ORIGINAL ARTICLE

Comparison of diagnostic and prognostic capabilities of ¹⁸F-FDG-PET/ CT, ¹³¹I-scintigraphy, and diffusion-weighted magnetic resonance imaging for postoperative thyroid cancer

Shigeki Nagamachi · Hideyuki Wakamatsu Shogo Kiyohara · Ryuichi Nishii · Youichi Mizutani Seigo Fujita · Shigemi Futami · Hideo Arita Masaomi Kuroki · Hiroshi Nakada · Noriko Uchino Shozo Tamura · Keiichi Kawai

Received: September 19, 2010 / Accepted: February 3, 2011 © Japan Radiological Society 2011

Abstract

Purpose. The first aim of this study was to compare the detectability of metastasis of postoperative differentiated thyroid cancer (DTC) among ¹³¹I whole body scintigraphy (IWBS), fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT), and diffusion-weighted magnetic resonance imaging (DWI). The second aim was to clarify the association between the image pattern and prognosis.

Materials and methods. We evaluated 70 postoperative DTC patients on both a patient basis and an organ basis (lymph nodes, lung, bone), and we analyzed the correlation between the image pattern and the prognosis.

Results. For the patient-basis analysis, the detectability by IWBS, PET/CT, and DWI was 67.1%, 84.2%, and 57.6%, respectively. IWBS provided complementary information to that provided by PET/CT in 11 of 70 (15.7%) cases. For the organ-basis analysis, IWBS was the best detector for lymph node metastasis (72.4%). PET/CT was superior to IWBS for detecting metastasis

Y. Mizutani · S. Fujita · S. Futami · H. Arita · M. Kuroki ·

H. Nakada · N. Uchino · S. Tamura

Department of Radiology, School of Medicine, Miyazaki University, 5200 Kihara, Kiyotake-cho, Miyazaki 889-1692, Japan

Tel. +81-985-85-1510 (ext. 2244); Fax +81-985-85-7172 e-mail: snagama@med.miyazaki-u.ac.jp

K. Kawai

Faculty of Health Science, School of Medicine, Kanazawa University, Kanazawa, Japan

of bone (85.7% vs. 71.4%) and lung (94.1% vs. 62.7%). For the correlation analysis, PET and DWI positivity were the factors predicting a poor prognosis. *Conclusion.* PET/CT was the best modality for detecting metastases in postoperative DTC patients, although IWBS provided complementary information. Because PET/CT and DWI gave similar information (e.g., positivity) suggesting poor prognoses, the combination of IWBS and DWI might be the method of choice for monitoring postoperative DTC.

Key words 131 I whole-body scintigraphy \cdot DWI \cdot DTC \cdot 18 F-FDG-PET/CT \cdot Prognosis

Introduction

¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) is a rapidly evolving imaging modality that has gained widespread acceptance in oncology.^{1,2} Clinical experience with FDG-PET in patients with differentiated thyroid cancer (DTC) has been reported.^{3–8} Several investigators have reported that FDG-PET and ¹³¹I whole-body scanning (WBS) had complementary roles in the detection of recurrent or metastatic DTC.^{3,4,9,10} Well-differentiated thyroid cancer was positive for ¹³¹I uptake and negative for FDG uptake, whereas poorly differentiated thyroid cancer was negative for ¹³¹I uptake and positive for FDG uptake.^{3–5,10} The combined images of ¹³¹I WBS and FDG-PET in the follow-up of DTC had a sensitivity of approximately 95% for detecting recurrence and metastasis.⁵

S. Nagamachi (🖂) · H. Wakamatsu · S. Kiyohara · R. Nishii ·

Few studies have compared FDG-PET/CT with ¹³¹I whole-body scintigraphy (IWBS).^{7,11,12} In particular, few studies have compared FDG-PET/CT with diffusion-weighted MRI imaging (DWI), which is known to be useful for diagnosing various cancers based on imaging the molecular mobility of water.^{13–20} Although DWI is not a routine investigation when evaluating thyroid cancer, it may become one of the choices owing to the versatility of MRI for tumor diagnosis.

To the best of our knowledge, the current study is the first to compare directly the findings of FDG-PET/CT and DWI in patients with DTC after total thyroidectomy. In addition, few studies have been conducted on the correlation of image patterns and prognosis.^{21,22}

The aim of this study was to evaluate the clinical significance of whole-body FDG-PET/CT in DTC patients by comparing the results with those obtained with IWBS and DWI. We also investigated the correlation of the prognosis with the image pattern.

Methods

Patients

This study included 70 patients with known metastatic differentiated thyroid cancer after total thyroidectomy (22 men, 48 women; ages 27–72 years, mean \pm SD 55.2 \pm 23 years). They were scheduled for ¹³¹I therapy between July 2005 and June 2009. There were 62 patients with papillary cancer and 8 with follicular cancer. All of them had stopped taking thyroxine (T_4) for 3 weeks for ¹³¹I therapy. The thyroid-stimulating hormone (TSH) level was >100 μ IU/ml for all patients at the time of ¹³¹I oral ingestion. Metastasis or recurrence had been diagnosed on the basis of the increased thyroglobulin levels (>30 ng/ ml), positive cytology findings, or positive findings on follow-up imaging including FDG-PET/CT, ¹³¹I scintigraphy, DWI magnetic resonance imaging (MRI), computed tomography (CT), ultrasonography (US), and bone scintigraphy. Written consent was obtained from the patients for all of the imaging studies.

Imaging

We performed FDG-PET/CT using a whole-body PET/ CT system (Biograph 16; Siemens/CTI, Knoxville, TN, USA). Patients fasted for at least 5 h. Whole-body FDG-PET/CT images were obtained 60 min after injection of 185 MBq FDG using the three-dimensional method. The blood glucose level, measured just before tracer administration, was <110 mg/dl in all patients. All patients were asked to remain at rest and quiet just before scanning. The images were obtained from the top of the brain to the femur in all patients. We did not use intravenous contrast media. All PET images were reconstructed using iterative algorithms (Fourier rebinning plus attenuation-weighted ordered-subset expectation maximization, two iterations, eight subsets, 5-mm Gaussian filter) with CT-based attenuation correction. The data were reconstructed with a 256×256 matrix and 3 mm slice thickness. To detect metastases in the lung field by low-dose CT, we reconstructed transaxial images, visualized using the window level, -600 Hounsfield units (HU) and width 1600 HU. We conducted all FDG-PET/ CT examinations under conditions without the influence of the TSH increase, before thyroid hormone depletion. To avoid possible metabolic stunning,²³ all FDG-PET/ CT studies were performed 3 weeks before ¹³¹I therapy.

 131 I whole-body scintigraphy was performed using a dual-head gamma camera (eCAM; Siemens/CTI) with high-energy collimators. The images were acquired 3–4 days after oral ingestion of the therapeutic dose (3.7 GBq) of 131 I.

The DWI was performed using a 1.5-T MRI imaging system (1.5-T Excelart Vantage, ZGV; Toshiba, Tokyo, Japan). Image analysis was done using the Power Plus Package (Toshiba). Both neck and chest images were obtained under the following conditions: TR/TE 11 000/70 ms; slice 6 mm; gap 1 mm; b value 1000 s/mm²; number of excitations (NEX) 4; field of view (FOV) 240 mm; matrix 256×256 ; flip angle (FA) 90°. Although the MRI protocol called for the imaging to be done 3–4 days before ¹³¹I administration and after hospitalization, it could not be done in 11 cases owing to unexpected machine problems or to the patient's condition, such as claustrophobia or hypothyroidism-induced depression or anxiety neurosis.²⁴

Analysis

Two experienced nuclear medicine physicians visually interpreted the FDG-PET/CT and IWBS images until they arrived at consensus. Lesions were defined as "positive" when there was a definite localized area of higher uptake than that in the surrounding normal tissue. In the interpretation of IWBS at ablation ¹³¹I therapy, we excluded uptake in the neck and upper mediastinum, so-called thyroid bed uptake, from the evaluation. With respect to equivocal uptake lesions, agreement was reached on the basis of the consensus of two nuclear medicine physicians. Positive findings were confirmed by the presence of carcinoma on histological examination or were confirmed by follow-up imaging examination, including US or diagnostic CT in the presence of persistent abnormal or increasing thyroglobulin (Tg) levels. Similarly, all DWI images were visually interpreted by three experienced radiologists including head and neck expert(s) and a chest specialist. There was no exchange of information between the nuclear medicine physicians and the radiologists. For the interpretation of DWI images, "positive" was diagnosed when a definite abnormal localized are of diffusion was noted as a highersignal lesion in accord with tumor location confirmed by histological examination or confirmed by follow-up imaging examination. With respect to equivocal lesions, the final decision was done by agreement of three radiologists.

The analyses of obtained images were done on both a patient basis and an organ basis. For the patient-basis analysis, "positive" was defined as a classification of "positive" in any organ. Organ-basis analysis was conducted by dividing anatomical regions into three organs: cervical or mediastinal lymph nodes; lung; bone. A classification of "positive" was assigned when at least one metastasis was detected in the organ (lungs, bones, lymph nodes). Multiple lesions in one organ were regarded as one lesion. Image patterns obtained with the three imaging methods were compared visually with regard to the distribution of metastasis.

We compared the possible influencing factors for influencing the prognosis in two groups: good or poor. Age, sex, serum Tg level before the examination, number of times therapy was applied, and histological differentiation were also possible factors. Based on (1) changes in the image findings and/or (2) changes in the serum Tg level being excellent indexes for persistent disease and recurrent disease diagnosis,^{25,26} we defined the "poor" prognosis group by referencing either condition, (1) or (2), in the correlation analysis. Thus, (1) the value of serum Tg persistently increased or re-increased during the follow-up periods after the last ¹³¹I therapy; and/or (2) the lesion's intensity or number increased during follow-up 1 year after the last ¹³¹I treatment. The patients who did not exhibit either of these conditions were categorized as being in the "good" prognosis group. The mean follow-up period from the last ¹³¹I therapy was 4.6 ± 0.6 years.

Statistical analysis

To determine the factors associated with survival rate, we performed multivariate analysis using the hazard model analysis of Cox. Factors included in analysis were sex, age, number of ¹³¹I treatments, image findings, serum Tg level, and histological examination of surgical specimens. Finally, we examined the association between FDG or DWI positivity and the survival rate using the Kaplan-Meier method. Continuous variables were expressed as a mean \pm SD and were tested by Student's *t*-test. Noncontinuous variables were analyzed by the chi-squared test. Differences were considered significant with P < 0.05.

Results

During the patient-basis analysis, 47 of 70 patients (67.1%) were detected by ¹³¹I-WBS and 34 of 59 (57.6%) by DWI. By means of FDG-PET/CT, the detectability notably improved to 84.2%. In all, 20 (28.6%) of 70 patients were detected only by FDG-PET CT or DWI (Table 1, Fig. 1a).

In the organ-basis analysis, IWBS was the best modality (72.4%) for detecting lymph node metastases (Table 2, Fig. 1b). The detectability of lymph node metastases by other modalities was 61.7% with DWI and 67.2% with PET/CT. Both IWBS and PET/CT showed concordance on 23 lesions (39.7%). Although findings of DWI were similar to those with FDG-PET/CT, six lesions (10.3%) were detected only by PET/CT.

As regards bone metastasis, PET/CT showed the highest detectability rate (85.7%). The detectability with IWBS (71.4%) was relatively lower than that with other modalities. The FDG uptake accorded with DWI high-signal intensity in 13 of 17 lesions (76.5%) for which both FDG-PET/CT and DWI were performed (Fig. 1c). For the diagnosis of lung metastasis, FDG-PET/CT showed

 Table 1. Detectability of metastasis (patient basis)

¹³¹ IWBS	DWI	FDG-PET/CT	
47/70	34/59	59/70	
67.1%	57.6%	84.2%	

¹³¹IWBS, iodine-131 whole-body scintigraphy; DWI, diffusionweighted magnetic resonance imaging; FDG-PET/CT, fluorodeoxyglucose-positron emission tomography/computed tomography

 Table 2. Detectability of metastasis (organ basis)

Organ	No. detected	
Lymph node ($n = 58$)		
¹³¹ IWBS	42 (72.4%)	
DWI (47 ^a)	29 (61.7%)	
FDG-PET/CT	39 (67.2%)	
Lung $(n = 51)$		
¹³¹ IWBS	32 (62.7%)	
DWI (40 ^a)	20 (50.0%)	
FDG-PET/CT	48 (94.1%)	
Bone $(n = 21)$		
¹³¹ IWBS	15 (71.4%)	
DWI (17 ^a)	13 (76.5%)	
FDG-PET/CT	18 (85.7%)	

^aTotal number of DWI scans performed

Fig. 1. Detectability of metastases illustrated by the Venn diagram. **a** Patient-based analysis (n = 70). DWI, diffusionweighted imaging; FDG-PET/CT, ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography; 131I, iodine-131. b-d Organ-based analyses. b Lymph node (n = 58). c Bone (n = 21). **d** Lung (n = 51)

3(2)

(): DWI was not done

131**J**

19(6)



3(2)

131₁

(): DWI was not done

3(2)

9(3)

d

FDG-

PET/CT

excellent detectability (94.1%) by visualizing small metastatic nodules with no FDG uptake (Table 2, Fig. 1d).

с

2

FDG-

PET/CT

a

A comparison of the clinical factors, including tracer uptake patterns, between the good prognosis and poor prognosis groups is summarized in Table 3. Regarding the imaging findings, both FDG and DWI positivity were significant prognostic indicators. However, ¹³¹I uptake pattern had no prognostic value. The histological differentiation, stage, and prior ¹³¹I therapy were also significant determinants (Table 3). Patients in the poor prognosis group were significantly older than those in the good prognosis group. The Tg level is also significantly higher in the poor prognosis group. Multivariate analysis indicated that age and the FDG positivity were significant factors influencing the survival rate (Table 4). Univariate analysis using the Kaplan-Meier method proved that the survival rate of the FDG-positive group was significantly lower than that of the FDG-negative group. Similarly, the survival rate of the DWI-positive group was significantly lower than that of the DWInegative group (Fig. 2). Representative FDG-negative cases and FDG-positive cases are demonstrated in Figs. 3 and 4, and in Figs. 5 and 6, respectively.

Discussion

Our current results demonstrated that FDG-PET/ CT provided excellent detectability in the detection of metastatic thyroid cancer on the patient-basis analysis, which agrees with data obtained by FDG-PET/CT that has recently become available.^{27–29} In the previous report, FDG-PET was reported to play a complementary role for IWBS.²⁻⁵ However IWBS provided information complementary to that obtained with PET/CT (15.7%) in the current study. With regard to lung metastases, previous studies showed FDG-PET cannot adequately assess nodules <6 mm.^{4,30} Using FDG-PET/CT, the detectability was impeccable for detecting small lung metastatic nodules, including FDG-negative uptake lesions. Nevertheless, the lack of resolution of low radiation dose CT renders it insufficient for visualising all miliary metastatic nodules. The problem should be further analyzed using diagnostic high-dose radiation CT.

As regards bone metastases, FDG-PET/CT showed excellent detectability. Nonetheless, it could not detect the FDG-negative metastatic lesions. Possibly, FDG-negative and ¹³¹I-positive metastatic bone lesions will show some morphological alteration. However, in the current investigation, plain CT showed no organic changes in accord with the ¹³¹I uptake. Because metastatic lesions without significant bone destruction are missed even by 64-slice multidetector (MD)CT with excellent image quality and high spatial resolution, the assessment of bony structures by FGD-PET CT (16-slice) might also be of insufficient quality.³¹

Factor	Good (<i>n</i> = 50)	Poor (<i>n</i> = 20)	Р
Sex (M:F)	14:36	8:12	NS
Age (years)	58.3 ± 11.8	68.2 ± 11.3	0.0041
Pathology (F:P)	4:46	4:16	NS
Differentiation (W:P)	48:2	12:8	0.004
Stage I–III:IV	37:13	2:18	< 0.0001
Prior ¹³¹ I therapy (yes:no)	7:43	9:11	0.0053
Thyroglobulin (ng/ml)	183.5 ± 13.8	1600.8 ± 79.6	0.0011
FDG-PET (positive: negative)	22:28	20:0	< 0.05
¹³¹ IWBS (positive: negative)	37:13	10:10	NS
MR-DWI $(n = 59)$ (positive:negative)	18:25	16:0	< 0.001

Table 3. Possible factors predicting prognosis

F, follicular; P, papillary; W, well differentiated; P, poorly differentiated; MR, magnetic resonance

Table 4. Factors influencing survival rate (multivariate analysis)

Variable	Relative risk	95% CI	Р
Age >45 years	4.64	3.89-5.26	0.034
Sex: male	2.17	1.22-2.43	0.069
Pathology: follicular	1.72	1.22-2.37	0.899
Thyroglobulin >30 ng/ml	1.35	0.91-1.84	0.439
Stage: IV	1.39	0.94-1.89	0.581
¹³¹ I irradiation: repeated	2.07	1.45-2.87	0.341
FDG-PET: positive	5.01	3.41-6.62	0.011
DWI: positive	2.51	1.60-3.42	0.065
¹³¹ I: negative	1.76	1.05-2.49	0.091

CI, confidence interval



Fig. 2. a Comparison of survival rates between FDG-positive and FDG-negative groups. The survival rate for the FDG-positive group was significantly lower than that for the FDG-negative

For the detection of lymph node metastasis, IWBS was the most sensitive modality of the four. However, FDG-PET/CT detected approximately 25% lesions that were not detected by IWBS. As papillary thyroid cancer has the highest incidence of DTC and showed a high occurrence of lymph node metastases,^{32,33} a combination of IWBS and FDG-PET/CT is necessary to detect metastatic lesions.^{28,29} Although in no case was the size of the lymph nodes a problem regarding diagnosis in the current study, it is difficult to evaluate the diameter of lymph nodes by low-dose plain CT alone. Contrast enhancement CT can overcome these limitations by accurately delineating the lymph node contour.

group. **b** Comparison of survival rates between DWI-positive and DWI-negative groups. The survival rate for the DWI-positive group was lower than that for the DWI-negative group

DWI has been proven to be useful for various thoracic diseases including pulmonary nodules such as primary lung cancer and thyroid cancer metastasis.^{13–16,20,34,35} The mechanism of DWI for depicting a malignant tumor depends on the diffusing capacity of a water molecule. High-intensity-signal DWI is associated with cellular edema, cellular high density, fibrosis, and gelatinous and viscous fluids.^{17,18,34} Therefore, within higher-grade carcinomas with high cell density, such as poorly differentiated adenocarcinoma, the diffusing capacity of a water molecule seems to be inhibited. Thus, the aggressive biological behavior of various cancers can be estimated by DWI.



Fig. 3. A 35-year-old woman with well-differentiated papillary cancer was categorized as having a good prognosis. Whole-body FDG-PET demonstrated no abnormal uptake (a). Chest FDG-PET/CT showed no abnormal findings (b). DWI shows no definitive abnormality (c). ¹³¹I whole-body scintigraphy (¹³¹IWBS)

shows diffuse and intense uptakes in bilateral lung fields (**d**). The serum thyroglobulin (Tg) level decreased from 900 ng/ml to 25 ng/ml after the first ¹³¹I therapy. Follow-up ¹³¹IWBS after 1 year showed no tracer uptake in the lung field (**e**)

Although the mechanisms for visualizing aggressive characteristics are different with the two imaging methods, the patterns of FDG uptake and DWI highsignal intensity were in relatively good agreement and were similar. Recently, some researchers reported that DWI and PET showed similar sensitivity in distinguishing malignant from benign pulmonary nodules.²⁰ They insisted that DWI showed significantly higher specificity than PET because it yielded fewer false-positive results for active inflammatory lesions.²⁰ In another comparison study between DWI and FDG-PET/CT in regard to breast cancer staging,³⁶ DWI seems to be a sensitive but unspecific modality for the detecting locoregional disease or metastasis. In the current study, certain discrepancies were also observed between FDG-PET/CT and DWI findings, in particular, lymph node metastases. One explanation is that the hypermetabolism of glucose in cancer cells is not always equal to the increase in cancer cell density or viscosity. In some metastases with a low density of cancer cells, hypermetabolic cancer cells can be detected by FDG-PET/CT. In contrast, lower metabolic metastasis with a high density of cancer cells can be identified with DWI. Another explanation could be that there is physiological uptake with each modality. For instance, in the thoracic region, the ribs, spinal cord, and mediastinal lymph nodes sometimes show nonspecific increased signal intensities.^{35,37,38} At the same time, lung fields contain few of the protons that are necessary for DWI. Respiratory movement is a restriction factor as well.³⁹ Recently, DWI has made remarkable progress with the development of hardware, such as the 3-tesla machine.⁴⁰The differences in findings between FDG-PET/ CT and DWI may be attributable to the performance of MRI. However, DWI could be an alternative imaging method in the future with a sequence adjustment. Future studies should compare higher-performance DWI with FDG-PET/CT findings.

With regard to the correlation between imaging patterns and prognosis, we could predict an unfavorable prognosis in patients with FDG uptake, as several authors previously reported.^{11,41-43} The survival of patients harboring FDG-positive tumor deposits was significantly shorter than that of subjects with FDGnegative metastases as Robbins et al. reported.²² FDG is often taken up by relatively poorly differentiated thyroid cancer or dedifferentiated cancers in which the glucose metabolism has increased^{5,6} and expression of glucose transporters (GLUT-1 and GLUT-3) is increased.¹¹ They generally grow faster than well-differentiated thyroid cancer.^{44,45} Joensuu and Ahonen also reported



Fig. 4. A 60-year-old woman with differentiated thyroid cancer (DTC) (well-differentiated papillary cancer) was categorized as having a good prognosis. Whole-body FDG-PET demonstrated no abnormal uptake (a). Chest FDG-PET/CT demonstrated multiple lung metastatic nodules (b). DWI shows no definitive abnor-

mality (c). ¹³¹IWBS shows multiple areas of intense uptake in the lung (d). Just after iodine therapy, the serum Tg level was 290 ng/ml. At 6 months later, the lung uptake had decreased (e). The serum Tg level decreased to 91 ng/ml during the follow-up period



Fig. 5. A 62-year-old man with DTC (poorly differentiated papillary cancer) was categorized as having a poor prognosis. Wholebody FDG-PET demonstrated intense uptake in the left subclavicular lymph node (*arrow*) (**a**), although ¹³¹IWBS shows uptake only in the thyroid bed (**b**). DWI shows no definitive abnor-

mality (c). Just after the initial iodine therapy, the serum Tg level was 28 ng/ml. At 6 months later, multiple areas of FDG uptake were noted in multiple organs, including the left lung, mediastinal lymph nodes, and neck lymph nodes (d). The serum Tg level increased to 1600 ng/ml during the follow-up period



Fig. 6. A 75-year-old woman with DTC (well-differentiated papillary cancer) was categorized as having a poor prognosis. ¹³¹IWBS showed no abnormal uptake (**a**). FDG-PET demonstrated multiple lung areas with uptake and left supraclavicular lymph node uptake (**b**). DWI demonstrated a high-intensity lesion (*arrow*) in

that metastases exhibiting high FDG uptake but low ¹³¹I uptake grow rapidly.⁴⁶ It has been reported in previous studies that most PET-positive metastases are of a histological aggressive subtype.^{41,42} In various cancer metastasis or recurrences, higher FDG concentrations were noted in connection with accelerated proliferative activity.⁴⁷ The degree of FDG uptake may have a certain correlation with proliferative activities, which is one of the major factors in aggressiveness. According to some molecular studies, FDG-positive/radioiodine-negative metastases have a mutational profile such as RAS or BRAF mutations.^{11,48,49} Such mutations in oncogenes is well known to be present in aggressive malignancies.¹¹ FDG positivity may be useful as a tool for estimating the abnormality of the genes and noninvasively predicting a bad prognosis.

In general, the standard treatment for DTC includes total surgical thyroidectomy followed by ¹³¹I therapy for residual or metastatic disease. The follow-up is based on

the left lung (c). Chest CT showed multiple lung metastases (d). At 9 months after ¹³¹I irradiation, lung metastases had increased in size and number compared with that before therapy (e). The serum Tg level increased from 480 ng/ml to 830 ng/ml during the follow-up period

monitoring the serum Tg level and IWBS. The natural history of DTC is long, and deaths that occur ≥ 20 years after the initial diagnosis can be attributed to it.³⁰ However, if FDG-positive lesions exist at any rate during the follow-up periods, they can potentially dedifferentiate and continuously progress despite repeated series of ¹³¹I therapy. In such cases, the therapeutic effect is insufficient, and another effective therapy, such as cytotoxic chemotherapy, should be chosen.²¹ For instance, after having given ¹³¹I therapy, an additional chemotherapy protocol is one of the choices. To determine the optimal treatment strategy depending on the situation, monitoring with FDG-PET/CT or DWI is necessary.

There were some limitations in the current study. The first is the differences in the quality of the equipment. Although FDG and IWBS showed different findings, the difference in the findings may have been caused by the different acquisition methods used for the PET/CT camera and planar scintigraphy by the gamma camera. A PET/CT camera has much higher sensitivity and spatial resolution than planar scintigraphy.⁵⁰ Generally, PET/CT is superior to planar scintigraphy for detecting various metastases and providing better image quality. Several small lesions, therefore, might be detected easily with FDG-PET/CT but only with difficulty with IWBS because of poor spatial resolution. In addition, 11 patients did not undergo the DWI examination, and so the DWI data that were analyzed comprised a smaller number. The detectability rate for DWI might improve if more patients are analyzed.

Another limitation is the method used for the organbasis analysis. Because individual comparisons of small and multiple lesions were difficult, solitary and multiple metastases were regarded as one lesion in each organ. In addition, we did not perform a quantitative analysis, such as for the standardized uptake value or the diffusion coefficient value (ADC). Although the great overlap of ADC values existed in malignant lesions and benign lesions including physiological uptake,³⁶ analysis using ADC values might be helpful when monitoring the therapeutic effect in individual cases.

Finally, the diagnosis was not always confirmed pathologically for each lesion. We performed clinical course observations, particularly with imaging analysis, and we could define metastases that showed ¹³¹I uptake or serial growth. However, we did not include several smaller lymph nodes with FDG uptake finally diagnosed as inflammation. Nevertheless, owing to the slowly progression of DTC metastasis, we might have underestimated FDG uptake-positive and ¹³¹I-negative lesions. Optimally, examination of biopsy would be preferable for confirming the clinical significance of FDG-PET/CT findings.

Conclusion

We found that FDG-PET/CT was the best modality for detecting metastases of DTC after total thyroidectomy, although IWBS provided complementary information. Patients with FDG high uptake or high-intensity-signal lesions on DWI tended to have a poor prognosis. Because DWI provides information similar to that obtained with FDG-PET in regard to predicting prognosis, the combination of IWBS and DWI might be the methods of choice for monitoring DTC.

References

 Hoh CK, Schiepers C, Seltzer MA, Gambhir SS, Silverman DH, Czernin J, et al. PET in oncology: will it replace the other modalities? Semin Nucl Med 1997;27:94–106.

- Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, et al. Recommendations on the use of ¹⁸F-FDG PET in oncology. J Nucl Med 2008;49:480–508.
- Grunwald F, Schomburg A, Bender H, Klemm E, Menzel C, Bultmann T, et al. Fluorine-18 fluorodeoxyglucose positron emission tomography in the follow-up of differentiated thyroid cancer. Eur J Nucl Med 1996;23:312–9.
- Dietlein M, Scheidhauer K, Voth E, Theissen P, Schicha H. Fluorine-18 fluorodeoxyglucose positron emission tomography and iodine-131 whole-body scintigraphy in the follow-up of differentiated thyroid cancer. Eur J Nucl Med 1997;24: 1342–8.
- 5. Feine U, Lietzenmayer R, Hanke JP, Held J, Wohrle H, Muller-Schauenburg W. Fluorine-18-FDG and iodine-131-iodide uptake in thyroid cancer. J Nucl Med 1996;37:1468–72.
- Grunwald F, Menzel C, Bender H, Palmedo H, Willkomm P, Ruhlmann J, et al. Comparison of ¹⁸FDG-PET with ¹³¹iodine and ^{99m}Tc-sestamibi scintigraphy in differentiated thyroid cancer. Thyroid 1997;7:327–35.
- Zoller M, Kohlfuerst S, Igerc I, Kresnik E, Gallowitsch HJ, Gomez I, et al. Combined PET/CT in the follow-up of differentiated thyroid carcinoma: what is the impact of each modality? Eur J Nucl Med Mol Imaging 2007;34:487–95.
- Robbins RJ, Larson SM. The value of positron emission tomography (PET) in the management of patients with thyroid cancer. Best Pract Res Clin Endocrinol Metab 2008;22:1047–59.
- Dietlein M, Scheidhauer K, Voth E, Theissen P, Schicha H. Follow-up of differentiated thyroid cancer: what is the value of FDG and sestamibi in the diagnostic algorithm? Nuklearmedizin 1998;37:12–7.
- Shiga T, Tsukamoto E, Nakada K, Morita K, Kato T, Mabuchi M, et al. Comparison of (18)F-FDG, (131)I-Na, and (201)Tl in diagnosis of recurrent or metastatic thyroid carcinoma. J Nucl Med 2001;42:414–9.
- Pace L, Nicolai E, Klain M, Salvatore M. Diagnostic value of FDG PET/CT imaging. Q J Nucl Med Mol Imaging 2009;53: 503–12.
- Razfar A, Branstetter BF, Christopoulos A, Lebeau SO, Hodak SP, Heron DE, et al. Clinical usefulness of positron emission tomography-computed tomography in recurrent thyroid carcinoma. Arch Otolaryngol Head Neck Surg 2010; 136:120–5.
- 13. Takano A, Oriuchi N, Tsushima Y, Taketomi-Takahashi A, Nakajima T, Arisaka Y, et al. Detection of metastatic lesions from malignant pheochromocytoma and paraganglioma with diffusion-weighted magnetic resonance imaging: comparison with ¹⁸F-FDG positron emission tomography and ¹²³I-MIBG scintigraphy. Ann Nucl Med 2008;22:395–401.
- Nakanishi K, Kobayashi M, Nakaguchi K, Kyakuno M, Hashimoto N, Onishi H, et al. Whole-body MRI for detecting metastatic bone tumor: diagnostic value of diffusion-weighted images. Magn Reson Med Sci 2007;6:147–55.
- Vilanova JC, Barcelo J. Diffusion-weighted whole-body MR screening. Eur J Radiol 2008;67:440–7.
- Bohlscheid A, Nuss D, Lieser S, Busch HP. Tumor search with diffusion-weighted imaging: first experience. Rofo 2008;180: 302–9 (in German).
- Choi JA, Kang EY, Kim HK, Song IC, Kim YI, Kang HS. Evolution of VX2 carcinoma in rabbit tibia: magnetic resonance imaging with pathologic correlation. Clin Imaging 2008;32:128–35.
- Baur A, Dietrich O, Reiser M. Diffusion-weighted imaging of bone marrow: current status. Eur Radiol 2003;13:1699–708.
- Bozgeyik Z, Coskun S, Dagli AF, Ozkan Y, Sahpaz F, Ogur E. Diffusion-weighted MR imaging of thyroid nodules. Neuroradiology 2009;51:193–8.

- Mori T, Nomori H, Ikeda K, Kawanaka K, Shiraishi S, Katahira K, et al. Diffusion-weighted magnetic resonance imaging for diagnosing malignant pulmonary nodules/masses: comparison with positron emission tomography. J Thorac Oncol 2008;3:358–64.
- Toubert ME, Hindie E, Rampin L, Al-Nahhas A, Rubello D. Distant metastases of differentiated thyroid cancer: diagnosis, treatment and outcome. Nucl Med Rev Cent East Eur 2007;10:106–9.
- Robbins RJ, Wan Q, Grewal RK, Reibke R, Gonen M, Strauss HW, et al. Real-time prognosis for metastatic thyroid carcinoma based on 2-[¹⁸F]fluoro-2-deoxy-D-glucose-positron emission tomography scanning. J Clin Endocrinol Metab 2006;91:498–505.
- Hung GU, Lee KW, Liao PY, Yang LH, Yang KT. The influence of I-131 therapy on FDG uptake in differentiated thyroid cancer. Ann Nucl Med 2008;22:481–5.
- Nagamachi S, Jinnouchi S, Nishii R, Ishida Y, Fujita S, Futami S, et al. Cerebral blood flow abnormalities induced by transient hypothyroidism after thyroidectomy: analysis by Tc-99m-HMPAO and SPM96. Ann Nucl Med 2004;18:469–77.
- 25. Eustatia-Rutten CF, Smit JW, Romijn JA, van der Kleij-Corssmit EP, Pereira AM, Stokkel MP, et al. Diagnostic value of serum thyroglobulin measurements in the follow-up of differentiated thyroid carcinoma, a structured meta-analysis. Clin Endocrinol (Oxf) 2004;61:61–74.
- 26. Schlumberger M, Baudin E. Serum thyroglobulin determination in the follow-up of patients with differentiated thyroid carcinoma. Eur J Endocrinol 1998;138:249–52.
- Palmedo H, Bucerius J, Joe A, Strunk H, Hortling N, Meyka S, et al. Integrated PET/CT in differentiated thyroid cancer: diagnostic accuracy and impact on patient management. J Nucl Med 2006;47:616–24.
- Freudenberg LS, Frilling A, Kuhl H, Muller SP, Jentzen W, Bockisch A, et al. Dual-modality FDG-PET/CT in follow-up of patients with recurrent iodine-negative differentiated thyroid cancer. Eur Radiol 2007;17:3139–47.
- Finkelstein SE, Grigsby PW, Siegel BA, Dehdashti F, Moley JF, Hall BL. Combined [¹⁸F]fluorodeoxyglucose positron emission tomography and computed tomography (FDG-PET/CT) for detection of recurrent, ¹³¹I-negative thyroid cancer. Ann Surg Oncol 2008;15:286–92.
- Nanni C, Rubello D, Fanti S, Farsad M, Ambrosini V, Rampin L, et al. Role of ¹⁸F-FDG-PET and PET/CT imaging in thyroid cancer. Biomed Pharmacother 2006;60:409–13.
- Buhmann Kirchhoff S, Becker C, Duerr HR, Reiser M, Baur-Melnyk A. Detection of osseous metastases of the spine: comparison of high resolution multi-detector-CT with MRI. Eur J Radiol 2009;69:567–73.
- Grebe SK, Hay ID. Thyroid cancer nodal metastases: biologic significance and therapeutic considerations. Surg Oncol Clin N Am 1996;5:43–63.
- Schlumberger MJ. Papillary and follicular thyroid carcinoma. N Engl J Med 1998;338:297–306.
- 34. Matoba M, Tonami H, Kondou T, Yokota H, Higashi K, Toga H, et al. Lung carcinoma: diffusion-weighted MR imaging: preliminary evaluation with apparent diffusion coefficient. Radiology 2007;243:570–7.
- 35. Hasegawa I, Boiselle PM, Kuwabara K, Sawafuji M, Sugiura H. Mediastinal lymph nodes in patients with non-small cell lung cancer: preliminary experience with diffusion-weighted MR imaging. J Thorac Imaging 2008;23:157–61.

- 36. Heusner TA, Kuemmel S, Koeninger A, Hamami ME, Hahn S, Quinsten A, et al. Diagnostic value of diffusion-weighted magnetic resonance imaging (DWI) compared to FDG PET/ CT for whole-body breast cancer staging. Eur J Nucl Med Mol Imaging 2010;37:1077–86.
- 37. Satoh S, Kitazume Y, Ohdama S, Kimula Y, Taura S, Endo Y. Can malignant and benign pulmonary nodules be differentiated with diffusion-weighted MRI? AJR Am J Roentgenol 2008;191:464–70.
- Rong R, Zhang CY, Wang XY. Normal appearance of large field diffusion weighted imaging on 3.0 T MRI. Chin Med Sci J 2008;23:158–61.
- 39. Horie T, Takahara T, Ogino T, Okuaki T, Honda M, Okumura Y, et al. Trial of artifact reduction in body diffusion weighted imaging development and basic examination of "TRacking Only Navigator" (TRON method). Nippon Hoshasen Gijutsu Gakkai Zasshi 2008;64:1157–66 (in Japanese).
- Kim CK, Park BK, Han JJ, Kang TW, Lee HM. Diffusionweighted imaging of the prostate at 3 T for differentiation of malignant and benign tissue in transition and peripheral zones: preliminary results. J Comput Assist Tomogr 2007;31: 449–54.
- Are C, Hsu JF, Ghossein RA, Schoder H, Shah JP, Shaha AR. Histological aggressiveness of fluorodeoxyglucose positronemission tomogram (FDG-PET)-detected incidental thyroid carcinomas. Ann Surg Oncol 2007;14:3210–5.
- Rivera M, Ghossein RA, Schoder H, Gomez D, Larson SM, Tuttle RM. Histopathologic characterization of radioactive iodine-refractory fluorodeoxyglucose-positron emission tomography-positive thyroid carcinoma. Cancer 2008;113:48–56.
- 43. Wang W, Larson SM, Fazzari M, Tickoo SK, Kolbert K, Sgouros G, et al. Prognostic value of [¹⁸F]fluorodeoxyglucose positron emission tomographic scanning in patients with thyroid cancer. J Clin Endocrinol Metab 2000;85:1107– 13.
- 44. Di Chiro G, DeLaPaz RL, Brooks RA, Sokoloff L, Kornblith PL, Smith BH, et al. Glucose utilization of cerebral gliomas measured by [¹⁸F] fluorodeoxyglucose and positron emission tomography. Neurology 1982;32:1323–9.
- Uematsu H, Sadato N, Ohtsubo T, Tsuchida T, Nakamura S, Sugimoto K, et al. Fluorine-18-fluorodeoxyglucose PET versus thallium-201 scintigraphy evaluation of thyroid tumors. J Nucl Med 1998;39:453–9.
- Joensuu H, Ahonen A. Imaging of metastases of thyroid carcinoma with fluorine-18 fluorodeoxyglucose. J Nucl Med 1987;28:910–4.
- 47. Watanabe K, Nomori H, Ohtsuka T, Naruke T, Ebihara A, Orikasa H, et al. [F-18]Fluorodeoxyglucose positron emission tomography can predict pathological tumor stage and proliferative activity determined by Ki-67 in clinical stage IA lung adenocarcinomas. Jpn J Clin Oncol 2006;36:403–9.
- Mian C, Barollo S, Pennelli G, Pavan N, Rugge M, Pelizzo MR, et al. Molecular characteristics in papillary thyroid cancers (PTCs) with no ¹³¹I uptake. Clin Endocrinol (Oxf) 2008;68:108–16.
- 49. Ricarte-Filho JC, Ryder M, Chitale DA, Rivera M, Heguy A, Ladanyi M, et al. Mutational profile of advanced primary and metastatic radioactive iodine-refractory thyroid cancers reveals distinct pathogenetic roles for BRAF, PIK3CA, and AKT1. Cancer Res 2009;69:4885–93.
- Aygun N. Imaging of recurrent thyroid cancer. Otolaryngol Clin North Am 2008;41:1095–106.