

## Technetium-99m Methoxyisobutylisonitrile Imaging in the Follow-up of Differentiated Thyroid Carcinoma

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### Abstract

**Objective:** To evaluate the potential of technetium-99m methoxyisobutylisonitrile (Tc-99m MIBI) imaging as an alternative to I-131 total-body scan (I-131 TBS) for the follow-up of patients with differentiated thyroid carcinoma (DTC). **Patients and Methods:** We performed 87 Tc-99m MIBI imaging studies in 76 DTC patients who had total or near-total thyroidectomy followed by a radioactive iodine ablation while receiving thyroxine therapy. The final diagnosis was correlated with I-131 TBS, serum thyroglobulin (Tg), other conventional imaging modalities, clinical outcome, and/or pathological report. **Results:** Seventy-six recurrent tumours or metastatic conditions in 58 DTC patients were detected. The overall findings of Tc-99m MIBI showed 72% sensitivity, 100% specificity and 77% accuracy. The figures for I-131 scan were 57%, 100% and 66%, respectively. When classifying upon tumour locations, Tc-99m MIBI imaging had sensitivity of 79% for cervical, 50% for mediastinal, 65% for skeletal and 69% for pulmonary metastases and the corresponding values for I-131 TBS were 33%, 67%, 94% and 75%, respectively. Furthermore, Tc-99m MIBI could detect only 44% of thyroid remnants demonstrated by radioiodine scan. **Conclusions:** Tc-99m MIBI imaging is more sensitive than I-131 TBS in detecting tumours in the neck but less sensitive for metastasis elsewhere, as well as thyroid remnants. Therefore, Tc-99m MIBI imaging should not substitute but rather complement I-131 TBS for evaluation of DTC patients post-radioiodine ablation.

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**Key words:** Iodine-131, Tc-99m MIBI, Thyroid carcinoma

### Introduction

Differentiated thyroid carcinoma (DTC) is not an uncommon tumour in Thailand.<sup>1</sup> A high percentage of 10-year survival results in long-term follow-up. I-131 total-body scan (I-131 TBS) is commonly used for monitoring the disease after surgery and radioiodine ablation in most centres. This study has an excellent specificity of almost 100%. However, the sensitivity is much lower and varies from 50% to 55% for the detection of metastases.<sup>2,3</sup> Furthermore, it requires 4 to 6 weeks of discontinuation of thyroid hormone therapy to achieve the appropriate thyroid stimulating hormone (TSH) level to stimulate the tumour uptake. On the other hand, Tc-99m methoxyisobutylisonitrile (Tc-99m MIBI), which is a non-specific tumour imaging agent, has been increasingly used for thyroid carcinoma imaging without the need for thyroid hormone discontinuation.

The aim of this study was to evaluate the potential role of whole-body Tc-99m MIBI imaging, to see whether it could

be used as an alternative to I-131 TBS for the follow-up of patients with DTC.

### Materials and Methods

We performed 87 Tc-99m MIBI imaging studies in 76 DTC patients who had total or near-total thyroidectomy followed by one or more treatment doses of radioactive iodine, while receiving levothyroxine (L-T<sub>4</sub>) therapy. There were 53 females and 23 males (age range, 18 to 82 years; mean, 48.2 ± 16.4 years). Histologically, 62 papillary or mixed papillary-follicular and 25 follicular carcinomas were included. All underwent Tc-99m whole-body imaging to follow-up or evaluate various suspected metastatic conditions according to the indications shown in Table I. A patient may be suspected for more than one metastatic conditions. Final diagnosis was correlated with I-131 TBS, chest radiograph, other conventional imaging modalities, such as ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI) etc., serum tumour

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TABLE I: INDICATIONS FOR Tc-99m MIBI IMAGING IN DIFFERENTIATED THYROID CARCINOMA PATIENTS

| Indication                       | No. of patients (cases) |
|----------------------------------|-------------------------|
| Lymph node metastasis            | 26                      |
| Bone metastasis                  | 13                      |
| Lung metastasis                  | 11                      |
| Mediastinal metastasis           | 2                       |
| Node and lung metastases         | 4                       |
| Node and mediastinal metastases  | 1                       |
| Bone and lung metastases         | 2                       |
| Bone and mediastinal metastases  | 2                       |
| Lung and mediastinal metastases  | 1                       |
| Raised thyroglobulin level alone | 3                       |
| Tumour recurrence                | 4                       |
| Confirmed remission              | 18                      |
| Total                            | 87                      |

marker called thyroglobulin (Tg) level, clinical outcomes, and/or pathological results.

### Scintigraphic Techniques

**Tc-99m MIBI imaging:** Tc-99m MIBI whole-body imaging was obtained immediately following intravenous injection of 740 MBq (20 mCi) of Tc-99m MIBI, using a scintillation camera equipped with a low-energy, high-resolution collimator in anterior and posterior views at a speed of 15 cm/min. Additional 1000-Kct static images at the neck and particular regions were also obtained if indicated.

**I-131 total-body scan (I-131 TBS):** I-131 TBS was regularly obtained after 2 weeks of discontinuation of triiodothyronine ( $T_3$ ) which had been replaced by L-thyroxine ( $L-T_4$ ) for the last 4 weeks to enhance TSH level to the optimal value of greater than 30  $\mu$ IU/mL and to shorten the period of hypothyroidism. Seventy-two hours following a diagnostic dose of 185 MBq (5 mCi) of I-131 or 3 to 7 days following the treatment dose, a whole-body imaging was obtained with a scintillation gamma camera attached with a high-energy collimator at a speed of 12 cm/min. In addition, 10-min static images of the thyroid region and other suspicious areas as requested were also performed.

**Thyroglobulin (Tg) measurement:** Serum Tg was measured by the immunoradiometric (IRMA) method (ELSA-hTG, CIS, France). The inter-assay coefficient of variation (CV) was 7.37% and the intra-assay CV was 4.72%. The cut-off value used in our laboratory to distinguish pathological from non-pathological Tg values in athyrotic patients was 4 ng/mL while receiving thyroid hormone suppression. Patients who had elevated Tg antibody were excluded from the study.

### Interpretation

All images were visually interpreted and the lesions were

considered positive if there was a definite localised area of higher uptake than the surrounding background activity. The regions of metastasis or recurrence were divided into four categories; neck, lung, mediastinum and bone. Positive localisation at the midline thyroid bed region may be due to normal thyroid remnant or local recurrence according to the clinical and other accompanying investigations. The lesions at the lateral side of the neck were considered lymph node metastasis.

### Statistical Analysis

The following formulas were used for statistical analysis: sensitivity =  $TP/(TP+FN)$ ; specificity =  $TN/(TN+FP)$ ; accuracy =  $TP+TN/(TP+FP+TN+FN)$ ; positive predictive value =  $TP/(TP+FP)$ ; negative predictive value =  $TN/(TN+FN)$ ; where T = true, F = false, P = positive, and N = negative.

### Results

Of 76 DTC patients, 58 cases had tumour recurrence or metastatic evidence, while 18 cases were in remission. Since 7 patients who had palpable cervical lymph node and positive Tc-99m MIBI uptake had undergone surgery, only 80 I-131 TBS (52 therapeutic and 28 diagnostic TBS) have remained for the study. The overall findings revealed that Tc-99m MIBI imaging had 72% sensitivity, 100% specificity and 77% accuracy. The positive predictive value (PPV) and negative predictive value (NPV) were 100% and 46%, respectively. The figures for I-131 TBS were 57 %, 100 %, 66%, 100% and 38%, respectively.

A total of 76 disease conditions including metastases in the regional lymph node (33), bone (17), lung (16) and mediastinum (6) as well as local tumour recurrence (4); and 16 cases with thyroid remnant were imaged with Tc-99m MIBI imaging. All but 7 cases with cervical node metastasis were also studied with radioiodine scan. The results of Tc-99m MIBI and I-131 scintigraphy in various tumour locations are summarised in Table II. Neither Tc-99m nor I-131 imaging in this study produced false-positive result; thus, excellent specificity and positive predictive value were achieved. Three cases with rising Tg level without clinical evidence of disease have shown accumulation of Tc-99m MIBI in metastatic cervical lymph nodes.

In terms of detection of thyroid remnant following radioiodine ablation, Tc-99m MIBI imaging revealed tracer uptake in only 7 of 16 cases (44%). These cases had positive I-131 scan.

### Discussion

Imaging with radioiodine, I-131, has long been accepted as a standard tool in the management of DTC patients. However, it is not convenient to perform as thyroid hor-

TABLE II: COMPARATIVE RESULTS OF Tc-99m MIBI IMAGING AND I-131 TOTAL-BODY SCAN IN VARIOUS TUMOUR CONDITIONS

| Disease condition      | No. | Tracers | Sensitivity | Specificity | Accuracy | PPV  | NPV  |
|------------------------|-----|---------|-------------|-------------|----------|------|------|
| Lymph node metastasis  | 33  | MIBI    | 0.79        | 1.00        | 0.92     | 1.00 | 0.89 |
|                        | 26* | I-131   | 0.35        | 1.00        | 0.75     | 1.00 | 0.72 |
| Bone metastasis        | 17  | MIBI    | 0.65        | 1.00        | 0.93     | 1.00 | 0.99 |
|                        | 17  | I-131   | 0.94        | 1.00        | 0.99     | 1.00 | 0.98 |
| Lung metastasis        | 16  | MIBI    | 0.69        | 1.00        | 0.94     | 1.00 | 0.93 |
|                        | 16  | I-131   | 0.75        | 1.00        | 0.95     | 1.00 | 0.94 |
| Mediastinal metastasis | 6   | MIBI    | 0.50        | 1.00        | 0.97     | 1.00 | 0.96 |
|                        | 6   | I-131   | 0.67        | 1.00        | 0.98     | 1.00 | 0.97 |
| Local recurrence       | 4   | MIBI    | 1.00        | 1.00        | 1.00     | 1.00 | 1.00 |
|                        | 4   | I-131   | 0.25        | 1.00        | 0.96     | 1.00 | 0.96 |

PPV: positive predictive value; NPV: negative predictive value

\* Seven patients had undergone surgical removal of the tumour following Tc-99m MIBI studies.

mone discontinuation for 4 to 6 weeks is necessary; thus, delaying results and also management of patients. In addition, some metastases may lose the capability to trap I-131. As an alternative, some non-specific tumour imaging tracers, such as Tl-201, Tc-99m MIBI and Tc-99m tetrofosmin, have been introduced to evaluate these tumours. Among these agents, Tc-99m MIBI is the radiopharmaceutical that has been most widely studied. This tracer is taken up by the tumour cells mainly via cellular mitochondrial content and metabolism,<sup>4</sup> and is not TSH-dependent.<sup>5</sup> Tc-99m MIBI study thus not only produces better image quality but also provides rapid assessment of tumour status without discontinuing thyroid hormone medications, unlike I-131 scan.

Although several reports have previously shown that thallium-201 is useful for detecting metastatic thyroid carcinoma, particularly when radioiodine image is negative,<sup>6-8</sup> this radionuclide is less available and more expensive as compared to Tc-99m MIBI.

A number of recent studies have been conducted to compare Tc-99m MIBI with other scanning methods, such as I-131,<sup>9-11</sup> Tl-201<sup>3,9,11-13</sup> and FDG PET scan,<sup>10,14</sup> in patients with thyroid carcinoma. Many investigators<sup>10,15,16</sup> observed higher sensitivity with Tc-99m MIBI but some reported conflicting results.<sup>9,11</sup>

Nemec et al<sup>15</sup> reported excellent sensitivity of Tc-99m MIBI in the detection of metastatic thyroid carcinoma to bone and lungs (100% and 94.7%, respectively). Rubello et al,<sup>16</sup> who compared Tc-99m MIBI study and neck ultrasonography, reported similar results for sensitivity to detect cervical, mediastinal, pulmonary and bone metastases—93.5%, 100%, 100%, and 85.7%, respectively. On the other hand, we found that the sensitivity of Tc-99m MIBI was somewhat lower. Nevertheless, our results suggest that Tc-99m MIBI scintigraphy is most useful for the detection of tumours in the neck and more sensitive than I-131 TBS, in contrast to the detection of bone and

lung metastases where I-131 TBS appears superior. Combining SPECT technique with planar whole-body scan may improve the detection of tumour at particular regions such as the lung and mediastinum.

For radioiodine-negative or non-functioning metastasis, Tc-99m MIBI certainly has a definite role to localising the tumour when Tg is elevated and/or there is clinical suspicion of recurrent or metastatic disease.

Concerning residual thyroid tissue following radioiodine ablation, Tc-99m MIBI, which is similar to Tl-201, appears to be far inferior compared to I-131.<sup>8</sup> Therefore, Tc-99m MIBI is much less accurate to evaluate the successfulness of the ablative treatment. In our study, only 44% of the patients whose I-131 scan demonstrated thyroid remnant revealed MIBI uptake, as compared to 64% reported by Roelants and Becker.<sup>17</sup> They also noted that the proportion of visualised residual thyroid tissue dropped down when the scan was performed late.

## Conclusion

Tc-99m MIBI imaging has an important role in the follow-up of DTC patients post surgery and after I-131 ablation, while continuing to receive thyroid medications, particularly in the neck. In addition, rapid evaluation of the disease will ensure that further appropriate treatment will be given. However, false-negative Tc-99m MIBI result with I-131 TBS giving a positive result can occur such as in mediastinal, bone and lung metastases; hence, Tc-99m MIBI could not be substituted but rather complement I-131 TBS. If clinical history or serum tumour marker suggests tumour evidence, further investigations or histological details should be obtained.

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