

## Usefulness of technetium-99m methoxyisobutylisotrile liver single photon emission computed tomography to detect hepatocellular carcinoma

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Technetium-99m methoxyisobutylisotrile (Tc-99m MIBI) has been shown to be useful in identifying several types of tumors, such as breast, lung and thyroid cancers. The usefulness of Tc-99m MIBI liver imaging in detecting hepatocellular carcinoma (HCC) is still controversial. In this study, 22 patients with HCC performed Tc-99m MIBI liver single photon emission computed tomography (SPECT). Twenty of 22 patients (90.9%) showed negative liver SPECT findings without significant Tc-99m MIBI uptake in HCC, and only 2 patients (9.1%) showed positive liver SPECT findings with significant Tc-99m MIBI uptake in HCC. In addition, no significant correlation between liver SPECT findings with sex, age, alpha fetoprotein serum level, HCC differentiation, and virus hepatitis status was found. We concluded that Tc-99m MIBI liver SPECT is not a sensitive tool to detect HCC.

*Key words:* Technetium-99m methoxyisobutylisotrile, hepatocellular carcinoma, single photon emission computed tomography.

Technetium-99m methoxyisobutylisotrile (Tc-99m MIBI), a member of the isonitrile class of coordination compounds, is a lipophilic cation used for myocardial perfusion imaging [14]. In addition, Tc-99m MIBI has been shown to be useful in identifying several types of tumors, such as breast, lung and thyroid cancers [1, 12]. Although its uptake mechanisms are not completely understood, it has been hypothesized that flow and metabolic status of cells are important with intracellular uptake dependent on mitochondria and the Na<sup>+</sup>/K<sup>+</sup> pump. However, there were only a few reports in the literature for Tc-99m MIBI uptake in hepatocellular carcinoma (HCC), and the results were conflicting [1, 5, 17]. HCC is the most common cancer in this country due a high prevalence of chronic HBV and HCV infection [2, 3, 19]. Therefore, the aim of this study was try to use Tc-99m MIBI liver single photon emission computed tomography (SPECT) to detect HCC and investigate the relationship between SPECT findings and various clinical parameters.

### Material and methods

*Patients.* Twenty-two patients (19 men, 3 women; age range, 23–73 years old; mean age 61.3 ± 13.4 years) with pathological proven HCC were enrolled in this study. No patient had been treated previously. Twelve cases had chronic hepatitis B virus infection, 5 cases had chronic hepatitis C virus infection, 2 cases had both chronic hepatitis B and C viral infections, and the remaining 3 cases had no known cause of HCC.

*Technetium-99m methoxyisobutylisotrile liver single photon emission computed tomography.* Before Tc-99m MIBI liver SPECT, there is a delay of 30 min from the oral intake of 500 mg perchlorate to the start of SPECT to prevent abnormal uptake of free Tc-99m pertechnetate. A commercial MIBI preparation (max. 5.56Gb (150 mCi) in approximately 1 to 3ml) is obtained from Dupont Company (Cardiolite). The labeling and quality control procedures are carried out according to the manufacturer's instructions. Labeling efficiencies are always higher than 95 percent. Each patient received intravenous injection of 20 mCi

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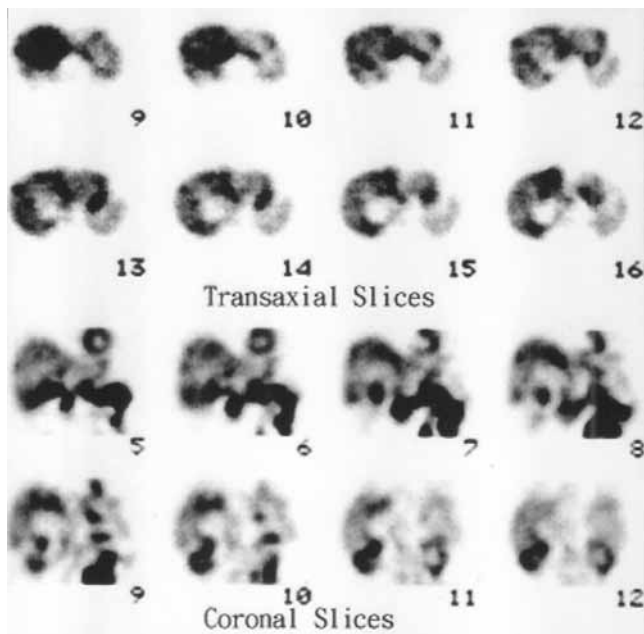


Figure 1. Positive Tc-99m MIBI liver SPECT findings reveal increased Tc-99m MIBI uptake in the HCC (the upper portion of the right hepatic lobe).

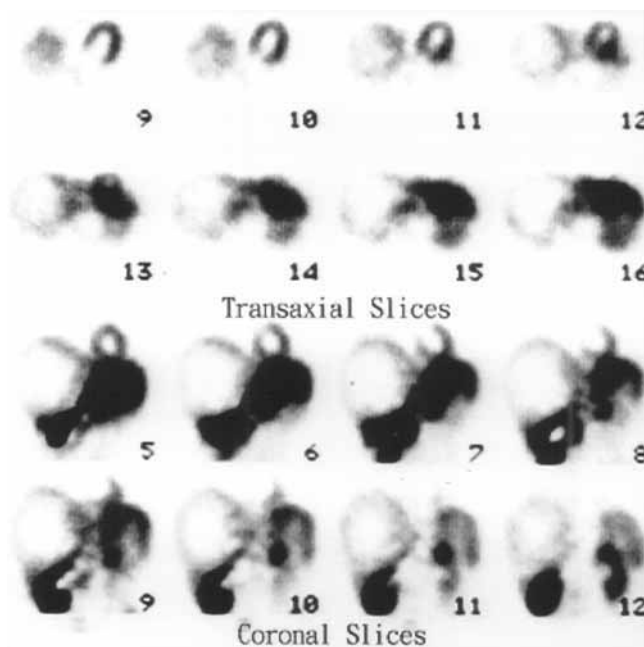


Figure 2. Negative Tc-99m MIBI liver SPECT findings reveal decreased Tc-99m MIBI uptake in the HCC (the upper portion of the right hepatic lobe).

(740 MBq) Tc-99m MIBI in the arm. Anterior and posterior planar and 360° SPECT images of the liver were performed at 10 minutes after injection using a dual-head gamma camera (GE Millennium, Milwaukee, Wisconsin, USA) equipped with a low-energy, high-resolution collimator. The energy peak was centered at 140 keV with a 10% win-

Table 1. The detailed data and Tc-99m MIBI liver SPECT findings of the patients

Case No.	Sex	Age (years)	AFP (ng/ml)	Tumor differentiation	Tc-99mMIBI liver SPECT
1	Woman	23	71433	Moderate	Positive
2	Man	36	6955	Moderate	Negative
3	Man	41	31	Undifferentiated	Negative
4	Man	48	6	Moderate	Negative
5	Man	49	144	Moderate	Negative
6	Woman	61	8508	Poor	Negative
7	Woman	62	8	Undifferentiated	Negative
8	Man	63	5	Undifferentiated	Negative
9	Man	63	8	Poor	Negative
10	Woman	65	35	Undifferentiated	Negative
11	Man	66	17	Poor	Positive
12	Man	66	7	Moderate	Negative
13	Man	67	5	Poor	Negative
14	Man	69	1567	Moderate	Negative
15	Man	69	327	Poor	Negative
16	Man	69	61	Poor	Negative
17	Man	70	17	Poor	Negative
18	Man	71	3464	Moderate	Negative
19	Man	72	1678	Undifferentiated	Negative
20	Man	72	6	Undifferentiated	Negative
21	Man	73	8	Poor	Negative
22	Man	73	2513	Moderate	Negative

dow. Tc-99m MIBI liver SPECT images are interpreted by the agreement of at least two of three experienced physicians. Tc-99m MIBI liver SPECT findings are defined as positive (focal abnormal accumulation at the tumor site seen on liver ultrasonography or CT) or negative (no abnormal focus of activity at the tumor site) (Fig. 1, 2).

**Statistical analysis.** The correlation between Tc-99m MIBI liver SPECT findings and various clinical features such as: sex, alpha feto-protein serum level, tumor differentiation, and virus hepatitis status was analyzed by chi-square tests.

## Results

The detailed data of the patients were listed in Table 1. Only 2 of 22 (9.1%) patients had positive Tc-99m MIBI liver SPECT findings and significant Tc-99m MIBI uptake in the HCC. However, the remaining 20 of 22 (90.9%) patients had negative Tc-99m MIBI liver SPECT findings without significant Tc-99m MIBI uptake in the HCC. The correlation was not significant ( $p$  values  $>0.05$ ) between Tc-99m MIBI liver SPECT findings and various clinical parameters.

## Discussion

There are still no satisfactory chemotherapy agents for HCC. One of the most important reasons for this resistance

is the over-expression of the multidrug resistance (MDR) gene after induction of chemotherapy. This gene encodes a 170-kDa glycoprotein, i.e. P-glycoprotein (Pgp) present in the plasma membrane and acts as an ATP-driven drug efflux pump [4, 15, 18]. There have been several reports concerning the expression of Pgp in HCC tissues [8, 13, 16] and ITSUBO et al reported 67.4% of HCC with positive Pgp expression [8].

Recently, it has also been reported that lipophilic and cationic Tc-99m MIBI is a substrate of Pgp, which functions as ATP-dependent efflux pumps, and thus Tc-99m MIBI is extruded from cancer cells like chemotherapy drugs [6, 7]. In addition, Tc-99m MIBI imaging was used as a noninvasive technique to predict the presence of Pgp expression in certain cancers [9–11]. Therefore, high incidence of Pgp expression of the HCC may be an explanation that 20 of 22 (90.9%) patients had negative Tc-99m MIBI liver SPECT findings without significant Tc-99m MIBI uptake in the HCC in our study.

In conclusion, Tc-99m MIBI liver SPECT imaging is not a sensitive tool to detect HCC. However, based on the previous literature reports, further studies are necessary to analyze the correlation of Tc-99m MIBI liver SPECT findings and MDR gene expression in HCC.

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