

Current state of oncologic ^{18}F -FDG PET/CT in Japan: A nationwide survey

Hajime Ichikawa^{1, 2}, Toyohiro Kato¹, Kenta Miwa³, Takayuki Shibutani², Koichi Okuda⁴, Akio Nagaki⁵, Hiroyuki Tsushima⁶, Masahisa Onoguchi^{2*}

¹Department of Radiology, Toyohashi Municipal Hospital, Toyohashi, Japan

² Department of Quantum Medical Technology, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Japan

³Department of Radiological Sciences, School of Health Sciences, International University of Health and Welfare, Tochigi, Japan

⁴Department of Physics, Kanazawa Medical University, Kanazawa, Japan

⁵Department of Radiological Technology, Kurashiki Central Hospital, Kurashiki, Japan

⁶Department of Radiological Sciences, Ibaraki prefectural University of Health Sciences, Ibaraki, Japan

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ABSTRACT

Objectives: Combined positron emission tomography/computed tomography (PET/CT) has gradually advanced with the introduction of newly developed techniques. However, the recent status of imaging techniques (e.g., scanning range, availability of correction methods, and decisions on performing delayed scan) in oncologic PET/CT with ^{18}F -fluorodeoxyglucose (^{18}F -FDG) in Japan is unclear. We conducted a nationwide cross-sectional survey to document ^{18}F -FDG PET/CT protocols and clarify the recent status of imaging techniques for oncologic ^{18}F -FDG PET/CT in Japan.

Methods: We conducted a web survey hosted by the Japanese Society of Radiological Technology between October and December 2017. The questionnaire included nine items on the demographics of the respondents, their scan protocols, and additional imaging to their routine protocols.

Results: We received responses from 119 Japanese technologists who performed ^{18}F -FDG PET/CT in practice. Almost all the respondents stated that the scanning range was from the top of the head to the pelvis or mid-thigh region. Newly developed techniques were used by fewer than half of the respondents. Most respondents performed additional imaging in consultation with physicians, such as delayed imaging (83%) or an extended scanning range for early imaging (55%).

Conclusions: Our survey helps in clarifying the recent state of oncologic ^{18}F -FDG PET/CT imaging techniques in Japan. Given that ^{18}F -FDG PET/CT practices most frequently performed additional imaging along with their routine scan protocol, the practice constitutes the most varied examination performed in Japanese nuclear medicine.

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Introduction

Positron emission tomography (PET) with ^{18}F -fluorodeoxyglucose (FDG) has been increasingly used for diagnosis, staging, or detecting recurrent

malignant tumors worldwide, including Japan (1).

The ^{18}F -FDG radiopharmaceutical provided by manufacturers has allowed easier application of ^{18}F -FDG PET procedures at Japanese medical

* Corresponding author: Masahisa Onoguchi. 5-11-80 Kodatsuno, Kanazawa, Ishikawa, 9200942, Japan. Tel: +81-76-265-2526; Fax No: +81-76-265-2526; E-mail: onoguchi@staff.kanazawa-u.ac.jp

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institutions since 2005. Combined PET/computed tomography (CT) hybrid scanners were available commercially in 2001, and thereafter time-of-flight (TOF) and point spread function (PSF) modeling reconstruction were implemented on PET/CT scanners (2). Moreover, semiconductor PET system and PET/magnetic resonance have become commercially available in recent years (3, 4).

Cancer has generally been diagnosed using ^{18}F -FDG PET/CT with visual interpretation and quantitative analysis for ^{18}F -FDG uptake, such as the standardized uptake value (SUV). However, in addition to the examination protocol, SUV variation is affected not only by the reconstruction method and its parameters but also by performance of attenuation correction, scatter correction, reconstruction incorporating TOF or PSF, respiratory-gated acquisition, and so forth (5-8). Consequently, in the United States and Europe, guidelines have been developed to achieve SUV harmonization (9, 10), and an additional worldwide survey was performed to assess the ^{18}F -FDG PET/CT protocols (11, 12). The survey assessed the examination protocol, imaging techniques (e.g., scanning range, correction method, and so forth), additional imaging techniques, and interpretation. The investigators stated that variability in the ^{18}F -FDG PET/CT protocols may cause degradation of the validity of the ^{18}F -FDG PET/CT practice.

Minamimoto et al. (13) performed a nationwide survey of cancer screening and described the examination protocol, imaging techniques, and diagnostic performance. However, in Japan and Asia, the oncologic ^{18}F -FDG PET/CT acquisition protocol was undefined, as was the use of new

technologies such as TOF or PSF correction. Therefore, we conducted a nationwide cross-sectional survey to document ^{18}F -FDG PET/CT protocols and to clarify the recent status of imaging techniques (e.g., scanning range, availability of correction methods, decisions on performing delayed scan) for oncologic ^{18}F -FDG PET/CT in Japan.

Methods

This study was approved by the human research ethics committee of our institution and was conducted between October 2 and December 20, 2017. We used a web survey system hosted by the Japanese Society of Radiological Technology. A link was mailed to approximately 9000 of their members who subscribed to an e-mail newsletter. However, only approximately 450 of 9000 members belonged to the nuclear medicine subgroup. The questionnaire included nine items on the demographics of the respondents (e.g., type of medical institution and kind of equipment), their scan protocols (e.g., scanning range and correction method), and additional imaging to their routine protocols (Table 1). We allowed multiple responses for all the questions and provided an explanation on the website that consent could not be withdrawn after completing the questionnaires because of the anonymous nature of data collection. Consent was assumed when a response was received and tabulated for each question. The responses were tabulated by medical institutions, the chi-square test was used to compare the responses among medical institutions; a p-value of <0.05 was considered significant.

Table 1. Questionnaire contents

Question	Option
Demographics	
Q1	Which is your type of medical institution? University hospital, public hospital, private hospital, other
Q2	How many years of experience in nuclear medicine examination do you have?
Q3*	What kind of equipment do you use? PET alone, PET/CT, SiPM-PET/CT, PET/MRI
Routine scan	
Q4	Scanning range Upper limite Lower limite Top of the head, base of the skull, neck, other Pelvis, mid-thighs, knees, ankles, feet, other
Q5*	What do you use for correction method of routine scan? PSF, TOF, uncorrected, high-resolution, respiratory-gated, MAR, other
Q6	Which body parts do you scan in delayed scan? same range as early scan, required body parts, chest, abdomen, other, non
Added imaging to routine scan	
Q7*	How do you determine addition to routine scan protocol? Institute guideline, consultation with physician, decision by technologist, other
Q8*	What additional scan and/or correction method do you perform? Extended scanning range, prolonged acquisition time, breath-hold acquisition, other Uncorrected, PSF, TOF, high-resolution, respiratory-gated, MAR, other Delayed scan; same range as early scan, required body parts, chest, abdomen, other
Q9*	What are the criteria for added imaging? Initial examination, follow-up examination, same as the previous examination, change in the previous examination, presence of abnormal lesions, absence of abnormal lesions, site of pain, agreement for each disease, other

PSF, point spread function correction; TOF, time-of-flight; MAR, metal artifact reduction. *Multiple-choice

Results

In all, 119 eligible responses were received: from university (42%), public (30%) and private (27%) hospitals, and other facilities (1%). The number of institutions that responded to this survey was estimated to be 95 of 389 Japanese PET centers. Two responses (out of total 121 responses received) were not found to be eligible and were excluded as they were from PET alone system users. The mean duration of experience as a nuclear medicine technologist for all the respondents was 11.0±7.9 years.

In routine protocols, almost all the respondents stated that the scanning range was from the top of the head (91%) through the pelvis (46%) or mid-thigh (44%, Figure 1). However, the percentage of upper limit in the scanning range

of public hospitals was significantly different from that in other medical institutions (p=0.0008). In contrast, the lower limit of the scanning range did not differ among types of medical institutions (p>0.05). PSF and TOF corrections were used by 50% and 42% of the respondents, respectively. One-third of the respondents reconstructed corrected and uncorrected PET images; other imaging techniques were not widely used (Table 2). Three quarters of the respondents performed delayed scans of the “required body parts” (Figure 2). Delayed PET/CT imaging of the same scan range as in early imaging was performed by 7% of the respondents. The scanning range of delayed scans showed no significant difference among types of medical institutions (p>0.05).

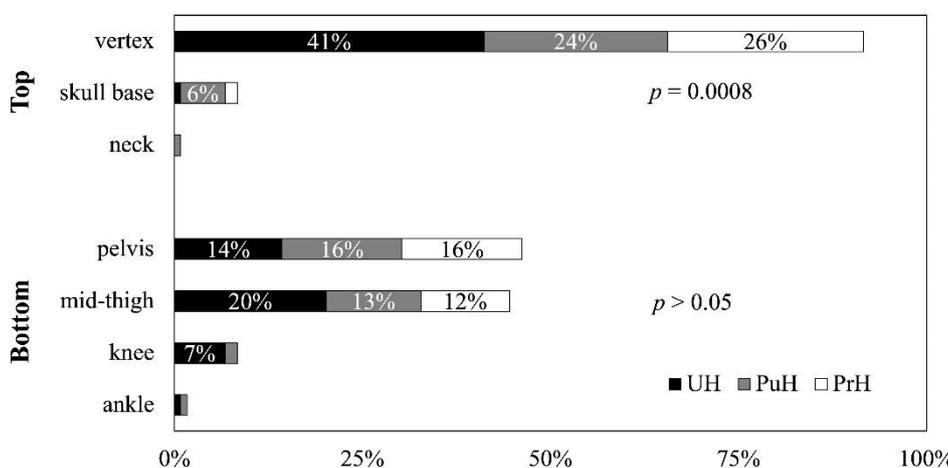


Figure 1. Responses regarding scanning range (upper and lower limits) provided by a medical institution (Q4)

Table 2. Percentage of the use for correction methods. Percentages in parentheses

	All (n = 119)	UH (n = 50)	PuH (n = 36)	PrH (n = 32)
PSF	60 (50)	28 (56)	18 (50)	13 (41)
TOF	50 (42)	26 (52)	14 (39)	10 (31)
Uncorrected	39 (33)	15 (30)	15 (42)	9 (28)
Respiratory-gated	13 (10)	4 (8)	4 (11)	5 (16)
High-resolution	8 (7)	4	3	1
MAR	8 (7)	3	4	1
Other	2	2	0	0

UH, university hospital; PuH, public hospital; PrH, private hospital

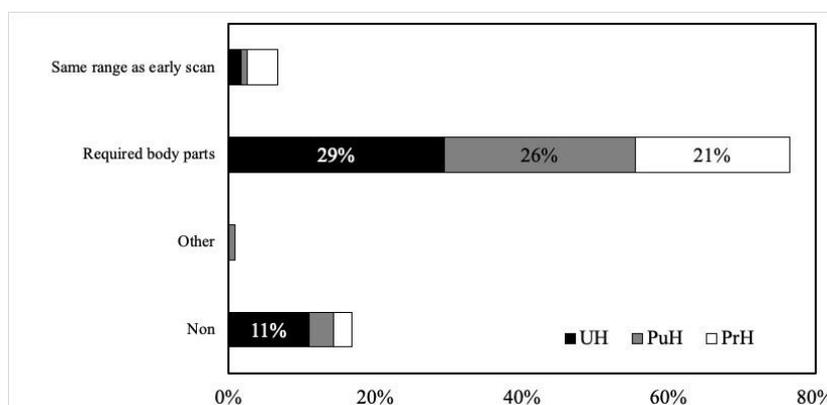


Figure 2. Responses to the question, "Which body parts do you scan in delayed scan?" (Q6)

Additional imaging to the early routine scan protocol was performed by 87% of the respondents. The additional imaging was decided on mostly based on “consultation with the physician” (56%) or “decision by the technologist” (50%), and the percentage varied by the medical institution (Figure 3); although there was no significant difference ($p>0.05$). The most used imaging type was delayed imaging (83%), and an expanding scan range was used for

early imaging (55%; e.g., patients with bone metastases, malignant melanoma, and malignant lymphoma; Figure 4). For additional scan, no significant difference was found among the types of medical institutions ($p>0.05$). Half of the respondents (54%) performed some additional imaging when abnormal lesions were detected (Figure 5). There was also no significant difference in the criteria for additional scan by type of medical institution ($p>0.05$).

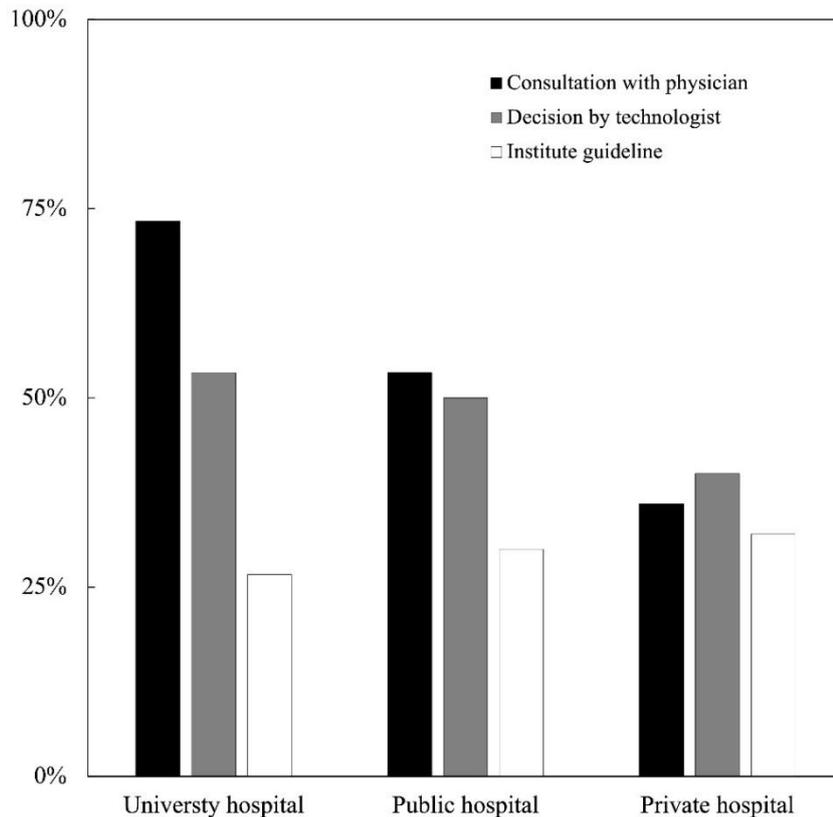


Figure 3. Responses to the question, “How do you determine addition to routine scan protocol?” (Q7)

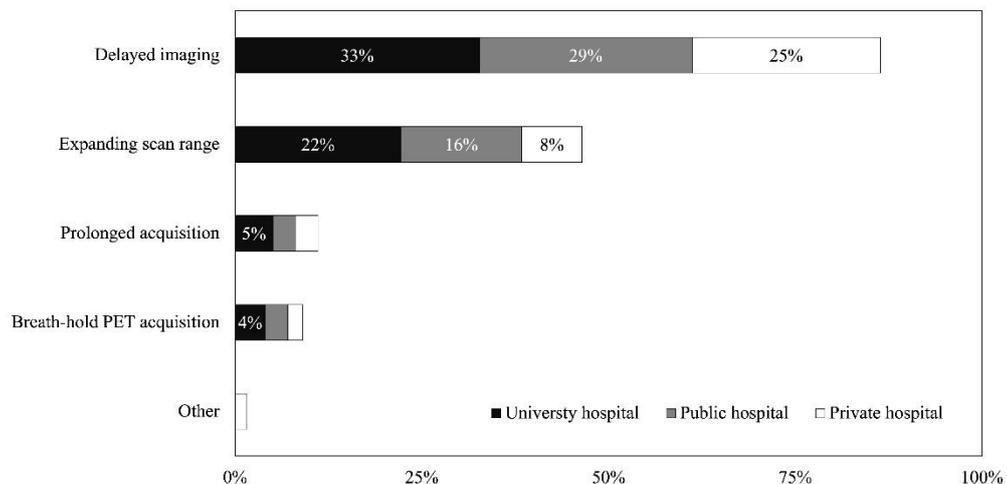


Figure 4. Responses to the question, “What additional scan and/or correction method do you perform?” (Q8)

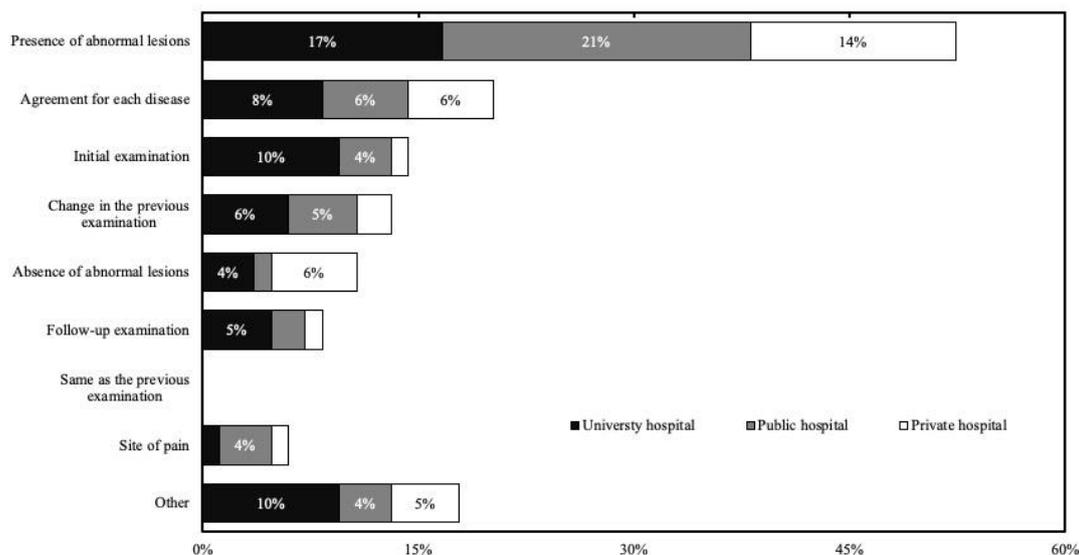


Figure 5. Responses to the question, “What are the criteria for additional imaging with your routine scan protocol?” (Q9)

Discussion

We performed a nationwide survey to document the ¹⁸F-FDG PET/CT protocols and to help clarify the recent state of oncologic ¹⁸F-FDG PET/CT protocols and practice in Japan. The PET/CT practice in Japan was hardly dependent on the type of medical institution, and the responses were highly varied. Nevertheless, for 90% of the respondents, the scanning range during a routine scan covered the top of the head to the pelvis or mid-thigh. A relatively new technology depending on hardware or software (i.e., modeling the PSF during the PET image reconstruction, TOF capability, respiratory-gated imaging, and so forth) was used by fewer than half of the respondents. These techniques may help differentiate between malignant and benign tumors due to improved SUV. Additional imaging was performed by >80% of the respondents and was mostly decided upon by physicians.

In Japan, the routine scanning range was from the top of the head through the pelvis or mid-thigh. However, in the United States and Europe, this range has been defined routinely as the neck (including the base of the skull) to the thighs (hereafter referred to as torso imaging) and constitutes added imaging as part of the routine scanning range as needed (9, 10). Public hospitals had a significantly higher frequency of skull base as the upper limit but a lower frequency of expanding the scan range than that of university hospitals (Figure 1, 4). In Japan and elsewhere, whether the head should be involved in the routine scanning range remains controversial. In our study, 39% of the respondents routinely acquired images extending beyond their normal scanning range. Equally, the scanning range for cancer screening

in Japan has been performed almost from the top of the head to the femur region (13). Osman et al. (14) described the necessity of including the brain in torso imaging of lung cancer patients, and this led to upstaging. Moreover, at more than half of the institutes, patients with head and neck cancer undergo head scanning in addition to torso imaging (12); however, to our knowledge, few studies report the usefulness of additional head scanning in torso imaging in cancer patients other than those with lung or head and neck cancer. Including the lower extremity, whether an extended scanning range, such as whole-body imaging, is necessary remains to be determined, although approximately 1% of cancer patients were demonstrated to have unexpected primary or metastatic lesions (15, 16).

The frequency of performing additional imaging in the routine PET/CT scan protocol was higher than that for other nuclear medicine practices (17). Most respondents (84%) performed delayed imaging, routinely (Figure 2) or when necessary (Figure 4), and many (56%) performed delayed imaging after consultation with the physician each time (Figure 3). The most common criterion for delayed imaging in all medical institutions was the presence of abnormal lesions (Figure 5). Many previous studies have shown the usefulness of delayed scans; for instance, the 90–120 min after intravenous injection show higher ¹⁸F-FDG uptake than routine scan images of most malignant lesions due to increased background clearance (18-26). Although details were unavailable, 20% of the respondents performed delayed imaging based on the agreement for each disease. Delayed imaging in

patients with head and neck cancers (18), hepatic metastasis (19-21), and esophageal (22, 23), lung (24, 25), and pancreatic (26) carcinomas have received considerable attention. Delayed imaging is also useful in patients with high background uptake, such as overweight patients or those with poorly controlled diabetes (27), but this indication was not observed in this study. However, exceptions exist, and a few reports showed that delayed imaging is not considered useful for the improvement of diagnostic performance in patients with lung cancer, colorectal cancer, malignant soft-tissue tumors, and pulmonary nodules with low accumulation (28-32). Given that the PET/CT system has been in use currently, particular consideration should be given to deciding on delayed imaging due to the increased CT radiation dose.

PSF and TOF improve the spatial resolution and signal-to-noise ratio of PET images (5, 6). In 2017, PET/CT system with TOF accounted for 38% PET/CT system in Japan (33), and in our study, 50% and 42% of the respondents performed PSF and TOF correction, respectively (Table 2). Because the percentage of TOF implementation and results of this questionnaire were almost in agreement, the performance of their PET/CT systems may have affected these results. The effect of incorporating PSF in the reconstruction process is clearer for smaller than for larger lesions; the maximum SUV (SUV_{max}) for small lesions of <10 mm, such as lymph node metastasis, may be increased two times (2, 7). Despite this fact, SUV_{max} has currently been used as a reference value of tumor metabolic activity (34). TOF information helps increase the signal-to-noise ratio or reduce the injection dose, and the improvement achieved from TOF is more significant in overweight patients (35). Respiratory-gated acquisition and breath-hold PET/CT acquisition were performed by 23% and 11% of the respondents, respectively. Respiratory-gated acquisition also improved the SUV_{max} for liver lesions (8), although improvement in decreasing signal-to-noise ratio due to respiratory-gated acquisition requires a prolonged acquisition time (36). The availability of features such as PSF, TOF, and respiratory-gated acquisition depends on the PET/CT system, and these features are implemented in relatively new systems. Given that imaging techniques are constantly being developed, SUV will be affected, and the techniques will be refractory to SUV harmonization between different PET/CT systems.

Uncorrected images may help in identifying artifacts due to patient motion (including breathing), metal implants (e.g., joint prostheses,

spine orthopedic braces, dental implants, and pacemakers), and intravenous contrast accumulation (7, 10). One-third of the respondents reported routinely processing uncorrected images, and 15% of the respondents processed when necessary. The MAR algorithm on CT images can improve PET images for patients with metal implants (37), although only 27% of the respondents used the processing method. On the contrary, higher-resolution head PET images are beneficial (12), and despite almost all the respondents performing a routine scan protocol including the head, only 21% of the respondents routinely or occasionally reconstructed high-resolution PET images.

Consultation with a physician on whether to perform additional imaging was more than twice as likely to occur in ^{18}F -FDG PET/CT practice than in bone scintigraphy practice (38). Possible explanations for this include the following: it is difficult for technologists to always judge accurately whether there is malignancy, inflammation, or benign or physiologic accumulation; the maximum percentage of the respondents were from university hospitals; a relatively large number of physicians were from hospitals in which PET/CT examination can be performed; and increasing radiation dose was associated with exposure to CT in additional PET/CT scanning such as delayed imaging or an extended scanning range. Moreover, given that many additional imaging was also performed, as decided by the technologist, variations of scanning protocol remain a challenge for standardization of ^{18}F -FDG PET/CT. Developing and utilizing the institution guideline is of critical importance, and the guideline may be interchangeable with standardized protocol in the future.

Our study had some limitations. Our survey has no information about administered dose, radiation dose in CT, wait time, or patient preparation. To facilitate standardization of the ^{18}F -FDG PET/CT imaging protocol, these pieces of information are needed. Although administered dose and radiation dose in CT will be reported by Japan Radioisotope Association and/or Japan Network for Research and Information on Medical Exposure every 5 years. Reports showed that the average administered dose in Japan is 196–220 MBq [1], which may assist in the standardization of the ^{18}F -FDG PET/CT practice. This survey had slightly fewer responses than desired, because the surveyed population consisted of members of the society. Otherwise, such a nationwide survey could not be performed. PET/CT systems and imaging techniques will rarely be unified throughout the country in the future. Consequently, nuclear medicine technologists must be aware of

variations in technical developments for ^{18}F -FDG PET/CT examination. A great need for professional education regarding new PET/CT software and hardware technology is evident.

Conclusions

Our survey found that the scanning range for the diagnosis of cancer using ^{18}F -FDG PET/CT was similar to that for cancer screening in Japan (from the top of the head through the femur region) at almost all medical institutions. Moreover, although the differences in the availability of TOF, PSF, and respiratory-gated acquisition were found, ^{18}F -FDG PET/CT practices did not significantly differ among the different types of medical institutions. Because the frequency of additional imaging was highest in ^{18}F -FDG PET/CT among all nuclear medicine practices, we suggest establishing a standardized imaging protocol. Delayed imaging has been performed because of consultation with physicians in the presence of abnormal lesions. Although almost all medical institutions have functioning PET/CT systems, the availability of technical developments (e.g., PSF and TOF) will constantly vary among institutions. This survey will be the first step toward standardization and is useful to decide protocols in clinical practice.

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Conflicts of interest

The authors declare that there is no conflict of interest.

Ethical considerations

This article does not contain any studies with human participants or animals performed by any of the authors.

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