Detecting Breast Cancer with Non-contrast MR Imaging:
Combining Diffusion-weighted and STIR Imaging

Seiko KUROKI-SUZUKI*, Yoshifumi KUROKI2, Katsuhiro NASU2, Shigeru NAWANO2, Noriuki MORIYAMA1, and Masatoshi OKAZAKI3

1Research Center for Cancer Prevention and Screening, National Cancer Center
5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan
2Department of Diagnostic Radiology, National Cancer Center Hospital East
3Department of Radiology, Fukuoka University School of Medicine
(Received November 9, 2006; Accepted February 14, 2007)

We combined diffusion-weighted (DWI) and short TI inversion recovery (STIR) imaging to evaluate the diagnostic capability of non-contrast magnetic resonance (MR) imaging to detect breast cancer. Seventy women patients underwent mammography and MR imaging with combined DWI (b factor: 1000) and STIR that revealed malignancy, and postoperative pathological examination confirmed breast cancer. Interpreted images were evaluated for sensitivity, false negative rate (FN), sensitivity by pT, and sensitivity by background density of the mammary gland. Of the 70 cases, 68 were diagnosed as cancer by DWI and STIR (sensitivity, 97±68/70; FN, 2.9±2/70). Sensitivities by pT were: pTis, 67% (4/6); pT1, 100% (33/33); and pT2–4, 100% (31/31). No significant differences were observed in sensitivity between pT1 and pT2–4 (P<0.001). Sensitivities by background density of mammary gland were: fatty scattered fibroglandular tissue, 95% (20/21) and heterogeneous fibroglandular tissue/mostly fibroglandular tissue, 98% (48/49). No significant differences were observed (P<0.001). Two cases, an intraductal and an apocrine carcinoma, were incorrectly diagnosed by MR imaging.

Precise diagnosis of breast cancer is possible with combined DWI and STIR, even in non-contrast MR imaging, regardless of the diameter or background density of mammary gland. It is hoped that non-contrast MR imaging that combines DWI and STIR will become an established clinical screening method.

Keywords: breast cancer, MRI, diffusion-weighted image (DWI), STIR

Introduction

As research on high-risk breast cancers has progressed, gene mutation and family and patient history of breast cancer have been accepted as risk factors.1,2 Several reports show that about 80% of women with BRCA-1 and BRCA-2 gene mutations developed breast cancers by age 70.2–4 It is accepted that a patient with a strong family history has a greater risk for developing nonhereditary, sporadic breast cancer as well as so-called “hereditary” breast cancer.2–5 For a patient with a personal history of breast cancer, the probability of developing cancer in the contralateral breast is reported to be 2 to 6 times higher than that of a patient without such history.6–8 Moreover, the probability of developing breast cancer is known to be significantly higher for a patient having a history of radiation therapy in the chest region.9 In those at high risk, medical examination from the early years of life is recommended. However, even conventional examination based on mammography (MMG) and clinical breast examination (CBE) may fail to detect lesions hidden by dense breast tissue.10–12

Remarkable progress has been made in MR imaging technology, and its time resolution and spatial resolution have been improved.13 Consequently, lesion morphology and analysis of enhancement pattern using Gd-DTPA enable diagnosis of breast cancer and precise determination of the extent of intraductal components, which were previously difficult to diagnose by MMG or ultrasound (US).14–16
Diffusion-weighted imaging (DWI) enables visualization of cellularity and has been applied by neuroradiologists to diagnose very early-stage cerebral infarction. Compared with conventional MR imaging, DWI is characterized by extremely high contrast resolution. Although the clinical application of DWI to the body was delayed because strong artifacts created non-uniformity of the magnetic field, recent development of MR imaging technology has enabled its clinical application, and DWI has been reported useful for evaluating the body and for diagnosing breast cancer.

We evaluated the diagnostic capability of non-contrast MR imaging to detect breast cancer by combining DWI and short TI inversion recovery imaging (STIR).

Materials and Methods

Target selection

In our hospital, 255 cases of breast cancer were diagnosed and operated from August 2003 to July 2004. This study included 70 women aged 24 to 83 years (median age, 55 years) who underwent MRI, including DWI and MMG, before operation and whose breast cancers were confirmed by postoperative pathological examination. Excluded from study were patients with neoadjuvant chemotherapy or history of breast cancer treatment.

According to the TNM classification of the International Union against Cancer (UICC), the 70 cancers comprised 6 pTis; 33 pT1; and 31 pT2-pT4. According to World Health Organization (WHO) classification, the cases comprised 48 invasive ductal carcinomas, 5 invasive ductal carcinomas with a predominant intraductal component, 6 intraductal carcinomas, 3 mucinous carcinomas, 3 apocrine carcinomas, and 5 invasive lobular carcinomas.

Imaging protocols

MR examinations were performed with a 1.5-Tesla MR imager (Gyroscan Intera 1.5T Master Grade; Philips Medical Systems, the Netherlands). Bilateral breast images were acquired using a SENSE body coil with patients in the prone position. All imaging was performed in the transaxial plane. Subsequent to DWI and STIR, dynamic study was carried out on each image using Gd-DTPA enhancement. Single-shot echo planar imaging was employed for DWI. Image acquisition parameters for DWI were: b factor, 0, 1000 s/mm²; repetition time/echo time (TR/TE), 4000/76 ms; flip angle, 90°; matrix, 101 × 256; SENSE factor, 2.0; thickness, 5 mm; gap, 0 mm; voxel size, 2.5 mm × 3.2 mm × 5 mm; field of view (FOV), 320 mm; and number of signal averages (NSA), 2. The fat suppression technique employed for this study was by spectral presaturation with inversion recovery. Motion-probing gradient pulses were placed along the x, y, and z axes. Image acquisition parameters for STIR were: TR/TE, 4100/60 ms; flip angle, 90°; TSE factor, 19; matrix, 256 × 512; SENSE factor, 1.7; thickness, 5 mm; gap, 0 mm; FOV, 320 mm; and NSA, 2. MMG was performed using LORAD M-IV (Hologic, USA) and FCR5000MA (Fuji Photo Films, Japan). Bilateral craniocaudal and mediolateral oblique views were taken with sampling size of 0.1 mm.

Imaging analysis

DWI is affected by T₂ or T₂* as well as diffusion. Therefore, interpretation of DWI minimally requires T₁WI. On the other hand, STIR is more stable than T₁WI for fat suppression of breast tissue. Therefore, we employed DWI and STIR for interpretation.

Two radiologists with 15 and 14 years of experience in diagnostic radiology interpreted MR images and MMG. DWI and STIR images were interpreted by the retrospective consultation of the 2 radiologists.

Table 1 lists the criteria followed for determining the presence of malignancy on MR images. The apparent diffusion constant (ADC) was not used for diagnosis, and images were evaluated visually. We classified the signal intensity in DWI and STIR of the area in question as high, iso, or low in comparison with the signal intensity of the corresponding background mammary gland. Areas of high intensity on DWI were located and then investigated on STIR with the help of signal intensity, marginal aspect, and internal structure. Based upon the results, they were classified as malignant, highly suspicious of malignancy and requiring further examination, and benign with low likelihood of malignancy and requiring no further examination. An area of high intensity on DWI and low or iso-intensity on STIR was classified into the malignant group (Fig. 1). In the case of high intensity on both DWI and STIR, the area was classified as malignant if there was marginal irregularity and/or internal structure, for example a papillary projection. As an exception, an area of extremely low intensity on STIR was classified as malignant based on morphologic findings, regardless of its signal intensity on DWI.

According to BI-RADS, surrounding mammary glands of MMG were classified into fatty, scattered fibroglandular tissue; heterogeneously fibroglandular tissue; and mostly fibroglandular tissue and further subdivided into two groups, fatty/
Table 1. Diagnostic criteria for breast cancer

<table>
<thead>
<tr>
<th>DWI signal</th>
<th>STIR signal</th>
<th>STIR Irregular margin</th>
<th>STIR Internal structure</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Low — Iso</td>
<td>—</td>
<td>—</td>
<td>Malignancy</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Positive</td>
<td>—</td>
<td>Malignancy</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Negative</td>
<td>Positive</td>
<td>Malignancy</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Negative</td>
<td>Negative</td>
<td>Benign</td>
</tr>
<tr>
<td>Low — Iso</td>
<td>Low — High</td>
<td>—</td>
<td>—</td>
<td>Benign</td>
</tr>
<tr>
<td>Low — Iso</td>
<td>Extremely low</td>
<td>—</td>
<td>—</td>
<td>Malignancy</td>
</tr>
</tbody>
</table>

Fig. 1. A 48-year-old woman with invasive ductal carcinoma of the right breast, a typical case. (a,b) Because it was highly intense on diffusion-weighted imaging (DWI) and iso intense on STIR (arrow), it was diagnosed as malignant. (c) This mass was enhanced on dynamic magnetic resonance (MR) imaging early phase (arrow head). (d) Mammography revealed an ill-defined mass in the right breast.

Results

Of 70 cases with breast cancer, 68 were diagnosed as malignant using DWI and STIR (Table 2). Sensitivity was 97% (68/70) and FN was 2.9% (2/70) in diagnosing malignant lesions. Sensitivities by pT were: pTis, 67% (4/6); pT1, 100% (33/33); and pT2–4, 100% (31/31) (Table 3). There were no significant differences in sensitivity between pT1 and pT2–4. Sensitivities by background density of mammary gland were: fatty/scattered fibroglan-
Table 2. Overall results of non-contrast magnetic resonance (MR) imaging (n = 70)

<table>
<thead>
<tr>
<th>DWI signal</th>
<th>STIR signal</th>
<th>STIR Irregular margin</th>
<th>STIR Internal structure</th>
<th>Diagnosis (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Low ~ Iso</td>
<td>—</td>
<td>—</td>
<td>Malignancy (44)</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Positive</td>
<td>—</td>
<td>Malignancy (22)</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Negative</td>
<td>Positive</td>
<td>Malignancy (2)</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
<td>Negative</td>
<td>Negative</td>
<td>Benign (1)</td>
</tr>
<tr>
<td>Low ~ Iso</td>
<td>Low ~ Iso</td>
<td>—</td>
<td>—</td>
<td>Benign (1)</td>
</tr>
<tr>
<td>Low ~ Iso</td>
<td>Extremely low</td>
<td>—</td>
<td>—</td>
<td>Malignancy (0)</td>
</tr>
</tbody>
</table>

Table 3. Sensitivity in pT types (n = 70)

<table>
<thead>
<tr>
<th>pT</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTis</td>
<td>66.7 (4/6)</td>
</tr>
<tr>
<td>pT1</td>
<td>100 (33/33)</td>
</tr>
<tr>
<td>pT2-4</td>
<td>100 (31/31)</td>
</tr>
</tbody>
</table>

Table 4. Sensitivity in background density of mammary gland (n = 70)

<table>
<thead>
<tr>
<th>Background density</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatty/Scattered fibroglandular tissue</td>
<td>95 (20/21)</td>
</tr>
<tr>
<td>Heterogeneously fibroglandular tissue/Mostly fibroglandular tissue</td>
<td>98 (48/49)</td>
</tr>
</tbody>
</table>

Fig. 2. A 53-year-old woman with intraductal carcinoma in the left breast. This case was incorrectly diagnosed. (a) It was difficult to recognize the lesion of low image quality caused by failure of fat suppression on diffusion-weighted imaging (DWI) (arrow head). (b) It was also difficult to recognize the lesion caused by its iso intensity on STIR. (c) Dynamic magnetic resonance (MR) imaging early phase revealed enhanced area (arrow). (d) Mammography revealed irregularly clustered microcalcifications in the left breast (arrow).

Two cases were incorrectly diagnosed by MRI, an intraductal carcinoma (Fig. 2) that showed low signal intensity on DWI and an apocrine carcinoma (Fig. 3) that showed high signal intensity on both DWI and STIR images but that was difficult to differentiate from a cyst.
Fig. 3. A 61-year-old woman with non-invasive apocrine carcinoma of the left breast. This case was incorrectly diagnosed. (a, b) Because of high intensity on both diffusion-weighted imaging (DWI) and STIR (arrow), it was diagnosed as benign. (c) Dynamic magnetic resonance (MR) imaging early phase revealed enhanced area in this mass (arrow head). (d) Mammography revealed a well defined mass in the left breast.

Discussion

Diffusion is a physical phenomenon that differs from conventional parameters such as T1 and T2. The principle underlying DWI is that the thermal motion of water molecules in extracellular fluid enables the acquisition of images that reflect both histological structure and cellularity. Diffusion studies of MRI started with epidermoid or cerebral ischemia and are now used for neuroradiological diagnosis of early cerebral infarction.17 Compared to conventional MR imaging, DWI is characterized by extremely high contrast resolution. However, its clinical application to the body was delayed because motion or strong susceptibility artifact resulted from non-uniformity of magnetic field. Recent hardware advancement, such as phased-array multicoil and software development, including parallel imaging, has allowed the application of DWI to the body. DWI is useful for both examining the body and diagnosing breast cancer.18–20

DWI can detect various lesions of the trunk, including malignant tumors, as areas of high signal intensity, regardless of its non-specificity. T2 relaxation time is short for most normal tissue in the body so that the signal of normal tissue is suppressed and lesions are clearly detected as areas of high signal intensity. The reason for decreased diffusion in malignant tumor is unclear. Possibly, the relatively increased cellularity in malignant tumors decreases the diffusion speed of water molecules in the extracellular fluid, and this signal is intensified on diffusion images.20 Diffusion conditions can be analyzed using apparent diffusion constant (ADC) value. Some publications have reported the differential diagnosis of breast malignancy from benign mass by the ADC value.19,20 Kuroki and associates report that the ADC value of an invasive ductal carcinoma is significantly lower than that of a benign mass and the ADC value of an intraductal carcinoma tends to be lower than that of a benign mass, but they did not observe significant differences.19 Intraductal and invasive ductal carcinomas are difficult to differentiate by ADC values as well as by other diagnostic imaging methods because their ADC values overlap. Therefore, it is reasonable to consider ADC value as a reference. Therefore, a differential diagnosis of malignancy from a benign mass was based on DWI and STIR signal intensities and morphological information without measuring the ADC value of the mammary mass.

With the combination of DWI and STIR, 68 of 70 cases were diagnosed as malignant. Sensitivity was 97%, and FN was 2.9%, confirming a high
diagnostic capability. Significant difference in sensitivity between pT1 and pT2–4 was not observed, and a high diagnostic capability was confirmed regardless of tumor size. It is inferred that DWI reflects cellularity and detects lesions as areas of high signal intensity regardless of their size. No significant differences were observed in sensitivity by background mammary gland between the fatty/scattered fibroglandular tissue group and heterogeneous fibroglandular tissue group, seemingly because of the strong suppression of the signal of background mammary gland in DWI. The signal of background mammary gland is effectively suppressed to the noise level even in the case of dense breast, thus making diagnosis difficult using other methods, such as MMG. Consequently, the signal of a lesion can be easily recognized. Detection of breast cancer is reliable regardless of its size and background mammary gland. Breast cancers with high sensitivity, including intraductal carcinomas, which were usually difficult to diagnose, can now be diagnosed. These characteristics of DWI may make it an advantageous modality for screening younger women, including those at high risk. Moreover, there is no radiation risk or adverse effects from contrast medium. Accordingly, it is concluded that non-contrast MR imaging that combines DWI and STIR is appropriate for screening women who are younger or who are at high risk.

However, this study is limited because specificity and false positives were not investigated. The study was designed for a feasibility evaluation of the clinical applications of a combination of DWI and STIR in breast-cancer screening. Therefore, we investigated the detectability of breast cancer by studying only sensitivity and false negatives. Large-scale reading sessions with mixed benign and malignant cases or prospective studies are recommended to prove the validity of this method of screening.

DWI as an independent indicator obviously has some limitations. Two cases, a non-invasive apocrine carcinoma and an intraductal carcinoma, were incorrectly diagnosed. In the former case, cellularity did not appear particularly elevated and the lesion did not show high signal intensity in DWI. In the future, it will be necessary to evaluate the diagnostic capability for intraductal carcinoma, with a cellularity that is not appreciably increased, and an invasive lobular carcinoma, which is conventionally difficult to diagnose and was rare in this study. In the latter case, it was difficult to recognize the lesion because of low image quality caused by failure of fat suppression. Because mammary glands protrude from the body, their structure may obstruct fat suppression. Sufficient fat suppression is dispensable for DWI and will require the development of new technology or improved positioning of the mammary gland during image acquisition. In the case of very severe mastopathy, background mammary gland signal should be suppressed with a much stronger diffusion-weighted imaging, such as DWI with b factor: 1500 s/mm². A contributing factor is the training of the image readers. Because DWI for the body remains a developing technology, optimization of imaging parameters and reader training are required. Once these problems are resolved, DWI should be recognized and clinically applied as the third contrast method for MR imaging, following T₁-weighted and T₂-weighted imaging.

**Conclusion**

DWI obviously excels at detecting malignant lesions of the mammary gland, even in the case of dense breast that cannot be diagnosed well by MMG, the principal conventional examination. However, many problems, such as artifact from sequence design and the need for optimization of imaging parameters and reader training, need to be resolved. In addition, whether malignant tumors are depicted as areas of high signal intensity with DWI must be clarified.

**Acknowledgments**

This work was supported in part by the Health and Labour Sciences Research Grants for Third Term Comprehensive Control Research for Cancer.

**References**