Comparison of Technetium-99m and Iodine-123 Imaging of Thyroid Nodules: Correlation with Pathologic Findings

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Three hundred and sixteen patients with solitary or dominant thyroid nodules were imaged both with technetium-99m- (99mTc) pertechnetate and iodine-123 (123I). The images were independently interpreted by five readers. lodine scans were preferred, but differences were small and in 27%-58% of the cases there was no difference in quality between the two radionuclides. Discrepancies between ^{99m}Tc and ¹²³I images were found in 5%-8% of cases, twice as often in multinodular goiters as in single nodules. Cytologic/histologic examination was performed on all nodules but no correlation was found between the pathology and the type of discrepancy. Twelve carcinomas were found (4%) but none in nodules showing a discrepancy. There was great variation among the observers about the preference for radionuclides and about the existence or type of discrepancies. The slightly better overall quality of ¹²³I scans is probably not of diagnostic significance and does not justify the routine use of 123 instead of 99mTc. Routine reimaging of 99mTc hot nodules with radioiodine for cancer detection does not appear to be necessary.

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Several systematic comparative studies using technetium-99m- (99m Tc) pertechnetate and radioiodine (131 I, 125 I, 123 I) have been performed in attempts to clarify their respective roles in thyroid imaging. Some showed definite superiority of radioiodine (1-4), but other authors found the results so similar that they were not able to choose one radionuclide as better (5-11). There is similar disagreement about the clinical significance of discrepant scan findings. The controversy becomes even more complex if economic factors are considered. Technetium is inexpensive and readily

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available from on-site generators. Iodine-123, however, is cyclotron-produced, considerably more expensive, and, with a 13-hr physical half-life, presents significant logistical problems. Finally, the issue is further complicated by the fact that the value of thyroid scanning for cancer detection has been challenged and its clinical usefulness questioned (12,13)

Since the introduction of [99m Tc]pertechnetate for routine thyroid imaging, a number of cases of thyroid carcinoma appearing scintigraphically hot with [99m Tc] pertechnetate and cold with radioiodine have been rather dramatically reported (14-21). The result of these findings has been the frequent recommendation that nodules appearing hot with pertechnetate should be re-imaged with an isotope of iodine in order that the diagnosis of thyroid malignancy is not overlooked. However, other case reports (22-29) and comparative studies of the two radionuclides (9,30,31) indicated that benign thyroid lesions are the more likely cause of discrepant findings. Thyroid carcinoma has also been found with another, less frequent type of discrepancy, increased iodine uptake relative to pertechnetate (32).

The Bureau of Radiological Health (BRH), Food and Drug Administration (FDA), being interested in reduction of radiation dose delivered to the organs during nuclear imaging procedures, appointed an Advisory Task Force on Short-Lived Radionuclides for Medical Applications. This group recommended that comparative studies of [99mTc]pertechnetate and 123I as imaging agents for nodular goiter be undertaken to clarify differences between these two radionuclides. The BRH designed a comprehensive study of this issue using these radiopharmaceuticals, including cytologic or histologic follow-up (33).

MATERIALS AND METHODS

The study was conducted in the University Hospital "Dr. Mladen Stojanović" in Zagreb, Yugoslavia according to a protocol developed by the BRH FDA's Nuclear Medicine

Laboratory in collaboration with the University of Cincinnati Medical Center.

Entry into the study was limited to patients with a solitary or dominant nodule on palpation of the thyroid, which was performed by two experienced thyroid specialists prior to imaging. Three hundred and sixteen patients (283 women and 33 men, mean age 42 yr) came from the northwest part of Yugoslavia, which, until recently, was an area of mild endemic goiter. No patient had a history of childhood neck irradiation. The procedure and purpose of the study were explained and individual signed consent was obtained. Controls were 20 clinically and biochemically euthyroid women, mean age 35 with normal thyroids on palpation and no history of thyroid disease.

The initial image was obtained 20 to 30 min after an injection of 185 MBq of [99mTc]pertechnetate. Two-hundred thousand counts were collected using the 140-keV photopeak and 20% window on a scintillation camera (GE 400T, Milwaukee, WI) with a 5-mm pinhole collimator. Images were recorded on x-ray film. A skin-to-aperture distance was recorded (in the majority of cases it was 7 cm). An anterior view with a marker on the thyroid cartilage and suprasternal notch also was obtained. The image was repeated with additional markers on any palpable nodules. Oblique views at 45° were obtained in all patients.

Within 1 wk, the patients were again studied, using an oral dose of 14.8-18.5 MBq of 123 I. This preparation (provided by Mallinckrodt, Vienna, Austria) was free of 124 I and had < 2% contamination with 125 I. Patients had only liquids for 4 hr prior to administration of activity. Images and uptakes were obtained at 1 hr and 20-24 hr after administration of 123 I. The same instrument, imaging view, and distance was used for both radionuclides. Images with 123 I were obtained with a total of 100,000 counts or an imaging time of 10 min, whichever came first, using the 159-keV photopeak and 20% window.

Cytologic examinations of all palpable nodules were performed subsequent to imaging studies. Sixty patients, who were subsequently treated surgically, had histologic findings available. The locations of the abnormalities found on palpation and areas biopsied were marked on anatomic drawings of the thyroid and correlation with scan findings was established by one of the physicians who had originally examined the patients.

In addition to the medical history and physical examination, laboratory tests were obtained including serum thyroxine, triiodothyronine, thyrotropin, TRH test, antithyroid antibodies, and ultrasound for the majority of patients. Hyperthyroidism was diagnosed in 18 patients, the rest were euthyroid.

Images were read independently by five experienced readers (DVB, RSB, ZL, WPL, and ELS) qualified in nuclear medicine image analysis who were not familiar with the patients or images. The images were presented to them without medical history, laboratory, cyto-histologic or technical data. All of the readers routinely use [99mTc]pertechnetate as a thyroid imaging agent in their institutions. The observations of the five readers were recorded on a form, which required categorized notations of: image quality (on a five-level scale from excellent to unusable); image thyroid size; image thyroid symmetry; image distribution of activity, if localized; location of irregularity; image interpretation (on a five-level scale from

definitely normal to definitely abnormal); impression (normal, multinodular goiter, cold nodule, hot nodule, and diffuse goiter); discrepant area; comparison of ^{99m}Tc and ¹²³I scan; and comparison of ¹²³I (1-hr) and ¹²³I (20-hr) scans.

Each patient had three films, one each for [99mTc]pertechnetate, ¹²³I at 1 hr, and ¹²³I at 20–24 hr. Each film contained four scans:

- Anterior view with a marker on thyroid cartilage and suprasternal notch.
- 2. Same view with a marker on the nodule.
- 3. Right oblique view.
- 4. Left oblique view.

The 1,008 films (three films for each of the 336 subjects: 316 patients and 20 controls) were coded, randomized, and grouped into five batches. In addition, for the first trial, the scans with the marker on the nodule were masked. It consisted of two readings, and was double blinded with respect to radionuclide and patient. Each reader read one batch (201 films) in the first reading. In the second reading, the readers changed batches so that each film was seen by 2 different readers constituting one pair. Five batches were read by five different pairs of readers, as follows: AB, CA, BD, EC, DE.

In the second trial, the films were unmasked and each reader read the same batch as in the first reading.

The third trial consisted of direct (simultaneous) comparison of the three films of each patient (^{99m}Tc, ¹²³I 1-hr, ¹²³I 20-hr). For this trial, the films were decoded, unmasked, and reorganized, and identified by patient and radionuclide.

There was no attempt to impose rules of interpretation or criteria evaluation on the readers because it was deemed important that each reader represent his individual experience and attitude. If rules of interpretation had been imposed, any conclusion of the study might have been less applicable to general (usual) clinical practice.

Statistical Methods

The data from the image reading forms for all 336 patients and controls were keyed with verification into a permanent computer file. The study was organized to follow a balanced incomplete block design (34). This method permitted the five readers to read only 40% of the films to complete the study.

Frequency tabulations and percentages were obtained by creating contingency tables. The amount of association represented by the data contained in the tables was computed by chi-square analysis using the method of Cramer (35). The presence of significant heterogeneity among readers for these tabulations was determined by log-linear model analyses.

The data for image quality and image interpretation were analyzed by variance analysis. The values that were not available due to the design of the study were estimated by the least squares method for these entries.

RESULTS

When [99mTc]pertechnetate and ¹²³I scans were evaluated simultaneously for each patient (Trial 3) there was almost general agreement that ¹²³I scans were "better" than ^{99m}Tc scans (Table 1). The number of cases reported as showing no difference was large (27%–

TABLE 1
Comparison of [99mTc]Pertechnetate and 123 I Scans

| Reader | ^{99m} Tc better than ¹²³ I, % of cases | than 99mTc, % of cases | No difference % of cases | |
|--------|--|--------------------------|-----------------------------|---------------------|
| Α | 27 | 38 | 35 | I > Tc |
| В | 38 | 35 | 27 | Tc > l |
| С | 2 | 40 | 58 | $I > Tc^{\dagger}$ |
| D | 2 | 51 | 47 | $I > Tc^{\dagger}$ |
| Ε | 14 | 41 | 45 | I > Tc [†] |

Nonsignificant difference.

58%). Among the reasons mentioned for preference of one radionuclide were: lower background, sharper edges resulting in better contrast, and absence of esophageal activity.

In a comparison of 1-hr and 20-hr ¹²³I scans, the 20-hr ¹²³I scans were preferred in a significant number of instances by all observers, but in 35%-58% of cases no difference was indicated.

Association of image interpretation with the comparison of [99mTc]pertechnetate and 123I scans for all readers combined is summarized in Table 2. For the majority of glands judged as normal, no difference between 99mTc and ¹²³I scans was found. However, for abnormal glands it was apparently easier to choose one radionuclide as better, and the ¹²³I images were generally preferred, although there remained a large number of cases in which no difference was indicated. Comparison of diagnostic "impression" for scans made with the two radionuclides (Table 3) shows a preference for ¹²³I in all categories, although there are large numbers of cases where no difference was noted, especially for glands considered "normal" or a "diffuse goiter." In all categories of image interpretation and impression, 20-hr ¹²³I images were considered better than 1-hr ¹²³I images but with a large percentage of cases reported as showing no difference.

Independent evaluation of each film based on image quality produced a ranking of preference for radio-

TABLE 2
Association of Image Interpretation with the Comparison of 99mTc and 123I Scans

| Image interpretation | ^{99m} Tc better than ¹²³ I, % of cases | than 99mTc, % of cases | No difference % of cases |
|-------------------------|--|--------------------------|-----------------------------|
| Definitely normal | 0 | 14 | 86 |
| Probably normal | 3 | 21 | 76 |
| Indeterminate | 4 | 22 | 74 |
| Probably abnormal | 23 | 36 | 41 |
| Definitely abnormal | 19 | 46 | 35 |

TABLE 3Association of Diagnostic Impression with the Comparison of ^{99m}Tc and ¹²³I Scans

| Impression | ^{99m} Tc better than ¹²³ I, % of cases | 123 better than 99mTc, % of cases | No difference % of cases |
|---------------------|--|--|-----------------------------|
| Normal | 3 | 16 | 81 |
| Multinodular goiter | 18 | 50 | 32 |
| Cold nodule | 19 | 42 | 39 |
| Hot nodule | 23 | 53 | 24 |
| Diffuse goiter | 9 | 34 | 57 |

nuclides. The reading was double blinded with respect to radionuclides and patient identification and with a mask obscuring scans showing location of the palpable nodules. All readers preferred 20-hr ¹²³I scans to [^{99m}Tc] pertechnetate scans; four readers also preferred 1-hr ¹²³I scans over [^{99m}Tc]pertechnetate scans. The same comparison with unmasked films demonstrated that knowing the location of the nodule did not make a substantial change in the preference for radionuclide.

Interobserver agreement did not differ significantly for ^{99m}Tc and ¹²³I scans in categories of image quality, image interpretation, and diagnostic impression. There was no correlation between uptake values (32%–55% at 20 hr) and preference for radionuclides. Correlation of location of palpable nodules with location of scan abnormality did not show significant difference between ^{99m}Tc and ¹²³I images.

Evaluation of categories of diagnostic impression based on ^{99m}Tc and ¹²³I scintigraphy was done blindly without knowledge of location of nodule. There was great variation among the readers, but every reader found the lowest percentage of normals and the highest percentage of multinodular goiter on ^{99m}Tc scintigraphy. This observation is in accordance with the finding that ^{99m}Tc images of abnormal glands were more likely to be classified as abnormal than were ¹²³I scans (on a scale from definitely normal to definitely abnormal). Both radionuclides were similar in demonstrating cold and hot nodules.

Because of the crossover nature of the trial, which precluded each reader from seeing all images, it is only possible to estimate the overall frequency of discrepancies at 5%-8%. Of the discrepancies reported, there was agreement about the type of discrepancy between two readers who saw the same cases in only one-fifth of these instances. In as many as two-thirds of the discrepant cases, there was disagreement about the very existence of a discrepancy. Some readers were more likely to find discrepancies than others—but most often in different images. The most frequent type of discrepancy was technetium, normal or cold with iodine, cold or normal. Technetium hot/iodine cold was somewhat less frequent. In one-sixth of the cases, discrepant scan

[†] Significant difference.

findings did not correspond to the palpated nodule. Discrepancies were found twice as often in multinodular than in solitary nodule goiter.

Examples of the types of discrepancies found are shown in Figures 1 through 3.

Table 4 lists cytologic or histologic findings of lesions with discrepant scan findings. There is no correlation between the observed type of discrepancy and cytology or histology of the nodule. There were 12 carcinomas found in the study, but none of them was found in the nodules showing discrepancy. Two cancers were found in the glands with discrepant images but did not correlate with scintigraphic discrepancy.

In two patients with technetium hot/iodine cold discrepancy, the TRH test was normal. In three patients with technetium hot/iodine normal discrepancy, TRH tests were: normal, blunted, and flat. In two patients with iodine hot/technetium normal discrepancy, TRH test was normal as well as in one patient with iodine hot/technetium cold discrepancy.

DISCUSSION

The overall quality of ¹²³I thyroid scans has been judged better than ^{99m}Tc scans in some reported comparative studies (1,4), although the clinical significance of such findings has not been conclusively demonstrated. In the present study, all readers showed a general preference for ¹²³I, but the differences between iodine and technetium images were small and could not be considered to be of diagnostic importance. In a large proportion of cases (27%–58%) scans with both radionuclides were judged by the different readers to be equal in quality. Differences between average scores for quality of ^{99m}Tc and ¹²³I scans were very small, but the large number of cases contributed to their significance.

The major reasons for preference of ¹²³I in this and other studies were lower background and the greater clarity of the picture, but images obtained with both radionuclides yielded essentially the same information.

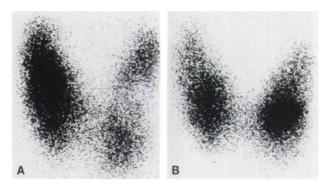


FIGURE 2Palpable nodule in the left lobe. (A) Nonfunctioning region on [99mTc]pertechnetate scan. (B) Increased uptake in the nodule on ¹²³I scan. Histology: follicular adenoma

Only two pairs of readers in our study had statistically significant agreement in preference for one radionuclide while three did not. There seemed a greater variation among the observers than between the radionuclides.

The 20-hr ¹²³I scans were preferred in our study to 1-hr scans, but the differences were small and there were a large number of cases in which no difference was noted. The relatively high uptake at 1 hr in our patients (5%-15%) and large dose (14.8-18.5 MBq) may account in part for the good quality of early ¹²³I scans, which were satisfactory for clinical purposes. To obtain 100,000 counts with ¹²³I at 1 and 20 hr required < 10 min in almost all our patients. Ryo et al. (11) found 1-hr ¹²³I scans of poor quality. The 4-hr and 24-hr scans with ¹²³I were found to be of equal diagnostic value (36). Our study indicates the possibility of obtaining satisfactory ¹²³I images in even shorter time if uptake is high. Normal values are still rather high in Yugoslavia (25%-45% at 24 hr).

The prevalence of reported discrepancies between 99m Tc and radioiodine scintigrams varies (1,2,3,7,8, 10,11,37) and probably depends on many factors: se-

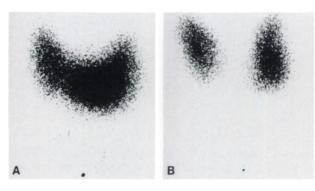


FIGURE 1Palpable nodule in the isthmus was about equal in function to the remainder of the gland on [99mTc]pertechnetate scan (A) and cold on 123I scan (B). Histology: follicular adenoma

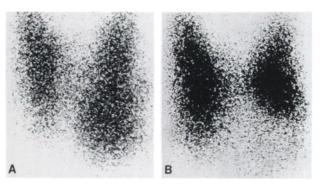


FIGURE 3Palpable nodule in the lower part of the left lobe corresponded to an area of apparently normal [99mTc]pertechnetate concentration (A) but absent 123 concentration (B). Histology: follicular adenoma

TABLE 4Discrepant Images: Cytologic or Histologic Findings

| | Number | |
|---------------------------|----------|--|
| Type of discrepancy | of cases | Cytology or histology |
| 99mTc hot/123 normal | 2 | Colloid goiter |
| | 1 | Hemorrhagic cyst [†] |
| | 1 | Severe acute inflammation [†] |
| | 1 | Colloid goiter with cyst |
| 99mTc hot/123l cold | 1 | Colloid goiter [†] |
| • | 1 | Hemorrhagic cyst [†] |
| | 1 | Lymphocytic thyroiditis† |
| | 1 | Colloid goiter with cyst |
| | 2 | Colloid goiter |
| 99mTc normal/123l cold | 4 | Colloid goiter [†] |
| • | 1 | Normal thyroid† |
| | 1 | Lymphocytic thyroiditis |
| | 1 | Follicular adenoma |
| 99mTc normal/123l hot | 1 | Follicular adenoma |
| 99mTc cold/123 normal | 4 | Colloid goiter [†] |
| · | 3 | Hemorrhagic cyst [†] |
| | 2 | Follicular adenoma |
| | 1 | Follicular neoplasm [†] |
| 99mTc cold/123I hot | 1 | Colloid goiter [†] |
| · | 1 | Hemorrhagic cyst [†] |
| | 1 | Follicular adenoma |
| * Histology. † Cytology. | | |

lection of patients, the imaging procedures (timing of the images, scanning equipment), use of 131 or 123 I, criteria used for evaluating images, etc. Usually 24-hr radioiodine images were reported, although some authors used earlier times, even 20 min after i.v. administration (4). In some studies, a large proportion of the subjects had no thyroid abnormality or had Graves' disease (1,3) and a low frequency of discrepancy was found. This is in contrast to the studies where a high proportion of the patient population had nodular or multinodular goiter (2,11,20). It appears in all studies that the patients with multinodular goiter have the highest frequency of discrepancy. In the present study, patients were selected for inclusion because of finding on palpation of a solitary or dominant nodule with presumed greater risk of malignancy. In addition, image evaluation and precise correlation of the pathologic or cytologic findings with scan abnormalities in multinodular goiter is usually difficult. However, a number of multinodular goiters were inevitably included. The relatively low frequency of discrepancies (5%-8%) in the present study, is probably due to patient selection. Discrepancies were found twice as often in multinodular image patterns than in images showing a solitary abnormality.

The radioiodine scan and technetium scan of auton-

omous nodules may have different degrees of function seen in the relatively suppressed normal thyroid tissue (38). One autonomous nodule with significantly better function in the suppressed tissue with 123 I as compared to 99mTc was found in the present study. In some patients with scan discrepancy and hot nodule seen only with one radionuclide, a TRH test was performed. In one-third of the cases with positive [99mTc]pertechnetate uptake and negative 123I uptake, the TRH test was abnormal (flat or blunted). In all cases with a positive ¹²³I uptake and negative [^{99m}Tc]pertechnetate uptake, the TRH test was normal. Although the most sensitive study (the suppression test) was not performed, the results suggest that not all nodules which are hot only with one radionuclide show autonomous function. There seems a greater probability of autonomy in nodules appearing hot only with 99mTc than in nodules appearing hot only with 123I but the number of such cases was rather small.

In the present study, the 99mTc images were more likely to be described as abnormal and classified as representing multinodular goiters than ¹²³I scans. The pathophysiology and significance of such findings has not been clarified. In 1983, Ryo et al. reported that more lesions with increased uptake can be demonstrated on 99mTc scintigraphy than on 123I scintigraphy (11). They concluded that the sensitivity of 99mTc scanning in detecting lesions is higher than that of ¹²³I. In our study, the frequency of that kind of discrepancy, however, was not high. The use of ultrasound is probably desirable to assist in establishing the diagnosis in such situations. Occurrence of the multinodular image pattern in a palpatory uninodular goiter is not uncommon (11,39). The value of finding multiple scan abnormalities in palpatory uninodular goiter has been questioned. Such findings may make cancer in the nodule less likely.

Few discrepancies between 1-hr and 20-hr ¹²³I scans were noted, although there were some variations in the degree of function in the present study. In two cases, 1-hr ¹²³I scans were more similar to ^{99m}Tc than to the 20-hr ¹²³I scans. The quantitative differences between areas of normal and deficient organic binding may increase with time (9).

Oblique views generally were felt to minimize the incidence of discrepancies in the present study. On rare occasions, however, oblique views introduced a discrepancy which was not seen on the anterior view. In multinodular goiters, different areas sometimes showed different kinds of discrepancies.

Cytologic and histologic examinations of nodules with discrepant images have revealed a variety of lesions (9,14-16,19,22,26,27,29,30). The lack of correlation reported in the literature between the type of discrepancy observed and histology of the nodule is confirmed in the present study. Microscopic foci of carcinoma that

could not be the cause of the discrepant scan finding have been reported (30). In the present study, a similar case of lack of correspondence of carcinoma and scan discrepancy in the same gland was found.

The most frequent explanation for positive 99mTc uptake and negative radioiodine uptake has been that these nodules retain the ability to concentrate monovalent anions (pertechnetate and iodine) but have lost the ability to organify iodine (23), allowing it to be readily discharged. Some lesions which are hot on 99mTc scan and not visualized on radioiodine scan may be autonomous and have a rapid iodine turnover in the nodule (24). In the present study, no malignancy was found in patients with 99mTc positive and radioiodine negative scans. Detailed review of the literature suggests that the frequency of thyroid carcinoma with such discrepancy is very low. In addition to four case reports (14,16,17,18) in three studies comparing the two radionuclides (15,20,21), only three cases were reported. In all of these studies, 131 was used for radioiodine scintigraphy with the relatively poor resolution of the rectilinear scans in some studies. In one study, the unusually high number of discrepancies caused by cancers particularly follicular (twice as many as all cases reported in the literature) remains unexplained (19). These cases, however, heavily influence literature recommendations for managing discrepant nodules.

Although these and similar findings are frequently quoted as the basis for the recommendation that nodules with positive [99mTc]pertechnetate uptake be reimaged with radioiodine, this may not be optimum strategy for evaluation of such findings. Since autonomous nodules are almost never malignant, the most appropriate next step would probably be the TRH test (40), measurement of TSH with sensitive assay, or suppression test to define possible autonomy in the nodule.

The present study and careful review of the literature lead to the conclusion that the slightly better overall quality of ¹²³I scans does not in itself provide sufficient advantage to justify recommendation of the use of 123I over [99mTc]pertechnetate for routine thyroid imaging. This is particularly true in view of the present tendency to consider the usefulness of thyroid imaging limited where its principal benefit is to differentiate cold from hot nodules. In addition, 99mTc may be a more practical agent than 123I for general use. Discrepancies in images are rare and appear most often in multinodular goiter where they are probably of only minimal importance. There is no correlation between the type of discrepancy and the histology of the lesions. Discrepancies are far more likely to be caused by benign thyroid disorders than malignancy. The risk of cancer in nodules appearing hot with 99mTc and cold with radioiodine is probably so low that routine re-imaging of hot nodules on the ^{99m}Tc scan with radioiodine is not necessary.

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REFERENCES

- Atkins HL, Klopper JF, Lambrecht RM, Wolf AP. A comparison of technetium-99m and iodine-123 for thyroid imaging. Am J Roentgen 1973; 117:195-201.
- Gorowski T, Chomicki OA. Some comparative studies using ^{99m}Tc and ¹³¹I in thyroid scanning. *Nuklearmedizin* 1976; 15:268-272.
- Prince JR, Zubi SM, Haag BL. Thyroid imaging with iodine-125 and technetium-99m. Eur J Nucl Med 1979; 4:37-41.
- Shapiro B, Britton K, Fountos A, et al. A multiobserver comparison of ^{99m}TcO₄ and ¹²³I thyroid imaging. Eur. J Nucl Med 1981; 6:135-138.
- Schultz JL, Hanner TG, Witcofski RL, Maynard CD. Comparison of ^{99m}Tc and ¹²⁵I thyroid scans [Abstract]. J Nucl Med 1966; 7:797.
- Weber PM, Dos Remedios L, Fish M, Pollycove M. Thyroid imaging: ¹³¹I or ^{99m}Tc: a clinical comparison [Abstract]. *J Nucl Med* 1969; 10:451.
- Marion MA, Ronai PM, Pain RW, Wise PH. Simultaneous assessment of thyroid structure and function with the gamma camera using pertechnetate: a comparison with radioiodine and biochemical diagnosis. Aust N Z J Med 1974; 4:379-384.
- Arnold JE, Pinsky S. Comparison of ^{99m}Tc and ¹²³I for thyroid imaging. J Nucl Med 1976; 17:261–267.
- Dige-Petersen H, Kroon S, Vadstrup S, Andersen ML, Roy-Poulsen NO. A comparison of ^{99m}Tc and ¹²³I scintigraphy in nodular thyroid disorders. *Eur J Nucl Med* 1978; 3:1-4.
- Kalk WJ, Van Drimmellan M, Klugman L, Silberman R, Levin J. Comparison of ^{99m}Tc and ¹³¹I scans in thyroid function studies. S Afr Med J 1979; 56:839-840.
- Ryo UY, Vaidya PV, Schneider AB, Bekerman C, Pinsky SM. Thyroid imaging agents: a comparison of I-123 and Tc-99m pertechnetate. *Radiology* 1983; 148:819-822.
- Miller JM. Evaluation of thyroid nodules. Accent on needle biopsy. Med Clin North Am 1985; 69:1063–1077.
- Rojeski MT, Gharib H. Nodular thyroid disease. Evaluation and management. N Engl J Med 1985; 313:428-436.
- Steinberg M, Cavalieri RR, Choy SH. Uptake of technetium-99m pertechnetate in a primary thyroid carcinoma: need for caution in evaluating nodules. J Clin Endocrinol 1970; 31:81– 84
- Shambaugh GE, Quinn JL, Oyasu R, Freinkel N. Disparate thyroid imaging. Combined studies with sodium pertechnetate Tc-99m and radioactive iodine. *JAMA* 1974; 228:866– 869
- 16. Turner JW, Spencer RP. Thyroid carcinoma presenting as a

- pertechnetate "hot" nodule, but without ¹³¹I uptake: case report. *J Nucl Med* 1976; 17:22-23.
- Quinn JL, Henkin RE. Scanning techniques to assess thyroid nodules. Ann Rev Med 1975; 26:193–201.
- O'Connor MK, Cullen MJ, Malone JF. A kinetic study of (1311) iodide and (99mTc) pertechnetate in thyroid carcinomas to explain a scan discrepancy: case report. J Nucl Med 1977; 18:796-798.
- Erjavec M, Movrin T, Auersperg M, Golouh R. Comparative accumulation of ^{99m}Tc and ¹³¹I in thyroid nodules: case report. J Nucl Med 1977; 18:346-347.
- Massin JP, Planchon C, Accard JL, Perez R. Discordances scintigraphiques entrele technetium 99m et l'iode 131 dans l'etude des nodules thyroidiens. Nouv Presse Med 1977; 6:97– 100.
- Szonyi G, Bowers P, Allwright S, et al. Comparative study of ^{99m}Tc and ¹³¹I in thyroid scanning. Eur J Nucl Med 1982; 7(10):444-446.
- Usher MS, Arzoumanion AY. Thyroid nodule scans made with pertechnetate and iodine may give inconsistent results. J Nucl Med 1971; 12:136-137.
- Demeester-Mirkine N, Van Sande J, Corvilain J, Dumont JE. Benign thyroid nodule with normal iodide trap and defective organification. J Clin Endocrinol Metab 1975; 41:1169-1171.
- Miller JM, Kasenter AG, Marks DS. Disparate imaging of the autonomous functioning thyroid nodule with ^{99m}Tc pertechnetate and radioiodine. *Radiology* 1976; 119:737-739.
- Kim E, Kumar B. Discrepant imaging of nodular hyperplasia with pertechnetate and radioiodine. Clin Nucl Med 1976; 1:204-205.
- Hirabayashi S, Koga Y, Kitahara T, Hishida T, Kiga M, Lindo S. Inconsistent images of thyroid nodule scintigrams made with iodine and pertechnetate: case report. J Nucl Med 1975; 16:918.
- Barth JD, Bakker WH, Hennemann G. Discrepancies between iodine and technetium thyroid scintigraphy. *JAMA* 1978; 240:463–464.
- 28. Thrall JH, Burman KD, Wortofsky L, Corcoran RJ, Johnson MC, Gillin MT. Discordant imaging of a thyroid nodule with

- ¹³¹I and ^{99m}Tc: concordance of ¹³¹I and fluorescent scans. *Radiology* 1978; 128:705–706.
- Browne HG. Report of a case of disparate imaging in thyroid scintigraphs with histopathologic correlation. J Tenn Med Assoc 1979; 72:368-370.
- Ryo UY, Vaidya P, Schneider A, Pinsky SM. Histopathology of thyroid lesions that caused discrepant findings between Tc-99m scan and I-123 scan [Abstract]. J Nucl Med 1979; 20:678.
- Tennvall J, Cederquist E, Moller T, Naversten Y, Akerman M. Preoperative scintigraphy with correlation to cytology and histopathology in carcinoma of the thyroid. *Acta Radio Oncol* 1983; 22:183-191.
- Vorne M, Jarvi K. 99mTc-pertechnetate in the detection of thyroid carcinoma in a ten year period. Eur J Nucl Med 1987; 13:362-365.
- Paras P, Saenger EL, Spaventi Š, Kusić Z. Comparative studies of I-123 and Tc-99m as imaging agents for thyroid disorders. Proceedings of the third world congress of nuclear medicine and biology. Paris: Pergamon Press; 1982; 1:794– 798.
- Fisher RA, Yates F, eds. Statistical tables for biological, agricultural and medical research. New York: Hafner Publishing Co.; 1953.
- Mathematical methods for statistics. Princeton, NJ: Princeton University Press; 1946.
- Rosenthal SL, Hofeldt FD, Verdon TA. Comparison of 4and 24-hr thyroid scans with ¹²³I: concise communication. J Nucl Med 1976; 17:1050-1052.
- Strauss HW, Hurley PJ, Wagner HN. Advantages of ^{99m}Tc pertechnetate for thyroid scanning in patients with decreased radioiodine uptake. *Radiology* 1970; 97:307-310.
- Massin JP, Planchon C, Perez R. Comparison of ^{99m}Tc-pertechnetate and ¹³¹I in scanning of thyroid nodules. *Clin Nucl Med* 1977; 2:324–333.
- Alderson PO, Sumner MW, Segel BA. The single palpable thyroid nodule. Evaluation by ^{99m}Tc pertechnetate imaging. Cancer 1976; 37:258-265.
- Ng Tang Fui S, Maisey MN. Thyroid disease. In: Maisey MN, Britton KE, Gilday DL, eds. Clinical nuclear medicine. Philadelphia-Toronto: WB Saunders Company; 1985;197-247.