The Technique of Intraoperative Nuclear Mapping to Facilitate Minimally Invasive Parathyroidectomy

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The use of intraoperative nuclear mapping to localize parathyroid adenomas is reviewed.

Background: Despite the fact that primary hyperparathyroidism (HPTH) is the result of a single adenoma in 85% to 92% of cases and is cured following the removal of this one gland, many surgeons continue to perform a complete bilateral neck exploration for patients with primary HPTH. The advent of the sestamibi scan now enables the identification of patients with a single adenoma.

Methods: The use of preoperative sestamibi scanning followed immediately by minimally invasive parathyroidectomy using intraoperative nuclear mapping allows cure for primary HPTH in properly selected patients.

Results: Reports have shown that preoperative sestamibi scanning has a sensitivity of approximately 90% and a specificity of almost 100% in identifying patients with a single adenoma. Intraoperative mapping allows a limited dissection to be performed under local anesthesia in an outpatient setting in approximately 80% of all patients with primary hyperparathyroidism. The details of this new technique — patient selection, timing, use of the intraoperative nuclear probe, and surgical exploration — are described.

Conclusions: When selected appropriately, most patients with primary HPTH can be successfully treated through a minimally invasive technique.

Introduction

Primary hyperparathyroidism (HPTH) is the result of a single adenoma in approximately 85% to 92% of cases and is cured long-term following the removal of this one gland. Despite this fact, most surgeons continue to favor a complete bilateral neck exploration for patients with primary HPTH. The purpose of this comprehensive dissection is to identify and even biopsy each gland so all hyperfunctional parathyroid tissue is identified and resected while normal glands are left behind. This conviction is a historical reflection of the inability of preoperative testing to accurately distinguish those patients harboring a single diseased gland from the 8% to 15% of patients with multiple adenomas or four-gland hyperplasia.

The advent of the sestamibi scan in the early 1990s has changed the management of primary HPTH for many surgeons. A number of recent reports, including one from our institution, has shown preoperative sestamibi scanning to have a sensitivity of approximately 90% and a specificity approaching 100% in identifying patients with a single adenoma. This suggests that the vast majority of all parathyroid adenomas will be identifiable using this technique. More important is the fact that when a single adenoma is identified, the scan is almost always correct.

Using the technique of sestamibi scanning followed immediately by surgical exploration, we have shown that the radioactive gland can be rapidly identified by using a miniature gamma detection device intraoperatively to guide the dissection. This technique allows a smaller, more directed approach to the adenoma that is easily completed using local anesthesia in a true outpatient setting.

Patient Selection and Anticipated Results

Once the diagnosis of primary HPTH has been confirmed, patients are counseled regarding the standard vs minimally invasive approach. We do NOT perform a sestamibi scan on patients prior to the day of the operation. No other localizing studies are warranted. Patients are scheduled for an operation, and the technique used will be dictated by the results of the sestamibi scan an hour or two prior to surgery.

Since not all patients will demonstrate a single adenoma on sestamibi (typical sensitivity in the literature is 86%), they are informed that some will not be candidates for minimal resection. The Figure details the selection of all patients with primary HPTH for minimal vs standard bilateral exploration. This diagram is given to each patient and is explained in detail. If a single adenoma is found on the preoperative scan, then a minimally invasive approach is used. If no localization occurs, a standard bilateral exploration will be performed at that time. Because of the referral pattern associated with the use of this minimally invasive approach, a rare patient will elect not to undergo a standard exploration if a single adenoma fails to visualize (the morbidly obese, or extremes of age with confounding medical problems).

During our first four months of performing this procedure, a total of 30 patients underwent preoperative sestamibi that yielded 25 positive scans of high quality. All 25 of these patients (83.3% of patients referred for primary HPTH) underwent minimal exploration under local anesthesia. A large adenoma was found in each of these patients (specificity of 100%) an average of 17.4 ± 1.1 minutes (range = 9 to 42 minutes) after making the skin incision. The average operating time was 45.8 ± 2.3 minutes, which includes the time from neck incision to
placement of the bandage. In our first report of this procedure detailing its feasibility and safety in 15 patients, we showed significant reductions in tumor location times, total operating times, and length of hospital stay. Of the remaining five patients in the current study who failed to localize on sestamibi, four underwent standard bilateral exploration at that time. Three were found to have a single adenoma, giving the sestamibi a sensitivity of 86.2% in locating single adenomas in this series of 30 patients. One of the patients with a negative sestamibi had four-gland hyperplasia (true-negative scan).

**Optimal Timing Between Sestamibi and Operative Exploration**

Several factors dictate the optimal time between the sestamibi scan and intraoperative nuclear mapping/resection. The first consideration is the half-life of the radiopharmaceutical, which is approximately 6.5 hours. This dictates that the two procedures must be carried out on the same day.

The most important consideration, however, is the speed at which the thyroid and parathyroid "wash out" the nuclear tag. Since the thyroid will lose its initial uptake of sestamibi-Tc at a faster rate than a hyperactive parathyroid gland, the optimal situation occurs when the thyroid has washed out and the parathyroid remains radioactive. Only when there is differential activity between the thyroid and the parathyroid adenoma can the gamma probe be helpful. We have found that this situation occurs within a window of between 1.5 and 3 hours.

Typically, 2 to 2.5 hours is ideal for the vast majority of patients, and we discourage an elapsed time over 3.5 hours. We have had the occasion to try this technique several times after 5.5 to 6.5 hours, and no differential radioactivity could be found and the gamma probe was useless. We typically schedule the sestamibi injection for 07:30, with the operating room scheduled for 10:00. If a second case will follow, the injection should follow the first case by about 1.5 to 2.0 hours. The details of how we perform sestamibi scanning have been reported previously and can also be found on our web page: www.endocrine-surgery.com.

We believe that the risk of recurrent nerve injury is neither lessened nor increased for the minimally invasive dissection on the dissected side. The contralateral side, however, is without risk. We have not experienced this complication but believe the incidence to be comparable to standard exploration at about 1%. Patients are counseled in this regard as well.

**Use of the Gamma Probe in the Operating Room**

When positioned on the operating room table, an 11-mm hand-held Neoprobe gamma counter (Neoprobe Corp. Dublin, OH) is used to measure radioactivity in four quadrants of the neck defined by the upper and lower poles of the thyroid on each side. There is typically a difference of approximately 500 counts per second difference overlying the adenoma. If this can be appreciated, the case should proceed very quickly because of the large differential radioactivity that will become apparent as the probe is placed deeper in the neck. Some patients will not demonstrate a difference in radioactivity at the skin level. Provided a single source was seen on sestamibi, these cases should still proceed since the radioactivity will increase dramatically as the dissection nears the source.

The skin and subcutaneous tissues are infiltrated with local anesthesia, and the patient is given intravenous sedation (we prefer propofol). The initial incision is placed according to the expected location of the adenoma as determined by both sestamibi scanning and measurement of gamma emissions on the skin. This will necessitate that the incision is occasionally higher or lower than usual, but all should be oriented transversely to allow extension as needed, or even conversion to bilateral exploration if necessary. Superficial adenomas (at the level of the thyroid lobe) can be removed through a 2.5-cm incision. Those adenomas lying in the tracheoesophageal groove, however, usually require a 3-cm incision.

Subplatysma flaps are created 2 to 3 cm in all directions and held open with a small self-retaining retractor. Radioactivity is again quantitated in all four quadrants. The strap muscles are now separated along the midline and another self-retaining retractor is placed at 90 degrees to the original. The dissection is carried deeper as directed by increasing gamma counts to locate the radioactive gland. Beyond this point, blunt dissection should be used exclusively to prevent damage to small vascular or nervous structures. Any deep cautery should be of the bipolar type. The recurrent laryngeal nerve is examined as it pertains to the operative field at hand. I do not make a specific point of locating the nerve during every case but am constantly aware of anatomical relationships in this regard.

The adenoma is located by continued use of the probe to direct the dissection. When placing the probe deep in the neck, it must be remembered not to aim it directly at the heart as the sestamibi-Tc is also used as a cardiac imaging agent and will give false-positive readings. Once identified, the adenoma is teased from its surrounding tissues bluntly and elevated to reveal its single pedicle, which is clamped with a single hemoclip and transected. A drain is not needed. At no time should safety be compromised by a hesitancy to extend the incision or even to convert to general anesthesia if necessary.

We routinely send these patients home within an hour or two of the procedure. Those patients with significant underlying medical problems are kept overnight, but this has been necessary in only two of our last 25 patients. Advanced age alone is probably not reason enough to preclude an outpatient approach if all has gone well.

**Discussion**

In contrast to the vast majority of published reports examining the accuracy of sestamibi scanning prior to the initial neck exploration, this technique takes advantage of the very high specificity this test offers and selects for minimal exploration only those patients identified as having single gland disease on delayed images. This selective approach allows the surgeon to avoid the false-negative tests afforded by the 85% to 94% sensitivity of sestamibi and to perform only a minimal exploration on those with a high-quality scan showing a single adenoma. The main concern, therefore, becomes elimination of the very rare false-positive scans that would suggest that a patient has a single adenoma when multiple adenomas or hyperplasia is present. This rare case is addressed by monitoring changes in radioactivity in all four neck quadrants and not just the one harboring the known adenoma.

There are several important points following removal of the adenoma that combine to acknowledge it as the sole source of radioactivity. The first is that the excised adenoma emits radioactivity at least 20% and occasionally higher than 50% of postexcision background (typical ex vivo emissions are always greater than 700 counts/sec and average 2900 counts/sec). Fat, lymph nodes, and even thyroid nodules will never show this level of radioactivity (typical ex vivo emissions are less than 110 counts/sec). Ex vivo radioactivity has proved to be 100% accurate in distinguishing parathyroid tissue from fat and lymph nodes. This should reduce the number of...
“Diagnostic” frozen sections since it becomes readily apparent what type of tissue has been removed. We have recently stopped getting frozen sections during these cases altogether, but we would not recommend this approach until the surgeon has gained significant experience in using the probe in this regard. Because of the systemic administration of the radiopharmaceutical, ex vivo counts must be performed several feet from the patient with the probe aimed away.

The second important observation is that removal of the radioactive gland will be associated with dramatically decreased gamma emissions within that quadrant of the neck. The loss of this main focus of radioactivity within the neck will give rise to the third observation: the establishment of a new background level of radioactivity in all quadrants of the neck, and most importantly, the radioactivity in all four quadrants will equalize. Failure of any of these expected observations to be manifest suggests that another hyperfunctional gland is present that contains more Tc99m-sestamibi than surrounding tissues. This is a direct result of the greater sensitivity of the Neoprobe placed within the tissues of the neck than the gamma camera used for routine sestamibi scanning. My approach to this situation is to identify and biopsy a normal ipsilateral gland or, very rarely, use the probe to direct the subsequent dissection if a second adenoma is suspected. It should be remembered that the risks of reoperation following this minimal approach are not as significant as when following a failed bilateral neck exploration.

When the use of the probe allows the resection to be performed rather quickly. Adenomas are identified at an average of 17 minutes after incision. We have had two patients with completely intrathyroidal parathyroid adenomas that were found in 24 and 31 minutes. Their hidden position was disclosed by a decline in radioactivity behind the thyroid and the demonstration of emissions several thousand per-second higher in one specific portion of the thyroid compared to the remainder of the gland. Our average operative time for adenoma resection is now under 46 minutes. Although the speed at which an operation is performed is not important in itself, we believe these times are a reflection of the simplicity of this technique.

Detailed monitoring of the potential radiation hazards has shown this procedure to pose no significant risk to operating room personnel, surgeon, or pathologist. The surgeon’s exposure is relatively insignificant, and we have reported that the cumulative radiation dose acquired over 15 cases is 1% of acceptable yearly exposure (5 REM) as determined by the Nuclear Regulatory Commission. Similarly, the radioactive adenoma sent to pathology contains only slightly more radioactivity than background (0.04 mR/hr) and therefore poses no exposure hazard to frozen section personnel and does not contaminate the cryostat or other instruments/liquids. The soaked linens and sponges do not require special handling and can be discarded as routine.

When selected appropriately, a majority of patients with primary HPTH may be successfully treated through a minimally invasive technique. The use of local anesthesia and the limited scope of the dissection afforded by intraoperative nuclear mapping may decrease the incidence of failed explorations and other potential complications associated with this operation. Although intraoperative nuclear mapping can be a very useful tool to minimize the efforts necessary to localize a diseased parathyroid, prior experience in parathyroid surgery is still mandatory since clinical judgment will continue to play the dominant role in determining when the operation is complete and when a bilateral exploration is required.

References


