Percutaneous RF Interstitial Thermal Ablation in the Treatment of Hepatic Cancer

S. Rossi1
M. Di Stasi1
E. Buscarini1
P. Quarretti2
F. Garbagnati3
L. Squassante4
C. T. Paties5
D. E. Silverman6
L. Buscarini1

OBJECTIVE. The aim of this study was to evaluate the usefulness of RF interstitial thermal ablation for treating hepatic cancer. 

SUBJECTS AND METHODS. Fifty patients, 39 who had 41 hepatocellular carcinoma nodules and 11 who had 13 hepatic metastatic nodules, underwent RF interstitial thermal ablation. In all but one, a thermal necrosis volume greater than the tumoral node volume was created to obtain total tumor destruction. One large tumor was treated for debulking purposes.

RESULTS. Hepatocellular carcinoma node destruction was achieved in a mean of 3.3 sessions of RF interstitial thermal ablation. During a mean follow-up of 22.6 months (range, 3–66 months), 16 (41%) of 39 patients had recurrences; two (5%) of these patients showed local recurrences and the remaining 14 (36%) had new lesions. Nine of these 16 patients underwent further RF interstitial thermal ablation that proved effective. RF interstitial thermal ablation was also successfully repeated in four patients who had a second recurrence. With RF interstitial thermal ablation, we treated 54 hepatocellular carcinoma nodules in 39 patients. Eleven (28%) of the 39 patients died: five from hepatic failure due to advanced cancer and six from causes other than cancer. Autopsy was performed on three patients who died from causes other than cancer, one had had two new courses of RF interstitial thermal ablation for two new lesions. Gross examination failed to detect two treated tumor nodules; histologic examination of three other treated tumor nodules showed total necrosis in two nodules and a 3-mm focus of viable cancer cells in the other nodule. Cumulative survival curves showed the median survival time to be 44 months. The survival rate for the first year was 0.94, 0.86 for the second year, 0.68 for the third year, and 0.40 for the fourth and fifth years. In the patients treated for metastatic nodules, posttreatment imaging studies showed necrosis that varied from 80% to 100% in all cases. Pathologic studies performed on two patients who underwent surgery after RF interstitial thermal ablation showed 100% necrosis in one case and 80% necrosis in the other.

CONCLUSION. RF interstitial thermal ablation is a useful percutaneous treatment for hepatic cancer.

Few patients affected by hepatocellular carcinoma are ideal candidates for surgical resection because of technical difficulties, age at the time of diagnosis, and advanced cirrhosis, which in Western and Far Eastern countries is a common background for hepatocellular carcinoma [1]. Moreover, the 5-year recurrence rate after resective surgery is about 80% [2]. Similarly, only 5–10% of patients with secondary hepatic tumors are suitable for surgical resection [3] with a resulting 5-year survival time of approximately 25% [4]. For all these reasons, percutaneous treatment, such as ethanol injection, has been proposed [5].

Work has focused on developing a new percutaneous ablative therapy founded on interstitial hyperthermia to achieve a more effective and rapid destruction of hepatic tumor.

Interstitial hyperthermia can be obtained by RF electrode needles, microwave electrodes, or laser fibers inserted into the tumor under sonographic guidance. Interstitial laser photocoagulation has been used mainly in patients with hepatic metastasis [6–8]; RF interstitial thermal ablation and percutaneous microwave coagulation therapy have been
mostly used in patients with small hepatocellular carcinoma [9-13].

RF interstitial thermal ablation can be carried out with monopolar or bipolar energy by inserting one or two electrode needles into the tumor. In either case, heat is generated in the tissue around the needle or between the needles by molecular friction and ionic dissipation. The bipolar method achieves a volume of necrosis more than twice that of a lesion made by a simple unmodified monopolar needle [14].

We report a 7-year experience with RF interstitial thermal ablation for treating both hepatocellular carcinoma and hepatic metastasis using monopolar or bipolar methods.

Subjects and Methods

Patients with Hepatocellular Carcinoma

From January 1989 to July 1995, 37 patients were selected for RF interstitial thermal ablation if they had the following characteristics: a single hepatocellular carcinoma nodule not more than 3.0 cm in diameter; absence of portal vein thrombosis or extrapleural spread; prothrombin activity more than 50%, partial thromboplastin time less than 40 sec, serum fibrinogen level more than 100 mg/dl, and platelet count more than 70,000/mm³; high surgical risk, postoperative relapse, or refused surgery; and informed consent. Moreover, two patients with two hepatocellular carcinoma nodules who met all the other criteria were included. The resulting RF interstitial thermal ablation series comprised 39 patients with 41 hepatocellular carcinoma nodules. Of these patients, 24 were men and 15 were women between 53 and 79 years old (mean, 66.7 years old).

All the hepatocellular carcinoma nodules were detected initially using sonography. Table 1 shows the largest tumor diameters. The sonographic tumoral patterns were classified as hypoechoic in 23 cases, as hyperechoic in three, and as iso- to hyperechoic with a hypoechoic rim in 15. Tumor location was defined by Couinaud’s nomenclature [15]: seven hepatocellular carcinoma nodules were located in the second hepatic segment, one in the third, seven in the fourth, seven in the fifth, 10 in the sixth, six in the seventh, and three in the eighth. Ten hepatocellular carcinoma nodules were subcapsular and deformed the hepatic margins.

Pathologic diagnosis was obtained in all cases by sonographically guided fine-needle biopsy with a 22-gauge Chiba needle (Ecojet; H. S. Hospital Service, Cavezzo, Italy), 22-gauge cutting needle (Surecut; H. S. Hospital Service), or both. Thirty-eight of the 39 patients had been diagnosed with cirrhosis after hepatic biopsy. At recruitment, Child-Pugh classification [16] for the prognosis was applied to all cirrhotic patients: 21 patients were in class A, 16 in class B, and one in class C.

To confirm the size and number of hepatocellular carcinoma nodules and to obtain basic information for evaluating the RF interstitial thermal ablation therapeutic effects, we performed the following techniques: dynamic CT on 37 (95%) of 39 patients (two were allergic to the contrast medium), which detected 35 of 39 hepatocellular carcinoma nodules; selective hepatic angiography on 30 (77%) of 39 patients, which detected 28 of 32 hepatocellular carcinoma nodules; and α-fetoprotein (AFP) serum assay (normal values, <20 ng/ml) in all patients. AFP was normal in 29 patients, between 51.8 and 423 ng/ml in nine, and 2700 ng/ml in one.

Contiguous 5- to 8-mm-thick axial CT scans were obtained with a Siemens Somatom HiQ scanner (Siemens, Erlangen, Germany) or with a Philips Tomoscan LX scanner (Philips, Best, Holland). Dynamic incremental scanning was performed after administration of 100-150 ml of iopromide (Ultravist 370; Schering Pharmaceuticals, Berlin, Germany) at a rate of 2 ml/sec with a power injector. A scanning time of 1.3-1.9 sec was used with a 2- to 3-sec interscan delay in the early and delayed phases.

Of the 21 patients with Child-Pugh class A cirrhosis, two were excluded from surgery because of technical difficulties; three because of advanced obstructive bronchopneumopathy; seven because they were more than 70 years old; two because of recurrences after surgery, one because of two tumor nodules located in different hepatic segments, and six because they refused surgery. The patient without cirrhosis was more than 70 years old and had advanced obstructive bronchopneumopathy and thus was excluded from surgery.

Patients with Metastases

From March 1991 to July 1995, 11 patients with 13 hepatic metastatic nodules underwent RF interstitial thermal ablation: nine were referred from their oncologists because no other treatment was considered appropriate; two had to delay surgery because of temporary high risk and, after RF interstitial thermal ablation, underwent hepatic resection. The five men and six women were 52-75 years old (mean, 60.6 years old).

The recruitment criteria were the same as those for the patients with hepatocellular carcinoma. We treated two patients with two metastatic nodules that were each smaller than 3.5 cm in diameter and one patient with a solitary tumor approximately 8.0 cm in diameter for debulking purposes before hepatic radiotherapy.

Before RF interstitial thermal ablation, all patients underwent sonography. The metastatic nodules were classified as iso- to hyperechoic with a hypoechoic rim in six cases, as hypoechoic in six cases, and as a complex mass in one case. One metastatic nodule was located in the third hepatic segment, one in the fourth, one in the fifth, three in the sixth, four in the seventh, and two in the eighth. Finally, one metastatic nodule had a centrolepatic location involving various segments. The histopathologic diagnosis of metastasis was obtained by sonographically guided fine-needle biopsy in all cases. Table 2 gives the largest metastatic nodule diameters and the primary tumors.

Dynamic CT performed on all 11 patients with metastases revealed 13 nodules. Gastrin serum dosage performed on the patient with gastrinoma reached 1470 pg/ml (normal value, <50 pg/ml) and the carcinomembryonic antigen performed on four patients was normal in two and ranged between 10 and 20 ng/ml in the others (normal value, 0-5 ng/ml).

Equipment

The RF delivery system used for the monopolar method was an RF-current generator (Radiomics RFG S; Radiomics, Burlington, MA; ZoMed International, Mountain View, CA) with an active needle electrode and a dispersive electrode. For the bipolar method, we used the same ZoMed RF Generator with two active electrode needles. Both generators had a 480-kHz frequency with a maximum power of 26 RF-watt and were a source of RF-voltage through their output terminals, which were connected to electrodes.

The active needle electrodes had an insulated (by 0.1-mm-thick plastic) stainless steel shaft that was 24-30 cm long. The exposed tip was of fixed length in the Radiomics equipment and varied in length (because of a moving plastic covering) in the ZoMed equipment. The tips contained one (Radiomics) or two thermistors (ZoMed) that allowed temperature monitoring in the tissue around the needle tip. The calibration of the thermistor was accurate to ±4°C in the region of 90°C.

Needle electrodes with an external diameter of 1.2, 1.3, and 1.6 mm and an exposed tip of 1.0 or 2.0 cm were used for the monopolar method. Needle electrodes with an external diameter of 1.3 mm and an exposed tip of 2.0 cm were used for the bipolar method.

To insert the electrode needles in the tumor, we used a 3.5-MHz convex probe (Aloka SSD-650; Tokyo, Japan) with a lateral biopsy apparatus for the monopolar method or with a multiholed guide specifically designed by our group for the bipolar method mounted on the transducer (Fig. 1).

Technique

The RF interstitial thermal ablation treatment was performed only on inpatients after an overnight fast, with a hospital stay of 1 day for each session. No sedative or analgesics were given. If multiple sessions were required, they occurred once or twice a week. Blood coagulation tests were performed before each session; RBC count and hemoglobin, serum alanine transference, and serum aspartic transference levels were evaluated before and 24 hr after each session.

The monopolar procedure has been described [9-11]. In short, after connecting the patient to the RF generator by a dispersive electrode, we administered lidocaine 1% (Lidrin; Bieffe Medicil, Modena, Italy) from the insertion point at the skin to the peritoneum along the puncture line. With sonographic guidance we used the lateral biopsy apparatus to
### RF Thermal Ablation for Hepatic Cancer

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Tumor Size (cm)</th>
<th>Sonographically Guided Biopsy</th>
<th>Dynamic CT</th>
<th>Selective Angiography</th>
<th>Posttreatment Studies</th>
<th>Recurrences</th>
<th>Outcome (mo)</th>
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<tr>
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<td>N</td>
<td>N</td>
<td>MD (4)</td>
<td>HCC (10)</td>
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<td>1.3 - 1.7</td>
<td>N</td>
<td>N</td>
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<td>AWT (third recurrence) (66)</td>
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<td>MD (40)</td>
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<tr>
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<td>P&lt;sup&gt;c&lt;/sup&gt;</td>
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<td>65</td>
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<td>N</td>
<td>N</td>
<td>N</td>
<td>NL (7)</td>
<td>AWOT (14)</td>
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<td>18</td>
<td>61</td>
<td>1.7 - 1.7</td>
<td>N</td>
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<td>1.5 - 2.0</td>
<td>N</td>
<td>N</td>
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<td>1.5 - 1.5</td>
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<td>AWOT (25)</td>
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<td>21</td>
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<td>2.5 - 2.8</td>
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<td>N</td>
<td>N</td>
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<td>69</td>
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<td>23</td>
<td>55</td>
<td>2.8 - 2.8</td>
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<td>—</td>
<td>NL (12)</td>
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<td>24</td>
<td>69</td>
<td>1.5 - 2.8</td>
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<td>—</td>
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<td>25</td>
<td>60</td>
<td>2.0 - 2.6</td>
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<tr>
<td>26</td>
<td>73</td>
<td>2.2 - 2.2</td>
<td>N</td>
<td>N</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>MD (5)</td>
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<tr>
<td>27</td>
<td>73</td>
<td>2.4 - 2.5</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>—</td>
<td>—</td>
<td>AWT (12)</td>
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<tr>
<td>28</td>
<td>71</td>
<td>1.8 - 3.0</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>—</td>
<td>—</td>
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<tr>
<td>29</td>
<td>69</td>
<td>1.7 - 2.1</td>
<td>N</td>
<td>N</td>
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<td>—</td>
<td>—</td>
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<td>30</td>
<td>60</td>
<td>1.9 - 2.1</td>
<td>N</td>
<td>N</td>
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<td>—</td>
<td>AWOT (11)</td>
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<tr>
<td>31</td>
<td>72</td>
<td>2.0 - 2.1</td>
<td>N</td>
<td>N</td>
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<td>—</td>
<td>—</td>
<td>Respiratory failure (9)&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td>32</td>
<td>68</td>
<td>1.6 - 1.6</td>
<td>N</td>
<td>N</td>
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<td>—</td>
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<tr>
<td>33</td>
<td>65</td>
<td>3.0 - 3.0</td>
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<td>N</td>
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<tr>
<td>34</td>
<td>70</td>
<td>3.0 - 3.0</td>
<td>N</td>
<td>N</td>
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<td>—</td>
<td>—</td>
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<td>61</td>
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<td>N</td>
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<td>N</td>
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<td>N</td>
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<td>39</td>
<td>60</td>
<td>2.1 - 2.1</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>—</td>
<td>—</td>
<td>AWOT (3)</td>
</tr>
</tbody>
</table>

Note.—AWOT = alive without tumor, AWT = alive with tumor, HCC = hepatocellular carcinoma, LR = local recurrence, MD = multicentric disease, N = negative for tumor, NL = new lesion, P = positive for tumor, TIPS = transjugular intrahepatic portosystemic shunt, — = not performed.

<sup>a</sup>Death.
<sup>b</sup>New course of RF interstitial thermal ablation.
<sup>c</sup>Biopsies became negative for tumor after additional RF interstitial thermal ablation. Dynamic CT and angiography were performed at this time.
<sup>d</sup>Underwent autopsy.
<sup>e</sup>Biopsies and CT were false-negative. Imaging became negative after a new course of RF interstitial thermal ablation.

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Introduce the active electrode needle tip into the chosen area of the tumor. The temperature at the needle tip was maintained at 90°C for 120 sec.

With the bipolar procedure, local anesthesia along the two prefixed puncture lines was done as described. Then we used sonographic guidance and a multiholed lateral needle guide to insert the two active electrode needles that were connected directly to the RF generator. The two active elec-
trode needles were held parallel and inserted, 2.0 cm apart, into the tumor. A temperature of 90°C at the needle tips was maintained for 20 min.

Both monopolar and bipolar procedures made a single thermal lesion with a volume that ranged from 1.0 to 1.8 cm³ with the monopolar method [17] and that was approximately 8.0 cm³ with the bipolar method.

At each insertion, the needle tip of the electrode was placed in the deepest part of the tumor. Multiple thermal lesions were created along the major axis of the electrode by withdrawing it from the thermal lesion and reactivating the RF generator. After making the prefixed thermal lesions, we turned off the RF generator, and all electrodes were removed.

When necessary because of tumor size, we performed multiple insertions of the needle electrodes in all strategic points of the tumor, not more than six insertions in a monopolar method session (the time required for each session ranged from 10 to 30 min) and not more than two in a bipolar session (the time required for each session ranged from 30 to 60 min). With the bipolar technique, when the tumor was smaller than 2.0 cm in diameter, the needles were placed at the opposite tumor boundaries to destroy the tumor in one pass. Access was intercostal in three cases and subcostal in all others.

For tumor nodules less than 3.0 cm in diameter, a necrosis volume of approximately twice the tumor volume was planned. For tumor nodules greater than 3.0 cm, the number of RF interstitial thermal ablation treatments was determined by imaging findings.

**Posttreatment and Follow-Up Studies**

Between 3 and 15 days after the last session of RF interstitial thermal ablation, multiple cytologic and histologic samples were taken by sonographically guided biopsies. Blood samples for serum AFP assay or other tumor marker levels were also collected. If the biopsies did not show tumor, dynamic CT was carried out. Dynamic CT was considered negative if a completely nonenhanced area was shown in the site of the treated tumor.

In the patients treated for hepatocellular carcinoma in whom both biopsies and dynamic CT were negative, hepatic angiography was done. It was considered negative if all the signs of neo-plastic vascularization of the arterial phase, portal phase, or both had completely disappeared. If one of the posttreatment investigations showed remaining tumor, additional treatment was carried out (except the metastasis treated for debunking purposes).

Follow-up study for hepatocellular carcinoma included sonographic examination every 2 months in the first year, every 3 months in the second year, and every 4 months thereafter and AFP assay and hepatic function tests every 4 months. A dynamic CT scan was obtained after 1 year. In patients with metastasis, sonographic examination and assay of serum tumor marker levels were performed every 3 months.

**Recurrences**

We defined the tumor nodules that appeared in the same hepatic segment as the treated one as local recurrences and other tumor nodules as new lesions. Sonographically guided fine-needle biopsy was used when possible to obtain a pathologic diagnosis of recurrences.

The patients with recurrences were treated with a new course of RF interstitial thermal ablation if they satisfied our eligibility criteria. Candidates for new RF interstitial thermal ablation courses had to receive all the pre- and posttreatment investigations we have described and had to give informed consent again.

**Statistical Analysis**

Survival rates of the 39 treated patients and cumulative recurrence rates for hepatocellular carcinoma were calculated according to the Life Table [18]. The date of the first RF interstitial thermal ablation was the starting point for the calculations.

**Results**

**Patients with Hepatocellular Carcinoma**

Thirty-seven patients with 38 hepatocellular carcinoma nodules were treated by monopolar method and two patients with three hepatocellular carcinoma nodules by combined monopolar and bipolar methods. With the monopolar method, the number of thermal lesions obtained in the same patient ranged from three to 24 and the number of sessions ranged from one to eight. With the bipolar method, one session was performed per patient. One monopolar session was added per patient either to complete the destruction of the hepatocellular carcinoma nodule or to destroy a second hepatocellular carcinoma nodule.

Sonography performed during RF interstitial thermal ablation showed an enlarging homogeneous hyperechoic area (Figs. 2A and 2B), often with posterior acoustic shadow, that appeared around the needle tip when the temperature reached 90°C. This sonographic structural change, visible at every thermal lesion, diminished dramatically as soon as RF power was switched off. However, some increased echogenicity in the treatment zone persisted as long as 12 hr. With the bipolar method, when the temperature reached 90°C, this hyperechoic area appeared around and between the needles.

At the end of the treatment, the sonographic patterns of hepatocellular carcinoma were modified. Usually, the hyperechoic hepatocellular carcinoma became isoechoic or hyperechoic (Figs. 2A and 2C). Iso- to hyperechoic hepatocellular carcinomas with hypoechogenic rims became iso- to hypoechoic, iso- to hyperechoic, or hypo- to hyperechoic. The hyperechoic hepatocellular carcinoma remained unchanged or became hypo- to hyperechoic.

At the end of the treatment, AFP levels dropped to the normal range in all 10 patients in whom they were elevated before RF interstitial thermal ablation.

Table 1 gives the results of posttreatment sonographically guided biopsies (performed a mean of 10.2 days after treatment ended), of posttreatment dynamic CT (Figs. 3A and 3B), and of posttreatment selective hepatic angiography (Figs. 3C and 3D).

The mean number of RF interstitial thermal ablation sessions needed to obtain tumor nodule destruction was 3.3 (range, 1–8 sessions). Excluding the first 15 patients, the mean number of RF interstitial thermal ablation sessions per tumor nodule was 2.3 (range, 1–5 sessions).

Mean follow-up time was 22.6 months (range, 3–66 months). On sonographic examination the treated hepatocellular carcinoma nodules slowly diminished in size. Several months after the end of the treatment, 10 were not detectable by sonograhpy, 14 appeared as hyperechoic areas less than 1.0 cm in diameter (Figs. 4A and 4B), four as isoechoic areas with a hyperechoic rim areas less than 1.0 cm in diameter, six as small heterogeneous areas, and one as a small hepatic margin deformity. Finally, the follow-up was not sufficient to evaluate the complete sonographic evolution of six treated tumoral nodules. Sometimes a posterior acoustic shadow was visible.

Table 1 shows recurrences and RF interstitial thermal ablation treatments of the recurrences; Figure 5 shows disease-free survival curves. The diagnosis of recurrences was confirmed by sonographically guided
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Fig. 2.—72-year-old man with hepatocellular carcinoma. A, Sonogram shows hypoechoic hepatocellular carcinoma nodule 2.0 cm in diameter (arrows) in segment VI. B, During RF interstitial thermal ablation (monopolar method), sonogram shows hyperechoic area (arrows) that appeared around needle tip when its temperature reached 90°C. C, Sonogram taken 4 days after B shows isoechoic area (arrows) larger than tumor nodule in segment VI. D, Gross specimen taken 3 months after RF thermal ablation shows total necrosis in treated area (arrows), which was confirmed by microscopic examination.

Fine-needle biopsy in 13 of 16 patients and by imaging (sonography and dynamic CT) in three patients in which AFP serum assay showed a level of more than 500 ng/ml. The recurrent tumors, when detected, were a single nodule less than 3.0 cm in diameter in 13 patients and multicentric disease in the others. As Table 1 shows, RF interstitial thermal ablation (31 sessions) successfully treated 13 recurrent hepatocellular carcinoma nodules in nine patients. Therefore, 54 hepatocellular carcinoma nodules in 39 patients were treated with RF interstitial thermal ablation.

No complications related to the treatment or invasive diagnostic techniques occurred; only five patients with subcapsular hepatocellular carcinoma experienced slight transitory pain during RF interstitial thermal ablation, which disappeared soon thereafter. After the treatment, no patients had fever or pain; no increase in serum alanine transferase and serum aspartate transferase levels or decrease in hemoglobin level was observed.

Eleven (28%) of the 39 patients died. Table 1 gives the causes of death. Three patients, who died of causes other than hepatocellular carcinoma, underwent autopsy. Five treated hepatocellular carcinoma nodules were analyzed. A 3.0-mm focus of viable cancer was detected in a hepatocellular carcinoma nodule 2.0 × 2.0 cm in diameter that had been treated 13 months before. Total necrosis without cancer cells was detected in two hepatocellular carcinoma nodules 2.1 × 2.0 cm (Fig. 2D) and 2.5 × 2.5 cm in diameter that had been treated 9 and 5 months before, respectively. Finally, gross examination failed to detect two hepatocellular carcinoma nodules 2.1 × 2.0 cm and 1.5 × 1.0 cm in diameter that had been treated 42 and 20 months before, respectively.

Cumulative survival curves indicate that the median survival time was 44 months, and Figure 6 shows survival rates.

Patients with Metastases

Seven patients with nine metastatic nodules were treated in 17 RF interstitial thermal ablation sessions with the monopolar method. Three patients with three metastatic nodules underwent 13 RF interstitial thermal ablation sessions (six with the monopolar method and seven with the bipolar method) (Figs. 7A and 7B). Finally, the patient with a large centrohepatic tumor had four bipolar RF interstitial thermal ablation sessions (Figs. 8A and 8B).

The immediate sonographic changes due to the temperature reaching 90°C around and between the needle tip(s) and the sonographic changes at the end of the treatment were the same as those described for hepatocellular carcinoma.

At the end of the treatment, in the two cases in which carcinoembryonic antigen levels were elevated before RF interstitial thermal ablation, they dropped into the normal range in one case and increased to 52 ng/ml in the other; gastrin serum levels dropped from 1470 to 870 pg/ml. Table 2 gives the results of post-treatment sonographically guided fine-needle biopsies, posttreatment dynamic CT (Figs. 7C, 7D, 8C, and 8D), and pathologic examinations on surgical specimens.

The mean follow-up time was 11 months (range, 3–27 months) in nine patients with
11 metastatic nodules, excluding the two patients who underwent surgery.

On sonographic follow-up, two metastatic nodules of about 1.0 cm in diameter were no longer visible; three metastatic nodules that ranged from 2.0 to 3.5 cm in diameter diminished in size and became small hyperechoic or heterogeneous areas less than 1.0 cm in diameter; three metastatic nodules, two about 3.5 cm in diameter and the large centrohepatic mass, changed in sonographic pattern but showed only a small volume reduction; one metastatic nodule 3.5 cm in diameter showed a local progression; and the follow-up was not sufficient to evaluate the complete sonographic evolution in two metastatic nodules.

Unfortunately, as Table 2 shows, only one patient seemed to be free from tumor 12 months after the end of the treatment.

As in patients with hepatocellular carcinoma, we did not observe any complications. No
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Fig. 5.—Disease-free survival curves of patients with hepatocellular carcinoma who underwent RF interstitial thermal ablation. Estimates of rates for local recurrences were 0 in 1 year, 0.04 in 2 and 3 years, and 0.16 in 4 and 5 years. Estimates of rates for new lesions were 0.08 in 1 year, 0.31 in 2 years, and 0.56 in 3 and 4 years. LR = local recurrence, NL = new lesion, T = total recurrence.

Fig. 6.—Cumulative survival curves for patients with small hepatocellular carcinoma who underwent RF interstitial thermal ablation. Survival rate for first year was 0.94, 0.86 for second year, 0.68 for third year, and 0.40 for fourth and fifth years. H = death from hepatocellular carcinoma, T = death from all causes.

Fig. 7.—59-year-old woman with single hepatic metastatic nodule from colorectal cancer. A, Sonogram obtained before RF interstitial thermal ablation shows hyperechoic metastatic nodule with hypoechoic rim (arrows) in segment VI. B, During RF interstitial thermal ablation (bipolar method), sonogram shows two activated needle electrodes in tumor. Hyperechoic areas around and between needle tips are visible (arrows). C, Dynamic CT scan obtained before B showed hyper- to isodense metastatic nodule (arrow) in segment VI. D, Dynamic CT scan obtained after B shows nonenhancing hypodense area larger than treated tumor nodule (arrows) in segment VI.

patients experienced pain during RF interstitial thermal ablation. After the treatment no patients had fever or pain, and no increase in serum alanine transferase and serum aspartate transferase levels or decrease in hemoglobin levels.

Discussion

RF interstitial thermal ablation is a technique capable of destroying hepatic tumors as shown by sonography, sonographically guided fine-needle biopsy, dynamic CT, selective angiography, and pathologic studies.

Sonography is a good technique to guide the RF electrode needles to the critical points of the tumors and to monitor the extent of the obtained necrosis [19]. Unfortunately, it is not suitable for detecting small areas of remaining viable tumor. Multiple sonographically guided fine-needle biopsies can also miss residual tumoral tissue because fine-needle biopsy samples are a limited volume of the treated area. Nevertheless, they are useful if positive.

Dynamic CT is important for evaluating the results of RF interstitial thermal ablation because posttreatment, nonenhancing foci indicate tumor necrosis [20]. Nevertheless, a posttreatment peripheral enhanced ring in the site of the treated tumor detected by our group and
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![Image of sonograms and CT scans](Fig. 8—73-year-old woman with single hepatic metastasis from ovarian sarcoma, which did not respond to chemotherapy.

A, Sonogram taken before RF interstitial thermal ablation shows centrohepatic complex mass 8.0 cm in diameter (arrows).

B, After RF interstitial thermal ablation, sonographic pattern became hypoechoic. Needle electrode insertion lines are visible (arrows).

C, Dynamic CT scan obtained before RF interstitial thermal ablation shows an iso- to hyperdense centrohepatic mass (arrows).

D, Dynamic CT scan obtained after RF interstitial thermal ablation shows 80% necrosis of treated metastatic mass; residual strip of enhancing tumor is visible near portal vein (arrows).

### Table 2: Results in Patients with Liver Metastases Treated by RF Interstitial Thermal Ablation

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Primary Tumor</th>
<th>Tumor Size (cm)</th>
<th>Sonographically Guided Biopsy</th>
<th>Dynamic CT (% Necrosis)</th>
<th>Histology on Surgical Specimens (% Necrosis)</th>
<th>Outcome (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>Colorectal cancer</td>
<td>3.5 x 3.5</td>
<td>—</td>
<td>100</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>60</td>
<td>Colorectal cancer</td>
<td>1.8 x 1.8</td>
<td>—</td>
<td>100</td>
<td>100</td>
<td>Alive without tumor (24)</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>Gastrinoma</td>
<td>3.0 x 3.5</td>
<td>—</td>
<td>80</td>
<td>—</td>
<td>Alive with residual liver tumor (27)</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>Colorectal cancer</td>
<td>3.0 x 3.5</td>
<td>—</td>
<td>80</td>
<td>—</td>
<td>Alive with local progression and other liver metastases (12)</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>Colorectal cancer</td>
<td>3.0 x 3.5</td>
<td>—</td>
<td>80</td>
<td>—</td>
<td>Alive with other liver metastases (12)</td>
</tr>
<tr>
<td>6</td>
<td>57</td>
<td>Colorectal cancer</td>
<td>3.0 x 3.5</td>
<td>N</td>
<td>100</td>
<td>—</td>
<td>Alive without tumor (12)</td>
</tr>
<tr>
<td>7</td>
<td>58</td>
<td>Colorectal cancer</td>
<td>2.8 x 2.8</td>
<td>N</td>
<td>100</td>
<td>—</td>
<td>Alive with lung metastases (10)</td>
</tr>
<tr>
<td>8</td>
<td>54</td>
<td>Breast cancer</td>
<td>2.0 x 2.0</td>
<td>1.0 x 1.0</td>
<td>100</td>
<td>—</td>
<td>Alive with lung and other liver metastases (10)</td>
</tr>
<tr>
<td>9</td>
<td>72</td>
<td>Ovarian sarcoma</td>
<td>8.0 x 9.0</td>
<td>—</td>
<td>80</td>
<td>—</td>
<td>Alive with other liver metastases (9)</td>
</tr>
<tr>
<td>10</td>
<td>52</td>
<td>Thymoma</td>
<td>2.0 x 3.5</td>
<td>—</td>
<td>100</td>
<td>—</td>
<td>Alive with spleen and lung metastases (4)</td>
</tr>
<tr>
<td>11</td>
<td>75</td>
<td>Gastric cancer</td>
<td>3.0 x 3.5</td>
<td>1.0 x 1.0</td>
<td>80</td>
<td>—</td>
<td>Alive with other liver metastases (3)</td>
</tr>
</tbody>
</table>

Note: — = negative for tumor, — = not performed.

* Surgery was performed within 35 days after RF interstitial thermal ablation.

b Death.

c Incomplete treatment due to technical difficulties.

d Not detected with sonography.
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others [6, 21], which corresponds to a high intensity ring on MR imaging [12], remains an intriguing observation. It may be caused by postnecrotic edema, neovascularization with microscopic arteriovenous shunting [17], or residual viable tumor [21]. Therefore, to avoid difficulties in imaging interpretation, dynamic CT scans should be obtained 3–4 days after the RF interstitial thermal ablation treatment because the size of necrosis is at a maximum and the vascular neogenesis is poor [17].

Angiography also plays a role in assessing treatment efficacy and is considered the gold standard. However, in this series it failed to detect small vascularized residual tumor foci. Therefore, none of the cited techniques alone was sufficient to evaluate the final results, nor did they always agree. In fact, sometimes both sonographically guided fine-needle biopsies and dynamic CT missed remaining tumor detected by angiography. For this reason, we think the use of multiple diagnostic techniques will prove valuable even though some authors have stressed that hepatocellular carcinoma ablation with percutaneous ethanol injection can be correctly evaluated by dynamic CT or MR imaging [21, 22]. We recognize that angiography is an expensive and invasive technique, but it could be replaced by other noninvasive technologies, such as color Doppler sonography, that evaluate tumor vascularization changes [23].

Measuring serum tumor markers such as AFP in hepatocellular carcinoma and carcinoembryonic antigen in colorectal hepatic metastases is another way to assess the efficacy of ablative therapies, but their predictive value is significant only if the starting levels are high. Serum AFP levels are normal in about 30% of patients with hepatocellular carcinoma and greater than 200 ng/ml in 20% of patients with hepatocellular carcinomas smaller than 3.0 cm [21]. Similarly, disappointing results have been found for carcinoembryonic antigen in colorectal hepatic metastases [7].

The effectiveness of RF interstitial thermal ablation in both hepatocellular carcinoma and hepatic metastases was confirmed in this series by pathologic studies performed on surgical samples or on autopsies. The percentage of hepatocellular carcinoma nodules with total destruction in our series was better than the 69% found in the largest series of the literature, which comprised 23 hepatocellular carcinoma nodules surgically controlled after percutaneous ethanol injection [24]. Moreover, histopathologic evaluation of two cases of hepatic metastases treated by percutaneous ethanol injection [25] and of two cases treated by interstitial laser photocoagulation [7] showed only partial necrosis.

The occurrence in a few cases of tumor remaining after RF interstitial thermal ablation treatment can be related to the difficulty of placing the RF electrode needles in all critical points of the tumors, especially for deep tumors. Nevertheless, we stress that the same difficulties exist for percutaneous ethanol injection, in which ethanol diffusion is haphazard and uncontrollable. Another problem is presented by the possible presence of large vessels near the tumor, which act as heat sinks [6]. For both these reasons the necrosis rate will be less than the theoretical amount calculated.

Follow-up of the treated hepatocellular carcinomas in some patients showed development of multiple hepatocellular carcinoma nodules some months after the end of the treatment; we think it is due to an underestimation of the extent of the disease at the time of recruitment. In fact, dynamic CT and angiography can miss about 20% of hepatocellular carcinomas less than 3.0 cm in diameter [26], as confirmed by the frequent presence of undetected hepatocellular carcinoma nodules in cirrhotic livers [27].

Tumors recurred in most treated patients. Early recurrences (within 2 years after the treatment) were both local and new lesions; late recurrences were mainly new lesions. Local recurrence is the result of a lack of aggressiveness or thoroughness in the technique, whereas new lesions are a part of the natural history of hepatocellular carcinoma in cirrhosis. The total recurrence rate of hepatocellular carcinoma we observed is similar to that reported after surgery or percutaneous ethanol injection [24, 28–30], and in all series most patients developed new lesions. The local recurrence rate we observed is low and comparable to that found in patients treated by percutaneous ethanol injection [24, 29, 30]. We may have overestimated this percentage by considering a hepatocellular carcinoma nodule that developed later in the same segment as the treated one to be a local recurrence. Most of our patients who developed local recurrences or new lesions underwent a successful new course of RF interstitial thermal ablation treatment, which gave good results in cases of second recurrences.

The survival rate of patients with hepatocellular carcinoma treated by RF interstitial thermal ablation treatment is similar to that found in surgical series [28] and in patients with small hepatocellular carcinoma treated by percutaneous ethanol injection [24, 29, 30], but our patients had a mean age of 66.7 years (it was 64.3 years in a large percutaneous ethanol injection series [30]), and causes other than hepatocellular carcinoma influenced survival. However, the comparison with surgical series is limited by various biases, such as different clinical characteristics of the patient population (disfavoring percutaneous techniques because many of these patients were not surgical candidates) and different methods of follow-up (probably disfavoring surgical series). The satisfactory survival rate we observed is in part related to our strict follow-up, which was designed to detect and treat recurrences early. Moreover, the identification of the tumors, the administration of therapy, and the follow-up investigations were performed by the same group of operators, permitting a more thorough therapeutic regimen. Nevertheless, we think that multicentric randomized trials to compare the results of different therapeutic options to treat hepatic cancer are needed and advisable.

In patients with metastases, the short-term results were good. However, in the follow-up, judging the real clinical impact of the administered therapy is difficult. Most patients showed intrahepatic, extrhepatic, or both kinds of metastases soon after the RF interstitial thermal ablation. This occurrence would have been dramatic if a major treatment like surgery had been performed. However, in the field of percutaneous treatment of hepatic metastasis, we believe only patients with relatively slow growth tumor histotype (colorectal and endocrine tumor) in whom a theoretical possibility of complete tumor destruction exists should be enrolled. With the technology we used, we believe the largest diameter of the lesion should be no more than 3.5 cm. RF interstitial thermal ablation treatment (bipolar method) and interstitial laser photocoagulation can achieve debulking with low secondary morbidity; nevertheless, they should be considered only in a multidisciplinary approach to metastatic disease.

An effective percutaneous ablative therapy, as RF interstitial thermal ablation has proven to be, has to achieve a complete result in a short time. The duration of the therapy is a crucial point both for the patient’s compliance and for medical costs. In our experience after the first period, when caution was mandatory with a consequently high number of sessions, the treatment time was short: one or two sessions even for tumor nodules of 3.0 cm in diameter. We believe that in some cases treatment could be done in outpatients.
Our results have been supported by the integrated use of mono- and bipolar methods, which can be considered complementary. The monopolar method is easier to perform than the bipolar one and can effectively obtain complete necrosis of tumors less than 2.0 cm in diameter in one session. For bigger tumors, the bipolar method proved more useful and any small areas of residual tumor can subsequently be destroyed using the monopolar method.

Moreover, electrode needles modified to reach the goal of large hepatic tumor destruction in one session are under investigation by our group and others (Goldberg et al., presented at the Radiological Society of North America meeting, November 1995) with promising preliminary results.

RF interstitial thermal ablation is a flexible technique; laparoscopic guidance can be used to ablate small hepatic tumors that are superficially located [31]. RF interstitial thermal ablation is safe and is not likely to provoke venous thrombosis at the border of thermal lesions as experimentally shown [17, 19], because such vessels induce a dispersion of heat. In contrast with other authors [32], we did not observe any tissue microbubbles, which usually occur at temperatures greater than 100°C. The danger of bleeding with RF interstitial thermal ablation is reduced by the coagulation power of the interstitial hyperthermia.

No cases of tumor seeding along the needle track were seen, in spite of the high number of punctures.

RF interstitial thermal ablation is effective in destroying both primary or metastatic hepatic tumors in a short treatment time. Large hepatic metastases can also be debulked. Both monopolar and bipolar methods are useful and safe, without pain or discomfort for the patients. We think this technique will play an important role in the treatment of hepatic tumors.

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References