Thermal Ablation Using Microwave Coagulation Therapy (MCT) and Radiofrequency Ablation (RFA) for Hepatocellular Carcinoma

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Abstract: Thermal ablation can be achieved using microwave coagulation therapy (MCT) and radiofrequency ablation (RFA), and has been developed as a curative and minimally invasive treatment for hepatocellular carcinoma (HCC). A percutaneous, endoscopic, or open body approach can be selected based on the size, number, and location of the tumors. MCT is achieved with monopolar-type electrodes to create a columnar ablative area with a 1 cm diameter centered around the electrode. RFA is achieved with internally cooled electrodes (Cool-tip™) or expandable electrodes (LeVeen™ and RITA™). RFA can produce a spheroidal ablative area with a 3 cm diameter surrounding the needle. Three- and 5-year overall survival rates are 80.0-81.0% and 43.0-78.0% for MCT, and 62.0-77.7% and 33.3-55.4% for RFA, respectively. Morbidity and mortality rates using thermal ablation are 2.2-8.9% and 0.3-0.5%, respectively. Thermal ablation, using MCT or RFA, can provide a favorable long-term prognosis with low morbidity rates for HCC patients with poor liver function reserves.

Key Words: hepatocellular carcinoma, thermal ablation, radiofrequency ablation, microwave coagulation therapy

Introduction

Thermal ablation, including microwave coagulation therapy (MCT) and radiofrequency ablation (RFA), is one of the less invasive and effective curative treatments for hepatocellular carcinoma (HCC) and has been used worldwide1-8. Thermal ablation is used for patients with unresectable HCC, and with poor liver function reserves, but sometimes even for patients with resectable tumors9,10. Percutaneous, endoscopic and open body approaches are selected according to the size, number and locations of the tumor9,10,11. In this paper, we have summarized differences in the efficacies, and in the adverse effects of MCT and RFA.
Indications for thermal ablation in hepatocellular carcinoma

Thermal ablation can be performed for patients with poor hepatic reserves, and indications for thermal ablation are described below. Relevant tumor parameters to be considered are: HCCs should be 5 cm or smaller; there should be no more than 3 tumors; the tumors should not be close to major vessels; and there should be no portal vein tumor thrombosis. If these conditions are satisfied, a patient is a good candidate. Other essential functional factors for the liver which must be considered are: total-bilirubin levels of less than or equal to 3 mg/dl; prothrombin activity equal to or higher than 40%; and the presence of no uncontrollable ascites. The percutaneous approach is selected for tumors with a diameter of 3 cm or less, and for the presence of no more than 3 tumors. Superficial HCCs must be excluded because of the possibility of tumor cell implantation. An endoscopic approach is performed for HCCs which are located near the surface of the liver, 4 cm or less in diameter, and for the presence of no more than 3 tumors. Thoracoscopic and laparoscopic approaches are chosen at the dome of the liver and for other sites, respectively. An open body approach is selected for HCCs equal to or less than 5 cm in diameter, and which have contraindications for the percutaneous and endoscopic approaches. It is important to select an appropriate approach in treating these tumors in order to generate sufficient surgical margins (Fig. 1).

Fig. 1. Changes in enhanced CT with pre- and post-thermal ablation.
(a) A HCC with lipiodol accumulation with an arterio-portal shunt, 5 cm in diameter, located in segment 7 in the liver was completely ablated with a percutaneous approach. (b) A HCC with dense lipiodol accumulation, 3 cm in diameter, located in the dome of the liver was completely ablated with a sufficient surgical margin using a thoracoscopic approach. (c) Two HCC nodules, 3 cm in diameter, adjacent to the IVC were ablated without injury to the IVC with an open body approach.
**Microwave coagulation therapy**

MCT was initially developed as a coagulation tool to be used after liver biopsy, and then adapted for hepatic tumor ablation\(^1\). The majority of the experiences obtained with MCT have been in Japan and China\(^1\). Endoscopic and open body MCT is accomplished primarily with monopolar-type electrodes. The microwaves act chiefly on the water component in tissues, producing dielectric heat and tissue coagulation\(^9\). The ablative area of MCT forms a column with a 1 cm diameter surrounding the electrode (Fig. 2)\(^3\). A relatively large number of needle insertions can be necessary to coagulate the entire tumor and the surrounding liver tissue using MCT\(^9\). Yu et al. reported on a comparison of standard single straight, triangular triple straight, and spherical triple-loop antennas along with pathologic findings\(^14\). They concluded that multiple straight or loop antennas can generate large coagulation volumes during short procedure times, and with low complication rates\(^14\).

**Radiofrequency ablation**

RFA for human liver tumors was first described by Rossi et al.\(^2,10\). The current technology for RFA was developed for general tissue ablation in 1997 in the United States\(^1\). RFA is achieved using internally cooled electrodes (Cool-tip\(^T\)) or expandable electrodes (LeVeen\(^T\) and RITA\(^T\))\(^10\). The ablative area for RFA with internally cooled electrodes forms a spheroid with a 3 cm diameter surrounding the needle (Fig. 3)\(^11\). Complete ablation of a tumor smaller than 2 cm can thus be accomplished with a single puncture. Shibata et al. reported on differences between internally cooled and expandable electrodes\(^10\). Both devices are equally effective, and have similar
complications, tumor progression free survivals, and overall survivals. However, the internally cooled needle is superior when being guided with ultra-sound during its placement.

**Therapeutic efficacies of MCT and RFA**

Among the papers describing the use of MCT and RFA in PubMed, reports referring to long term survival (5-year survival) were selected (Table I). In Table I, the results from 238 patients treated with MCT, and 1321 patients treated with RFA are summarized. Mean tumor sizes ranged from 1.8 cm-3.3 cm. Three- and 5- year overall survival rates were 80.0-81.0% and 43.0-78.0% for MCT, and 62.0-77.7% and 33.3-55.4% for RFA, respectively. Kawamoto et al. reported on the long-term outcomes of 69 laparoscopic MCT-treated patients. The cumulative 5-year survival rate was 63.9%. In patients with well differentiated HCC tumors, or with tumors having diameters of less than or equal to 2.0 cm, the cumulative 5-year survival rates were significantly better (78.9% and 76.0%, respectively). Tateishi et al. reported on long-term outcomes and complications for 664 RFA treated patients. For 319 naïve patients, the cumulative 5-year survival rate was 54.3%, and there were no treatment-related deaths. Lencioni et al. described 3- and 5-year local recurrence rates of 10% in 187 HCC patients treated with percutaneous RFA. Risk factors affecting local recurrence after thermal ablation were: larger tumor size, tumors in a subcapsular location, tumors adjacent to major vessels, poor pathologic differentiation, advanced tumor stage, insufficient safety margin, high level of serum AFP, and the existence of hepatitis.

**Table I. Long-term results of thermal ablation for hepatocellular carcinoma**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of Patients</th>
<th>Tumor size (cm)</th>
<th>Route</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence-Free Survival Rate</th>
<th>Local Recurrence Rate</th>
<th>Overall Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossi et al.</td>
<td>1996</td>
<td>RFA 39</td>
<td>&lt;3.0</td>
<td>P</td>
<td>22.6</td>
<td>30.0% (4-yr)</td>
<td>68.0%</td>
<td>40.0%</td>
</tr>
<tr>
<td>Seki et al.</td>
<td>1999</td>
<td>MCT 48</td>
<td>mean 1.8</td>
<td>P</td>
<td></td>
<td>30.0% (4-yr)</td>
<td>78.0%</td>
<td></td>
</tr>
<tr>
<td>Buscarini et al.</td>
<td>2001</td>
<td>RFA 88</td>
<td>&lt;5.0</td>
<td>P</td>
<td>34</td>
<td>24.0%</td>
<td>62.0%</td>
<td>33.0%</td>
</tr>
<tr>
<td>Seki et al.</td>
<td>2005</td>
<td>MCT 68</td>
<td>mean 2.0</td>
<td>E</td>
<td>54</td>
<td>37.4%</td>
<td>81.0%</td>
<td></td>
</tr>
<tr>
<td>Kawamoto et al.</td>
<td>2005</td>
<td>MCT 69</td>
<td>&lt;4.0</td>
<td>E</td>
<td>54</td>
<td>17.8%</td>
<td>80.0%</td>
<td></td>
</tr>
<tr>
<td>Tateishi et al.</td>
<td>2005</td>
<td>RFA 319</td>
<td>mean 2.6</td>
<td>P</td>
<td>27.6</td>
<td>2.4%</td>
<td>62.4%</td>
<td>38.2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(naïve)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA 345</td>
<td>mean 2.6</td>
<td>P</td>
<td>24</td>
<td>10.0%</td>
<td>71.0%</td>
<td></td>
</tr>
<tr>
<td>Lencioni et al.</td>
<td>2005</td>
<td>RFA 187</td>
<td>mean 2.8</td>
<td>P</td>
<td>24</td>
<td>10.0%</td>
<td>71.0%</td>
<td></td>
</tr>
<tr>
<td>Machi et al.</td>
<td>2005</td>
<td>RFA 65</td>
<td>mean 3.2</td>
<td>P (49)</td>
<td>24.8</td>
<td>27.9%</td>
<td>39.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>E (20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>O (15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raut et al.</td>
<td>2005</td>
<td>RFA 194</td>
<td>mean 3.3</td>
<td>P (140)</td>
<td>34.8</td>
<td>43.1%</td>
<td>68.1%</td>
<td>55.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>O (54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xu et al.</td>
<td>2005</td>
<td>MCT 53 and RFA 84</td>
<td>mean 2.6</td>
<td>P</td>
<td>24.1</td>
<td>18.8%</td>
<td>42.8%</td>
<td>20.1%</td>
</tr>
</tbody>
</table>

RFA: radiofrequency ablation, MCT: microwave coagulation therapy, P: percutaneous approach, E: endoscopic approach, O: open body approach
Table II. Comparison of outcomes of MCT and RFA for hepatocellular carcinoma

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>No. of Patients</th>
<th>Tumor size (cm)</th>
<th>Route</th>
<th>Mean Follow-up (months)</th>
<th>Recurrence-Free Survival Rate</th>
<th>Local Recurrence Rate</th>
<th>Overall Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shibata et al.</td>
<td>2002</td>
<td>MCT 36</td>
<td>mean 2.2</td>
<td>P</td>
<td>18</td>
<td>12.0% 24.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA 36</td>
<td>mean 2.3</td>
<td>P</td>
<td>18</td>
<td>4.0% 12.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lu et al.</td>
<td>2005</td>
<td>MCT 49</td>
<td>mean 2.5</td>
<td>P</td>
<td>25.1</td>
<td>26.9% 13.4%</td>
<td>50.5%</td>
<td>36.8% (4-yr)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA 53</td>
<td>mean 2.6</td>
<td>P</td>
<td>24.8</td>
<td>15.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beppu et al.</td>
<td>2006</td>
<td>MCT 200</td>
<td>mean 2.6</td>
<td>P (55%) E (30%) O (15%)</td>
<td>30</td>
<td>65.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA 220</td>
<td>mean 2.5</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td>62.0%</td>
</tr>
<tr>
<td>Ohmoto et al.</td>
<td>2006</td>
<td>MCT 48</td>
<td>mean 1.7</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RFA 70</td>
<td>mean 1.6</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td>5.0% 15.0% 77.0%</td>
</tr>
</tbody>
</table>

MCT: microwave coagulation therapy, RFA: radiofrequency ablation, P: percutaneous approach, E: endoscopic approach, O: open body approach

Morbidity with MCT and RFA

Morbidity rates encountered with MCT and RFA are similar12). Mulier et al. reviewed this and found that the mortality rate was 0.5% and that the morbidity rate was 8.9% in 3670 RFA treated patients38). Livraghi et al. reported that the mortality rate was 0.3%, the major complication rate was 2.2%, and the minor complication rate was less than 5% in 2,320 RFA-treated patients38). Complications consisted of abdominal bleeding, abdominal or intrahepatic infection, intestinal perforation, biliary tract damage, liver failure, pulmonary complications, dispersive skin burns, hepatic vascular damage, visceral damage, cardiac complications, myoglobinemia or myoglobinuria, renal failure, coagulopathy, hormonal complications, and tumor seeding35,36). Llovet et al. reported a high rate of tumor seeding (12.5%), whereas, Livraghi et al. concluded that the rate of tumor seeding was only 0.9% in 1314 patients, and the risk factor for seeding is a prior tumor biopsy12,13). Recently, intrahepatic dissemination of HCCs37–40) or sarcomatous changes after thermal ablation41) have been reported. These unusual recurrences are serious problems because of their poor outcomes.

Comparison of MCT and RFA

There were four reports comparing MCT and RFA from the viewpoint of local recurrences, complications, and prognosis3,27–29). Shibata et al. and Lu et al. concluded that RFA and MCT had equivalent therapeutic effects, complication rates, and rates of incomplete tumor necrosis27,28). Ohmoto et al. reported that RFA can achieve a lower local recurrence rate and a higher survival rate29). RFA has an advantage in that complete ablation can be achieved with fewer sessions27,28). RFA is more beneficial in coagulating the tumor itself with a surgical margin, and MCT is useful in obtaining adequate surgical margins9).

In this department, between 1991 and 2004, 430 patients underwent thermal ablation therapy. MCT was performed in 200 patients, and since 1999, RFA was performed in 230 patients9). There were no differences in clinical factors such as age, gender, etiology, liver damage grade, clinical stage, and tumor
size between MCT treated and RFA treated patients. Although, the number of tumors treated with RFA (average : 2.5, max : 10) was greater than the number treated with MCT (average : 1.9, max : 6) (p<0.01). Among the MCT treated patients, percutaneous, endoscopic and open body approaches were selected for 48%, 30% and 22% of the patients, respectively. Among the RFA treated patients, percutaneous, endoscopic and open approaches were selected in 58%, 30% and 12% of the patients, respectively. More percutaneous approaches were selected among the RFA treated patients than among the MCT treated patients. Complication rates with MCT and RFA were 10% and 5%, respectively. Complications with MCT were 2 disseminations, 2 hepatic failures, 1 bleeding, 8 liver abscesses, 1 biliary fistula, 2 bilomas, 2 massive effusions, and 2 acute respiratory distress syndromes. Complications with RFA were 2 hepatic failures, 1 bleeding, 2 bilomas, 1 skin burn, 2 port hernias, and 2 massive effusions. Liver abscesses were never observed in RFA treated patients. Cumulative survival rates were very similar in patients treated with MCT (3 and 5-year survival rates : 70% and 45%, respectively) and RFA (3 and 5-year survival rates : 70% and 42%, respectively) (Fig. 4).

![Fig. 4. Cumulative survival curves after MCT and RFA in HCC patients.](image)

The survival curves were calculated with the Kaplan-Meier method and were equivalent for the two groups.

Conclusions

Thermal ablation with MCT and RFA can provide a favorable long-term prognosis with low complication rates for HCC patients with poor liver functional reserves.

References


