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Correlation between ^{99m}Tc-MIBI uptake and angiogenesis in MIBI-positive breast lesions

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Abstract

This study was undertaken to assess the correlation between the degree of accumulation and the washout of 99m technetium methoxyisobutylisonitrile (^{99m}Tc-MIBI) and angiogenesis in MIBI-positive breast lesions. Twenty-eight patients (mean age, 51±11 years) with 31 breast lesions who underwent scintimammography were studied. Anterior, left and right prone lateral images were obtained 20 min and 3 h after the injection of 740 MBq ^{99m}Tc-MIBI. All breast lesions showed increased ^{99m}Tc-MIBI uptake. Early and delayed tumor to background activity ratios (T/BG) and washout index (early tumor uptake−delayed tumor uptake divided by early tumor uptake) were calculated. Vascular endothelium was immunohistochemically labeled using a biotinylated monoclonal antibody directed against the factor-VIII-associated antigen using standard biotin–avidin technique. Angiogenesis was evaluated by assessing the vascular surface density (VSD) and the microvessel number (NVES) within 10 randomly chosen areas. All pathological data were compared with early and delayed T/BG activity ratios and washout index of ^{99m}Tc-MIBI. Statistical analysis was performed using Spearman correlation test. There was no statistically significant correlation between the degree of angiogenesis and early T/BG (r=.287, P>.05 with VSD, r=.351, P>.05 with NVES), delayed T/BG (r=.277, P>.05 with VSD, r=.315, P>.05 with NVES) and the washout index (r=.268, P>.05 with VSD, r=.285, P>.05 with NVES) of ^{99m}Tc-MIBI in all breast lesions. There was no statistically significant correlation between the degree of angiogenesis and early T/BG (r=.235, P>.05 with VSD, r=.356, P>.05 with NVES), delayed T/BG (r=.181, P>.05 with VSD, r=.285, P>.05 with NVES) and the washout index (r=.158, P>.05 with VSD, r=.187, P>.05 with NVES) of ^{99m}Tc-MIBI in 24 invasive breast lesions. No statistically significant correlation was found between the degree of angiogenesis and early T/BG (r=−.036, P>.05 with VSD, r=−.107, P>.05 with NVES), delayed T/BG (r=−.500, P>.05 with VSD, r=−.429, P>.05 with NVES), but there was a high correlation between angiogenesis and the washout index (r=.893, P<.05 with VSD, r=.964, P<.05 with NVES) of ^{99m}Tc-MIBI in seven noninvasive breast lesions. Amount of ^{99m}Tc-MIBI uptake in breast lesions is dependent on several factors. Our study indicates that early and delayed ^{99m}Tc-MIBI uptakes in MIBI-positive breast lesions are not related to angiogenesis in both invasive and noninvasive breast lesions. But washout index of ^{99m}Tc-MIBI in noninvasive breast lesions is highly correlated with angiogenesis. ^{99m}Tc-MIBI scintigraphy does not seem to be able to indicate angiogenic property of invasive breast lesions.

Keywords: ^{99m}Tc-MIBI; Angiogenesis; Breast

1. Introduction

Since 1992, 99m technetium methoxyisobutylisonitrile (^{99m}Tc-MIBI) is used for breast imaging and was proved to be highly accurate in the diagnosis of primary breast cancer [1–3]. Methoxyisobutylisonitrile is known as a nonspecific tumor marker. It is a small lipophilic cation and is sequestered within the cytoplasm and mitochondria. The mechanism of uptake of ^{99m}Tc-MIBI is still under investigation, but it appears to be related to the lipophilicity and negative charge of the radiopharmaceutical. According to some studies, uptake of MIBI in both benign and malignant lesions is related to the degree of angiogenesis, percentage of ill-formed blood vessels, high mitotic activity reflected by high tumor grade and high percentage of proliferating cell nuclear antigen, mitosis and PGP expression [4–8]. Several studies have evaluated the correlation between the

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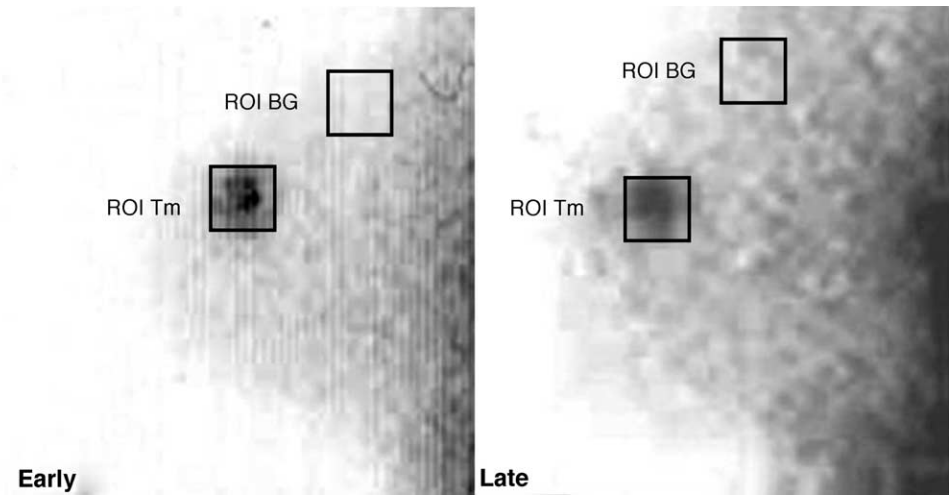

Fig. 1. Early and delayed tumor region of interests are placed over the highest ^{99m}Tc-MIBI uptake on the early and late prone lateral images. Background region of interest is placed over a uniform portion of the same normal breast tissue.

degree of angiogenesis and ^{99m}Tc-MIBI uptake in breast lesions [9–14].

Angiogenesis is described as formation of new blood vessels. The process of tumor angiogenesis results in an increased number of vessels in the tumor tissue, which is essential for tumor growth, metastasis and prognosis [15]. Angiogenesis can be quantified by NVES, which is calculated by counting microvessels, in tumors [16]. Additionally, the vascular surface density (VSD) in a tumor is a putative target of tumor cell adhesion and invasion, as well as consecutive local and systemic spread [17–19].

The aim of this study was to search for a correlation between the degree of ^{99m}Tc-MIBI accumulation in early and delayed phase of the scan, the washout index of ^{99m}Tc-

Table 1
The values of scintigraphic and pathological data

Patients	Early T/BG	Delayed T/BG	Washout index	VSD	NVES	Histopathology
1	2.5	2	0.20	27.6	153	Infiltrative ductal+lobuler carcinoma
2	1.4	1.32	0.50	10.02	62.12	Fibroadenoma
3	2.33	1.94	0.49	20.21	169	Infiltrative lobuler carcinoma
4	2.65	2.26	0.63	31.60	159	Infiltrative ductal carcinoma
5	1.65	1.73	0.44	18.24	107.61	Infiltrative ductal carcinoma
6	3.99	4.5	0.52	42.7	251	Infiltrative ductal+lobuler carcinoma
7	2.25	2.06	0.42	14.08	91.57	In situ ductal carcinoma
8	2.58	2.62	0.55	33	227	Infiltrative lobuler carcinoma
9	1.85	1.81	0.64	33.41	212.5	Infiltrative ductal carcinoma
10	1.92	1.45	0.61	16.99	100	Comedomastitis
11	1.71	1.33	0.58	23.6	158	Radial scar
12	3.54	3.30	0.25	34.69	193.63	Infiltrative ductal carcinoma
13	4.69	3.62	0.70	16.6	145	Infiltrative ductal carcinoma
14	2.07	1.94	0	18.4	125.69	Infiltrative ductal+lobuler carcinoma
15	3.44	2.48	0.29	4.53	24.34	Fibrocystic disease
16	1.14	1.47	0.19	15	73	Infiltrative lobuler carcinoma
17	2.40	2.37	0.29	28.49	210	Infiltrative ductal+lobuler carcinoma
18	2.25	2.42	0.31	25.57	185	Infiltrative ductal+lobuler carcinoma
19	1.36	1.34	0.70	25.41	112	Infiltrative ductal carcinoma
20	3.41	3.85	0.46	14.28	71.57	Infiltrative ductal carcinoma
21	1.73	2.19	0	25.82	121	Infiltrative ductal carcinoma
22	3.95	3.09	0.38	13.87	64.73	Mucinous carcinoma
23	3.06	2.93	0.62	49.2	251	Infiltrative ductal carcinoma
24	2.01	1.74	0.74	33.88	246	Infiltrative ductal carcinoma
25	1.6	1.58	0	4.55	21.21	Fibrocystic disease
26	2.1	1.93	0.34	20.8	38.21	Infiltrative ductal carcinoma
27	1.5	1.4	0.37	7.3	42.1	In situ ductal carcinoma
28	2.2	2.1	0.67	15.9	25.5	Infiltrative ductal carcinoma
29	1.8	1.9	0.52	15.9	25.5	Infiltrative ductal carcinoma
30	1.75	1.85	0.39	16.6	111.4	Infiltrative ductal carcinoma
31	1.95	1.87	0.50	16.6	100.5	Infiltrative ductal carcinoma