Real-Time Evaluation of the Effectiveness of Microwave Coagulation Therapy for Hepatocellular Carcinoma Using Color Doppler Imaging

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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.

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

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

PMCT: Percutaneous microwave coagulation therapy; F: Female; M: Male; OPE: Hepatic resection; PEIT: Percutaneous ethanol injection therapy; TAE: Transcatheter 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).
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
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 angioembolization in small HCC (6). PEIT is
widely performed as a percutaneous local treatment be-
cause of its simplicity and low cost. However, this
modality is occasionally ineffective because of inhomoge-
neous distribution of ethanol within the tumor (7).
Therefore, there is a need for a more effective tech-
nique 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 imag-
ing. 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 dye-
ing. 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 deter-
mined 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.

References
1. Couinaud C: Les enveloppes vasculo-biliaires du foie au capsule de
2. Takeuchi H, Konaga E, Nishizaki M, Murakami T, Yunoki Y, Tana-
kaya K and Yasui Y: Real-time evaluation of the effectiveness of
percutaneous microwave coagulation therapy using color Doppler
Shioyama Y, Terada R and Kimura M: Transcatheter arterial chemo-
eombolization (TACE) in the treatment of unresectable liver cancer.
Y and Takanashi R: Percutaneous ethanol injection in the treatment of
5. Saito H, Muta M and Andou K: Determination of objective prognosis
of resected hepatocellular carcinoma using the method of discrimina-
K, Wakisaka K, Okamura J and Kozuka T: Limitation of transcatheter
arterial chemoembolization using iodized oil for small hepatocellular
F and Kondo Y: Percutaneous ethanol injection for the treatment of
small hepatocellular carcinoma: Study of 95 patients. J Gastroenteral
8. Tabuse K: A new operative procedure of hepatic surgery using a
9. Tabuse K, Kobayashi Y and Katsumi M: Microwave surgery; he-
patectomy using a microwave tissue coagulator. World J Surg (1985)
9, 136-143.
10. Seki T, Wakabayashi M, Nakagawa T, Itoh T, Shiro T, Kunieda K,
Satô M, Uchiyama S and Inoue K: Ultrasonically guided percutaneous
microwave coagulation therapy for small hepatocellular carcinoma.
Cancer (1994) 74, 817-825.

E: Histopathological evaluation of microwave coagulation for rat liver
and Hirai H: Percutaneous microwave coagulation therapy by the new
synchronous use of microwave and dissociating electric method. J

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