

^{99m}Tc -Sestamibi and Minimally Invasive Radioguided Surgery for Primary Hyperparathyroidism

The management of primary hyperparathyroidism is not without controversy. There is controversy as to which imaging technique (if any) should be used to localize a parathyroid adenoma (1,2). There is controversy as to when surgery should be recommended in an asymptomatic patient; although some would argue that all patients are symptomatic but simply do not realize it! There is also controversy as to which surgical technique should be used—that is, bilateral neck exploration or minimally invasive surgery (MIS) (2). This Invited Perspective is timely and stimulated by a paper from Rubello et al. (3) reporting the results of a multicenter experience of radioguided (probe-guided) MIS (MIRS).

On pages 220–226 of this issue of *The Journal of Nuclear Medicine*, Rubello et al. (3) report a study evaluating 384 consecutive patients from 7 centers who underwent MIRS or bilateral neck exploration for hyperparathyroidism. MIRS was successfully performed on 268 (96.8%) of 277 patients. The other 9 patients (3.3%) were converted to bilateral neck exploration because of parathyroid carcinoma, unsuspected multigland disease, or glands that were difficult to access by MIRS. Importantly, the group reported successful MIRS in 32 (78.0%) of 41 patients who had undergone previous thyroid or parathyroid surgery. The probe technique was not found to be helpful if there was concomitant uptake of ^{99m}Tc -sestamibi in thyroid nodules or no uptake in parathyroid tissue. In these

instances, the quick assay for parathyroid hormone was found to be useful. In the group of 20 patients with ^{99m}Tc -sestamibi-negative preoperative imaging results (6 of whom had concomitant multinodular goiter), 40% had multiglandular disease (6 with hyperplasia and 2 with double adenomas).

In many ways, this was an admirable study dealing with an important clinical problem in a large patient population, with careful analysis of the data and a comprehensive discussion of the results. However, there are some problems. It was not made clear whether this was a prospectively planned study or a retrospective analysis (one assumes the latter), and as the study was not randomized, the opportunity was missed to provide information on any real benefits of MIRS over MIS with an intraoperative quick parathyroid hormone assay. As Dr. John L. Doppman asserted at the National Institutes of Health Consensus Conference on asymptomatic hyperparathyroidism (4), “The most difficult challenge in preoperative localization in primary hyperparathyroidism is locating the parathyroid surgeon.” An experienced parathyroid surgeon would expect a cure in more than 95% of cases of primary hyperparathyroidism by bilateral neck exploration (5). Thus, any new procedure has to provide real benefits. MIS can be performed only if the parathyroid adenoma has been localized. Preoperative localization requires imaging, and the combination of ultrasound and ^{99m}Tc -sestamibi imaging allows detection of adenomas in a high proportion of patients (6), potentially allowing MIS to approach the success rates of bilateral neck exploration. However, MIS has several other advantages such as reducing operative time and allowing surgeons to perform parathyroidectomy as

an outpatient procedure with the attendant cost-savings (7,8). Rubello et al. (3) confirmed this advantage by finding a mean operating time of 37 min and a mean hospital stay of 1.2 d. Locoregional anesthesia was possible in 72 patients and allowed surgery in 56 patients considered at high risk of complications from anesthesia.

Although MIRS may have some theoretic advantages such as improved sensitivity for the detection of a parathyroid adenoma, these advantages have not been proven. Similarly, the utility of MIRS in difficult reoperative cases has yet to be proven in comparative trials, especially when multiple adenomas may be an issue (9). Furthermore, MIRS is not a new concept and has been practiced since 1997 by Norman’s group (10) in patients presenting for the first time as well as in patients with recurrent disease (11). Thus, the study of Rubello et al. (3) would appear simply to provide additional supportive data from a European population. Although MIRS has been known for many years, its use has not been widely adopted, presumably because of the inconveniences attached to the use of the probe (e.g., cost, regulations relating to radioactivity, sterilization, and additional training). At present, it is a rare procedure in the United States (J. Bilezikian, oral communication) and United Kingdom (P. Selby, oral communication), and we presume that this is the case in most other countries. What is nevertheless controversial is the suggestion that MIRS can be used in reoperative cases (3), as has been recommended previously (11). This requires additional study, as a previous operation is generally considered to be a relative contraindication for MIS (12).

There appears to be a clear division of surgical opinion about MIS. The 2 largest single-center studies on MIS were by Norman’s group (7,10) and Udelsman’s

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For correspondence or reprints contact: Hans Van der Wall, MB BS, PhD, Department of Nuclear Medicine, Concord Hospital, Hospital Rd., Concord 2139, Australia.

E-mail: hansv@nmrf.org.au

group (8). Although both advocate MIS, Norman's group uses a radioguided probe to confirm that the excised adenoma is indeed the index lesion identified preoperatively by ^{99m}Tc -sestamibi scanning. Udelsman's group does not use a radioguided probe but uses the quick parathyroid hormone assay to confirm successful removal of the index adenoma, which is preoperatively identified on ^{99m}Tc -sestamibi scanning. Reported success rates are similar, with identical operative times and all advantages associated with MIS. Other centers that eschew the radioguided probe use frozen sections to confirm that the excised lesion is indeed the culprit adenoma. The potential benefit of using a radioguided probe in addition to localizing the adenoma intraoperatively is the ability to confirm that the excised lesion is indeed the culprit lesion. Dr. Norman emphasizes the latter point (written communication).

The advent of the rapid parathyroid hormone assay has led to its adoption as an intraoperative safeguard for successful localization of a parathyroid adenoma (13). A 50% reduction in the hormone level at 10 min after excision of the parathyroid adenoma was associated with successful treatment (14). Although Rubello et al. (3) enthusiastically support this use, others would disagree. There is a small but significant false-negative rate (13), and a recent study has demonstrated that the technique may not be cost-effective in MIS (15). Some centers have since abandoned the routine intraoperative use of the assay (13), whereas others continue to use it as a confirmatory tool. However, a case can be made for its use when the ^{99m}Tc -sestamibi findings are negative or suspected of being false-positive at a second site, when multiple adenomas are suspected, or when complex repeated surgery is needed.

If nuclear medicine wishes to influence clinical practice, then studies have to be well designed and the results have to be published in the major clinical journals (16). There seems little point in nuclear medicine physicians' impressing each other (17) but being ignored by the clinical community, as those who need convincing are the general physicians/

endocrinologists who investigate patients and refer them to surgeons. Experienced parathyroid/endocrine surgeons do very well indeed with or without nuclear medicine assistance. Many but not all surgeons do wish to know where the parathyroid adenoma is before surgery, and it seems likely that MIS will increasingly be used. We suggest, however, that most surgeons would require considerable convincing that any potential benefits from MIRS would outweigh the extra hassles.

In conclusion, the study of Rubello et al. (3) substantiates the utility of ^{99m}Tc -sestamibi across multiple centers in the diagnosis and treatment of primary hyperparathyroidism by MIRS. Their experience confirms that MIS provides substantial savings in operative time and hospital costs over bilateral neck exploration. However, although many centers including our own have welcomed MIS in view of the obvious benefits to the patient and, indeed, the surgeon, they have chosen not to use an intraoperative probe, and we wonder whether its use will ever become routine. From an imaging perspective, we should strive to improve our sensitivity in the detection of parathyroid adenomas with ^{99m}Tc -sestamibi, optimizing the technical aspects of the technique and its coregistration with anatomic modalities (18) and in particular ultrasound (6). Alternate imaging approaches such as ^{11}C -methionine PET have shown promise in very sensitive detection of primary parathyroid adenomas (16,19) and recurrent disease (16,17). Indeed, we wonder whether optimizing imaging would have a greater overall impact on operative success than the routine use of a probe with MIS. Although this study provided additional information supporting the use of MIRS, we believe that it is MIS for sure but MIRS not so sure.

Hans Van der Wall, MB BS, PhD
Hugh Carmalt, MB BS
Concord Hospital
Sydney, New South Wales, Australia

Ignac Fogelman, MD
King's College
London, United Kingdom

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