Quick Diagnosis of Hyperthyroidism with Semiquantitative 30-Minute Technetium-99m-Methoxy-Isobutyl-Isonitrile Thyroid Uptake

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Ten normal volunteers and 14 patients with hyperthyroidism had pinhole thyroid imaging 30 min after an intravenous injection of 10 mCi ^{99m}Tc-MIBI. Technetium-99m-MIBI thyroid uptake was calculated by the formula: [total counts with a region of interest (ROI) over the whole thyroid gland] ÷ [(mean counts of every pixel in the neck soft tissue) × (total number of pixels in ROI over the whole thyroid gland)]. The results showed that the 30 min ^{99m}Tc-MIBI thyroid uptake ratios had positive relationships with the 24 hr ^{131}I-thyroid uptake ($r = 0.79$), and that the patients with hyperthyroidism had significantly higher 30 min ^{99m}Tc-MIBI thyroid uptake than the normal volunteers (5.31 ± 0.78 s.e.m. versus 2.35 ± 0.14 s.e.m., $p < 0.005$ using the Mann-Whitney U-test). Technetium-99m-MIBI thyroid uptake may be useful for the rapid diagnosis of hyperthyroidism.

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Conventional ^{131}I thyroid uptake and scans reflect thyroid function. However, ^{131}I uptake may be influenced by antithyroid drugs, and the measurement is usually made 24 hr after oral intake of ^{131}I. Technetium-99m-MIBI thyroid uptake is related to the mitochondria of the cells. Both the number and activity of the mitochondria are measured in thyroid glands with hyperthyroidism. In two recent articles, ^{99m}Tc-TBI (tertiary butyl isonitrile) and ^{99m}Tc-MIBI were used for visualization of suppressed thyroids (*1,2*). The uptake was higher in hyperfunctional nodules than in suppressed normal thyroid tissues. In our study, ^{99m}Tc-MIBI thyroid uptake was used as an index to predict thyroid function and to differentiate between euthyroid and hyperthyroid glands. It is based on another mechanism which is different from the traditional 24-hr ^{131}I thyroid uptake study.

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MATERIALS AND METHODS

Ten normal volunteers (3 M, 7 F; 22–78 yr) with normal thyroid function and 24 hr ^{131}I thyroid uptake (Table 1) and 14 patients with hyperthyroidism (2 M, 12 F; 20–72 yr) who had been diagnosed by typical clinical features, abnormal thyroid hormones and increased 24 hr ^{131}I thyroid uptake (Table 2), were studied.

A commercial MIBI preparation (max. 5.55 GBq [150 mCi] in approximately 1 to 3 ml) was obtained from the Dupont Company (Cardiolite). The labeling and quality control procedures were carried out according to the manufacturer's instructions. Labeling efficiency was always higher than 90%. Patients were pretreated with 500 mg perchlorate to prevent uptake of free [^{99m}Tc]pertechnetate in the thyroid glands 30 min before intravenous injection of 370 MBq (10 mCi) ^{99m}Tc-MIBI. After an additional 30 min, the thyroid was imaged by a gamma camera with a pinhole collimator for a total of 100,000 counts. The distance from the collimator to the neck was consistently 7 cm.

The ^{99m}Tc-MIBI thyroid uptake was calculated by the formula: [total counts with an ROI over the whole thyroid gland] ÷ [(the mean counts of every pixel in the neck soft tissue) × (total number of pixels in the ROI over the whole thyroid gland)] (Fig. 1A,B).

RESULTS

The results (Table 1,2) showed that 30-min ^{99m}Tc-MIBI thyroid uptake ratios correlated with 24-hr ^{131}I thyroid uptake ($r = 0.79$) (Fig. 2) and that patients with hyperthyroidism had significantly higher 30-min ^{99m}Tc-MIBI thyroid uptake than the normal volunteers (5.31 ± 0.78 s.e.m. versus 2.35 ± 0.14 s.e.m., $p < 0.005$ using the Mann-Whitney U-test) (Fig. 3).

DISCUSSION

Hexakis (2-methoxyisobutyl isonitrile) technetium (I) (^{99m}Tc-sestamibi) is a monovalent cation with a central Tc(I) core that is surrounded by six lipophilic ligands coordinated through the isonitrile carbon. Piwnica-Worms et al. (*3*) investigated the fundamental myocellular uptake mechanism of technetium sestamibi and found that its transport involves passive distribution across plasma and mitochondrial membranes, and at equilibrium it is sequestered largely within mitochondria by the large negative transmembrane potentials. When plasma membrane po-

TABLE 1
Comparison of ^{99m}Tc-MIBI and ^{131}I Thyroid Uptake in Normal Volunteers

Subject no.	Sex	Age	% 30-min ^{99m}Tc-MIBI thyroid uptake	% 24-hr ^{131}I thyroid uptake
1	F	78	2.89	35
2	M	71	2.77	37
3	F	48	2.77	40
4	F	22	2.48	32
5	F	28	2.50	30
6	F	29	2.37	28
7	M	69	2.33	35
8	F	48	2.12	27
9	M	35	1.76	25
10	F	51	1.52	23

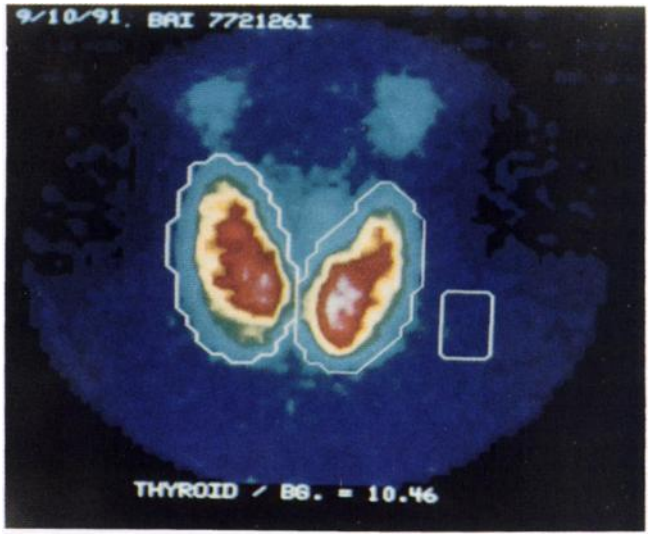

FIGURE 1. A 20-yr old female with hyperthyroidism had a free T4 > 4.4 ng/dl (reference normal: 0.7–2.2), T3 = 408 ng/dl (reference normal: 85–165), T4 = 22.03 μg/dl (reference normal: 6.0–12.0), and TSH = 0.24 μU/ml (reference normal: 0.4–5.0). The 30-min ^{99m}Tc-MIBI thyroid uptake was 10.46 and the 24-hr ^{131}I thyroid uptake was 79%.

tentials or mitochondrial membrane potentials are depolarized, there is inhibition of net uptake and retention of ^{99m}Tc-sestamibi. When mitochondrial and plasma membrane potentials are hyperpolarized, there is increased ^{99m}Tc-sestamibi cellular uptake and retention. Metabolic derangements could conceivably result in diminished ^{99m}Tc-sestamibi uptake independent of flow. This could occur with metabolic-induced membrane polarization changes (*4*).

The thyroid uptake mechanism of ^{99m}Tc-MIBI is not yet clearly understood. Based on microscopic findings, more abundant mitochondria and blood flow are often described in the thyroid glands of hyperthyroidism (*5*). We suppose that it should bind to the cytosol in the follicular cell as in myocardium. The cationic charge and lipophilicity of ^{99m}Tc-MIBI, mitochondrial and plasma membrane potentials of the follicular cell as well as cellular mitochondrial content can play a significant role in thyroid uptake of this agent (*6,7*). However, uptake may be caused by an indirect phenomenon such as increased thyroid blood flow and capillary permeability.

In a review of the literature, ^{99m}Tc-MIBI is taken up by normal thyroid tissue and the metastases of thyroid carcinoma. This uptake cannot be affected by exogenous thyroxine therapy (*8*). In two recent articles, ^{99m}Tc-TBI (an earlier ^{99m}Tc-isonitrile complex) and ^{99m}Tc-MIBI were used for visualization of suppressed thyroids without TSH stimulation (*1,2*). The biodistribution of ^{99m}Tc-MIBI is characterized by rapid blood clearance and, consequently, early uptake by target organs (*9*). The early imaging time of thyroid glands, 20–40 min after intravenous injection of ^{99m}Tc-MIBI, is adequate (*1,10*).

Another study found that perchlorate failed to inhibit ^{99m}Tc-MIBI uptake by the thyroid (*10*). Pretreatment of patients with perchlorate, either as sodium or potassium perchlorate, can markedly alter the biological distribution of [^{99m}Tc]pertechnetate. Perchlorate is a monovalent negative ion of approximately the same ionic size as [^{99m}Tc] pertechnetate. It blocks pertechnetate uptake in the thyroid gland, salivary gland, gastric mucosa and choroid plexus by competitive inhibition (*11,12*). Its effect on thyroid uptake persists for up to 72 hr (*13*). Perchlorate may also be given after tracer administration, since pertechnetate is readily discharged from the thyroid and salivary glands. In the present study, thyroid uptake should not be due to free [^{99m}Tc]pertechnetate, because we did not use ^{99m}Tc-MIBI if the radiochemical purity was less than 90%. We also

TABLE 2
Comparison of ^{99m}Tc-MIBI and ^{131}I Thyroid Uptake in Patients with Hyperthyroidism

Patient no.	Sex	Age	% 30-min ^{99m}Tc-MIBI thyroid uptake	% 24-hr ^{131}I thyroid uptake
1	F	31	12.82	84
2	F	20	10.46	79
3	F	62	7.52	74
4	F	54	5.17	73
5	F	21	4.66	70
6	F	65	3.87	60
7	F	38	4.72	68
8	M	34	4.01	62
9	F	42	3.78	63
10	F	34	3.71	60
11	F	72	3.67	65
12	M	53	3.54	62
13	F	20	3.34	54
14	F	27	3.10	45

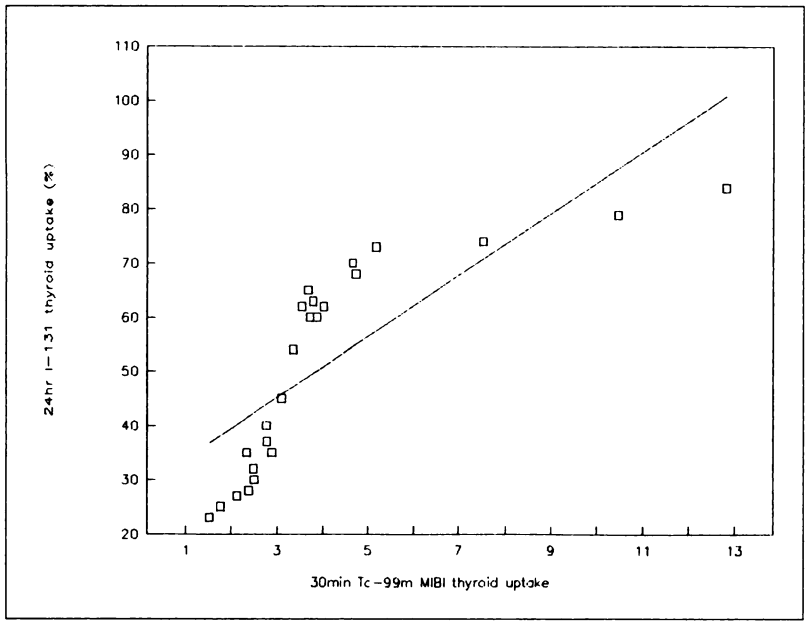

FIGURE 2. Thirty minute ^{99m}Tc-MIBI thyroid uptake ratios correlated well with 24-hr ^{131}I thyroid uptake (r = 0.79).

pretreated the patients with perchlorate, which inhibits the thyroid uptake form of free [^{99m}Tc]pertechnetate.

In conclusion, these studies suggest that ^{99m}Tc-MIBI uptake may be useful for the diagnosis of hyperthyroidism.

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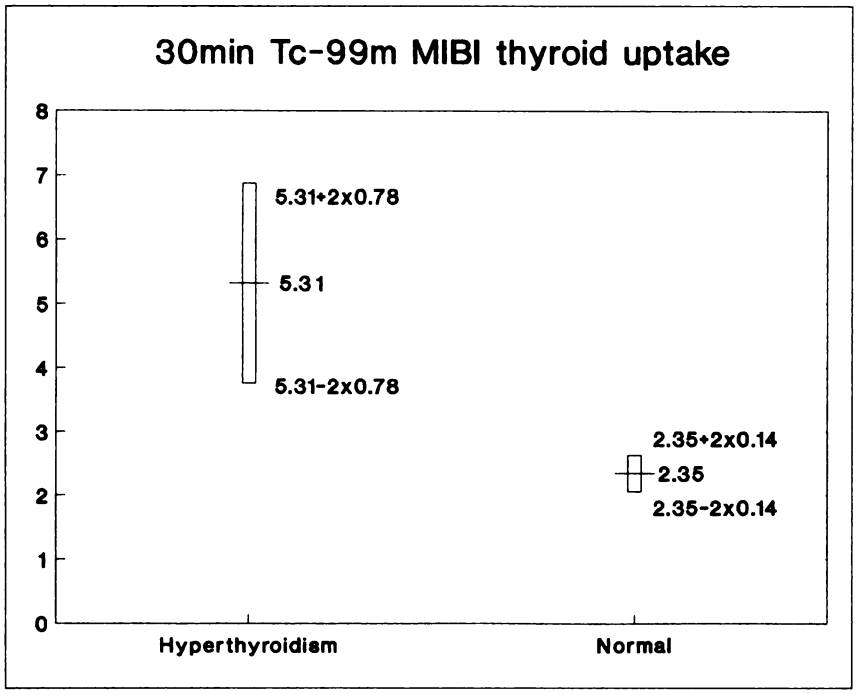

FIGURE 3. Patients with hyperthyroidism had significantly higher 30-min ^{99m}Tc-MIBI thyroid uptake than normal volunteers.

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(continued from page 70)

SELF-STUDY TEST
Pulmonary Nuclear Medicine
ANSWERS

fibrosis, a process leading to widespread interstitial fibrosis, bronchiolectasis, and distortion of pulmonary architecture.

Gallium-67 images of the lungs are frequently abnormal in patients with pulmonary sarcoidosis. There is evidence from in vitro experiments that the macrophages associated with the alveolitis and granulomas of the active disease become labeled with more ^{67}Ga on a per-cell basis than do normal macrophages. Furthermore, this increased macrophage uptake of ^{67}Ga in vitro correlates with the presence of positive ^{67}Ga scintigrams.

Although the role of ^{67}Ga scintigraphy, as a means to stage or monitor the disease is controversial, patients with normal studies generally have stable pulmonary function, suggesting that their diseases are quiescent. Conversely, positive ^{67}Ga studies have been associated with deterioration of pulmonary function in most, but not all, patients. Furthermore, several authors have demonstrated a close correlation between positive gallium scintigrams and responsiveness to therapy. Most authors seem to agree that corticosteroid therapy is unlikely to benefit a patient with sarcoidosis who has a negative ^{67}Ga study. On the other hand, it appears that positive ^{67}Ga scintigrams do not reliably distinguish patients who will improve spontaneously (without treatment) from those who require medical intervention.

Thus, it appears that ^{67}Ga uptake marks the presence of one or more components of the disease stages associated with active alveolitis and granuloma formation. Gallium-67 localization has not been associated with pulmonary fibrosis per se, and hence may not correlate closely with pulmonary function or with the appearance of the chest roentgenogram. Patients who have pulmonary fibrosis but no ^{67}Ga localization are unlikely to benefit from corticosteroid therapy, which appears to be most successful during the inflammatory phase of the disorder.

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For further in-depth information, refer to the syllabus pages in Nuclear Medicine Self-Study I.