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Dual-tracer subtraction parathyroid SPECT using Tc-99m pertechnetate and Tc-99m MIBI

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Dual-tracer subtraction parathyroid SPECT using Tc-99m pertechnetate and Tc-99m MIBI

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Abstract. The aim of this study was to develop software for dual-tracer subtraction parathyroid SPECT using Tc-99m pertechnetate and Tc-99m MIBI. The software was developed using MATLAB and designed into 3 main steps: image registration, image normalization, and subtraction SPECT. Image registration was performed for all transaxial, coronal and sagittal planes with option to manually adjust slice-by-slice. For normalization, a region of interest (ROI) was manually drawn around the thyroid gland for all transaxial slices of pertechnetate SPECT and the thyroid contours were automatically copied to the MIBI SPECT. A normalization factor was then calculated and used to normalize the pertechnetate SPECT. Finally, MIBI SPECT was subtracted from pertechnetate SPECT to generate subtraction SPECT images. Retrospective data from patients were used to evaluate the software. The abnormal findings on subtraction SPECT were confirmed with the surgical pathologic report used as the gold standard. A total of 10 abnormal glands were surgically removed of which 8 were identified by the subtraction SPECT. These findings corresponded to the pathologic results that confirmed 2 adenomas and 6 hyperplastic glands. However, 2 hyperplastic glands were missed due to their small size. This software is user-friendly, efficient and can be used for dual-tracer subtraction parathyroid SPECT.

1. Introduction

Parathyroid imaging is useful for localizing hyperfunctioning parathyroid glands (adenomas or hyperplasia) before surgery to help the surgeon localize the lesion. At present, there are several techniques for parathyroid imaging including dual-phase planar Tc-99m MIBI, dual-isotope or dual-tracer planar subtraction, Tc-99m MIBI SPECT and SPECT/CT [1]. For the dual-tracer subtraction technique, Tc-99m MIBI is used in conjunction with Tc-99m pertechnetate or I-123 which is taken up only in thyroid tissue. Subtraction between the two sets of images is performed to produce the subtraction image. However, there are several disadvantages to using I-123 including high cost and long procedure time. For this reason, Tc-99m pertechnetate is widely used instead of I-123 for dual-tracer imaging.

The dual-tracer subtraction technique is mostly based on planar imaging between Tc-99m pertechnetate and Tc-99m MIBI. However, SPECT imaging has been demonstrated to provide more precise anatomical location [1] and improved detection of abnormal parathyroid glands [2, 3]. Several studies have reported the use of dual-tracer subtraction SPECT, which provides good results for the detection of abnormal parathyroid glands, and these studies were performed using I-123 in combination with Tc-99m MIBI [4-6]. Previously, we studied dual-tracer SPECT using Tc-99m pertechnetate and

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Tc-99m MIBI, with and without subtraction SPECT, using Monte Carlo simulation [7]. We found that this technique provides good performance with area under the ROC curve (AUC) higher than 0.80 in the detection of simulated abnormal parathyroid gland. Though dual-tracer SPECT imaging is currently used in the clinic, there is no software for subtracting dual-tracer SPECT images. For this reason, we performed this study aimed to develop software for dual-tracer subtraction parathyroid SPECT using Tc-99m pertechnetate and Tc-99m MIBI.

2. Materials and methods

2.1. Software development

Software was developed by using MATLAB program version R2017a, under an academic license supported by Mahidol University, and the graphic user interfaces (GUIs) of the software designed using the Graphic User Interface Development Environment (GUIDE). There were 4 main user interfaces (UIs), 'Patient Data UI', 'Registration UI', 'Draw ROI UI', and 'Subtraction UI', as shown in figure 1.

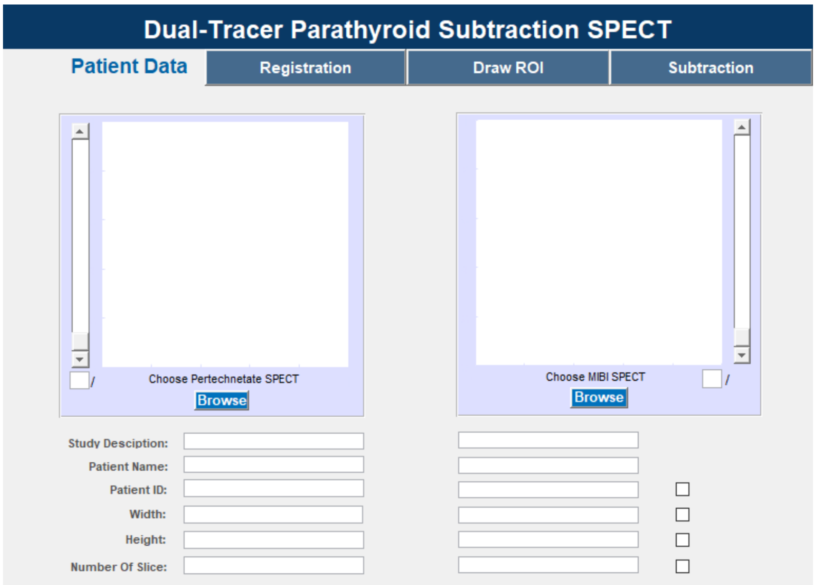

Figure 1. Dual-tracer subtraction SPECT software included 4 main UIs; 'Patient Data UI' is the first UI for reading patient images as DICOM files.

2.1.1. Image data of patient. When the software was opened, the 'Patient Data UI' was presented first (figure 1) to read DICOM files which are transaxial SPECT images of Tc-99m pertechnetate and Tc-99m MIBI. Study information, including study description, patient's name, ID, width, height and number of slices, were automatically read from the DICOM header. It was very important to read both sets of images from the same patient, and thus the study information from both were matched and checked by software. If both SPECT data sets were obtained from the same patient, the next process, which was image registration, continued.

2.1.2. Image registration. The 'Registration UI' was created to perform registration of both Tc-99m pertechnetate SPECT and Tc-99m MIBI SPECT as shown in figure 2. First, transaxial SPECT images of both radiotracers were reformatted into coronal and sagittal planes. After that, image registration was performed for all 3 planes (transaxial, coronal and sagittal). In addition, this UI provided options for translation and rotation of the Tc-99m pertechnetate images to register with Tc-99m MIBI images.

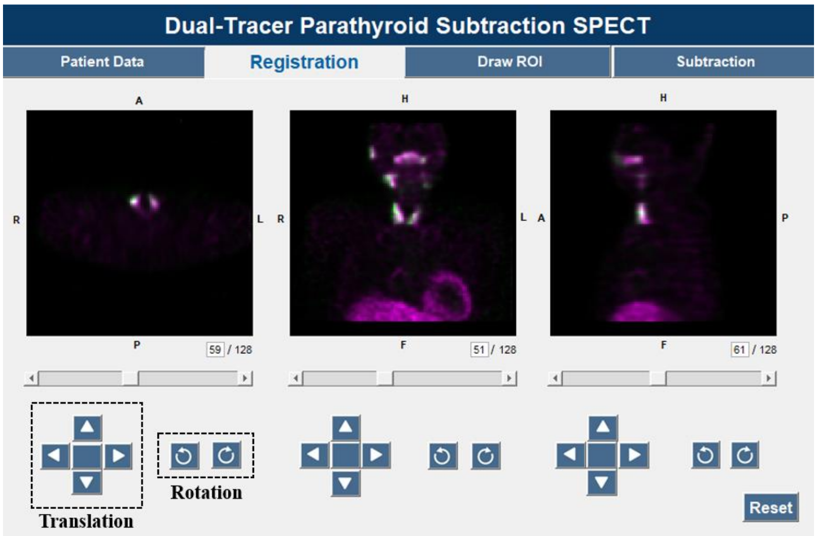

Figure 2. The 'Subtraction UI' was used for image registration of Tc-99m pertechnetate SPECT and Tc-99m MIBI SPECT for all 3 image planes.

2.1.3. Image normalization. For parathyroid imaging, the amount of administered activity of Tc-99m pertechnetate (2-10 mCi) is much lower than that of Tc-99m MIBI (20-30 mCi) [1]. The goal of 'Draw ROI UI' was to normalize thyroid counts in the Tc-99m pertechnetate SPECT to be similar to those in the Tc-99m MIBI SPECT before performing subtraction. To do normalization, the region of interest (ROI) was manually drawn around the thyroid gland slice-by-slice in the Tc-99m pertechnetate SPECT as shown in figure 3. After that, these ROIs were automatically copied to the Tc-99m MIBI SPECT. The normalization factor was calculated as:

$$\text{Normalization Factor} = \frac{C_M}{C_P} \tag{1}$$

where C_M and C_P were the total thyroid counts in ROIs of Tc-99m MIBI and Tc-99m pertechnetate, respectively. Tc-99m pertechnetate SPECT was then normalized by using this factor.

2.1.4. Subtraction SPECT

Subtraction SPECT was easily performed using 'Subtraction IU' as shown in figure 4. The normalized Tc-99m pertechnetate SPECT images were subtracted from Tc-99m MIBI SPECT images to generate dual-tracer subtraction SPECT images. In addition, this UI allowed the user to adjust the normalization factor to increase or decrease the level of subtraction until the thyroid gland disappeared into the background of subtraction SPECT images. Moreover, image contrast could be adjusted using window width (WW) and window level (WL), and exported via DICOM file.

2.2. Software evaluation

Retrospective data of 4 patients who underwent dual-tracer SPECT imaging using Tc-99m pertechnetate and Tc-99m MIBI at the Division of Nuclear Medicine, Siriraj Hospital, were used to evaluate the software. The data collection process of this study was approved by Mahidol University's Central Institutional Review Board. All SPECT data were reconstructed using a 3D OS-EM algorithm with 4 iterations and 10 subsets, and scatter correction using a dual-energy window and resolution recovery. In addition, CT-based attenuation correction was applied only in Tc-99m MIBI SPECT because the CT scan was acquired only in this session (to reduce radiation dose of patient).

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To evaluate the software, transaxial SPECT images of both radiotracers were read into the software and were then carefully registered until both sets of images were superimposed. In the subtraction process, the normalization factor was manually adjusted until the subtraction SPECT images were subjectively satisfactory. Finally, abnormal findings on the subtraction images were recorded and these results were confirmed with surgical histologic reports.

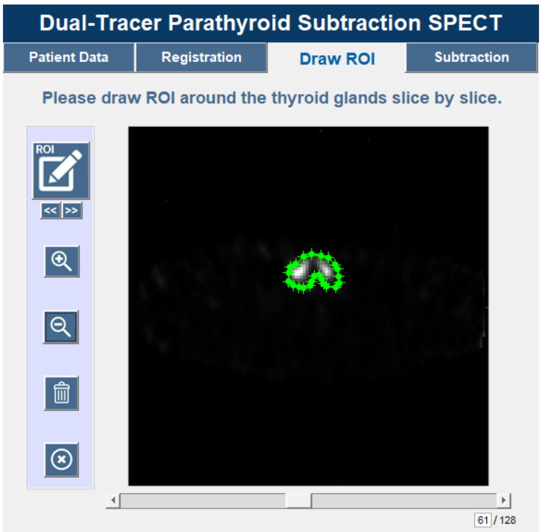

Figure 3. The 'Draw ROI UI' was created to draw ROIs around the thyroid gland slice-by-slice in Tc-99m pertechnetate SPECT and perform normalization.

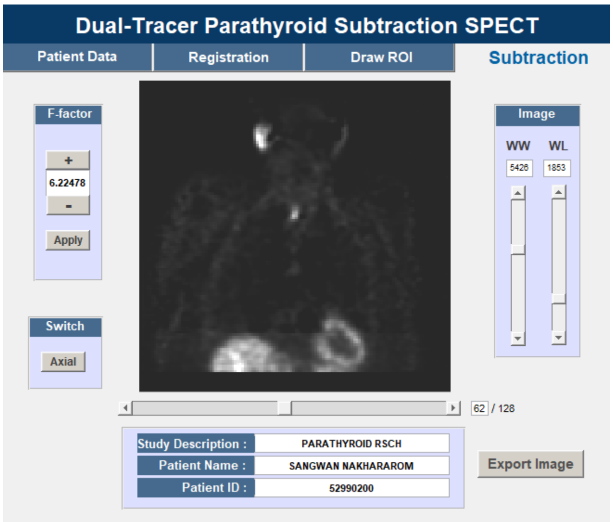

Figure 4. The 'Subtraction UI' was created to perform subtraction between normalized Tc-99m pertechnetate SPECT and Tc-99m MIBI SPECT. The normalization factor could be adjusted in this UI.

3. Results and discussion

A total of 10 abnormal parathyroid glands were surgically removed in 4 patients. Histology revealed parathyroid hyperplasia of all 4 glands found in 2 patients and solitary parathyroid adenomas in 2 patients. In this study, dual-tracer subtraction SPECT was able to localize 8 abnormal parathyroid glands while it missed 2 glands that were hyperplastic according to histologic reports (shown in table 1).

Table 1. Results of dual-tracer subtraction SPECT and surgical histologic report.

Case Number	Dual-Tracer Subtraction SPECT		Surgical Histologic Report
	Location[a]	(+/–)[b]	
1	LU	–	Parathyroid hyperplasia
	LL	+	Parathyroid hyperplasia
	RU	+	Parathyroid hyperplasia
	RL	+	Parathyroid hyperplasia
2	LU	–	Parathyroid hyperplasia
	LL	+	Parathyroid hyperplasia
	RU	+	Parathyroid hyperplasia
	RL	+	Parathyroid hyperplasia
3	RL	+	Parathyroid Adenoma
4	LL	+	Parathyroid Adenoma

[a] LU = left upper; LL = left lower; RU = right upper; RL = right lower
[b] + = positive; − = negative

A sample patient case with dual-tracer subtraction SPECT is shown in figure 5. The figure shows that 3 abnormal glands were clearly visible on the subtraction SPECT as indicated by white arrows. However, one abnormal gland was not visible at the upper pole of left thyroid lobe. The histologic result of this case was that there were 4 glands with hyperplasia.

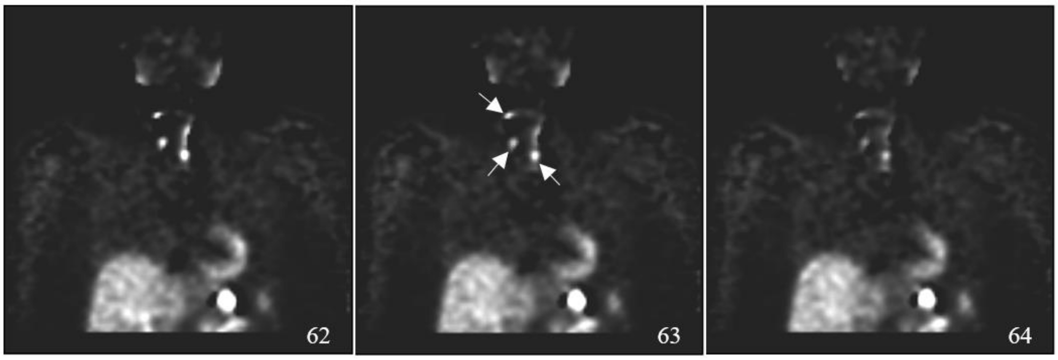

Figure 5. A patient case with 4 hyperplastic glands. Three abnormal parathyroid glands were clearly seen as indicated by white arrows, but one gland which was located at the upper pole of the left thyroid lobe was not visible on dual-tracer subtraction SPECT.

In this study, two hyperplastic glands were not visible in the subtraction SPECT and both glands were located at the upper pole of thyroid lobes. The location of lower parathyroid glands is commonly located beneath the thyroid gland, whereas upper glands usually lie behind the thyroid gland [8]. For this reason, abnormal parathyroid glands at upper poles of the thyroid might be difficult to visualize and negative findings can occur. In addition, several factors can affect the localization of abnormal parathyroid glands including variability of patient anatomy, gland size and shape. Moreover, system resolution and the amount of radiotracer uptake by abnormal parathyroid tissue may also limit detectability [9].

It has been reported that Tc-99m MIBI parathyroid imaging is less sensitive for detecting hyperplastic parathyroid glands than adenomatous glands because hyperplastic glands are usually smaller in size than adenomatous glands [9]. Moreover, Neumann *et al.* [6] reported a positive correlation between hyperplastic gland size and detectability using dual-tracer subtraction SPECT, with larger glands more likely to be detected. In this study, two hyperplastic parathyroid glands were not visible in the subtraction SPECT and their sizes according to histologic reports were 1×0.5×0.3 cm and 1.1×1.0×0.7 cm which were smaller than those of detected hyperplastic glands.

With the dual-tracer subtraction technique, it was essential to use dual-tracer SPECT images with the same patient position to avoid misregistration. In addition, patient motion during acquisition could lead to misregistration of two images resulting in in-correct subtraction images and misinterpretation. Furthermore, adjustment of the normalization factor should be done carefully because over-subtraction can remove lesion activity and result in a false-negative finding.

4. Conclusion

The software for dual-tracer subtraction SPECT using Tc-99m pertechnetate and Tc-99m MIBI was developed in this study. Retrospective data from 4 patients who underwent dual-tracer parathyroid SPECT imaging with surgical histologic results were used to evaluate the software. This evaluation showed that the dual-tracer subtraction SPECT provided good results in the detection of abnormal parathyroid glands. However, two hyperplastic parathyroid glands were missed due to their small size. This software is graphic user interface-based, user-friendly, and may be useful for clinical work.

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