Radiofrequency Tumor Ablation for Hepatocellular Carcinoma - Therapeutic Significance of Approaching Methods and the Device differences.

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Abstract:

Aim

Based on our experiences of treating hepatocellular carcinomas (HCC), we discuss some of the techniques that are required in order to gain appropriate outcomes. We also report the clinical significance of different radiofrequency devices.

Methods

One hundred and forty-seven cases with HCC were treated using radiofrequency ablation. Either a percutaneous approach or a laparoscopic approach was selected depending on the location and the size of tumors. A guiding needle technique was routinely applied to the percutaneous approach in order to make it safer and easier to target the tumor. Laparoscopy under general anesthesia was assisted by the ultrasound guidance to locate the tumor.

Two different radiofrequency devices: an expandable electrode with a thermo-controlled generator (Model 30, RITA) and a cool-tip electrode with an impedance-controlled generator (Cooltip-system, Radionics) were compared. The clinical advantages of both devices were assessed.

Results

Of the 94 cases that were treated by RFA as the initial treatment for the tumor, 50 were bearing a single nodule smaller than 30mm. After RFA, most cases of this group were diagnosed as completed ablation, and there were three cases (6%) with local recurrences.

A guiding needle technique was applied to all the percutaneous approaches which not only enabled us to target the tumor precisely, but also offered a safe route for biopsy and hematostatic procedure. For the laparoscopic approach, the ultrasonic guidance was essential when the tumor was located under the liver surface.

Compared to the expandable electrode, the use of the cool-tip electrode resulted in the reduction of the number of punctures by half, thus shortening the operation time by half. This difference may be attributed to the difference in the capacity of the generator power.

**Conclusions**

Radiofrequency ablation may play a major role in treating hepatocellular carcinoma provided the techniques and procedures are adequate.

**Key Words:** radiofrequency ablation, hepatocellular carcinoma, laparoscopy

**Introduction**

Although radiofrequency ablation (RFA) for tumors was introduced several years ago\(^1\), its clinical advantage as a local therapy proved to be most useful in treating primary liver cancers\(^2\) only in recent years. In countries in which vigorous efforts have been made to detect hepatocellular carcinoma (HCC) in the early stage, that is less than 3cm and limited in number, RFA may play a major role in the treatment of HCCs. Local ablation therapies for HCC include percutaneous ethanol injection (PEI)\(^3\), percutaneous microwave coagulation therapy (MCT)\(^4\), and RFA. PEI is superior to MCT in that it can destroy a larger volume of tissue. MCT is superior to PEI in that its coagulation area is not disturbed by septa within nodules that prevent ethanol diffusion. RFA, which came up last of all, has the advantages of both PEI and MCT\(^5\). It can control the coagulation area as precise as MCT and as wide as PEI can. For RFA to be the choice of treatment for the early stage HCCs, it must be as efficient as partial hepatectomy. HCC nodules are not always located where they are easily approached percutaneously. Some may be located right beneath the diaphragm where percutaneous ultrasound can hardly demonstrate them, and others may be protruding from the liver surface. There is a strong demand for overcoming these difficulties. Some essential techniques are required to bring forth satisfactory therapeutic outcomes\(^6\). This article discusses these techniques with our experiences.

**Patients and Methods**

**Patients**

Since April 1999, we have adopted RFA as one of our major therapeutic strategies for hepatocellular carcinoma. Until June 2001, 147 patients underwent the procedure. The inclusion criteria are; clinically documented HCCs with less than 4 nodules and 30mm in diameter, or solitary nodule smaller than 50mm, better than grade C of the liver damage (LD)\(^7\) according to the General Rules for the Clinical and Pathological Study of Primary Liver Cancer (Liver Cancer Study Group of Japan), no major organ failures that must be harmful to the procedure. Of 147 patients, 94 never had any prior cancer therapy, and the rest had therapy for recurrence of HCCs previously treated.

**Ablation procedure**

Either a percutaneous or laparoscopic approach was selected depending on the location and the size of tumor, and 18 patients underwent the laparoscopic approach. Most of the percutaneous cases could be treated under local anesthesia although all the laparoscopic cases required general anesthesia. Either
an expandable electrode with a thermo-controlled generator system (Model30, RITA, USA)\(^9\), or an internally water-cooled electrode with an impedance-controlled generator (Cool-tip system, Radionics, USA)\(^9\) was used.

The expandable electrode (Model30, RITA) is a 15G probe which has four retractable hooks (curved electrodes), and an extra electrode at the probe tip. The shaft of the probe is insulated with plastic down to 1cm from the distal tip where the electrode is located. Thus, this RF probe consists of five electrodes, four of which are retractable hooks, each containing a thermocouple for monitoring the temperature of the electrode-tissue interface during thermal ablation. The geometry of these electrodes is such that the separate elliptical lesions created overlap with one another to form a spheroid of 2-3cm in diameter. The RF generator (PA500, RITA) can deliver power up to 50W maximum which is servo-controlled during treatment to maintain the temperature collected from the four thermocouples to the target temperature (usually 80 to 100°C). Our treatment protocol for this device is 8 minutes under thermal control.

The Cool-tip system (Radionics, USA) electrode is a single shaft 17G probe within which cooled water circulates internally to cool the tissue adjacent to the electrode, maximizing energy deposition and reducing tissue impedance (charring). The generator (Radionics, USA) can deliver power up to 200W maximum which is automatically controlled according to the tissue impedance. The power delivery is automatically shut off for 15 seconds when the tissue impedance starts to rise. This resting period allows the electrode tip to cool down before the next power delivery. Usually this power on and off occurs cyclically during 12 minutes of the treatment enabling a large amount of energy to go into the tumor lesion. Temperature monitoring from the tip of the electrode just after completion of the session indicates that the lesion is heated up to more than 70°C.

**Guiding needle technique**

When the tumor is larger than 25mm, more than one puncture is usually required to cover the entire tumor with a sufficient surgical margin. This is made safe and easy by the guiding needle technique that is routinely applied to the percutaneous approach. Briefly, one or more 21G fine guiding needles were first inserted percutaneously under the ultrasonic guidance to the center and near the edges of the tumor so that the ablation areas cover the entire tumor with a sufficient surgical margin. Then, one of these needles was replaced by inserting a 15G hollow over tube. Through this second tube, the RF electrode or a biopsy needle if needed was inserted into the tumor for ablation. One by one, all the guiding needles were replaced with over tubes and the part of the tumor was ablated. Before pulling out each over tube after ablation, the needle tract was coagulated using a microwave tissue coagulator (Azwell, Japan), or filled up with gelatin sponge in order to prevent bleeding.

**Peritoneal saline infusion technique**

In some cases in which it is difficult to demonstrate the entire tumor by the percutaneous ultrasound because of the tumors located behind the lung field in the subphrenic area, a peritoneal saline infusion technique is required. A 17G paracenthesis needle was inserted from the right lower quadrant of the abdomen through which sterile saline heated up to 36 degrees Celsius was infused into the peritoneal cavity until the perihepatic space was immersed and the tumor behind the lung became clearly detectable.
This technique was advantageous when a tumor was located in the dorsal deep area of segment 8 (superior anterior of the right hepatic lobe).

**Laparoscopic procedure**

The tumor locations suitable for the laparoscopic approach were; anteriorly protruding tumors, located right on or under the ventral surface of the liver, and in the subphrenic area where percutaneous ultrasound hardly detects the tumor\(^1\). A laparoscope was inserted through a 10mm trocar under general anesthesia. After endoscopic observation, an ultrasound probe (Aloka Inc., Japan) was inserted through the second trocar to detect the tumor and decide the puncture point. The RF electrode was inserted under the ultrasonic guidance as many time as needed to complete the tumor ablation.

**Evaluation of the treatment**

After one session of treatment, enhanced thin sliced biphasic CT was performed within a week to evaluate the outcome. If there was no detectable enhancement of the original tumor nodule in the early arterial phase and the ablated area indicated by non-enhanced area of the late equilibrium phase exceeded the size of original tumor nodule in every direction, the procedure was evaluated as complete. If there was any enhancement of original tumor nodule detected or insufficient ablated area was noted, the procedure was considered incomplete and another session of treatment was given until remaining viable lesions were no longer detected. The treatment was evaluated 4 weeks after the end of the procedure by enhanced thin sliced biphasic CT. It was classified as complete response (CR) when there was no remaining or recurrent viable tumor portion detected, as partial response (PR) when there was less than 50% of remaining or recurrent viable tumor portion, as progressive disease (PD) when the remaining tumor grew up more than 25% of the original size, or as no change (NC) otherwise. Periodical liver imaging together with a serum tumor marker follow-up was performed every 3 months after treatment. If the outcome was evaluated as other than CR, or recurrence was found, re-treatment was planned as long as the ablation therapy was still indicated.

**Clinical impact of the two different devices**

Two different radiofrequency devices: an expandable electrode with a thermo-controlled generator system (Mode130, RITA, USA), and an internally water-cooled electrode with an impedance-controlled generator (Cool-tip system, Radionics, USA) were used for the treatment. The initial 76 cases were treated using the expandable electrode (Mode130) system until January 2000 and the rest were treated using the Cool-tip system, that was available thereafter. The clinical advantages (operation time, number of guide needle insertions, number of ablations, number of sessions, clinical outcome) of both devices were assessed.

**Results**

One hundred forty-seven cases were safely treated by RFA with the average of 2.2 sessions. Most of the cases were treated successfully without residual viable tumor nodules. Those who could not be completely treated after several sessions underwent additional transcatheter arterial embolization.
Table I
Number of Puncture Required and Number of Coagulation Required for Treatment according to the Tumor Size.

<table>
<thead>
<tr>
<th>Tumor size</th>
<th>number of puncture</th>
<th>number of coagulation</th>
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<tbody>
<tr>
<td>less than 21mm</td>
<td>1.4 ± 0.7</td>
<td>2.6 ± 1.9</td>
</tr>
<tr>
<td>more than 20mm</td>
<td>2.0 ± 0.9</td>
<td>3.7 ± 2.2</td>
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Statistics: student t

A small nodule about 2cm or less in diameter could easily be treated with a single puncture of electrode. However, when a nodule exceeded 2cm, more than one puncture were required to cover the entire tumor within the coagulation area. (Table I) As a result, the number of coagulation (heating) increased as the size of the treating tumor increased.

Several approaching methods were employed in order to solve technical obstacles that might otherwise prevent the surgeon from reaching the tumor. A guiding needle technique was uniformly employed when the tumor was treated percutaneously. (Case 1, Fig. 1)

A peritoneal saline infusion technique was employed in 3 of the 20 cases treated for the liver segment.

Fig. 1 66yo, Male, CH (HCV) S5-S6 30mm RFA with expandable handpiece (RITA)
Eighteen patients underwent laparoscopy. (Case 3, Fig. 3) This approach was selected, first, when the tumor was located in the anterior segments or protruding from the liver surface, and second, when laparoscopic approach was not contraindicated. All of the 18 cases were successfully treated.

Two of the three radiofrequency devices: an expandable electrode with a thermal controlled generator system (Model30, RITA, USA) and an internally water cooled electrode with an impedance controlled generator system (Cool-tip System, Radionics, USA) were examined for their clinical significance. Coagulated areas tended to show an irregular form when the expandable electrode was used because of the uneven distribution of the RF current in the area\(^\text{[11]}\). In order to avoid this irregular formation and to acquire a smooth round shaped coagulation area, it was necessary to rotate the expandable electrode at 45 degrees for additional coagulation. In contrast, the cool-tip electrode could produce a larger and smoother coagulation area. These differences may be attributed to the difference in the capacity of the generator power, 50W maximum with RITA and 200W maximum with the Cool-tip system. Further investigation is required to clarify the relationship between the amount of power supply
and clinically measured coagulation area.

There were no major complications among the 147 cases treated with RFA. Some minor complications included limited abdominal wall heat burn at the puncture site (5 cases), self-limiting biloma (3 cases), temporary pleural effusion (5 cases), temporary elevation of transaminases to two to three-fold the previous value (43 cases), and grade 1 skin burn under a neutralising electrode plate (3 cases). No worsening of jaundice, ascites, hepatic encephalopathy, bleeding from puncture site, nor other vital organ damages were noted.

Fig. 1-a showed a 66 years old male with chronic hepatitis C complicated with HCC in the right liver lobe, 30mm in diameter, which required 4 punctures with the expandable electrode and 12 coagulations. This procedure was carried out with the guiding needle technique that enabled precise targeting and the smooth exchange of the electrode from one puncture line to the other. CT scans with a contrast medium taken after the treatment revealed complete ablation (Fig. 1-b). This case was tumor recurrence free even after six months (Fig. 1-c).

Another 66 years-old male with hepatitis C virus related liver cirrhosis was referred to us when HCC was detected in the liver segment 8 just beneath the diaphragm (Fig. 2-a). This case was treated by the
peritoneal saline infusion technique because the tumor was not detected by percutaneous ultrasonography. The tumor became clearly detectable after 700ml of normal saline heated up to 36 degrees Celsius had been infused into the peritoneum (Fig. 2-b). After a single percutaneous puncture and ablation with the cool-tip electrode, the nodule was completely coagulated (Fig. 2-c).

One of the 18 patients who underwent the laparoscopic approach was a 55-years-old male with hepatitis C virus related liver cirrhosis. He was treated laparoscopically because the tumor was undetectable by percutaneous ultrasonography and half protruding from the surface of the liver bordering on the diaphragm (Fig. 3-a). This location was, however, easily accessible by laparoscopy, which would also make it possible to avoid burning the diaphragm when a protruding nodule was ablated (Fig. 3-b). After several punctures and coagulations, the nodule was completely ablated (Fig. 3-c).

**Discussions**

Radiofrequency ablation is a thermal ablation technique which results in a sharply demarcated area of coagulative necrosis. Recently, three different RFA systems became available and they were capable of giving efficient local therapy for hepatocellular carcinomas. Since 1999, we have employed the first RITA system with expandable electrodes and after 2000 we have mainly used the Cool-tip system. Both devices have their own advantages and disadvantages. The single electrode of the Cool-tip system is easy for puncture and placement in the tumor, whereas the expandable electrode can be held within the tissue so that the electrode displacement seldom occurs.

The shape and volume of the coagulated areas seem to be different between these two devices. They tended to show a rather irregular form when the expandable electrode was used. On the other hand, the cool-tip electrode could produce a larger and smoother coagulation area. This difference may be attributed to the structure of the electrode and the surrounding electric current distribution. The single shaft electrode would produce an oval and smooth treatment lesion compared with a complicated form of the expandable electrode that radiates an uneven distribution of the RF current in the area. Furthermore, the blood flow near the treating tumor modifies the heat delivery around the ablated area by conveying heat away from the area or "cooling it down", know as the "radiator effect". These complicated factors result in unexpected irregular ablation areas. In order to avoid this irregular formation and to acquire a smooth round coagulation area, it would have be necessary to rotate the expandable electrode at 45° for additional coagulation.

Although there was no difference in the number of needle puncture required for treatment between two devices, apparently a larger therapeutic area was obtained by the single ablation procedure with the Cool-tip system. This difference may be attributed to the difference in the capacity of the generator power, 50W maximum with RITA and 200W maximum with the Cool-tip system. Further investigation is required to clarify the relationship between the amount of power supply and clinically measured coagulation area.

**Conclusions**

Since treating HCC entails a high recurrence rate, less invasive therapies such as radiofrequency ablation play an important role and should be carried out with adequate techniques, including multiple
guiding needles, peritoneal saline infusion, and laparoscopic approach, when HCCs treated with satisfactory outcomes are few.

References

肝細胞癌に対するラジオ波熱凝固療法
—方法と機種の違いによる特徴—

野口 修・泉 並木 建 隆宏・川村 央信
鈴木比有万・土 谷 薫・濱野 耕 靖・板倉 潤
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要　旨：肝細胞癌 (HCC) に対する当院のラジオ波治療 (RFA) 経験を踏まえ、適切な治療成績を得るための治療手技について検討した。腫瘍の占拠部位とサイズに応じて経皮的または腹腔鏡的に治療を行った。経皮治療では穿刺を確実に行うためにガイドニードルによる穿刺を行った。腹腔鏡治療では超音波プローブの利用が腫瘍の治療範囲同定に不可欠であった。適切な手技と方法を用いることにより、RFA は HCC の局所療法として中心的な役割を果たすと考えられる。