Economic Benefits and Diagnostic Quality of Diffusion-Weighted Magnetic Resonance Imaging for Primary Lung Cancer

Katsuo Usuda, MD,1 Aika Funazaki, MD,1 Ryo Maeda, MD,1 Atsushi Sekimura, MD,1 Nozomu Motono, MD,1 Munetaka Matoba, MD,2 and Hidetaka Uramoto, MD1

This paper focuses on the latest research of diffusion-weighted magnetic resonance imaging (DWI), and deals with economic benefits, diagnostic benefits, and prospects of DWI for lung cancer. The medical cost of a magnetic resonance imaging (MRI) is 81%–84% cheaper than that of 18-fluoro-2-deoxy-glucose positron emission tomography/computed tomography (FDG-PET/CT). DWI is reported to be useful for differential diagnosis of malignancy or benignity for neoplasm in various organs. Diagnostic efficacy by DWI for pulmonary nodules and masses and the evaluation of N factor and M factor in lung cancer are equivalent to or more than that of FDG-PET/CT. The diagnostic capability of whole-body DWI (WB-DWI) for the staging of clinically operable lung cancers is equivalent to that of FDG-PET/CT and brain MRI, and WB-DWI is now becoming a more main stream procedure. Although the diagnostic performance of DWI for lung cancer may be equivalent to that of FDG-PET/CT, prospective randomized controlled trial for comparison of diagnostic efficacy between FDG-PET/CT and DWI for lung cancer is necessary for an accurate comparison. DWI may have an advantage in the aspect of the cost and diagnostic efficacy in lung cancer management.

Keywords: magnetic resonance imaging, diffusion-weighted magnetic resonance imaging, 18-fluoro-2-deoxy-glucose positron emission tomography/computed tomography, lung cancer, pulmonary nodule and mass

Introduction

Diffusion-weighted magnetic resonance imaging (DWI) utilizes the random, translational motion, or so-called Brownian movement, of water molecules in biologic tissue.1 Recently, DWI has been applied to detect the restricted diffusion of water molecules in the body. DWI has been used primarily in brain imaging, mainly for the assessment of acute ischemic stroke, demyelinating diseases, and intracranial tumors.2 Malignant tumors have usually inhibited diffusions of the water molecule in DWI compared to the normal tissue, and apparent diffusion coefficients (ADC) of the malignant tumors become lower values.

For the last two decades, indication of magnetic resonance imaging (MRI) in lung cancer staging has been limitedly used in mediastinum invasion or chest wall invasion of lung cancer after Webb et al.3 of the Radiologic Diagnostic Oncology Group reported in 1991 that the diagnostic ability of MRI was the same as computed tomography (CT) concerning T factor or N factor except mediastinum invasion or chest wall invasion of lung cancer. Recently,
the technology of MRI has improved dramatically. In Japanese lung cancer practice guidelines 2016,\textsuperscript{4}) DWI is described as being useful in the assessment of benign and malignant pulmonary nodules and masses and in the judgment whether an additional examination is necessary.

In the paper, we focus on the recent finding of the DWI and give an outline about the economic benefits and diagnostic efficacy of DWI for primary lung cancer.

Medical cost of examinations

Recently, the medical cost of health for people has been increasing dramatically. It is caused not only by increasing life spans, but also by the increasing medical cost of examinations and various kinds of therapies. The medical cost of each medical examination is 10,000 yen (around $88) for CT, 13,300 yen (around $116) for MRI of 1.5T, and 16,000 yen (around $140) for MRI of 3T. An additional cost of 5,000 yen (around $43) is needed when using contrast medium in CT or MRI. And other medical cost is 22,000 yen (around $192) for bone scintigraphy and 18,000 yen (around $157) for gallium scintigraphy. Furthermore, the cost of 18-fluoro-2-deoxy-glucose positron emission tomography/computed tomography (FDG-PET/CT) is 86,250 yen (around $756), which is considerably expensive. In general, medical examinations using radionuclide are usually expensive, especially FDG-PET/CT is the most expensive. Actually, the cost of an MRI is 81\%–84\% cheaper than that of FDG-PET/CT. MRIs have economic advantages compared to FDG-PET/CT.

Advantage and disadvantage of MRI

There are several advantages with MRIs. MRI involves no contrast agents and requires less time for the examination. Furthermore, MRI has no radiation exposure for patients and is suitable and ideal for the examination of the children.\textsuperscript{5)}

On the other hand, there are some disadvantages with MRIs. An MRI examination is prohibited for people who have a metal such as a pacemaker or a tattoo on the skin. An MRI examination produces a noisy sound which is uncomfortable for patients.

Diagnosis of lung cancer and the pulmonary nodule and mass

DWI has been reported to be useful for differential diagnosis of malignancy and benignity in the lungs,\textsuperscript{6–9)} the mediastinum,\textsuperscript{10)} the thorax,\textsuperscript{11)} the prostate,\textsuperscript{12)} the breast,\textsuperscript{13)} and the liver.\textsuperscript{14)} There were two meta-analysis of DWI for differential diagnosis of malignancy and benignity for pulmonary nodules and masses,\textsuperscript{15,16)} and the both concluded that DWI was useful in differential diagnosis of malignancy and benignity for pulmonary nodules and masses. However, the use of DWI is restrictive for the lungs and has not become popular yet.

For detecting malignancy, diagnostic ability of DWI was reported to be similar to that of FDG-PET/CT,\textsuperscript{6)} or to be superior to FDG-PET/CT.\textsuperscript{17)} An important value of FDG-PET is prediction of tumor aggressiveness. While it is well known to predict tumor aggressiveness by standardized uptake value (SUV) on FDG-PET, ADC value and imaging pattern on DWI are also reported to be well correlated with FDG-accumulation and tumor aggressiveness.\textsuperscript{6)} Recently, Nomori et al.\textsuperscript{18)} divided the imaging pattern on DWI in primary lung cancer into three, that is, faint-homogenous, dark-homogenous, and heterogenous patterns, reporting that the imaging pattern not only showed histological heterogeneity, but also histological invasiveness, such as lymphatic, vascular, and pleural invasion. DWI could be used for prediction of tumor aggressiveness as well as FDG-PET. In FDG-PET/CT, solid lung cancer is usually associated with positive FDG-accumulation, but well-differentiated adenocarcinoma and small-sized lung cancer with a little metabolic activity have little FDG-accumulation, and are usually judged as negative. ADC value of adenocarcinoma with bronchioloalveolar carcinoma features was almost same to that of solid lung cancer, but SUV\textsubscript{max} of adenocarcinoma with bronchioloalveolar carcinoma features was similar to that of benign pulmonary lesions, which is one of the reasons that some lung cancers are likely to be false negative in FDG-PET/CT.\textsuperscript{19)}

On the other hand, DWI has two limitations. First, one of the pulmonary lesions which showed restricted diffusion and lower ADC values in DWI is pulmonary abscess with histopathological necrosis. Abscesses and thrombi impede the diffusivity of water molecules because they have hyperviscous nature.\textsuperscript{20,21)} The heavily impeded water mobility of pus may be caused by its high cellularity and viscosity, and shows the low ADC values.\textsuperscript{22)} In DWI, 22\% of benign lesions were reported to be able to exhibit restricted diffusion in images with high b values.\textsuperscript{23)} These articles on the properties of abscesses and thrombi can explain false-positive results in DWI for some benign pulmonary nodules and masses with abscesses. Second, in DWI, mucinous carcinomas were usually hypointense and showed higher ADC values,
which could be misjudged as benign lesions in DWI.\(^{19}\) Mucinous carcinomas had lower DWI signal intensity and higher ADC values than tubular adenocarcinoma in the ano-rectal region because mucinous carcinomas had lower cellularity than tubular adenocarcinomas.\(^ {24}\)

There were two articles which compared diagnostic capability of DWI with that of FDG-PET/CT for pulmonary nodules and masses.\(^6,19\) The sensitivity and the accuracy of DWI were significantly better than those of FDG-PET/CT for pulmonary nodules and masses.\(^6\) For pulmonary nodules and masses, the sensitivity (80.0\%) of DWI was significantly better than that (70.0\%) of FDG-PET/CT.\(^ {19}\) The specificity (65.5\%) of DWI was as same as that (65.5\%) of FDG-PET/CT, and the accuracy (77.8\%) of DWI was not significantly better than that (69.3\%) of FDG-PET/CT.\(^ {19}\)

Because there was no prospective randomized controlled trial between DWI and FDG-PET/CT for pulmonary nodules and masses, we do not conclude which diagnostic capability is higher, but can speculate that the diagnostic capability of DWI is compatible to that of FDG-PET/CT for pulmonary nodules and masses.

**Diagnostic capability of lymph node metastasis in lung cancer (Fig. 1)**

Non-invasive examinations including CT and FDG-PET/CT are used for the evaluation of lung cancer and lymph node metastases. However, FDG-PET/CT do not always determine a precise stage of lung cancer. Although FDG-PET/CT is reported to be superior than CT in the evaluation of lymph node metastases of lung cancer, it is
pointed out that there are some cases of false-positive assessment in FDG-PET/CT for the evaluation of lymph node metastases of lung cancer. Recently, the diagnostic capability of MRI has developed and two articles of meta-analysis reported that DWI was effective for the evaluation of N factor of lung cancer. Meta-analysis of the MRI by Peerlings et al. revealed high diagnostic capability that the sensitivity was 0.87, the specificity 0.88 for nodal assessment in the non-small-cell lung cancer.

DWI has some advantages in comparison with FDG-PET/CT. First, the sensitivity and accuracy of hilar and mediastinal lymph nodes by DWI were significantly higher than those of FDG-PET/CT. Nomori et al. reported that the accuracy (89%) of DWI was significantly higher than that (78%) of FDG-PET/CT in 88 lung cancer cases, due to the fact that there was less understaging cases with DWI compared with FDG-PET/CT.

Besides, it was reported that there were some cases of understaging with lung cancer in FDG-PET/CT. In 147 cases of clinical stage IA by FDG-PET/CT, 21 cases (14.3%) were pathologic N1 to N2 cases. We reported that the accuracy (96.2%) of N factor by DWI was significantly higher than that (94.3%) of FDG-PET/CT in 160 lung cancer cases. FDG-PET/CT examination for miner workers was reported to be inappropriate because of high false-positive rate for lymph nodes due to pneumoconiosis. Lymph nodes affected by silicosis have an accumulation of moderate FDG in FDG-PET/CT, and they may be incorrectly evaluated as positive. In FDG-PET/CT, we often feel it is difficult to diagnosis when there is an accumulation of FDG of multiple hilar and mediastinal lymph nodes in lung cancer cases. In lung cancer patients with an accumulation of FDG of multiple hilar and mediastinal lymph nodes, the specificity and the accuracy of DWI were significantly higher than those of FDG-PET/CT. For the etiology of 100 patients who had an accumulation of FDG in hilar and mediastinal lymph nodes in FDG-PET/CT, there were 11 patients with metastases of cancer, 40 anthracosis, 39 reactive lymphadenitis, 4 granulomas, and 3 silicosis. These reports show that the diagnostic capability of DWI is equivalent or more than that of FDG-PET/CT. However, the silicosis and granulation tissue in the lymph nodes were also reported to be also false positive in DWI, which is due to that an architectural change with granulation tissue decreases the diffusion of water molecules on DWI. Further studies are necessary for the assessment.

Diagnosis of staging for lung cancer by whole-body DWI

Some reported that the diagnostic ability of whole-body DWI (WB-DWI) was equivalent to that of FDG-PET/CT. Others reported that the diagnostic ability of WB-DWI was superior to that of FDG-PET/CT. In this decade, clinical staging of lung cancer is usually performed by FDG-PET/CT and brain MRI. FDG-PET/CT cannot assess brain metastasis because of metabolism of glucose in the brain, and brain MRIs make up for the disadvantage of FDG-PET/CT. Diagnostic efficacy by WB-DWI for operable lung cancer was equivalent to that by FDG-PET/CT + brain MRI. From now, WB-DWI will become more widely accepted for clinical staging of lung cancer.

Conclusion

This paper focuses on the latest research of DWI, and the economic benefits, diagnostic benefits, and prospects of DWI for lung cancer. DWI is reported to be useful for differential diagnosis of malignancy or benignity for neoplasm in various organs. Diagnostic efficacy by DWI for pulmonary nodules and masses, the evaluation of N factors and M factors in lung cancer is equivalent to or more than that of FDG-PET/CT. DWI might have several economic and diagnostic advantages.

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Disclosure Statement

The authors have no conflict of interest to declare.

References


4) [Qualitative imaging, lung cancer practice guidelines by the EBM technique on 2016 version], The Japan Lung Cancer Society, Tokyo, Kanehara Publication, 2016: 29-32. (in Japanese)


29) Usuda K, Sagawa M, Motono N, et al. Advantages of diffusion-weighted imaging over positron emission...


