Comparative Analysis of Capability for Bone Metastases Assessment among Whole-Body Diffusion-Weighted Imaging, Whole-Body MR Imaging without and with Diffusion-Weighted Imaging, Bone Scan and Whole-Body FDG-PET/CT in Non-Small Cell Lung Cancer Patients

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INTRODUCTION: The treatment regimen for non-small cell lung cancer (NSCLC) depends on preoperative TNM staging, with curative surgical resection possible for the early stages, while for the late stage chemoradiotherapy, chemotherapy or best supportive care is considered advisable, depending on the patients' performance status (1, 2). Accurate tumor staging is therefore essential for choosing the appropriate treatment strategy. To achieve the aforementioned goal, CT, bone scan, whole-body positron emission tomography with [18F] fluoro-2-D-glucose (FDG-PET) is commonly utilized. Moreover, technologic advances have promoted FDG-PET image fused with CT (PET/CT) as the new modality in various oncology imaging (3-5). Recently, whole-body MR imaging has been put forward as another whole-body technique for assessment of distant metastases in patients with pediatric and various malignancies due to no need for ionizing radiation exposure, information from various sequences without and with administration of contrast media and improved temporal resolution due to newly developed parallel imaging technique, moving table scheme and/ or multiple body-array coils (6-8). Moreover, it has been suggested that diffusion-weighted imaging (DWI) could be useful for assessment of primary malignancy, lymph node and/or distant metastases, as well as detection of additional benign and/or malignant tumors (9-11). However, no direct comparison of diagnostic accuracy for bone metastasis assessment has been made among whole-body DWI, whole-body MR imaging without and with DWI, bone scan 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 bone metastases in NSCLC patients with a capability similar to that of integrated FDG-PET/CT and bone scan. The purpose of this study was to prospectively and directly compare the capability for bone metastasis assessment among whole-body DWI, whole-body MR imaging with and without DWI, integrated FDG-PET/CT and bone scintigraphy with SPECT, and determine the utility of whole-body DWI as a component of whole-body MR examination for detection of bone metastasis.

MATERIALS AND METHODS: 115 consecutive NSCLC patients (66 men, 49 women; mean age 72 years) prospectively underwent standard whole-body MRI, whole-body DWI, integrated FDG-PET/CT, bone scan for diagnosis of bone metastases and more than one-year follow-up examinations. Final diagnosis of bone metastases in each patient was determined according to the results of pathological and/ or 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 bone scans were performed by using standard bone scan protocol on a SPECT scanner (e-CAM, Siemens Medical Solution). 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 prospectively and independently assessed by two radiologists. All bone scans were prospectively and independently assessed by two nuclear medicine physicians. All integrated FDG-PET/CT were prospectively and independently assessed by two nuclear medicine physicians with more than three years experience of diagnostic radiology and no information about whole-body MR and PET/CT examinations. Probabilities of presence of metastases on whole-body DWI, whole-body MRI without and with DWI, bone scan and integrated FDG-PET/CT were evaluated by using 5-point visual scoring systems on a per site basis. Final diagnosis in each site 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, for bone scan and for integrated FDG-PET/CT on a per-site basis. To compare capability for bone metastases assessment on a per-site basis, ROC analysis was used. This was followed by a statistical comparison of sensitivity, specificity and accuracy by means of McNemar's test. To compare capability for bone metastasis assessment on a per-patient basis, ROC analysis was also used. This was also followed by a statistical comparison of sensitivity, specificity and accuracy by means of McNemar's test.

RESULTS: The results of kappa statistics are shown in Table 1. The interobserver agreement of each method were substantial (0.61<kappa<0.81). The results of ROC analyses and comparative analysis of the diagnostic capability on a per site basis are shown in Table 2. There were no significant differences of area under the curve (Az) in each other (p>0.05). The feasible threshold value for the visual scoring system for each method was set at 4. Specificity and accuracy of other method except whole-body DWI were significantly higher than those of whole-body DWI (p<0.05). Specificity and accuracy of whole-body MRI without DWI were significantly higher than those of bone scan (p<0.05). Specificity of whole-body MRI without DWI was significantly higher than that of integrated FDG-PET/CT (p<0.05). Specificity and accuracy of whole-body MRI with DWI were significantly higher than those of bone scan and integrated FDG-PET/CT (p<0.05). The results of comparative analysis of the diagnostic capability on a per patient basis are shown in Table 3. Specificity and accuracy of whole-body MRI with DWI were significantly higher than those of whole-body DWI.

CONCLUSION: Whole-body MR imaging without and with DWI has potential for more specific and/or accurate method for bone metastasis assessment than bone scan and integrated FDG-PET/CT on a per site basis. In addition, whole-body MR imaging without and with DWI can be used for bone metastasis assessment of NSCLC patients with accuracy as good as that of bone scan and integrated PET/CT. When whole-body DWI is adopted as an adjunct for whole-body MR examination, the diagnostic capability of whole-body MR imaging for bone metastases assessment can be improved.

Table 1. Results of kappa statistics in all methods.

		Visual score					Kappa value
		1	2	3	4	5	
Whole-body DWI	Reader 1 (cases)	424	352	138	54	57	0.64
	Reader 2 (cases)	415	323	177	54	56	
Whole-body MRI without DWI	Reader 1 (cases)	405	384	141	41	54	0.68
	Reader 2 (cases)	412	372	143	45	51	
Whole-body MRI with DWI	Reader 1 (cases)	433	345	148	43	56	0.66
	Reader 2 (cases)	410	345	171	45	54	
Bone scan	Reader 1 (cases)	394	291	229	66	45	0.67
	Reader 2 (cases)	375	288	251	68	43	
Integrated PET/CT	Reader 1 (cases)	400	375	140	59	50	0.65
	Reader 2 (cases)	361	370	184	61	48	

Table 2. Results of ROC analysis and comparative analysis of diagnostic capability on a per site basis.

	Az	SE (%)	SP (%)	PPV (%)	NPV (%)	AC (%)
Whole-body DWI	0.96	95.5 (64/67)	93.7 (898/958)	52.9 (64/121)	99.7 (898/901)	93.9 (962/1025)
Whole-body MRI without DWI	0.95	89.6 (60/67)	96.3* (923/958)	63.2 (60/95)	99.2 (923/930)	95.9* (983/1025)
Whole-body MRI with DWI	0.96	95.5 (64/67)	96.1* (921/958)	63.4 (64/101)	99.7 (921/924)	96.1* (985/1025)
Bone scan	0.96	95.5 (64/67)	95.2*, **, *** (912/958)	58.2 (64/110)	99.7 (912/915)	95.2*, **, *** (976/1025)
Integrated PET/CT	0.97	97.0 (65/67)	95.4*, **, *** (914/958)	59.6 (65/109)	99.8 (914/916)	95.5*, *** (979/1025)

*: Significant difference with whole-body DWI (p<0.05)
**: Significant difference with whole-body MRI without DWI (p<0.05)
***: Significant difference with whole-body MRI with DWI (p<0.05)

Table 3. Results of comparative analysis of diagnostic capability on a per patient basis.

	SE (%)	SP (%)	PPV (%)	NPV (%)	AC (%)
Whole-body DWI	96.0 (24/25)	78.9 (71/90)	55.8 (24/43)	98.6 (71/72)	82.6 (95/115)
Whole-body MRI without DWI	80.0 (20/25)	88.9* (80/90)	66.7 (20/30)	94.1 (80/85)	87.0 (100/115)
Whole-body MRI with DWI	96 (24/25)	88.9* (80/90)	70.6 (24/34)	94.1 (80/85)	90.4* (104/115)
Bone scan	96.0 (24/25)	84.4 (76/90)	63.2 (24/38)	98.7 (76/77)	90 (100/115)
Integrated PET/CT	96.0 (24/25)	84.4 (76/90)	63.2 (24/38)	98.7 (76/77)	90 (100/115)

*: Significant difference with whole-body DWI (p<0.05)

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