EDITORIAL

Radionuclide Parathyroid Imaging

Controversy in the management of hyperparathyroidism revolves around several issues. Do all patients need a parathyroidectomy? Which patients (if any) require preoperative localization, and if so, which procedure or set of procedures are optimal for the purpose? Is there a danger that improved preoperative localization may increase the risk of the tyro surgeon chancing his hand? In the hands of an experienced parathyroid surgeon, 90%–95% of the abnormal parathyroid glands would be localized using total thyroid bed exploration. Therefore, for a first exploration, localization may be considered unnecessary (*1*). However, up to 20% of parathyroid adenomas are ectopic (*2*) and need detection, if at all possible, to save surgical exploration of the thyroid bed and the potential morbidity associated with localization of all parathyroid tissue. Also, 80%–85% of the causes of hyperparathyroidism are due to single adenomas. Therefore, if the site can be detected, the possibility of shortening surgery time is feasible (*3*), or a local approach through a unilateral incision (*4*), thereby reducing the extent of postoperative scarring, is a reasonable and some say preferable surgical approach. However, this view is disputed by others (*5,6*). It is possible that selected patients may be suitable for localized resection and same-day discharge (*7*). Another interesting possibility is keyhole/thoracoscopic surgery for patients in good health (*8*).

The argument for preoperative localization is greatest in patients who are undergoing re-exploration after a failed procedure. Although many re-explorations find the parathyroid gland in a normal site or accessible from the neck (*9*), a variable percentage is due to abnormally sited glands (*10,11*). Second operations have a higher morbidity and a lower chance of establishing normocalcemia. Some surgeons would advise that localization in these circumstances be confirmed by at least two techniques (*12*). There is then a rationale for performing preoperative localization in these patients to exclude as much as possible the ectopic gland and hopefully reduce the chance of missing normally sited glands.

The question we must ask ourselves is: Can imaging guarantee the site of the parathyroid gland, and if so, how is this best achieved? There are a variety of techniques used to find the hyperfunctioning parathyroid gland, and these methods—MRI, CT, USS and radionuclide imaging (single photon and positron) have been recently reviewed (*13,14*).

All of the techniques give variations in sensitivity of detection varying between 38% and 100% (*13*). The large variation in these modalities is dependent on local expertise, the selection bias in each study and the technology available. What is clear is that no imaging modality has a definite advantage over radionuclide imaging and often falls short of the best radionuclide imaging. The difficulty is that all technology is advancing, and often the latest technique in one modality is not compared with the state-of-the-art technique in another.

Although several radionuclide techniques have been explored (*14,15*), the two most widely used and tested are $^{201}Tl/^{99m}Tc$-sestamibi subtraction imaging. For thallium imaging, despite various twists on the theme, a subtraction scan using either pertechnetate or iodine (^{123}I) to outline the thyroid has been the standard technique. Several researchers (*16,17*) have demonstrated that the sensitivity of ^{99m}Tc-sestamibi subtraction imaging of the thyroid is as good, if not better, than thallium imaging with a lower radiation dose. Reported sensitivities were greater than 90% for adenomas and far lower for hyperplastic glands (*14*). Taillefer et al. (*18*) raised the question as to whether subtraction imaging is really necessary. He demonstrated that differential washout rates for thyroid and parathyroid tissue allowed for early (thyroid and parathyroid) and late imaging (parathyroid) to visualize the parathyroid gland after a single injection. Others have confirmed this finding, but recent articles question this principle and suggest that late images may be inferior to early images and that a thyroid image should be obtained for comparison (*19,20*). There are a variety of methods of data acquisition and processing, but it would appear, regardless of the acquisition method, localization of adenomas should be greater than 90%; otherwise, the technique is suboptimal.

SPECT imaging with sestamibi has met with varying success. Billotey et al. (*21*) reported an increased sensitivity when SPECT was used in addition to the dual-phase planar technique. This was particularly evident in the mediastinum but also provides an occasional advantage in the neck when the SPECT was performed early, i.e., 30–60 min after injection. Chen et al. (*19*) also found a minor advantage with SPECT for early images but did not find any advantage in neck imaging when imaging was performed 2–3 hr following injection. Neumann et al. (*22*) showed no difference in sensitivity between early and late SPECT although there was an improved specificity; both SPECT acquisitions were worse than the dual-phase study in this group. Furthermore, these sensitivity and specificity measurements were lower than those reported in other studies using these techniques. There are clear potential advantages with SPECT: it provides better anatomical localization of an adenoma situated in the carotid sheath or within the mediastinum, but the majority of lesions will be detected on planar imaging. SPECT imaging of the mediastinum may determine the location to be within the aortopulmonary window rather than the thymus and thus prevent median sternotomy and encourage a left or a right thoracotomy (*23*). When SPECT is used, a minimum activity of 600 MBq of sestamibi should be administered.

What improvements can be expected in parathyroid imaging? Newer radiopharmaceuticals are under investigation, including ^{99m}Tc-tetrofosmin, which has also been shown to localize in parathyroid glands postinjection (*24*), but the optimal time for imaging has only now been identified (*20*). The initial image was not obtained until 5 min, which is unfortunate since the uptake kinetics into the thyroid and parathyroid would be of interest. However, there is a clear difference in the washout kinetics between sestamibi and tetrofosmin. Tetrofosmin remains in the thyroid, and therefore delayed imaging [similar to the technique described by Taillefer (*18*)] will provide no additional information. Arbab et al. (*25*) suggest that the distribution of thallium, sestamibi and tetrofosmin intracellularly are quite different and may ex-

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plain the slight differences in accumulation in the thyroid and parathyroid tissue. Both sestamibi and tetrofosmin accumulated in their tissue culture cells, but there was a dramatic difference in the uptake of sestamibi in the cells, with large numbers of mitochondria compared with those with reduced numbers, whereas this difference was not marked with tetrofosmin. The residence times were similar between the two agents but the total percentage of the injected dose taken up was far less with tetrofosmin. It is important that any new agents be treated in much the same way as in the early studies with sestamibi and that an optimum imaging time be derived rather than assuming it to be the same as that for sestamibi. A large comparative study of tetrofosmin with sestamibi needs to be performed using the best imaging protocol for each technique. If there is no difference between the techniques, then from an economic point of view, the radiopharmaceutical used for myocardial imaging is likely to be the one favored by any one department.

The use of PET tracers have met with variable success. Neumann et al. (*22,26*) found fluoro-2-deoxy-D-glucose (FDG) to be useful in the detection of parathyroid adenomas; others have not met with this success (*27,28*). The recent article by Neumann et al. (*22*) demonstrated a sensitivity of 94% and a specificity of 78%. The study was in primary operative intervention and has yet to be tested in the reoperative patient. The results compare favorably with sestamibi subtraction scan results, but the dual-phase comparison in this article had poor results, far worse than in most published reports. Carbon-11-methionine is perhaps the more interesting imaging technique and has promise (*29,30*). Limited experience has been obtained, but Sundin et al. (*30*) have demonstrated the ability of the technique to localize adenomas in patients requiring primary and reoperation with greater success than CT or ultrasound examination. The technique is probably best reserved for those patients who have had a failed surgical procedure and no localization with sestamibi.

CONCLUSION

At this time, the radionuclide technique of choice for preoperative localization of abnormal parathyroid tissue would appear to be a subtraction sestamibi scan of the neck, and I believe that this study should be combined with a mediastinal view. This should identify in excess of 90% of parathyroid adenomas. If used in the correct clinical situation, limited neck exploration should be possible as well as the removal of a single gland. For surgical re-exploration, a subtraction scan of the neck, a mediastinal view and a tomogram of the mediastinum should be obtained. Failure to localize a parathyroid adenoma in a patient should be explored with a PET study, with PET methionine scanning as the first choice and FDG as the second choice. This should also be combined with CT or MRI. Localization of an adenoma in the mediastinum on planar sestamibi imaging should be accompanied by an anatomical imaging technique, either CT or MRI. The only possible reason for imaging secondary hyperparathyroidism would be to exclude ectopic glands, and therefore neck and mediastinal images should be obtained. Routine imaging in chronic renal failure, however, is unnecessary.

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