Comparison of the accuracy of MIBI scan and SPECT/CT scan in patients with hyperparathyroidism with reference to the surgical and pathological results - our local 12 years experience

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Learning objectives

After reading this E poster, readers would be able to:

- recognise the radiological manifestations of different types of hyperparathyroidism in MIBI scan and SPECT/CT scan
- learn about the accuracy of the MIBI scan and SPECT/CT scan for preoperative localization of abnormal parathyroid tissue
- revise on the causes, pathophysiology and electrolyte abnormalities in patients with hyperparathyroidism

Background

Patients with hyperparathyroidism have increased calcium and decreased phosphate reabsorption in the kidney, increased osteoclast activity and increased 1,25 dihydroxy vitamin D3 production in the kidney. The overall effect would be increased serum calcium and decreased serum phosphate.

The cause of hyperparathyroidism could be divided into primary, secondary and tertiary categories. Up to 80% of primary hyperparathyroidism is caused by a single adenoma. The second most common cause is diffuse hyperplasia, accounting for about 4%. Parathyroid cancer only accounts for 1.5% of primary cases. [1] For secondary hyperparathyroidism, it is usually caused by chronic renal failure, or less commonly dietary deficiency of vitamin D. Tertiary hyperparathyroidism occurs after prolonged secondary hyperparathyroidism, when the glands acts autonomously, causing excessive secretion of parathyroid hormone and hypercalcaemia.

Surgery is indicated if patient's symptoms are not responding to medical treatment. Preoperative localization of abnormality can reduce operative time, cost and patient morbidity. Nuclear medicine is one of the commonly employed methods. Studies have shown that Technetium Tc99m Sestamibi scan has a higher sensitivity and similar specificity compared with high resolution ultrasound. [2] While others advocate using radiologist performed sonography as the principal imaging modality for patients with hyperparathyroidism, and selective use of Technetium 99m sestamibi in cases with negative or equivocal sonographic findings before parathyroid resection. [3]
Imaging findings OR Procedure details

Material and Method

This retrospective study was approved by the local institutional review board.

Population

The inclusion criteria were all patients who had undergone both preoperative localization nuclear medicine scan (either MIBI scan or SPECT/CT) and subsequent parathyroidectomy in our hospital in the 12 year period between 1 July, 1997 and 30 April, 2010. Cases without preoperative localization scan, those did not eventually undergo surgery or those that were lost to follow up were excluded from the study.

Data Acquisition

The respective protocols for data acquisition by the two different kinds of scan are shown below as reference.

1. Parathyroid MIBI Scan Imaging Protocol

Our hospital's nuclear medicine section used MIBI scan for parathyroid scan before March 2008.

We injected patient with 20mCi Tc-99m-MIBI intravenously. MIBI scintigraphy images were acquired according to a specific protocol. An anterior planar view and an anterior view were obtained at 10 minutes. The anterior planar view was taken when patient extended his or her neck. The thyroid was positioned at the top of the field of view and the mid mediastinum was included. The anterior view was obtained also when patient extended his or her neck. The thyroid was positioned at the center of the field of view. Acquisition times for both views were 300 second each. At 3 hours post injection, we obtained anterior, 30 degree RAO and 30 degree LAO views in extended neck position and thyroid at the center of field of view, also with acquisition time of 300s, matrix 128x128.

2. SPECT/CT
Our nuclear medicine section employed SPECT/CT as the mode of preoperative localization since March 2008.

The protocol for acquisition of images was similar as before with modifications. That is, we injected patient with 20mCi Tc-99m-MIBI intravenously. Static MIBI scintigraphy images were acquired at 10 minutes and 3 hours as before with matrix 256x256. SPECT images were obtained after the 10 minutes planar images, with 6 degrees per step, and a 30 second acquisition for each step in the continuous mode with a matrix of 128x128. The images were reconstructed using two dimensional ordered subset expectation maximization iterative technique (for subsets and eight iterations) and Gallssian three dimesional post filter. Non contrast CT scan of the neck and upper mediastinum was performed for the corresponding region for further correlation (1mm collimation with reconstruction to 1.25mm slice thickness, pitch 1.6, soft tissue algorithm: 25mAs, 130kVp). Soft ware with image fusion function was used for image analysis.

**Methodology**

Patients were divided into two groups according to the mode of preoperative localization: MIBI scan and SPECT/CT scan. Their demographic factors, serum parathyroid hormone and electrolyte levels, scan, surgical and pathological reports were reviewed. The surgical and pathological reports were regarded as the gold standard.

There were five area of interest in each people which were classified as left superior, left inferior, right superior, right inferior and ectopic locations. Each area of interest was being looked at separately. The results were interpreted by comparing the uptake in the scan and the operative and pathological results.

**Statistical Analysis**

With the surgical and pathological reports regarded as the gold standard, the sensitivity, specificity, positive and negative predictive values of MIBI scan and SPECT /CT scan were calculated. The diagnostic capability of the two modes of localization was measured by calculating a receiver operating characteristic curve. The area under the curve was estimated with the Delong, Delong, and Clark-Pearson method. [4]. Statistical software, MedCalc (version 11.1, Broekstraat, Mariakerke, Belgium) was used for statistical analysis. P value less than 0.001 was taken as statistically significant.

**Result**
100 patients had undergone Tc-99m MIBI subtraction scintigraphy and parathyroidectomy between 1 July, 1997 and 30 June, 2007. They were included in our study, which amounted to a total of 500 sites of interest. Of the 100 patients, there were 33 males and 67 females, with age range of 24 to 85 years old and a mean of 58.6 years old. The abnormal parathyroid tissue could be seen as area of persistent radiotracer uptake in the delayed phase. *(figure 1-4).*

For patients using MIBI scan as preoperative localization, the range of serum parathyroid hormone right before operation in this patient group was 5.9nmol/L to 343.1nmol/L. The mean was 62.3nmol/L. 95 patients had elevated parathyroid hormone levels and 4 had normal levels.

The range of serum calcium right before operation in this group of patient was from 1.85mmol/L to 3.26mmol/L. The mean median was 2.74mmol/L. 83 patients had elevated serum calcium levels, while 15 patients had normal serum calcium levels and 2 had lower levels.

Similarly, all the patients who had undergone SPECT/CT scan and parathyroidectomy in the 25 month period after the implementation of SPECT/CT between 1 March, 2008 and 30 April, 2010 were included in the study. These amounted to a total of 21 cases and 105 sites of interest. There were 5 males and 16 females, with age range of 44 to 88 years old. The abnormal parathyroid tissue could be seen in the reconstructed image as area of persistent radiotracer uptake superimposed on an abnormal parathyroid nodule. *(figure 5-7).*

The range of serum parathyroid hormone in the second group of patient ranges from 9.3nmol/L to 331nmol/L. All patients in this group had elevated parathyroid level. The mean value was 88.5nmol/L.

The range of serum calcium right before operation was from 1.95mmol/L to 3.28mmol/L. The mean was 2.6mmol/L. 16 patients had elevated serum calcium level, 4 had normal and 1 had reduced levels.

Using MIBI scan as the mode of pre operative localization of abnormal parathyroid tissue in 100 patients in 10 years period, the total number of persistent uptake foci as reported by our department's radiologists amounted to 107, in which 87 turned out to be true positive and 20 turned out to be false positive. The total number of sites reported as normal were 393, in which 355 were true negative and 38 were false negative. *(table 1)*
As for the accuracy of MIBI scan in our study, the sensitivity, specificity, positive predictive value and negative predictive value were 69.9%, 94.7%, 81.3% and 90.3% respectively. (table 3)

As for SPECT/CT scan in the second group of 21 patients in 25 months period, the total number of persistent uptake foci as reported by our department's radiologists amounted to 23, in which 21 turned out to be true positive and 2 turned out to be false positive. The total number of sites reported as normal were 82, in which 81 were true negative and 1 was false negative. (table 2)

As for the accuracy of SPECT/CT scan in our study, the sensitivity, specificity, positive predictive value and negative predictive value were 95.5%, 97.6%, 91.3% and 98.8%. (table 3)

Comparison of the accuracies of MIBI scan and SPECT/CT scan were also done by looking at their respectively area under the ROC curve. (figure 8, 9) For MIBI scan, the area under curve, standard error and 95% confidence interval calculated were 0.821, 0.0215 and 0.785-0.854 respectively; while that for SPECT/CT scan were 0.950, 0.060 and 0.890-0.983 respectively. The P value was less and 0.001 and it was proved to be of statistical significance. (table 4)

As mentioned before, the MIBI scan had 38 sites of false negative and 20 sites of false positive. For the false negative, these included 15 sites of adenoma, 17 sites of hyperplasia and 5 sites with abnormal parathyroid tissue that could not be further classified into subtypes. For the false positive, these included 8 sites that were in patient diagnosed with adenoma, 5 sites in patient with hyperplasia, 5 sites in patient with abnormal parathyroid tissue and 1 site in patient with parathyroid cancer. (table 5)

As for SPECT/CT scan, there was 1 site of false negative that turned out to be hyperplasia. For the 2 sites of false positive, these included 1 site that was in patient diagnosed with adenoma and the other with hyperparathyroidism but uncertain cause. (table 5)

<table>
<thead>
<tr>
<th>Pathological Positive</th>
<th>Reported Positive</th>
<th>13+32+10+32+0=87</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Negative</td>
<td>1+7+3+8+1=20</td>
<td>77+55+73+53+97=355</td>
</tr>
</tbody>
</table>

Table 1. True positive, false positive, true negative and false negative results of MIBI scan (a+b+c+d+e=f) = (Lt sup + Lt inf + Rt sup + Rt inf + Ect = Total)
### Table 2. True positive, false positive, true negative and false negative results of SPECT/CT scan ($a+b+c+d+e=f$) = ($Lt\ sup + Lt\ inf + Rt\ sup + Rt\ inf + Ect$ = Total)

<table>
<thead>
<tr>
<th></th>
<th>Reported Positive</th>
<th>Reported Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathological Positive</td>
<td>$4+8+0+9+0=21$</td>
<td>$0+0+0+0+1=1$</td>
</tr>
<tr>
<td>Pathological Negative</td>
<td>$0+1+0+1+0=2$</td>
<td>$17+12+21+11+20=81$</td>
</tr>
</tbody>
</table>

### Table 3. Comparison of accuracy of MIBI scan and SPECT/CT with reference to their sensitivities, specificities, positive predictive values and negative predictive values

<table>
<thead>
<tr>
<th></th>
<th>MIBI</th>
<th>SPECT/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>69.6%</td>
<td>95.5%</td>
</tr>
<tr>
<td>Specificity</td>
<td>94.9%</td>
<td>97.6%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>81.3%</td>
<td>91.3%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>90.3%</td>
<td>98.8%</td>
</tr>
</tbody>
</table>

### Table 4. Comparison of the AUC of MIBI scan and SPECT/CT scan

<table>
<thead>
<tr>
<th></th>
<th>MIBI scan</th>
<th>SPECT/CT scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.821</td>
<td>0.950</td>
</tr>
<tr>
<td>Standard error</td>
<td>0.0215</td>
<td>0.0306</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>0.785-0.854</td>
<td>0.890-0.983</td>
</tr>
<tr>
<td>Z statistic</td>
<td>14.977</td>
<td>14.696</td>
</tr>
</tbody>
</table>

### Table 5. Comparison of false negative and positive results of MIBI scan and SPECT/CT scan

<table>
<thead>
<tr>
<th></th>
<th>MIBI scan</th>
<th>SPECT/CT scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>False negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>17</td>
<td>1</td>
</tr>
<tr>
<td>Nonspecific</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>False positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Nonspecific</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>2</td>
</tr>
</tbody>
</table>
Table 5. Comparison of the sites of false negative and positive in MIBI scan and SPECT/CT scan

Images for this section:

Fig. 1: A 44 year old woman presented with peptic ulcer. She was found to have elevated parathyroid hormone and calcium level and diagnosed with primary hyperparathyroidism. Left: Anterior view obtained 10 minutes post injection showing focal increase uptake at the lower pole of right thyroid lobe; Right: Anterior view obtained 3 hours post injection showing delayed washout of uptake; Pathology: parathyroid adenoma
Fig. 2: A 51 year old woman with known history of end stage renal failure, was found to have persistently elevated parathyroid hormone (170pmol/L) and calcium levels. Left: Anterior view obtained 10 minutes post injection showing focal increase uptake at the upper pole of right thyroid lobe and lower pole of left thyroid lobe; Right: Anterior view obtained 3 hours post injection showing delayed washout of uptake; Pathology: parathyroid adenoma
Fig. 3: A 59 year old female presented with fractured right big toe. Blood results were suggestive of primary hyperparathyroidism. Left: Anterior view obtained 10 minutes post injection showing focal increase uptake at the lower pole of left thyroid lobe; Right: Anterior view obtained 3 hours post injection showing delayed washout of uptake; Pathology: parathyroid neoplasm
Fig. 4: A 58 year old female presented with goiter. Blood results showed elevated parathyroid hormone and calcium levels. Left: Anterior view obtained 10 minutes post injection showing increase uptake overlying the left thyroid lobe; Right: Right anterior oblique view obtained 3 hours post injection showing no persistent uptake; Pathology: reactive lymphadenopathy
Fig. 5: A patient with unexplained hyperparathyroidism. Left lower: The delayed image of the MIBI scan showed persistent uptake at the left superior pole. Right upper: Corresponding plain axial CT images showed a round hypodense lesion at the left superior pole. Right lower: Superimposed MIBI and CT images showed that the functional and structural abnormalities corresponded to each other.
Fig. 6: Same patient as above. Third and forth images from the left: reconstructed sagittal and coronal images from the plain CT scan superimposed with SPECT images of the delayed phase of the MIBI scan: Hypodense round lesion with persistent uptake at the left superior pole. Pathology: parathyroid adenoma
**Fig. 7:** A patient with elevated serum parathyroid hormone and calcium. Left lower: The delayed image of the MIBI scan showed persistent uptake at the left inferior pole. Right upper: Corresponding plain axial CT images showed a round hypodense lesion at the left inferior pole. Right lower: Superimposed MIBI and CT images showed that the functional and structural abnormalities corresponded to each other. Pathology: parathyroid adenoma
**Fig. 8:** ROC curve of MIBI scan
Fig. 9: ROC curve of SPECT/CT
**Conclusion**

From our study, the accuracy of the SPECT/CT scan for preoperative localization of abnormal parathyroid tissue in patients with hyperparathyroidism showed statistical significance compared with that of MIBI scan. Based on these findings, we conclude that SPECT/CT scan should be the first line of investigation for patients with hyperparathyroidism requiring surgery, in contrary to some of the published studies.

**Personal Information**

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