Assessing Thyroid Malignancy with Double-Phase Scintigraphy Using Technetium-99m-MIBI

TO THE EDITOR: In a recent article, Kresnik et al. (1) reported on double-phase thyroid scintigraphy (30 min and 2 hr postinjection) with $^{99m}$Tc-sestamibi in patients with cold thyroid nodules and concluded that the uptake and retention of the tracer by thyroid nodules is not specific for malignancy.

![Figure 1](Image)

**FIGURE 1.** All nodules appearing cold on the $^{99m}$Tc image (Patients A, B and C) show intense uptake of MIBI in the early image (MIBI #1). In the late image, the retention was present both in the raw image (MIBI #2A) and in the image normalized for acquisition time and $^{99m}$Tc decay (MIBI #2B) for Patients A and B, respectively. The retention was not present in Patient C. The washout rate was 21% per hr$^{-1}$ and 13% per hr$^{-1}$ for Patient A, 20% per hr$^{-1}$ and 16% per hr$^{-1}$ for Patient B and 20% per hr$^{-1}$ and 20% per hr$^{-1}$ for Patient C for normal thyroid tissue and for nodules, respectively. Histopathology revealed Hürthle cell tumor in Patient A, follicular carcinoma in Patient B and adenoma in Patient C.

We agree in part with their conclusions. In our experience (2), we have witnessed oxyphilic tumors take up and retain $^{99m}$Tc-sestamibi in contrast with other thyroid tumors (Fig. 1). We were able to conclude this by calculating the washout rate of the tracer from the nodule and from the normal thyroid tissue using double-phase scintigraphy (15–30 min and 3–4 hr postinjection). The washout rate was lower in oxyphilic tumors than in other nodules and in normal thyroid tissue. This index proved to be much more specific than visual inspection in evaluating such retention.

The uptake of sestamibi by thyroid nodules is related to vascularity and cellularity (3), but its retention is related mainly to mitochondrial concentration (4) and secondarily to the initial uptake. As a result, the retention could be either true or apparent according to the washout rate and initial uptake. Therefore, visual inspection could be misleading in such evaluation.

REFERENCES


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REPLY: We are pleased with the interest that our study on $^{99m}$Tc-MIBI scintigraphy of thyroid nodules published in the January issue of JNM (1) has raised, and in particular with the detailed interest by Vattimo et al.

In our study, 62 patients with single-injection, dual-phase scintigraphy were investigated. The scintigrams were rated visually by two experienced observers. There were 12 patients with thyroid carcinoma. Five patients were classified as $^{99m}$Tc-MIBI positive (superior tracer uptake to normal surrounding thyroid tissue). Seven patients were $^{99m}$Tc-MIBI negative (lower tracer uptake to surrounding thyroid tissue). There were 27 patients with thyroid adenoma (8 oxyphilic, 10 follicular and 9 microfollicular). All patients with microfollicular histological cell type were classified as $^{99m}$Tc-MIBI positive. Follicular and oxyphilic adenoma were positive in only 50% of cases.

Vattimo et al. (2) report in their study on double-phase scintigraphy with $^{99m}$Tc-MIBI that persistent tracer uptake seems to be characteristic of Hürthle cell tumor in contrast to other thyroid tumors. Visual inspection of the images was performed using a scoring method (0 = no uptake to 3 = uptake superior to the thyroid gland).

There was a group of eight patients that were scored 3 on the late-performed scans. Two patients revealed oxyphilic adenoma and three patients oxyphilic carcinoma, but the histology in three patients was not available. Perhaps it would be helpful also to provide the cytological or histological data from these patients. In another group of 23 patients, the late-performed scans showed no tracer retention; therefore, they were scored 0. Within this group, there were two patients with elevated nodular-to-extranodular normal thyroid tissue (N/T) ratios (1.35 in Patient 17 and 1.56 in Patient 18). It is not clear why they were not visible on the scan.

We agree with Vattimo et al. (2) that oxyphilic tumors have increased tracer uptake, but in our study, all patients with microfollicular adenomas, four patients with papillary carcinoma and one patient with follicular carcinoma also took up and retained the tracer. They were also all visible on the scan. The retrospective calculated mean values (nodule-to-thyroid counts, N/T) for microfollicular adenomas was 1.28 ± 0.22 for early and 1.48 ± 0.28 for the late-performed scan. The washout rate for the normal thyroid tissue was 32%/hr ± 0.64%/hr and for the nodules 26.5% ± 17%/hr.

Similar results could be obtained in our study for the cationic complex $^{99m}$Tc-tetrofosmin dual-phase scintigraphy of thyroid nodules (3). There were 57 patients (11 carcinoma, 21 adenoma, 24 degenerative goiter and 1 Hashimoto’s disease). All microfollicular and oxyphilic adenomas showed visible tracer uptake superior to the normal thyroid gland on the early scan and retention on the late images. On the delayed scan, the N/T ratio for microfollicular adenomas was 1.38 ± 0.28 and 1.70 ± 0.43 for oxyphilic adenomas. It also could be demonstrated that the tetrofosmin uptake by the adenomas exceeded that by the thyroid gland on the early scan, with mean values of 1.46 ± 0.5 for microfollicular and 1.75 ± 0.45 for oxyphilic adenomas. The mean washout rate for nodules was 33.13% ± 8.66%/hr, and the washout rate for the normal thyroid tissue was 30.96% ± 7.07%/hr.
most important asymmetry, 23-pixel circular ROIs (about 9 cm²) were drawn around any hypoactive area and its contralateral.

The most important right-to-left asymmetry observed in the first studies was between 5.4% and 16.5% (mean 10.4%, s.d. 3.4%). In the repeat studies, the asymmetry was between 6.1% and 15.9% (mean 9.9%, s.d. 3.3%).

In only two of the ten volunteers was the most important hypoactivity located in the same area in the first and second brain SPECT images. In three volunteers, it was located elsewhere in the same hemisphere, while it was located on the opposite hemisphere in the five other volunteers.

Because of these topographical changes, a quantitative evaluation of replicability seems hazardous. For example, the first SPECT image of one volunteer showed a 16.5% hypoactivity located in the left temporal area, while the second SPECT image showed an 11.4% right parietal lobe hypoactivity.

We consider that, with our setting, important variability in ⁹⁹ᵐTc-HMPAO regional distribution is frequently observed. When comparing two ⁹⁹ᵐTc-HMPAO studies performed in the same patient, a change less than 18% should not be considered abnormal.

In their work, Deutsch et al. (1) concluded that they had "good within-subject replicability." However, it is obvious from the standard deviations presented in their Table 1 that differences between Scan 1 and Scan 2 of more than 20% have been observed in some cortical areas of some volunteers.

Our data are in agreement with those of Deutsch et al. (1); we differ only in the interpretation of the results.

REFERENCES


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REPLY: In response to Tondeur et al.'s letter, above, it is misleading to say that our respective studies show the same results but that we "differ only in the interpretation." The results cannot even be rightfully compared because the two studies (where they overlap at all) examined variability in two completely different ways. We looked at changes in identical, carefully defined regions of interest (ROIs); Tondeur et al. (1) defined their ROIs in terms of any area that showed a large asymmetry with the homologous side. Their ROIs were different in each study; ours were the same. It is not appropriate to point to some of our values for the difference between Scan 1 and Scan 2 and say that we also had 20% variability in some ROIs. Where such differences exist in our data, they clearly represent an extreme; that is, they represent values at 2 s.d. or greater extreme—approximately 4% of the population estimate. Tondeur et al. claim this kind of variability to be typical. Table 1 in our article shows that the mean variability was in fact 2.8% (range 0%-7.8%) for our 36 cortical ROIs (within-subject Scan 1:Scan 2 percentage difference for each ROI) (2).

Tondeur et al.'s (1) approach of looking for maximum differences or asymmetries in each scan may, as they say, be of some interest in its implication for methods of clinical interpretation. It reinforces the fact that such methods do not constitute good clinical practice, not that these methods are even normally used by most clinicians. To reduce the interpretation of a brain SPECT scan to merely observing for areas of hypoactivity is a vast oversimplification of the proper approach to clinical brain SPECT scan diagnosis.