Impact of Localization Studies and Clinical Scenario in Patients With Hyperparathyroidism Being Evaluated for Reoperative Neck Surgery

Joyce J. Shin, MD; Mira Milas, MD; Jamie Mitchell, MD; Eren Berber, MD; Louis Ross, BS; Allan Siperstein, MD

Background: Previous studies have focused on the success of localization studies (LSs) in patients undergoing reoperative parathyroid surgery; however, patients who did not undergo reexploration surgery have been excluded from analysis. In addition, the concept of whether clinical scenario (CS) suggests single- vs multiple-gland disease in reoperative strategy is often underemphasized.

Objective: To evaluate how LSs and CS direct operative strategy in patients being considered for reexploration.

Design: Retrospective review of a prospective database.

Setting: Tertiary referral center.

Patients: Two hundred three patients with hyperparathyroidism who underwent previous neck surgery. The CS stratified patients as candidates for single- or multiple-site exploration (or unknown).

Main Outcome Measure: Ability of CS and LSs to direct successful reexploration.

Results: Of 203 patients, 27 were not explored owing to nonlocalizing studies. Of the remaining 176 patients, LSs accurately guided reexploration in 85%. However, when including the 27 nonexplored patients, the success of LSs decreased to 73%. The cure rate in reoperated patients was 96% but was reduced to 83% when including nonexplored patients. Of the reoperated patients, 83% had single-site disease and 17% had multiple-site disease. The positive predictive value of LSs in predicting single- or multiple-site disease was 92% and 73%, respectively. However, when stratified by CS, the positive predictive value increased to 95% for single-site disease and to 100% for multiple-site disease.

Conclusions: Failure to cure patients was 4 times more likely to be due to nonlocalizing studies than to a failed reexploration. Stratification by CS was useful in the interpretation of LSs and in determining the most accurate reoperative approach.
disease status, stratifying the patient as having a single diseased gland or multiple diseased glands remaining in the neck and/or mediastinum. Consequently, patients who are predicted to have single-site disease (SSD) by clinical history are candidates for single-site exploration (SSE), and those who are predicted to have multiple-site disease (MSD) are candidates for multiple-site exploration (MSE). Clinical scenario (CS) can assure surgeons that the LSs correspond to their clinical expectations and is a helpful strategy in decision making for the reoperative approach. Although this clinical stratification process may be obvious and already practiced by many surgeons, it is an important concept that is often not systematically scrutinized or reported in the literature.

This study was designed to analyze our clinical strategies in the management of patients with HPT requiring reoperative neck surgery. Information provided by LSs and clinical history was applied in the stratification of patients by disease status and reoperative approach. To our knowledge, this is the first study to consider a very critical view of the success rates of LSs and reoperative parathyroid surgery by including all patients with HPT being evaluated for reoperative neck surgery in an intent-to-treat analysis, even those who were not reexplored owing to nonlocalizing studies.

### METHODS

Between May 1, 2000, and November 30, 2009, 203 patients with HPT were evaluated for reoperative neck surgery at the Cleveland Clinic (Cleveland, Ohio) by 4 endocrine surgeons (M.M., J.M., E.B., and A.S.) and studied from a prospective database. These patients had symptoms and/or associated conditions of HPT that warranted reoperation. They also had a history of neck operations involving the same surgical territory as in parathyroid exploration (previous parathyroid, thyroid, and esophageal surgical procedures). Diagnoses of primary, secondary, persistent, and recurrent HPT were confirmed. Persistent HPT was defined as hypercalcemia (serum calcium level >10.5 mg/dL [to convert to millimoles per liter, multiply by 0.25]) occurring within 6 months of parathyroidectomy, and recurrent HPT was defined as hypercalcemia recurring after at least 6 months of postoperative normocalcemia. Clinical scenario (determined by the type of HPT and findings at previous explorations) stratified patients into the following disease categories: (1) strongly suspected of having a single remaining abnormal gland, (2) strongly suspected of having multiple remaining abnormal glands, and (3) unknown (inadequate clinical information to determine clinical status). The various clinical conditions used to stratify these patients are listed in Table 1.

All 203 patients underwent surgeon-performed ultrasonography and sestamibi-iodine subtraction scan (MBI) with or without computed tomography (CT) (co-registration of single-photon emission CT with CT images performed with MBI starting in July 2005). When the results of these studies were negative or inconclusive, parathyroid fine-needle aspiration biopsy under ultrasonographic guidance, magnetic resonance imaging, CT (before the use of single-photon emission CT/CT with MBI), and/or selective venous sampling for intact parathyroid hormone (PTH) was performed. The success rates of each LS were evaluated on a per-patient basis, as previously described by Shen et al. A study was defined as completely correct if it identified all abnormal parathyroid glands in a patient with no false-positive or false-negative findings. The term correct with false-positive results was used if the LS identified all abnormal glands in a patient but also had false-positive results (imaged suspected tumors not identified at surgery). The term correct with false-negative results was used if the localization study identified all abnormal glands in a patient but also had false-negative results (additional nonimaged tumors found at exploration). Finally, a study was defined as completely incorrect if it produced the following results: (1) a completely negative study result in a patient with an abnormal gland(s), (2) a completely false-positive study result that localized all abnormal glands in incorrect positions, or (3) the localization of the abnormal gland(s) remaining unknown after reexploration. The sensitivity of LSs was defined as the proportion of studies that correctly located all abnormal parathyroid glands (completely correct and correct with false-positive results) in patients with abnormal glands.

In addition, the accuracy of these LSs in guiding the surgeon to perform an appropriate and curative exploration was assessed based on the aggregate interpretation of LSs for each patient. For this study, LSs were considered to be accurate if a focal signal led to a curative exploration and excision of only the single localized gland (completely correct) or if multifocal signals guided the surgeon to perform a curative exploration and excision of at least 2 localized glands (completely correct or correct with false-negative results). Surgical cure was determined by the assessment of serial serum calcium and PTH values at least 6 months postoperatively (range, 6 months to 9 years), in which the patient did not meet the criteria for persistent or recurrent primary HPT. After reexploration and from

### Table 1. Stratification of Disease Status and Reoperative Approach by Clinical Scenario

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>LS Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSD</td>
<td>Persistent</td>
</tr>
<tr>
<td>MSD</td>
<td>Recurrent</td>
</tr>
</tbody>
</table>

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surgically confirmed pathology laboratory findings, the positive predictive value (PPV) of disease status (SSD or MSD) derived only from the CS was analyzed. Last, the PPV of disease status based on the interpretation of LSs in the context of the patient's CS was also evaluated.

Statistical analysis was performed using a commercially available statistical software package (JMP 8.0, SAS Institute, Inc.). We determined statistical significance between the PPVs using a z score for proportions. The level of statistical significance for this study was defined as $P < .05$.

### RESULTS

Of the 203 patients, 147 were women and 56 were men (female to male ratio of 2.6 to 1). Their mean age was 58 years (age range, 21-87 years). Indications for previous cervical operations are listed in Table 2. Previous surgical procedures included parathyroid surgery in 126 patients (62.1%), parathyroid and thyroid surgery in 24 (11.8%), and nonparathyroid surgery (thyroid or esophageal) in 53 (26.1%).

For each group, the aggregate interpretation of LSs (focused as having SSD (n=145, 82.4%), MSD (n=16, 9.1%), or unknown disease status (SSD or MSD) (n=15, 8.5%). For each group, the aggregate interpretation of LSs (local or multifocal signal), surgical approach (SSE or MSE), operative success (cure, fail, or negative exploration), and surgically confirmed outcome (SSD, MSD, or no disease) were evaluated. For details, refer to the Appendix eFigures 1, 2, and 3 (http://www.archsurg.com).

We determined statistical significance between the PPVs using a z score for proportions. The level of statistical significance for this study was defined as $P < .05$.

#### Table 2. Indications for Previous Cervical Explorations

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patients, No. (N = 203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary hyperparathyroidism (HPT)</td>
<td>96</td>
</tr>
<tr>
<td>Secondary HPT</td>
<td>6</td>
</tr>
<tr>
<td>Tertiary HPT</td>
<td>9</td>
</tr>
<tr>
<td>Parathyroid cancer</td>
<td>1</td>
</tr>
<tr>
<td>Multiple endocrine neoplasia type 1</td>
<td>12</td>
</tr>
<tr>
<td>Multiple endocrine neoplasia type 2A</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid disease (benign or cancer)</td>
<td>48</td>
</tr>
<tr>
<td>Thyroid disease and primary HPT</td>
<td>22</td>
</tr>
<tr>
<td>Thyroid disease and secondary HPT</td>
<td>1</td>
</tr>
<tr>
<td>Thyroid disease and tertiary HPT</td>
<td>1</td>
</tr>
<tr>
<td>Esophageal disease</td>
<td>5</td>
</tr>
</tbody>
</table>

Of the 203 patients, 147 were women and 56 were men (female to male ratio of 2.6 to 1). Their mean age was 58 years (age range, 21-87 years). Indications for previous cervical operations are listed in Table 2. Previous surgical procedures included parathyroid surgery in 126 patients (62.1%), parathyroid and thyroid surgery in 24 (11.8%), and nonparathyroid surgery (thyroid or esophageal) in 53 (26.1%). Indications for reoperative parathyroid surgery included persistent HPT (primary, secondary, and tertiary HPT and multiple endocrine neoplasia type 1) in 110 patients (54.2%), recurrent HPT (primary, secondary, and tertiary HPT and multiple endocrine neoplasia types 1 and 2A) in 40 (19.7%), primary HPT in 52 (25.6%), and secondary HPT in 1 (0.5%). Of the 203 patients, 176 (86.7%) were candidates for reexploration due to concordance on 2 LSs (n=165, 93.8%), localization by only selective venous sampling when all other study results were negative (n=6, 3.4%), or localization by only 1 study when also undergoing thyroid surgery (n=5, 2.8%). On the other hand, 27 patients (13.3%) did not meet the criteria for reexploration due to nonlocalizing studies. Of the 176 reoperative candidates, localization by only ultrasonogram and MIBI (with or without co-registration of CT images) was achieved in 63 patients (35.8%). Thirty-seven patients (21.0%) required fine-needle aspiration biopsy as the only additional preoperative study, and 46 (26.1%) needed other noninvasive imaging modalities (CT and/or magnetic resonance imaging) with or without fine-needle aspiration biopsy. Magnetic resonance imaging was used more frequently in the earlier years of this study and is now rarely used owing to its low sensitivity, and CT alone without MIBI was performed before July 2005. Thirty patients (17.0%) underwent selective venous sampling for PTH. A total of 517 LSs were performed in these reoperative candidates. The success rates of LSs analyzed individually are demonstrated in Table 3.

For the 176 reoperative candidates, their CSs as previously described were reviewed, and they were stratified as having SSD (n=145, 82.4%), MSD (n=16, 9.1%), or unknown disease status (SSD or MSD) (n=15, 8.5%). For each group, the aggregate interpretation of LSs (local or multifocal signal), surgical approach (SSE or MSE), operative success (cure, fail, or negative exploration), and surgically confirmed outcome (SSD, MSD, or no disease) were evaluated. For details, refer to the Appendix eFigures 1, 2, and 3 (http://www.archsurg.com).

For each group, the aggregate interpretation of LSs (local or multifocal signal), surgical approach (SSE or MSE), operative success (cure, fail, or negative exploration), and surgically confirmed outcome (SSD, MSD, or no disease) were evaluated. For details, refer to the Appendix eFigures 1, 2, and 3 (http://www.archsurg.com).

Surgically confirmed outcomes of HPT in reoperative neck surgery in 176 patients who were candidates for reexploration were as follows: SSD removed in 144 cured patients (81.8%), MSD excised in 25 cured patients (14.2%), SSD removed in 4 failed patients (2.3%), and no disease found in 3 patients (1.7%).

The SSE group achieved cure by removing 90% SSD and 6% MSD (with the last 4% representing 3 failures and 3 negative explorations), the MSE group achieved cure by excising 19% SSD and 81% MSD, and the unknown disease status group achieved cure by removing 67% SSD and 27% MSD (with the last 6% representing 1 failure). The LSs accurately guided reexploration (either SSE or MSE) in 84.7% of patients (149 of 176), consisting of 88% in the SSE group, 75% in the MSE group, and 67% in the unknown disease status group. However, when including the 27 patients who were not reexplored owing to nonlocalizing studies, the success of LSs to direct reexploration was decreased to 73%. The cure rate in reoperated patients was 96% (3 negative explorations and 4 persistent disease). When including the 27 nonexplored patients, the overall cure rate of the entire cohort was reduced to 83%.

The PPV of disease status derived only from the CS was then evaluated. When patients were strongly suspected of having a single remaining abnormal gland and, therefore, were candidates for SSE based on CS alone, 92.3% (131 of 142) had surgically confirmed SSD and 7.7% (11 of 142) had MSD. Conversely, when patients were strongly suspected of having multiple remaining abnormal glands and, therefore, were candidates for MSE based on the CS alone, 81.3% (13 of 16) had surgically confirmed SSD and 18.8% (3 of 16) had MSD. Therefore, when patients were stratified by CS, 92% actually had SSD (increased from 83%, $P = .008$) and 81% actually had MSD (increased from 17%, $P < .001$). Although the stratification process could not be applied in the group with unknown or unclear history, 66.7% (10 of 15) had surgically confirmed SSD, and 33.3% (5 of 15) had MSD.

The PPV of disease status from the interpretation of LSs in the context of the patient’s CS was then analyzed (Table 5). From the entire cohort with a focal signal on LSs, 91.8% of patients (135 of 147) were found to have SSD based on completely correct LSs alone. However, when an accurate focal signal was seen in the SSE
group, 95.3% of patients (123 of 129) had surgically confirmed SSD. When a focal signal was seen in the MSE group, 60.0% of patients (3 of 5) had SSD. Lastly, when a focal signal was seen in the group with unknown disease status, 69.2% of patients (9 of 13) actually had SSD.

On the other hand, from the entire cohort with multifocal signals on LSs, 73.1% (19 of 26) were found to have MSD based on LSs alone (completely correct or correct with false-negative results). However, when accurate multifocal signals were seen in the SSE group, 53.8% of patients (7 of 13) had surgically confirmed SSD. When multifocal signals were seen in the MSE group, 100% of patients (11 of 11) had MSD. Lastly, when multifocal signals were seen in the group with unknown disease status, 50.0% of patients (1 of 2) actually had MSD. From this analysis, we can conclude that a focal signal on LSs has a PPV for SSD of 92%. However, if the patient can be stratified by CS to have SSD, the PPV of the focal signal on LSs is increased to 95% (P = .12). Conversely, multifocal signals on LSs have a PPV for MSD of 73%. However, if the patient can be stratified by CS to have MSD, the PPV of the LSs is increased to 100% (P = .03). Although the PPV of disease status improved for both groups, it was statistically significant only for the MSE group, supporting previous studies12-14 that have shown LSs to be superior at detecting single adenomas vs multigland disease.

Thirty-four of 176 patients (19.3%) had more extensive exploration than indicated by LSs due to concomitant thyroid surgery (29 in the SSE group and 5 in the unknown disease status group). However, for this study, patients were considered to have SSE if a completely correct focal signal on LSs guided the surgeon to explore only the index site, and, therefore, the concomitant thyroid surgery would not have changed the surgical approach. Only 3 of 34 patients were considered to have MSE due to completely or partially incorrect LSs that led the surgeon to explore other nonlocalized sites, even if no thyroidectomy was being performed.

Table 3. Success Rates of Localization Studies Analyzed Individually in 176 Reoperated Patients

<table>
<thead>
<tr>
<th>Resultsa</th>
<th>Ultrasound (n = 176)</th>
<th>MIBI (n = 103)</th>
<th>MIBI + CT (n = 73)</th>
<th>FNAB (n = 62)</th>
<th>MRI (n = 53)</th>
<th>CT (n = 20)</th>
<th>SVS (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely correct, No.</td>
<td>119</td>
<td>69</td>
<td>56</td>
<td>57</td>
<td>18</td>
<td>9</td>
<td>24</td>
</tr>
<tr>
<td>Correct + FP, No.</td>
<td>2</td>
<td>7</td>
<td>70</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Correct + FN, No.</td>
<td>11</td>
<td>7</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Completely incorrect, No.</td>
<td>44</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>32</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Sensitivity, %b</td>
<td>69</td>
<td>74</td>
<td>86</td>
<td>92</td>
<td>34</td>
<td>45</td>
<td>87</td>
</tr>
</tbody>
</table>

Abbreviations: CT, computed tomography; FN, false-negative results; FNAB, fine-needle aspiration biopsy; FP, false-positive results; MIBI, sestamibi-iodine subtraction scan; MIBI + CT, MIBI with co-registration of CT; MRI, magnetic resonance imaging; SVS, selective venous sampling. 

See the “Methods” section of the text for definitions.

b Sensitivity was calculated as (completely correct + correct with FP) / total.

Table 4. Surgically Confirmed Disease Status When Stratified by Clinical Scenario

<table>
<thead>
<tr>
<th>Disease Status</th>
<th>Total, No. (%) (n = 173)</th>
<th>Candidate for SSE, No. (%) (n = 142)a</th>
<th>Candidate for MSE, No. (%) (n = 16)</th>
<th>Unknown Disease Status, No. (%) (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgically confirmed SSD</td>
<td>144 (83)</td>
<td>131 (92)</td>
<td>3 (19)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Surgically confirmed MSD</td>
<td>29 (17)</td>
<td>11 (8)</td>
<td>13 (81)</td>
<td>5 (33)</td>
</tr>
</tbody>
</table>

Abbreviations: MSD, multiple-site disease; MSE, multiple-site exploration; SSD, single-site disease; SSE, single-site exploration.
a Excluding 3 negative explorations.

Table 5. Accuracy of Disease Status Based on the Interpretation of Localization Studies in Context of the Clinical Scenario

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total, No. (%) (n = 173)</th>
<th>Candidate for SSE (n = 142)d</th>
<th>Candidate for MSE (n = 16)</th>
<th>Unknown Disease Status (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy of focal signal on LSs in predicting SSDb</td>
<td>135/147 (92)</td>
<td>123/129 (95)</td>
<td>3/5 (60)</td>
<td>9/13 (69)</td>
</tr>
<tr>
<td>Accuracy of multifocal signals on LSs in predicting MSDc</td>
<td>19/26 (73)</td>
<td>7/13 (54)</td>
<td>11/11 (100)</td>
<td>1/2 (50)</td>
</tr>
</tbody>
</table>

Abbreviations: LSs, localization studies; MSD, multiple-site disease; MSE, multiple-site exploration; SSD, single-site disease; SSE, single-site exploration. 

b No. of patients with SSD/No. of patients with focal signal on LSs. 

c No. of patients with MSD/No. of patients with multifocal signals on LSs. 

d Excluding 3 negative explorations.
patients, where the Miami criterion15 (an intraoperative PTH decline ≥50% from the highest of either the preincision or preexcision level 10 minutes after gland excision) was met in 110 patients (64.3%) but was not satisfied in 10 (5.8%). In patients with multiple abnormal glands removed, operative cure was achieved in 28, where the Miami criterion was met in 26 patients (15.2%) but was not satisfied in 2 (1.2%). In 11 patients, the preincision or preexcision value was within the reference range and decreased at least 50% after gland excision in 8 patients (4.7%) but fell less than 50% after gland excision in 3 (1.8%). Of the remaining 12 patients, intraoperative PTH measurements were not interpretable in 6 (3.5%), 3 (1.8%) failed postoperatively (2 met the Miami criterion and 1 did not), and 3 (1.8%) had negative explorations and did not meet the Miami criterion. Overall, the Miami criterion correctly predicted postoperative cure in 144 of 159 interpretable intraoperative PTH values (90.6%).

From this cohort, 220 parathyroid specimens were excised in 173 patients (excluding 3 negative explorations). As shown in the Figure, 136 parathyroid glands (61.8%) were located in their normal anatomical positions (24 left lower, 43 left upper, 24 right lower, and 45 right upper). Of the remaining 84 ectopic parathyroid specimens (38.2%), 15 were previously autotransplanted parathyroid tissue in the sternocleidomastoid or strap muscles, and the most common ectopic location was intrathymic (Table 6).

### Table 6. Anatomical Locations of 84 Ectopic Parathyroid Specimens

<table>
<thead>
<tr>
<th>Location</th>
<th>Ectopic Parathyroid Glands, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrathympic</td>
<td></td>
</tr>
<tr>
<td>RL thymus</td>
<td>8</td>
</tr>
<tr>
<td>LL thymus</td>
<td>8</td>
</tr>
<tr>
<td>Superiormost aspect of RL thyrothymic ligament</td>
<td>2</td>
</tr>
<tr>
<td>Superiormost aspect of LL thyrothymic ligament</td>
<td>2</td>
</tr>
<tr>
<td>Descended</td>
<td></td>
</tr>
<tr>
<td>RU</td>
<td>5</td>
</tr>
<tr>
<td>LU</td>
<td>3</td>
</tr>
<tr>
<td>LU and within tracheoesophageal groove</td>
<td>2</td>
</tr>
<tr>
<td>LU and retroesophageal</td>
<td>1</td>
</tr>
<tr>
<td>Undescended</td>
<td></td>
</tr>
<tr>
<td>LU</td>
<td>2</td>
</tr>
<tr>
<td>RU</td>
<td>2</td>
</tr>
<tr>
<td>LU and retroesophageal</td>
<td>1</td>
</tr>
<tr>
<td>LU and within carotid sheath</td>
<td>1</td>
</tr>
<tr>
<td>RU and within carotid sheath</td>
<td>1</td>
</tr>
<tr>
<td>Infrathympid</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>5</td>
</tr>
<tr>
<td>Right</td>
<td>3</td>
</tr>
<tr>
<td>Carotid sheath</td>
<td>7</td>
</tr>
<tr>
<td>LL</td>
<td>4</td>
</tr>
<tr>
<td>LU</td>
<td>2</td>
</tr>
<tr>
<td>RU</td>
<td>1</td>
</tr>
<tr>
<td>Esophageal</td>
<td></td>
</tr>
<tr>
<td>LU paraesophageal</td>
<td>2</td>
</tr>
<tr>
<td>RU retroesophageal</td>
<td>3</td>
</tr>
<tr>
<td>RL retroesophageal</td>
<td>1</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>10</td>
</tr>
<tr>
<td>Right ventricular outflow tract</td>
<td>1</td>
</tr>
<tr>
<td>Adjacent to brachiocephalic artery</td>
<td>1</td>
</tr>
<tr>
<td>Aortic arch</td>
<td>3</td>
</tr>
<tr>
<td>Anterior mediastinum and within thymus</td>
<td>2</td>
</tr>
<tr>
<td>Posterior mediastinum</td>
<td>3</td>
</tr>
<tr>
<td>Autotransplants</td>
<td>15</td>
</tr>
<tr>
<td>Left sternocleidomastoid muscle</td>
<td>9</td>
</tr>
<tr>
<td>Right sternocleidomastoid muscle</td>
<td>3</td>
</tr>
<tr>
<td>Left strap muscle</td>
<td>2</td>
</tr>
<tr>
<td>Right strap muscle</td>
<td>1</td>
</tr>
</tbody>
</table>

Abbreviations: LL, left lower; LU, left upper; RL, right lower; RU, right upper.

Reoperative neck surgery for HPT in patients with previous cervical explorations can pose diagnostic and technical difficulties.1-6,8,9,10-21 With the higher risk of morbidity, surgeons need to rely heavily on the patient’s clinical history and LSs to perform curative reexploration. When sufficient data can be obtained from both clinical information and imaging studies, reoperative parathyroid surgery can have success rates that are comparable with those of initial parathyroidectomy.4,5,8,10 However, most of the recognition has been given to the success of LSs, whereas the wealth of data that can be gained from the clinical history has not been as well acknowledged. In addition, previous studies1-10 in the literature have not analyzed patients in whom the LSs are unable to local-

![Figure](http://archsurg.jamanetwork.com/pdfaccess.ashx?url=/data/journals/surg/22575/)

**Figure.** Distribution of 220 parathyroid specimens: 136 parathyroid glands (61.8%) located in their normal anatomical positions and 84 ectopic parathyroid glands (38.2%). Reprinted with permission from Cleveland Clinic Center for Medical Art & Photography 2011. All rights reserved.
ize the abnormal gland(s), and, therefore, only report the success of LSs in those who actually undergo reopera-
tive parathyroid surgery. In this study, we took an intent-
to-treat approach by evaluating all patients presenting for
reoperative neck surgery. The ability of LSs to accu-
rately direct reexploration was 85% in those who met the
criteria for reexploration; however, it was decreased to
73% when including those who never underwent reex-
ploration. Similar to other series, the present cure rate in
reoperated patients was 96%; however, 27 nonex-
plorated patients remain with disease, thereby reducing the
overall cure rate to 83%. In conclusion, the failure to cure
patients with HPT and previous neck surgery was 4 times
more likely to be due to nonlocalizing studies than to a
failed reexploration.

One of the aims of this study was to emphasize the
importance of clinical history in this patient popula-
tion. From the entire cohort of patients who were reex-
plored and in whom pathologic abnormalities were found,
83% had SSD and 17% had MSD. However, by applying
CS to the stratification of disease status, the likelihood of
actually having either a single or multiple remaining
abnormal glands was improved (from 83% to 92% in the
SSE group and from 17% to 81% in the MSE group). Fur-
thermore, the PPV of the disease status based on LSs also
increased when a patient was stratified as having either
a single or multiple remaining abnormal glands (from 92%
95% in the SSE group and from 73% to 100% in the
MSE group). Therefore, the CS allows surgeons to cat-
gerize patients according to their disease status, aids in
the interpretation of LSs, and helps correctly direct the
reoperative approach.

The incidence of concomitant thyroid and parathy-
roid diseases is growing.22-23 Twenty-four percent of this
patient population initially underwent thyroid surgery, and
12% had simultaneous parathyroid and thyroid op-
eration as their previous cervical exploration. Fur-
thermore, 19% of patients had concomitant thyroidectomy
during reexploration for HPT, which meant requiring more
extensive exploration than indicated by LSs. This
represents realistic groups of patients who are being evalu-
ated for reoperative neck surgery, and our approach to
these patients is extremely relevant to the true clinical
setting.

Although the best strategy is to prevent reoperative
surgery, failures do occur after initial surgery for HPT.
Owing to the potential difficulties of reoperative neck ex-
plorations, surgeons must seek data that can help re-
duce the complexity and morbidity of these operations.
These results demonstrate the significance of LSs and clin-
cal history used in conjunction to achieve operative cure.
With the use of all available information, the success of
reexploration for HPT has the potential to equal that of
initial parathyroid surgery in patients with concordant
LSs. However, there remain many patients with unsuccess-
ful LSs who continue to live with the disease.

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The Bayes Theorem Wins

“Torture numbers and they will confess to anything,”
(Gregg Easterbrook, 1999, New Republic)

“There are three kinds of lies: lies, damned lies, and statistics.” (misattributed to Disraeli by Mark Twain, 1906)

Endocrine surgeons are known to be friendly, humble, and thoughtful intellectuals rather than chestthumpers. The main socially acceptable mode of competition among endocrine surgeons is their excellence in surgical outcome. One measure of endocrine surgeons’ prowess is their parathyroidectomy success rate. For primary operations, the success rate is expected to be 96% to 99%. Even for reoperations, the success rate is expected to be 90% to 95%. Success rate is a simple fraction with a numerator and a denominator. As surgeons, we try to improve the percentage by having more accurate diagnosis and localization studies (LSs) and better knowledge of anatomy and embryology. Usually, we concentrate on improving the outcome of individual patients (the numerator). Shin et al1 remind us that the denominator is just as important. They analyzed a large series of reoperative parathyroidectomy from Cleveland Clinic, a center of excellence for complex parathyroid surgery. They show that the expected success rate depends on how and when you measure it. For a patient already scheduled for a reoperative parathyroidectomy, the expected success rate is 96%, but for a patient who has an indication for reoperative parathyroidectomy who has not yet undergone LSs, the expected success rate is only 83% because those with negative LSs usually could not undergo parathyroidectomy. Similarly, the PPVs of their LSs depended on whether nonoperated patients were included in the calculation and whether clinical scenarios (CSs) were considered.

It may seem artificial or a trivial point that “patient selection” and “exclusion criteria” would significantly affect the success rate of an operation. Patients and referring physicians, however, reading Web site postings and surgical literature may, nevertheless, have different perceptions about the 2 statistically equivalent statements of “we have an 83% chance of curing you” vs “we have a 96% chance of curing you if your LSs are positive.” Adding such conditional statements allows for a more optimistic interpretation of the same facts.

So, are endocrine surgeons guilty of minimizing their denominators to improve their success rates or of “torturing the numbers” and “lying with statistics”? I do not think that is the message of this article. I think this article shows the importance of thinking and talking about probability precisely, on a time continuum, and in a clinically relevant manner. As additional information is accumulated about a patient, the expected probability of an outcome needs to be adjusted.

The Bayes theorem tells us that posttest probability is determined by pretest probability. To evaluate statistical numbers appropriately, complete clinical context is absolutely necessary. In the end, the Bayes theorem wins.

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