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Review

Microwave coagulation therapy for liver cancer: laparoscopic microwave coagulation

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Introduction

A microwave coagulator was developed in 1979 by Tabuse.[1] Originally, it was invented as a new cautery device designed to reduce the volume of hemorrhage during hepatectomy. Using the same device, Saitsu et al.[2] reported intraoperative and laparoscopic microwave coagulation (MC) therapy for hepatocellular carcinoma (HCC) in 1991. Percutaneous MC was then described by Seki et al.[3] in 1994, and the use of MC has rapidly spread since that time. MC for HCC was included in medical insurance coverage in Japan in 1996, and it has since been employed percutaneously, endoscopically (laparoscopy, thoracoscopy), and in open surgery. However, as it has been only 4 years since MC became covered by insurance (and, thus, used widely) in Japan, its clinical value has not yet been established.

A representative local therapy for HCC before the advent of MC was percutaneous ethanol injection therapy (PEI), which was introduced around 1983.[4,5] Although controversy still continues, there is a general consensus that the results of PEI are comparable to those of surgical resection for HCCs 20 mm or less in diameter.

Recently, radiofrequency coagulators developed in the United States have been introduced to Japan, and a number of facilities are performing radiofrequency ablation (RA).[6–13] The appearance of newer RA devices makes the future position of MC unclear. In particular, as the procedure used for percutaneous MC, which is the most widely performed modality, varies among facilities, and as the criteria for evaluation of its efficacy also differ slightly among facilities, the situation is rather confusing. If the methods differ, the results will also be different. Differences in the approach to cancer are expected to further widen the differences in the results obtained. In this article, we summarize the characteristics and procedures of MC, and review the advantages and disadvantages of MC that have been documented to date, in terms of the approach to cancer. Problems experienced with MC are considered to be similar to those experienced with RA.

Characteristics of MC

The principle of MC is the thermal coagulation of tissues around the electrode by the generation of electromagnetic waves at its tip. Unlike radiofrequency coagulation, no opposite electrode is necessary. In MC, the tumor must be punctured with the electrode. Several monopolar-type electrodes have been developed, and they are classified as percutaneous electrodes for tumors in deep regions (Figs. 1, 2) and as superficial electrodes for tumors near the hepatic surface (Figs. 3, 4). Percutaneous monopolar-type electrodes for deep regions are 1.6–2.0 mm in diameter. With a 1.6-mm electrode, an elongated spherical coagulation area (an elliptical area) 24 × 16 mm is obtained by irradiation at 60 W for 120 s.[3] With a 2.0-mm electrode, an elongated spherical coagulation area of 31 × 26 mm is obtained by irradiation at 80 W for 60 s.[14] Because the percutaneous electrode for deep areas is a single needle with no changes in diameter, tumors in

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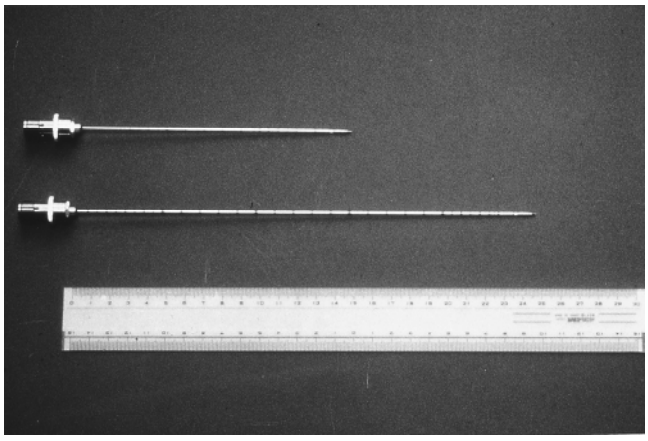

Fig. 1. Monopolar-type electrodes: percutaneous electrodes for tumors in deep regions. This type of electrode is used in percutaneous, laparoscopic, and thoracoscopic microwave coagulation

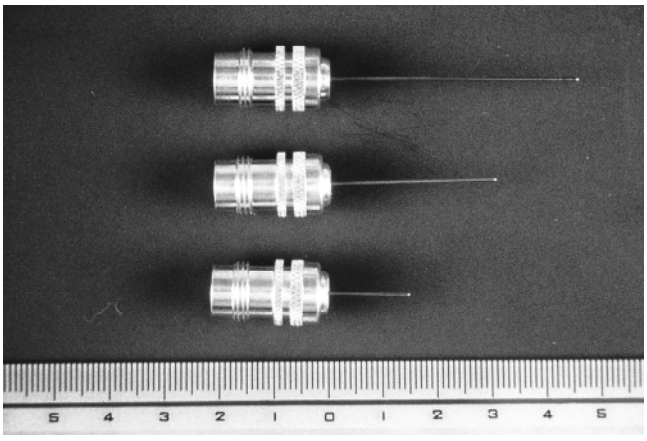

Fig. 3. Monopolar type electrodes: superficial electrodes for tumors near the hepatic surface. This type of electrode is used in intraoperative microwave coagulation

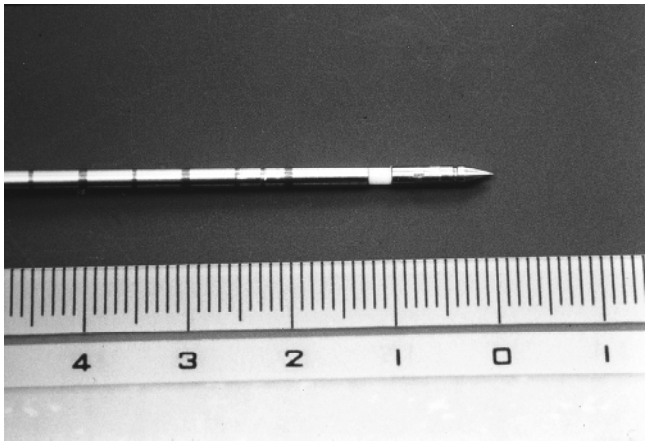

Fig. 2. Tip of percutaneous electrode is 1.6-mm-thick, and the monopolar electrode is 1-cm-long

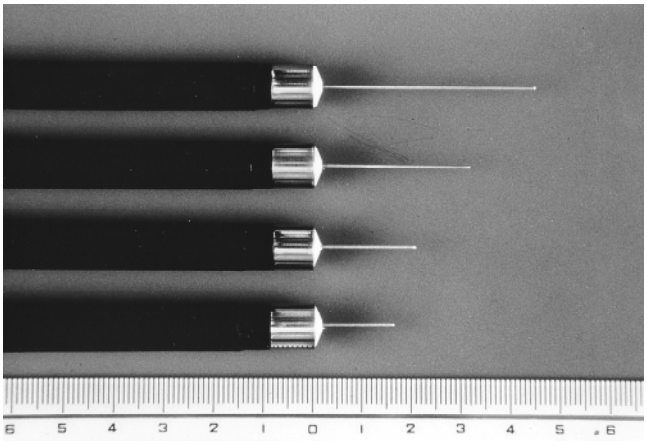

Fig. 4. Monopolar type electrodes: superficial electrodes for tumors near the hepatic surface. This type of electrode is used in laparoscopic and thoracoscopic microwave coagulation

shallow as well as deep areas of the liver can be treated if the tip of the electrode can be monitored with an imaging modality. Superficial electrodes having needle-like electrodes that are 15-, 20-, 30-, or 45-mm-long are available. The coagulation area obtained with a superficial electrode is nearly as long as the electrode itself, but its smaller diameter is less than that in the coagulation area obtained with a percutaneous electrode for deep areas.[15] With a superficial electrode, only areas near the liver surface (to a depth nearly equal to the length of the electrode) can be treated, for structural reasons.

Unlike PEI, MC is not affected by the HCC capsule, and consistently causes coagulation in the area of heating. However, the coagulation area is simply enlarged, retaining its elongated spherical shape, when the duration of irradiation is extended. For this reason, if the coagulation area obtained by a single puncture is insufficient, coagulation must be repeated by changing the puncture site. Therefore, puncture must be repeated if the shorter diameter of the coagulation area obtained by a single puncture is insufficient. These are characteristics of MC.

From these characteristics, it can be concluded that the maximum diameter of a tumor that would be sufficiently coagulated by a single puncture with a 2-mm electrode for deep regions would be about 15 mm, in consideration of a surgical (safety) margin of 5 mm on each side. This characteristic of MC may well be a major cause of the variation among facilities in regard to the results of MC in HCCs that are 15 mm or greater in diameter. Nevertheless, it is surprising that a coagu-

lation area with a 26-mm short diameter can be obtained consistently at an irradiation time of only 1 min. An electrode of 1.4 mm in external diameter, with which an even wider coagulation area can be obtained, has been reported abroad.[16]

Percutaneous MC (PMC)

A percutaneous electrode for deep regions is used for this procedure. PMC is the most widely performed MC, presumably because it is regarded as an extension of the conventional PEI and can be performed readily with the patient under local anesthesia.[17–30] If PMC can be performed safely and easily with consistent effects, it may be an ideal procedure. At present, however, the treatment must be repeated several times to ensure its effectiveness; thus, the duration of hospitalization is considerably extended.[3,14] To complete the therapy in one stage and to shorten the treatment period, tumors 15 mm or greater in diameter must be punctured several times.[22,24] This increases discomfort for the patient and also increases the risk of postoperative bleeding. The greatest problem is the difficulty of confirming hemostasis. Because a 1.6-mm microwave electrode is much larger than the 21 G needle used for PEI, the risk of hemorrhage must always be considered, and careful hemostatic treatment is required after withdrawal of the electrode. If coagulation of the puncture route is insufficient, the possibility of intraperitoneal dissemination remains, even if hemorrhage poses no major problem. Therefore, in PMC, confirmation of hemostasis after removal of the electrode, and hemostatic procedures to be taken if there is bleeding, are nearly impossible unless the electrode is inserted through an outer needle. Few reports have mentioned such minor maneuvers.[14,18,21] On the other hand, multiple punctures can be made readily, and hemostasis can be confirmed easily, in MC other than by the percutaneous approach. Moreover, hemostatic procedures can be carried out easily and with certainty.

Intraoperative MC (OMC)

MC was derived from microwave hepatectomy.[1] Therefore, intraoperative MC using a hepatectomy (superficial) electrode is a result of natural development.[31–38] Generally, however, performing MC by laparotomy is inconsistent with the less invasive nature of MC. Therefore, we consider that intraoperative MC is justified only when percutaneous or endoscopic MC is difficult. Actually, HCC often seems to be treated by open surgery for resectable lesions, combined with MC for residual tumors.[33,35] A superficial electrode is used to treat HCC near the liver surface.[31,36] HCC in deep areas of the liver can also be treated by MC if an electrode for deep areas is used under ultrasound guidance.[34] An advantage of this technique is that the route of puncture can be selected with considerable freedom in the field of operation.[34] Whatever treatment is selected, the recurrence rate of HCC at other sites is characteristically high, and if adhesions develop intraperitoneally after the initial treatment, subsequent laparoscopic procedures become difficult. Therefore, it must be taken into consideration that as wide a selection as possible of subsequent treatments will be required.

Thoracoscopic MC (TMC)

In approaching HCC near the diaphragm, the route of puncture can be shortened by thoracoscopic transdiaphragmatic puncture of the nontumorous part. Thoracoscopic MC was developed to treat HCC near the diaphragm (segments VII, VIII) by this approach.[39–41] Although this is a reasonable technique, it provides a smaller field of operation than the laparoscopic approach and is applicable only to lesions in the right hepatic lobe, and not to those in the left lobe. An incision in the diaphragm is desirable for reliable treatment, but this increases both the invasiveness and the complexity of the procedure. Laparoscopically, the entire liver can be scanned readily with a linear electron scanning type ultrasonograph by the immersing method recently developed by us, but the area of scanning under thoracoscopy is limited. Therefore, thoracoscopic MC is indicated only when laparoscopic MC is difficult. Also, more careful anesthetic management is required for this thoracoscopic procedure, because, naturally, ventilation is possible only with the left lung during this procedure.[39–41]

Laparoscopic MC (LMC)

Laparoscopic MC is our first choice,[44] because we are accustomed to laparoscopy and laparoscopic procedures.[43–47,54–60] However, we are ready to adopt any treatment if it leads to safe, certain, and speedy cure. In our 70 patients with solitary HCCs up to 40 mm in diameter, the mean period of hospitalization after laparoscopic MC was 9.4 days, and the 5-year survival rate was 75%. Postoperative hemorrhage was observed in none of these patients. Also, we have not excluded any patient, except those in whom marked adhesion was disclosed, since we started performing laparoscopic MC with patients under general anesthesia. TMC was performed in only 3 patients, and OMC was not performed in the 70 patients who have received LMC

under general anesthesia. The advantages of LMC are as follows.

Multiple punctures can be done safety and readily

There are facilities that use superficial electrodes (applicable to HCC near the liver surface)[2,19,46] and those that use electrodes for deep regions (applicable to HCC at any site).[44,47] The greatest advantage of LMC is that no hesitation is needed in undertaking multiple punctures of the lesion with an electrode for deep regions. At present, the coagulation area obtained by a single puncture is reported to be larger with RA than with MC.[6,13] In laparoscopic procedures, however, only the operation time is important, and the size of the coagulation area obtained by a single puncture has no significance. It would be best if the treatment could be finished by a single puncture, but we have not observed shortening of the operation time by RA. Our experience with the two modalities of LMC and LRA has revealed that a single-rod type electrode is better than a forked type electrode, because the entire length of a single-rod type electrode can always be readily and consistently visualized in its entirety by ultrasonography.

Hemostasis can be confirmed and hemostatic maneuvers can be made readily

Bleeding from the puncture site into the peritoneal cavity is often experienced even when the electrode is withdrawn by simultaneously coagulating the puncture route.[44] Under laparoscopic monitoring, hemorrhage at this time can be minimized by reinsertion of the electrode. In addition, hemostasis can be achieved easily by re-coagulation. In percutaneous MC, confirmation of hemostasis is difficult unless an outer needle is used for guiding the electrode.[14,18]

General anesthesia makes LMC applicable to HCCs at all sites

LMC can be performed with the patient under local anesthesia,[44] but the patient's discomfort is much less under general anesthesia.[42,43,46,47] Complete muscle relaxation under general anesthesia offers a broader intraperitoneal operation field, so that the range of selection of the puncture route is widened. Furthermore, HCC in segment VII or VIII, which is often considered a poor indication, may also be treated by the concomitant use of the immersion method. Tumors in segment VII, the treatment of which under local anesthesia has been avoided because of the presence of a large portal vein in the puncture route,[44] can be approached by puncturing from the right lateral abdominal wall in the right elevated position. Adhesiotomy makes LMC applicable for nearly all patients with intraperitoneal adhesion caused by a history of surgery. Adhesiotomy is usually difficult to perform with a patient under local anesthesia.

Sites of treatable HCCs can be extended by the use of different electrode types

With an electrode for deep regions, most tumors in all liver regions, including the surface, can be treated as mentioned above. Naturally, it is a prerequisite that tumors at all sites can be punctured under laparoscopic ultrasonography.[44,47] With a superficial electrode, on the other hand, only tumors near the liver surface can be treated.[2,19,46] Moreover, the thoracoscopic procedure is the only choice for HCC just below the diaphragm.

Indications for and results of MC

Indications

Indications for MC for HCC are considered to be clinical stages I to III and part of Child-Pugh grade C, probably reflecting the noninvasive nature of MC. Indications for PMC are considered to be a tumor diameter of 30 mm or less and a number of tumors between one and three.[3,15,25] The frequency of complications, including abscess, is reported to increase in tumors 40 mm or greater in diameter, regardless of the approach.[24] The possibility of infarction and bile duct stenosis increases when HCC is located near the porta hepatis, so that MC should be performed carefully in such conditions. At many facilities, HCCs 40 mm or less in diameter are considered to be indications for endoscopic or intraoperative MC.[32,44,46] We regard all HCCs of 40 mm or less in diameter as treatable, regardless of their location. However, even at many facilities that perform LMC, only HCC near the liver surface is considered treatable.[16,32,42,46] The most important reason is probably the technical difficulty in pinpointing punctures of deep-seated cancers. Indications for MC must be established after the evaluation of long-term prognosis, which will be reported in future. Indications for MC concerning metastatic liver cancer are unclear because of lack of data.

Results

There have been few reports on long-term prognosis after MC treatment of HCC. Complete coagulation necrosis was observed by dynamic computed tomo-

graphy (CT) in 75%–100% of patients immediately (a few days to 1 week) after treatment.[3,15,25,28,34,42,47] Complete coagulation necrosis generally tended to be achieved more frequently by endoscopic MC than by percutaneous MC. At most facilities, judgments are made a few days to 1 week after treatment, by dynamic CT. Differences in therapeutic effects appear to reflect differences in the judgments of therapeutic effects and differences in MC techniques. In HCCs 15 mm or greater in diameter, which require multiple punctures,[14] the cure rate varies, with consequent variation in the local recurrence rate. The local recurrence rate 1–3 years after treatment, in patients assessed as cured by dynamic CT immediately after the treatment, is reported to be 12%–35%[7,14,25,27] with PMC and 7%–18%[32,44,46,47] with LMC, rates which are considered nearly satisfactory.

Complications

Postoperative hemorrhage, hematoma under the hepatic capsule, and subcutaneous hematoma have been reported as MC complications related to hemorrhage.[51] Other complications described to date include bile duct stenosis, liver infarction, and liver abscess.[24,51] Although postoperative ascites and thoracic effusion have also been reported,[21,51] there has not been a report of severe liver failure. A few cases of tumor seeding in the puncture route and intraperitoneal dissemination have been noted as complications.[21,24,48,51] These conditions, which were rare after PEI, are considered to be caused by withdrawal of the electrode. They were observed not only after PMC but also after intraoperative MC. The electrode must always be withdrawn with coagulation to minimize hemorrhage. The incidence of complications is reported to be high in HCCs 40 mm or greater in diameter.[24] Because there have been reports of liver infarction extending over the entire left lobe in association with HCC near the porta hepatis as mentioned under the heading "Indications", MC should be employed carefully for HCC at this site. We treat HCC located along a large portal tract by a combination of MC and local ethanol infusion in the periportal area, to prevent complications. Most complications of MC are common to all MC modes. However, pneumothorax has occurred due to intercostal insertion of the electrode as a complication specific to LMC.[42] In LMC, which involves pneumoperitoneum, there is the possibility of pneumothorax even if the electrode is not inserted intercostally.[47] Installation of an information (insurance) drain is extremely effective for the early detection of postoperative hemorrhage.[44] Because postoperative hemorrhage has been reported even after LMC,[47] in which confirmation of intraoperative hemostasis is easy, the insurance drain is highly valuable.

Common problems of MC to be addressed

Development of a method for the accurate intraoperative evaluation of therapeutic effect

In MC, the coagulation area usually includes a safety (surgical) margin of 5 mm on each side.[14,44] Evaluation of the therapeutic effect by intraoperative ultrasonography (including the color Doppler technique), is possible, to an extent, but it is not completely reliable. Therefore, the effectiveness of the treatment is evaluated by dynamic CT or by magnetic resonance imaging 1 week after operation, at most facilities.[49–53] We study not only changes in ultrasonograms immediately after coagulation but also the distribution of traces of the routes of needle puncture observed on ultrasound images of the tumor. Because the short diameter of the coagulation area produced by a single coagulation is known, the needle traces are useful as an objective marker for evaluation of the therapeutic effect. The situation that there is no reliable intraoperative evaluation method has not changed from the days of PEI. The development of an accurate method for intraoperative evaluation is a major problem that also needs to be solved so that the postoperative hospitalization period can be shortened. Reports of the use of ultrasound contrast media have begun to appear, but final evaluation of these media must still be made. Imaging procedures play a key role in MC, as they provide a reliable assessment of the therapeutic effect of the procedure.

Selection of the optimal approach

The present situation, in which various approaches are employed for MC and the same approach is obtained by different techniques, makes accurate evaluation of MC even more difficult. The advantages of MC cannot be exploited if the percutaneous approach is selected merely because of technical simplicity. We might have felt comfortable with the laparoscopic approach because we have enough experience in laparoscopic therapeutic procedures.[46,47,54–59] However, we have no intention of adhering to laparoscopic procedures, because the use of less invasive treatments is our primary concern. We are ready to accept any approach if it is safe and consistently effective and if it shortens the duration of treatment and the hospitalization period. After all, the original motive for our adoption of laparoscopic treatment was that it was expected to shorten the duration of treatment. It was for this purpose that we started laparoscopic PEI (LEI).[55] Selection of the most appropriate approach for each patient, without being obsessed with a particular approach, is important. To ensure this selection, the acquisition of the skill needed

for each approach is absolutely necessary. The considerable differences observed in regional cure rates and incidences of complications after MC, even with the same approach, among facilities provide evidence of the importance of technical proficiency.

Prospective randomized studies of MC and RA are needed

Prospective randomized studies of MC and RA, performed by the same approach, are needed for precise comparison of the two modalities.[61] Otherwise, differences between the two treatments are difficult to clarify in a short period. As noted above, confusion simply increases if individual facilities continue to report results based on different approaches and different procedures.

Future developments in LMC

Development of laparoscopic ultrasound devices that facilitate electrode insertion

The development of laparoscopic ultrasound probes that facilitate electrode insertion into the tumor is urgently needed. At present, at many facilities, indications for LMC are limited to HCC on or near the liver surface, although the staff are aware of its safety and effectiveness.[42,45,46] The primary reason for this limitation is the technical difficulty of puncturing deep-seated tumors. The local cure rate for HCCs on the liver surface by LMC is higher than that for HCCs in deep areas of the liver, probably for the same reason.[47] It is true that some skill is required for laparoscopic tumor puncture using a linear electron scanning type ultrasound probe. Therefore, the reliability and safety of the treatment are expected to be improved remarkably if puncture of tumors in deep areas of the liver is facilitated.

Development of electrodes that produce larger coagulation areas

In Japan, as well as in other countries, test models of monopolar electrodes that produce markedly larger coagulation areas than the existing electrodes have been developed. In addition, the shape of the coagulation area obtained is nearly spherical, and commercial production of these electrodes is anticipated. The development of improved electrodes is an important matter that is related to shortening of the operation time, and improvements in the consistency of therapeutic effects and the safety of the treatment.

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