Percutaneous Treatment of Small Hepatic Tumors by an Expandable RF Needle Electrode

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OBJECTIVE. The aim of this study was to evaluate the usefulness of expandable RF needle electrodes in the treatment of hepatic cancer.

SUBJECTS AND METHODS. Thirty-seven patients, 23 of whom had 26 hepatocellular carcinoma nodules and 14 of whom had 19 hepatic metastatic nodules, underwent treatment by RF interstitial thermal ablation with expandable needle electrodes. Forty-five tumor nodules were treated in 64 RF interstitial thermal ablation sessions with 83 needle electrode insertions. The mean diameter of the tumor nodules was 2.5 cm (range, 1.1–3.5 cm). Immediate posttreatment tumor necrosis was evaluated by dynamic CT in all cases. Two patients with hepatocellular carcinoma and three patients with metastases underwent surgical resection 20–60 days after RF treatment. The remaining 32 patients were followed up clinically.

RESULTS. The mean number of RF interstitial thermal ablation sessions to complete tumor nodule treatment was 1.4. Mean number of needle electrode insertions was 1.8. No complications were observed. Posttreatment dynamic CT showed a completely nonenhancing area in the site of the treated tumor in 44 of 45 cases. The remaining patient with metastatic disease had persistent enhancing tissue. Histology showed complete necrosis in four treated tumor nodules and residual viable cancer in one. Twenty-one patients with hepatocellular carcinoma were followed up for 6–19 months (mean, 10 months). Of these patients, six showed recurrences and 15 remained apparently disease-free. Two patients died, one from advanced cancer and one from other causes. Eleven patients with hepatic metastases were followed up for 7–20 months (mean, 12 months). Of these patients, nine showed recurrent disease and only two remained apparently disease-free. Two patients died from disseminated disease.

CONCLUSION. RF interstitial thermal ablation of hepatic tumor by expandable needle electrodes is a safe and effective technique. Local ablation of tumors not exceeding 3.5 cm in diameter is achieved in a short time without complications.

Interstitial hyperthermia generated by RF needle electrodes, microwave electrodes, or laser fibers has recently been used to treat hepatic tumors percutaneously [1–5]. Preliminary trials of RF interstitial thermal ablation have yielded satisfactory results in the treatment of both primary and secondary hepatic tumors with no serious complications [6, 7]. Histopathologic examination showed a complete response in some treated tumors, and the treatment efficacy was confirmed during a long follow-up period [6, 7].

However, to obtain complete necrosis of tumor nodules with a mean diameter of 2.2 cm, multiple needle electrode insertions and a mean of 3.3 RF interstitial thermal ablation sessions per tumor nodule were required [6]. In fact, with the monopolar technique, the maximum volume of necrosis obtained for each thermal lesion was only about 1.8 cm3 [8]. The bipolar and multipolar techniques, which require the simultaneous parallel insertion into the tumor and activation of two or more needle electrodes, can achieve a larger volume of necrosis per thermal lesion [6, 7, 9, 10] and therefore reduce the number of needle electrode insertions and sessions. Nevertheless, much operational skill is required because incorrect placement of the needle electrodes will lead to either a lack of fusion of the thermal lesion between the electrodes or an irregular thermal lesion [6, 10].

Because patient compliance is greatly reduced by multiple treatment sessions occurring during a long period of time and resulting in
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high medical and social costs, a treatment technique is needed that is as simple to use as the monopolar technique but capable of producing at least as large a volume of thermal necrosis as the multipolar technique.

A large volume of necrosis was obtained by infusing saline solution through the needle electrode during production of the RF thermal lesion, probably because of reduced tissue impedance, but in most instances the lesions were irregular [11]. A significant increase in necrosis volume, compared with that obtained with simple monopolar needle electrodes, was achieved in an experimental model by using a cooled needle, which avoids the increase of tissue impedance even with high power [12]; this possibility has been confirmed in a preliminary clinical trial [13].

Another method of enlarging the volume of necrosis is based on the use of a needle electrode, the active surface of which can be expanded by hooks deployed laterally from the tip. This needle electrode can create spherical thermal lesions larger than 3.0 cm in diameter for each activation of the RF generator, as shown by preliminary results [14, 15].

We report our experience in 37 patients with 45 hepatic tumor nodules treated with expandable RF needle electrodes. The number of RF interstitial thermal ablation sessions needed to obtain the necrosis of the tumors was evaluated, and all patients were followed up for at least 6 months.

Subjects and Methods

Patients

Between October 1995 and October 1996, 37 patients with primary and metastatic hepatic cancer underwent RF interstitial thermal ablation in our departments. The patients had to meet the following criteria: presence of a single tumor nodule of not more than 3.5 cm in diameter or not more than three tumor nodules, none of which exceeded 3.0 cm in diameter; absence of extrhepatic spread; absence of portal thrombosis; prothrombin time of not less than 50% and platelet count of not less than 70,000/mm³ (70 x 10³/μl); inoperability or delay or refusal of surgery; and signed informed consent. Patients with hepatocellular carcinoma and accompanying cirrhosis had to be in the Child-Pugh risk class A or B [16] without refractory ascites. Patients with metastases had to have resection of the primary tumor and contraindication, refusal, or failure of chemotherapy.

Of the 37 patients treated with RF interstitial thermal ablation, 23 had 26 hepatocellular carcinoma nodules and 14 had 19 metastatic hepatic nodules. Of the 23 patients with hepatocellular carcinoma, 15 were men and eight were women between 61 and 82 years old (mean, 69 years). Of the 14 patients with hepatic metastases, nine were men and five were women between 46 and 75 years old (mean, 60 years).

Prereatment Studies

All patients underwent sonography. The sonographic patterns of the tumor nodules were classified as hypoechoic in 11 hepatocellular carcinoma nodules and in eight metastatic nodules, as hyperechoic in two hepatocellular carcinoma nodules and in one metastatic nodule, and as iso- to hyperechoic with hypoechoic rim in 13 hepatocellular carcinoma nodules and in 10 metastatic nodules. The mean hepatocellular carcinoma nodule diameter was 2.6 cm (range, 1.3-3.5 cm), the mean metastatic nodule diameter was 2.3 cm (range, 1.1-3.5 cm), and the overall mean tumor nodule diameter was 2.5 cm (range, 1.1-3.5 cm). The hepatic location of tumor nodules was defined using Couinaud's nomenclature [17]: one was in the first hepatic segment, four in the second, one in the third, five in the fourth, seven in the fifth, eight in the sixth, 14 in the seventh, and five in the eighth. Nine tumor nodules were subcapsular, deforming the liver margins.

Histologic or cytologic diagnosis was obtained in all tumor nodules by sonographically guided fine-needle biopsy with a 22-gauge Chiba needle (Coejekt; H. S. Hospital Service, Cavezzo, Italy) or a 22-gauge cutting needle (Surecut; H. S. Hospital Service). The primary tumors in the patients with metastases were colorectal cancer in six patients and miscellaneous in the others.

All patients with hepatocellular carcinoma had histologically proven liver cirrhosis at recruitment and were classified according to Child-Pugh grading [16]; 17 patients were in class A and the remaining six in class B.

Dynamic CT was performed in all patients. Continuous 5-mm-thick axial CT scans were obtained with a Somatom HiQ scanner (Siemens, Erlangen, Germany) or with a Tomoscan LX scanner (Philips, Best, Holland). Dynamic incremental scanning was performed after administration of 100-150 ml of iopromide (Ultravist 370; Schering, Berlin, Germany) at a rate of 2 ml/sec with a power injector. The scanning time was 1.0-1.9 sec with a 2- to 3-sec interscan delay in both early and delayed phase. Dynamic CT revealed 40 of 45 tumor nodules; it failed to detect four hepatocellular carcinoma nodules and one colorectal cancer metastatic nodule, all smaller than 2.5 cm in diameter.

Selective hepatic angiography was performed in five patients with hepatocellular carcinoma and detected all tumor nodules revealed by other imaging techniques.

Serum levels of α-fetoprotein (normal value, ≤20 ng/ml [≤20 μg/l]) were assayed in all patients with hepatocellular carcinoma, and carcinoembryonic antigen (normal value, 0-5 ng/ml [0-5 μg/l]) serum levels were assayed in four patients with colorectal cancer metastases to obtain further parameters on which to evaluate the efficacy of RF interstitial thermal ablation treatment. Levels of α-fetoprotein were normal in 10 patients, ranged between 20 ng/ml (20 μg/l) and 500 ng/ml (500 μg/l) in 11 patients, and were more than 500 ng/ml (500 μg/l) in two patients. Carcinoembryonic antigen levels were normal in one patient and more than 5 ng/ml (5 μg/l) in the others.

Equipment

The RF delivery system was an RF current generator (Electrosurgical Generator; Radiofrequency Interstitial Thermal Ablation Medical System, Mountain View, CA) in monopolar mode with an active expandable needle electrode and a large dispersive electrode. The RF generator had a 480-kHz frequency, supplied 50 RF watts of power output, and was a source of RF voltage through its output terminals, which were connected to electrodes. The RF generator displays indicating hook temperatures, tissue impedance value, and procedure time. The generator was connected to a computer (Think-Pad 360; IBM-ASISTEL, Milan, Italy) through dedicated software (Micro Interactive; Micro Interactive, New York, NY), continuously recorded the temperature curves obtained during the treatment by the four thermistors placed on the hook tips.

The active nickel-titanium hooks could be deployed laterally and retracted manually by moving the graduated control mechanism on the handle of the needle. The maximum deployment diameter of the hooks was 3.0 cm, and each hook had a thermistor on its tip to monitor the temperature in the surrounding tissue. The calibration of the thermistor was accurate to ±4°C in the region of 90°C to 120°C.

The RF needle electrode was inserted in the tumor under sonographic guidance using a 3.5-MHz convex probe (Alokå 2000; Alokå, Tokyo, Japan; or ATL HDI, ATL, Seattle, WA) with a lateral biopsy apparatus.

Technique

The RF interstitial thermal ablation treatment was performed on inpatients after 12 hr of fasting without any sedation and with a hospital stay of 1 day. Blood coagulation tests were performed before each session; RBC, hemoglobin, serum alanine transferase, and serum aspartate transferase levels were evaluated before and 24 hr after each treatment. Serum aminotransferase levels were also evaluated 7 days after the last session of RF interstitial thermal ablation treatment.

The patient was connected to the RF generator by a large dispersive electrode. Local anesthesia was achieved by injecting lidocaine 1% (Lidrian; Bierfe Medidal, Modena, Italy) from the skin to the peritoneum along the predetermined puncture line. The skin was pricked with a small pointed lancet. The active needle electrode was then introduced into the chosen area of the tumor under sonographic guidance through a needle biopsy apparatus. After the hooks had been deployed, the RF generator was activated, and the power needed to maintain a temperature from 90°C to 115°C at the hook tips was delivered for 8 min. Impedance values ranged be-
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Fig. 1.—Photograph of type of active expandable RF needle electrode used in this study before and after deployment of hooks.

Fig. 2.—Photomicrograph of specimen shows thermal lesion 3.2 cm in diameter (arrows) obtained in pig liver using RF needle electrode with external diameter of 1.9 mm, exposed tip of 1.0 cm, and four hooks. Deployment diameter of hooks was 3.0 cm. Temperature between 95°C and 115°C was applied for 8 min. Pig was killed 48 hr after RF interstitial thermal ablation performed during laparotomy.

tween 30 and 50 ohm. These parameters were chosen on the basis of preliminary experimental studies (Rossi S, unpublished data) (Fig. 2).

For tumor nodules smaller than 2.5 cm, the needle electrode was inserted through the center of the nodule. The tip of the needle electrode was advanced until it reached the deepest margin of the nodule and then the hooks were deployed. When necessary, after creation of the first thermal lesion the hooks were retracted and the needle electrode was withdrawn 1.0 cm along its major axis; the hooks were then redeployed, and the RF generator was reactivated. At the end of the procedure, the RF generator was turned off and the needle electrode was removed. For tumors larger than 2.5 cm, two or three needle electrode insertions were planned, depending on the tumor shape, and at every insertion two or three thermal lesions were created as described. In any case, further insertions of the needle electrode were made according to the findings on posttreatment dynamic CT.

Access was intercostal in four patients and subcostal in the others.

Posttreatment and Follow-Up Studies

Sonography was performed between 24 and 48 hr, dynamic CT within 5 days, selective hepatic angiography within 10 days, and tumor marker assay between 10 and 15 days after the RF interstitial thermal ablation treatment.

During posttreatment dynamic CT, once the treated area was found, an additional 50 ml of contrast medium was injected and further contiguous 5-mm-thick axial incremental scans were obtained for minute evaluation of the resulting necrosis. The findings of dynamic CT were considered negative if a completely nonenhancing area with a diameter equal to or larger than the treated tumor was shown at the site of the tumor. If residual enhancing tissue persisted, further RF thermal lesions were made and posttreatment dynamic CT was repeated.

The findings of selective hepatic angiography were considered negative if all the signs of neoplastic vascularization had completely disappeared.

In the patients treated with delayed surgery, the treatment efficacy was further assessed by histologic examination of resected specimens.

The follow-up after the RF treatment included evaluation of tumor markers every 2 months, sonographic examination every 3 months, and dynamic CT every 3 months in patients with hepatic metastases and every 6 months in patients with hepatocellular carcinoma. If sonographic examination or dynamic CT revealed new tumor nodules, local recurrences, or even only doubtful images that might indicate local recurrences, multiple sonographically guided fine-needle biopsies were performed.

Tumor nodules that appeared in the same hepatic segment as the treated one were defined as local recurrences, and others were defined as new tumor nodules.

Statistical Analysis

Statistical comparison was performed using the Student’s paired t test. Because of the abnormal distribution of α-fetoprotein serum levels, values were log-transformed. Geometric mean values were calculated before and after the RF interstitial thermal ablation treatment. A p value of less than .05 was considered statistically significant.

Results

Forty-five tumor nodules in 37 patients were treated in 64 RF interstitial thermal ablation sessions with 83 needle electrode insertions. The mean number of RF interstitial thermal ablation sessions and needle electrode insertions needed to obtain apparent tumor nodule destruction as seen on imaging results is shown in Table 1.

Sonographic examination soon after RF generator activation showed an increasing hyperechoic area, often with a posterior acoustic shadow, that appeared around the needle electrode and its hooks, reproducing the needle shape. This area became round at the end of the thermal lesion and sometimes included some hyperechoic spots (Fig. 3B). These sonographic changes, which were visible at each thermal lesion, diminished rapidly as soon as the RF generator was switched off and completely disappeared within 12 hr. The sonographic changes visible after 24 hr varied depending on the initial sonographic pattern of the tumor. Generally, hyperechoic lesions acquired echogenicity; hyperechoic lesions either became isoechoic or remained unchanged. In some patients with good sonographic visibility and with superficially located tumor nodules, after more than 24 hr the thermal lesions appeared as iso- to hypoechoic areas clearly defined from the surrounding tissue by a thin peripheral hyperechoic rim (Figs. 4A and 4B).

Posttreatment dynamic CT on all patients showed a completely nonenhancing area, with a diameter equal to or larger than the diameter of the treated tumor in 39 of 40 nodules with a positive pretreatment CT pattern (Figs. 3D, 3E, 4C, and 4D), and a nonenhancing area in the five nodules with a negative pretreatment CT pattern. In one patient with metastases, dynamic CT showed persistent enhancing tissue after treatment was discontinued because of
the difficulty of correctly inserting the needle electrode tip into the tumor located in the subdiametrical region of an obese patient.

Posttreatment selective hepatic angiography showed disappearance of tumor stain in all cases.

Levels of α-fetoprotein decreased in all 13 patients who had high pretreatment values, becoming normal in nine but remaining between 20 and 100 ng/ml (20–100 μg/l) in four. The decrease in α-fetoprotein serum levels was statistically significant (p < .001). Caringoembryonic antigen levels came within the normal range in one of the three patients who had high pretreatment values and continued to be abnormal in the other two.

No fatal or major complications related to the treatment or to the diagnostic procedure were observed. Only six patients experienced mild abdominal pain during the procedure, which required analgesia (propacetamol chloride [Pro-erfetan; UPSA Laboratories, Agen, France]). One patient who was asymptomatic during the procedure experienced intense abdominal pain 2 hr after the treatment; the pain required analgesia (10 mg of morphine chloride and 0.5 mg of atropine sulfate [Cardiostenol; L. Molteni, Florence, Italy]) and persisted for 2 days. In this patient, dynamic CT showed capsular necrosis. One patient had fever (>38°C) the day after the treatment that did not require therapy. A slight increase of serum alanine transaminase and serum aspartate transaminase was seen in all patients. Before the treatment, the serum alanine transaminase levels were 82 ± 9 IU/ml (82 ± 9 U/l) (normal value, 0–37 IU/ml [0–37 U/l]) in patients with hepaticocellular carcinoma and 26 ± 4 IU/ml (26 ± 4 U/l) in patients with metastases. The serum aspartate transaminase levels were 92 ± 8 IU/ml (92 ± 8 U/l) (normal value, 0–40 IU/ml [0–40 U/l]) in patients with hepaticocellular carcinoma and 26 ± 4 IU/ml (26 ± 4 U/l) in patients with metastases. After treatment, the serum alanine transaminase levels were 155 ± 11 IU/ml (155 ± 11 U/l) in patients with hepaticocellular carcinoma and 142 ± 7 IU/ml (142 ± 7 U/l) in patients with metastases; the serum aspartate transaminase levels were 152 ± 9 IU/ml (152 ± 9 U/l) in patients with hepaticocellular carcinoma and 143 ± 6 IU/ml (143 ± 6 U/l) in patients with metastases. Aminotransferase levels returned to the baseline values within a week in all patients.

Surgical Control Subjects

Five patients underwent surgery from 20 to 60 days after percutaneous RF interstitial thermal ablation treatment. Of these patients, two had hepaticocellular carcinoma and three had hepatic metastasis from colorectal cancer.

Histopathologic examination of the resected specimens failed to detect any residual viable cancer cells in one patient with a hepaticocellular carcinoma node smaller than 2.5 cm in diameter and in three patients with metastatic nodules (two smaller and one larger than 2.5 cm in diameter), whereas it showed 90% necrosis with three remaining 3-mm tumor foci in a patient with a hepaticocellular carcinoma node larger than 2.5 cm in diameter (false-negative at both dynamic CT and selective angiography).

Follow-Up

Patients with hepaticocellular carcinoma.—Excluding the two patients who underwent surgery, 21 patients with 24 tumor nodules were followed up for at least 6 months (range, 6–19 months; mean, 10 months). Of these patients, one showed local recurrence, two had new tumor nodules, three had multicentric disease, and 15 remained apparently disease-free. Two patients died, one from hepatic failure due to advanced cancer and one from causes other than cancer.

On the 6-month sonographic examination, four treated tumor nodules were no longer visible; five appeared as a hyperechoic spot not exceeding 1.0 cm in diameter, six as inhomogeneous or hyperechoic areas not exceeding 2.0 cm in diameter, and three as iso- to hyperechoic areas between 2.0 and 2.5 cm with a hyperechoic rim; one showed lack of regression with reappearance of posterior acoustic enhancement; and five were involved in multicentric disease. A posterior acoustic shadow was frequently visible.

On 6-month dynamic CT, four treated tumor nodules were no longer visible; and 14 appeared as decreasing nonenhancing areas not exceeding 2.5 cm in diameter (Fig. 4E), one as a nonenhancing area with enhancing half-moon, and five as nonenhancing areas within an enhancing tumor tissue.

Levels of α-fetoprotein in the follow-up were significantly high in only one patient who developed multicentric disease but remained at insignificant values in the others.

Patients with metastases.—Excluding the three patients who underwent surgery, 11 patients with 16 metastatic nodules were followed up for at least 7 months (range, 7–20 months; mean, 12 months). Of these patients, three showed other hepatic metastases, one had local recurrences, five had extraparenchymal metastases, and two had hepatic and extraparenchymal metastases. At 12-month follow-up, only two patients (who underwent new courses of RF interstitial thermal ablation) seemed to be tumor-free. Two patients died from disseminated disease.

On 6-month sonographic examination, three treated tumor nodules were no longer visible; five appeared as hyperechoic or inhomogeneous areas not exceeding 1.0 cm in diameter, three as inhomogeneous decreasing areas not exceeding 2.0 cm in diameter, two as inhomogeneous areas without decrease in diameter, and one as a growing area; one was involved in multicentric disease; and one was not evaluated.

On 6-month dynamic CT, three treated tumor nodules were no longer visible; five appeared as nonenhancing areas about 1.0 cm in diameter, three as decreasing nonenhancing areas not exceeding 2.0 cm in diameter, two as nonenhancing areas without decrease in diameter, one as a growing enhancing area, and one as a nonenhancing area within diffuse enhancing tumor tissue; and one was not evaluated.

<table>
<thead>
<tr>
<th>Tumor Nodule</th>
<th>No.</th>
<th>Mean No. of Sessions (Range)</th>
<th>Mean No. of Needle Electrode Insertions (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2.5 cm</td>
<td>24</td>
<td>1.1 (1–2)</td>
<td>1.3 (1–2)</td>
</tr>
<tr>
<td>&gt;2.5 cm</td>
<td>21</td>
<td>1.7 (1–6)</td>
<td>2.4 (1–7)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>26</td>
<td>1.5 (1–6)</td>
<td>1.9 (1–7)</td>
</tr>
<tr>
<td>Metastases</td>
<td>19</td>
<td>1.3 (1–6)</td>
<td>1.7 (1–4)</td>
</tr>
<tr>
<td>Liver segment</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>18</td>
<td>1.3 (1–6)</td>
<td>1.6 (1–2)</td>
</tr>
<tr>
<td>Posterior</td>
<td>27</td>
<td>1.4 (1–6)</td>
<td>1.9 (1–7)</td>
</tr>
<tr>
<td>Overall</td>
<td>45</td>
<td>1.4 (1–6)</td>
<td>1.8 (1–7)</td>
</tr>
</tbody>
</table>

* In some patients, two tumor nodules were treated in a single RF session.
Carcinoembryonic antigen levels remained in the normal range in one apparently disease-free patient and were significantly high in three other patients because of local recurrence or extrahepatic disease.

Discussion

Surgical resection is considered the only curative therapy for malignant hepatic tumors, but few patients with hepatic tumors are ideal candidates for surgery [18]. Therefore, alternative treatments that are less invasive and potentially equally effective are being investigated.

This study confirms that RF interstitial thermal ablation is a technique capable of ablating hepatic tumors [2, 6, 7]. The appearance of multincentric disease in about 10% of cases some months after the end of the RF treatment is probably due to an underestimation of the disease on radiologic imaging, especially in patients with underlying cirrhosis [19].

The design of the new expandable RF needle electrodes increases the active electric field, producing spherical necrosis with a diameter larger than that previously reported using simple monopolar RF needle electrodes [8]. Primary and metastatic hepatic tumors having a diameter of up to 2.5 cm were treated in only one session, generally with a single needle electrode insertion. Further needle electrode insertions were required in only a few instances, depending on the tumor location and on the patient’s cooperation. In some patients, two tumor nodules could be ablated during the same session. For tumor nodules from 2.5 to 3.5 cm in diameter, multiple needle electrode insertions were required to create a thermal necrosis volume larger than the treated tumor volume, thus ensuring therapeutic adequacy. In these cases, according to our results, the treatment could nevertheless be accomplished in one or two sessions.

Factors other than tumor volume, such as the tumor location and the presence of vessels near the tumor [20, 21], influenced the success of the treatment and the number of needle electrode insertions required.

As in all percutaneous treatment of hepatic tumors, a deep liver location made the therapy more difficult. In our experience, a deep location resulted in a larger number of needle electrode insertions compared with the number needed to treat superficially located tumors. However, the number of sessions was practically unchanged. In one case, the subdiaphragmatic location of the tumor in an obese patient made completing the treatment impossible.

The presence of large vessels near the needle electrode can lead to incomplete necrosis because the vessels act as heat sinks and dissipate the heat [20, 21]. On the other hand, this pitfall can be avoided by retracting the hooks and redeploying them after slightly rotating the needle electrode to change the hook position, or by completely repositioning the needle electrode until killing temperatures are obtained near all
hook tips. Small vessels do not substantially influence the procedure because RF energy can overcome the low flow in these vessels.

Obviously, the patient’s ability to breathe deeply and then hold the breath is crucial; in fact, a patient’s inability to comply with this procedure renders needle electrode tip placement difficult, so a larger number of needle electrode insertions than planned is required.

Another factor affecting the results is the temperature used. In this study, the temperatures were kept between 90°C and 115°C to maximize the necrosis volume. Even if some gas microbubbles formed, we did not observe either irregular popping lesions or related complications. Impedance values of less than 50 ohm indirectly ensured the absence of significant charring.
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As for all percutaneous ablative therapies, the major problem was verifying the complete destruction of the tumors. Previous investigators used a combination of imaging techniques to evaluate tumor necrosis after percutaneous ablative therapies, but no established protocol exists [5, 6, 22, 23].

Sonography cannot be used to confirm complete tumor necrosis soon after the treatment because necrotic tumor and viable tumor may have similar sonographic patterns. Similarly, posttreatment sonographically guided biopsy is not a reliable way of solving the problem because even multiple biopsies will provide data on only a limited volume of the treated tumor [6, 7, 22, 23]. For this reason, the role of sonographically guided biopsies is limited to evaluating a doubtful area visible with the imaging technique.

Measuring serum tumor markers such as α-fetoprotein in hepatocellular carcinoma and carcinoembryonic antigen in colorectal hepatic metastases is another way of assessing the efficacy of ablative therapies, but the predictive value of these markers is significant only if the starting levels are high. Serum α-fetoprotein levels are normal in about 35% of patients with hepatocellular carcinoma [24]. Similarly disappointing results have been found for carcinoembryonic antigen in colorectal hepatic metastases [25]. In fact, the lack of a posttreatment decrease in carcinoembryonic antigen can be due to either unsatisfactory response of the treated tumor, the appearance of other metastases, or occult tumor relapse.

In patients with hepatocellular carcinoma treated by transarterial embolization [26] or percutaneous ethanol injection [22, 23], dynamic CT played a major role in evaluating the necrosis obtained by RF interstitial thermal ablation treatment, with a good correspondence with histopathologic findings in four (80%) of five resected specimens. In one patient, dynamic CT failed to identify three remaining tumor foci smaller than 3.0 mm. Unlike some authors [11] who performed dynamic CT 1 month after the treatment, we preferred to perform it within 5 days from the end of the therapy because an early examination made it possible to finish an incomplete treatment without delay. Besides, at this time the size of the necrosis is largest and the vascular neogenesis is poor [8], facilitating the avoidance of the posttreatment peripheral enhanced ring that sometimes appears around the thermal necrosis because of either a residual tumor or a reactive inflammation with microscopic arteriovenous shunts [8]. This peripheral enhanced ring poses a problem of interpretation if the thermal necrosis does not clearly exceed the tumor margins. Otherwise, the peripheral enhanced ring can be attributed with certainty to neovascularization.

However, we believe that at present no imaging or biopsy technique can exclude conclusively the persistence of a small amount of viable cancer cells after percutaneous ablative treatment; only an adequate follow-up with imaging examination and tumor marker assay can confirm the radical nature of the treatment.

The primary goal of this technique is to produce the largest volume of necrosis in the shortest time. Our results represent a clear improvement from the previously reported data using RF monopolar, bipolar, or multipolar methods in which two to three treatment sessions were required for small tumor nodules [6, 7]. Likewise, the results of this study are far better than those of using percutaneous ethanol injection, which requires almost five sessions to treat hepatocellular carcinoma nodules of less than 2.0 cm in diameter and eight to 10 sessions to treat hepatocellular carcinoma nodules of less than 3.5 cm in diameter [27].

The outcome of RF interstitial thermal ablation did not depend on the kind of tumor (primary or metastatic) or, in the case of metastases, on tumor histotype, although sporadic cases of difficulty in treating rapidly growing metastases from sarcoma have been reported [7]. The same applies to laser ablation, which always requires multiple fiber insertions [5] and is more expensive than RF interstitial thermal ablation, and to cryotherpy, which necessitates open surgery [28].

Nevertheless, the crucial point is the real impact of RF interstitial thermal ablation treatment on survival, because neither tumor necrosis nor tumor response to therapy necessarily prolongs life expectancy. In a nonrandomized study, satisfactory results have been shown in a series of 39 patients with hepatocellular carcinoma followed up for a mean of 23 months after RF thermal ablation [6]; however, in patients with hepatic metastasis, the results are different. A disease-free survival rate of 30% was reported in a series of 16 patients with at least 9 months follow-up (mean, 16 months) [7]. On the contrary, in a previous study [6] we observed only one (11%) of nine apparently disease-free patients 1 year after RF thermal ablation treatment, and similar results occurred in our study in which only two (18%) of 11 patients seemed to be apparently disease-free after 1 year. This overall biologic failure may be due to understaging of disease at recruitment. The pretreatment staging probably can be improved using more advanced imaging techniques (helical CT, MR imaging). Nevertheless, it is likely that one group overestimates and the other underestimates disease-free survival. We believe that only multicentric, randomized clinical trials can provide a definitive answer. In the meantime, the use of RF interstitial thermal ablation in patients with metastases must in any case be decided in agreement with medical oncologists in a multidisciplinary approach to the disease.

The short treatment time, combined with the practically pain-free procedure, resulted in better compliance. We think that further improvement can be obtained in selected patients if the treatment is carried out on an outpatient basis.

Our study confirms that RF interstitial thermal ablation is safe. In fact, we did not observe any major complications. However, we believe caution is needed, with careful sonographic monitoring of the position of the needle electrode tip and hooks. No tumor seeding has been reported [6, 7, 11], probably because the cancer cells adhere to the needle electrodes, where they burn and die. In spite of the needle gauge, only one case of self-limiting peritoneal hemorrhage has been described [7], and no bleeding was observed in our series, probably because of the coagulating power of the RF interstitial hyperthermia.

When expandable needle electrodes are used, a transient increase in serum aminotransferase levels is observed, probably because of the large volume of necrosis, whereas no enzymatic change was found in previous experiences of RF thermal ablation with simple monopolar needle electrodes [2, 6]. Finally, new RF needle electrodes that are capable of creating large thermal lesions either by modifying the electrode tip design or by avoiding the impedance-related problems (e.g., by cooling the needle electrode tip using circulating liquid) are under investigation by others [12, 13] and ourselves with promising results.

In conclusion, RF interstitial thermal ablation is a safe and effective technique for obtaining local control of selected hepatic tumors in patients with no surgical prospects. With modified expandable RF electrode needles, both primary and metastatic tumor nodules not exceeding 2.5 cm in diameter can be treated in about one session and those between 2.5 and 3.5 cm in diameter in a short time without complications.

References
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