRI examination without contrast material was scheduled for a few days after the administration of the second dose. The study protocol was approved by the authors' institutional review board. Informed written consent was obtained from all of the patients.

Tumor response to chemotherapy was assessed based on the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines.17 Tumor sizes were measured on coronal and sagittal contrast-enhanced MRI and on transverse multiplanar reconstructions of contrast-enhanced MR images. The maximum size of each tumor was recorded.

Magnetic resonance imaging

The MRI was performed using a 1.5-T system (Avanto; Siemens Medical Solutions, Erlangen, Germany). All patients were examined in a prone position. A double breast coil (breast matrix coil; Siemens Medical Solutions) was used for both MRI and MRS. Before the administration of contrast material, bilateral sagittal fat-suppressed T2-weighted images (TR/TE 4780/97 ms; field of view (FOV) 16 cm; matrix 256 × 256; slice thickness 3 mm; gap 0; time of acquisition 78 s) and coronal T1-weighted images (TR/TE 8/4.8 ms; flip angle 25°; FOV 33 cm; matrix 320 × 320; interpolated slice thickness 3 mm; partition 40; time of acquisition, 52 s) were obtained. In addition, coronal diffusion-weighted images were acquired with a spin-echo-type single-shot echo-planar imaging sequence incorporating the generalized autocalibrating partially parallel acquisition (GRAPPA) algorithm for parallel acquisition. The parameters were as follows: TR/TE 8000/96 ms; FOV 33 cm; matrix 110 × 110; receiver bandwidth 1684 Hz/pixel; parallel acquisition factor 2.0; slice thickness 3 mm; gap 0; time of acquisition 2.5 min. Motion-probing gradient pulses were applied along the X, Y, and Z directions with b values of 500, 1000, 1500, 2000, and 3000 s/mm², respectively. Spectrally adiabatic inversion recovery (SPAIR) was used for fat suppression.

Dynamic MRI using a three-dimensional fat-suppressed volumetric interpolated breath-hold examination (VIBE) sequence with parallel acquisition was obtained before and three times after the bolus injection of 0.1 mmol Gd-DTPA/kg (Magnevist; Bayer Schering Pharma, Berlin, Germany) at a rate of 2 ml/s, followed by a 20-ml saline flush using an automatic injector. Both breasts were examined in the coronal plane on first-, second-, and third-phase dynamic images, acquired at 30 s, 1.5 min, and 4.5 min, respectively. The dynamic MRI parameters were as follows: TR/TE 5.2/2.3 ms; flip angle 12°; FOV 33 cm; matrix 448 × 318; receiver bandwidth 430 Hz/pixel; interpolated slice thickness 0.9 mm; partition 144; time of acquisition, 60 s. The right and left breasts were examined sagittally using the VIBE sequence without parallel acquisition at 2.5 and 3.5 min (i.e., between the second- and third-phase images, respectively) (TR/TE 4.0/2.2 ms; flip angle 15°; FOV 16 cm; matrix 256 × 256; receiver bandwidth 390 Hz/pixel; interpolated slice thickness 1.2 mm; partition 80; time of acquisition 60 s).

Non-contrast-enhanced MRI after the first cycle of chemotherapy included sagittal fat-suppressed T2-weighted images, coronal T1-weighted images, and coronal diffusion-weighted images.

1H magnetic resonance spectroscopy

After scanning with all of the MRI sequences, single-voxel 1H MRS was performed using a point-resolved spectroscopy sequence (PRESS).18 The parameters of