

Tc-99m-sestamibi alone. Both methods are cumbersome, and new strategies to improve parathyroid localization are needed.

This study differs from previous work with Tc-99m-sestamibi in the method in which the thyroid gland is imaged. Rather than using a time-consuming and cumbersome iodine-123 subtraction technique, we imaged the thyroid gland using a rapid Tc-99m-pertechnetate technique. Because one of the most important aspects of parathyroid localization is the ability to subtract the thyroid image completely, adequate thyroid imaging without motion artifacts is crucial. In this prospective study of Tc-99m-pertechnetate and Tc-99m-sestamibi subtraction scanning, we achieved a high sensitivity rate for localizing solitary parathyroid adenomas or residual hyperplastic parathyroid glands. Because the parathyroid glands are located near the thyroid gland and hyperplastic glands are smaller compared with a dominant solitary adenoma, Tc-99m-sestamibi imaging of diffuse parathyroid glandular hyperplasia does not always occur. When both isotopes are used, there may not be enough contrast to separate the thyroid and the parathyroid glands, especially in multiple gland hyperplasia. The radionuclide localization of solitary parathyroid adenomas or solitary residual hyperplastic parathyroid glands may be more successful because of increased concentration and uptake of Tc-99m-sestamibi in a single focus of abnormal parathyroid tissue. Glandular size ultimately may be the important determinant for the limits of resolution of Tc-99m-sestamibi radionuclide imaging. The results of this study compare favorably with results of previous work using iodine-123 subtraction or Tc-99m-sestamibi alone. Direct comparison to determine which technique is better cannot be done now. Tc-99m-sestamibi subtraction imaging of abnormal parathyroid glands is less cumbersome and quicker using a Tc-99m-pertechnetate technique.

Most experienced surgeons who perform parathyroid operations advocate bilateral neck exploration to ensure the success of the initial operation. If a radiologic method that could localize every abnormal parathyroid gland were developed, it might be possible to limit the extent of surgical exploration for parathyroid disease and to reduce the morbidity from complete neck exploration. In this study, although no effect was evident in those patients having initial neck exploration for hyperparathyroid disease, the radionuclide scans did help direct the surgeon to the area of abnormal parathyroid glands in those patients having reoperation. Above all, a thorough understanding of the principles and physiology of hyperparathyroid disease should guide the surgeon in the operation for that disease. Until more studies have elucidated the mechanisms and limitations of Tc-99m-sestamibi parathyroid imaging, clinical and operative decisions should not be based only on radiologic images.

Acknowledgment

The authors thank Laura Burton for editorial assistance.

References

1. Kaplan EL, Yashiro T, Salti G. Primary hyperparathyroidism in the 1990s: choice of surgical procedure for this disease. *Ann Surg* 1992; 215:300-317.
2. Doppman JL, Miller DL. Localization of parathyroid tumors in patients with asymptomatic hyperparathyroidism and no previous surgery. *J Bone Miner Res* 1991; 6:S153-158.
3. O'Doherty MJ, Kettle AG, Wells P, Collins REC, Coakley AJ. Parathyroid imaging with technetium-99m-sestamibi: pre-operative localization and tissue uptake studies. *J Nucl Med* 1992; 33:313-318.
4. Taillefer R, Boucher Y, Potvin C, Lambert R. Detection and localization of parathyroid adenomas in patients with hyperparathyroidism using a single radionuclide imaging procedure with technetium-99m-sestamibi (double-phase study). *J Nucl Med* 1992; 33:1801-1807.
5. Levin KE, Clark OH. The reasons for failure in parathyroid operations. *Arch Surg* 1989; 124:911-914.
6. Clark OH, Duh QY. Primary hyperparathyroidism, a surgical perspective. *Endocrinol Metab Clin North Am* 1989; 18:701-714.
7. Wei JP, Burke GJ, Mansberger AR Jr. Prospective evaluation of the efficacy of technetium-99m-sestamibi and iodine-123 radionuclide imaging of abnormal parathyroid glands. *Surgery* 1992; 112:1111-1117.
8. Casas AT, Burke GJ, Sathyanarayana, Mansberger AR Jr, Wei JP. Prospective comparison of Tc-99m-sestamibi/I-123 radionuclide scan versus high-resolution ultrasonography for the preoperative localization of abnormal parathyroid glands in previously unoperated primary hyperparathyroidism. *Am J Surg* 1993; 166:369-373.

Discussion

DR. WILLIAM C. MCGARITY (Atlanta, Georgia): We do not use routine localizing studies before the initially neck exploration in parathyroids in patients with primary hyperparathyroidism, except as already mentioned in patients who have had previous neck surgery and in an occasional poor risk patient. Our experience with technetium 99m sestamibi iodine 123 imaging reoperative parathyroid surgery has been very good. And, Dr. Mansberger, we have also found that the technique is better in identifying adenomas than hyperplasia. In our series, 14 patients had 14 adenomas correctly localized. Seven of these were reoperative case, four were in the mediastinum, and we had three false positives due to thyroid lesions. There were no false negatives. However, only 11 of the 15 enlarged glands were correctly localized in patients with hyperplasia. There were two false positives due to thyroid lesions and four false negatives. As pointed out, the I¹²³ subtraction is more difficult and more expensive than the pertechnetate. However, up until this time, we have preferred the sestamibi I¹²³ imaging for reoperative surgery because we thought that the background activity was good, the image was clear, and we thought that it picked up smaller lesions than the pertechnetate. However, after hearing the paper by Dr. Mansberger this morning, we may have to rethink our position in that regard. For reoperative surgery, we need the best study available. Dr. Mansberger, I'd like to ask you the following questions. What tissues in the neck take up

sestamibi other than the parathyroids? Can this be confusing? All of your adenomas were in the field of surgical exploration. I know that localizing studies were not necessary for you to find them, but did it save you any operative time? Did you do conventional technetium 99m sestamibi I¹²³ in any of the same patients that had the pertechnetate with sestamibi to compare the sensitivity and specificity? What test do you now advise for reoperative surgery? In a consecutive series of 600 patients followed for five to 30 years, our cure rate for initial surgical exploration for primary hyperparathyroidism was 96 percent. The incidence of persistent disease was 3.2%, and the incidence of recurrent was 0.7%. In the series of 600 cases, we had an incidence of multiglandular disease, double adenomas, and nodular and diffuse hyperplasia of 34%. Because of the significant incidence of multiglandular disease, we feel that all glands should be identified, if possible, and proven by biopsy. The patients referred to us with persistent disease, after initial exploration, the cause of persistent disease has been primarily due to inadequate exploration. I feel that if localizing procedures are performed on all cases before initial exploration that the incidence of inadequate exploration and persistent disease would probably increase because it's likely that some surgeons would limit the operation to removal of the lesion shown on the scan and not further explore for possible multiglandular disease. Dr. Irvin, maybe your new approach will prevent this problem. In cases referred to us that have had localizing procedures by the referring physician, we have not found that the operating time was significantly less than in patients that have not had the localizing procedures. In summary, for the following reasons we do not use preoperative localization studies for our initial exploration: 1) there is a failure rate of only four to five percent after initial exploration without the use of localizing studies when done by an experienced endocrine surgeon; 2) there is a significant incidence of multiglandular disease, and one should identify all the parathyroid glands, if possible; 3) localizing procedures are not perfect, as already pointed out; sestamibi with the I¹²³ subtraction is near perfect for adenomas, but it does not show all the enlarged glands in patients with hyperplasia or multiglandular disease; and, 4) localizing studies are expensive and are not cost effective, as shown by Dr. Burns. So at the present time, unless Dr. Irvin's new approach changes my mind, I agree with Dr. Burns that preoperative parathyroid localization studies should not be routinely performed in those patients undergoing initial cervical exploration for primary hyperparathyroidism. In my experience, they do not increase surgical success or significantly decrease operative time. However, the newer localizing studies are invaluable in reoperative parathyroid surgery. Dr. Burns, 79% of your series of 104 patients had preoperative studies. Why were these done? What has been

your experience in using technetium 99m sestamibi in patients with hyperplasia? And, Dr. Irvin, I'd like to ask you one question. With a cure rate of 90% to 96%, or a failure rate of only 4 to 5% following initial exploration without localizing studies, how can you justify the cost of the sestamibi study plus the PTH assays in all de novo cases?

DR. JOHN WEI (Closing Discussion): In closing, our current recommendations at our institution for initial operations for primary hyperparathyroidism are that we do not perform any preoperative localizing test. By and large, we never performed technetium-thallium scans because we knew it didn't work. High-resolution ultrasonography was not very good, anyway. Currently, every patient who gets a sestamibi scan at our institution is done on an investigational protocol. As such, I think that until more experience and more data can be obtained on this, patients who get this study should be done in a study setting so that as much scientific data as possible can be generated so that we can learn as much as possible about the limitations of this agent. Now, in response to Dr. McGarity's question, there is differential uptake of the sestamibi in the various tissues of the neck. In unpublished data that we've generated in patients who have received sestamibi alone and have had biopsies of various tissues, we know that because sestamibi is sequestered in metabolically active tissues, or tissues which are high in mitochondrial content, such that in comparison of the relative ratios of radioactive counts measured under a scintillator, peripheral blood and fat and non-active muscle in the neck will have an uptake ratio in comparison to an abnormal parathyroid gland of approximately 40. The parathyroid adenoma, or a hyperplastic gland, will have a relative ratio uptake in comparison to normal thyroid of approximately tenfold. In comparison to a normal parathyroid gland, however, an abnormal adenoma will have a relative ratio of around 10 or so. This has been in the first ten patients that we've studied with in vivo uptake studies. In terms of savings in operative time, in a retrospective review of our patients who we had not performed sestamibi localization on, and in comparison to the initial operations for primary hyperparathyroidism, we had a mean savings time of approximately 45 minutes. In terms of multiple scans using either technetium pertechnetate in comparison to iodine 123 subtraction, we have not done that. The main reason is because the institutional review board would never approve a triple isotope study in a patient under these circumstances.

Currently, as it stands and as you see via our study, we do what we need to for our reoperative patient. At least in this series we had three reoperative cases that we were able to localize the abnormal parathyroid glands with the pertechnetate and sestamibi combination.