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| Author(s) | Nakayama, Jun; Miyasaka, Kazuo; Omatsu, Tokuhiko; Onodera, Yuuya; Terae, Satoshi; Matsuno, Yoshihiro; Cho, Yasushi; Hida, Yasuhiro; Kaga, Kichizo; Shirato, Hiroki |
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Title

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Metastases in Mediastinal and Hilar Lymph Nodes in Patients with Non-Small Cell Lung Cancer: Quantitative Assessment with Diffusion-Weighted MR Imaging and Apparent Diffusion Coefficient.

(b)

Jun Nakayama, MD

Kazuo Miyasaka, MD, PhD

Tokuhiko Omatsu, MD

Yuuya Onodera, MD

Satoshi Terae, MD

Yoshihiro Matsuno, MD

Yasushi Cho, MD, PhD

Yasuhiro Hida, MD, PhD

Kichizo Kaga, MD, PhD

Hiroki Shirato, MD, PhD

From Medical Image Lab, Inc. (J.N., K.M.) Kita 15-jyo Nishi 2-chome 1-8
Kita-ku Sapporo 001-0015, Japan,

Department of Radiology, Hokkaido University Hospital (T.O., Y.O., S.T.)
North 14, West 5, Kita-ku, Sapporo, 060-8648, Japan.

Department of Surgical Pathology, Hokkaido University Hospital (Y.M.)
North 14, West 5, Kita-ku, Sapporo, 060-8648, Japan.

Departments of General Surgery/Thoracic surgery, Shinnittetsu Muroran
Hospital (Y.C) 1-45 Chilibetsu-cho Muroran, 050-0076, Japan

Department of Surgical Oncology, Division of Cancer Medicine, Hokkaido
University Graduate School of Medicine (Y.H., K.K.) North 15, West 7,
Kita-ku, Sapporo, 060-8638, Japan.

Department of Radiology, Hokkaido University Graduate School of
Medicine (H.S.) North 15, West 7, Kita-ku, Sapporo, 060-8638, Japan.

(c)

Address correspondence to J.N. (Tel: +81-11-738-9688, Fax: +81-11-738-9689,
e-mail: jnakaj@nifty.com)

Abstract:

Objective: To evaluate DW MR imaging for detection of metastases in lymph nodes by using quantitative analysis.

Methods: Seventy patients with NSCLC were examined with DW and STIR TSE MR imaging. ADC of each lung cancer and lymph node was calculated from DW MR images. Difference of the ADC in a lung cancer and a lymph node was calculated (D1). From STIR TSE MR images, ratios of signal intensity in a lymph node to that in a 0.9% saline phantom was calculated (LSR1). For quantitative analysis, the threshold value for a positive test was determined on a per-node basis and tested for ability to enable a correct diagnosis on a per-patient basis. Results of quantitative analyses of DW and STIR MR images were compared on a per-patient basis with McNemar testing.

Results: Mean D1 in the lymph node group with metastases was lower than that in the group without metastases ($P < .001$). When an D1 of $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$. was used as the positive-test threshold, sensitivity, specificity, and accuracy were 69.2%, 100%, and 94.0%, respectively on a per-patient basis. There was no significant difference ($P > .05$) between quantitative analyses of DW MR images and STIR MR images.

Conclusion: Quantitative analysis of DW MR images enables differentiation

of lymph nodes with metastasis from those without.

Keywords:

1. diffusion-weighted (DW) MR imaging
2. apparent diffusion coefficient (ADC)
3. lung cancer
4. lymph node
5. metastasis

Introduction: Lung cancer is the leading cause of cancer death in both men and women worldwide (1). Non-small cell lung cancer (NSCLC) accounts for 80% of all lung cancers, and small cell lung cancer accounts for the remainder (2). Mortality rates and the success of therapeutic approaches depend on the histologic type of cancer, the involvement of mediastinal and hilar lymph nodes, and the presence of remote metastases. Therefore, accurate tumor staging is essential for choosing the appropriate treatment strategy for patients with lung cancer, and mainly, tumor staging depends on imaging procedures.

Various diagnostic techniques and procedures, such as computed tomography (CT), magnetic resonance (MR) imaging, bronchoscopy,

mediastinoscopy, and positron emission tomography (PET), are used for preoperative staging of lung cancer. CT is the most commonly used method for staging of lymph nodes. However, CT is limited in the evaluation of nodal status because it provides only presumptive evidence of metastatic disease on the basis of size criteria. Sensitivity and specificity of CT in this regard are approximately 60%, which is not optimal for clinical decision making (3-9). A more accurate noninvasive method for determining lymph node status in patients with early-stage NSCLC would be useful for assigning patients to the most appropriate staging procedure.

Promising results have been reported for PET performed with fluorine 18 fluorodeoxyglucose (FDG). Positron emission tomography has been used to differentiate lymph nodes with metastasis from those without on the basis of the biochemical mechanisms of increased glucose metabolism and duplication tumor cells (10-13); however, elevated glucose metabolism may be secondary to tumor, infection, or inflammation (14,15). Moreover, the diagnostic capability of FDG-PET is limited because standard uptake values at FDG-PET are affected by lymph node size (12).

Some investigators have discussed the utility of short inversion time inversion recovery (STIR) MR imaging for detection of lymph nodes with metastasis in various malignant cancers (16-20). In addition, it was reported that quantitative and qualitative analyses of STIR turbo-spin-echo(TSE) MR imaging enable differentiation of lymph nodes with metastasis from those without with sensitivity values that are greater than or equal to those of FDG-PET (20).

Diffusion-weighted (DW) MR images and apparent diffusion coefficient (ADC) values add important information to findings obtained with conventional MR imaging and have been widely used in brain imaging, primarily for the evaluation of acute ischemic stroke, intracranial tumors, and demyelinating disease (21-23). With the advent of the echo-planar MR imaging technique, DW MR imaging of the abdomen and thoracic cavity has become possible with fast imaging times, which minimize the effects of gross physiologic motion from respiration and cardiac movement (24). The application of DW echo-planar MR imaging has extended to the breast and prostatic regions and allows for differentiation between tumor and normal tissue (25,26). DW MR imaging has also been used in the hepatic and thoracic lesion to help differentiate between malignant and benign lesions (27,28). Therefore, we hypothesized that the ADCs of the lymph nodes with metastasis is different from those of the lymph nodes without metastasis and the ADCs of the lymph nodes with a high ratio of metastatic cell nests is approximated to ADCs of the primary lung cancer.

Thus, the purpose of our study was to evaluate DW MR imaging for detection of metastases in lymph nodes by using quantitative analysis.

Materials & Methods: This retrospective study was approved by the institutional review board, and informed consent was waived.

Patients

Seventy patients suspected of having NSCLC on the basis of findings at CT were examined with contrast material-enhanced CT, DW- and STIR- MR imaging, and either mediastinoscopy before thoracotomy and resection of the primary lesion or thoractomy for primary lesion resection with random hilar lymph node sampling at Hokkaido University Hospital within two weeks before operation, during the period of (2007 and 2008). These 70 patients (mean age, 68 years; age range, 48-82 years) included 38 men and 32 women. The final diagnosis of lung cancer was based on pathologic findings in resected specimens. Fifty-two of 70 patients had adenocarcinoma and 18 patients had squamous cell carcinoma. There were no patients with large cell carcinoma, or other histologic types of lung cancer in this series.

MR Imaging Examination

All MR examinations were performed with a 1.5-T clinical imager (Avanto; Siemens, Erlangen, Germany) by using a body phased-array coil. Patients were in the supine position throughout the examination. Prior to DW-and STIR-MR imaging, T1-and T2-weighted images were obtained in the transverse plane in each patient. Transverse DW MR images were obtained with b values of 50 and 1000 sec/mm². The components of the applied gradients for diffusion weighting, which consisted of three orthogonal gradients, were equal in read, phase, and section orientation to obtain maximum total gradient strength. DW half-Fourier single-shot turbo spin-echo imaging was used in this study. Other parameters were as follows: repetition time msec/echo time msec, 3000/69; effective band width, 2056

Hz/pixel; number of signals acquired, two; matrix, 78×128 ; field of view, 45×28.1 cm; and section thickness, 6mm. Transverse breath-hold STIR MR images were obtained with the following parameters: 3830/91; inversion time, 170msec; matrix, 320×192 ; field of view, 35×26.3 cm; and section thickness, 6mm; a 0.9% saline phantom was placed alongside the chest wall at imaging of each patient. The saline phantom consisted of 100 mL of 0.9% saline within a plastic tube covered by a plastic cap.

Lymph Node Sampling and Histopathologic Examination

At thoracotomy, hilar and mediastinal lymph node dissection was systematically performed by the surgeon. The sites of surgically dissected lymph nodes were matched to the lymph nodes identified at CT and MR imaging according to the American Joint Committee on Cancer and Union International Contre le Cancer (AJCC-UICC) regional lymph node classification system for lung cancer staging (29).

All resected lymph nodes were fixed in 10% buffered formalin and were routinely processed before histologic examination. Each histologic specimen contained the largest cut surface of each lymph node and evaluated by at least two pathologists. In addition, all lymph nodes were histologically reviewed for confirmation independently by a single pathologist (Y.M.).

Analysis of DW- and STIR- MR images

Quantitative analysis

On DW MR images, all ADC values were measured for each lung cancer,

mediastinal and hilar lymph nodes by a chest radiologist with 11 years of experience (J.N.). ADC values were calculated with a linear regression analysis of the natural log of signal intensity versus the gradient factor according to the following equation: $ADC = -[\ln(S_h/S_l)] / (b_h - b_l)$. S_h and S_l were the signal intensities in the region of interest obtained with two different gradient factors (b_h and b_l). In this study, b_h was 1000 sec/mm² and b_l was 50 sec/mm². A region of interest with a diameter of 3-10 mm was positioned for the measurement of ADC in each lung cancer and lymph node. The region of interest was placed on the center of the lung cancer and lymph node. ADC_{LC} is the ADC of the lung cancer, ADC_{LN} is that of the lymph node. The D1 was the formula $D1 = |ADC_{LC} - ADC_{LN}|$.

On STIR MR images, all signal intensities were measured in circular or oval regions of interest drawn over each mediastinal and hilar lymph node and the phantom of 100 mL of 0.9% saline by a chest radiologist with 11 years of experience (J.N.). The regions of interest drawn over the lymph node encompassed the entire cross-sectional area of the lymph node and saline phantom (3-10 mm in diameter). So that we could quantitatively evaluate the signal intensity of lymph nodes at STIR MR imaging, all signal intensities of lymph nodes were normalized by comparing them with the signal intensities of the 0.9% saline phantom to produce the lymph node-saline ratio (LSR1). The LSR1 was the formula $LSR1 = SI_{LN} / SI_{SP}$, where SI_{LN} is the signal intensity of the lymph node, SI_{SP} is the signal intensity of the saline phantom.

Data and Statistical Analysis

The ADC_{LN} , D1, and LSR1 of lymph nodes with metastasis and those of nodes without metastasis were compared by Tukey honestly significantly difference multiple comparison testing.

To evaluate the ability of ADC_{LN} , D1, and LSR1 to enable the differentiation of lymph nodes with metastasis from those without, the feasible threshold of ADC_{LN} , D1, and LSR1 on a per-node basis was determined by using a receiver operating characteristic-based positive test.

Receiver operating characteristic analysis was used to evaluate the effectiveness of the ADC_{LN} , D1, and LSR1 for revealing lymph nodes with metastasis. Sensitivity, specificity were calculated for each level of ADC_{LN} , D1, and LSR1 by varying the ADC_{LN} , D1, and LSR1 that signified a positive test (ie, the threshold value). Sensitivity was defined as the percentage of lymph nodes with metastasis that had an ADC_{LN} , D1 less than or equal to the given threshold level, and specificity was defined as the percentage of lymph nodes without metastasis that had an ADC_{LN} , D1 greater than the given threshold level. Sensitivity was defined as the percentage of lymph nodes with metastasis that had an LSR1 greater than or equal to the given threshold level, and specificity was defined as the percentage of lymph nodes without metastasis that had an LSR1 less than the given threshold level.

Feasible threshold values at quantitative analyses of DW- and STIR- MR images were tested for their ability to enable lymph nodes with metastasis to distinguished from lymph nodes without metastasis on a per-patient basis. Overlapping lymph nodes evaluated with the feasible threshold value were

also histologically reviewed.

The ability of quantitative analysis of DW MR images to enable a correct diagnosis were compared with the ability of STIR MR images on a per-node basis excluding lymph nodes that were not detected by using the McNemar test.

The ability of quantitative analysis of DW MR images to enable a correct diagnosis were compared with the ability of STIR MR images on a per-patient basis including lymph nodes that were not detected by using the McNemar test.

For all statistical analyses, a *P* value of less than .05 was considered to indicate a statistically significant difference.

Results: At pathologic examination, 16 of 70 patients were pN positive (pN1:9, pN2:7). Thirty-seven of 441 lymph nodes were pathologically diagnosed as containing metastatic carcinoma; 404 nodes without metastatic carcinoma included nodes with anthracosillicotic nodes, silicotic nodes, hyalinized nodes, epithelioid cell granulomas such as sarcoid reaction or sarcoidosis, and reactive lymph nodes not otherwise specified. Nodal involvement of malignant lymphoma was also found in lymph nodes. On DW MR images, 56 of 441 lymph nodes (12.7%) were able to be detected. On STIR MR images, 45 of 441 lymph nodes (10.2%) were able to be detected. The numbers of lymph nodes that were able to be detected on either DW- and STIR-MR images are shown in Table 1. On DW MR images, five metastatic lymph

nodes with a long-axis diameter of greater than 5 mm that were not able to be detected were lymph nodes directly invaded by a primary tumor. On STIR MR images, five metastatic lymph nodes with a long-axis diameter of greater than 5 mm that were not able to be detected were lymph nodes directly invaded by a primary tumor mass. Five metastatic lymph nodes with a long-axis diameter of greater than 5 mm that were not able to be detected were lymph nodes along bronchi. Representative examples of lymph nodes with metastasis and without metastasis are shown in Figures 1 and 2, respectively.

The numbers and mean ADC_{LN} , D1, and LSR1 with metastasis and those without metastasis among histologic types of lung cancer are shown in Table 2-4. In all groups and in adenocarcinoma group, the mean ADC_{LN} , D1, and LSR1 for the lymph nodes with metastasis were significantly different from those for the lymph nodes without metastasis. In squamous cell carcinoma group, the mean ADC_{LN} , D1, and LSR1 for the lymph nodes with metastasis were not significantly different from those for the lymph nodes without metastasis.

Results with the receiver operating characteristic-based positive test for ADC_{LN} , D1, and LSR1 on a per-node basis are shown in Figure 3-5. An ADC_{LN} of $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$ was adopted as the threshold for a positive test (ie, an ADC_{LN} of $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$ or less indicated that a lymph node contained metastasis). The sensitivity and specificity for differentiating lymph nodes with metastasis from those without metastasis by using this threshold ADC_{LN} were 82.6% (19 of 23 nodes) and 84.8% (28 of 33 nodes),

respectively. The ADC_{LNS} of four (17.4%) of 23 lymph nodes with metastasis were overlapped with those of lymph nodes without metastasis (ie, the ADC_{LNS} of four lymph nodes were greater than $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$). In two of them, metastatic adenocarcinoma was producing abundant intra- and extra-cellular mucin. One overlapped lymph node had micrometastasis less than 0.2mm. One overlapped lymph node had metastasis from well-differentiated adenocarcinoma. The ADC_{LNS} of five (15.1%) of 33 lymph nodes without metastasis were overlapped with those of lymph nodes with metastasis (ie, the ADC_{LNS} of two lymph nodes were less than or equal to $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$). Five overlapped lymph nodes without metastasis were infiltrated by inflammatory cells including many eosinophils, suggesting a specific inflammatory process of uncertain etiology in these cases.

An D1 of $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$ was adopted as the threshold for a positive test (ie, an D1 of $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$ or less indicated that a lymph node contained metastasis). The sensitivity and specificity for differentiating lymph nodes with metastasis from those without metastasis by using this threshold D1 were 87.0% (20 of 23 nodes) and 100% (33 of 33 nodes), respectively. The D1s of three (13.0%) of 23 lymph nodes with metastasis were overlapped with those of lymph nodes without metastasis (ie, the D1s of three lymph nodes were greater than $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$). In two of them, metastatic adenocarcinoma was producing abundant intra- and extra- cellular mucin. One overlapped lymph node had micrometastasis.

An LSR1 of 0.354 was adopted as the threshold for a positive test (ie, an LSR1 of 0.354 or greater indicated that a lymph node contained metastasis).

The sensitivity and specificity for differentiating lymph nodes with metastasis from those without metastasis by using this threshold LSR1 were 88.2% (15 of 17 nodes) and 89.3% (25 of 28 nodes), respectively. The LSR1 of two (11.8%) of 17 lymph nodes with metastasis was overlapped with that of lymph nodes without metastasis (ie, the LSR1 of one lymph node was less than 0.354). This overlapped lymph node had micrometastasis. The LSR1 of three (10.7%) of 28 lymph nodes without metastasis was overlapped with that of lymph node with metastasis (ie, the LSR1 of one lymph node was greater than or equal to 0.354). This overlapped lymph node without metastasis had a hyalinized nodule. There was no significant difference ($P > .05$) between the results on a per-node basis of D1 and those of LSR1 of lymph nodes that were detected on both DW- and STIR- MR images.

In terms of the results of quantitative analyses of DW- and STIR- MR images on a per-patient basis including lymph nodes that was not detected (Table 5), the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of D1 were greater than those of LSR1. However, there was no significant difference ($P > .05$) between the results of D1 and those of LSR1. Additionally, Table 6 shows the results of assessments excluding of lymph nodes directly invaded by a primary tumor.

Discussion: Accurate evaluation of the presence or absence of metastases in mediastinal and hilar lymph nodes is a critical factor which may determine the appropriate treatment strategy for patients with lung cancer.

Computed tomography and FDG PET are most commonly used method for staging of lymph nodes. However, CT and MRI are limited in the evaluation of nodal status because it provides only presumptive evidence of metastatic disease on the basis of size criteria (3-9). Recently, DW MR imaging has also been used in the hepatic and thoracic lesion to help differentiate between malignant and benign lesions (27,28) Although the total number of patients in this study was small, we found that ADC_{LN} and the difference between ADC_{LN} and ADC_{LC} (D1) had a significant correlation with the differential diagnosis of lymph nodes with metastasis and those without.

In this study, our results show that mean D1 and ADC_{LN} of detected lymph nodes with metastasis were significantly lower than those of lymph nodes without metastasis. The mean D1 produced a more significant difference than the mean ADC_{LN} . ADC refers to the specific diffusion capacity of a biologic tissue. ADC depends largely on the presence of barriers to diffusion within the water microenvironment, namely, cell membranes, tight junctions, fibers, macromolecules, and cell organelles (30). Consequently, compartments within different cellular structures may exhibit dissimilar ADCs, and the ADC can therefore aid in determining different tissue types and tissue characteristics (31,32). Therefore, significant differences between lymph nodes with metastasis and lymph nodes without metastasis were observed in this study.

When $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$ was adopted as the feasible D1 threshold value, D1s of three (13.0%) of 23 lymph nodes with metastasis were overlapped with those of lymph nodes without metastasis. Two overlapped lymph nodes

were mucin-producing-cell-rich lymph nodes. One overlapped lymph node had micrometastasis. Previous studies have revealed a significant correlation between ADC and tumor cellularity (25,28,33,34). Tumor cellularity may be an important factor influencing ADCs in viable tumor tissue. In this study, it was thought that the degree of such pathologic changes as size of metastatic cell nests, amount of mucin production, necrosis, and infiltrating eosinophils within a lymph node affected the changes in ADC and result in some overlap between lymph nodes with metastasis and those without. Oppositely, it was thought that the degree of such pathologic changes as hyalinization and anthracosis, as well as epithelioid cell granulomas did not affect the changes in ADC. Therefore, these results suggest that the ADCs of the lymph nodes with a high ratio of metastatic cell nests is approximated to ADCs of the primary lung cancer. And D1s of lymph nodes with metastasis were lower than D1 of those without.

At comparison of the results of quantitative analyses of STIR-and DW- MR images on a per-patient basis, we found that for distinguishing lymph nodes with metastasis from those without, quantitative analysis of DW MR images had high sensitivity, specificity and accuracy equal to that of STIR MR images.

In previous reports of results for differentiating lymph nodes with metastasis from lymph nodes without metastasis by using FDG PET, sensitivities, specificities, and accuracies ranged from 67% to 80%, from 97% to 100%, and from 87.5% to 88%, respectively (10-13). In our study, because

lymph nodes directly invaded by a primary tumor mass were included, the quantitative analysis of DW MR images had low sensitivity than that of FDG PET on a per-patient basis. However, the quantitative analysis excluding assessment of lymph nodes directly invaded by a primary tumor had equal sensitivity and specificity to that of FDG PET and greater accuracy than that of FDG PET on a per-patient basis. Therefore, quantitative analysis of DW MR images enables differentiation of detected lymph nodes with metastasis from those without metastasis with sensitivity, specificity, and accuracy values than that are greater than or equal to those of FDG PET.

There were several limitations to our study. First, lymph nodes with a long-axis diameter of less than 5 mm were not able to be detected on DW MR images. And, there were lymph nodes with micrometastasis that was not detected as abnormal signal intensity lesion. And, ADCs of necrotic lymph nodes with metastasis are relatively higher. In addition, lymph nodes directly invaded by a primary tumor mass were not able to be detected by separating the lymph nodes from the lung cancer. Second, we performed radiologic-pathologic correlation with DW- and STIR- MRI imaging but not with FDG PET. Therefore, a larger prospective directly comparative study involving FDG PET would be required to determine the true value of DW MR imaging for the diagnosis of metastasis in lymph nodes.

In conclusion, quantitative analysis of DW MR images enable lymph nodes with metastasis to be differentiated from those without.

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Figure 1. Images in 78-years-old man with lymph nodes containing metastasis from squamous cell carcinoma.

- (a) Transverse contrast-enhanced CT scan shows right anterior mediastinal node.
- (b) Transverse DW MR image obtained with diffusion gradient 50sec/mm² shows lymph node as high-signal-intensity area.
- (c) Transverse DW MR image obtained with diffusion gradient 1000sec/mm² also shows lymph node as high-signal-intensity area.
- (d) Transverse STIR MR image (repetition time msec/effective echo time msec/inversion time msec, 3830/91/170) shows lymph node as high-signal-intensity area.

ADCs of the lymph node and lung cancer were respectively $1.31 \times 10^{-3} \text{mm}^2/\text{sec}$, $1.21 \times 10^{-3} \text{mm}^2/\text{sec}$, and the difference (D1) was $0.10 \times 10^{-3} \text{mm}^2/\text{sec}$. The lymph

node-saline ratio (LSR1) was 0.485. Analysis of histologic specimen from right anterior mediastinal node revealed nodular lesions composed of metastasizing squamous cell carcinoma.

Figure 2. Images in 79-years-old man with lymph nodes free of metastasis from adenocarcinoma.

- (a) Transverse contrast-enhanced CT scan shows pretracheal and right tracheobronchial nodes.
- (b) Transverse DW MR image obtained with diffusion gradient 50sec/mm² shows lymph nodes as high-signal-intensity area.
- (c) Transverse DW MR image obtained with diffusion gradient 1000sec/mm² also shows lymph nodes as intermediate-signal-intensity area.
- (d) Transverse STIR MR image (repetition time msec/effective echo time msec/inversion time msec, 3830/91/170) shows lymph nodes as high-signal-intensity area.

ADCs of the lymph nodes were respectively $1.69 \times 10^{-3} \text{mm}^2/\text{sec}$, $1.55 \times 10^{-3} \text{mm}^2/\text{sec}$, $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$, and ADCs of the lung cancer was $1.07 \times 10^{-3} \text{mm}^2/\text{sec}$. The differences (D1s) were respectively $0.52 \times 10^{-3} \text{mm}^2/\text{sec}$, $0.47 \times 10^{-3} \text{mm}^2/\text{sec}$, $0.48 \times 10^{-3} \text{mm}^2/\text{sec}$. The lymph node-saline ratios (LSR1s) were respectively 0.33, 0.22, 0.23. Analysis of histologic specimen from pretracheal and right tracheobronchial nodes revealed no evidence of metastatic cell nests.

Figure 3. Graph shows results with receiver operating characteristic-based positive test at quantitative analysis with the ADC_{LN} on a per-node basis. ● = sensitivity, ○ = specificity. An ADC_{LN} of $1.54 \times 10^{-3} \text{mm}^2/\text{sec}$ was adopted as the threshold for a positive test.

Figure 4. Graph shows results with receiver operating characteristic-based positive test at quantitative analysis with the D1 on a per-node basis. ● =

sensitivity, \circ = specificity. An D1 of $0.24 \times 10^{-3} \text{mm}^2/\text{sec}$ was adopted as the threshold for a positive test.

Figure 5. Graph shows results with receiver operating characteristic-based positive test at quantitative analysis with the LSR1 on a per-node basis. \bullet = sensitivity, \circ = specificity. An LSR1 of 0.354 was adopted as the threshold for a positive test.

TABLE 1

Number of Lymph nodes that were able to be detected on either DW- and STIR- MR images

| Diagnostic Group | DWI | | | STIR | | |
|--------------------------------|-----------------|----------------|-----------------|-----------------|----------------|-----------------|
| | All | < 5mm | > 5mm | All | < 5mm | > 5mm |
| | No.of Nodes | No.of Nodes | No.of Nodes | No.of Nodes | No.of Nodes | No.of Nodes |
| Lymph nodes with metastasis | 23 / 37 (62.2%) | 3 / 12 (25.0%) | 20 / 25 (80.0%) | 18 / 37 (48.6%) | 3 / 12 (25.0%) | 15 / 25 (60.0%) |
| Lymph nodes without metastasis | 33 / 404 (8.2%) | 5 / 376 (1.3%) | 28 / 28 (100%) | 27 / 404 (6.7%) | 6 / 376 (1.6%) | 21 / 28 (75%) |

TABLE 2

Number and mean ADC_{LN} of Lymph nodes with metastasis and those without metastasis among histologic types of lung cancer

| Diagnostic Group | All | | Adenocarcinoma | | Squamous cell carcinoma | |
|--------------------------------|----------------|---------------------|----------------|---------------------|-------------------------|---------------------|
| | No.of Nodes | ADC _{LN} * | No.of Nodes | ADC _{LN} * | No.of Nodes | ADC _{LN} * |
| Lymph nodes with metastasis | 23 | 1.352±0.178† | 14 | 1.383±0.194‡ | 9 | 1.305±0.168 |
| Lymph nodes without metastasis | 33 | 1.652±0.213 | 24 | 1.653±0.173 | 9 | 1.650±0.313 |

Note. ADC_{LN}= the ADC of the lymph node.

* Data are means ± SDs.(×10⁻³mm²/sec)

† Mean ADC_{LN} significantly lower ($P<0.001$) than that of lymph nodes without metastasis.

‡ Mean ADC_{LN} significantly lower ($P<0.01$) than that of lymph nodes without metastasis.

There were no significant differences in the mean ADC_{LN} for lymph nodes with metastasis among histologic types of lung cancer.

TABLE 3

Number and mean D1 of lymph nodes with metastasis and those without metastasis among histologic types of lung cancer

| Diagnostic Group | All | | Adenocarcinoma | | Squamous cell carcinoma | |
|--------------------------------|----------------|--------------|----------------|--------------|-------------------------|-------------|
| | No.of Nodes | D1* | No.of Nodes | D1* | No.of Nodes | D1* |
| Lymph nodes with metastasis | 23 | 0.092±0.098† | 14 | 0.122±0.117‡ | 9 | 0.048±0.038 |
| Lymph nodes without metastasis | 33 | 0.465±0.224 | 24 | 0.443±0.176 | 9 | 0.522±0.336 |

Note. D1=the formula $D1 = |ADC_{LC} - ADC_{LN}|$.

ADC_{LC} = the ADC of the lung cancer.

ADC_{LN} = the ADC of the lymph node.

* Data are means ± SDs.($\times 10^{-3} \text{mm}^2/\text{sec}$)

† Mean D1 significantly lower ($P < 0.0001$) than that of lymph nodes without metastasis.

‡ Mean D1 significantly lower ($P < 0.001$) than that of lymph nodes without metastasis.

There were no significant differences in the mean D1 for lymph nodes with metastasis among histologic types of lung cancer.

TABLE 4

Number and mean LSR1 of lymph nodes with metastasis and those without metastasis among histologic types of lung cancer

| Diagnostic Group | All | | Adenocarcinoma | | Squamous cell carcinoma | |
|--------------------------------|----------------|--------------------------|----------------|--------------------------|-------------------------|-------------|
| | No.of Nodes | LSR1* | No.of Nodes | LSR1* | No.of Nodes | LSR1* |
| Lymph nodes with metastasis | 18 | 0.392±0.115 [†] | 12 | 0.456±0.055 [‡] | 6 | 0.329±0.132 |
| Lymph nodes without metastasis | 27 | 0.227±0.081 | 15 | 0.224±0.081 | 12 | 0.240±0.095 |

Note. LSR1= lymph node-0.9% saline phantom ratio

* Data are means ± SDs.

[†] Mean LSR1 significantly higher ($P<0.001$) than that of lymph nodes without metastasis.

[‡] Mean LSR1 significantly higher ($P<0.0001$) than that of lymph nodes without metastasis.

There were no significant differences in the mean LSR1 for lymph nodes with metastasis among histologic types of lung cancer.

TABLE 5

Results at Quantitative Analyses of DW- and STIR- MR Images on a per-Patient Basis

| Parameter | Quantitative Analysis of DW MR Images | Quantitative Analysis of STIR MR Images |
|----------------------------------|---------------------------------------|---|
| | (D1) | (LSR1) |
| Sensitivity (%) | 56.3 (9/ 16) | 50.0 (8/16) |
| Specificity (%) | 100 (54/ 54) | 98.1 (53/ 54) |
| Positive predictive value (%) | 100 (9/ 9) | 88.9 (8/ 9) |
| Negative predictive value (%) | 88.5 (54/ 61) | 86.9 (53/ 61) |
| Accuracy (%) | 90.0 (63/ 70) | 87.1 (61/ 70) |

Note. Numbers on parentheses are raw data

D1=the formula $D1 = |ADC_{LC} - ADC_{LN}|$.

ADC_{LC} = the ADC of the lung cancer.

ADC_{LN} = the ADC of the lymph node.

LSR1= lymph node-0.9% saline phantom ratio

TABLE 6

Results at Quantitative Analyses of DW- and STIR- MR Images on a per-Patient Basis (Assessments excluding Lymph Nodes directly invaded by a primary tumor)

| Parameter | Quantitative Analysis of DW MR Images (D1) | Quantitative Analysis of STIR MR Images (LSR1) |
|----------------------------------|---|---|
| Sensitivity (%) | 69.2 (9/ 13) | 61.5 (8/ 13) |
| Specificity (%) | 100 (54/ 54) | 98.1 (53/ 54) |
| Positive predictive value (%) | 100 (9/ 9) | 88.9 (8/ 9) |
| Negative predictive value (%) | 93.1 (54/ 58) | 91.4 (53/ 58) |
| Accuracy (%) | 94.0 (63/ 67) | 91.0 (61/ 67) |

Note. Numbers on parentheses are raw data

D1=the formula $D1 = |ADC_{LC} - ADC_{LN}|$.

ADC_{LC} = the ADC of the lung cancer.

ADC_{LN} = the ADC of the lymph node.

LSR1= lymph node-0.9% saline phantom ratio



















