Sestamibi Scans Are Not All Created Equally

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Hypothesis: The sensitivity of sestamibi scanning techniques used for preoperative localization in primary hyperparathyroidism is a function of the parameters of image acquisition and processing.

Design: Criterion standard vs optimized technique.

Setting: Tertiary referral center.

Patients: One hundred forty-eight consecutive patients with primary hyperparathyroidism were analyzed. Under the initial protocol, 97 patients underwent a preexisting standard sestamibi–single-photon emission computed tomographic scan and surgical exploration. The scanning technique was modified and in the revised protocol, 51 patients underwent imaging and surgical exploration.

Intervention: Image acquisition and processing revisions as follows: patient positioning standardized, collimator resolution adjusted, radioactive tracer delay extended, visualization field broadened, data extraction refined, and image processing filter modified.

Main Outcome Measure: Concordance among the scan and operative localization, lateralization, and cure rate.

Results: Initial protocol: 97 patients underwent surgery for primary hyperparathyroidism with the initial sestamibi design. Eighty-one patients (83%) had a positive result, that is, at least 1 gland was identified; 77 patients (79%) had correct lateralization; and 49 patients (51%) had precise localization. Revised protocol: 51 patients underwent imaging under the optimized protocol. Forty-nine patients (96%) had a positive result; 47 patients (92%) had correct lateralization; and 36 patients (70%) had precise localization. These improvements were significant, with \( P < .05 \) for localization and \( P < .01 \) for lateralization. Cure rates were 96% in both groups, confirmed by laboratory and pathologic findings.

Conclusions: Sestamibi optimization in primary hyperparathyroidism can improve scan sensitivity. This may permit a focused minimally invasive operation.

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Primary hyperparathyroidism (HPTH) is a disorder of calcium metabolism caused by excess secretion of parathyroid hormone (PTH). In 80% of cases, the cause of the HPTH is a solitary adenoma, for which surgical resection is the treatment of choice.\(^1,2\) Resection of parathyroid adenomas has historically involved surgical exploration of the cervical neck bilaterally conducted with the patient under general anesthesia, with cure rates by experienced surgeons reported from 95% to 98%.\(^3,5\)

Surgery for primary HPTH has recently undergone a dramatic change with the introduction of minimally invasive techniques, which are driven by the following objectives: minimize the length of the incision, decrease the duration of the procedure, and permit the use of a regional anesthetic. These objectives have financial justification as well as improving the parameters of patient care. Minimally invasive parathyroidectomy (MIP) is the procedure of choice for primary HPTH in most endocrine surgical units worldwide.

The MIP procedure is predicated on preoperative localization of a lesion, thereby permitting a focused operative plan. Nuclear medicine scans have provided the best localizations, and among them the delayed technetium Tc 99m sestamibi–single-photon emission computed tomographic (sestamibi-SPECT) scan has been shown to be more sensitive than double-tracer thallium 201 chloride, \(^{99m}\)Tc pertechnetate, or iodine I 123 subtraction scanning.\(^12-15\) Accurate lateralization correctly indicates the ipsilateral side of the neck where the parathyroid adenoma is found; correct localization provides precise anatomical information thereby optimizing the operative plan. An incorrect or ambiguous scan may force the
primary HPTH, with a range reported from 43% to 91%.17 There can be variation in localization sensitivity for specific localization of choice. However, among sestamibi HPTH. This has been corroborated over the past decade in the preoperative workup of patients with primary parathyroid adenomas in patients who undergo initial or remedial surgical exploration. This work demonstrated the use of 2 sestamibi-SPECT protocols is described.

**Table 1. Comparison of Image Acquisition Parameters**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Initial Protocol</th>
<th>Revised Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delay after injection, h</td>
<td>2</td>
<td>1½</td>
</tr>
<tr>
<td>Gamma camera Collimator</td>
<td>IRIX 3 head</td>
<td>IRIX 3-head*</td>
</tr>
<tr>
<td></td>
<td>Low-energy, ultra high-resolution, parallel hole</td>
<td>Low-energy, high-resolution, parallel hole</td>
</tr>
<tr>
<td>Image matrix size, pixels</td>
<td>64×64</td>
<td>128×128</td>
</tr>
<tr>
<td>Projection time, s</td>
<td>45</td>
<td>30</td>
</tr>
<tr>
<td>Step rotation, No./step</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Mode</td>
<td>Continuous</td>
<td>Step-and-shoot</td>
</tr>
</tbody>
</table>

*The 3-head multidetector IRIX is manufactured by Royal Philips, Amsterdam, the Netherlands.

The injection of a standard dose (20 mCi) of the radioactive tracer was followed by a 2-hour delay prior to image acquisition. Data for tomographic images of the neck and chest were obtained with a 3-head multidetector IRIX (Royal Philips, Amsterdam, the Netherlands) gamma camera, equipped with a low-energy, ultra high-resolution, parallel hole collimator. The 64×64-pixel image matrix size was acquired 3 per step for 45 seconds per projection in continuous mode. The images were available both on a computer workstation, with image display options, as well as in hardcopy form, reviewed by the surgeon prior to the procedure.

**PATIENT POPULATION**

From September 11, 2001, to October 14, 2003, 148 consecutive patients with biochemical evidence of primary HPTH underwent preoperative sestamibi-SPECT at our institution and then underwent surgical exploration by an endocrine surgeon (R.U.). The sestamibi scan protocol was modified in March 2003. Ninety-seven patients had a sestamibi scan at our institution prior to this date and 51 were scanned and then underwent surgical exploration between March 12, 2003, and October 14, 2003. Each of these patients had unequivocal evidence of primary HPTH, demonstrated by a quantitative elevation of their serum calcium concentration and an elevated or inappropriate intact PTH level.

**DATA ACQUISITION AND PROCESSING**

**Initial Protocol**

The delay after injection of radioactive tracer was decreased to ½ hours; the washout of signal with a delay of 2 hours appeared excessive and, thus, the decrease in delay time improved the signal-to-noise ratio. Data for computed tomograms were obtained with the same 3-head multidetector IRIX gamma camera, only now equipped with a low-energy, high-resolution, parallel hole collimator that which permits collection of more counts. The ultrahigh resolution used in the initial protocol appropriately blocked nonparallel photons, but it also blocked useful signal, and so the use of the high-resolution collimator can improve capture of the relevant photons. The image matrix size was increased to 128×128 pixels, acquired 3 per step, for 30 seconds per projection in step-and-shoot mode. The larger size image permits inclusion of areas of interest in the mediastinum. Increased count rates from the shorter delay after tracer injection correspondingly require a shorter projection time, and this results in less patient motion artifact. Finally, the change from a continuous to step-and-shoot mode also minimizes motion artifact. Image acquisition parameters under the initial and revised protocols are summarized in **Table 1**. There was only 1 change in the postacquisition image-processing phase, namely, the transverse sections were generated with a Hamming filter with a 0.4-cycle/cm filter. No changes were made to the precision of oblique reformat or to the attenuation correction.

One hundred forty-eight consecutive sestamibi-SPECT parathyroid localization scans were retrieved, processed, and re-evaluated by the nuclear medicine service that was blinded to the clinical, laboratory, surgical, and pathological information. These films were then reviewed again in a blind fashion by a single, experienced nuclear imaging expert (D.C.). Images were available both on a computer workstation, with image display options, as well as in hardcopy form, reviewed by the surgeon prior to the procedure.

**Revised Protocol**

The delay after injection of radioactive tracer was decreased to ½ hours; the washout of signal with a delay of 2 hours appeared excessive and, thus, the decrease in delay time improved the signal-to-noise ratio. Data for computed tomograms were obtained with the same 3-head multidetector IRIX gamma camera, only now equipped with a low-energy, high-resolution, parallel hole collimator that which permits collection of more counts. The ultrahigh resolution used in the initial protocol appropriately blocked nonparallel photons, but it also blocked useful signal, and so the use of the high-resolution collimator can improve capture of the relevant photons. The image matrix size was increased to 128×128 pixels, acquired 3 per step, for 30 seconds per projection in step-and-shoot mode. The larger size image permits inclusion of areas of interest in the mediastinum. Increased count rates from the shorter delay after tracer injection correspondingly require a shorter projection time, and this results in less patient motion artifact. Finally, the change from a continuous to step-and-shoot mode also minimizes motion artifact. Image acquisition parameters under the initial and revised protocols are summarized in **Table 1**. There was only 1 change in the postacquisition image-processing phase, namely, the transverse sections were generated with a Hamming filter with a 0.4-cycle/cm filter. No changes were made to the precision of oblique reformat or to the attenuation correction.

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**Scan Interpretations**

A focal area of increased 99mTc uptake in the thyroid bed, neck, or mediastinum seen on planar or SPECT images was defined as a positive sestamibi-SPECT study for localization of a parathyroid adenoma; if no such area is identified, the scan is reported as negative. Given a positive sestamibi-SPECT scan, the location of increased uptake was described as either on the right or on the left side, and either in an upper or a lower position, corresponding to the 4 quadrants of typical parathyroid locations. In the case of uncertainty about whether the gland is in the upper or lower position, the lesion is simply identified by which side it is on. Additional information is available about the anterior or posterior planes. Full 3-dimensional localization of the lesion is a great asset to operative resection. At the conclusion of a given operation, the locations of all identified parathyroid glands are recorded both in a diagram by the surgeon and as a code that corresponds to the quadrants used in the designating lesions preoperatively, for example, both the scan and the operative findings may indicate that the lesions were found in the right upper quadrant. The correlation between the scintigraphic finding and the operative results can be in terms of either precise localization, in which specific quadrant is correct, or correct lateralization whereby the correct side...
of the neck is indicated on the preoperative scan. Sensitivity of the scan is expressed in terms of its ability to localize or lateralize the lesion. Surgical success is determined by normalization of postoperative calcium levels.

STATISTICAL ANALYSIS

The ability of the sestamibi-SPECT scan to demonstrate focal radiotracer uptake (a positive result) and then to correctly localize and lateralize the parathyroid lesion is determined under each protocol. The χ^2 goodness-of-fit test using P < .05 was used to determine if the improvement shown for positive sestamibi-SPECT scans as well as in the localization and lateralization of the revised protocol was statistically significant.

RESULTS

Data are expressed as mean±SEM. Under the initial protocol 97 patients with primary HPTH underwent a sestamibi-SPECT scan. A representative scan is shown in Figure 1. Of these 97 patients, 75 were women and 22 were men, with a mean age of 57.0±3.3 years. At presentation, the mean serum calcium concentration was 11.4±0.1 mg/dL (reference range, 8.8-10.2 mg/dL) falling to 9.4±0.4 mg/dL postoperatively. Similarly, the preoperative intact serum PTH value was 143.0±10.1 pg/dL (reference range, 12-72 pg/mL) and ranged from 48 to 865 pg/mL, and it fell to 40.7±3.5 pg/mL. Of this group of 97 patients, 93 (96%) were cured with respect to biochemical markers.

Fifty-one patients (43 women and 8 men), with a mean age of 55.4±4.2 years, underwent the revised protocol. Representative SPECT images are shown in Figure 2A and B, with the corresponding operative results shown in Figure 2C. These patients had a mean preoperative serum calcium level of 11.4±0.1 mg/dL and an intact PTH level of 119.5±10.2 pg/mL. Postoperatively, these values were 9.4±0.6 mg/dL for the calcium concentration, and a correspondingly normalized PTH level of 25.5±2.10 pg/mL. Forty-nine (96%) of the 51 patients were cured.

The proportion of patients undergoing MIP was similar under the initial protocol, 69 patients (71%), and under the revised protocol, 35 patients (67%), while there were slightly more patients undergoing a remedial cervical surgical exploration in the initial protocol group: 11 (11%) vs 2 (4%) in the revised protocol group. Thirteen patients (13%) in the first group underwent bilat-
eral cervical surgical exploration while 10 patients (20%) in the second group did so. In the first group, there were 4 (4%) conversions from the MIP procedure to full cervical surgical exploration and 4 (7%) in the second group.

Eighty-one patients (84%) scanned under the initial protocol had a positive sestamibi-SPECT result, that is, at least 1 gland was identified. Seventy-six patients (78%) had correct lateralization; 48 patients (49% of the original 97 patients) had precise localization. Of the 51 patients who underwent surgical exploration under the revised protocol, 49 patients (96%) had a positive result, 46 patients (92%) correctly lateralized, and 35 patients (69% of the original 51 patients) had precise localization. These improvements are statistically significant (Table 2).

Under the initial protocol, there were 28 patients (29%) who did not localize correctly but did lateralize correctly. From this group, 16 instances (57%) were due to upper glands residing in posteroinferior positions that were interpreted as lower quadrant adenomas. Because of the improvement in localization, only 11 patients (22%) scanned under the revised protocol lateralized without correct localization. Of these 11 patients, 9 (82%) did not have precise localization because of posteroinferior lesions. This indicates that given correct lateralization, the ability to embed the image within a more refined grid may result in improved localization.

Nuclear medicine researchers are concurrently investigating the acquisition and processing parameters of sestamibi-SPECT scans, focused on image quality without further comment on clinical context. O’Doherty and Kettle identified the type of collimator and the use of a subtraction vs delayed-imaging/dual-phase technique as areas of investigation. They concluded that for the neck a subtraction technique using a pinhole collimator and for the mediastinum a parallel hole collimator is optimal.

Improvement in sestamibi-SPECT scan sensitivity can be accomplished by meticulous attention to the technical aspects of scan acquisition, processing, and interpretation. In addition to the technical considerations, we found that a close interaction between the surgeon and nuclear medicine physician is essential. We acquire our images in the cervical hyperextended position to capture the operative area. Furthermore, our nuclear medicine physicians understand the embryonic variation of parathyroid anatomy where a gland located posteriorly in the inferior aspect of the neck or mediastinum represents an ectopic upper gland.

**CONCLUSION**

Sestamibi-SPECT is an important component of preoperative localization in patients with primary HPTH and enhances the ability to perform cost-effective MIP. Optimization of the imaging protocol can markedly improve scan sensitivity. Surgical experience can compensate for suboptimal scans; however, the operative plan is altered and minimally invasive potential is compromised.

**REFERENCES**


**COMMENT**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive Images</th>
<th>Lateralized</th>
<th>Localized</th>
<th>Cure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial protocol, % (N = 97)</td>
<td>84</td>
<td>78</td>
<td>49</td>
<td>96</td>
</tr>
<tr>
<td>Revised protocol, % (N = 51)</td>
<td>96</td>
<td>92</td>
<td>69</td>
<td>96</td>
</tr>
</tbody>
</table>

*Percentages are for the total population under each protocol.

Table 2. Comparison of Sestamibi Results Under the Initial Protocol and the Revised Image Acquisition and Processing Protocol*

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