Background: Improvements in the accuracy of preoperative localization and the availability of the rapid parathyroid hormone assay have permitted minimally invasive parathyroidectomy in patients with primary hyperparathyroidism.

Hypothesis: The use of intraoperative radioguidance is beneficial during targeted parathyroid operations.

Design: A retrospective analysis of a prospective database of patients.

Setting: Tertiary care referral center.

Patients: During a 2 1/2-year period, 130 patients underwent minimally invasive, targeted parathyroidectomy with intraoperative monitoring of the parathyroid hormone level. Of these, 60 patients underwent radioguided parathyroidectomy. Prior to surgery, a solitary parathyroid adenoma was visualized on technetium Tc 99m sestamibi scintigraphy in all patients selected for radioguided parathyroidectomy. A gamma probe was used to guide the surgical dissection.

Results: All patients were cured following radioguided parathyroidectomy. In 29 patients (48%), the probe provided confusing or inaccurate information; however, a unilateral neck exploration with excision of a parathyroid adenoma was successfully completed in each of these patients. Forty-three cases were completed under local anesthesia and 85% were discharged home on the same day of surgery. There was 1 temporary recurrent laryngeal nerve palsy.

Conclusion: In the era of improved preoperative localization and intraoperative parathyroid hormone monitoring, the routine use of radioguidance is not recommended during parathyroidectomy.

Arch Surg. 2002;137:967-970

Over the last decade, minimally invasive, or “targeted,” parathyroidectomy has gained acceptance among many endocrine surgeons. Several factors have contributed to the development of these focused surgical techniques, such as improved preoperative localization with high-resolution ultrasonography and/or technetium Tc 99m sestamibi scintigraphy, the availability of intraoperative monitoring of the parathyroid hormone (PTH) levels, and more recently, the use of nuclear mapping during surgery. These advances have permitted the use of a targeted approach while the patient is under local anesthesia and the development of video-assisted and complete endoscopic techniques.

Unilateral neck exploration for primary hyperparathyroidism was first reported by Tibblin et al in 1982. Advantages of unilateral neck exploration include a shorter operating time, a quicker recovery, and avoidance of surgical dissection around the normal parathyroid glands. Since then, many large series using a unilateral approach have been reported with results equal to or better than conventional bilateral neck exploration. The use of local anesthesia and same-day discharge home has been used with a high degree of success.

See Invited Critique at end of article

Recently, some surgeons have advocated the routine use of radioguidance during parathyroidectomy; however, others believe that radioguidance adds little benefit during parathyroidectomy, especially when being performed by experienced endocrine surgeons who have a high annual volume of parathyroid surgery. In this study, we report our experience with radioguided parathyroidectomy.
PATIENTS AND METHODS

From September 1, 1998, to April 30, 2001, 130 patients underwent minimally invasive, targeted parathyroidectomy with intraoperative monitoring of the PTH level at a university medical center. Selection criteria for a targeted approach included the success of preoperative localization of a solitary parathyroid adenoma on technetium Tc 99m sestamibi scintigraphy and/or high-resolution ultrasonography and no history of multiple endocrine neoplasia or familial hyperparathyroidism. Of these, 60 patients underwent radioguided parathyroidectomy and will constitute the focus of this analysis.

Many factors influenced the selection of patients for radioguided parathyroidectomy, the most important of which was favorable kinetics of the radionuclide on sestamibi scintigraphy. For example, appropriate candidates for radioguided parathyroidectomy should have a sestamibi scan showing retention of the radioisotope in a solitary adenoma and preferential washout from the thyroid gland and surrounding tissues. Other factors that influenced the recommended use of radioguidance included a history of neck surgery, persistent or recurrent hyperparathyroidism, and patient preference.

Among the patients undergoing radioguided parathyroidectomy, there were 13 men and 47 women with a mean age of 64 years (age range, 38-92 years). The mean (SD) preoperative calcium and PTH levels were 11.2 (0.88) mg/dL (2.80 [0.22] mmol/L) and 193 (160) pg/mL (20.3 [16.8] pmol/L), respectively. All patients selected for radioguided parathyroidectomy had a solitary parathyroid adenoma visualized on preoperative sestamibi scanning, which was performed prior to the day of surgery.

On the day of surgery, patients received 18 to 20 mCi of technetium Tc 99m sestamibi in an antecubital vein approximately 1.5 to 3 hours prior to surgery. In the operating room, an 11-mm gamma probe (Neoprobe 2000; Ethicon Endo-Surgery Inc, Cincinnati, Ohio) was used to measure radioactivity in each quadrant of the neck. The region over the thyroid isthmus was used to determine background radioactivity. After administering intravenous sedation, 1% lidocaine hydrochloride was injected in the skin and subcutaneous tissue over the area of maximal radioactivity and along the anterior border of the ipsilateral sternocleidomastoid muscle. A 2- to 3-cm incision was made and the strap muscles were separated, but not divided. For deeply located glands, the incision was placed in a more lateral location and the parathyroid adenoma was approached lateral to the strap muscles. The gamma probe was periodically inserted into the wound to determine the optimal direction of surgical dissection. In most cases, an attempt was made to identify the recurrent laryngeal nerve, especially if the adenoma was located in the tracheoesophageal groove or in a deep location. Once the adenoma was identified, the vascular pedicle was isolated, clipped, and divided. Ex vivo counts of the parathyroid adenoma were measured. Specimens were rarely submitted for frozen section analysis.

Intraoperative monitoring of the serum PTH level was used in all cases (Nichols Institute, Cincinnati, Ohio) with an assay performance time of 12 minutes. Serum was drawn from an antecubital vein or radial arterial line at the following intervals to assess PTH levels: baseline (prior to incision), after isolation, and 5, 10, and 30 minutes after excision. If there was a greater than 50% reduction in the PTH level from the highest preexcision value, the operation was terminated without visualizing the remaining parathyroid glands and the later PTH measurements were obtained in the recovery room. Calcium and PTH levels were measured in the office 2 to 3 weeks after surgery and again at 6 months.

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<th>Levels</th>
<th>Preoperative</th>
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<td>Calcium, mg/dL</td>
<td>11.2 (0.88)</td>
<td>9.3 (0.64)</td>
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<tr>
<td>PTH, pg/mL</td>
<td>193 (160)</td>
<td>88 (54)</td>
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*Data are given as mean (SD). To convert calcium levels to millimoles per liter, multiply by 0.25; to convert parathyroid hormone levels to picomoles per liter, multiply by 10.53.
†Data are available for only 25 patients.

All patients were cured following radioguided parathyroidectomy as determined by normal serum calcium levels in the postoperative period. Three weeks after surgery, the mean serum calcium and intact PTH levels were 9.3 (0.64) mg/dL (2.33 [0.16] mmol/L) and 88 (54) pg/mL, respectively (Table). Six-month or longer follow-up data were available on 25 patients. In these 25 patients, who had a mean follow-up of 10.9 months, the mean serum calcium level was 9.2 (0.9) mg/dL and the PTH was 86 (42) pg/mL.

In 29 patients (48%), the gamma probe was deemed unhelpful by the surgical team for the following reasons: confusing or inaccurate information of radioactivity counts (n=17), detection of increased radioactivity only when the probe was placed directly on top of a dissected and exposed adenoma (n=9), equipment failure (n=2), or logistical problems with the administration of the radioisotope (n=1). In each of these cases, a unilateral neck exploration was successfully completed with excision of a solitary parathyroid adenoma. In 24 patients (40%), the gamma probe detected increased radioactivity on the correct side of the neck and helped direct the surgical dissection.

In the 6 cases of persistent or recurrent hyperparathyroidism, the gamma probe aided in the surgical dissection by allowing optimal placement of the incision and by minimizing the surgical dissection in the reoperative neck. Forty-three cases were completed under local anesthesia, whereas 10 patients requested general anesthesia. Seven patients required conversion from local to general anesthesia, 4 of whom had had prior neck surgery. Fifty-one patients (85%) were discharged home the same day of surgery.

There was one temporary recurrent laryngeal nerve palsy secondary to excessive retraction of the thyroid.
gland. This patient experienced complete recovery 3 months after surgery as documented by normal vocal cord function on indirect laryngoscopy. Additional morbidity included 1 case of pneumonia and 1 case of pneumothorax. One patient with hypercalcemic crisis, adult respiratory distress syndrome, and a tracheostomy died of multiple system organ failure following surgery. Interestingly, a definite solitary parathyroid adenoma was visualized on the preoperative sestamibi scan, however, due to the contorted position of the patient and the central location of the tracheostomy, the side of the lesion could not be determined (right vs left) on the sestamibi scan. In this case, the gamma probe successfully identified the correct side of the neck for exploration and a 3-g adenoma was excised uneventfully. Radioguided parathyroidectomy was completed in 25 minutes. However, the patient died 6 days after surgery of causes unrelated to the operation.

**COMMENT**

Since sporadic primary hyperparathyroidism is caused by a solitary adenoma in 85% to 90% of the cases, a more focused surgical approach has gained popularity among endocrine surgeons. Many factors have made these targeted approaches feasible including improvements in the accuracy of preoperative localization as well as the availability of intraoperative PTH monitoring. Taking advantage of these improvements, multiple techniques have been developed, ranging from unilateral neck exploration under local anesthesia to video-assisted and complete endoscopic techniques. Many large series reporting experiences with minimally invasive parathyroidectomy have demonstrated equal or superior results when compared with conventional bilateral neck exploration, which historically has achieved a 95% cure rate when performed by an experienced surgeon.

The use of radioguidance during parathyroid surgery was first reported by Martinez et al in 1995. Since then, this technique has received a great deal of attention in the surgical literature with many investigators reporting excellent results. The use of radioguidance during parathyroid surgery takes advantage of the fact that the cells in a parathyroid adenoma contain a proportionally higher number of mitochondria compared with normal parathyroid glands and surrounding tissues. Mitochondria take up and retain 99mTc sestamibi to a greater degree than surrounding tissues and this increased radioactivity can be assessed intraoperatively with a gamma probe. Proponents of radioguided parathyroidectomy state that the use of a gamma probe helps minimize incision length, permits the use of local anesthesia, accurately directs the surgical dissection, and obviates the need for frozen section analysis.

Many endocrine surgeons have questioned the true benefit of radioguidance during parathyroidectomy. Multiple large series reporting unilateral neck exploration without radioguidance have demonstrated similar results with the same benefits reported for radioguided parathyroidectomy, including decreased duration of surgery, improved cosmetic results, and favorable technical conditions for reoperation. The use of local anesthesia and intraoperative PTH monitoring was first popularized by Chapuis et al and later by Irvin et al, both preceding the introduction of intraoperative radioguidance. Significant improvements in the accuracy of preoperative localization have allowed a more targeted surgical approach. For example, ultrasonography provides important anatomical information to the surgical team, such as the size and location of the parathyroid adenoma as well as its relationship to surrounding structures. This anatomical information greatly facilitates the intraoperative localization of enlarged parathyroid glands during targeted parathyroidectomy. The use of the rapid serum PTH assay during parathyroidectomy has also contributed to the development of focused techniques. An appropriate reduction in intraoperative PTH levels reliably predicts eucalceemia following parathyroidectomy.

The cost-effectiveness of radioguided parathyroid operations has not been established. It has been suggested that when compared with bilateral, conventional neck exploration, radioguided parathyroidectomy offers a cost benefit due to shorter duration of surgery, the use of local anesthesia, and same-day discharge. Since the efficacy of focused parathyroidectomy without radioguidance has also been well established, it is unlikely that the gamma probe itself is the cause of costs savings. Rather, the use of accurate preoperative localization and surgical experience would seem to be the main contributing factor to lowering overall costs. At certain centers, conventional bilateral neck exploration is performed as an outpatient procedure and has been shown to be more cost-effective than radioguided parathyroidectomy. These conflicting reports underscore the need for additional studies on the cost-effectiveness of the various approaches for parathyroidectomy.

Early in our experience of focused parathyroid explorations, radioguided parathyroidectomy was offered routinely to eligible patients. However, it soon became apparent that radioguidance added little information to preoperative imaging results, which alone permitted successful unilateral neck exploration. Moreover, the gamma probe often provided confusing data to the surgical team and proved to be unreliable in a high percentage of cases. After our initial experience, radioguidance is now used only in cases of persistent or recurrent hyperparathyroidism, a patient population in which the use of intraoperative radioguidance has been shown to be helpful. In the reoperative neck, the gamma probe may help guide the surgical dissection through previously dissected tissue planes, but the probe is no substitute for experience and sound surgical technique.

The results of this series confirm that targeted parathyroidectomy can be safely performed with excellent short-term results in patients with nonfamilial hyperparathyroidism and successful preoperative localization of a solitary parathyroid adenoma. Long-term follow-up is necessary to confirm the efficacy of focused neck exploration for primary hyperparathyroidism. The findings in this study do not support the routine use of intraoperative radioguidance during initial surgery for primary hyperparathyroidism. Radioguidance may be beneficial in cases of persistent or recurrent hyperparathyroidism and in the reoperative neck.
REFERENCES


Invited Critique

Recently we have seen some remarkable changes in the way that we approach the patient who has primary hyperparathyroidism. Although not all concur, many surgeons now believe that as a result of several technological advances, minimally invasive parathyroidectomy is the preferred approach for such patients. These advances include preoperative localization with technetium Tc 99m sestamibi scanning, high-resolution ultrasonography, the availability of intraoperative parathyroid hormone level monitoring, and intraoperative nuclear mapping via the use of the handheld gamma-detection device. Interestingly, all were relatively unheard of (or declared not useful) just a decade ago!

Inabnet, a strong proponent of the minimally invasive parathyroidectomy, argues that use of the gamma-detecting probe for intraoperative radioguidance is unnecessary during initial surgery for primary hyperparathyroidism. Inabnet et al., however, suggest that radioguidance is helpful in the reoperative neck and in cases of persistent or recurrent hyperparathyroidism. It is ironic that Inabnet et al. suggest that we reserve the use of radioguidance for those patients who represent the greatest challenge to even the most experienced parathyroid surgeons; yet, their data suggest that they are unable to successfully use the technology in a simpler and less complicated patient population! In the 48% of patients for whom they felt the gamma probe was unhelpful, most of the difficulties appear to be of a technical and/or learning curve category as opposed to a failure of the specific technology itself. It seems that if we are to reserve this approach for our most challenging patients, we must be completely comfortable and facile with its use in “routine” patients where success of the procedure does not have to be as greatly dependent on the satisfactory application of the technology.

Inabnet himself has said, “as parathyroid surgeons, we should have multiple techniques to offer patients.” There is ample evidence that the use of a radioguided probe serves as one of the exciting emerging new technologies whereby this disease is now approached. I agree, radioguidance may not be “necessary” during initial parathyroidectomy on all patients who have primary hyperparathyroidism; however, it is a technology with valid utility and has the potential to be very helpful to surgeons at all experience levels. It is unrealistic to assume that all patients with primary hyperparathyroidism will be operated on by surgeons of a similar, highly expert nature relative to experience and ability. Radioguidance should be further refined such that it can become an easily employed and reliable tool in the armamentarium of surgeons who undertake the care of patients with primary hyperparathyroidism—both simple and complicated!

Arthur J. Ross III, MD
La Crosse, Wis