Increase of Tc-99m RBC SPECT Sensitivity for Small Liver Hemangioma using Ordered Subset Expectation Maximization Technique

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Tc-99m RBC SPECT에서 Ordered Subset Expectation Maximization 기법을 이용한 작은 간 혈관종 진단 예민도의 향상

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전태주[1,3] · 봉정균[3] · 김희중[1,3] · 김명진[2,3] · 이종두[1,3]

국문 초록

목적: 적혈구 혈액 풀 SPECT는 높은 특이도로 인하여, 간의 대표적인 양성 종양인 혈관종의 진단에 널리 사용되어 왔지만 낮은 해상도가 이 검사의 단점 중 하나였다. 최근 들어 ordered subset expectation maximization (OSEM)이라는 기술이 임상 핵의학 분야에서 단층영상의 재구성에 도입되고 있는 바, 저자들은 간 혈관종을 대상으로 기존의 역투사방식과 새로운 수정된 반복영상구성법인 OSEM을 비교하고자 하였다. **대상 및 방법:** 24명의 간 혈관종 환자의 28개의 병변들 각각으로부터 이중 헤드 감마 카메라를 이용하여 단층영상 재구성을 위한 64개의 투사 영상을 얻었다. 이들 raw data는 LINUX운영체계의 개인용 컴퓨터에 보내서, 각각의 header file을 interfile로 대체하여 OSEM프로그램이 인식할 수 있도록 하였다. 최상의 영상을 구성하는 조건을 알아보기 위하여 다양한 subset 수(1, 2, 4, 8, 16 그리고 32) 및 반복계산 수 (1, 2, 4, 8, 그리고 16)하에서 재구성을 시도하여 4번의 반복계산과 16개의 subset일 때를 최적 조건으로 선택하였다. 이후 이 조건 하에서 OSEM과 역투사 방법으로 각각 모든 대상을 재구성한 후에 3명의 핵의학 및 방사선과 전문의가 특별한 정보 없이 모든 영상을 검토하였다. **결과:** 28개의 병변을 맹검한 결과, 거의 모든 증례에서 OSEM이 역투사에 비교하여 최소한 대등하거나 우수한 영상의 질을 보여주었다. 비록 3 cm 이상의 큰 병변의 검출에는 차이가 없었으나 1.5-3 cm 크기의 병변 5개는 OSEM을 통하여서만 발견되었다. 하지만 1.5 cm 미만의 작은 병변 4개는 양쪽 모두에서 검출되지 않았다. **결론:** OSEM은 작은 크기의 간 혈관종을 발견하는데 보다 높은 민감도를 보였으며 전체적인 영상의 질에 있어서도 보다 좋은 대조도와 윤곽을 보여주었다. OSEM은 이와 같은 장점 뿐만 아니라 높은 사양의 컴퓨터를 요하지않고 계산시간이 길지 않기 때문에 임상에서 간 혈관종의 진단을 위한 적혈구 혈액풀 SPECT에 쉽게 적용될 수 있는 좋은 방법으로 사료된다. **(대한핵의학회지 2002;36;344-56)**

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Introduction

Cavernous hemangioma is one of the most common benign neoplasm of liver, occurring up to 7.3% of the population.[1,2] Most of this tumors can be easily diagnosed by routine ultrasonography (US) due to its characteristic findings,[3,4] however, hemangioma mimic atypical hepatocellular carcinoma (HCC) can make a trouble in accurate diagnosis.[5] Therefore, diagnostic modality having high specificity as well as sensitivity is necessary.

Currently, various diagnostic modalities including US, computed tomography (CT), magnetic resonance imaging (MRI) and radionuclide study have been introduced for diagnosis of hemangioma.[6] Among these diagnostic methods, RBC blood pool single photon emission computed tomography (SPECT) using Tc-99m labeled RBC is one of the most widely used diagnostic tool for liver hemangioma owing to its high specificity and relatively low cost .[7] The limitation of this method is low sensitivity in case with small sized lesion and which is partly originated from its data acquisition and reconstruction technique.

Filtered back projection (FBP) method has been the only reconstruction method applied to SPECT for many years. Although FBP is a good method that can be used in clinical context due to its rapid reconstruction with low computer hardware, it has several inherent problems such as streaking artifact, negative values, and loss of resolution associated with filter selection.[8-10]

Recently, iterative reconstruction (IR) has emerged as alternative method for reconstruction of SPECT images as well as positron emission tomography (PET). Maximum likelihood of expectation maximization (MLEM) is classic IR technique which is free from streak artifact and shows better image quality, however MLEM has been rarely used in clinical practice due to its requirement for tremendous amount of calculation.[11] Ordered subset expectation maximization (OSEM) technique is a modified IR method that can reduce the reconstruction time using divided data processing.[12] There have been several reports about application of OSEM in clinical usage including bone and parathyroid SPECT.[13,14] Now, we applied the OSEM technique to reconstruction of RBC blood pool liver SPECT.

The aims of this study were to identify the best iteration condition for diagnosis of focal liver lesion, cavernous hemangioma in clinical context and to determine whether OSEM has better sensitivity and image quality compared with conventional FBP technique in reconstruction of RBC liver SPECT for cavernous hemangioma of liver.

Materials and Methods

1. Materials

Twenty-four cases of RBC blood pool SPECT of liver were analyzed. All cases selected in this study represented typical imaging findings of cavernous hemangioma in various diagnostic modalities. All the patients underwent one of the following diagnostic imaging among US (n=7), CT (n=11) and MRI (n=6). Diagnostic criteria of hemangioma in CT and MR were based on characteristic findings such as delayed peripheral enhancement with eventual filling and high signal intensity like light bulb on T2 weighted MR image. In cases of US, diagnostic criteria was both well defined echogenic nodule without evidence of cirrhotic change of liver parenchyma and no interval change of nodule size on 1 year follow up study. Because hemangioma is highly vascular mass with benign character, biopsy was not performed due to the risk of massive bleeding. The ten of 11 CT scans were performed as iodide contrast enhanced dynamic study and all 6 MR were dynamic enhanced scan using Gadollinum-DTPA.

The mean age of the patient group was 52.93±8.93 year-old (M:F=9:15). Total 28 lesions of 24 patients were included in this investigation and divided into three groups according to its diameter; less than 1.5 cm, 1.5 to 3 cm and more than 3 cm. The size criterion defining each group was retrospective matter and was based on the best way that can clearly represent difference in detection ability between OSEM and FBP

2. Imaging Procedures

Original RBC blood pool SPECT studies were performed 2 to 3 hour after an intravenous injection of 740 MBq of Tc-99m RBC. The 64 projection data were obtained using a dual-head gamma camera (VERTEX, ADAC Lab., USA) equipped with low energy, high resolution (LEHR) parallel hole collimators on each case. SPECT images were acquired in a 64×64 matrix with 6 degree of angular increment for 40 minutes (40 sec per projection). At first, trans-axial tomographic images were obtained by FBP method using a Butterworth filter. Cut off frequency and order Number were 0.45 cycles/cm and 6, respectively. These were the conditions recommended by manufacturer and also a routine protocol for blood pool liver SPECT in my institute.

The raw projection data of each case were introduced to LINUX based personal computer via ethernet, because OSEM software was not available on Windows based system. The personal computer used in this study had Pentium II 266 MHz of CPU with 64 MB RAM and hard disk capacity was 3 GB. The original data cannot be used in OSEM software, so some manipulation of the data was needed. At first, we deleted the 2048 bytes of header portion from raw data then rearranged remaining net projection data into each axial slice using custom software programed by IDL. However, this data form could not be recognized by OSEM software and we substituted header portion with interfile in order to achieve the communication between each slice data and OSEM software (Fig. 1).

Iterative reconstruction was performed on the each axial slice data to obtain the each axial slice image. Preliminary image reconstruction using OSEM was applied in various conditions of subsets (1, 2, 4, 8, 16, and 32) and iteration numbers (1, 2, 4, 8, and 16) to obtain the best quality image of liver SPECT, because increase the number of subset resulted in blurring of images and maximal iteration number could not guarantee best image quality shown as Fig. 2. We used no filter in OSEM reconstruction. All 3 investigators agreed to choose 4 iterations and 16 subsets as best condition for RBC blood pool liver SPECT. After the decision, OSEM were performed in all the cases using these parameters. The results from FBP and OSEM were displayed with an inverted gray scale by Scion image software, a free PC version of NIH image (http://www.scioncorp.com) and 3 investigators evaluated the both images. Neither attenuation correction nor other post processing was performed on this study.

3. Analysis

Twenty-four cases of SPECT images reconstructed by both FBP and OSEM were evaluated by 3 investigators (one radiologist and two nuclear medicine physicians). All the observers have no information about reference image findings such as US, CT, and MRI.

Three investigators compared and evaluated the images reconstructed by FBP and OSEM in each case. The criteria for comparing image qualities between OSEM and FBP technique consists of lesion detection ability, image quality including define, contrast, and anatomic details.

Results

Results are presented in several categories including detection ability, image qualities, and artifacts.

1. Ability of lesion detection

The three observers investigated the number of detected lesion in 28 lesions of 24 patients with liver hemangioma.

Nineteen of 28 cases larger than 3 cm in diameter were successfully diagnosed by both methods.

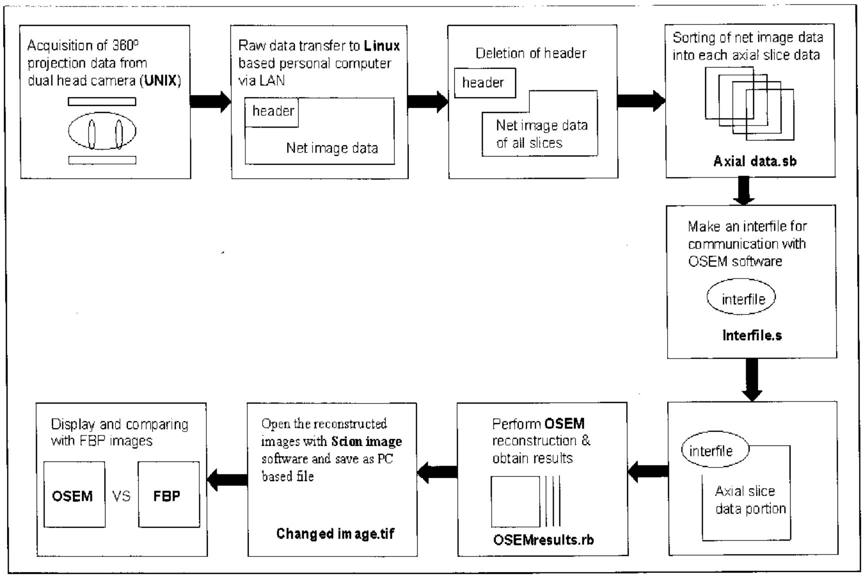

Fig. 1. Schematic diagram represents the each steps of image processing from raw data acquisition to reconstruction and evaluation.

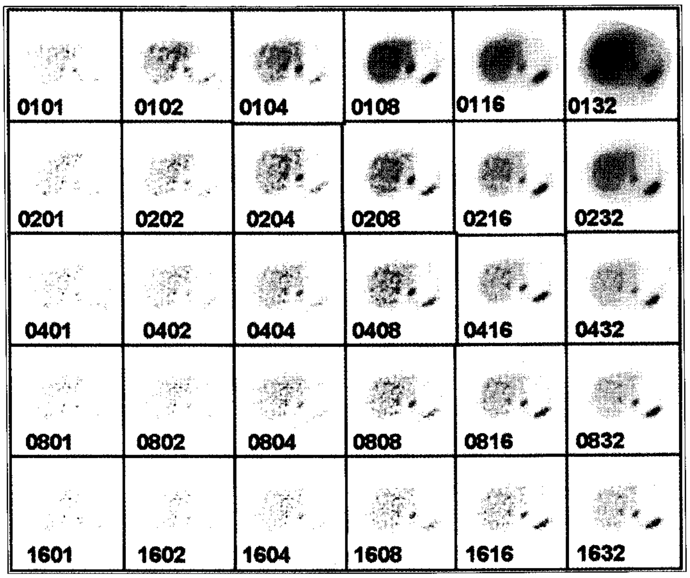

Fig. 2. Preliminary study of OSEM reconstruction using various conditions of iteration (first two digit) and subset number (last two digit) shows different texture of image in each condition.

However, 5 cases of small lesions around 1.5 to 3 cm in diameter were detected by OSEM only (Table 1). On remaining 4 cases less than 1.5 cm, both OSEM and FBP failed to depict hemangioma. Mean diameter of the lesion measured in diagnostic imaging including US, CT and MRI shows some differences but statistical comparison could not be performed due to different size and small number of population.

Figure 3 is the case that has about 1.5 cm sized focal lesion on lateral portion of segment 7 and MRI showed typical finding including peripheral enhancement and light bulb like high signal intensity on T2 weighted image. Axial SPECT image obtained by

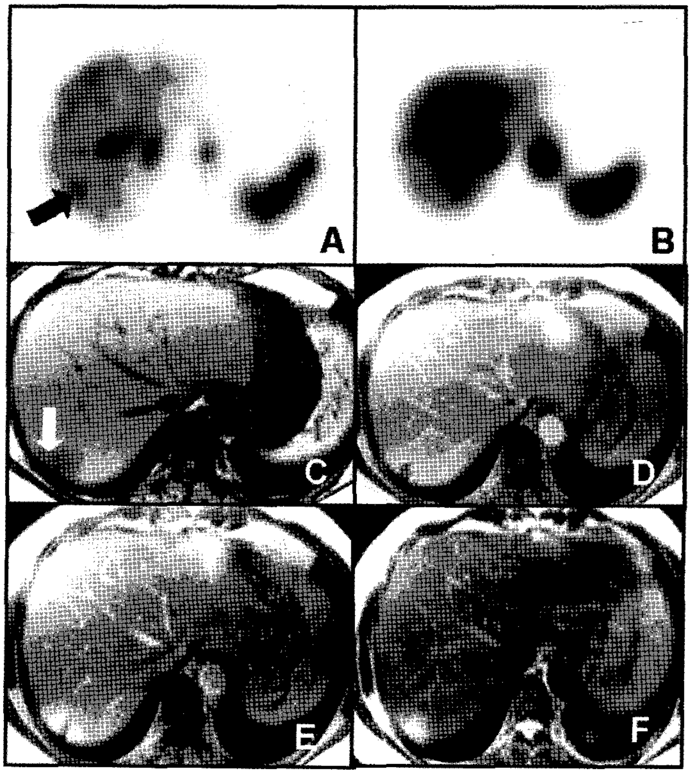

Fig. 3. Only OSEM image (A) represents focal hot uptake (arrow) on segment 7. FBP failed to depict the same lesion (B). MR images show typical finding of hemangioma at segment 7 (C–F).

Table 1. Comparison of Detection Ability of OSEM and FBP in Liver Hemangioma

Lesion size (mean diameter)	No. of lesions	Sensitivity (*)	
		OSEM (%)	FBP (%)
<1.5 cm (0.85±0.48)	4	0%	0%
1.5~3 cm (1.7±0.35)	5	100% (55.6)	0% (0)
> 3 cm (3.31±1.42)	19	100% (85.7)	100% (67.9)

* accumulation rate

OSEM represented focal hot uptake at corresponding area, while FBP images showed no focal uptake at the same region.

Similar result was also reported in figure 4 which had two hemangioma on anterior and posterior portion of segment 7. The larger lesion about 2.5 cm at anterior portion was successfully detected by both methods but the small lesion at posterior portion was more clearly depicted by OSEM. Although FBP image also showed faint uptake on same area, that was hardly differenciated true lesion from normal variation owing to its very low activity. This results might be influenced by focal activity as well as size and the characteristics of OSEM having better results in low count statistics is clearly demonstrated on this result.

2. Image qualities

Authors also investigated the qualities of images obtained by OSEM and FBP. First, we checked define, contrast and size of liver, spleen, and great vessels as well as hemangioma per se comparing with the findings of radiological imaging. In our observation, although both OSEM and FBP had detected hemangioma with more than 3 cm size, most of FBP image represented overestimated size of the lesion comparing with the results of US, CT, and MR.

Figure 5 demonstrated a case with hemangioma on lateral margin of lower posterior portion (segment

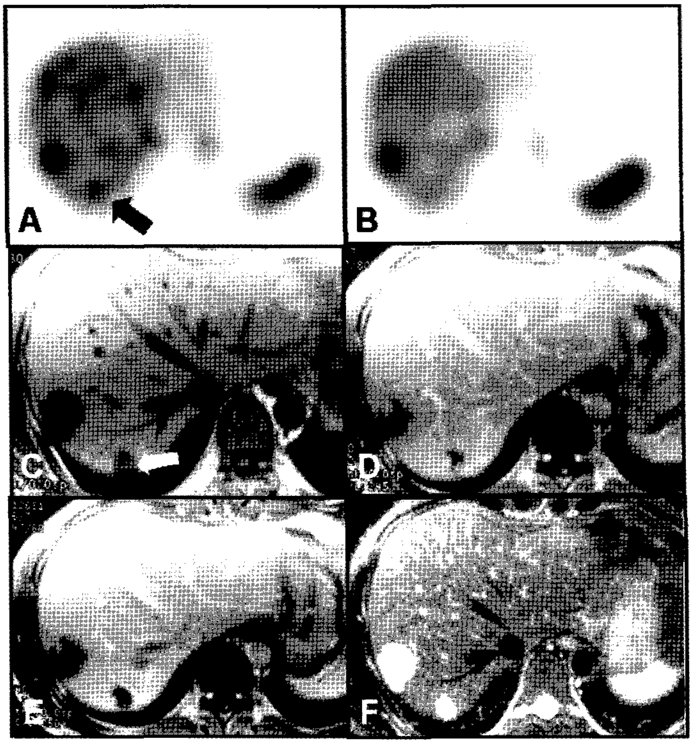

Fig. 4. The large hemangioma involving anterior portion of segment 7 is well depicted on both OSEM (A) and FBP (B), however small lesion on posterior portion (arrow) is detected by OSEM only (A). Dynamic enhanced MRI (C-F) clearly demonstrated two heamngiomas having typical findings, the peripheral enhancement and T2 high signal intensity.

6) of right lobe of liver, both OSEM and FBP showed well defined hot nodule at the same area where the CT scan showed the lesion. However, contrast between liver and hemangioma looked considerably higher in OSEM than in FBP. Fortunately, this lesion has fairly high activity enough to be detected by two methods, but if the same sized lesion with lower activity was located at same area, FBP might fail to detect this lesion.

Another example, figure 6 demonstrated OSEM

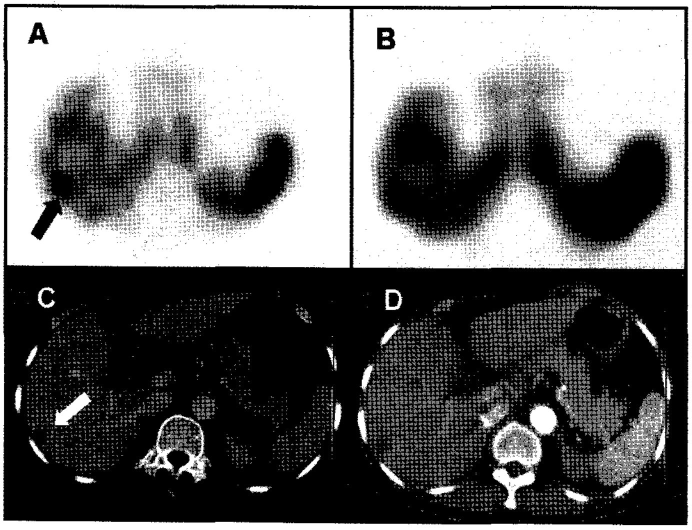

Fig. 5. OSEM image (A) shows higher contrast than that of FBP and better estimation of real size of the lesion considering the CT findings (C, D).

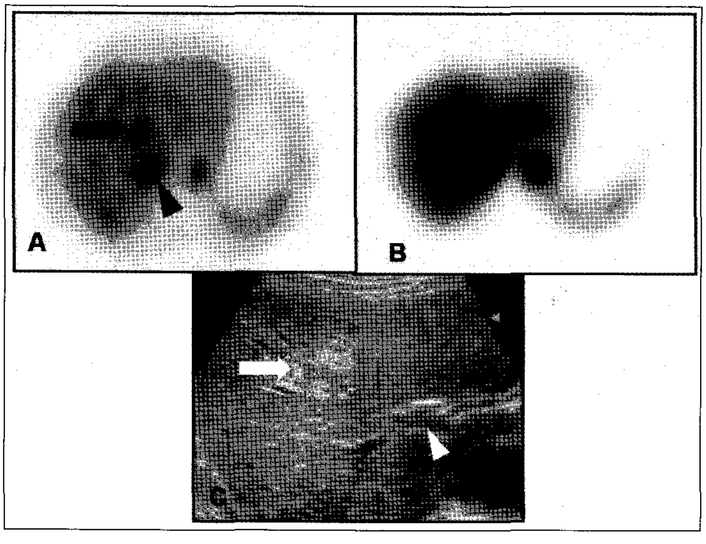

Fig. 6. Axial SPECT images obtained using OSEM (A) and FBP (B). OSEM shows focal hot nodule (arrow) separated from inferior vena cava (arrow head). Ultrasonography (C) reveals echogenic mass lesion separated with inferior vena cava (arrow head) but FBP falsely noted ill defined mass abutting the great vessel (B)

was superior to FBP in depiction of main lesion and adjacent structure. An echogenic round nodular lesion was detected by routine ultasonography and this lesion was located at anterior to inferior vena cava (IVC) with gap. Comparing with previous cases, the lesion was deeply located and axial SPECT image reconstructed by OSEM reveal well correlated focal lesion apart from this great vessel while FBP image falsely represent the lesion as round hot nodule abutting the IVC. On this study, we did not apply any attenuation correction technique to both methods. We also found that OSEM presented better define in showing deeply located lesion. For example, deeply located structure such as IVC and aorta revealed better define in OSEM.

On figure 7, about 3 to 4 cm sized mass lesion with lobulated margin is noted at the posteror inferior portion (segment 6) of right lobe of liver and dynamic CT scan revealed peripheral enhancement and posterior margin of this lesion had concave contour due to right kidney. On the image reconstructed by OSEM, concave contour of posterior portion is clearly described and right kidney is also well visualized, however FBP image represented round hot nodule regardless the existence of right kidney.

Final case, figure 8 is another example showing that the image resolution of OSEM is superior to that of FBP. In this case, both methods can detect focal hot nodule on lower portion of right lobe of liver, however, when we inspect the morphology of the lesion, two reconstruction methods revealed considerably different results. On the CT scan performed by contrast enhanced study, this lesion had oval shape with mild lobulation. OSEM image showed nearly the same contour with that of CT but FBP depict this lesion as simply round one.

We presented several clinical cases demonstrating better detection and description ability of OSEM comparing with FBP. All three reviewers agreed with these points and Table 2 is summary of these results. Nearly all cases had the same or better

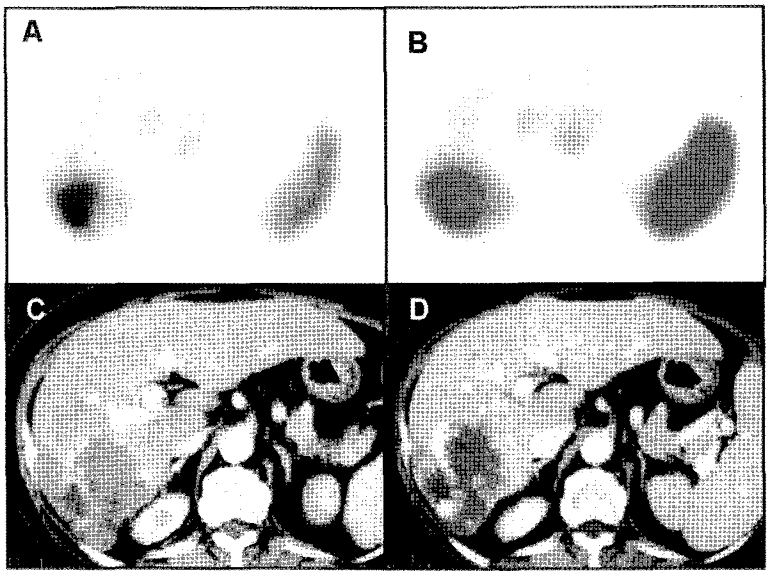

Fig. 7. A large lobulated hemangioma is noted on both OSEM (A) and FBP (B) images. Considering the shape of the hemangioma seen on CT scan (C,D), OSEM image shows better result in accurate imaging of true contour of the lesion.

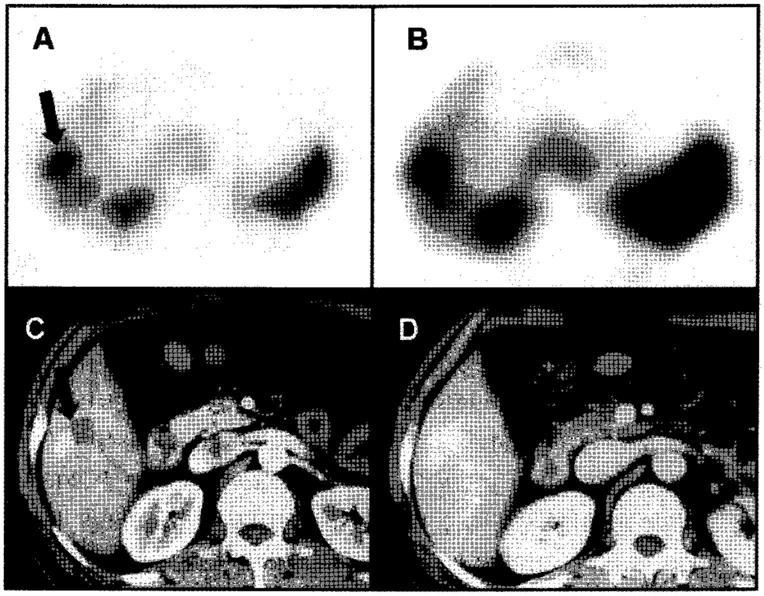

Fig. 8. OSEM image (A) represents hot nodule (arrow) with oval shape and FBP image (B) showed larger hot nodule with round contour. On dynamic CT scan (C, D), oval shaped enhanced lesion (arrow) is noted on lower anterior portion (segment 5) of right lobe and this lesion has somewhat lobulated contour on posterior margin. Retrospectively, same contour can be found on OSEM images.

Table 2. Comparison of Image Qualities between OSEM and FBP

Parameter	No of lesions	%
Anatomic define of margin		
Superior with OSEM	10	35.7
Identical with both	14	50
Inferior with OSEM	0	0
Disagreement	4	14.3
Accuracy in lesion extent		
Superior with OSEM	19	67.9
Identical with both	7	25
Inferior with OSEM	0	0
Disagreement	2	7.1
Contrast between liver and lesion		
Superior with OSEM	17	60.7
Identical with both	5	17.9
Inferior with OSEM	3	10.7
Disagreement	3	10.7
Total number of lesions	28	100

results in OSEM, though 3 observers could not reach complete agreement in small number of cases.

3. Artifacts

Usually, streak artifact has been known to be common problem occurring on FBP. Liver SPECT using FBP on these cases also had this artifact when we adjusted background activity to higher level, however in clinical context, this artifact was rarely seen because background activities diminished as low as possible in practical interpretation.

Although negative values at the neighboring area of hot activity were reported on several reports, there was no result having critical negative values on our cases of hemangioma.

Discussion

In this study, we tried to find the best condition of iteration and subset number for RBC blood pool SPECT using OSEM for liver hemangioma and apply this to clinical cases. The OSEM images reconstructed according to that condition (4 iteration and 16 subset number) represented satisfactory result in detection of liver hemangioma, especially in relatively small lesion around 1.5 to 3 cm comparing with those reconstructed by convention FBP

Filtered back projection (FBP) is conventional reconstruction method for emission tomographic images. In nuclear medicine field, there has been no substitutional method for this until recently. Although FBP easily can be applied to reconstruction of SPECT image due to its rapid processing time, inherent problems such as streak artifact and poor image quality on low counts have been obstacle to achieve images with good quality.[15]

Since Shepp and vardi had applied maximum likelihood (ML) reconstruction to emission tomography in 1982,[16] many kinds of reconstruction techniques were suggested. Among them, expectation maximization (EM) algorithm is a general statistical procedure for processing ML estimates. However, EM requires high performance computer and has slow convergence, while quality of reconstructed image is good.[15]\

OSEM is one of modified iteration reconstruction methods that can shorten reconstruction time by processing the data in several subsets, so called 'divide and conquer'.[12] As filter and acquisition parameter play an important role in FBP images, optimization of subset and iteration number is very important in OSEM technique. The more the subset numbers the faster the reconstruction time, but beyond the critical number, the noise artifact of ML solution is magnified by OSEM.[12] Number of iteration is also an important factor that changes image quality and this factor has optimal point. For example, the mean square error between estimated and true activity improves in early iterations, but excessive iteration can make the noise increase.[15] The results obtained in this study also showed convergence of image quality according to increment of number of iteration and subset.

The best setting of number of iteration and subset might be different according to imaging modalities and target organ as well as preference of interpreter. In this study, we chose 4 iterations and 16 subsets for SPECT image reconstruction and this choice might be different in other group due to the difference in preferring image texture of interpreter. For instance, the choice of Blocklet et al was 2 iterations and 8 subsets.[13] However, there was no wide range of choice and only 2 iteration or 8 subset combinations could make similar image quality with that of ours, although we also nominated 4 iterations and 8 subsets as well as 2 iterations and 8 subsets.

These days, OSEM is being applied to positron emission tomography (PET) as well as SPECT[17,18] and several investigators report good results. Comparing with PET scan, application of tomographic technology to SPECT study is limited due to its relatively low resolution and difficulty in attenuation correction. Therefore, most of attempt to this field has been concentrated in Tc-99m labeled radionuclide study such as bone[13] and parathyroid lesion[14] that can provide best resolution in SPECT study. RBC blood pool liver SPECT for diagnosis of cavernous hemangioma is considered to be another good indication for OSEM, because applying OSEM can improve detection rate. Moreover, current situation that fairly high performance computer system can be obtained at fairly low price owing to rapid improvement of computer hardware is another factor that accelerate adoption of iteration technique.

As shown in results, OSEM represented better performance in many fields. In the point of detection ability, 5 of 28 lesions (17.9%) could be detected by OSEM only, while 19 (67.9%) lesions were successfully diagnosed by both methods. However, the latter cases have more than 3 cm in size and the former is smaller, less than 3 cm, which means OSEM is superior to FBP in detection of small lesions. This difference might be originated from the nature of OSEM, such as less streak artifact, strength in low count data and non-using filter etc. Anyway, OSEM could improve the detection ability of small hemangioma. This result will encourage the usage of RBC liver SPECT for diagnosis of hemangioma.

We also estimated the quality of reconstructed images by OSEM and FBP. There were several factors that could define this, for example, in same lesion, which one is more distinct. This can be influenced by contrast between lesion to background (high or low) and define of margin (sharp or blurred). In addition, accurate depiction of original lesion with less distortion is also important point, because co-registration between functional (SPECT, PET) and anatomical (CT, MRI) images are important for better diagnosis in these days.

As shown in results, there were many OSEM-examples that represented better result in these points. We thought difference in contrast could make difference in diagnosis.

For example, although there is no problem in diagnosis of the lesion with very high activity (Fig 5), small lesion with relatively low activity can be missed by FBP. This result can be explained by difference of both methods. While FBP make constant noise across the reconstruction field, noise in OSEM is correlated with the signal, so the amplitude of noise is lower in region with low counts.[11] Several cases of FBP noted in this study represented blurred contour of hemangioma and their shapes were round in almost all cases regardless the true contour of the lesion. This discordance can be an effect of filters used in FBP reconstruction. There are several investigations of applying the post reconstruction filtering to reduce the noise.[19] On the contrast, OSEM need no filter in image reconstruction and this can be an advantage.

In addition, most new modalities require new or up-graded hardware and this is another obstacle to adopt new method, however, OSEM need no high performance computer system and minimal investment for computer system make OSEM possible to use in clinical practice.

On the view point of reconstruction time, it took only several seconds per slice under the condition of 4 iterations and 16 subsets, and higher number of subset and iteration resulted in blurring of images. Therefore, reconstruction time is not a problem for introducing OSEM.

The limitation of this study was insufficient number of cases, especially cases with small sized hemangioma around 1 cm diameter was not enough to estimate the statistical difference of detection ability on both methods. However, the promising point is that OSEM could make same or better results in most of cases in spite of their minimal settings. OSEM has many potential factors that improve the image quality including scatter correction technique and combination with another algorithm[20] and this means OSEM can make better image in near future.

Conclusion

OSEM is one of the modified iterative reconstruction methods that can achieve both better image quality and short processing time. Currently, this technique has been widely applied to various fields. Authors tried to adopt OSEM to RBC blood pool SPECT that has long been used for the diagnosis of cavernous hemangioma involving liver in clinical context. In this study, we found that 4 iteration and 16 subset number is the best condition for OSEM imaging and this method could improve the resolution of RBC blood pool SPECT for liver hemangioma as well as image qualities. Furthermore this can be easily used without requirement of high performance computer system. Therefore, OSEM is considered to be reasonable method that can improve the sensitivity of RBC blood pool SPECT in defection of small hemangioma of liver.

Abstract

Purpose: RBC blood pool SPECT has been used to diagnose focal liver lesion such as hemangioma owing to its high specificity. However, low spatial resolution is a major limitation of this modality. Recently, ordered subset expectation maximization (OSEM) has been introduced to obtain tomographic images for clinical application. We compared this new modified iterative reconstruction method, OSEM with conventional filtered back projection (FBP) in imaging of liver hemangioma. **Materials and Methods:** Sixty four projection data were acquired using dual head gamma camera in 28 lesions of 24 patients with cavernous hemangioma of liver and these raw data were transferred to LINUX based personal computer. After the replacement of header file as interfile, OSEM was performed under various conditions of subsets (1,2,4,8,16, and 32) and iteration numbers (1,2,4,8, and 16) to obtain the best setting for liver imaging. The best condition for imaging in our investigation was considered to be 4 iterations and 16 subsets. After then, all the images were processed by both FBP and OSEM. Three experts reviewed these images without any information. **Results:** According to blind review of 28 lesions, OSEM images revealed at least same or better image quality than those of FBP in nearly all cases. Although there showed no significant difference in detection of large lesions more than 3 cm, 5 lesions with 1.5 to 3 cm in diameter were detected by OSEM only. However, both techniques failed to depict 4 cases of small lesions less than 1.5 cm. **Conclusion:** OSEM revealed better contrast and define in depiction of liver hemangioma as well as higher sensitivity in detection of small lesions. Furthermore this reconstruction method dose not require high performance computer system or long reconstruction time, therefore OSEM is supposed to be good method that can be applied to RBC blood pool SPECT for the diagnosis of liver hemangioma.

Key Words: Iterative reconstruction, Ordered subset expectation maximization, Hemangioma

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