Diffusion-weighted magnetic resonance imaging in preoperative assessment of non–small cell lung cancer

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Background: Diffusion-weighted magnetic resonance imaging (DWI) frequently shows heterogeneity of signal intensity (SI) in non–small cell lung cancer (NSCLC). The purpose of our study was to examine the association of SI and DWI patterns with histology, tumor invasiveness, lymph node metastasis, and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) uptake in NSCLC.

Methods: One hundred forty-five patients with NSCLC underwent preoperative DWI and FDG-PET. DWI patterns were visually classified as homogenous (HOM) (n = 81) or heterogeneous (HET) (n = 64). The former was further classified as faint (faint-HOM) (n = 27) or dark (dark-HOM) (n = 54) according to a cutoff value of SI. Associations of SI and DWI patterns with tumor histology, lymphatic or vascular invasion, pleural invasion, lymph node metastasis, and FDG uptake were evaluated.

Results: All faint-HOM tumors were well-differentiated adenocarcinoma, whereas dark-HOM and HET tumors were less-differentiated adenocarcinoma or nonadenocarcinoma. Although the dark areas in HET tumors showed a dense aggregation of tumor cells, their faint areas showed abundant fibrovascular stroma or necrosis, or a well-differentiated part of adenocarcinoma. Tumor size and the frequencies of lymphatic or vascular invasion, pleural invasion, and nodal metastasis were highest in HET tumors, followed by dark-HOM and faint-HOM ($P = .1$-$P < .001$) tumors. Sixty-five tumors having at least 1 of the invasions or metastasis showed significantly higher SI than the 81 tumors without ($P < .001$). HET tumors had the highest FDG uptake, followed by dark-HOM and faint-HOM tumors; differences between the groups were significant ($P < .01$ to $P < .001$).

Conclusions: The SI and heterogeneity of DWI reflect the histologic heterogeneity, tumor aggressiveness, and FDG-PET uptake in NSCLC. (J Thorac Cardiovasc Surg 2015;149:991-6)

See related commentary on page 997.

Although positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG) has been used for TNM staging and evaluating tumor aggressiveness of non–small cell lung cancer (NSCLC), it is not a popular device all around the world because of its high cost. In contrast, magnetic resonance imaging (MRI) is popular because of not only lower cost, but also applicability for various diseases, including those that are benign. Recent diffusion-weighted magnetic resonance imaging (DWI) technology has enabled imaging of various types of malignant tumors similar to FDG-PET, including breast tumors,[1] musculoskeletal tumors,[2] prostate cancer,[3] rectal cancer,[4,5] and lung cancer.[6] The mechanism of action of imaging malignant tumors by DWI is that the diffusion of water molecules is affected by cellularity and nuclear/cytoplasmic ratio, which are different between malignant tumors and benign tissue.[7-9]

Although we have used DWI to image NSCLC since 2006,[10-12] we frequently see heterogeneity on the imaging. From the theory of DWI, its heterogeneity may reflect histologic heterogeneity within tumors, such as cellularity and nuclear/cytoplasmic ratio, which are strongly associated with tumor aggressiveness. On the other hand, conventional imaging modalities such as computed tomography (CT), FDG-PET, and T1- and T2-weighted MRI can hardly image the histologic heterogeneity of NSCLC. On the basis of our hypothesis that DWI can image the histologic heterogeneity of NSCLC, we examined the signal intensity (SI) and heterogeneity of DWI in patients with NSCLC, which were compared with histology, lymphatic or vascular invasion, pleural invasion, lymph node metastasis, and FDG uptake on PET in surgically resected specimens.

MATERIALS AND METHODS

Eligibility

The study protocol for examining DWI in patients with NSCLC before surgery was approved by the Kameda Medical Center Ethics Committee. Informed consent was obtained from all patients after detailed information was given by their surgeons.

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Abbreviations and Acronyms

CR = contrast ratio
CT = computed tomography
DWI = diffusion-weighted magnetic resonance imaging
FDG = ^{18}F-fluorodeoxyglucose
HET = heterogeneous
HOM = homogenous
NSCLC = non–small cell lung cancer
MRI = magnetic resonance imaging
PET = positron emission tomography
ROI = region of interest
SI = signal intensity
SUV = standardized uptake volume

Patients

Between October 2012 and December 2014, 174 patients with NSCLC underwent DWI and FDG-PET followed by surgical treatment. Of these, 11 tumors <1 cm in size and 18 tumors with pure ground-glass opacity appearance were excluded. As a result, 145 tumors in 143 patients were enrolled in the study. Table 1 shows the tumor characteristics, including tumor histologic types, lymphatic or vascular invasion, pleural invasion, and lymph node metastasis. Of the 145 tumors, 63 had at least 1 of lymphatic, vascular, or pleural involvement, and lymph node metastasis, whereas 82 had none of those.

Twenty benign nodules in 20 patients who underwent DWI during the same period were used for determining the cutoff value of SI between benign and malignant nodules, which was finally used for determining the cutoff value between tumors producing faint and dark contrasts on DWI.

DWI

All MRI images were obtained with a 1.5-T system (MAGNETOM Avanto; Siemens, Munich, Germany). Conventional MRI images and DWI were acquired during the same session. The former consisted of a coronal T1-weighted sequence (repetition time/echo time = 177 ms/4.7 ms) and coronal and axial single shot spin echo T2-weighted sequences (1000 ms/102 ms). The T1- and T2-weighted images were acquired at a section thickness of 5 mm with a 0 mm gap, with a 320 × 156 and 256 × 194 matrix, respectively, and a 263 × 350 mm and 280 × 350 mm field of view, respectively. DWI was performed in the axial plane using a spin-echo, echo-planar imaging sequence with pacing to each breath by using the following parameters: repetition time/echo time = 3100 ms/73 ms with each breath, diffusion gradient encoding in 3 orthogonal directions: b = 0-800 s/mm^2, field of view = 310 × 350 mm, 118 × 118 matrix, and section thickness = 5 mm with a 0 mm gap. Fusion images were made by T2-weighted imaging and DWI for confirmation of the lesions.

Measurement of SI on DWI

The SI was measured using the region of interest (ROI) on the lesion by using Virtual Space software (AZE Co, Tokyo, Japan). The ROI was drawn around the tumor. The maximum SI within the ROI was measured for each tumor. To eliminate the fluctuations of SI caused by imaging conditions in each lesion, the contrast ratio of SI (SI-CR) was calculated by maximum SI of the lesion/mean SI of spinal cord at the same level of the lesion.

Classification of DWI Patterns

Based on visual assessment, DWI patterns were classified into homogenous (HOM) (n = 81) and heterogeneous (HET) (n = 64) (Figures 1-3). The former was further classified into faint (faint-HOM) (n = 27) and dark (dark-HOM) (n = 54) based on the cutoff value of SI-CR, as determined on the receiver operating characteristic curve to discriminate between the 20 benign and 109 malignant nodules <3 cm in size; that is, 0.45.

PET-CT Scanning

PET scanning was conducted by using PET/CT (Discovery ST; GE Medical Systems, Amersham, UK). The dose of FDG was 185 to 230 MBq, which was determined according to body mass index. The acquisition time for PET was 2.5 or 3 minutes per table position.

PET Data Analysis

PET data were evaluated by a contrast ratio of standardized uptake value (SUV-CR) as described previously.[13,14] Briefly, the SUV-CR was calculated by the equation maximum SUV of the lesion/maximum SUV of the contralateral lung.

Comparison Between DWI and Histologic Findings

Table 2 shows the relationship of DWI pattern with tumor histologic type. Although all of the 27 faint-HOM tumors were well-differentiated adenocarcinoma, the dark-HOM and HET tumors were less-differentiated adenocarcinoma or nonadenocarcinomas. To compare histologic findings between the faint and dark areas of HET tumors histologically, the materials resected by surgery were sliced on the axial plane to correspond to the plane of the DWI images. The maximum cut surface of resected tumors was compared with its axial view on DWI. The dark and faint areas were marked on sections stained with hematoxylin and eosin.

Pathologic Analysis

Hematoxylin and eosin and Elastica-van Gieson staining were performed in all sections to investigate pleural and intratumoral lymphatic

TABLE 1. Tumor characteristics

Characteristic	Value
Tumor size (cm)	
Mean ± standard deviation	2.5 ± 1.5
Range	1.0-7.5
Histologic type	
Adenocarcinoma	114
Squamous cell carcinoma	24
Large cell carcinoma	4
Adenosquamous cell carcinoma	2
Large cell neuroendocrine tumor	1
Lymphatic or vascular invasion	
−	98
+	47
Pleural invasion	
P0	118
P1-P3	27
Pathologic N stage	
N0	125
N1-N2	20
Lymphatic, vascular, or pleural invasion or nodal metastasis	
−	82
+	63
Total	145

Values are presented as n unless otherwise noted.