Diffusion-Weighted MRI (DWI) with Fast Advanced Spin-Echo Sequence: Comparison of N-Stage Assessment with DWI with Echo-Planar Imaging and FDG-PET/CT in Non-Small Cell Lung Cancer Patients

Yoshiharu Ohno[1,2], Shinichiro Seki[3], Hisanobu Koyama[3], Takeshi Yoshikawa[1,2], Sumiaki Matsumoto[1,2], Yoshiko Ueno[3], Katsusuke Kyotani[4], Yoshimori Kassai[5], Masao Yui[5], Hitoshi Yamagata[5], and Kazuro Sugimura[3]

[1]*Advanced Biomedical Imaging Research, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan,* [2]*Division of Functional and Diagnostic Imaging Research, Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan,* [3]*Division of Radiology, Department of Radiology, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan,* [4]*Center for Radiology and Radiation Oncology, Kobe University Hospital, KObe, Hyogo, Japan,* [5]*Toshiba Medical Systems Corporation, Tochigi, Japan*

Introduction: Despite advances in radiation therapy and chemotherapy, surgery is currently considered the best curative option for non-small cell lung cancer (NSCLC). Therefore, clinicians are frequently asked to evaluate the accurate N-stage because it is essential for choosing the appropriate surgical treatment for NSCLC patients. In the last decade, FDG-PET/CT and MR imaging with short inversion time (TI) inversion-recovery (STIR) turbo spin-echo imaging and diffusion-weighted imaging (DWI) on 1.5T or 3T MR systems have been suggested as useful in this setting (1-3). However, DWI has a limited capability as compared with STIR turbo SE imaging due to motion artifact as well as relatively severe image distortion (3). Therefore, several investigators have been suggested the necessity of DWI to improve image quality by sequence development since 2006 (4). To improve image quality of DWI in not only skull base, but also chest fields, a few investigators have been suggested to apply turbo spin-echo, fast-spin-echo or fast advanced spin-echo (FASE) rather than echo-planar imaging (EPI) sequences because formers are more tolerant to susceptibility and motion artifacts than latter. In this situation, we develop the new DWI sequence with FASE sequence, and can test its' potential for N-stage assessment in NSCLC patients. In addition, to the best of our knowledge, no direct comparison of N-stage assessment capability has been made among DWIs with FASE and EPI sequence at 3T system and FDG-PET/CT in NSCLC patients.

We hypothesized that diagnostic performance for N-stage assessment on DWI with FASE sequence had higher than that on DWI with EPI sequence and FDG-PET/CT in NSCLC patients. The purpose of this study was directly compare the capability for N-stage assessment of DWI using an FASE sequence (FASE-DWI) with that of DWI using the EPI sequence (EPI-DWI) and PET/CT in NSCLC patients.

Materials and Methods: Sixty-four consecutive operable NSCLC patients (37 men, 27 women; mean age 71 years) prospectively underwent FASE-DWI and EPI-DWI at a 3T system (Vantage Titan 3T, Toshiba Medical Systems Corporation, Otawara, Tochigi, Japan), integrated FDG-PET/CT, surgical treatments and pathological and follow-up examinations. In each subject, both DWI sequences were applied with b-value at 300 sec/mm^2. All DWIs obtained by both sequences and integrated PET/CT were independently evaluated by two different pairs of chest radiologists with more than 8 years experiences and two PET physicians with more than 10 years CT examinations. Then, image quality of each DWI sequence, detection capability of lymph node on each DWI sequence and probability of lymph node metastasis at each station on both DWIs and PET/CT were visually assessed by a 5-point visual scoring system in all patients. Final score for each evaluation was made by consensus of two readers in all patients.

To compare image quality of DWI between EPI and FASE sequence, overall image quality was compared between both sequences by means of Wilcoxon-signed rank test. To determine diagnostic performance and feasible threshold value for lymph node metastasis assessment, ROC-analyses were also performed on a per node basis. Then, sensitivity, specificity and accuracy on a per node basis were compared among all methods by McNemar's test. Finally, sensitivity, specificity and accuracy for N-stage assessment on a per patient basis were also compared among all methods by McNemar's test. P value less than 0.05 was considered as significant in this study.

Results: Representative case is shown in Figure 1. Image quality of FASE-DWI (3.3±0.6) was significantly higher than that of EPI-DWI (2.8±0.5, $p<0.05$). On comparison of diagnostic performance for lymph node metastasis among all methods on a per node basis, the mean area under the curve (Az) of FASE-DWI (Az=0.89) was significantly larger than that of EPI-DWI (Az=0.78, $p<0.0001$) and PET/CT (Az=0.83, $p=0.03$). In addition, Az of PET/CT was also significantly larger than that of EPI-DWI ($p=0.02$). Feasible threshold values of both DWIs were determined as 4, and that of PET/CT was determined as 3. Sensitivity (SE) and accuracy (AC) of FASE-DWI (SE: 80.0 [60/75] %, AC: 95.3 [427/448] %) were significantly higher than those of EPI-DWI (SE: 56.0 [42/75] %, $p<0.0001$; AC: 91.5 [410/448] %, $p<0.0001$) and PET/CT (SE: 72.0 [54/75] %, $p<0.0001$; AC: 94.0 [421/448] %, $p<0.0001$) on a per node basis assessment. Results of compared diagnostic performance of N-stage assessment among all methods on a per patient basis are show in Table 1. Sensitivity (96.9 [31/32] %) and accuracy (95.3 [61/64] %) of FASE-DWI were significantly higher than those of EPI-DWI (SE: 75.0 [24/32] %, $p=0.02$; AC: 86.0 [55/64] %, $p=0.03$) and PET/CT (SE: 75.0 [24/32] %, $p=0.02$; AC: 86.0 [55/64] %, $p=0.03$).

Conclusion: On 3T MR system, FASE sequence can improve image quality and diagnostic performance of lymph node metastasis as compared with EPI sequence. FASE-DWI is significantly more sensitive and accurate than EPI-DWI and PET/CT for N-stage assessment in NSCLC patients

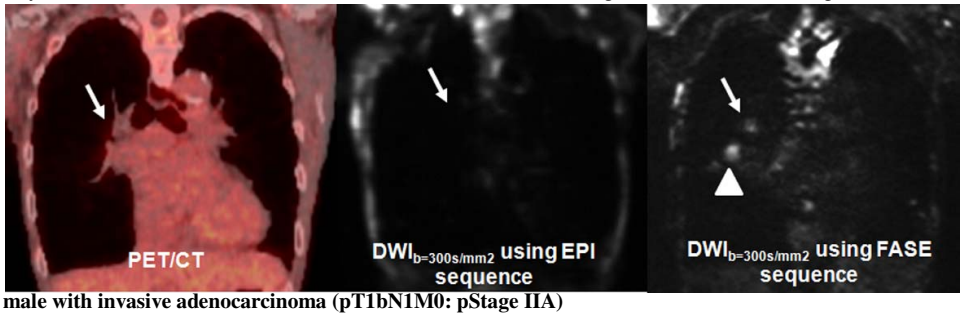

Figure 1. 74-year-old male with invasive adenocarcinoma (pT1bN1M0: pStage IIA)

FDG-PET/CT shows a hilar lymph node with littele uptake of FDG (arrow), and this lymph node (arrow) can not be visualized on EPI-DWI. This lymph node was assessed as non-metastatic lymph node, and this case was false-negative case on PET/CT and EPI-DWI. However, a hilar lymph node (arrow) and primary lesion (arrow head) are demonstrated as high signal intensity on FASE-DWI. This lymph node was evaluated as metastatic lymph nodes, and this case was true-positive case on FASE-DWI.

Table 1. Comparison of diagnostic performance by four methods for N-stage assessment in NSCLC patients.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
FASE-DWI	96.9 (31/32)	93.8 (30/32)	93.9 (31/33)	96.8 (30/31)	95.3 (61/64)
EPI-DWI	75.0* (24/32)	96.9 (31/32)	96 (24/25)	79.5 (31/39)	86.0* (55/64)
PET/CT	75.0* (24/32)	96.9 (31/32)	96 (24/25)	79.5 (31/39)	86.0* (55/64)

*: Significant difference with FASE-DWI ($p<0.05$).

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