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Technetium-99m-MIBI Scintigraphy of Thyroid Nodules in an Endemic Goiter Area

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Technetium-99m-methoxyisobutylisonitrile (MIBI) was introduced for myocardial imaging as an alternative to ^{201}Tl. According to biodistribution studies, MIBI also accumulates in the thyroid gland. The aim of this study was to find out which thyroid nodules retain MIBI and whether preoperative evaluation of malignancy is possible. **Methods:** Single injection, dual-phase (30 min and 2 hr) thyroid scintigraphy with ^{99m}Tc-MIBI was performed on 62 patients who showed a cold nodule on previously performed ^{99m}Tc scintigraphy. MIBI scans were considered positive if there was a clear tracer retention in the late 120-min image compared to the early 30-min image. Sonographic examination and fine-needle aspiration biopsy, guided by ultrasonography, was also done on each patient. In the following days and weeks, all patients underwent surgery. **Results:** Histopathological diagnoses revealed a total of 12 thyroid carcinomas, five were MIBI positive and seven MIBI negative. Out of 27 patients with thyroid adenomas (nine microfollicular, ten follicular, eight oxyphilic), 18 were MIBI positive and nine MIBI negative. There was no MIBI retention on the scans of 22 patients with degenerative changes in the goiter and the one with Hashimoto's disease. **Conclusion:** These results indicate that MIBI accumulation and retention is not specific for thyroid malignancy. Indeed, all evidence points to the fact that a positive MIBI scan is more likely to indicate thyroid adenoma than a malignant tumor.

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Technetium-99m-methoxyisobutylisonitrile (MIBI), a cationic complex molecule, was primarily introduced for perfusion myocardial imaging. Over the years, MIBI scintigraphy has also become one of the most sensitive methods in the detection of parathyroid adenomas (*1,2*). Briele et al. (*3*) also detected thyroid cancer metastases with MIBI scintigraphy. Until recently, ^{201}Tl still played an important role in the follow-up of thyroid cancer as well as in the preoperative evaluation of thyroid nodules (*4*). In 1980, Harada et al. (*5*) examined 55 patients using ^{201}Tl as a preoperative evaluation of thyroid nodules. Scintigraphy visualized 13 of 16 thyroid carcinomas, but thyroid adenomas were also depicted by ^{201}Tl scintigram. Thus, ^{201}Tl could not differentiate conclusively between benign and malignant thyroid nodules. It is, therefore, valid to ask whether ^{99m}Tc-MIBI is more suitable for evaluation purposes in the preoperative clarification of hypofunctional goiter nodules. Furthermore, it would be advantageous to use ^{99m}Tc-MIBI instead of ^{201}Tl, as it requires a smaller radiation dose (*6*) and is more readily available. Moreover, MIBI can be kept in stock and is easily labeled with ^{99m}Tc, in contrast to ^{201}Tl.

TABLE 1
Behavior of Technetium-99m-MIBI in 62 Patients with Cold Thyroid Nodules

No. of patients	Histology	MIBI after 2 hr	No.	MIBI after 30 min		
				A	B	C
11	Differentiated thyroid carcinoma	Positive	5	–	–	5
		Negative	6	–	6	–
1	Nondifferentiated carcinoma	Positive	–	–	–	–
		Negative	1	1	–	–
9	Microfollicular adenoma	Positive	9	–	1	8
		Negative	–	–	–	–
10	Follicular adenoma	Positive	5	–	1	4
		Negative	5	1	3	1
8	Oxyphilic adenoma	Positive	4	–	–	4
		Negative	4	3	1	–
22	Degenerative goiter	Positive	–	–	–	–
		Negative	22	3	19	–
1	Hashimoto's disease	Positive	–	–	–	–
		Negative	1	–	1	–
62	Total	Positive	23	–	2	21
		Negative	39	8	30	1

A = no uptake; B = uptake in the nodule equal to the thyroid tissue; C = uptake in the nodule superior to the normal thyroid tissue; MIBI-positive = clear retention after 2 hr in comparison to the 30-min image; MIBI-negative = no retention after 2 hr.

MATERIALS AND METHODS

Over a period of 9 mo, 62 patients (46 women, 16 men; aged 32–81 yr) selected from a group with solitary ^{99m}Tc hypofunctional thyroid nodules were studied. All patients underwent ^{99m}Tc-pertechnetate scanning, sonographic examination (5 MHz transducer) and fine-needle aspiration biopsy guided by ultrasonography. After an interval of at least 3 days, MIBI scintigraphy was also performed. In the following days and weeks, all patients underwent surgery, and thyroid nodules were evaluated histologically. Technetium-99m-MIBI scintigrams were obtained 30 min and 2 hr after 370 MBq intravenous injection. Planar images were taken using a double-headed camera with a 256 × 256 pixel matrix. Imaging time was 7–10 min. The scintigraphic images were rated visually by two experienced observers. Only nodules that showed clear tracer retention on the 2-hr delayed images in comparison with those taken at 30 min were evaluated as MIBI-positive; all nodules with continuing washout up to the 2-hr image were classified as MIBI-negative. Additional visual inspection of the nodules on the 30-min images were performed to compare MIBI uptake with that of normal thyroid tissue.

RESULTS

The results for ^{99m}Tc-MIBI scintigraphy are summarized in Table 1. Five of the 11 patients with differentiated thyroid carcinoma were MIBI-positive on the 2-hr delayed image. They also demonstrated MIBI uptake superior to the thyroidal tissue after 30 min. Figure 1 shows a 48-yr-old woman with focal MIBI retention in the caudal nodule of the left thyroid in the image taken at 30 min and clear MIBI retention on the 2-hr delayed image. Histology revealed a follicular thyroid carcinoma (2.5 cm in diameter). Six of the malignant tumors were MIBI-negative, but in the 30-min image the thyroid showed homogeneous MIBI uptake. Figure 2 shows a 59-yr-old man with a follicular thyroid carcinoma (3 cm in diameter) on the left side that showed homogeneous MIBI activity uptake at 30 min but continual washout on the 2-hr delayed image without late retention. One nondifferentiated thyroid carcinoma had no MIBI uptake after 30 min and no uptake after 2 hr; therefore, it was classified as MIBI-negative. Histology revealed thyroid adenoma in 27 patients. It is striking that all nine microfollicular adenomas demonstrated MIBI uptake on the 30-min image (one nodule equal to and eight nodules superior to the thyroid gland) with clear retention on the 2-hr delayed image. Figure 3 is a scintiscan with circumscribed increased uptake located on the left side of the thyroid gland at 30 min and clear retention on the 2-hr image. Histology revealed a microfollicular adenoma (5 cm in diameter). Only four of eight oxyphilic adenomas were MIBI-positive. They also showed superior uptake to the thyroidal tissue in the early image. Five of 10 follicular adenomas

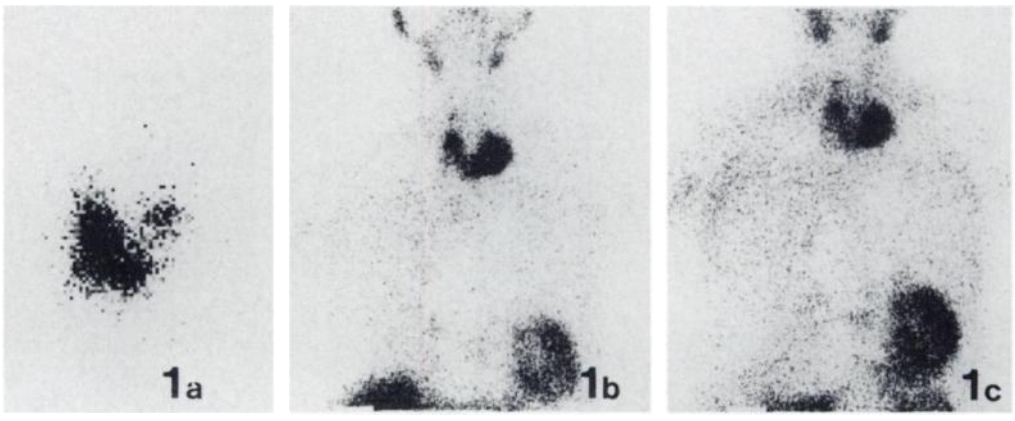

FIGURE 1. Technetium-99m-MIBI scintigraphy in a patient with a cold thyroid nodule (A). Thirty-minute early image (B). Clear MIBI retention on the 2-hr delayed image (C). Histology: a 2.5-cm follicular carcinoma of the left thyroid nodule.

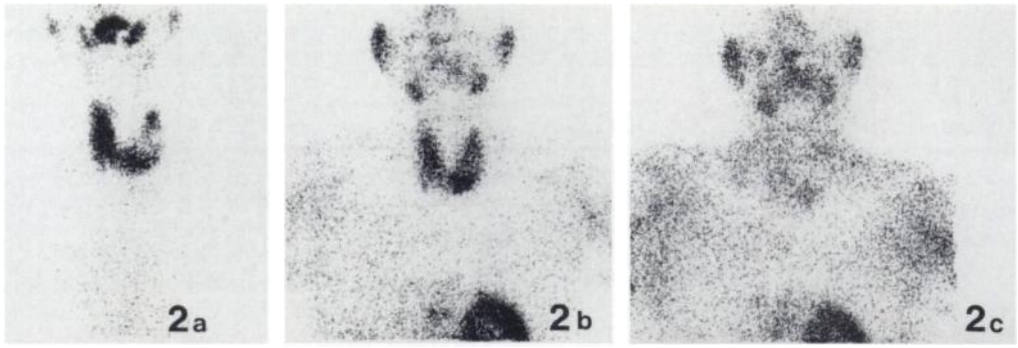

FIGURE 2. Technetium-99m-pertechnetate image in a patient with a cold nodule on the left side (A). Homogeneous MIBI activity at 30 min (B) but with continual washout after 2 hr (C). Histology: 3-cm follicular carcinoma of the left thyroid gland.

were MIBI-positive. Four already demonstrated increased and one identical MIBI uptake to the thyroid after 30 min. Nineteen patients of 22 with degenerative changes in the nodules of the goiter demonstrated MIBI uptake in the early image, but all of them were MIBI-negative after 2 hr. Ultrasonography showed decreased echogenity in 10 of 12 patients with thyroid carcinoma and an echogenity similar to the surrounding tissue in two. Of the 27 patients with thyroid adenomas, 23 patients also had decreased echogenity; two adenomas had a similar echogenity to normal thyroid tissue, and two had an echocomplex structure. Fifteen of the 22 patients with degenerative goiter had nodules with decreased echogenity, six had a normal and one had an enhanced echo structure. The diagnosis of thyroid cancer was suspected by cytology in 8 of 12 patients using ultrasonography guided FNAB. In four patients, cytology revealed follicular proliferation (Table 2). Histologically diagnosed adenomas were suspected cytologically in 23 of 27 patients (Table 3). Cytology for degenerative changes in the nodules of the goiter was true-positive in 13 of 22 patients.

DISCUSSION

Most hypofunctional thyroid nodules are benign, but, depending on iodine supply, about 5%–15% are malignant. If tumors are suspected to be malignant or benign, a different operational procedure is required. Therefore, pertechnetate scintigraphy, sonography and cytology and ^{201}Tl scintigraphy are also useful in the preoperative evaluation of thyroid nodules. At present, there is no radiopharmaceutical that has satisfactory specificity in the detection of thyroid cancer. Although ^{201}Tl has been used with high sensitivity until now, it only has low specificity for malignant thyroid tumors.Thus, as early as 1980, Harada et al. (*5*) showed that ^{201}Tl could not differentiate between benign and malignant thyroid nodules in 55 patients. Nodules with a low degree of differentiation or degenerative cystic changes had lower ^{201}Tl uptake than hyperplastic thyroid tissue. The aim of our study was to find out which thyroid nodules retain MIBI and whether preoperative evaluation of malignancy is possible.

Most MIBI thyroid scintigraphy studies addressed a small patient population. For example, Briele et al. (*3*) described the detectability of thyroid carcinoma metastases in 12 patients using MIBI scintigraphy, but lung metastases showed no recognizable MIBI uptake. Other cases described how primary thyroid tumors retain sestamibi (*7,8*). Comparative investigations by Földes et al. (*9*) on the imaging of thyroid nodules with pertechnetate and ^{99m}Tc-MIBI revealed great differences. Only one of the pertechnetate hot nodules was hot on MIBI scintigraphy. Of the pertechnetate cold nodules, 46% showed no MIBI uptake. Because some patients underwent surgery, histological classification was possible. There was no specific uptake of MIBI in malignant thyroid tumors, but uptake was dependent on the ability of viable thyroid tissue to accumulate MIBI.

Similar results were obtained by Sundram et al. (*10*) who studied the imageability of thyroid nodules with MIBI in a small group of patients. Some patients underwent surgery and the nodules were histologically classified. Malignant thyroid tumors had no increased MIBI uptake. Adenomas demonstrated various uptake behaviors, probably corresponding to histological type, as in our study. It should be noted, however, that Sundram did not classify the adenomas histologically. In their study of cellular MIBI retention, Piwnica-Worms et al. (*11*) established that MIBI uptake in thyroid cells depends on the number of mitochondria and the potential of plasma and mitochondria membranes because MIBI is held inside the mitochondria. The cells of malignant tumors in particular maintain more negative mitochondria transmembrane potential and, subsequently, encourage increased MIBI accumulation due to their increased metabolic needs.

An important aspect of our work was to determine how the degree of histological differentiation of thyroid nodules influences MIBI accumulation. In our study, all 9 microfollicular adenomas, 5 of 10 follicular and 4 of 8 oxyphilic adenomas had a high degree of differentiation and MIBI retention after 2 hr. Similar results were obtained for differentiated thyroid cancer, in which MIBI accumulation was depicted on the 2-hr delayed images of 5 of 11 patients. The five MIBI-positive cancers

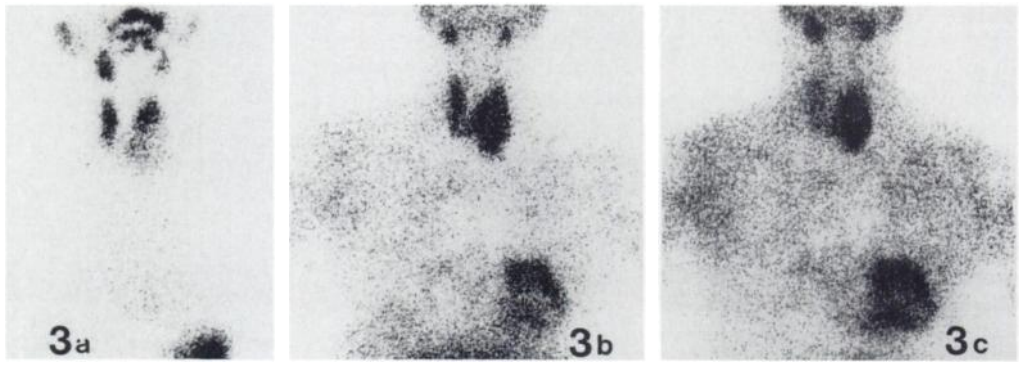

FIGURE 3. Technetium-99m-pertechnetate scintigraphy in a patient with a cold nodule on the left side (A). Recognizable MIBI uptake to the left at 30 min (B) and clear retention on the 2-hr image (C). Histology: 5-cm microfollicular adenoma.

TABLE 2
Cytological and Sonographic Results in 12 Patients with Thyroid Carcinoma

Sonography	P	F	M
Decreased echo	8	–	2
Similar echo	–	2	–

P = papillary carcinoma; F = follicular proliferation; M = microfollicular proliferation.

either had G1 or G2 differentiation. The remaining malignant thyroid tumors had lower degrees of histological differentiation. Patients with degenerative goiter changes had no MIBI retention after 2 hr. Therefore, MIBI scintigraphy gives information on the degree of differentiation in thyroid nodules but not on their potential malignancy. In our study, MIBI-positive nodules related to both adenomas and malignant tumors. Tumor size also appears to play a role in MIBI accumulation; both adenomas and malignant tumors with a diameter greater than 1 cm could be imaged. Conversely, two papillary carcinomas that were smaller than 1 cm were not visualized on MIBI scintigraphy after 2 hr. Valuable additional information for the histological classification of thyroid nodules can be provided by FNAB guided by ultrasonography. Hamming et al. (*12*) established that if a malignant tumor is suspected clinically, the sensitivity is 88%–95% and the specificity 67%–88%. We found that a malignant thyroid tumor could be confirmed cytologically in 8 of 12 patients. Histologically diagnosed adenomas in 23 of 27 patients could also be confirmed cytologically.

TABLE 3
Cytological and Sonographic Results in 27 Patients with Thyroid Adenoma

Sonography	No. of patients	M	F	A	O	D	ON	P
Decreased echo	23	6	9	1	4	–	1	2
Similar echo	2	–	–	1	1	–	–	–
Complex echo	2	–	1	–	–	1	–	–

M = microfollicular proliferation; F = follicular proliferation; A = adenomatose hyperplasia; O = oxyphilic proliferation; D = degenerative changes; ON = oxyphilic neoplasia; P = papillary carcinoma.

CONCLUSION

MIBI accumulation and retention is not specific for thyroid malignancy. In combination with all other findings, a positive MIBI scan would appear to indicate an adenoma rather than a malignant tumor.

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