Percutaneous microwave coagulation therapy for hepatocellular carcinoma: Increased coagulation diameter using a new electrode and microwave generator

RYOSUKE INOKUCHI, TOSHIHITO SEKI, KOZO IKEDA, RINAKO KAWAMURA, TOSHIKI ASAYAMA, MASATO YANAGAWA, HIDETO UMEHARA and KAZUICHI OKAZAKI

Department of Gastroenterology and Hepatology, Kansai Medical University, 10-15 Fumizono-cho, Moriguchi, Osaka 570-8507, Japan

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Abstract. We performed percutaneous microwave coagulation therapy (PMCT) using a new microwave electrode and microwave generator to lessen the number of microwave electrode insertions for hepatocellular carcinoma (HCC) measuring ≤ 3.0 cm in diameter. In this study, we assessed the efficacy of this new system. Fifty-two patients with liver cirrhosis and HCC measuring ≤ 3.0 cm in diameter (tumor size: ≤ 2 cm, 27 patients; >2 to ≤ 2.5 cm, 13 patients; >2.5 to ≤ 3 cm, 12 patients) underwent PMCT using a new microwave coagulation system under ultrasonographic guidance. Fortytwo of 52 patients showed complete necrosis of the tumor lesion with a treated margin ≥ 5 mm on dynamic computed tomography. Necrosis of HCC and the non-cancerous area surrounding the tumor was obtained by a single needle insertion in 23 patients (tumor size: ≤ 2 cm, 23 patients), by two needle insertions in 11 patients (tumor size: ≤2 cm, 4 patients; >2 to ≤ 2.5 cm, 5 patients; >2.5 to ≤ 3 cm, 2 patients), and by three needle insertions in 8 patients (tumor size: >2 to ≤ 2.5 cm, 5 patients; >2.5 to ≤ 3 cm, 3 patients). During the follow-up period of 5-34 months, all patients remained alive. Among the patients showing complete necrosis of HCC with a treated margin ≥ 5 mm, we have not detected local recurrences. On the other hand, 4 of the 10 patients who could not obtain the treated margin of ≥ 5 mm, experienced a local recurrence. No fatal complications were observed. However, bile duct stricture was observed in 2 patients. The new microwave coagulation system can induce extensive necrosis with a small number of microwave electrode insertions. This system may enhance the efficacy of PMCT for HCC measuring <3.0 cm in diameter.

Correspondence to: Dr Toshihito Seki, Department of Gastroenterology and Hepatology, Kansai Medical University, 10-15 Fumizonocho, Moriguchi, Osaka 570-8507, Japan E-mail: sekit@takii.kmu.ac.jp

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Introduction

Percutaneous microwave coagulation therapy (PMCT) has been used for the local treatment of either hepatocellular carcinoma (HCC) or metastatic liver tumors (1-5). In previous studies, PMCT has demonstrated the feasibility of efficaciously treating small HCC measuring ≤ 2.0 cm in diameter with a 5-year survival rate of about 70% (3).

However, despite its good coagulation capability and clinical results, PMCT has a major problem. The coagulated areas induced by PMCT with one microwave electrode insertion are small. Therefore, to produce extensive necrosis not only of the tumor but also including the neighboring non-cancerous tissue, multiple microwave electrode insertions were required (3,4). For example, 3-6 electrode insertions were required for HCCs measuring ≤ 2.0 cm and more than 6 electrode insertions were required for HCCs measuring ≥ 2.0 to ≤ 3.0 cm in diameter. Therefore, to significantly reduce the number of microwave electrode insertions and improve patient compliance, we developed a new microwave coagulation system. In this study, we report our clinical experience using this system for nodular HCCs measuring ≤ 3.0 cm in diameter.

Materials and methods

This clinical study was performed according to the guidelines of the Helsinki Declaration and the study was approved by The Clinical Research Board of Kansai Medical University Takii Hospital.

Between September 2005 and August 2008, 52 patients with cirrhosis and a single nodular HCC measuring ≤ 3.0 cm in diameter (tumor size: ≤ 2 cm, 27 patients; >2 to ≤ 2.5 cm, 13 patients; >2.5 to ≤ 3 cm, 12 patients) participated in the study. The pathogenesis of cirrhosis was hepatitis C virus in 50 patients and hepatitis B in 2 patients. The follow-up period ended in January 2009.

To evaluate the efficacy of PMCT for local control of the lesions, we decided on the following requirements: i) no extrahepatic metastases or portal tumor thrombosis were detected by various modes of imaging. ii) The object of treatment was limited to a solitary nodular tumor. iii) The size of the lesion was <3.0 cm in diameter. iv) The tumor

was located on one subsegment. v) Liver function was Child-Pugh Class A or B without refractory ascites and severe bleeding tendency. vi) The patient requested no surgical treatment. vii) Informed consent was obtained from the patient and his or her family member.

In this study, tumors showing extrahepatic extension were excluded because of the difficulty in maintaining the puncture line and tumors located near the hilar region, the gall bladder, or gastrointestinal organs were also excluded because of the possibility of bile duct stricture, bile leakage to the peritoneal cavity or perforation by heat injury.

Cancer staging was performed using ultrasonography (US), dynamic computed tomography (CT), dynamic magnetic resonance imaging (MRI) and CT angiography (CT-A) and CT arterioportgraphy (CT-AP).

In all patients, an iodized oil (4-6 ml, Lipiodol, Andre Guerbet, Aulnay-sous-Bios, France) was injected from the hepatic artery to evaluate the advance grade of cancer in detail and to visualize the tumor area for easy assessment of treated margin after treatment. The histological diagnosis of tumors measuring \leq 2.0 cm in diameter was confirmed by US-guided fine needle biopsy.

Equipment

Microwave coagulation system. To achieve tissue coagulation over an area larger than that for which a conventional system is intended in microwave coagulation therapy, it is necessary to apply greater energy and to apply it more efficiently to heat the tissue. For this purpose, the microwave irradiation power (in watts) must be sufficiently high; irradiation time must be extended; and the electrodes used must be able to withstand the conditions.

Microwave generator. The frequency of the microwave used for our system was 2450±50 MHz, which is internationally recognized as an Industrial, Scientific and Medical (ISM) Band. The electric energy of the microwave was supplied to a high frequency coaxial cable with an impedance of 50 ohms via an isolated sympathizer cavity in the generator and then conducted to an electrode attached to another end of the cable for irradiation from the tip to the tissue. In view of a rise in the inside temperature, the upper threshold for continuous microwave irradiation for a conventional microwave generator was set at 99 sec. For the new microwave generator (Microtaze AZM-520; Alfresa-Pharma, Tokyo, Japan; Fig. 1) used in this study, however, the impedance that was specific to the microwave transmission path was made uniform to prevent a rise in the inside temperature; and the radiation was intensified by adding a fan where the most heat is generated so that continuous microwave irradiation can be extended to 15 min, a much greater irradiation time than that allowed with conventional devices.

Microwave electrode. The new microwave electrode (Nesco PercuPro DP; Alfresa-Pharma) measures 2.0 mm in diameter and 25 cm in length (Fig. 2). The structure of the electrode from the tip to the other end consists of an antenna 10 mm long. Designed to withstand microwave irradiation for an extended period, the end of the center conductor of the microwave electrode was constructed of stainless steel and insulated



Figure 1. The microwave generator Microtaze AZM-520. This generator can supply microwaves with high power, until 110 W and irradiates microwaves continuously for 15 min.

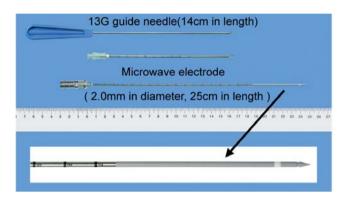


Figure 2. The guide needle for a new microwave electrode measure 13 G in diameter and 14 cm in length. The new microwave electrode Nesco PercuPro DP measure 2 mm in diameter and 25 cm in length and can withstand high power microwave irradiation up to 80 W. Its surface was insulated with Polytetrafluoroethylene from the tip of electrode to 6 cm (black arrow).

with Polytetrafluoroethylene (PTFE). The outer conductor was made of brass plated with nickel. To prevent adhesion of the coagulated tissue to the electrode, which constitutes a problem when irradiating over an extended period, the surfaces of the center and outer conductors were coated with PTFE. The thickness of the insulation (the distance between the center and outer conductors) was increased from 2 mm (for a conventional electrode) to 6 mm, a thickness at which the radiation efficiency improves when irradiating over an extended period. Within the tissue, microwaves cause the water molecules in the dielectric substance to vibrate markedly at a frequency of 2450 MHz, which generates frictional heat among the water molecules and coagulates the tissue. In an electrode with insulation of 2 mm, however, irradiation by microwaves causes a rapid loss of water at the electrode tip: thus coagulation occurs early around the insulation, limiting the area of coagulation. By increasing the insulation thickness to 6 mm, rapid loss of moisture is prevented; and for equal microwave irradiation power, coagulation over an area larger than that possible with a conventional 2 mm electrode became available with a longer irradiation time.

Power output assessment. In vitro evaluation of heat extension was performed by assessing temperature changes in egg white

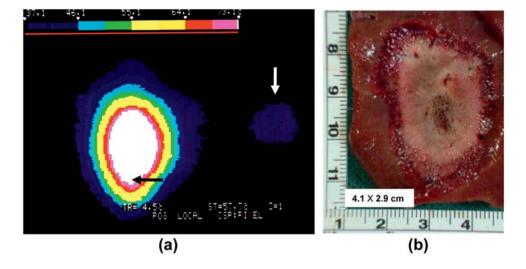


Figure 3. (a) Thermo graphic appearance of microwave-irradiated (80 W, 5 min) egg white. White arrow, a 10-yen coin (about 2.3 cm in diameter) used as a reference point. Black arrow, the tip of the new microwave electrode. The temperature in the interior of the yellow area increased to >55°C. (b) Gross appearance of coagulated lesion with the *in vivo* porcine liver produce by the new microwave electrode. The microwave output was set at 80 W for 5 min. The range of tissue coagulation with maximal and minimal diameters of 4.1 and 2.9 cm, respectively.

heated by the microwave electrode. The extent of heating was measured using a thermographic camera (Infra-Eye180, Fujitu Limited, Tokyo). The result of such thermographic imaging is shown in Fig. 3a. Microwaves heated egg white in a glass chamber. With irradiation at 80 W for 5 min, it was possible to raise the temperature above 55°C in an area 5.4 cm in long diameter and 3.9 cm in short diameter at the tip of the electrode. At this power and duration, the temperature of the shaft of the electrode did not exceed 46°C. If the power and duration of irradiation exceed 80 W and 5 min, respectively, the temperature of the shaft exceeded 50°C. At this temperature, the skin may burn where the electrode has been inserted. Therefore, we decided to set the power and duration of microwaves at 80 W and 5 min, respectively.

The following protocol for this study using healthy pigs was prepared in compliance with the Guidelines for Animal Experiments of Kansai Medical University, and approved by the Animal Experimentation Committee, Kansai Medical University. The animals were handled according to the guidelines of the National Institutes of Health (Guide for the Care and Use of Laboratory Animals, NIH publication no.90-23, revised 1990).

For the experiment *in vivo* porcine liver, 6 healthy, fasted adult pigs (35-40 kg body weight) were used (liver weight ~950 g). Under light anesthesia induced by intramuscular injection of ketamine hydrochloride (Ketalar for intravenous injection, 200 mg; Daiichi Sankyo, Tokyo, Japan) at a dose of 500 mg, endotracheal intubation was performed (Traquilon, inside diameter 7.0 mm, outside diameter 9.3 mm, 28 Fr; Terumo, Tokyo, Japan), and the tube was connected to a respirator (model 55-0715; Harvard Apparatus, MA, USA). Frequency of respiration and tidal volume were set at 20 strokes/ min and 15 ml/kg, respectively. An animal anesthesia apparatus was used (SN-487; Shinano Manufacturing, Tokyo, Japan) and anesthesia was maintained with a mixture of gas (oxygen and air) and 0.5-5% isoflurane (Isoful; Dainippon Sumitomo Pharma, Osaka, Japan).

The hepatic lobe was exposed via a median incision on the abdomen. We intentionally chose regions located in hepatic parenchyma away from the liver surface, porta hepatis and large vessels. The new microwave electrode was inserted into the hepatic parenchyma under ultrasonographic guidance to avoid major blood vessels and the area was irradiated at 80 W for 5 min. The abdomen was then closed. One day later, the animals were sacrificed with an overdose (25 ml) of potassium chloride solution (Shimizu Pharmaceutical, Shizuoka, Japan).

The excised liver was cut along to the tract of electrode insertion and was sliced at the width of 5 mm. The part showing clear discoloration (white zone including hemorrhagic rim) induced by microwave irradiation was judged to be a coagulation area according to a previous report (6). The coagulated area with the new microwave electrode was elliptical (Fig. 3b), the measurements of the diameter of the length of the area of coagulation along the electrode tract and the area of coagulation perpendicular to the electrode axis were obtained by consensus of two observers who were unaware of the coagulation modality.

The coagulation diameter along and perpendicular to the antenna tract was described in terms of maximal vertical diameter and maximal transverse diameter. The range of coagulation area of maximal vertical diameter and maximal transverse diameter was 4.3 ± 0.4 and 2.7 ± 0.2 cm.

Clinical study. For clinical use, the new microwave electrode and generator were approved by the Ministry of Health, Labor and Welfare (MHLW, Japan) in January, 2005 in accordance with the Pharmaceutical Affairs Act.

PMCT. The PMCT procedure was carried out as previously described (3). After local anesthesia, under ultrasonic guidance, a 13-gauge guide needle was inserted into the vicinity of the tumor. After the inner needle of the guide was removed, the microwave electrode was inserted through the outer needle of

the guide to place the electrode in the tumor area. The electrode was connected to the microwave generator via a flexible coaxial cable. The tumor area was irradiated with microwaves. To prevent skin burns, skin around the needle was cooled using a cold saline drip during microwave irradiation.

The electrode and the outer needle of the guide were removed. The puncture track was irradiated with microwaves to prevent bleeding from the hepatic surface when the electrode was removed. At each session, one to three electrode insertions were performed for the tumor, including different sites in its proximity and one microwave irradiation at 80 W for 5 min was performed for each electrode insertion, until the extensive hyperechogenic change covered the tumor area, including not only the tumor but also the neighboring non-cancerous tissue, to obtain a treated margin of \geq 5 mm. When this change in the echo images was achieved, we finished the initial session. To obtain reliable local control of the tumor, we attempted to induce a \geq 5-mm margin of necrosis in the non-cancerous tissue surrounding the tumor, the treated margin.

To assess the necrotic area, dynamic CT was performed 2-3 days after each treatment. When the initial session failed to obtain the treated margin, the next session was performed under ultrasonic guidance with reference to post-dynamic CT images taken after the initial session. Therefore, the total number of sessions was determined by dynamic CT image findings. Long diameters and short diameters of the necrotic areas were measured by dynamic CT one week after the completion of treatment. PMCT was performed twice per week.

Follow-up. Following discharge from the hospital, all patients were closely followed. Follow-up US was performed every 2 months. Dynamic CT and dynamic MRI were carried out every 3-5 months. Clinical observation periods following treatment ranged from 5 to 34 months. When intrahepatic recurrence was suspected from imaging studies, we performed CT angiography (CT-A, CT-AP) and/or US-guided tumor biopsy to confirm the diagnosis. In the patients with recurrence, we performed transcatheter arterial chemoembolization (TACE) + PMCT or TACE.

Results

None of the patients dropped out during the follow-up period in this study.

Treatment efficacy. PMCT of the tumors was finished within one week in all patients. The number of sessions was 1 or 2 (mean, 1.2 sessions). Forty-two of 52 patients showed complete necrosis of the tumor lesion with a treated margin \geq 5 mm on dynamic CT. Necrosis of the tumor and the non-cancerous area surrounding the tumor was obtained by a single needle insertion in 23 patients (tumor size: \leq 2 cm, 23 patients), by two needle insertions in 11 patients (tumor size: \leq 2 cm, 4 patients >2 to \leq 2.5 cm, 5 patients; >2.5 to \leq 3 cm, 2 patients) and by three needle insertions in 8 patients (tumor size: >2 to \leq 2.5 cm, 5 patients; >2.5 to \leq 3 cm, 3 patients) (Table I).

In 42 patients showing complete tumor necrosis, the mean long diameter and short diameter (mean \pm SD) of the necrotic area measured by dynamic CT after the session was, respectively, 3.8 ± 0.6 and 2.8 ± 0.6 cm by one needle insertion (Fig. 4),

Table I. The number of cases with complete necrosis (treated margin ≥ 5 mm) according to tumor size and the number of needle insertion.

No. of needle insertions		
1	2	3
23ª	4	0
0	5	5
0	2	3
	1	1 2

^aNo. of cases. One irradiation: 80 W, 5 min.

 3.8 ± 0.4 and 3.3 ± 0.7 cm by two needle insertions, 4.3 ± 0.3 and 3.8 ± 0.5 cm by three needle insertions (Fig. 5).

In the other 10 patients, the treated areas showed that the necrosis induced by one or two needle insertions covered the entire tumors on dynamic CT. However, the treated margin of ≥ 5 mm could not be obtained. Since, 9 patients (tumor size: >2 to ≤ 2.5 cm, 3 patients; >2.5 to ≤ 3 cm, 6 patients) refused further treatment (PMCT) to obtain an adequate treated margin due to social problems (they requested an earlier hospital discharge) and 1 patient (tumor size, 2.7 cm) refused the second session due to pleural effusion induced by the first session. Therefore, these patients were followed without further treatment.

Side effects and complications. As for the side effects, almost all patients complained of a heat sensation in the upper abdominal region during PMCT. Half the patients felt some pain during treatment but it was not severe enough to warrant cessation of the PMCT. In addition, all patients developed fever. One patient (tumor size, 2.7 cm) suffered from pleural effusion on the right side after the initial treatment, but he was discharged 2 weeks after conservative therapy. No other clinically relevant complications, such as bleeding, subcapsular hematoma or burn injury of the skin, were noted. However, during the follow-up period, we detected bile duct dilatations due to bile duct stricture at peripheral sites of treated area in 2 patients with HCC measuring >2.5 to \leq 3 cm in diameter after 3 and 4 months, respectively. However, the bile duct dilatations did not worsen during the follow-up period. Therefore, we are presently observing these strictures without treatment. None of the patients developed local dissemination of the cancer cells along the puncture line in this study.

Prognosis (survival and recurrence). All patients were alive at the end of this study. During the follow-up period, no evidence of local recurrence (recurrent nodule at the intra-treated area or the margin of the treated area) was observed in patients who showed complete necrosis of the tumor lesion with a treated margin ≥5 mm on dynamic CT. However, within follow-up period, 2 patients showed recurrences in the same subsegment after 6 and 8 months, respectively. Furthermore, 6 patients experienced recurrences in different subsegments after 7, 8, 8, 11, 12 and 14 months, respectively.

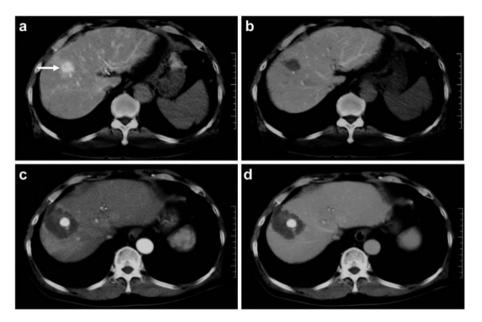


Figure 4. CT angiography (CT-A) and CT arterioportgraphy (CT-AP) were performed and dynamic computed tomography (CT) obtained one week after PMCT. Before treatment [CT-A (a), CT-AP (b)]. The tumor site (white arrow, tumor size = 1.7 cm in greatest dimension) is demonstrated as an enhanced area and perfusion defect is observed on CT-AP. This tumor was treated with one needle insertion. One week after treatment [early phase (c), portal phase (d)]. PMCT induced a sufficient treated margin. The tumor and the surrounding area were not enhanced. Accumulation of iodized oil was observed in the tumor. The coagulated area was 3.9 cm in maximal diameter and 3.3 cm in minimal diameter.



Figure 5. Dynamic CT obtained before treatment, one week after PMCT. Before treatment [early phase (a)]. The tumor site (white arrow, tumor size = 3.0 cm in greatest dimension) was partially enhanced. This tumor was treated with three needle insertions. One week after treatment [early phase (b), portal phase (c)]. The coagulated area was 4.5 cm in maximal diameter and 4.1 cm in minimal diameter and accumulation of a small amount of iodized oil was observed in the treated area.

On the other hand, of the 10 patients who could not obtain the treated margin of ≥ 5 mm, 4 patients (tumor size: 2.3 cm, 1 patient; >2.5 to ≤ 3 cm, 3 patients) experienced a local recurrence within 6 months. Moreover, 1 patient showed recurrences in the same subsegment after 7 months and 3 patients experienced recurrences in different subsegments after 7, 9 and 12 months, respectively.

Discussion

In previous studies, we reported that PMCT was a useful treatment for small HCC because of reliable coagulation capability (1,3,4). However, PMCT has a disadvantage. To obtain complete tumor necrosis with an appropriate treated margin, multiple microwave electrode insertions and micro-

wave irradiations are needed. Based on our experience, 3-6 electrode insertions were required for HCCs measuring ≤ 2.0 cm and more than 6 electrode insertions were required for HCCs measuring >2.0 to ≤ 3.0 cm in diameter using the conventional system (3).

To produce extensive necrosis with one needle insertion, various approaches may be considered. The extent of the coagulation achieved by microwave irradiation is related to the diameter of the electrode, the amount of electric power used, the irradiation time (1,4) and the heat loss via circulation. Therefore, thickening of the electrode, long irradiation or increasing electric power can enlarge tissue necrosis. However, thickening of the electrode may increase the incidence of post-bleeding. On the other hand, to reduce the heat loss, segmental hepatic blood flow (both arterial flow and portal flow) occlusion or transcatheter arterial chemoembolization (TACE) was performed as a procedure for PMCT reported previously (7-9). However, occlusion of both vessels using 2 balloon catheters is complex. Furthermore, we tried the combination of TACE and PMCT a using conventional microwave coagulation system but this combination therapy for HCC measuring >2.0 cm to \leq 3.0 cm in diameter required 4-6 electrode insertions to induce complete tumor necrosis with an adequate treated margin (9). Therefore, in the present study, we used a new microwave generator that can supply a significantly greater irradiation time than that allowed with conventional microwave generator and a new electrode that can withstand long microwave irradiation and prevent rapid loss of moisture in the tissue. With regard irradiation time, we chose 5 min to avoid burning injury of the skin and peritoneum.

In a previous study, with microwaves at 80 W for 60 sec using the conventional microwave coagulation system, the coagulated area was elliptical, measuring 3.1±0.5 cm in maximal vertical diameter and 2.2±0.4 cm in maximal transverse diameter on *in vivo* test (3). In the present study, with microwaves at 80 W for 5 min using the new microwave generator and electrode, the coagulated area was elliptical, with maximal vertical and transverse diameter of 4.3±0.4 and 2.7±0.2 cm, respectively. Therefore, the use of the new microwave coagulation system can result in increased volumes of tissue necrosis compared with the conventional microwave coagulation system in experimental studies. Furthermore, in this clinical study, the coagulated areas induced by one needle insertion at 80 W for 5 min was 3.8±0.6 cm in long diameter and 2.8±0.6 cm in short diameter. The dimensions of the coagulated area observed in the in vivo test using porcine liver was reproduced in a clinical study.

In the clinical results of the present study, of 27 patients with HCC measuring ≤ 2.0 cm in diameter who underwent PMCT, 23 patients showed complete necrosis with a treated margin of ≥ 5 mm by one needle insertion and only 4 patients required two needle insertions. Moreover, 10 of 13 patients with HCC measuring >2 to ≤ 2.5 cm in diameter and 5 of 12 patients with HCC measuring >2.5 to ≤ 3 cm in diameter revealed complete necrosis by two or three needle insertions. Compared with previous clinical results (3), the new microwave coagulation system markedly reduced the number of needle insertions required, because the tissue necrosis induced by the new microwave coagulation system

by one needle insertion was larger than that by the conventional microwave coagulation system.

In the present study, patients who could obtain a treated margin ≥ 5 mm showed no definite local recurrence. However, some patients who could not obtain a treated margin ≥ 5 mm showed definite local recurrence. This may have been due to incomplete necrosis of the marginal tumor area including microscopic metastasis adjacent to the primary tumor (10-12). Therefore, the treated margin of ≥ 5 mm should be obtained to eliminate tumor cells at the periphery and reduce the incidence of local recurrence (13,14). When PMCT cannot induce an adequate treated margin, patients should be observed closely for local recurrence.

It is suggested that the causes of the incomplete treatment may be the cooling effects of the regional circulated blood and/or large vessel (portal vein, hepatic vein or inferior vena cava) blood flow adjacent to the tumor, because previous reports demonstrated that blood flow exerts a strong negative influence on the volume of thermal coagulation achieved by radiofrequency ablation (15-17).

In the current study, unfortunately, 2 patients with HCC measuring >2.5 to \leq 3 cm in diameter experienced bile duct stricture. The cause of this complication may be bile duct injury because of the direct heat by microwaves. At present, it is difficult to predict the occurrence of this complication. Accordingly, close observation is needed to detect this complication after treatment, especially, when PMCT was performed for large sized HCC.

It was reported that the lesions induced by percutaneous radiofrequency ablation therapy (PRFA) for HCC by one needle insertion for 10-20 min ablation ranged in diameter from 3 to 4 cm (18-20). PRFA requires a longer ablation time than that of microwaves, but a larger area can be ablated in each session. Long-time RF ablation may be stressful for patients and may increase the possibility of complications, such as post-bleeding, subcapsular hematoma. Furthermore, long-time RF ablation may increase the risk of tumor cell seeding (21-25). One can then surmise that the internal pressure within the HCC that is encased by a capsule is raised by the temperature elevation of the tumor area due to RF ablation. If this rise in the internal pressure is long, the risk of tumor cells releasing and carrying into the peritoneal cavity along the puncture line may increase during ablation (26). Llovet et al reported that RF ablation with a cooled-tip needle for HCC locating near the liver surface and showing a poorly differentiated histological grade is associated with a high risk of neoplastic seeding (22).

On the other hand, we did not experience tumor cell seeding associated with PMCT in this study, although this condition of tumors showing extrahepatic expansion were not contained in this study. Of course, we cannot deny that there is likelihood of tumor cell seeding during PMCT. However, it is suggested that the short ablation time of PMCT may decrease the risk of tumor cell seeding along the puncture line. Therefore, based on the present results, it is suggested that PMCT using the new microwave coagulation system should be chosen for small HCC, although further clinical studies are required to document the effectiveness of this new microwave coagulation system. In conclusion, the new microwave coagulation system can induce extensive necrosis with a small number of microwave electrode insertions. This system may enhance the efficacy of PMCT and improve patient compliance.

References

- 1. Seki T, Wakabayashi M, Nakagawa T, *et al*: Ultrasonically guided percutaneous microwave coagulation therapy for small hepatocellular carcinoma. Cancer 74: 814-825, 1994.
- Matsukawa T, Yamashita Y, Arakawa A, *et al*: Percutaneous microwave coagulation therapy in liver tumors. A 3-year experience. Acta Radiol 38: 410-415, 1997.
- Seki T, Wakabayashi M, Nakagawa T, *et al*: Percutaneous microwave coagulation therapy for small hepatocellular carcinoma: comparison with percutaneous ethanol injection therapy. Cancer 85: 1694-1702, 1999.
- 4. Horigome H, Nomura T, Saso K and Itoh M: Standards for selecting percutaneous ethanol injection therapy or percutaneous microwave coagulation therapy for solitary small hepatocellular carcinoma: consideration of local recurrence. Am J Gastroenterol 94: 1914-1917, 1999.
- Seki T, Wakabayashi M, Nakagawa T, *et al*: Percutaneous microwave coagulation therapy for solitary metastatic liver tumors from colorectal cancer: a pilot clinical study. Am J Gastroenterol 94: 322-327, 1999.
- Sugimori K, Nozawa A, Morimoto M, *et al*: Extension of radiofrequency ablation of the liver by transcatheter arterial embolization with iodized oil and gelatin sponge: results in a pig model. J Vasc Interv Radiol 16: 849-856, 2005.
- Murakami T, Shibata T, Ishida T, *et al*: Percutaneous microwave hepatic tumor coagulation with segmental hepatic blood flow occlusion in seven patients. Am J Roentgenol 172: 637-640, 1999.
- Shibata T, Murakami T and Ogata N: Percutaneous microwave coagulation therapy for patients with primary and metastatic hepatic tumors during interruption of hepatic blood flow. Cancer 88: 302-311, 2000.
- Seki T, Tamai T, Nakagawa T, *et al*: Combination therapy with transcatheter arterial chemoembolization and percutaneous microwave coagulation therapy for hepatocellular carcinoma. Cancer 89: 1245-1251, 2000.
- Kondo Y, Kondo F, Wada K and Okabayashi A: Pathologic features of small hepatocellular carcinoma. Acta Pathol Jpn 36: 1149-1161, 1986.
- Wakasa K, Sakurai M, Okamura J and Kuroda C: Pathological study of small hepatocellular carcinoma: frequency of their invasion. Virchows Arch A Pathol Anat Histopath 407: 259-270, 1985.
- Nakajima Y, Nagabuchi E, Sato N, *et al*: A clinical study of liver resections in patients with small hepatocellular carcinoma less than three centimeters in diameter. Nippon Geka Gakkai Zasshi 93: 1087-1090, 1992.

- 13. Ikeda K, Seki T, Umehara H, *et al*: Clinicopathologic study of small hepatocellular carcinoma with microscopic satellite nodules to determine the extent of tumor ablation by local therapy. Int J Oncol 31: 485-491, 2007.
- 14. Nakazawa T, Kokubu S, Shibuya A, et al: Radiofrequency ablation of hepatocellar carcinoma: correlation between local tumor progression after ablation and ablative margin. Am J Roentgenol 188: 480-488, 2007.
- 15. Patterson EJ, Scudamore CH, Owen DA, Nagy AG and Buczkowski AK: Radiofrequency ablation of porcine liver in vivo: effects of blood flow and treatment time on lesion size. Ann Surg 227: 559-565, 1998.
- Goldberg SN, Hahn PF, Tanabe KK, *et al*: Percutaneous radiofrequency tissue ablation: does perfusion-mediated tissue cooling limit coagulation necrosis? J Vasc Interv Radiol 9: 101-111, 1998.
- Goldberg SN, Hahn PF, Halpern EF, Fogle RM and Gazelle GS: Radio-frequency tissue ablation: effect of pharmacologic modulation of blood flow on coagulation diameter. Radiology 209: 761-776, 1998.
- De Baere T, Denys A, Wood BJ, *et al*: Radiofrequency liver ablation: experimental comparative study of water-cooled versus expandable systems. Am J Roentgenol 176: 187-192, 2001.
- Goldberg SN and Gazelle GS: Radiofrequency tissue ablation: physical principles and techniques for increasing coagulation necrosis. Hepatogastroenterology 48: 359-367, 2001.
- Shibata T, Shibata T, Maetani Y, Isoda H and Hiraoka M: Radiofrequency ablation for small hepatocellular carcinoma: prospective comparison of internally cooled electrode and expandable electrode. Radiology 23: 346-353, 2006.
 Seki T, Tamai T, Ikeda K, *et al*: Rapid progression of hepato-
- Seki T, Tamai T, Ikeda K, *et al*: Rapid progression of hepatocellular carcinoma after transcatheter arterial chemoembolization and percutaneous radiofrequency ablation in the primary tumor region. Eur J Gastroenterol Hepatol 13: 291-294, 2001.
- Llovet JM, Vilana R, Bru C, *et al*: Increased risk of tumor seeding after percutaneous radiofrequency ablation for single hepatocellular carcinoma. Hepatology 33: 1124-1129, 2001.
 Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF and
- Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF and Goldberg SN: Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. Radiology 226: 441-451, 2003.
- De Baere T, Risse O, Kuoch V, *et al*: Adverse events during radiofrequency treatment of 582 hepatic tumors. Am J Roentgenol 181: 695-700, 2003.
- Curley SA, Marra P, Beaty K, *et al*: Early and late complications after radiofrequency ablation of malignant liver tumors in 608 patients. Ann Surg 239: 450-458, 2004.
 Kotoh K, Nakamuta M, Morizono S, *et al*: A multi-step,
- 26. Kotoh K, Nakamuta M, Morizono S, *et al*: A multi-step, incremental expansion method for radio frequency ablation: optimization of the procedure to prevent increases in intratumor pressure and to reduce the ablation time. Liver Int 25: 542-547, 2005.