# Ultrastructural Histology Correlates with Results of Thallium-201/Technetium-99m Parathyroid Subtraction Scintigraphy

Dirk Sandrock, Maria J. Merino, Jeffrey A. Norton and Ronald D. Neumann

*Department of Nuclear Medicine, Warren G. Magnuson Clinical Center, Laboratory of Pathology and Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland*

Specimens from 15 scintigraphically true-positive adenomas (golden standard: histology), 15 false-negative adenomas, 15 true-positive hyperplasias, 15 false-negative hyperplasias, 15 true-negative normal glands from patients with hyperparathyroidism, and 15 normal glands from patients without hyperparathyroidism, all selected randomly, were studied. After fixation, sectioning and H and E staining, in all 90 tissues the number of oxyphil, chief, and clear cells was counted in five randomly selected squares (103 × 103 $\mu$m). In 30 tissues, the number of mitochondria per cell was counted in five randomly selected cells from each lesion in transmission electron photomicrographs. Total cell counts in each group and number of chief cells showed no correlation with lesion detectability by scintigraphy. However, true-positive lesions had a significantly higher number of oxyphil cells than false-negative or normal glands. Twenty-one of 30 true-positive lesions had a oxyphil-to-clear cell ratio > 1; in contrast to only two of 30 false-negative lesions and 0 of 30 normal glands ($p < 0.0005$). The number of mitochondria per cell was higher in oxyphil cells in true-positive lesions (adenomas: 155 ± 58, hyperplasias: 55 ± 18) than in chief or clear cells in false-negative or normal lesions (30 ± 15, $p < 0.001$). Our data suggest that the detectability of abnormal parathyroid glands by $^{201}Tl/^{99m}Tc$ subtraction scintigraphy is in part dependent upon the presence of mitochondria-rich oxyphil cells.

**J Nucl Med 1993; 34:24–29**

Parathyroid scintigraphy has been used routinely to detect abnormal parathyroids since the introduction of the $^{201}Tl/^{99m}Tc$ subtraction method of injecting $^{99m}Tc$ first by Ferlin et al. (*1*). Reported sensitivity values, however, range from 38% to 92% (*2–4*); no generally accepted explanation for these differences has been presented (*5*). Patient selection and especially technical modifications of the scintigraphic technique have been discussed. Reversing the order of tracer injection gave higher sensitivity numbers in the hands of some groups (*2,6–9*). Color processing and modifications in the subtraction algorithms also claimed to get better results (*10–12*).

The exact mechanism for $^{201}Tl$ accumulation in abnormal parathyroid tissue is presently unknown. Increased perfusion, functional activity and/or cellularity have been discussed (*2–4,8,13*). On the cellular level, three different uptake mechanisms for $^{201}Tl$ ions have been studied: Na/K ATPase, the $Tl^+$-$Na^+$-$2Cl^-$-cotransport, and the $Ca^{++}$-dependent ion channel (*14,15*) which are partly energy dependent requiring mitochondria. Parathyroid tumors with abundant mitochondria–rich cells should be good targets for thallium scintigraphy if the cellular mitochondria content predicts thallium uptake. Thus, our hypothesis was that we would find differences at the cellular level between parathyroid adenomas and/or hyperplasias detected by $^{201}Tl/^{99m}Tc$ subtraction scintigraphy and those lesions that were missed.

## PATIENT POPULATION AND METHODS

Between 1983 and 1988, 113 consecutive patients (42 men, 71 women, age 52 ± 14 yr) with primary hyperparathyroidism (elevated blood calcium and parathormone (PTH) level, 53 patients with prior parathyroid surgery and recurrent hyperparathyroidism) had $^{201}Tl/^{99m}Tc$ parathyroid subtraction scintigraphy and subsequent surgical exploration at the National Institutes of Health. For subtraction scintigraphy, a modified technique of Ferlin et al. (*1,4*) was used with injection of 74 MBq (2 mCi) $^{99m}Tc$ as pertechnetate. After 15 min, acquisition (4- or 6-mm pinhole and/or high-resolution parallel-hole collimator) of a 5-min image in the technetium window (140 keV ± 10%) was followed by a 5-min (background) image in the thallium window (70 keV ± 10%). Then, after injection of 74 MBq (2 mCi) $^{201}Tl$ as thallous chloride, a dynamic acquisition was done for 30 min in the thallium window. The subsequent processing of these digital images included background correction and subtraction of the technetium image from the corrected and normalized composite thallium image. In cases with patient movement during the thallium acquisition, motion correction was performed by actually shifting the affected frames using a region of interest over the thyroid as the reference, or by using only the frames prior to the patient's movement. The gold standard for our

Received Apr. 27, 1992; revision accepted Aug. 12, 1992.

For reprints or correspondence contact: Dirk Sandrock, MD, Georg-August-University, Department of Nuclear Medicine, Robert-Koch-Str. 40, D-3400 Goettingen, Germany.

comparisons and classification as "true" or "false" "positive" or "negative", respectively, was the surgeon's intraoperative localization of the lesion and the pathologist's tissue diagnosis after neck exploration (*16*).

In this group of 113 patients, 127 benign lesions were found surgically. Of these, scintigraphy detected 48 lesions (38% sensitivity) in 48 patients (30 adenomas, 18 hyperplastic glands). Data from parathyroid angiography (*17*) were available on 19 of these glands.

We excluded from further analysis patients with intrathyroidal and mediastinal lesions and those patients whose lesions had a diameter less than 1 cm. For the histologic review, we used randomly selected specimens from 15 scintigraphically true-positive adenomas, 15 false-negative adenomas, 15 true-positive hyperplasias, and 15 false-negative hyperplasias. We compared these with 15 true-negative glands, meaning they were not visualized by scintigraphy and were considered normal according to the pathologist's diagnosis from patients with primary hyperparathyroidism. In these patients, at least one other abnormal gland presumably responsible for the clinical hyperparathyroidism had been removed during surgery. Finally, we used 15 normal glands from patients without any evidence of calcium or phosphate metabolism disorder. The "normal" patients had neck surgery for thyroid disorders or head and neck tumors not of parathyroidal origin, or the normal glands were obtained by autopsy. The relevant clinical data of the three groups (true-positive, false-negative, true-negative, and normal) are listed in Table 1. Despite frequent modifications of the PTH assays, mean serum levels and normal ranges are matched for the groups "True-Positive" and "False-Negative". The PTH levels of the "Negative/Normal" group are not listed (slightly elevated mean PTH level) because this group contains 15 specimens from (intraoperatively biopsied) "normal" glands from patients *with* hyperparathyroidism (elevated PTH) and 15 glands from patients *without* hyperparathyroidism (normal PTH).

All 90 formalin-fixed tissues were sectioned (10 $\mu$m thickness), hematoxylin and eosin stained, and the number of oxyphil, chief and clear cells [according to the classification of Altenähr (*18*)] in five randomly selected areas of 103 × 103 $\mu$m was counted by two pathologists, blinded to the results of scintigraphy and in a random order. In total, 18,265 cells were scored. Intra- and interobserver variance was found to be <5%. In 30 tissues (five from each group), the number of mitochondria per cell was counted in five randomly selected cells of each lesion from transmission electron photomicrographs (magnification × 15,000). A total of 8,191 mitochondria were counted.

## RESULTS

In a multivariate analysis of the original data (127 lesions in 113 patients) and the data of the randomly selected patients, we found no correlation between scintigraphic detectability and the parameters of age, sex, adenoma (defined as single gland disease) versus hyperplasia (defined as multiple gland disease), anatomic location (upper versus lower, right versus left glands), serum parahormone levels prior to surgery, or prior head/neck surgery versus no prior surgery. The mean greatest diameter of abnormal glands was not significantly different between lesions detected and lesions missed. However, below a diameter of 1 cm, only two of 23 abnormal glands were detected by scintigraphy. This is near the in vivo resolution limit of scintillation cameras employed; and, thus, was our reason to exclude these small glands from further analysis.

There was no correlation between results of contrast angiography and scintigraphy in the 19 lesions costudied; negating significantly enhanced lesion perfusion as the main determining parameter. In these 19 lesions, eight were detected and five were missed by both methods (with no correlation with the parameters listed above). In three patients, lesions were detected by scintigraphy but missed by angiography. In three different patients, however, angiography detected lesions missed by scintigraphy.

No correlation was found between the total cell counts or the absolute number of chief, clear or oxyphil cells and the parameters listed above (all p values > 0.05). There was also no correlation between the scintigraphic detectability and the total cell count or absolute chief cell number ($p > 0.05$). No significant difference in the overall chief

**TABLE 1**
Clinical Data

| Parameter | True-Positive n=30 | False-Negative n=30 | Negative/Normal n=30 |
|---|---|---|---|
| Men:Women | 7:23 | 10:20 | 12:18 |
| Age (mean ± s.d.) | 51 ± 16 | 53 ± 13 | 49 ± 16 |
| Upper glands | 18 | 19 | 15 |
| Lower glands | 12 | 11 | 15 |
| Gland size (cm) | 1.9 ± 1 | 2.0 ± 0.8 | 0.4 ± 0.3 |
| Previous neck surgery | 16 | 11 | 00 |
| No previous neck surgery | 14 | 19 | 30 |
| Serum PTH-level | | | |
| 0.06–0.22 ngeq/ml* | 0.57 ± 0.40 (15) | 0.60 ± 0.27 (9) | not given, see text |
| 0.04–0.18 ngeq/ml* | 0.50 ± 0.21 (6) | 0.38 ± 0.08 (9) | |
| 2–50 fmoleq/ml* | 166.2 ± 209 (4) | 138.0 ± 86 (6) | |
| 0.002–0.05 pmoleq/ml* | 0.11 ± 0.01 (5) | 0.11 ± 0.04 (6) | |

* Normal range. Numbers in parentheses are the glands in each group.

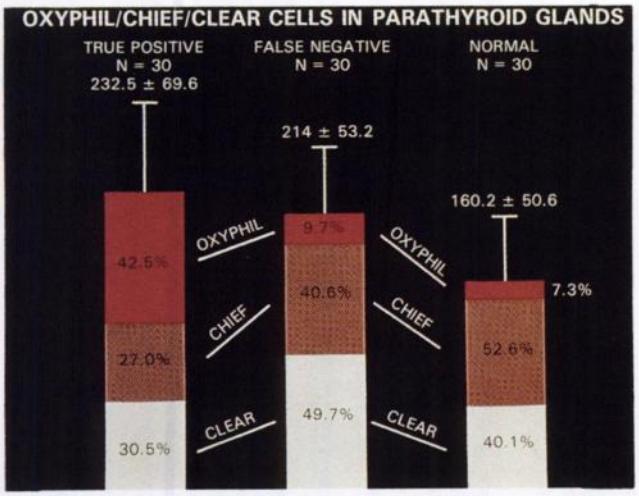


**FIGURE 1.** Overall cell numbers versus parathyroid scintigraphy.

cell number between the three groups was found ($p > 0.05$). The absolute cell numbers (mean ± standard deviation) and the distribution of the different cell classes for the three groups are listed in Figure 1. Abnormal glands detected by scintigraphy had a significantly higher number of oxyphil cells (98.7 ± 88.9) than false-negative (20.7 ± 32.8) or normal glands (11.7 ± 9.9, $p < 0.001$), and a lower number of clear cells (true positive: 70.9 ± 93.4, false-negative: 106 ± 68.2, negative/normal: 64.3 ± 32.9 cells, $p < 0.05$).

A typical example of an adenoma (right lower gland) detected by scintigraphy (true-positive) is shown in Figure 2 (left panel). On the right side of Figure 2, the subtraction scan of a different patient with an adenoma (same location) missed by scintigraphy (false-negative) is shown. Figure 3 gives the light microscopic appearance and Figure 4 the electromicroscopic appearance of the parathyroid tumors

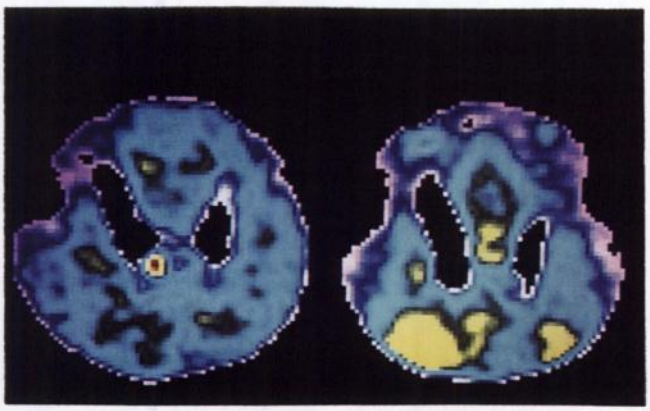

**FIGURE 2.** (Left) Subtraction scintigraphy showing a true-positive adenoma of the right lower gland. (Right) False-negative study (also adenoma of the right lower gland).

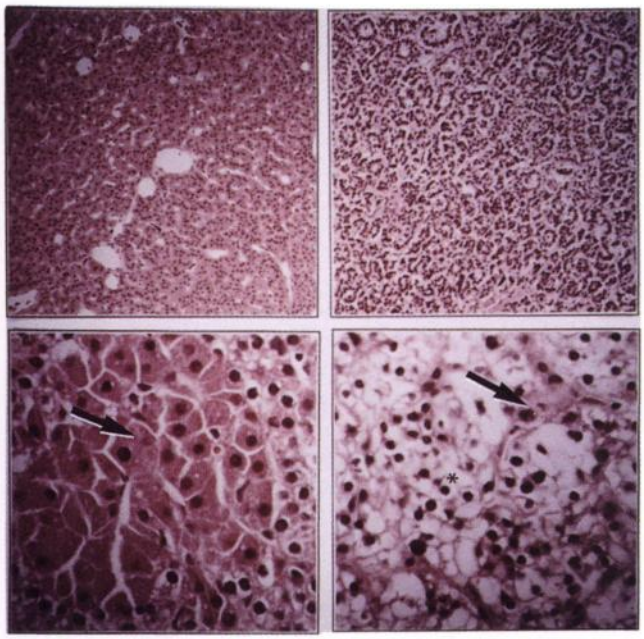

**FIGURE 3.** (Left) H & E stained specimen (low (top) and high (bottom) magnification) of the adenoma seen in Figure 2 (left): multiple oxyphil cells (arrow). (Right) Specimen of the adenoma missed by scintigraphy in Figure 2 (right): chief cells (arrow) and clear cells (*).

(true-positive study on the left, false-negative study on the right).

Overall, 21 of 23 abnormal glands with an oxyphil/clear cell ratio > 1 were detected by scintigraphy. In contrast, 58 of 67 glands with a ratio < 1 were false-negatives or true-negatives or normal (Fig. 5, $p < 0.0005$). Mean ratios were 1.4 (true-positive glands) and 0.2 (true/false-negative or normal glands). There were, however, five true-positive glands with clear cell numbers > 200 and oxyphil cell numbers < 40.

In oxyphil cells of lesions detected by scintigraphy, the number of mitochondria per cell was higher than in chief

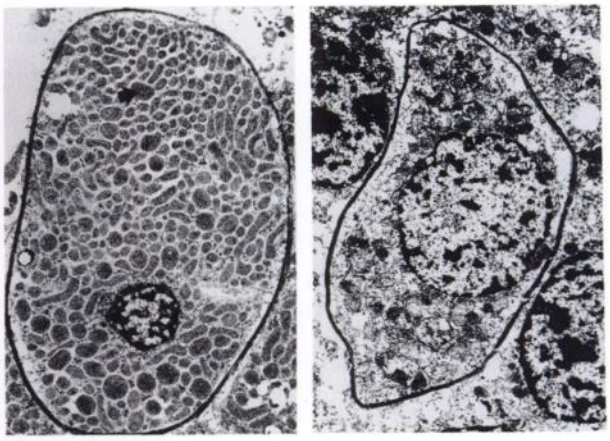

**FIGURE 4.** (Left) Electronmicrography × 16000, oxyphil cell with multiple mitochondria (arrowhead). (Right) Chief cell with lighter appearance (less mitochondria).

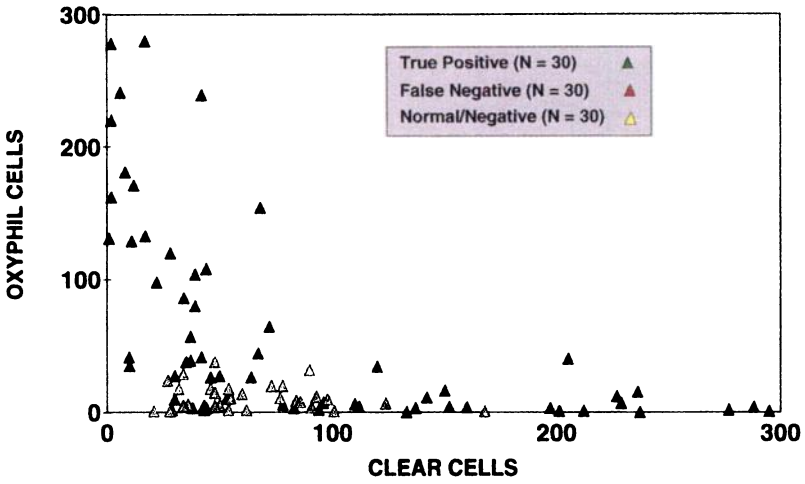


**FIGURE 5.** Oxyphil and clear cells versus parathyroid scintigraphy.

or clear cells of the lesions missed by scintigraphy or in normals (Table 2, $p < 0.001$). Figure 4 (left) shows an oxyphil cell of the scintigraphically detected adenoma; the right side shows a chief cell from the adenoma missed by scintigraphy. The number of mitochondria per cell was not related to age, sex, location or size of the lesion, prior neck surgery, or serum parathormone levels prior to surgery. By combining the results of cell and mitochondria counting and by assuming an equal number of mitochondria in the selected specimen and cells counted as in the others not counted, 22 of 26 glands could be detected by scintigraphy if >6000 mitochondria (number of cells multiplied by number of mitochondria per cell; e.g., oxyphil cells > 60 × 105 mitochondria per cell, or clear cells > 220 × 28 mitochondria per cell) were present in the counted area.

## DISCUSSION

In normal and abnormal parathyroid glands, several different cell types can be found (*18*): chief cells are normally the active endocrine cells; oxyphil cells are slightly larger in size, have a more eosinophilic cytoplasm and are also thought capable of PTH production (*19,20*); and clear cells with foamy, waterclear cytoplasm are fundamentally inactive cells with unknown function. Some authors also include a subclass of transitional oxyphil cells or distinguish different cell steps of a secretory cycle (*18, 21*). No direct correlation between a distinct light microscopic histologic pattern and the PTH level has been reported. An ultrastructural analysis by Altenähr et al. (*22*) found a moderate correlation between the PTH level and volumetric density of mitochondria in chief cell adenomas. They created a morphometric index of weight and volume density of mitochondria, secretory granules, Golgi apparatus and glycogen, which correlated well ($r = 0.95$) with the PTH level. More recently, Juhlin et al. (*14,23–25*) reported reduced expression of a parathyroid cell calcium receptor which may play an important role in hyperparathyroidism. These authors produced a series of monoclonal antibodies that stain the calcium receptor antigens in the cell membrane of normal parathyroid cells. At least one of these antibodies can also interfere with the receptor's function in the sensing and gating of calcium ion traffic. In frozen tissue immunohistochemistry studies, these authors showed reduced staining of adenomatous and hyperplastic parathyroid tissue, suggesting that hyperparathyroidism of either type is associated with reduced expression of this calcium receptor in pathologic parathyroid tissues. We found a correlation between the number of cell mitochondria and positive scintigraphy, but not between cell type, PTH level and/or overall cellularity in general. This can be explained by the fact that the number of chief cells, commonly said to be the endocrine active cells, was not significantly different between the groups with true-positive or false-negative scintigraphy. There was, on the other hand, a small number of glands with a very high clear cell number (and therefore a high number of mitochondria) correctly localized by scintigraphy suggesting that the overall number of mitochondria may play a role for the detectability.

No model for uptake of thallium or, more recently, for $^{99m}$Tc-sestamibi (*26*) in parathyroid (tumor) cells has been

**TABLE 2**
Thallium-201/Technetium-99m Subtraction Scintigraphy Versus Mitochondria/Cell (mean ± s.d.)

| | Subtraction scintigraphy | | | |
|---|---|---|---|---|
| | True-Positive | False-Negative | | |
| Adenomas | 155 ± 58* | 27 ± 15* | Negative | 30 ± 16* |
| Hyperplasias | 55 ± 18* | 29 ± 11* | Normal | 32 ± 18* |

* Five cells in each group.

reported. By analogy to cardiac myocytes and to other tumor cells, one can expect at least three different cellular uptake mechanisms for $^{201}Tl$ ions: Na/K ATPase, the $Tl^+$-$Na^+$-$2Cl^-$-cotransport, and the $Ca^{++}$-dependent ion channel (*14,15*). The first two mechanisms are known to be energy dependent and therefore require functioning mitochondria. That may explain the higher likelihood for mitochondria-rich tissues to give a positive result by $^{201}Tl$ scintigraphy as observed in our study. The third mechanism's need for energy is not yet known. Other tumors with abundant oxyphil (also called eosinophilic) cells should be good targets for thallium scintigraphy if the cellular mitochondria content predicts thallium uptake. In fact, Mueller et al. (*27*) observed the best scanning results in patients with eosinophilic cell tumors of the thyroid compared with mixed eosinophilic/follicular or papillary tumors. We do not yet have data from an immunohistologic exam of our patients' parathyroid lesions for the relative presence of the calcium receptor recognized by the monoclonal antibodies of Juhlin et al. (*25*). But the near absence of this receptor on the oxyphil-rich lesions which were detected best in our scintigraphy results make this calcium sensor/receptor unlikely as the mechanism for thallium uptake.

Could differences in perfusion or vascularization of the parathyroid tumors alone explain our results? The absence of a positive correlation between angiography and the results of scintigraphy implies little influence of gross blood flow on $^{201}Tl/^{99m}Tc$ scan results. Sufficient perfusion of the abnormal gland is, of course, a requirement for radionuclide transport to the cell. Angiographic studies of parathyroid adenomas demonstrated an usually homogenous staining and a blood supply by a single feeding artery (*17*).

Tumor size clearly affects the result of parathyroid scintigraphy because of the resolution limits in vivo scintigraphy by gamma cameras. Some authors have found differences in detectability between large and small glands; "small" generally defined as weight below 500–620 mg (*6,28,29*). In other studies, however, no significant difference in weight or mean diameter was found between glands detected and missed by scintigraphy (*7,30,31*). In order to avoid the controversial discussion about the influence of size on cell counts and lower limits of resolution in scintigraphy, we excluded small glands <1 cm from our study. We also excluded intrathyroidal and mediastinal glands, because sensitivity numbers in these locations have been reported to range from 0% (*32*) or 100% (*3*); and we wanted our review to be independent of the "location" parameter. Our two scintigraphic groups with 30 patients each (true-positive, false-negative) also were matched for adenoma versus hyperplasia. This distinction was also previously reported to affect the sensitivity of scintigraphy; half of the studies with more than 20 patients (*28,29,33, 34*) detected two times more adenomas than hyperplasias while the other half (*2,4,7,32*) found no difference. Finally, different acquisition protocols may also affect the results of scintigraphy (*10–12*). Some groups reversing the order of tracer injection ($^{201}Tl$ first) reported high sensitivities for this technique (*2,6–9*). A recent study, however, carefully analyzing physical and physiological behavior of $^{201}Tl$ and $^{99m}Tc$ in phantom and patient studies, did not find any beneficial effect injecting $^{201}Tl$ first (*12*). Large differences in sensitivity numbers are therefore probably better explained by patient selection. For example, our low overall sensitivity at NIH is probably due to a high number of patients with more complicated recurrent hyperparathyroidism and perhaps unsuccessful outside diagnostic studies. A meticulous scintigraphic procedure should be beneficial, especially for the detection of small glands.

In conclusion, the detectability of parathyroid adenomas or hyperplasias (with a diameter >1 cm) in patients with primary hyperparathyroidism by $^{201}Tl/^{99m}Tc$ subtraction scintigraphy may depend upon the presence of mitochondria-rich oxyphil cells within the abnormal parathyroid tissue.

## REFERENCES


1. Ferlin G, Borsato N, Perelli R, et al. Technetium-thallium subtraction scan: a new method in the preoperative localization of parathyroid enlargement. *Eur J Nucl Med* 1981;6:A12.
2. Okerlund MD, Sheldon K, Corpuz S, et al. A new method with high sensitivity and specificity for localization of abnormal parathyroid glands. *Ann Surg* 1984;200:381–388.
3. Basarab RM, Manni A, Harrison TS. Dual isotope subtraction parathyroid scintigraphy in the preoperative evaluation of suspect hyperparathyroidism. *Clin Nucl Med* 1985;10:300–314.
4. Sandrock D, Merino MJ, Norton JA, Neumann RD. Parathyroid imaging by Tc/Tl scintigraphy. *Eur J Nucl Med* 1990;16:607–613.
5. Coakley AJ. Parathyroid localization—how and when? *Eur J Nucl Med* 1991;18:151–152.
6. Winzelberg GG, Hydowitz JD, O'Hara KR, et al. Parathyroid adenomas evaluated by Tl-201/Tc-99m pertechnetate subtraction scintigraphy and high-resolution ultrasonography. *Radiology* 1985;155:231–235.
7. Gooding GAW, Okerlund MD, Stark DD, Clark O. Parathyroid imaging: comparison of double-tracer (Tl-201, Tc-99m) scintigraphy and high resolution US. *Radiology* 1986;161:57–64.
8. Krubsack AJ, Wilson SD, Lawson TL, Collier BD, Hellman RS, Isitman AT. Prospective comparison of radionuclide, computed tomographic, and sonographic localization of parathyroid tumors. *World J Surg* 1986;10: 579–585.
9. Park CH, Intenzo C, Cohn HE. Dual tracer imaging for localization of parathyroid lesions. *Clin Nucl Med* 1986;11:237–241.
10. Liehn J-C, Amico S, Delisle M-J, Flament J-B. Improvement of parathyroid Tl-Tc scintigraphy by using a new image subtraction method. *Eur J Nucl Med* 1988;14:184–189.
11. Blue PW, Crawford GC, Dydek GJ. Parathyroid subtraction imaging—pitfalls in diagnosis. *Clin Nucl Med* 1989;14:47–57.
12. Sandrock D, Dunham RG, Neumann RD. Simultaneous dual energy acquisition for $^{201}Tl/^{99}Tc^m$ parathyroid subtraction scintigraphy: physical and physiological considerations. *Nucl Med Commun* 1990;11:503–510.
13. Ferlin G, Borsato N, Camerani M, Conte N, Zotti D. New perspectives in localizing enlarged parathyroids by technetium thallium subtraction scan. *J Nucl Med* 1983;24:438–441.
14. Nygren P, Gylfe E, Larsson R, et al. Modulation of the $Ca^{2+}$-sensing function of parathyroid cells in vitro and hyperparathyroidism. *Bioch Biophys Acta* 1988;968:253–260.
15. Sessler MJ, Geck P, Maul FD, Hör G, Munz LD. New aspects of cellular thallium uptake: $Tl^+$-$Na^+$-$2Cl^-$ cotransport is the central mechanism of ion uptake. *Nucl Med* 1986;24–27.
16. Norton JA. Reoperative parathyroid surgery: indication, intraoperative decision-making and results. In: Farthmann EH, ed. *Progress in surgery, volume 18*. Basel: Karger; 1986:133–145.
17. Doppmann JL. Parathyroid localization: arteriography and venous sampling. *Radiol Clin North Am* 1976;14:163–188.

18. Altenähr E. The parathyroid glands. In: Johannessen JV, ed. *Electron microscopy in human medicine, volume 10.* New York: McGraw-Hill, 1981:111–146.
19. Ordonez NG, Ibanez ML, Mackay B, Samaan NA, Hickey RC. Functioning oxyphil cell adenomas of parathyroid gland: immunoperoxidase evidence of hormonal activity in oxyphil cells. *Am J Clin Pathol* 1982;78: 681–689.
20. Wolpert HR, Vickery AL, Wang CA. Functioning oxyphil cell adenomas of the parathyroid gland. A study of 15 cases. *Am J Surg Path* 1989;13: 500–504.
21. Shannon WA, Roth SI. An ultrastructural study of acid phosphatase activity in normal, adenomatous and hyperplastic (chief cell type) human parathyroid glands. *Am J Path* 1974;77:493–506.
22. Altenähr E, Arps H, Montz R, Dorn G. Quantitative ultrastructural and radioimmunologic assessment of parathyroid gland activity in primary hyperparathyroidism. *Lab Invest* 1979;41:303–312.
23. Juhlin C, Johannson H, Holmdahl R, et al. Monoclonal antiparathyroid antibodies interfering with a $Ca^{2+}$-sensor of human parathyroid cells. *Biochem Biophys Research Comm* 1987;143:570–574.
24. Juhlin C, Klareskog L, Nygren P, et al. Hyperparathyroidism is associated with reduced expression of a parathyroid calcium receptor mechanism defined by monoclonal antiparathyroid antibodies. *Endocrinology* 1988; 122:2999–3001.
25. Juhlin C, Rastad J, Klareskog L, Grimelius L, Akerstrom G. Parathyroid histology and cytology with monoclonal antibodies recognizing calcium sensor of parathyroid cells. *Am J Path* 1989;135:321–328.
26. Coakley AJ, Kettle AG, Wells CP, O'Doherty MJ, Collins REC. $^{99m}$Tc sestamibi—a new agent for parathyroid imaging. *Nucl Med Commun* 1989; 10:791–794.
27. Müller SP, Guth-Tugelidis B, Piotrowski B, Farahati J, Reiners C. Tl-201 scintigraphy in the follow-up of eosinophilic thyroid carcinoma. *J Nucl Med* 1990;31:767.
28. Ferguson WR, Laird JD, Russell CFJ. Experience with technetium-thallium subtraction imaging of parathyroid lesions [Abstract]. *J Nucl Med* 1984;25:P19.
29. Percival RC, Blake GM, Urwin GH, Talbot CH, Williams JL, Kanis JA. Assessment of thallium-pertechnetate subtraction scintigraphy in hyperparathyroidism. *Br J Radiol* 1985;58:131–135.
30. Skibber JM, Reynolds JC, Spiegel AM, et al. Computerized technetium/thallium scans and parathyroid reoperation. *Surgery* 1985;98:1077–1082.
31. Clark OH, Okerlund MD, Moss AA, et al. Localization studies in patients with persistent or recurrent hyperparathyroidism. *Surgery* 1985;98: 1083–1094.
32. Miller DL, Doppman JL, Shawker TH, et al. Localization of parathyroid adenomas in patients who have undergone surgery: I. Noninvasive imaging methods. *Radiology* 1987;162:133–137.
33. Young AE, Gaunt JI, Croft DN, Collins REC, Wells CP, Coakley AJ. Location of parathyroid adenomas by thallium-201 and technetium-99m subtraction scanning. *Br Med J* 1983;286:1384–1386.
34. MacFarlane SD, Hanelin LG, Taft DA, Ryan JA Jr, Fredlund PN. Localization of abnormal parathyroid glands using thallium-201. *Am J Surg* 1984;148:7–12.