Technetium-99m-Sestamibi Scintigraphy Compared with Thallium-201 in Evaluation of Thyroid Tumors

Hiroshi Nakahara, Shiro Noguchi, Nobuo Murakami, Hiroaki Hoshi, Seishi Jinnouchi, Shigeki Nagamachi, Takashi Ohnishi, Shigemi Futami, Leo G. Flores II and Katsuji Watanabe

Noguchi Thyroid Clinic and Hospital Foundation, Beppu, Oita; and Department of Radiology, Miyazaki Medical College, Miyazaki, Japan

Technetium-99m methoxyisobutylisonitrile (MIBI) is a myocardial perfusion imaging agent that has been reported to effectively localize in various tumors (e.g., lung and thyroid carcinomas and osteogenic sarcoma). To determine its usefulness in thyroid tumors, we compared 99mTc-MIBI with 201Tl imaging. Method: We evaluated 25 patients with thyroid tumors (papillary carcinoma in 11, follicular carcinoma in 2, follicular adenoma in 7, adenomatous goiter in 5). Fifteen metastatic lesions from differentiated thyroid carcinomas were also evaluated. Early (10 min after injection) and delayed images (120 min after injection) were obtained for both 99mTc-MIBI and 201Tl scintigraphy. Results: The early images showed very similar findings for both 99mTc-MIBI and 201Tl. However, the delayed images showed that malignant tumors tended to retain more tracer agent than benign nodules. A slight difference in clarity was seen that may have been due to the effect of the 99mTc. Conclusion: Although 99mTc-MIBI scintigraphy does not have particularly good results in differentiating malignant from benign thyroid tumors, it may be useful in evaluating metastases or predicting recurrence because of its better imaging characteristics.

Key Words: technetium-99m-sestamibi; thallium-201; thyroid tumors


For correspondence or reprints contact: Hiroshi Nakahara, MD, Miyazaki Medical College, 5200 Ohaza Kirara, Kyotake, Miyazaki, Japan 889-16.
tumor-to-normal thyroid tissue activity ratio (T/N ratio), or the ratio of activity in the ROI of the tumor to the activity of the ROI that was positioned on the normal thyroid tissue.

For metastatic lesions from thyroid carcinomas, only those 1 cm in diameter or larger were evaluated. Both 99mTc-MIBI and 201Tl accumulations in metastatic lesions were classified as positive (accumulation was clearly depicted); equivocal (accumulation was ambiguously depicted); or negative (accumulation was not depicted).

RESULTS

Primary Tumors

Figure 1 shows the correlation between the 99mTc-MIBI and 201Tl T/N ratios on the early images from 25 patients with thyroid tumors (correlation coefficient r = 0.83; p < 0.001; slope of computed regression line 0.65). Figure 1 reveals a relative linear relationship between the T/N ratios of 99mTc-MIBI and 201Tl images.

Figure 2 shows the correlation between 99mTc-MIBI and 201Tl T/N ratios on the delayed images from the same patients (correlation coefficient r = 0.71; p < 0.001; slope of computed regression line 0.57). On the delayed images, the relationship between the T/N ratios of 99mTc-MIBI and 201Tl was not as linear as on the early images.

Table 1 details the scintigraphic findings in 25 patients with primary thyroid tumors. All 11 papillary carcinomas showed iso or high accumulation of both 201Tl and 99mTc-MIBI on the early images. The delayed images revealed a high accumulation of 201Tl (7 of 11 tumors), nearly identical to that for 99mTc-MIBI (6 of 11 tumors) (Fig. 3).

On early imaging of the two follicular carcinomas, one had a high accumulation of both 201Tl and 99mTc-MIBI, and the second had a nearly identical accumulation of both 201Tl and 99mTc-MIBI. On delayed imaging, the first tumor had a high accumulation, but the second had washed out both tracers.

Of the seven follicular adenomas, two revealed relatively low accumulation, four had iso accumulation and one had high accumulation in both early images compared with normal thyroid tissue. On delayed imaging, the same two tumors revealed low accumulation, only three revealed iso accumulation and two had relatively high accumulation compared with normal thyroid tissue.

In the five patients with adenomatous goiter, two low and three iso accumulations were seen on the early images of both 201Tl and 99mTc-MIBI. On the delayed images, the same two tumors revealed low accumulation, and two had iso accumulation. The remaining tumor showed high accumulation in one part of the adenomatous nodules on both images. In all 25 primary thyroid tumors, 201Tl and 99mTc-MIBI images had nearly identical findings, but 99mTc-MIBI images were slightly clearer than 201Tl images.

Metastatic or Recurrent Lesions from Thyroid Carcinomas

Table 2 shows the scintigraphic findings in patients with metastatic lesions from thyroid carcinomas. In 10 patients with metastatic lymph nodes, 29 were over 1 cm in diameter. Of

TABLE 1
Scintigraphic Results for Thyroid Tumors

<table>
<thead>
<tr>
<th>T/N ratio</th>
<th>Scintigraphic appearance</th>
<th>Papillary carcinoma (n = 11)</th>
<th>Follicular carcinoma (n = 2)</th>
<th>Follicular adenoma (n = 7)</th>
<th>Adenomatous goiter (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>201Tl Early</td>
<td>99mTc-MIBI Early</td>
<td>201Tl Delayed</td>
<td>99mTc-MIBI Delayed</td>
</tr>
<tr>
<td>Mean (s.d.)</td>
<td>Low</td>
<td>Iso</td>
<td>High</td>
<td>Mean (s.d.)</td>
<td>Low</td>
</tr>
<tr>
<td>1.39 (0.41)</td>
<td>0</td>
<td>8</td>
<td>3</td>
<td>1.27 (0.25)</td>
<td>0</td>
</tr>
<tr>
<td>1.10 (0.21)</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>1.21 (0.29)</td>
<td>2</td>
</tr>
</tbody>
</table>
these 29 lymph nodes, 25 were clearly depicted (positive) (Fig. 4), and 4 were equivocal or had no depiction (equivocal or negative) on both 201TI and 99mTc-MIBI images. Of these four less clearly depicted metastatic lymph nodes, three were in the submandibular regions below the mandibular angle, and one was the paratracheal lymph node just below the thyroid gland.

In three patients with lung metastases, nine metastatic nodules were estimated to be over 1 cm in diameter by CT. Six of seven of these nodules were clearly depicted on both 201TI and 99mTc-MIBI scintigrams. Accumulation was unclear in two of three images for both 201TI and 99mTc-MIBI. These findings were nearly identical, but 99mTc-MIBI images were slightly clearer than 201TI images.

In two patients with metastatic bone tumors, metastases of cervical vertebrae and the left eighth rib were evaluated. Both metastases were clearly depicted on both images, but a high accumulation 201TI in the liver and small intestine and 99mTc-MIBI in the liver/biliary system and small intestine hid the lower thoracic/lumbar vertebral regions.

**DISCUSSION**

Technetium-99m-MIBI is a superior myocardial perfusion agent (1,2). It is a lipophilic cationic agent whose myocardial distribution is proportional to regional blood flow. It has been reported that 99mTc-MIBI accumulates within the mitochondria and cytoplasm of cells on the basis of the electrical potentials generated across the membrane bilayers (17), whereas 201TI mostly follows the potassium pathway through the ATPase-dependent Na⁺/K⁺ pump (18,19).

Recently, 99mTc-MIBI has been reported to accumulate in benign and malignant lesions, such as lung (3,4), brain (5,6), carcinoid (20) and parathyroid tumors (7,8) and bone lesions (9). In thyroid tumors, this tracer is reported to accumulate in recurrent Hurthle cell carcinoma (21) and primary thyroid lymphoma (22).

In thyroid tumors, 201TI has been used to differentiate benign from malignant nodules (10–12) and to find metastatic or recurrent lesions during follow-up studies (13–15). Delayed imaging has been reported to be useful in differentiating malignant tumor from benign tumor, but the results were not very satisfactory. Like 201TI, 99mTc-MIBI does not require stopping thyroid medications before beginning the study. We think that 99mTc-MIBI scintigraphy is advantageous over 131I scintigraphy in that it requires no preparation before study.

In the present study, 99mTc-MIBI images were very similar to 201TI images. In papillary carcinoma, 6 (54.5%) of 11 tumors showed marked retention of 99mTc-MIBI, and 7 (63.6%) of 11 tumors showed marked retention of 201TI on the delayed image. In differentiating malignant from benign thyroid nodules, El-Desouki et al. (11) and Ochi et al. (12) reported a sensitivity of over 90% (for tracer retention in tumors on the delayed images) for 201TI, but Koizumi et al. (10) reported a 74% sensitivity in 246 thyroid nodules. We think that these results are dependent on tumor size to some degree. In the present study, one of two follicular carcinomas showed marked accumulation on both early and delayed images, whereas the other showed high accumulation on the early image only and no accumulation on the delayed image for both 99mTc-MIBI and 201TI. In well-differentiated follicular carcinomas, neoplastic follicles are similar to those of histologically normal thyroid tissue. We agree with Ochi et al. (12) that differentiation of well-differen-

**TABLE 2**

| Scintigraphic Results in Metastatic Lesions (> 1 cm) from Thyroid Carcinomas |
|---------------------------------|--------|--------|--------|
| Positive                        | Equivocal | Negative |
| 201TI (n = 9) in ten patients   | 25      | 1      | 3      |
| 99mTc-MIBI                      | 25      | 2      | 2      |
| Lung metastases (n = 9) in patients | 6      | 3      | 0      |
| 201TI                           | 25      | 2      | 2      |
| 99mTc-MIBI                      | 7      | 2      | 0      |
| Bone metastases (n = 2) in two patients | 2      | 0      | 0      |
| 201TI                           | 2      | 0      | 0      |
| 99mTc-MIBI                      | 2      | 0      | 0      |

LN = lymph node.

**FIGURE 3.** (A) Early 99mTc-MIBI image in a patient with papillary carcinoma in the right lobe of the thyroid. Accumulation in the tumor was nearly identical to normal thyroid tissue. (B) Delayed 99mTc-MIBI image in the same patient showing a high accumulation in the tumor but low accumulation in normal thyroid tissue. (C) Early 201TI image in the same patient. Accumulation in the tumor was nearly equal to that in the normal thyroid tissue. (D) Delayed 201TI image in the same patient. The tumor had high accumulation, and the normal thyroid tissue had low accumulation. Findings were nearly identical for both 99mTc-MIBI and 201TI scintigraphy, but 99mTc-MIBI images were slightly clearer.

**FIGURE 4.** (A) Early 99mTc-MIBI image in a patient with papillary carcinoma with cervical lymphadenopathy showing several metastatic lymph nodes in the bilateral neck region and one in the upper mediastinum. (B) Early 201TI image in the same patient shows findings similar to those on the 99mTc-MIBI image. The 99mTc-MIBI image is clearer than the 201TI image, and one lymph node in the upper mediastinum is slightly clearer on the 99mTc-MIBI image than the 201TI image.
tiated follicular carcinoma may be beyond the scope of a scintigraphic study. For benign nodules (follicular adenoma and adenomatous goiter) in our series, 8 (66.7%) of 12 nodules had no marked retention of either $^{99m}$Tc-MIBI or $^{201}$TI on the delayed images. Previously, benign thyroid nodules were reported to show no increased thallium activity in 92% (11) and 89.7% (12), but 58% showed no increased thallium activity on visual evaluation of 246 lesions (10). These results are disappointing compared with those for aspiration cytology, with a sensitivity of 65% to 98% and a specificity of 72% to 100% (23,24). However, critics point out that fine-needle biopsy has limitations according to the skill of aspirator, the expertise of the cytologist and the difficulty in differentiating some benign adenomas from malignancies (23). Therefore, $^{99m}$Tc-MIBI or $^{201}$TI imaging should be used to supplement aspiration cytology in the differentiation of the thyroid tumors.

As for the evaluation of metastases or recurrences, $^{99m}$Tc-MIBI and $^{201}$TI images and results were nearly identical. About 34 (85.0%) of 40 metastases or recurrences were clearly revealed on the early images for both $^{99m}$Tc-MIBI and $^{201}$TI. These results are relatively satisfactory. The $^{99m}$Tc-MIBI images were slightly clearer than those of $^{201}$TI. However, Brendel et al. (13) reported that $^{201}$TI imaging is not recommended as the only modality for follow-up studies in patients with well-differentiated thyroid carcinoma because the sensitivity of $^{201}$TI imaging for detecting tumor location is not 100%, and serum thyroglobulin measurements are more reliable in successful thyroid ablation. We share this opinion and recommend the combination of $^{99m}$Tc-MIBI or $^{201}$TI imaging with thyroglobulin measurement during the follow-up period.

CONCLUSION

Technetium-99m-MIBI images were similar to $^{201}$TI images. In differentiating malignant from benign tumors in thyroid masses, both $^{99m}$Tc-MIBI and $^{201}$TI were insufficient compared with aspiration cytology. However, these studies help with the diagnosis when the aspiration study results are unsatisfactory and when imaging reveals metastatic lymph nodes or strong accumulation on the delayed image. Technetium-99m-MIBI studies are also useful in follow-up evaluation of thyroid carcinoma because of the superior imaging characteristics of $^{99m}$Tc-MIBI compared with $^{201}$TI.

REFERENCES