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Abstract

Percutaneous microwave coagulation therapy (PMCT) is a new technique for the treatment of hepatocellular carcinoma (HCC). However, it is difficult to distinguish those lesions in which necrosis has been induced from the viable residual lesions during the procedure, because the margin of the tumor becomes unclear during PMCT. We determined the area of necrotic lesions during the procedure using color Doppler imaging. PMCT was performed on 10 patients (17 lesions) with recurrent HCC. The electrode of the microwave delivery system was moved around the tumor and the surrounding area until color mosaic images disappeared from the entire area of the tumor. The areas in which necrotic tissue was indicated by color Doppler imaging were later confirmed by other modalities such as angiography or contrast-enhanced computed tomography. This leads us to believe that real-time, effective evaluation of PMCT is possible with color Doppler imaging.

KEYWORDS: microwave coagulation therapy, color Doppler imaging, hepatocellular carcinoma

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Percutaneous microwave coagulation therapy (PMCT) is a new technique for the treatment of hepatocellular carcinoma (HCC). However, it is difficult to distinguish those lesions in which necrosis has been induced from the viable residual lesions during the procedure, because the margin of the tumor becomes unclear during PMCT. We determined the area of necrotic lesions during the procedure using color Doppler imaging. PMCT was performed on 10 patients (17 lesions) with recurrent HCC. The electrode of the microwave delivery system was moved around the tumor and the surrounding area until color mosaic images disappeared from the entire area of the tumor. The areas in which necrotic tissue was indicated by color Doppler imaging were later confirmed by other modalities such as angiography or contrast-enhanced computed tomography. This leads us to believe that real-time, effective evaluation of PMCT is possible with color Doppler imaging.

Key words: microwave coagulation therapy, color Doppler imaging, hepatocellular carcinoma

Percutaneous microwave coagulation therapy (PMCT) is a new technique for the treatment of hepatocellular carcinoma (HCC). One of the problems inherent in this procedure is the difficulty in evaluating its effectiveness during the procedure, because the margin of the tumor becomes unclear under the influence of PMCT. This makes it difficult to distinguish necrotic lesions from viable residual lesions. Herein, we report a new technique employing color Doppler imaging to determine in real-time the extent of tissue necrosis induced by PMCT.

Materials and Methods

Apparatus. PMCT was performed using a color Doppler imaging system (SSA-270, Toshiba Co., Tokyo, Japan). The microwave delivery system consists of a magnetron (HS-15M, Nippon Shoji Co., Osaka, Japan), a flexible coaxial cable, and a microwave electrode 1.6 mm in diameter and 25 cm in length (TMD-16CB-10/250, Nippon Shoji Co., Osaka, Japan).

Assessment of irradiation time and the change of ultrasound imaging in the bovine liver. Before PMCT was applied to clinical cases, we evaluated the extent of heating by irradiating bovine livers with a microwave electrode at 55 W for various lengths of time. The change in color of the freshly cut surface of the liver was compared with that of ultrasound imaging during PMCT.

Clinical subjects. Ten patients with recurrent HCC underwent PMCT. Surgical resection, transcatheter arterial embolization (TAE) and ultrasonography-guided percutaneous ethanol injection therapy (PEIT) had been performed alone or in combination in all patients before PMCT. Subjects included eight men and two women ranging from 57 to 75 years old (mean, 68). All were diagnosed with liver cirrhosis and were positive for hepatitis B virus antigen or hepatitis C virus antibody. Each had 1 or 2 HCC lesions (total, 17 lesions) measuring from 1.0 to 7.0 cm in greatest dimension (mean, 2.7 cm). The site of the lesion was defined according to Couinaud's segmental model (1) of the liver. For these tumors, PMCT was performed once to 7 times (mean, 2.8). All procedures were thoroughly explained to the patients and their families, and informed consent was

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Table 1 Summary of 10 patients with recurrent hepatocellular carcinoma treated by PMCT

Case	Age (years)	Sex	Treatment before PMCT	Tumor site	Tumor size (cm)	Number of sessions	Recurrence	Outcome (months)
1	74	F	OPE, PEIT	S7, S8	2.5, 1.0	1, 1	+	Died (24)
2	70	M	OPE, TAE	S2-3, S7	7.0, 3.0	4, 3	+	Died (19)
3	71	M	OPE, PEIT, TAE	S2, S3	2.0, 2.5	3, 3	+	Alive (36)
4	65	M	OPE, TAE	S4, S7	3.0, 2.0	4, 2	−	Alive (35)
5	65	M	TAE, PEIT	S4	3.0	2	−	Alive (33)
6	57	M	TAE, PEIT	S6-7, S8	3.0, 1.3	2, 2	−	Alive (33)
7	70	M	TAE, PEIT	S2-3, S4	4.5, 1.0	7, 5	+	Alive (31)
8	72	F	OPE, PEIT, TAE	S7-8	3.3	2	−	Died (11)
9	75	M	PEIT, TAE	S2	1.5	2	−	Alive (27)
10	60	M	PEIT, TAE	S6, S8	1.3, 1.3	2, 2	−	Alive (27)

PMCT: Percutaneous microwave coagulation therapy; F: Female; M: Male; OPE: Hepatic resection; PEIT: Percutaneous ethanol injection therapy; TAE: Trancatheter arterial embolization.

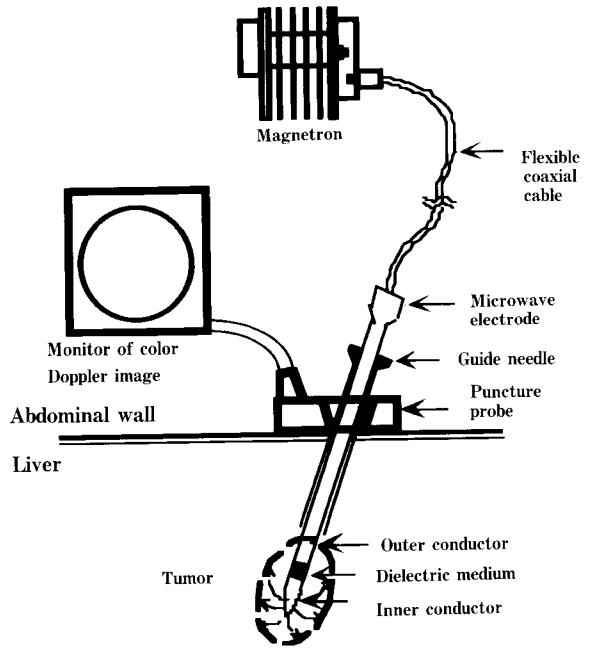

Fig. 1 Illustration of the percutaneous microwave coagulation therapy (PMCT) apparatus.

obtained in each case. These patients were followed-up from 11 to 36 months (Table 1).

Clinical method. Under local anesthesia, a 14 gauge 15 cm guide needle was inserted into the vicinity of the tumor guided by ultrasonography. After the inner needle of the guide was removed, a microwave electrode was inserted through the outer needle of the guide to place the electrode in the tumor area. The electrode was connected to a microwave generator through a flexible coaxial cable (Fig. 1). For tumors larger than 1 cm in diameter, one part of the area was irradiated with microwaves 2450 MHz in frequency at 55 W for 60 sec. Then, the electrode was moved and reinserted into the tumor and the area surrounding the tumor to irradiate the whole area of the tumor.

We determined the effective area of PMCT by changes in color Doppler images monitored during the procedure. The ultimate effectiveness of the procedure was evaluated by the loss of tumor vessels revealed by angiography (performed in 7 cases) and by contrast-enhanced computed tomography (performed in all cases).

Results

The extent of heating in the bovine liver is shown in Fig. 2. In the cut surface, the change in color spread 5 mm in a short dimension and 1.5 cm in a long dimension after 30 sec, and 1 cm in a short dimension and 2 cm in a long dimension after 60 sec. However, the affected area did not become wider after 90 sec. Following this, we decided to irradiate at 55 W for 60 sec. The B-mode image changed into a highechoic pattern 1 cm in diameter with acoustic shadows immediately after the irradiation and showed no remarkable change thereafter. B-mode images did not reflect the extent of the change in color of the cut surface of the bovine liver. On the other hand, the change of the color Doppler image after 30 sec was different from those after 60 and 90 sec. Color mosaic patterns gradually changed into a monochromatic pattern in proportion to the irradiation time.

In the first clinical case of HCC 1 cm in diameter, the color Doppler image changed from a monochromatic pattern to a color mosaic pattern at the beginning of

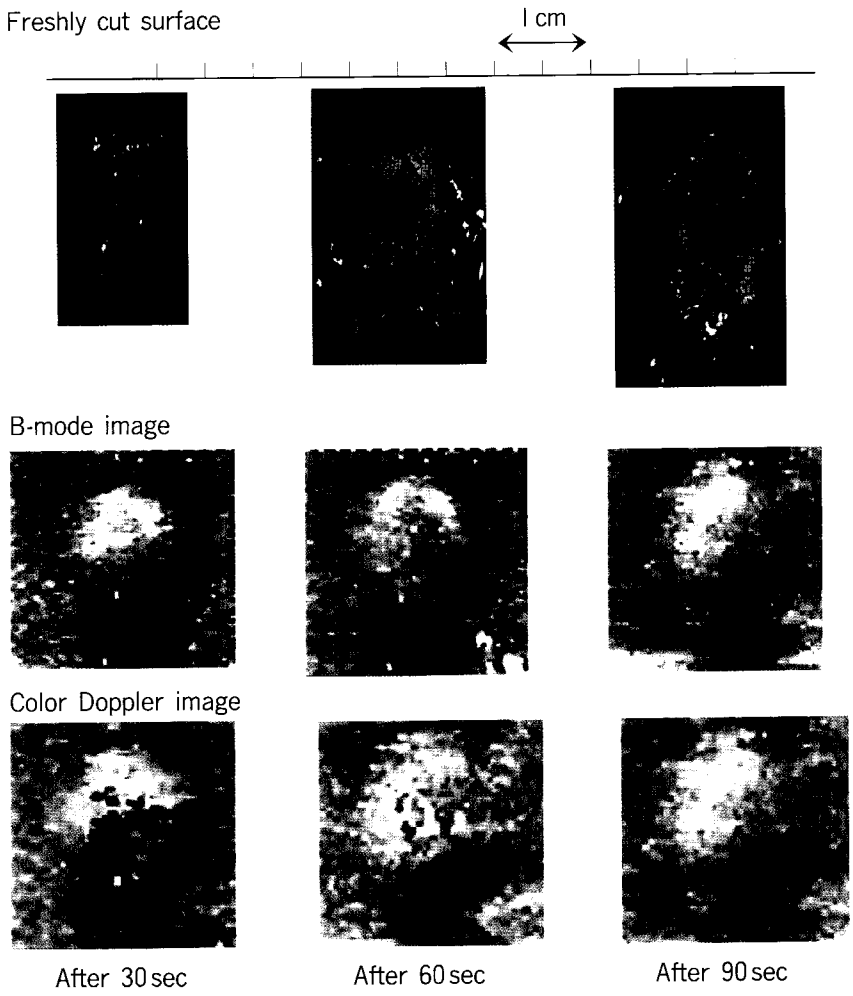

Fig. 2 Macroscopic findings in freshly cut surface of the bovine liver and ultrasound images during percutaneous microwave coagulation therapy. The cut surface turned white and expanded 1 cm after 60 sec, but it did not expand further. The B-mode image immediately became hyperechogenic, making the margins of the tumor unclear. There were no remarkable changes thereafter. On the other hand, color Doppler images changed in proportion to the extent of irradiation.

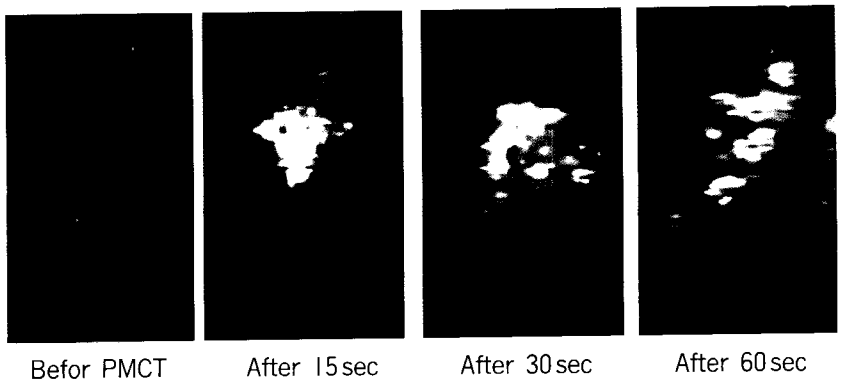

Fig. 3 Changes in the color Doppler image of hepatocellular carcinoma 1 cm in diameter after percutaneous microwave coagulation therapy (PMCT).

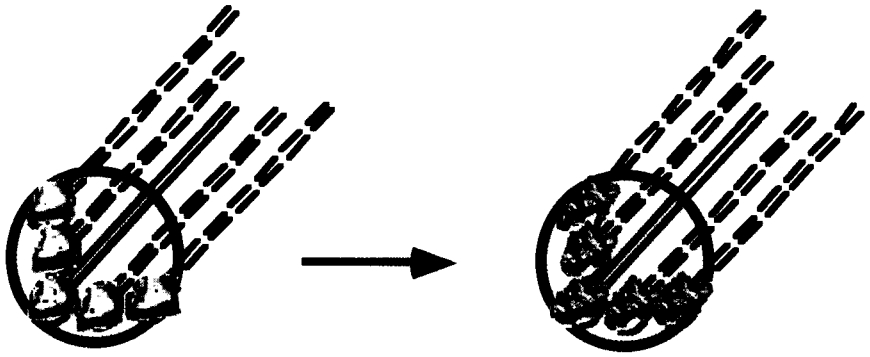

Fig. 4 Illustration of the percutaneous microwave coagulation therapy method for tumors larger than 1 cm in diameter.

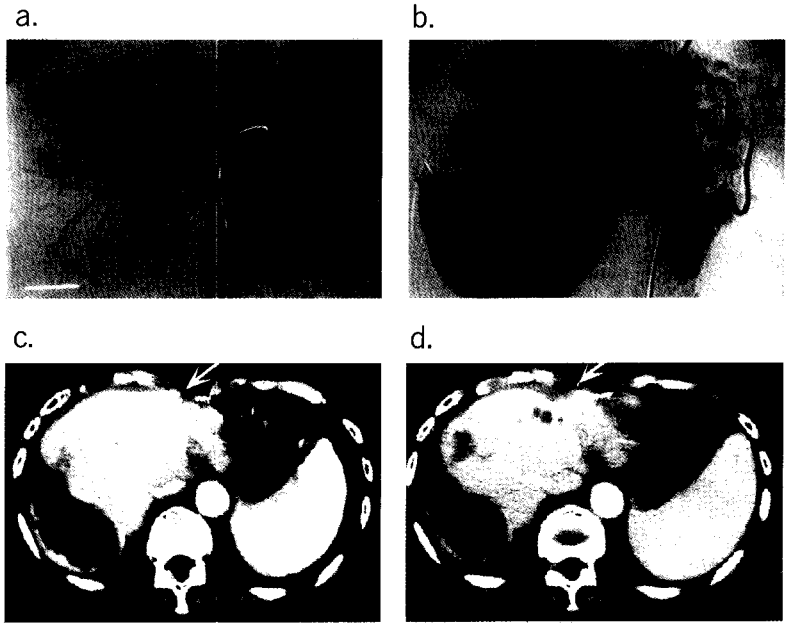

Fig. 5 Changes in angiography images and contrast-enhanced computed tomography (CE-CT) after percutaneous microwave coagulation therapy (PMCT).
a: Angiography before PMCT; **b**: Angiography after PMCT; **c**: CE-CT before PMCT; **d**: CE-CT after PMCT.

irradiation. Then, the color mosaic pattern increased in width immediately after irradiation followed by a monochromatic change in the center. Finally, the color mosaic pattern diminished and changed into a monochromatic pattern with irregular internal echo in the whole area of the tumor after 60 sec (2) (Fig. 3). Following this case, PMCT was applied to tumors larger than 1 cm in diameter several times until the color mosaic image had disappeared in the whole area of the tumor (Fig. 4).

The areas in which the color mosaic pattern disappeared coincided with those areas where the loss of the tumor vessels was confirmed by other modalities such as angiography (13 of 14 lesions) or contrast-enhanced computed tomography (CE-CT) (16 of 17 lesions) after PMCT.

In Fig. 5, the vessels of a tumor 7 cm in diameter diminished after 4 sessions of PMCT. This was confirmed by angiography and CE-CT. Complete tumor remission was achieved in six patients, and HCC recurred in four patients. However, we did not observe any tumor recurrence in the areas treated with PMCT. At the time

of writing, seven patients have been alive from 27 months to 36 months. Three cases died at 11, 19 and 24 months after PMCT because of hepatic failure and/or recurrent tumors. In 4 patients, recurrent nodules appeared in other subsegments, but did not appear in the original sites treated with PMCT.

More than half of the patients complained of a slight heat sensation at the puncture point and some pain in the upper abdominal region during PMCT. However, we neither discontinued treatment nor administered sedatives. After treatment, a transient fever developed in all patients but dissipated the following day. There were no serious complications of PMCT.

Discussion

As an initial treatment for HCC, surgical resection, TAE (3) and PEIT (4) have been performed alone or in combination. However, these treatments have various limitations. Surgical resection is not a viable option for all patients due to poor liver function induced by liver cirrhosis (5). TAE is sometimes ineffective because of inadequate angioneogenesis in small HCC (6). PEIT is widely performed as a percutaneous local treatment because of its simplicity and low cost. However, this modality is occasionally ineffective because of inhomogeneous distribution of ethanol within the tumor (7).

Therefore, there is a need for a more effective technique to induce tumor necrosis. Tabuse *et al.* (8, 9) used microwave radiation for tissue coagulation and hemostasis in hepatic resection during open surgery. Seki *et al.* (10) developed a new type of needle-electrode which allows coagulation of deep lesions in the liver percutaneously. This new modality of percutaneous local treatment for HCC has now been accepted widely in Japan. The advantage of PMCT is that the local area irradiated with microwave radiation is completely killed.

However, one of the problems of this procedure is that it is difficult to evaluate the effective area during the procedure, because the margin of the tumor becomes unclear immediately after irradiation under B-mode imaging. We could detect a difference in the echo pattern between 30 and 60 sec after initiation of treatment by color Doppler imaging. Color Doppler imaging was therefore useful to overcome the problems encountered with B-mode imaging.

It is difficult to distinguish a necrotic cell from a viable cell in histological findings with hematoxylin-eosine dyeing. Yoshimoto *et al.* (11) reported that DNA damage was observed in the area where the tumor turned white under macroscopic observation. This was in accordance with our experimental results in which macroscopic changes in tissue irradiated for 60 sec correlated well with changes in color Doppler images taken after 60 sec of irradiation in the bovine liver.

Color mosaic images seem to occur due to repeated expansion and explosion of the liver cells induced by irradiation with microwaves. PMCT heats tissue by molecular vibration of dipoles, particularly those of water contained in the tissue, and induces thermal coagulation in the target area (12). It seems that color mosaic images change to a monochromatic pattern when the tumor cells stop moving after thermal coagulation. Thus, we believe that the area of effective PMCT treatment can be determined by monitoring changes in echo patterns as revealed by color Doppler imaging.

Another problem of PMCT is that the effective area is limited. For this reason, Seki *et al.* (10) applied PMCT for only small HCC lesions less than 2 cm in diameter. Our method which employs color Doppler imaging can overcome the limitations of PMCT. We also expect that it will allow PMCT to be used for treatment of large HCC.

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