Whole-Body MR Examination for M-Stage Assessment in Non-Small Cell Lung Cancer: How to Use Whole-Body Diffusion-Weighted Imaging as Compared with Integrated FDG-PET/CT

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Introduction: Assessment of M-stage is very important for management in non-small cell lung cancer (NSCLC) patients. Currently, FDG- PET/CT has been suggested as more useful than FDG-PET in this setting. FDG-PET/CT can assess morphological and metabolic information at same time, and widely utilized for cancer screening and TNM staging in lung cancer patients (1-3). Recently, whole-body MR imaging (MRI) has been also suggesting as another technique in this setting (4). In addition, whole-body diffusion-weighted image (DWI) has been suggested as useful for assessment of tumor staging and metastases (5, 6). However, no direct comparison of capability for M-stage assessment has been made among whole-body DWI only, whole-body MR imaging without and with DWI and integrated FDG-PET/CT in NSCLC patients. In this study, we attempted to validate the hypothesis that whole-body MR imaging with DWI has potential as an alternative technique for the detection of distant metastases in NSCLC patients with a capability similar to that of integrated FDG-PET/CT. To this end, we prospectively and directly compared the capability of whole-body MR imaging with and without DWI and of integrated FDG-PET/CT for M-stage assessment in NSCLC patients, and to determine the utility of whole-body DWI as a component of whole-body MR examination for detection of metastases.

Materials and Methods: 203 consecutive NSCLC patients (109 men, 94 women; mean age 72 years) prospectively underwent standard whole-body MRI, whole-body DWI, integrated FDG-PET/CT, pre-therapeutic standard radiological examinations for diagnosis of M-stage and more than one-year follow-up examinations. Final diagnosis of M-stage in each patient was determined according to the results of standard radiological and follow-up examinations. As whole-body MR imaging, short TI inversion-recovery turbo spin-echo images (TR 3200ms/ TE 60ms/ TI 165ms) and dual-phase T1-weighted gradient-echo images (TR 100ms/ TE 2.3 and 4.6ms/ FA 75°) with and without contrast-media (Gadoteridol, ProHans, Eizai, Japan) were obtained on coronal and sagittal planes by using moving-table system and body coil on two 1.5 T MR scanners (Gyroscan Intera and Achieva, Philips Medical Systems). Whole-body DWI (TR 5759ms/ TE 70 ms/ TI 180 ms/ ETL 141/ b=0, 1000 sec/mm^2) was also obtained in each patient. All FDG-PET/CT examinations were performed by using standard whole-body PET/CT protocol on a PET/CT scanner (Discovery ST; GE Health Care). All whole-body MR images were prospective assessed by two chest radiologists, and all FDG-PET/CT images were prospectively assessed by two nuclear medicine physicians with more than 3 years experiences of diagnostic radiology. Probabilities of presence of metastases on whole-body DWI, whole-body MRI without and with DWI, and integrated FDG-PET/CT were evaluated by using 5-point visual scoring systems on a per patient basis. Final diagnosis in each patient was made by consensus of two readers. A kappa statistic was used to determine the inter-observer agreement for whole-body DWI, whole-body MR imaging with and without DWI and for integrated FDG-PET/CT on a per-patient basis. To compare capability for M-stage assessment including brain metastases, ROC analysis was used on a per-patient basis. This was followed by a statistical comparison of sensitivity, specificity and accuracy by means of McNemar's test. To compare capability for M-stage assessment excluding brain metastases, ROC analysis was also used on a per-patient basis. This was also followed by a statistical comparison of sensitivity, specificity and accuracy by means of McNemar's test.

Results: The assessments demonstrated that interobserver agreements were substantial (whole-body DWI: k=0.62, whole-body MR imaging without DWI: k=0.64, whole-body MR imaging with DWI: k=0.66, and FDG-PET/CT: k=0.68). When brain metastases were included in M-stage assessment stage including of NSCLC patients, the results on a per-patient basis of ROC analyses of whole-body DWI, whole-body MR imaging with and without DWI and FDG-PET/CT are shown in Figure 1. The feasible threshold value for the visual scoring system for each method was set at 4. The area under the curve for whole-body DWI (Az=0.79) was significantly smaller than those for whole-body MR imaging with DWI (Az=0.87, $p<0.05$) and integrated FDG-PET/CT (Az=0.89, $p<0.05$). Tables 1 shows the results on a per-patient basis of a comparative analysis of the diagnostic capability, including assessment of brain metastases, whole-body DWI, whole-body MR imaging with and without DWI and integrated FDG-PET/CT. When brain metastases were included, specificity and accuracy of whole-body DWI were significantly lower than those of whole-body MR imaging with and without DWI and integrated FDG-PET/CT ($p<0.05$). When brain metastases were excluded from M-stage assessment of NSCLC patients, the results on a per-patient basis of ROC analyses of whole-body DWI, whole-body MR imaging with and without and with DWI and FDG-PET/CT are shown in Figure 2. The feasible threshold value for the visual scoring system for each of the methods was set at 4. The area under the curve for whole-body MR imaging without DWI (Az=0.81) was significantly smaller than that for integrated FDG-PET/CT (Az=0.89, $p<0.05$). The results of a comparative analysis on a per-patient basis of the diagnostic capability, with the exclusion of brain metastasis assessment, of whole-body DWI, whole-body MR imaging with and without DWI and integrated FDG-PET/CT are shown in Table 2. Specificity and/or accuracy of whole-body DWI was significantly lower than that of whole-body MR imaging with and without DWI and integrated FDG-PET/CT ($p<0.05$). Moreover, accuracy of whole-body MR imaging without DWI was significantly lower than that of integrated FDG-PET/CT ($p<0.05$).

Conclusion: Whole-body MR imaging with DWI can be used for M-stage assessment of NSCLC patients with accuracy as good as that of integrated PET/CT. In addition, when whole-body DWI is adopted as an adjunct for whole-body MR examination, the diagnostic capability of whole-body MR imaging for M-stage assessment can be improved, especially when evaluation of brain metastases on whole-body MR imaging is not included.

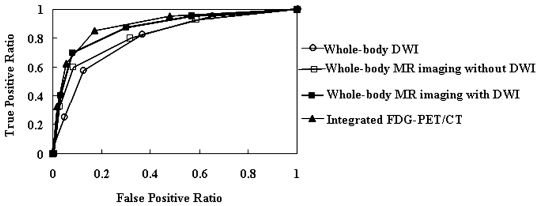

Figure 1. ROC analyses of whole-body DWI, whole-body MR imaging with and without DWI and integrated FDG-PET/CT for M-stage assessment inclusive of brain metastases on a per-patient basis.

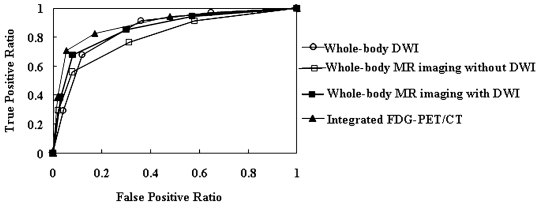

Figure 2. ROC analyses of whole-body DWI, whole-body MR imaging with and without DWI and integrated FDG-PET/CT for M-stage assessment not including brain metastases on a per-patient basis.

Table 1. Comparison of diagnostic capability on a per-patient basis, including assessment of brain metastases, of whole-body DWI, whole-body MRI with and without DWI and Integrated FDG-PET/CT.

	SE (%)	SP (%)	PPV (%)	NPV (%)	AC (%)
Whole-body DWI	57.5 (23/40)	87.7*, **, *** (143/163)	53.5 (23/43)	89.4 (143/160)	83.3*, **, *** (166/203)
hole-body MRI without DWI	60.0 (24/40)	92.0 (150/163)	64.9 (24/37)	90.4 (150/166)	85.7 (174/203)
Whole-body MRI with DWI	70.0 (28/40)	92.0 (150/163)	68.3 (28/41)	92.6 (150/162)	87.7 (178/203)
Integrated FDG-PET/CT	62.5 (25/40)	94.5 (154/163)	73.5 (25/34)	91.1 (154/169)	88.2 (179/203)

SE: Sensitivity, SP: Specificity, PPV: Positive predictive value; NPV: Negative predictive value,
AC: Accuracy
*: Significant difference with whole-body MRI without DWI ($p<0.05$).
**: Significant difference with whole-body MRI with DWI ($p<0.05$).
***: Significant difference with integrated FDG-PET/CT ($p<0.05$).

Table 2. Comparison of diagnostic capability on a per-patient basis, excluding assessment of brain metastases, of whole-body DWI, whole-body MRI with and without DWI and Integrated FDG-PET/CT.

	SE (%)	SP (%)	PPV (%)	NPV (%)	AC (%)
Whole-body DWI	67.6 (23/34)	87.7*, **, *** (143/163)	53.5 (23/43)	92.9 (143/154)	84.3**, *** (166/197)
Whole-body MRI without DWI	55.9 (19/34)	92.0 (150/163)	59.4 (19/32)	90.9 (150/165)	86.2*** (169/197)
Whole-body MRI with DWI	67.6 (23/34)	92.0 (150/163)	63.9 (23/36)	93.2 (150/161)	88.2 (173/197)
Integrated FDG-PET/CT	70.6 (24/34)	94.5 (154/163)	72.7 (24/33)	93.9 (154/164)	90.6 (178/197)

SE: Sensitivity, SP: Specificity, PPV: Positive predictive value; NPV: Negative predictive value,
AC: Accuracy
*: Significant difference with whole-body MRI without DWI ($p<0.05$).
**: Significant difference with whole-body MRI with DWI ($p<0.05$).
***: Significant difference with integrated FDG-PET/CT ($p<0.05$).

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