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Do short-time SPECT images of bone scintigraphy improve the diagnostic value in the evaluation of solitary lesions in the thoracic spine in patients with extraskeletal malignancies?

Kana KOBAYASHI, Chio OKUYAMA, Takao KUBOTA, Takako NAKAI, Yo USHIJIMA and Tsunehiko NISHIMURA

Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine

Objective: Single photon emission computed tomography (SPECT) images provide many details of the anatomical structure. Also about bone scintigraphy, there are many reports of the improvement of diagnosis by SPECT images. Although SPECT is useful, it requires much time. So to perform SPECT for all cases is difficult in the clinical situation. Recently, due to technical improvements in gamma cameras, we can get SPECT images in a short time. We examined diagnosis of solitary hot spots of thoracic spine in cancer patients using short-time SPECT. And we considered whether short-time SPECT contributes to the precise diagnosis of the lesion. ***Material and Methods:*** We performed bone scintigraphy image acquisition and both planar and short-time SPECT of the chest. Short-time SPECT was acquired in 6 minutes. We selected 36 cases with malignancy, whose bone scintigraphy demonstrated a solitary accumulation hot spot in the thoracic spine. Three experienced radiologists in nuclear medicine and 4 beginners diagnosed the images. They interpreted planar, short-time SPECT and maximum intensity projection (MIP) view of the chest of each case. The observers' response data were analyzed with receiver operating characteristic (ROC) curve analysis. ***Results:*** Of the three types of images, the Az (the area under ROC curve) values of short-time SPECT were the highest in all the observers except for only one beginner. Compared with experienced observers, beginners scored lower Az values of short-time SPECT. MIP images were constructed using SPECT data, but the Az values of MIP images were not higher than those of planar images. As to diagnosis, beginners tended to interprete most of the accumulations as metastatic lesions. ***Conclusion:*** Short-time SPECT can be helpful to some degree, but to provide greater benefit, the observers require considerable exercise and experience.

Key words: bone metastasis, bone scintigraphy, ^{99m}Tc-HMDP, SPECT, thoracic spine

INTRODUCTION

FOR PATIENTS with malignancy, bone scintigraphy is widely used to detect skeletal metastasis owing to its high sensitivity.[1–7] Bone metastases may be visualized on bone scintigraphy 2 to 6 or even 12 months earlier than detected by radiographic methods before their symptoms occur.[1] Early detection of metastatic bone tumors contributes to the decision of the next treatment plan, and improvement of the quality of life. Some solitary abnormal accumulations, however, often cause diagnostic confusion because of their low specificity.[8,9] For example, in vertebral bones, to which tumors metastasize the most frequently, an abnormally increased focal accumulation does not always mean a metastasis, and abnormal findings are often caused by many other conditions such as osteoarthrosis, compression fracture, discitis, and spondylitis.

It is particularly difficult to detect small abnormalities and evaluate the exact anatomic site of abnormalities of the thoracic vertebrae by planar bone scintigraphy; because of the existence of the ribs and sternum, the morphological complexity of the thoracic vertebrae.

Recently, mechanical developments in the construction of gamma cameras have made it possible to obtain

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For reprint contact: Kana Kobayashi, M.D., Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajiicho, Kawaramachi Hirokoji, Kamigyo-ku, Kyoto 602–8566, JAPAN.

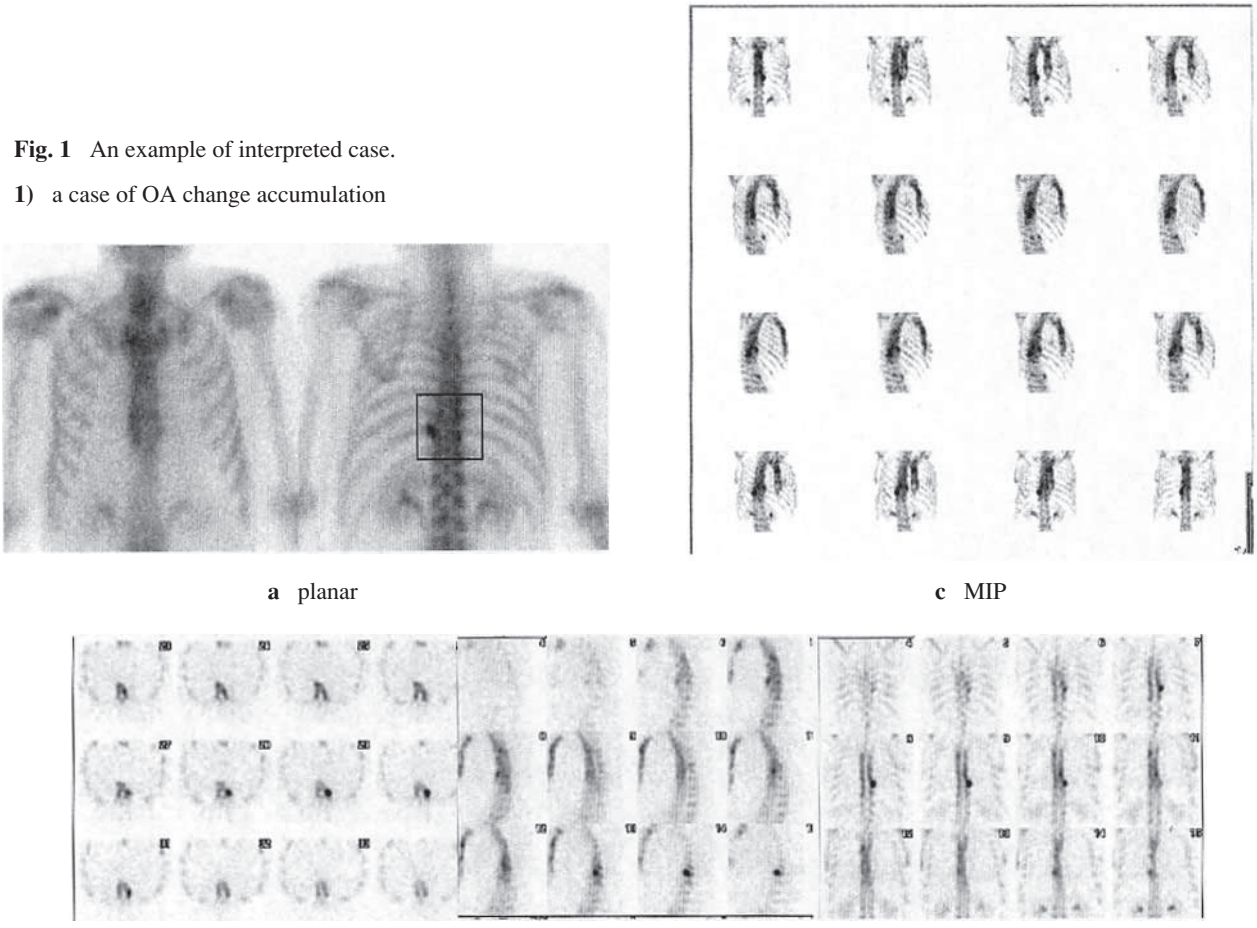


Fig. 1 An example of interpreted case.

1) a case of OA change accumulation

a planar

c MIP

b SPECT

single photon emission computed tomography (SPECT) images in a short acquisition time, and the merged processing technique can display whole body SPECT images. Maximum intensity projection (MIP) images reconstructed from the SPECT data can display the stereo-static images, which help with the recognition of anatomical structures. The usefulness of whole body MIP images has been reported for tumor-seeking radiopharmaceuticals, for example, ^{67}Ga citrate and ^{201}Tl chloride, and the data suggested that whole body SPECT is an excellent technique as an alternative to whole body planar scanning.[10]

For bone scintigraphy, many authors have reported the benefits of SPECT.[3–7] It is no wonder that SPECT increases image contrast and improves lesion detection and localization compared with planar scintigraphy. Although whole body SPECT might replace the whole body planar scan, it is not clinically practical for routine examinations, because it requires much time.

To obtain further information about the thoracic spine, where planar scans often fail to visualize abnormal accumulation, we routinely perform bone SPECT of the chest. On the basis of a routine examination protocol, the acquisition of SPECT is completed in a short time. If the SPECT images obtained in a short time are superior to planar images, whole body SPECT might replace whole body planar scan.

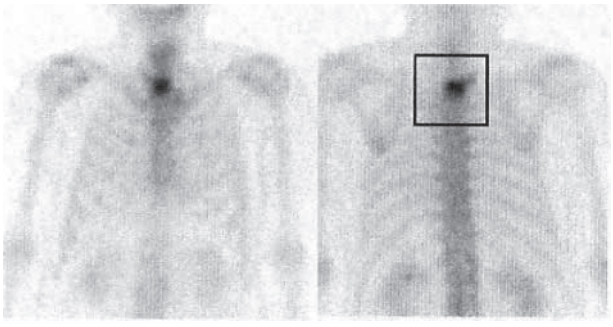
In this study, we compared the diagnostic value of short-time SPECT of bone scintigraphy to planar and MIP images in a group of patients with solitary increased accumulations in the thoracic spine.

MATERIALS AND METHODS

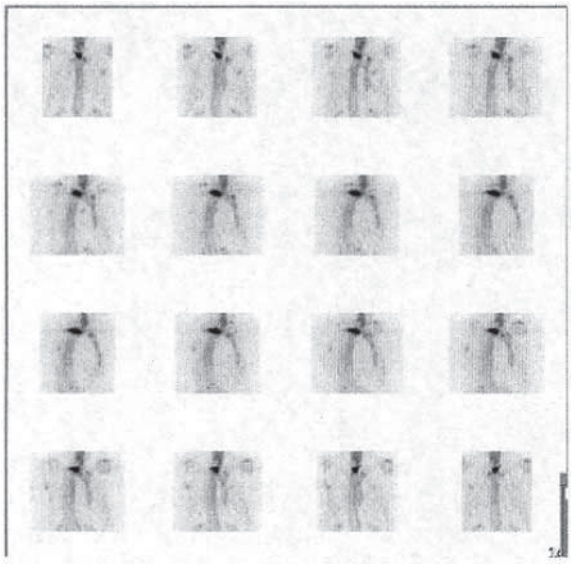
Patient Selection

We reviewed 940 patients (380 males and 560 females), who had been diagnosed as having some malignancy and underwent bone scintigraphy in the Hospital of Kyoto Prefectural University of Medicine for the survey of bone metastasis between February 2001 and December 2002. Of these patients, 36 cases (20 males and 16 females, mean age 67, age range 40–87 years old) with solitary abnormal increased accumulations on the thoracic spine, of which the final diagnosis had been confirmed, were included in this study. The final diagnosis (the malignant or benign nature) of the thoracic spine lesion was proved by other imaging methods (plain X-ray, computed tomography [CT], magnetic resonance imaging [MRI]) or more than 6 months of follow up examinations including sub-

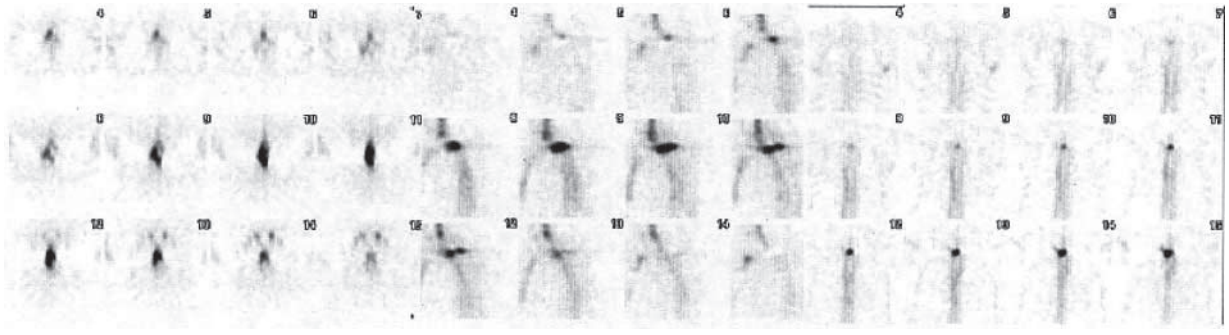
2) a case of bone metastasis



a planar



c MIP



b SPECT

sequent bone scintigraphy. The primary sites of malignancy were 12 breast cancers, 6 lung cancers, 5 prostate cancers, 5 renal cell carcinomas, 3 esophageal cancers, 2 colon cancers, and 1 bile-duct, oral, bladder and ureteral cancers. One case had double cancers of the lung and colon. The final diagnosis of the thoracic spine lesions included bone metastasis, 16; osteoarthrosis, 13; and non-pathological compression fractures; 7.

Imaging Acquisition

Patients received 555–740 MBq of ^{99m}Tc-hydroxymethylene diphosphonate (^{99m}Tc-HMDP, Nihon Medi-Physics Co., Nishinomiya, Japan) by intravenous injection, and 3 hours later the whole body scan and short-time SPECT of the chest were performed using a triple-head gamma camera equipped with high-resolution low energy collimators (PRISM-IRIX, Philips, Cleveland, USA). The anterior and posterior whole body was scanned for 15 minutes. For patients with a heights of 150 cm and 180 cm, the scan speeds were 10 cm/minute and 12 cm/minute, respectively. Short-time SPECT images were acquired in a 128 × 128 matrix at 6° angular steps, 15s each step. Transaxial, coronal, and sagittal slices 2 pixels thick (pixel size was 4.7 mm) were reconstructed using the filtered back projection method and a Butterworth filter was applied (6.0 order and cutoff frequency of 0.27 cycles per centimeter). Maximum intensity projection [MIP] images were reconstructed with the software program "Max Pixel Raytrace" on the Odyssey Fx machine using the data after filtering.

Image Interpretation

Anterior and posterior planar images of the chest, transaxial, coronal, and sagittal SPECT images of the thoracic vertebrae, and the MIP images were separately displayed at random in each series. Observers interpreted the images on a monitor as to the region of interest where an open square delineated the images printed on paper (Fig. 1). The observers included 4 beginner radiologists with 3 to 15 months of clinical experience in general nuclear medicine, and 3 experienced radiologists (experts), who had more than 6 years' experience in general nuclear medicine, and were licensees of the nuclear medicine board by the Japanese Society of Nuclear Medicine. Before the interpretation, the beginners were given a 10-minute review about some typical patterns of pathological

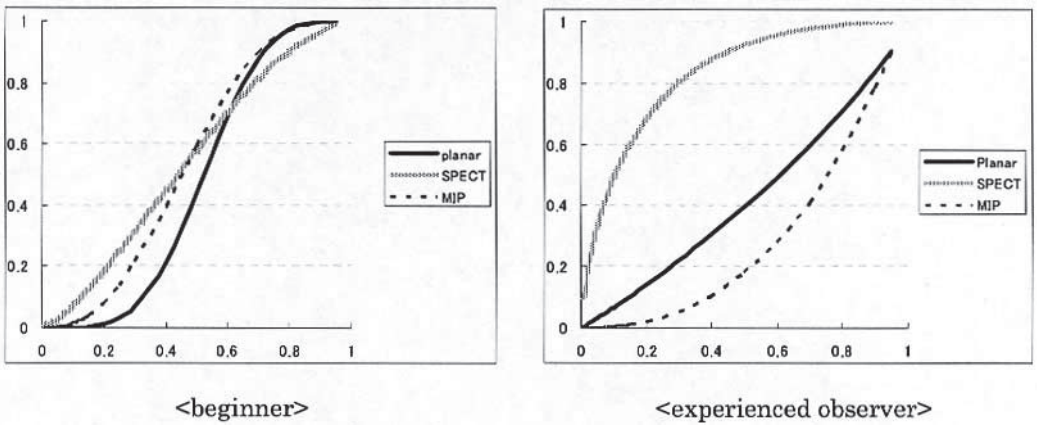


Fig. 2 ROC curves of one experienced radiologist and beginner (examples).

and anatomical features of bone metastasis, osteoarthrosis, and compression fracture of the vertebrae. All observers were given only the information that the bone scintigraphy had been performed to check for metastatic bone tumors, but they were blinded to the final diagnosis of the thoracic spine lesions. They interpreted the planar series first, then short-time SPECT series, and lastly MIP series, with brief breaks between each interpretation series.

The observers were asked to rate the degree of certainty of the diagnosis of bone metastasis in each subject by using the following confidence rating scale (1–5): 1, no evidence of bone metastasis; 2, a pattern that probably does not indicate bone metastasis; 3, an indeterminate pattern; 4, a probable bone metastasis pattern; 5, a definite bone metastasis pattern.

Data Analysis

The observers' response data were analyzed with a receiver operating characteristic (ROC) curve analysis (CORROC2 program). With this program, the area under the ROC curve (Az) and the two-tailed p values were calculated. A two-tailed paired Student's t test was used to assess the statistical significance of differences between Az values obtained by each image series. A significant level of 0.05 was used for the statistical tests.

We also calculated sensitivity, specificity, positive predictive value, negative predictive value and accuracy. For this evaluation, from the point of view of the decision of the next examination or treatment, we regarded the interpreting rating of 3, 4 and 5 (an intermediate pattern, a probable and definitive bone metastasis pattern) as a positive diagnosis of bone metastasis, and of 1 and 2 (no evidence and not indicative of bone metastasis pattern) as a negative diagnosis, because it is important whether further examination or treatment is recommended, or is not necessary. We evaluated the effect of experience in nuclear medicine to the diagnostic values, with the comparison of the results by 4 beginners and 3 experts using Mann-Whiteny-U statistical tests.

Table 1 The results of ROC analysis of each image based on each observer

a) Az scores

		Planar	SPECT	MIP
Beginner	1	0.4778	0.5416	0.5416
	2	0.4356	0.7701	0.3802
	3	0.5849	0.4808	0.4596
	4	0.5527	0.6675	0.3810
Experienced observer	1	0.3797	0.7272	0.2913
	2	0.4254	0.8296	0.2902
	3	0.4254	0.8296	0.2902

b) p values

		S vs. P (S > P)	S vs. M (S > M)	P vs. M (P > M)
Beginner	1	0.6528	0.9738	0.651 (P < M)
	2	0.0019	0.0047	0.7803
	3	0.4759 (P < S)	0.8771	0.3645
	4	0.3430	0.0139	0.1130
Experienced observer	1	0.0127	0.0117	0.6643
	2	0.0001	<0.0001	<0.0001
	3	0.0001	<0.0001	<0.0001

*S; SPECT, P; Planar, M; MIP

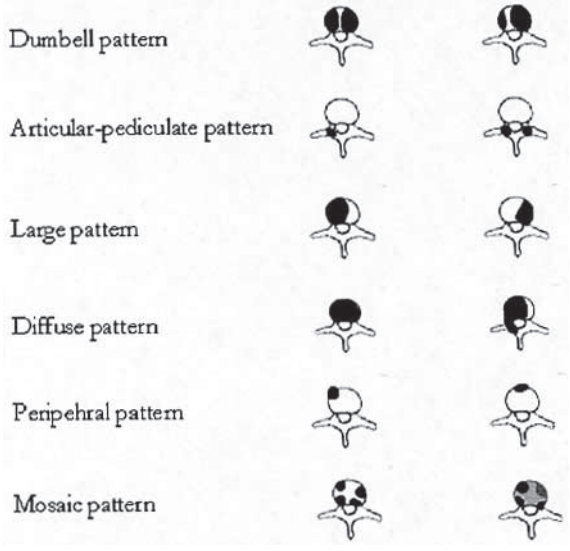
The pattern of the site of abnormally increased accumulation was classified into 5 groups based on the previous report by Kosuda et al.[14] Our classifications were defined as follows: mosaic pattern, accumulation scattered in the vertebral body; peripheral pattern, hot spot at a peripheral lesion; diffuse pattern, accumulation in most part of a vertebra; large pattern, large hot spot on either side of the vertebra; articular-pediculate pattern, accumulation in lamina or facet joint, and we added dumbbell pattern, large accumulation divided into the left and right part of the vertebra (Fig. 3).

Based upon the results of the ROC analysis, diagnostic values, and the diagnostic tendency, we evaluated how

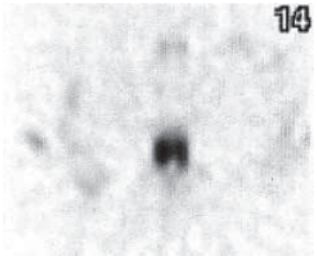
routinely performed short-time SPECT might be useful in the diagnosis of solitary thoracic spine lesions.

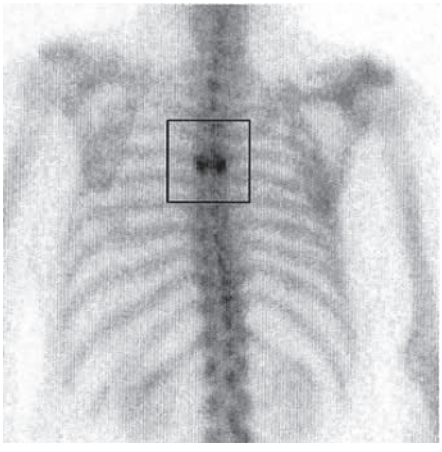
RESULTS

The results of the ROC analysis (Az scores) of each image based on each observer are shown in Table 1. The examples of ROC curves of one beginner and experienced observer were shown at Figure 2. For all the observers except for only one beginner, the Az values of short-time SPECT were the highest; they were significantly higher than those of the planar images by 1 beginner ($p < 0.005$) and all the experts (2, $p < 0.05$; 1, $p < 0.0005$), and not significantly higher in 2 beginners, and it was also significantly higher than that of MIP images in 2 beginners (1, $p < 0.05$; 1, $p < 0.005$) and all the experts (2, $p < 0.05$; 1, $p < 0.0005$). The values of planar images showed a tendency to be higher than those of MIP images, but no significant difference existed between the Az values of planar images and MIP images in any observers. Comparing the experts with the beginners, there was a significant difference in Az values of short-time SPECT ($p < 0.01$).



a patterns





b-1 SPECT **b-2** planar

b an example of dumbbell pattern of SPECT images and that of planar image

Fig. 3 The patterns of the site of abnormally increased accumulation on SPECT images.

MIP images were constructed using SPECT data, but the Az values of MIP images were not higher than those of planar images.

Figure 4 shows the sensitivity, specificity, positive predictive value, negative predictive value, and the accuracy, of each observer. First as with the ROC analysis, higher sensitivity, specificity, PPV, NPV, and accuracy in short-time SPECT images compared with the planar images were seen by all but one observer. On the planar images, although there was no significant difference, beginners tended to have higher sensitivities (mean ± S.D.; 0.531 ± 0.064) than experienced observers (0.292 ± 0.036), and lower specificities (0.500 ± 0.003) than experienced observers (0.550 ± 0.003). On the short-time SPECT images, the sensitivity of experienced observers was not significantly higher than that of the beginners (beginner; 0.734 ± 0.003, experienced observers; 0.771 ± 0.009), but the experienced observers showed significantly higher specificities (0.717 ± 0.001) than the beginners (0.488 ± 0.036) ($p = 0.048$). Though sensitivity was higher on short-time SPECT than on the planar images for most observers, on the short-time SPECT images some beginners had lower specificity than on planar images. On MIP images, both sensitivity (beginner, 0.609 ± 0.022; experts, 0.292 ± 0.021) and specificity (beginner, 0.388 ± 0.027; experts, 0.583 ± 0.023) showed wide-ranging variances. No significant difference between beginners and experienced observers was seen in either the positive or negative predictive values of planar and MIP images, whereas the experts had higher predictive values on short-time SPECT images. The accuracy of short-time SPECT images was also significantly higher for the experienced observers (0.741 ± 0.002) than the beginners (0.597 ± 0.014) ($p = 0.043$).

The 16 metastatic lesions were classified based on the abnormally increased site on SPECT findings into 1

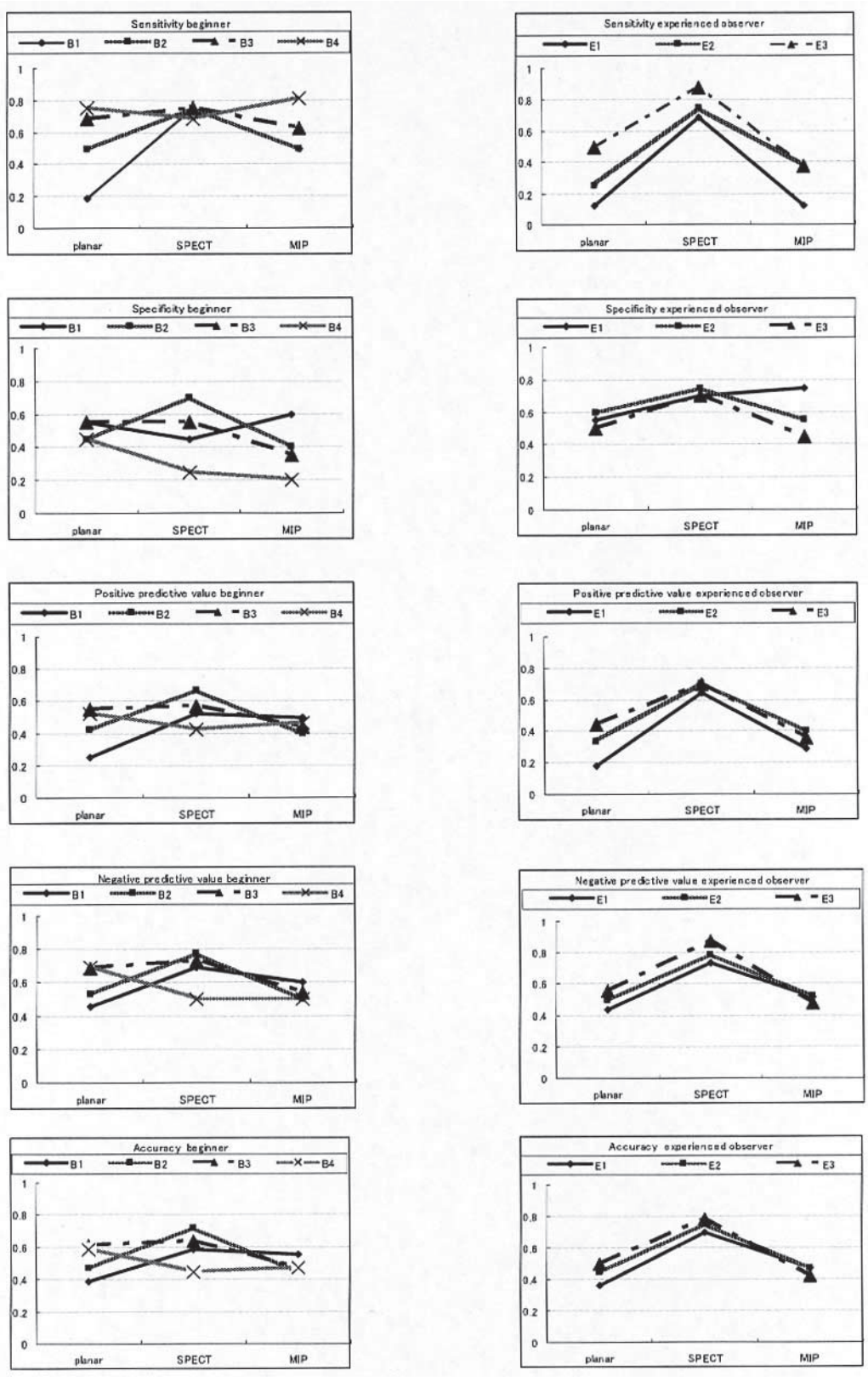
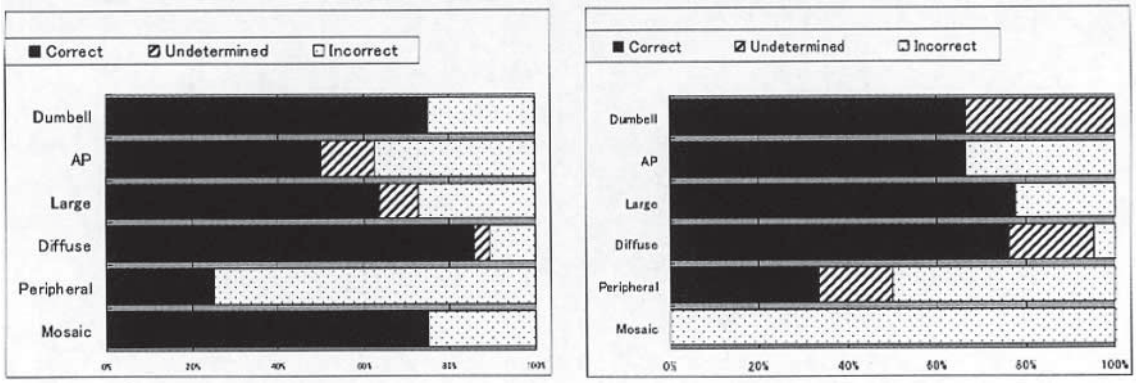


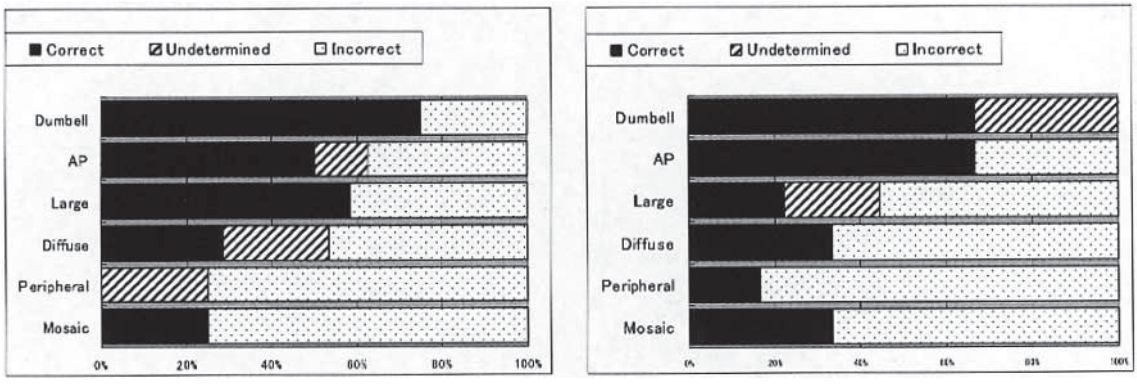
Fig. 4 The sensitivity, specificity, positive predictive value, negative predictive value, and the accuracy (*left;* beginners, *right;* experienced observers).

a The diagnosis on SPECT images



<beginner> <experienced observer>

b The diagnosis on planar images



<beginner> <experienced observer>

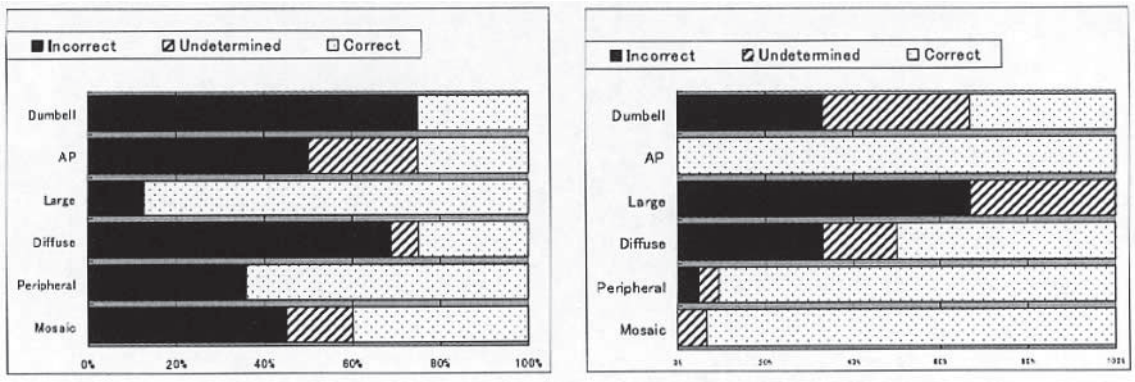
Fig. 5 The diagnosis of metastatic lesions by each pattern on short-time SPECT images and those of planar images by beginners and experienced observers.

mosaic pattern, 2 peripheral patterns, 7 diffuse patterns, 3 large patterns, 2 posterior patterns, and 1 dumbbell pattern, while 20 non-metastatic lesions were classified into 5 mosaic, 7 peripheral, 4 diffuse, 2 large, 1 posterior, and 1 dumbbell pattern. Figure 5 shows the scintigraphic interpretation of the metastatic lesions with each pattern on the planar images and short-time SPECT images by the beginners and experienced observers, and Figure 6 shows those of non-metastatic lesions. The closed bar shows the percentage diagnosed as "suspected metastatic lesion, 5, 4"; the slanted bar shows the percentage diagnosed as "undetermined lesion, 3"; and the dotted bar shows the percentage diagnosed as "not suspected as metastatic lesion, 1, 2". As for the diffuse and large patterns, short-time SPECT imaging was useful for the experienced observers. In the short-time SPECT interpretation, beginners were likely to mark higher scores (which meant metastasis). For the beginners, on diagnosis of non-metastatic lesions, short-time SPECT was not always beneficial. For the experienced observers, short-time SPECT made the interpretation of large and diffuse pattern metastases easier and more precise. For both groups of observers (beginners and experienced observers) short-time SPECT was useful for the differential diagnosis between benign and metastatic lesions. The trend was more prominent for experienced observers than beginners.

DISCUSSION

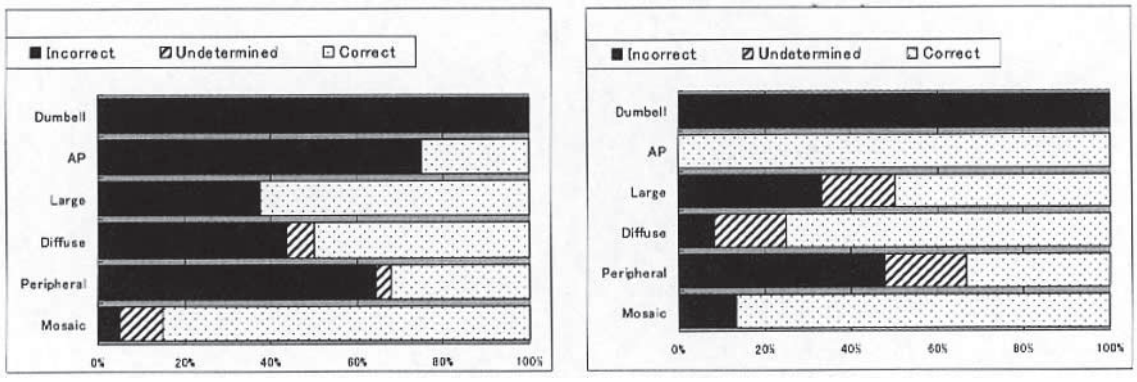
In patients with malignancy, the screening for metastatic lesions plays a very important role in making the adequate treatment plans. Bone scintigraphy is one of the most-accepted and frequently performed diagnostic procedures with a high sensitivity for the evaluation of skeletal metastases. On the other hand, the assessment of the pathological findings often poses a diagnostic dilemma as either a benign disease or a metastatic lesion may be the source of intraosseous abnormal accumulations. Though the interpretation as metastases is not very difficult when the scintigrams visualize multiple abnormal accumulations or typical large lesions, the evaluation of a solitary

a The diagnosis on SPECT images



<beginner> <experienced observer>

b The diagnosis on planar images



<beginner> <experienced observer>

Fig. 6 The diagnosis non-metastatic lesions by each pattern on short-time SPECT images and those of planar images by beginners and experienced observers.

lesion of the vertebrae with no further typical osseous involvement is often problematic.

In our study, we evaluated only the selected cases with solitary hot spots in the thoracic spine, in which the nature of the lesions was strictly confirmed by other modalities or follow-up. Many others, whose scintigrams showed typical metastatic patterns, and who underwent the next treatment with no additional studies to confirm the nature of the "hot-spot" lesions, were excluded from our study. This caused the relatively low sensitivity of the diagnosis of this study.

Even-Sapir et al. mentioned that isolated vertebral lesions were usually benign,[11] but actually, a metastasis usually grows up as a solitary small lesion at first. For the interpretation of a solitary "hot spot" on bone scintigrams, comparisons with the images performed previously or other imaging modalities are the most important.

Though an abnormality on a bone scan is observed in many different pathologies, such as metastasis, osteoarthrosis, compression fracture, discitis, spondylitis, primary bone tumors, and so on, each pathology has characteristics which depend on its anatomic localization. Reinarts et al. reviewed hot spots at the lumbar spine and mentioned that the percentages of malignancy of the hot spots in vertebral body, pedicle, facet joint and spinous process were 46.9, 100, 6.5, and 50%, respectively.[6] Understanding of the anatomy and the pathologically particular localization of osseous lesions often helps the interpretation of the scintigrams.

The structural complexity of the spine makes it difficult to detect the abnormality on conventional planar scintigrams. Particularly in the case of the thoracic vertebrae, the sternum and ribs as well as the parts of the vertebrae are superimposed on the anterior-posterior projection and it is difficult to determine the exact anatomic location of an abnormality.

SPECT images not only help the comprehension of the anatomic structure, but also allow the detection of small lesions because of the tomographic methods. Many studies have reported on the benefit of SPECT images of bone scintigraphy. Sedonja et al. described that more metastases were detected by SPECT (SPECT, 58 of 64;

planar 42/64),[3] and that about 90% of lesions of the lumbar spine can be differentiated correctly between being malignant or benign.

As to the localization of the lesion, planar bone scintigraphy failed in detection of about 60–80% of spine osseous lesions, which were detected by ^{18}F-FDG PET, while they failed in 10–20% of skull, rib, and extremities.[12] Savelli et al. evaluated studies of 118 patients with bone metastases and they mentioned that SPECT showed high sensitivity, specificity, and accuracy and in particular improved the predictive value of planar scan in the diagnosis of vertebral metastases.[7]

It can not be argued that SPECT is superior to planar images, but is not practical for routine examination protocols. In most of the studies in which the utility of bone SPECT is described, the acquisition time of the SPECT ranged from about 20 to 40 minutes, and the total protocol schedule of bone scintigraphy (i.e. planar images and one position SPECT images) takes about an hour or more. Recently, the times of the study for CT and MRI have been shortened. We were able to conclude the examination in less than 25 minutes using the same device to acquire both planar and SPECT images.

Kawamura et al. tried whole body SPECT images in ^{67}Ga scintigraphy.[10] In their study, the SPECT data were acquired with the matrix 128 × 128, 64 views and 10 sec/view, and under this protocol 6.4 minutes was needed for one position of SPECT acquisition. They compared the SPECT with planar scans, and concluded that the SPECT images combined with MIP images were superior to planar images. To think of whole body SPECT images in bone scan, we can expect better sensitivity and accuracy of diagnosis. But to perform whole body SPECT in bone scan, which is good for precise diagnosis, takes such a long time that is undesirable for patients with a malignancy. Recently other modalities such as whole-body MRI[15] can realize fast scans, and examinations which take over thirty minutes are not acceptable as routine exams.

From these points of view, we evaluated the utility of short-time SPECT, whose acquisition time was 6 minutes in bone scintigraphy for the interpretation of solitary hot spot lesions of the thoracic spine. This protocol is acceptable in the clinical situation. Appropriate lesions are those which demonstrate solitary accumulation and are difficult to diagnose. We examined the difference in diagnosis between beginners and experienced observers. The Az scores of short-time SPECT were significantly higher than those of planar images in the experienced observers, while there were no significant differences between short-time SPECT and planar Az scores in some beginners (Fig. 2). For the diffuse type, large type, and peripheral type lesions, short-time SPECT is useful for exact diagnosis, especially for the experienced observers. On the peripheral type, short-time SPECT can clearly discriminate the vertebral arch and facet joint. Beginners tend to diagnose all accumulations as metastases. The sensitivity of metastasis on short-time SPECT is good, whereas the specificity of non-metastatic lesions is not good on short-time SPECT. This may show the usefulness of short-time SPECT for experienced observers who tend to have a clearer understanding of the anatomical structure, but does not apply to beginners. One of the reasons may be the beginner's unfamiliarity with the anatomical structures with short-time SPECT. The second reason is technical limitations of short-time SPECT with many noise related artifacts.

In the present study, MIP images were not useful, and if anything, worsened the accuracy of the diagnosis for experienced observers. On oncological scintigraphy, such as ^{67}Ga citrate, ^{201}TlCl and ^{18}F-FDG PET, MIP images are often needed for the interpretation, and their utility is recognized. These tumor-seeking agents visualize the abnormal lesion as a positive accumulation against background low accumulation. MIP image can thus emphasize the lesions with a greater accumulation than the background. On the other hand, bone scans are disadvantageous for MIP, because the tracer accumulates in normal bone tissue as well as in abnormal lesions. Moreover MIP images often fail to visualize cold lesions. When the osteoblastic activity of a bone metastatic lesion is poor, the lesion can be photopenic, or sometimes a cold area is surrounded by a hot rim. Kober et al. reported that 2% of metastases are visualized as cold lesions.[13] Compared with oncological scintigraphy, which represents positive accumulation alone, bone scans are disadvantageous for MIP, because data of both normal bone tissue and abnormal lesions are accumulated. It is thus not good for precise diagnosis to rely highly on the short-time SPECT.

CONCLUSION

It is certain that SPECT images give more information than planar images and this is helpful for diagnosis. Short-time bone SPECT can be helpful to some degree. Short-time SPECT images make the location of the lesion clearer in the thoracic spine than planar images which are not good for the perception of anatomical localization. To receive benefit from short-time SPECT images, however, the observers require considerable practice, experience and a sufficient knowledge of anatomy and pathology. To obtain useful short-time bone SPECT images, further improvements in image acquisition technology are needed. Much improvement would be needed to make whole body bone SPECT practical enough to replace planar scans.

REFERENCES

1. Galasko CSB. Skeletal metastases. *Clin Orthop Rel Res* 1986 (210): 18–30.
2. Krasnow AZ, Hellman RS, Timins ME, Collier BD, Anderson T, Isitman AT. Diagnostic bone scanning in oncology. *Semin Nucl Med* 1997; 27 (2): 107–141.

3. Sedonja I, Budihna NV. The benefit of SPECT when added to planar scintigraphy in patients with bone metastasis in spine. *Clin Nucl Med* 1999; 24: 407–413.
4. Nagele-Wohrle B, Nickel O, Hahn K. SPECT bone scintigraphy of benign and malignant lesions of the spine. *Neurosurg Rev* 1989; 12: 281–283.
5. Sarikaya I, Sarikaya A, Holder LE. The role of single photon emission computed tomography in bone imaging. *Semin Nucl Med* 2001; 36: 3–16.
6. Reinartz P, Schaffeldt J, Sabri O, Zimmy M, Nowak B, Ostwald E, et al. Benign versus malignant osseous lesions in the lumbar vertebrae: differentiation by means of bone SPET. *Eur J Nucl Med* 2000; 27: 721–726.
7. Savelli G, Maffioli L, Maccauro M, De Deckere E, Bombardieri E. Bone scintigraphy and the added value of SPECT (single photon emission tomography) in detecting skeletal lesions. *Q J Nucl Med* 2001; 45 (1): 27–37.
8. Tryciecky EW, Gottschalk A, Ludema K. Oncologic imaging: interactions of nuclear medicine with CT and MRI using the bone scan as a model. *Semin Nucl Med* 1997; 27 (2): 142–151.
9. Jacobson AF, Cronin EB, Stomper PC, Kaplan WD. Bone scans with one or two new abnormalities in cancer patients with no known metastases: frequency and serial scintigraphic behavior of benign and malignant lesions. *Radiology* 1990; 175 (1): 229–232.
10. Kawamura S, Ishibashi M, Fukushima S, Kurata S, Umezaki N, Morita S, et al. Study on the usefulness of whole body SPECT coronal image, MIP image in ^{67}Ga scintigraphy. *Ann Nucl Med* 2002; 16: 221–216.
11. Even-Sapir E, Martin RH, Barnes DC, Pringle CR, Iles SE, Mitchell MJ, et al. Role of SPECT in differentiating malignant from benign lesions in the lower thoracic and lumbar vertebrae. *Radiology* 1993; 187: 193–198.
12. Schirrmeister H, Glatting G, Hetzel J, Nüssle K, Arslandemir C, Buck AK, et al. Prospective evaluation of the clinical value of planar bone scans, SPECT, and ^{18}F-labeled NaF PET in newly diagnosed lung cancer. *J Nucl Med* 2001; 42: 1800–1884.
13. Kober B, Hermann HJ, Wetzel E. "Cold lesions" in bone scintigraphy. *Fortschr Rontgenstr* 1979; 131: 545–549.
14. Kosuda S, Arai S, Yokoyama H, Katayama M, Wada Y, Kusano S. Differential diagnosis between osseous metastasis and degenerative joint disease of the vertebrae by bone SPECT: Analysis by accumulation pattern. *KAKU IGAKU (Jpn J Nucl Med)* 1994; 31: 613–618.
15. Tamada T, Nagai K, Iizuka M, Imai S, Kajihara Y, Yamamoto S, et al. Comparison of whole-body MR imaging and bone scintigraphy in the detection of bone metastases from breast cancer. *Nippon Igaku Hoshasen Gakkai Zasshi* 2000; 60 (5): 249–254.