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Study on the usefulness of whole body SPECT coronal image, MIP image in ^{67}Ga scintigraphy

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In this study, we examined the usefulness of whole body coronal images and whole body cine display MIP images (CMIP) upon which image processing was carried out after whole body SPECT in comparison to the usefulness of whole body images (WB/SC) compensated by scattered radiation in tumor/inflammation scintigraphy with ^{67}Ga-citrate (^{67}Ga). Image interpretation was performed for the 120 patients with confirmed diagnoses, and the accuracy of their diagnoses was studied by three nuclear medical physicians and two clinical radiological technologists by means of sensitivity, specificity and ROC analysis. The resultant data show that sensitivity, specificity, accuracy and the area under the ROC curve Az in the WB/SC were approximately 65%, 86%, 74% and 0.724, respectively, whereas sensitivity, specificity, accuracy and Az of the image reading system in which CMIP is combined with whole body coronal images reconstructed by the OS-EM method were approximately 93%, 95%, 94% and 0.860, respectively. Furthermore, coronal images reconstructed by the OS-EM method tended to be superior to those produced by the FBP method in both diagnostic accuracy and ROC analysis. In conclusion, the image reading system in which CMIP is combined with whole body coronal images reconstructed by the OS-EM method was shown to be superior in diagnostic accuracy and ROC analysis. Our data suggest that whole body SPECT is an excellent technique as an alternative to WB/SC.

Key words: whole body SPECT, ^{67}Ga-citrate, ordered subset expectation maximization (OS-EM), filtered back projection (FBP), maximum intensity projection (MIP)

INTRODUCTION

TUMOR/INFLAMMATION SCINTIGRAPHY with ^{67}Ga-citrate (^{67}Ga) has been widely used as a visualization technique for malignant tumors for approximately 30 years, ever since a 1969 report[1] discussed the accumulation of ^{67}Ga in the lymph nodes of patients with Hodgkin's disease.[2] In conventional ^{67}Ga scintigraphy, diagnoses have been made by taking whole body planar images in conjunction with anterior and posterior spot images obtained with a gamma camera. The acquisition time for these front and rear images can now be shortened by approximately 15–20 minutes with a dual detector gamma camera together with a wide view collimator. The conventional whole body image is referred to as (WB) and the whole body image compensated by scattered radiation is referred to as (WB/SC).

More recently, not only has whole body SPECT become possible, but it has also bocome possible to take transaxial images as well as coronal and sagittal images which are the reconstructed images. This has improved the ability to detect foci which were previously difficult to detect with only WB/SC and spot images. Furthermore, it

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is anticipated that anatomical sites of lesions will be readily identified by displaying whole body SPECT images with maximum intensity projection (MIP) as used in magnetic resonance imaging (MRI) and computerized tomography (CT).[4–6] Whole body SPECT and MIP display techniques have also recently been used in the field of nuclear medicine. Moreover, the ordered subset expectation maximization (OS-EM) method, a reconstruction method based on the stochastic technique, may now be applied clinically due to the sophistication of new nuclear medicine processing instruments.[7–10] Nevertheless, there has been no published report to date comparing the diagnostic ability of whole body SPECT and MIP images utilizing the OS-EM method and WB/SC.

This study examines the usefulness of whole body coronal images prepared by the OS-EM method and MIP images; this study examines the usefulness of both MIP images and whole body coronal images prepared by the OS-EM method together with the reconstruction of whole body SPECT in comparison with WB/SC with specific reference to diagnostic accuracy (sensitivity, specificity, accuracy and ROC analysis).[11,12]

MATERIALS AND METHODS

Subjects

We evaluated 120 patients with diagnosis confirmed by surgery, autopsy, angiography, CT, MRI, ultrasound and so forth who were selected from 200 cases on which WB/SC and whole body SPECT were carried out between March 30, 2000 and October 31, 2000. The 67 males and 53 females were chosen for their confirmed diagnoses: 40 cases of malignant lymphoma, 10 of lung cancer, 9 of pharyngeal cancer, 9 of sarcoidosis, 4 of hepatic cancer, 4 of interstitial pneumonia, 3 of malignant melanoma, 2 of thyroid cancer, 2 of adult T cell leukemia and 37 cases of other diagnoses including fever of unknown origin. The patients ranged in age from 5 to 83 years, with a mean of 57.8 years.

Methods of imaging and image display of WB/SC and whole body SPECT

At 48 hours after administering ^{67}Ga (74 MBq), WB/SC of the front and rear were obtained with a gamma camera (Siemens Medical System, E. CAM) provided with a low and medium energy general purpose (LMEGP) collimator with a 256×1024 matrix and a scanning rate of 20 cm/min. Radiation scatter compensation was then carried out by the triple energy window (TEW) method with a nuclear medicine image processing instrument (Toshiba, GMS-5500A/PI).[13–15] After WB/SC imaging, SPECT images were examined three times to obtain SPECT data on three sections from the parietal region to the femur region in a nearest-neighbor continuous swing collection mode with the matrix at 128×128, 64 views and 10 sec/view. Radiation scatter compensation was then carried out a second time, again by the TEW method. Reconstruction of SPECT was also done by merging three SPECT data followed by the filtered back projection (FBP) and OS-EM methods in order to obtain a SPECT images (whole body image) as a sheet of images from the parietal to the femur region. For reconstruction by the FBP method, a Butterworth filter (order 8, cut-off frequency 0.25 cycles/cm) and a Ramp filter were used as a pretreatment filter and a reconstruction filter, respectively. For reconstruction by the OS-EM method, a Butterworth filter of the same specifications as the above was used as a pretreatment filter in all cases, and SPECT reconstruction was carried out with iteration 3 and subset 8. Compensation of absorbance was not performed with either method.

In order to visually evaluate WB/SC and whole body SPECT images, WB/SC and whole body coronal images as well as MIP images were developed on the films. These images were reconstructed into the following five systems: WB/SC, Coronal-FBP/MIP, a combination of a MIP image with a whole body coronal image reconstructed by the FBP method; Coronal-OSEM/MIP, a combination of an MIP image with a whole body coronal image reconstructed by the OS-EM method; Coronal-OSEM/CMIP, a combination of an MIP image cine-displayed on a monitor together with a whole body coronal image reconstructed by the OS-EM method; and Coronal-OSEM/CMIP/WB, a combination of an MIP image cine-displayed on a monitor with a whole body coronal image reconstructed by the OS-EM method and WB/SC. The display examples of each image are shown in Figure 1.

Data analysis

Calculation of sensitivity, specificity and the accuracy and analysis of ROC: Calculation of sensitivity, specificity and the accuracy and analysis of ROC were carried out in order to evaluate the diagnostic ability of the above five systems for image display. With image displays for each of the five systems, the 120 test cases were evaluated by three nuclear medical physicians with 25, 20 and 7 years' experience in nuclear medicine, and by two radiological technologists with 12 and 5 years' experience in nuclear medicine. Here, WB, coronal-OSEM/WB, coronal-FBP/MIP and coronal-OSEM/MIP were diagnosed by using the films, and coronal-OSEM/CMIP and coronal-OSEM/CMIP/WB were diagnosed by CRT together with the films. The CRT diagnosis was carried out with the workstation which is an image processing apparatus specific for Toshiba E-CAM. The diagnostic ability of the above five systems was further evaluated by ROC analysis (method for continuously distributed test results with full certainty = 100 points). Prior to evaluation, first interpretation of the radiogram was significantly trained for whole body, coronal, MIP and CMIP images having only physiological accumulation. Then the interpretation of images was carried out for the five systems mentioned above, and

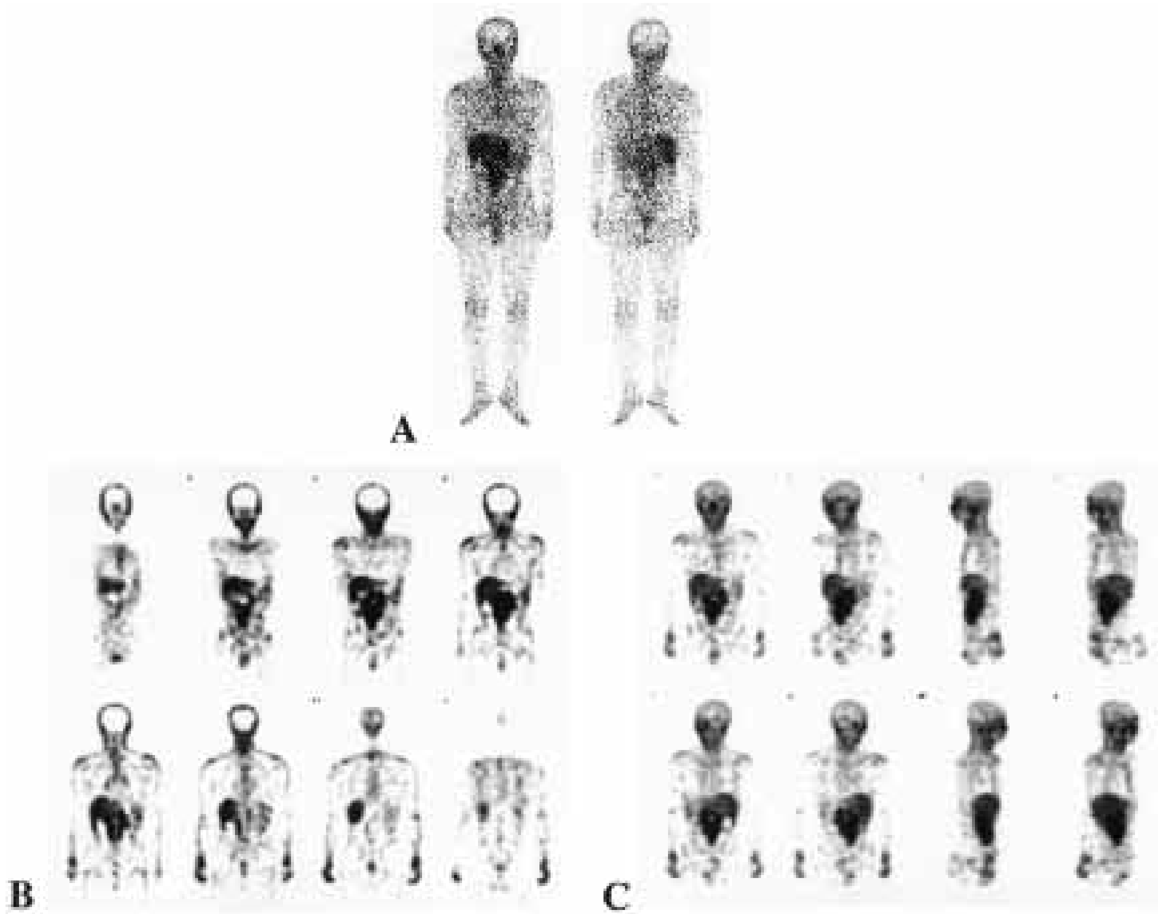

Fig. 1 The three imaging patterns. A shows the whole body image; B shows the Coronal OSEM image; C shows the MIP image.

abnormal accumulation sites were checked. Interpretation was carried out in the manner in which potential sites of abnormal accumulation were marked with a pencil on the schemes for whole body images. The continuously-distributed tests in ROC analysis were also conducted on a parallel with the check for the abnormal accumulation sites. On a free scale from 0 to 100 points, 100 points were given for the case in which the accumulation site definitely seems to be abnormal accumulation, and 0 points were given for the case with absolutely no abnormal accumulation site. Based on these criteria, points from 0 to 100 were given for each case depending on the judgment of each reader for the abnormal accumulation sites. Statistically significant difference was tested by the jackknife method which employs the area under the ROC curve Az. Az was shown by the mean ± standard deviation obtained from five readers.The interval between image readings for all five systems was approximately 3 weeks. The image readers were not given any information approximately the patients and they performed the evaluation independently of each other. The environment at image reading illumination in the image interpretation room, brightness of film viewers and CRT monitors were constant. The image examiners themselves selected the distances and time periods for observation. The order of presentation of the specimens was altered to eliminate the effects of the order of examining images.[11] The software used for ROC analysis was LABROC1 developed by Metz et al.,[12] and distributed by Met's ROC Software Users Group of the Japanese Society of Radiological Technology, Image Workshop.

RESULTS

Sensitivity, specificity and accuracy

The results of tests for sensitivity, specificity and accuracy are shown in the table. For sensitivity, Coronal-OSEM/MIP (approximately 93%), Coronal-OSEM/CMIP/WB (approximately 93%) and Coronal-OSEM/CMIP (approximately 93%), which are all systems which include Coronal-OSEM and MIP or CMIP, showed relatively higher values than those found for WB/SC (approximately 65%), and Coronal-FBP/MIP (approximately 88%). For specificity, similar results were found: the systems including Coronal-OSEM and MIP or CMIP showed values of approximately 95%, which is a higher

Table The sensitivity, specificity and accuracy for the five imaging patterns

	(WB)	(Coronal FBP/ MIP)	(Coronal-OSEM/ MIP)	(Coronal-OSEM/ CMIP)	(Coronal-OSEM/ CMIP/WB)
Sensitivity (%)	65.2 ± 5.3	87.5 ± 1.7	93.6 ± 1.3	92.5 ± 1.9	93.1 ± 2.5
Specificity (%)	86.2 ± 2.6	83.3 ± 2.2	94.6 ± 1.6	94.9 ± 1.1	95.4 ± 1.2
Accuracy (%)	73.9 ± 4.9	85.7 ± 2.5	92.9 ± 1.6	93.2 ± 1.0	93.7 ± 3.5

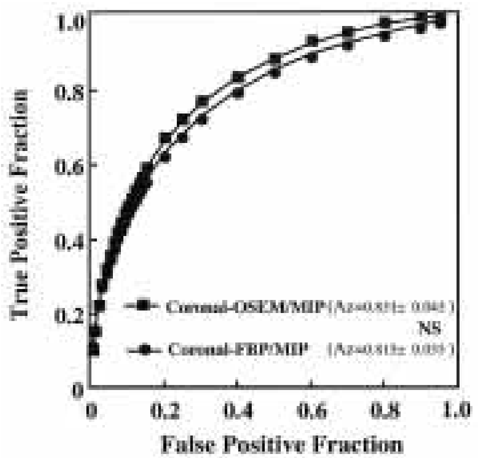

Fig. 2 ROC analysis of Coronal-OSEM/MIP and Coronal-FBP/MIP images. Az indicates the area under the ROC curve and is represented by mean ± standard deviation obtained from five readers.

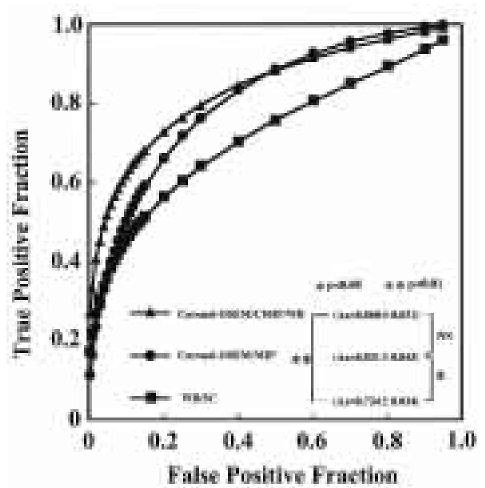

Fig. 3 WB/SC, Coronal-OSEM/MIP, and Coronal-OSEM/CMIP/WB images. Az indicates the area under the ROC curve and is represented by mean ± standard deviation obtained from five readers.

value than found with the other systems. For accuracy as well, the systems including Coronal-OSEM and MIP or CMIP showed higher values than those of the other systems, at approximately 93%. In summary, the systems including Coronal-OSEM and MIP or CMIP showed higher values than those of the other systems not only for sensitivity, but also for specificity and accuracy.

ROC analysis

The results of ROC analysis for Coronal-OSEM/MIP and Coronal-FBP/MIP are shown in Figure 2. The area under the ROC curve Az in Coronal-OSEM/MIP and Coronal-FBP/MIP are 0.831 ± 0.043 and 0.815 ± 0.033, respectively. Coronal-OSEM showed higher values, but no statistically significant difference was observed. The results of ROC analysis for WB/SC, Coronal-OSEM/MIP and Coronal-OSEM/CMIP/WB are shown in Figure 3. The area under the ROC curve Az in WB/SC, Coronal-OSEM/MIP and Coronal-OSEM/CMIP/WB was 0.724 ± 0.034, 0.831 ± 0.043 and 0.860 ± 0.031, respectively, with Coronal-OSEM/CMIP/WB showing the highest value. Both Coronal-OSEM/MIP and Coronal-OSEM/CMIP/WB showed higher Az values than WB/SC, and here a statistically significant difference was observed (See Fig. 3). And the systems which included Coronal-OSEM, which is tomographic and has the maximum value projection with MIP or CMIP, showed higher Az values than WB/SC, and a statistically significant difference was observed in this case also.

DISCUSSION

The image quality of WB and SPECT images in ^{67}Ga scintigraphy is inferior to that in bone scintigraphy due to the effects of image taking time periods, dosages of ^{67}Ga and scattered radiation. But recently, with advances in the development of software have permitted image preparation of whole body Coronal, MIP,[4–6] and CMIP images by SPECT reconstruction by the OS-EM method or the FBP method after performing whole body SPECT.

The sensitivity of WB/SC is approximately 65%. The sensitivity, specificity and proper diagnosis rate of Coronal-OSEM-MIP were compared to those of Coronal-FBP-MIP, and the former showed superior values. The difference between Coronal-OSEM/MIP and Coronal-FBP/MIP is found only in the reconstruction method. Therefore, the OS-EM method is considered to be useful for reconstruction of SPECT images in ^{67}Ga scintigraphy, which produces projection data with the lowest counts due to its dosages and exposure. In this study, the system of Coronal-OSEM/CMIP/WB, which is a combination of most image displays, showed good values in sensitivity, specificity and accuracy, but no statistically significant difference was observed in comparison with either Coronal-OSEM/MIP or Coronal-OSEM/CMIP. Thus it may be concluded that it is important that diagnosis be made by combining Coronal-OSEM images with MIP or CMIP images.

In ^{67}Ga scintigraphy, discrimination of normal distribution from abnormal accumulation is difficult when excretion of feces is not complete in spite of giving fecal softener or an enema. Nevertheless, even in these cases, additional image taking after stool elimination could be avoided in all cases by image reading combining Coronal, MIP and further CMIP images. Discrimination of abnormal accumulation from feces in particular became easier by displaying CMIP images on the monitor. And the use of CMIP images made it easier to determine if physiological or abnormal accumulation was present in other accumulation sites such as the cervical and thoracic regions. The diagnostic system incorporating CMIP was superior in this study. One of advantages of MIP and CMIP is the ability to avoid overlaps of accumulation due to profile views in various directions. In particular, CMIP images may take accumulation sites stereoscopically resulting in easier determination of either physiological or abnormal accumulation. It therefore appears that the reading system combining CMIP images provides better results.

Tests of significant difference were performed for Az in each display system since the area under the ROC curve, Az, represents the accuracy of image reading. As the results indicate, the area under the ROC curve was the highest in Coronal-OSEM/CMIP/WB and Coronal-OSEM/CMIP, i.e., when the images were read by combining Coronal-OSEM images with MIP images cine-displayed on the monitor. The Az values of these systems were higher than that of Coronal-OSEM/MIP, but no statistically significant difference was found. This may be due to CMIP's ease in discriminating physiological from abnormal accumulation because it readily constructs visually stereoscopic images. The shapes of the ROC curves and the Az values of Coronal-OSEM/WB and Coronal-OSEM/MIP were almost identical. In these results, CMIP, which is a cine image on the monitor, appeared to increase diagnostic accuracy more than MIP on the film. The contribution to diagnosis of WB/SC in Coronal-OSEM/CMIP/WB appeared to be minimal.

The difference in the diagnostic ability of OS-EM and FBP methods was studied by ROC analysis. The shapes of the ROC curve (Fig. 2) in Coronal-OSEM/MIP and Coronal-FBP/MIP were similar, and no statistically significant difference in Az was found between them. Nevertheless, the OS-EM method showed a stronger tendency than the FBP method to increase Az, suggesting that the OS-EM method might be an excellent reconstruction method. The OS-EM method has the disadvantage that it needs approximately 5.6 times more time for calculation than the FBP method, but it appeared to be a method suitable for reconstruction of SPECT in the case of projection data with low counts as is the case of ^{67}Ga scintigraphy since it has the advantages of good S/N at low count areas and suppression of artifacts from high accumulation sites.[7–10,16] The order of diagnostic accuracy in visual evaluation and in the shape and Az value of the ROC curve was identical for all five observers. A streak artifact occurred in images from the FBP method and appeared to affect diagnosis and ROC analysis. The OS-EM method appears to be a reconstruction method more suitable for ^{67}Ga scintigraphy than the FBP method because the extension of the true positive fraction (TPF) was found to be better in the OS-EM method when the false positive fraction (FPF) in the ROC curve was allowed to be large. It was considered that the OS-EM method is suitable for reconstruction of SPECT in ^{67}Ga scintigraphy and contributes to improvement of diagnostic ability.

The acquisition time periods for WB/SC and whole body SPECT were approximately 11 and approximately 18 minutes, respectively. The test can always be completed within approximately 31 minutes even including bed transfer and the swing time period for the gamma camera. If the acquisition time period for whole body SPECT is increased, the whole body coronal image quality, and therefore diagnostic ability appear to be improved. But accuracy and diagnostic ability by combining whole body Coronal images and CMIP images is remarkably improved over WB/SC even when the whole body SPECT test is carried out in only 18 minutes. It is important to remember that significant training in image reading is thought to be necessary for transfer from WB/SC and spot images to the image reading systems with Coronal-OSEM/CMIP and the like.

CONCLUSION

In this study we examined the usefulness of whole body Coronal images, MIP images, CMIP images in which whole body SPECT was introduced into ^{67}Ga scintigraphy and the OS-EM method was applied for reconstruction of SPECT with specific reference to the accuracy of diagnosis and ROC analysis. The results indicate that when whole body Coronal and CMIP images are used for diagnosis in ^{67}Ga scintigraphy, their sensitivity, specificity and accuracy are all clearly better than those provided by WB/SC. Similarly, whole body Coronal images and CMIP images were also shown to be excellent display systems for ROC analysis. Finally, the OS-EM method was shown to be superior to the FBP method in the reconstruction of whole body SPECT after studying diagnostic accuracy and conducting ROC analysis.

These data provide strong evidence in favor of the idea that image reading systems with Coronal images reconstructed by the OS-EM method after whole body SPECT, CMIP images and MIP images are excellent systems to improve diagnostic ability, and we recommend whole body SPECT as a test which should be actively used.

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