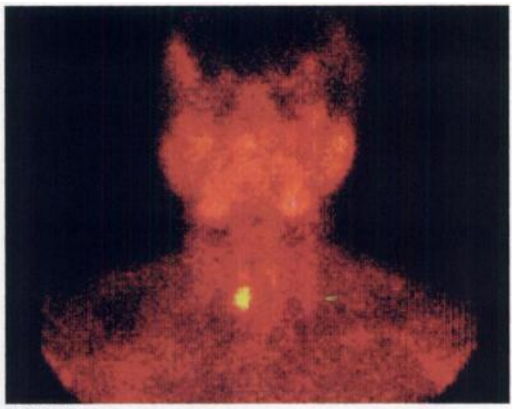
Part 1—
Parathyroidectomy

Advancing Medical Care: The Role of Nuclear Medicine in Radioguided Surgery

About 2 years ago, Katherine Abrahamsen had a nagging feeling that something was not quite right. She seemed more tired than usual and had been having difficulty concentrating when a diagnosis of hyperparathyroidism was made. Abrahamsen, a 51-year-old registered nurse from Hollywood, FL, went to see an endocrinologist, who monitored her calcium and parathyroid hormone levels for about 18 months before he urged her to have surgery. "My doctor told me about a new, minimally invasive surgery that was being performed at the University of South Florida [USF], and I decided to travel 200 miles to Tampa to have the innovative procedure," Abrahamsen said. On the day of the surgery in February 1998, Abrahamsen checked into the hospital at 6:00 a.m., was injected with the radiopharmaceutical ^{99m}Tc-sestamibi at around 11:00 a.m. and had a series of early and delayed nuclear scans to localize her adenoma before she was wheeled into the operating room at 1:00 p.m.

Within 30 minutes, James G. Norman, MD, director of endocrine surgery at USF, made a tiny incision in her neck, inserted a radioguided probe that produces a series of high-pitched tones when aimed at the enlarged gland (still radioactive from the sestamibi uptake) and removed the adenoma. By 5:00 p.m., Abrahamsen was on her way home with a small bandage covering her incision. "By the next morning, I felt wonderful," said Abrahamsen. "Over the next 3 months, I gradually noticed a remarkable increase in my energy level. I feel so fortunate to have had a procedure available to me that was painless and that left no noticeable scar."

Radioguided surgeries are rapidly becoming the standard of care at many cancer institutions and teaching hospitals. These surgeries require the injection of a radionuclide that is taken up by the target organ or surrounding lymph nodes, which are then detected by a radioguided probe. The most established use for the probe is to localize and remove the sentinel lymph nodes in melanoma and breast cancer patients, sparing many patients the morbidity associated with full lymphadenectomies. *Newsline* first reported on this topic last year (*J Nucl Med* 1997;38(6):15N–20N) when sentinel node mapping was still limited to clinical trial protocols. Now more than 100 teaching and community hospitals throughout the U.S. have sent their surgeons, nuclear physicians and pathologists to various training courses to learn the technique. Sentinel lymph node mapping will be covered in a future issue in Part 2 of this series.



Photos courtesy of James G. Norman, MD, University of South Florida, Tampa, FL.

FIGURE 1

FIGURE 2

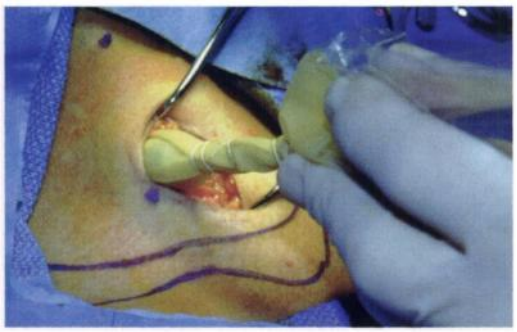


FIGURE 3

The use of radioguided surgery for the treatment of hyperparathyroidism is less than 2 years old, yet its high success rate has many endocrine surgeons eager to learn this outpatient procedure, which is called minimally invasive radioguided parathyroidectomy. The technique is performed by using ^{99m}Tc-sestamibi scans immediately before the surgery to localize the adenoma. Nuclear physicians inject the radiopharmaceutical, perform the

FIGURE 1. Typical sestamibi scan showing a solitary parathyroid adenoma.

FIGURE 2. Gamma-detecting probe (Navigator; U.S. Surgical, Norwalk, CT). Three probes are shown. From left to right, miniature parathyroid probe, standard parathyroid probe and standard melanoma/breast lymph node probe.

FIGURE 3. Probing for radioactive adenoma through 2-cm incision. Lines show sternal notch and location and size of standard parathyroid incision.

imaging and identify the exact location of the enlarged gland. The nuclear scans have a sensitivity of 90%–95% for identifying the hyperactive parathyroid gland, according to Hamant Chheda, MD, clinical assistant professor of radiology at USF College of Medicine, who performs the nuclear imaging before the parathyroid surgeries. In contrast to the adenoma, which has a high uptake, the three normal parathyroid glands will have little or no uptake of the radiopharmaceutical because their function is shut down to compensate for the hyperactive gland.

Within 45 minutes of the delayed imaging, the patient undergoes surgery in which the surgeon makes an incision where the probe detects the highest radioactivity, inserts the radioguided probe and listens for a series of high-pitched sounds to indicate the exact location of the adenoma. "The probe tells us the location of the adenoma to within half a millimeter, and the patient walks away with a 2-cm incision," said Norman. He started performing outpatient parathyroidectomies about 18 months ago and currently performs 5 or 6 procedures a week. He estimates that a couple of dozen surgeons in the U.S. are performing the radioguided surgery, but the numbers are rapidly growing. "I get at least one or two calls a day from surgeons who have heard about the procedure and are eager to learn it," Norman said.

"The probe tells us the location of the adenoma to within half a millimeter, and the patient walks away with a 2-cm incision," said Norman.

Armando E. Guiliano, MD, chief of surgical oncology at John Wayne Cancer Center, Santa Monica, CA, began performing the minimally invasive procedure about 4 months ago after training with Norman. "We've performed it on about 20 patients and have had very good results," Guiliano said. "So far, all of the patients who had sestamibi imaging have qualified for the minimally invasive surgery."

The traditional treatment for hyperparathyroidism usually involves exploratory surgery under general anesthesia, in which each of the four glands is identified and sometimes biopsied to see if it is hyperfunctional. "It's necessary to make up to an 8-in. incision to find the adenoma, often no larger than an almond, and the three other pea-sized glands, which could be located anywhere from the neck down to the sternum," Norman said. "During residency training, we were told to eat a big breakfast on the day of a parathyroid surgery because we were likely to be in the operating room for hours."

In a study of 150 patients submitted for publication, Norman and his colleagues documented a 100% cure rate for hyperparathyroidisim with a mean follow-up period of 8.2 months. "This is the highest cure rate ever documented for this disease," he said. The more invasive surgery has a cure rate of 95% at teaching hospitals but can be as low as 80%. Even more promising is the fact that as many as 85% of patients with hyperparathyroidism are eligible for the radioguided surgery, according to Norman.

Of the 15% of patients who are not good candidates for the procedure, about 10% do not have sestamibi uptake in a single gland because they have multiple adenomas or hyperplasia (usually in all four glands); the other 5% of patients have a single adenoma that is too small or not functional enough to be detected by a sestamibi scan, said Chheda. In a small number of patients (approximately 1%), the nuclear scan could potentially detect one adenoma and miss smaller adenomas in other glands. Some of these patients may have recurrent disease and require repeat surgery. Norman said he has not encountered this problem but emphasized that nuclear physicians need to be knowledgeable in determining true-positive scans from those merely suggestive of a single adenoma.

Role of Sestamibi Imaging

One of the biggest selling points of sestamibi imaging in the eyes of managed care executives could turn out to be that it is cost-effective. In a study published in March 1998 (*J Am Coll Surg* 1998;186:293–305), Norman and his colleague, Daphne Denham, MD, performed a meta-analysis of 175 studies and determined that sestamibi scanning had an average sensitivity of 90.7% and specificity of 98.8% and that nearly 90% of patients had solitary adenomas. Thus, 80% of patients were eligible for the minimally invasive surgery. If all patients with hyperparathyroidism were given sestamibi scans, the study found there would be an average cost savings of $650 per patient, resulting from shortened hospital stays and reduced time in the operating room. "It's clearly cost-effective to scan all patients with hyperparathyroidism even though about 15%–20% will still have to undergo the more extensive surgery," said Norman.

In other research to be published in an upcoming issue of *Surgery*, Norman has found that the probe is very useful in the 5% of patients with recurrent disease who had traditional parathyroidectomies but had a missed primary lesion. Norman has found that the probe can help surgeons navigate around the scar tissue and obliterated surgical planes caused by previous surgery.

A Matter of Timing

The success of the minimally invasive surgery, said Norman, depends on close coordination between the surgery and nuclear medicine departments. Norman said he and Chheda spent over a year fine-tuning the technique to get the timing just

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mission. The practitioner is responsible for the acts of anyone using his or her provider number.

- During May and June of 1998, the OIG revealed its 1998 Work Plan. It contains new initiatives enacted to detect fraud and abuse committed by health care providers. The plan's two primary responsibilities are (1) to protect the Department of Health and Human Services (HHS) from fraud, waste and abuse and (2) to improve programs and operations within HHS.
- Targeted areas include reimbursement practices, governance and administrative issues, health care provider billing practices and clinical appropriateness.

It is more important now than ever before that nuclear medicine physicians have a seat on their local Medicare carrier liaison and advisory committees. If a liaison committee does not exist, then nuclear medicine physicians should help to form one, possibly with the help of the state radiological society. Nuclear medicine physicians must be involved as well as assist leadership through committee membership and participation.

Also, physicians should be aware that they could become the victim of a "whistle-blower." An individual might accuse a practitioner of fraud or abuse simply by reporting to HCFA or the OIG. There are enormous incentives for such individuals. There is no grace period. The deadline for establishing a compliance program is yesterday. If a practitioner is cited for any violations, the existence and application of a well-conceived compliance program may serve to reduce the severity of any actions taken against him or her.

I recommend two sources of information. The first is a compliance document that is soon to be available from the American College of Radiology. The second is *Effective Affordable Compliance* by Janice K. Bucsko and Leif C. Beck (Conshocken, PA: Advisory Publications; 1998). For more information, contact Wendy J.M. Smith, Director of Health Care Policy, Society of Nuclear Medicine, at (703) 708-9000, ext. 242, or by email at wsmith@snm.org.

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Radioguided Surgery

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right. "Timing is critical," Chheda concurred. "The patient must be in the operating room no more than 2.5 hours after the sestamibi is injected in order to retain count rates in the adenoma that are high enough to be detected with the probe." This means that the nuclear physician must do delayed images about 90 minutes after the injection, enough time for the radiopharmaceutical to clear from the thyroid while leaving high counts in the hyperactive parathyroid for surgery.

"When we first started doing the procedure, we waited the traditional 2–3 hours to get delayed images, but the surgeons then found that they were not getting high enough count rates," Chheda recalled. "Nuclear physicians need to realize that they will have to make this major adjustment to the delayed imaging protocol in order to coordinate with the surgical procedure." He contends that shortening the time between initial and delayed imaging does not affect the ability of the scan to pinpoint the depth and location of the adenoma.

Another important factor that helps determine the procedure's success is the types of views that are taken. Oblique images, said Chheda, are the most useful because they can determine whether a hot spot that appears to be on the thyroid is actually on a posterior parathyroid gland. Moreover, these images can give some indication of depth. "Superficial adenomas appear to move from one side of the neck to the other when comparing the left and right anterior obliques, while deep adenomas in the tracheoesophageal groove will stay near the midline," Chheda explained.

Patients who have the nuclear scan receive an injection of about 20 mCi ^{99m}Tc-sestamibi (although the dose may vary from 15 to 25 mCi depending on the patient's weight). Chheda and his colleagues in the nuclear medicine department use a low-energy, high-resolution collimator to obtain 5 early views 15 minutes after the injection and 4 delayed views about 90 minutes after the injection. "We take anterior neck views and anterior mediastinum views as well as right and left anterior oblique views," said Chheda. Norman emphasized the importance of taking multiple views. "I've been asked to interpret many scans sent to me from across the country by surgeons," he said. "And often I can't tell where the adenoma is because of the poor quality of the scan or because oblique views have not been performed."

At this point, it is difficult to predict whether radioguided parathyroidectomies will become the standard of care at most hospitals. For instance, one newly trained endocrine surgeon, William Inabnet, MD, assistant professor of surgery at Mt. Sinai Medical Center, New York, said he favors ultrasound imaging over sestamibi imaging to localize the adenoma because ultrasound is less expensive, easier to use and more readily available in surgeons' offices.

Although sestamibi imaging is far more reliable than sonography, it requires close coordination between nuclear physicians and surgeons, which may pose insurmountable difficulties for small-staffed community hospitals. "The nuclear medicine department must complete the imaging quickly, and an operating room must be available at the exact scheduled time in order for the procedure to work," said Guiliano. He also emphasized that each team of surgeons and nuclear physicians needs to be properly trained in the new technique and perform self-assessments to ensure that patients receive optimum care. For more information on the role of sestamibi imaging in minimally invasive parathyroidectomies, physicians can log onto a web site, http://www.endocrineweb.com.

—Deborah Kotz