Radiofrequency Ablation of the Liver: Current Status

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Hepatocellular carcinoma (HCC) and metastases from colorectal carcinoma are the two most common malignant tumors to affect the liver. When these tumors are left untreated, the prognosis for both is dismal, with essentially 100% mortality at 5 years. Conventional therapies such as systemic chemotherapy or radiation have proven ineffective. Surgical resection of the tumors is considered the only potentially curative therapy [1–4]. Successful resection of targeted tumors with negative tumor margins is achieved in approximately 80–90% of patients undergoing hepatic resection [5–7]. Unfortunately, surgical resection has many factors limiting its overall usefulness. Of all patients presenting with a malignant hepatic tumor, few are surgical candidates. Contraindications to hepatic resection include too many tumors, tumors in unresectable locations, insufficient hepatic reserve to tolerate resection, and other medical conditions that make the patient a poor surgical risk. It has been estimated that only 5–15% of patients with HCC or hepatic metastases are eligible for resection [1–4]. For those patients who undergo hepatic resection, there is considerable postoperative morbidity—a small but real risk of death related to the operation—significant monetary expense, and only a modest improvement in long-term prognosis. The 5-year survival rate for patients undergoing resection of HCC or hepatic metastases is only 20–40% [1–3]. Most patients die from recurrent hepatic tumors. Although in some instances surgery may be repeated to resect recurrent tumor, at most institutions hepatic resection is a “one-shot” therapy. In light of these shortcomings, an effective, minimally invasive technique is needed for treating these tumors—one that can be repeated as necessary to treat recurring tumor.

A number of alternative therapies have been used for the treatment of malignant hepatic tumors. These include chemoembolization, ethanol injection therapy, and thermal ablation techniques. Chemoembolization has been studied extensively and is often reserved for patients with unresectable hepatic tumors [8, 9]. Ethanol injection therapy has gained fair international acceptance as a safe, inexpensive, and effective therapy for small HCC tumors [10, 11]. However, it has failed to generate much enthusiasm in the United States. This lack of enthusiasm is based in part on the need to perform multiple consecutive therapeutic sessions to completely kill even the smallest HCC tumor and the fact that the technique is typically performed under sonographic guidance [11]. Furthermore, ethanol injection therapy has been shown to be ineffective for the treatment of colorectal metastases [12].

Thermal ablation techniques for the treatment of malignant hepatic tumors include both freezing (cryoablation) and heating (radiofrequency, microwave, laser, and high-intensity focused sonography) techniques. Of these techniques, cryoablation has been the most extensively investigated [13, 14]. The two advantages of cryoablation over surgical resection are that it can be used to treat liver tumors that, by number or location, are not surgically resectable, and that it is associated with diminished morbidity and mortality relative to resection. The overall prognosis for patients undergoing cryoablation is reported to be the same as for hepatic resection. However, the limitations of cryoablation are similar to the limitations of hepatic resection—namely, it is invasive, with a laparotomy being performed in most cases [14].

During the last 10 years, considerable interest has developed in the thermal ablation techniques that produce heat. Methods that are being investigated include microwave, laser, high-intensity focused ultrasound, and radiofrequency ablation. Most of the research on microwave ablation has been performed in Japan, with minimal experience or knowledge of the technique outside that country [15, 16]. Laser ablation has been tested most rigorously outside the United States [17–19]. One group of German researchers, Vogl et al. [19], claim that the technique is highly effective for the treatment of both HCC and colorectal metastases. However, one of the primary investigators of laser ablation in England has essentially abandoned the technique in favor of radiofrequency ablation [20]. High-intensity focused ultrasound has been shown to be successful in ablating hepatic tumors in animal models but has not been used to treat liver tumors in humans [21]. Overall, the interest and enthusiasm for radiofrequency thermal ablation has far exceeded that for either microwave or laser ablation. This article will...
review the current status of radiofrequency ablation in the treatment of liver neoplasms

**Background**

The initial investigation of the use of radiofrequency waves in the body is credited to d'Arsonval [22] in 1891, who showed that radiofrequency waves that pass through living tissue cause an elevation in tissue temperature without causing neuromuscular excitation. These observations eventually led to the development in the early to mid 1900s of electrocautery and medical diathermy [23–25]. The best known of these developments is the surgical Bovie knife [Liebel Flarsheim, Cincinnati, OH] [26]. This device is used to cauterize bleeding tissue. The device consists of an alternating electric current generator operated in the range of radiofrequency, a small knifelike electrode, and a large grounding pad. The physical principles of the operation of the device are fairly simple. The alternating electric current passes back and forth through the patient between the grounding pad and the Bovie knife. The grounding pad is applied to the patient’s thigh and acts as a large dispersive electrode that allows the current to pass freely through the patient without producing any significant heat except around the point of the Bovie knife. The Bovie knife has a small tip and, when brought into contact with the patient, acts as a focal point for the electric current. The current arcs between the Bovie knife and the patient, desiccating and charring the tissue at the point of contact. Work by Organ [27] elucidated the physical principles of the interaction of the alternating electric current with living tissue. He showed that at low-power settings, the alternating current causes agitation of the ions in the adjacent tissue. The ionic agitation causes frictional heat that extends into adjacent tissues by conduction. However, at high-power settings the ions are quickly destroyed through desiccation and charring of the superficial tissue, and heat production is minimal [27, 28]. Subsequent modifications of the Bovie knife have led to its use in other superficial applications, such as destruction of the neuronal pathways in the heart in patients with intractable arrhythmias [29, 30].

In the early 1990s, two independent groups of investigators using modified radiofrequency equipment studied the percutaneous creation of focal thermal injuries deep in the liver [31, 32]. In their studies they used equipment similar to that of the Bovie knife; that is, an alternating electric current generator operated in the radiofrequency range, a grounding pad placed on the tissue, and an insulated needle as a monopolar electrode. The original needle design was simple and used standard stock needles insulated to the distal tip (Fig. 1). The studies consisted of placing needle electrodes deep in the liver and creating focal thermal injuries around the noninsulated tip of the needles. Gross and histologic examination of the ablated livers showed that the process produced a well-defined concentric region of coagulative necrosis around the exposed needle tip. This was similar to coagulative necrosis as described in prior experimentation [33]. However, the size of the thermal injuries was small; the radius of the coagulated tissue surrounding the exposed needle tip was approximately 1 cm (Fig. 2). Superficial charring around the needle tips similar to that produced by the Bovie knife limited the size of the thermal injury that could be created in the liver. Nonetheless, both investigators proposed that radiofrequency ablation might be an effective technique for destroying small malignant liver tumors [31, 32].

Subsequent research has shown that effective tissue coagulation requires local temperatures in excess of 50°C [34]. Furthermore, several factors, including a slow increase in generator power, prolonged radiofrequency application, and an increase in the exposed surface area of radiofrequency needle electrodes, have been shown to increase the volume of coagulated tissue [34–36].

Modern radiofrequency ablation equipment can create thermal lesions of sufficient size (3–4.5 cm) to be clinically relevant. In the United States, three primary companies (RITA Medical Systems, Mountain View, CA; Radiotherapeutics, Mountain View, CA; and Radionics, Burlington, MA) market radiofrequency devices for tissue ablation. Each of the companies received approval of their devices from the Food and Drug Administration under a 510K-like device exemption. The radiofrequency tissue ablation devices were deemed similar enough to the Bovie knife in design and application that a full Food and Drug Administration application was unnecessary. Each company was allowed to market its device for generic tissue ablation; however, none could market its device specifically for the ablation of hepatic tumors. However, just recently the Food and Drug Administration has approved the use of these devices for the treatment of liver tumors that are surgically unresectable.

**Equipment**

To overcome the problem of tissue desiccation and charring and a limited radius of coagulated tissue around the radiofrequency needle electrode, each of the three companies in the United States has experimented with different radiofrequency needle designs and generator algorithms. Each of the marketed devices uses a different radiofrequency needle design, generators of different wattage, and generator algorithms that vary significantly from each other. The following is a description of the different equipment and operating parameters.

![Fig. 1— Original needle design. A, Photograph of original needle design shows standard stock needle that is insulated (arrow) to distal tip. Needle tip is not insulated. B, Drawing shows theoretic lesion that would be produced if noninsulated needle tip were used during monopolar radiofrequency electrocautery. (Reprinted with permission from [75])](image-url)
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One of the manufacturers markets a system with two retractable needle electrodes (Model 70 and Model 90 Starburst XL Needles; RITA Medical Systems). The needle electrodes consist of a 14- or 15-gauge insulated outer needle that houses seven or nine (respectively) retractable curved electrodes of various lengths. When the electrodes are extended, the devices assume the approximate configuration of a Christmas tree, with the length and diameter of the electrode clusters measuring 3 or 5 cm, respectively (Fig. 3A). Four of the electrodes are hollow and contain thermocouples in their tips that are used to measure the temperature of the adjacent tissue. The alternating electric current generator comes in either a 50- or 150-W model; both are operated at 460 kHz.

To perform a typical ablation, one or two grounding pads are placed on the patient’s back or thigh. The tip of the needle (with retracted electrodes) is advanced to the desired location. The needle is inserted into the target lesion, and the alternating current is delivered to create a radiofrequency coagulation lesion.

Fig. 2.— In vivo sonographic and histologic correlation for radiofrequency coagulation of swine liver. A, Sonogram of monopolar radiofrequency lesion shows hyperechoic regions surrounded by hypoechoic rim (arrow). B, Photograph of in vivo liver reveals central area of charred tissue (1) surrounded by coagulative necrosis (2) and hyperemic rim (arrow, 3). L = healthy liver. (Reprinted with permission from [28])

Fig. 3.— Photographs of radiofrequency needle designs. A, Prongs protrude in “Christmas tree” configuration from tip of needle manufactured by RITA Medical Systems, Mountain View, CA. B, Ten prongs protrude in umbrella configuration from tip of needle manufactured by Radiotherapeutics, Mountain View, CA. C, Single (solid arrow) and clustered (open arrow) cooled-tip needles manufactured by Radionics, Burlington, MA.
location, and the electrodes are deployed to approximately two thirds their length. The generator is turned on and run by an automated program. The program starts the generator at approximately 25 W and then gradually increases the wattage to peak power in 30–120 sec. The program monitors the temperature at the tips of the electrodes and maintains peak power until the temperature exceeds the preselected target temperature (typically between 95° and 105°C). The operator watches the temperature display, and after the target temperature is achieved, advances the curved electrodes slowly to full deployment while maintaining the target temperature. When the electrodes are fully deployed, the program maintains the target temperature by regulating the wattage. As the tissue begins to desiccate, the amount of power needed to maintain the target temperature decreases. The company recommends that the target temperature be maintained for 8–12 min for the smaller electrode and 25 min for the larger electrode. After the ablation cycle is completed, a temperature reading from the extended electrodes in excess of 50°C at 1 min is reported to indicate a satisfactory ablation [34].

Another radiofrequency ablation device (LeVeen Needle Electrode; Radiotherapeutics) has retractable curved electrodes and an insulated 14-gauge outer needle that houses 10 solid retractable curved electrodes that, when deployed, assume the configuration of an umbrella [37] (Fig. 3B). The electrodes are manufactured in different lengths (2- to 3.5-cm umbrella diameter), with most users choosing the 3.5-cm device. The alternating electric current generator is 100 W operated at 480 kHz. Two ground pads are used with the device; both are placed on the patient’s thighs. In application, the tip of the electrodes and maintains peak power until the temperature exceeds the preselected target temperature (typically between 95° and 105°C). The operator watches the temperature display, and after the target temperature is achieved, advances the curved electrodes slowly to full deployment while maintaining the target temperature. When the electrodes are fully deployed, the program maintains the target temperature by regulating the wattage. As the tissue begins to desiccate, the amount of power needed to maintain the target temperature decreases. The company recommends that the target temperature be maintained for 8–12 min for the smaller electrode and 25 min for the larger electrode. After the ablation cycle is completed, a temperature reading from the extended electrodes in excess of 50°C at 1 min is reported to indicate a satisfactory ablation [34].

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The generator provided with the cooled-tip radiofrequency needles is the most powerful of the three commercially available generators. It has a peak power output of 200 W and is operated at 480 kHz. In clinical application, four grounding pads are placed on the patient’s thighs. The tip of the single or cluster electrode is advanced to the desired location in the tissue to be treated. To maintain the correct spacing and triangular configuration of the cluster needle, a guidance thimble is used (Fig. 4). The single or cluster electrode needles are connected both to the generator and to a perfusion pump. The pump is switched on and sterile chilled water is circulated through the needle. To begin the ablation, an automated program gradually increases the power for 1 min to a peak of 200 W and maintains the power at that level until the impedance rises 20 Ω over the starting level. The power is then reduced automatically to 10 W for 15 sec and then returned to maximal power until the impedance increases again. If the power cannot be maintained for at least 10 sec without a rise in the impedance, the power is reduced for subsequent cycles to minimize elevations in impedance. Successive cycles are continued for a total ablation time of 12 min. Successful ablations usually increase the temperature of the ablated tissue to between 60° and 80°C.

Clinical Application

The clinical application of radiofrequency ablation of hepatic tumors usually includes these steps: preoperative evaluation; choice of approach: percutaneous, laparoscopy, or laparotomy; anesthesia and medications; needle placement and treatment strategy; and follow-up. The following represents a summary of the practice in our programs, but the practice may vary from institution to institution.

Preoperative Evaluation

The preoperative evaluation begins with a review of the pertinent imaging studies. Good-quality abdominal CT or MR imaging is the fundamental imaging examination on which the candidacy of a patient for radiofrequency ablation is based. These preoperative imaging studies are used to determine the number and size of tumors and their relationship to surrounding structures such as blood vessels, bile ducts, gallbladder, diaphragm, and bowel. Patients are considered potential candidates if they have fewer than five tumors, each less than 5 cm in diameter, and no evidence of extrhepatic tumor [6, 40–42]. In practice, patients with more than two tumors approaching 5 cm are poor candidates because of the sheer...
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Radiofrequency ablation is performed using a technique that involves the direct application of high-frequency electrical energy to a tumor, resulting in the destruction of the tumor tissue. The procedure is typically performed under local anesthesia and is less invasive than surgical resection. Radiographic guidance is used to ensure accurate targeting of the tumor.

Choice of Approach: Percutaneous, Laparoscopy, or Laparotomy

The choice of approach depends on the location and size of the tumor, as well as the patient's medical history. Percutaneous ablation is often the first line of treatment for small tumors located near the liver surface. Laparoscopy is used for tumors located deeper in the liver or those that are more difficult to access. Laparotomy is reserved for large tumors or those that cannot be treated with the other approaches.

Ablation Procedure

The ablation procedure is performed under radiographic guidance, typically using ultrasound or CT imaging. A small incision is made in the skin, and a needle is inserted into the tumor. The needle is then attached to a generator that delivers high-frequency electrical energy to the tumor, causing it to heat up and destroy itself.

Contraindications

Contraindications to radiofrequency ablation include the presence of certain types of tumors, such as those that are highly vascular or those that have a high risk of metastasizing. Other contraindications include the presence of certain medical conditions, such as infection or coagulopathy, that could affect the outcome of the procedure.

Complications

Complications of radiofrequency ablation include pain, infection, and bleeding. These complications are typically managed with appropriate medical therapy and can usually be avoided with proper technique and patient selection.

Conclusion

Radiofrequency ablation is a safe and effective treatment for liver tumors, offering patients an alternative to surgery. It is particularly useful for patients with small, well-localized tumors or those who are not candidates for surgical resection. However, it is important to note that the procedure may not be appropriate for all patients, and careful patient selection is essential to achieve the best possible outcome.

References


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cent hepatic parenchyma. The result is a larger thermal injury than is possible with normal blood flow [42].

Anesthesia and Medications

General anesthesia is required for laparoscopy or open surgical treatment. However, conscious sedation is usually sufficient for a percutaneous approach. At our institutions, we use the services of the anesthesiology department for percutaneous radiofrequency ablation. On the morning of the procedure, an anesthesiologist or nurse—anesthetist evaluates the patient for suitability for anesthesia. The medical history is reviewed, the laboratory test results are checked, and the ECG is interpreted. If deep conscious sedation is not contraindicated, the patient is prepared for the procedure. A peripheral IV line is started, and the patient is monitored to track blood pressure, pulse, respiratory rate, and peripheral oxygenation. The site of the planned percutaneous puncture with the radiofrequency electrode is anesthetized with 1% lidocaine hydrochloride (Xylocaine; AstraZeneca, Wilmington, DE). The anesthesiologist or nurse—anesthetist administers an IV sedative. This can be a combination of the traditional drugs fentanyl (fentanyl citrate injection; El-

Fig. 5.—62-year-old man with metastases to liver from colon cancer. A, Both preoperative CT scan (not shown) and sonogram show only a single large metastasis in right lobe of liver (arrow) that was scheduled for operative resection. B, At surgery, intraoperative sonography revealed several 4-mm metastases scattered throughout liver (arrow). Resection was not performed.
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76-year-old man with colon cancer and metastases to liver.

A, Sonogram shows guide for placement of needle into isolated hyper-echoic colon metastasis (arrow).

B, CT scan shows deployed prongs (arrow) in lesion.

kins-Sinn, Cherry Hill, NJ or Baxter Healthcare, Deerfield, IL) and midazolam hydrochloride (Versed; Roche Laboratories, Nutley, NJ) that are used for many percutaneous intervention procedures, or, as we prefer, the more potent and short-acting agents propofol (Diprivan; AstraZeneca) or remifentanil hydrochloride (Ultiva; Glaxo Wellcome, Research Triangle Park, NC) [48]. These newer agents are administered by a constant drip infusion. The major advantages of these agents are the deep level of anesthesia that can be obtained and their short duration of action. If the cooperation of a patient is needed to achieve satisfactory placement of the needle electrode, the patient is easily aroused within minutes of stopping the infusion of the agent. Likewise, if a patient has respiratory suppression due to oversedation, he or she is quickly recovered by stopping the infusion and ventilating the patient using a bouche bag for a few minutes.

At the end of a radiofrequency ablation session, the patient can experience severe nausea and pain with the decrease of the sedative. Because of the frequency of these two side effects, we established a routine protocol to treat these problems. Immediately after the conclusion of the procedure and before transporting the patient to the recovery area, we administer both an antiemetic and morphine IV. After the patient is transferred to the recovery area, combined oral hydrocodone bitartrate and acetaminophen tablets (Vicodin; Knoll Laboratories, Mount Olive, NJ), are given to control subacute pain. This medication regime is usually sufficient to keep the patient comfortable for 3–4 hr, at which time the side effects of the ablation have usually diminished to a tolerable level. Fewer than 50% of patients require additional analgesics during the immediate recovery period, and even fewer require analgesics after discharge. If pain persists, the patient is typically given a 3-day prescription for combined oral hydrocodone bitartrate and acetaminophen tablets (Vicodin).

Occasionally, patients may be unable to tolerate percutaneous radiofrequency ablation with just conscious sedation. This may be true for patients with cancer with chronic pain who have been taking routine analgesics, patients with a history of alcohol or drug abuse, or patients with a low tolerance for pain. General anesthesia may be indicated for these patients. Likewise, general anesthesia may be preferred if an ablation is going to be extensive and the procedure is expected to last 3 hr or longer.

Although there has been no trial to validate the use of prophylactic antibiotics, such use has become routine at some institutions. One of us routinely administers IV cephalosporin just before treatment and continues with oral cephalosporin for 5 days after treatment.

Needle Placement and Treatment Strategy

Radiofrequency needles can be placed under sonographic, CT, or MR guidance using a percutaneous approach. The needles are usually well revealed by each technique (Fig. 7). However, without question sonography is the most common method used to guide percutaneous radiofrequency tumor ablation [49–59]. Its advantages over CT and MR are its real-time capabilities, vascular visualization, availability, speed, and low cost.

Regardless of the method used to guide radiofrequency tumor ablation, strategy must be established before placement of the needle. The objective in treating a tumor must be to kill the entire tumor as well as a tumor-free margin of normal liver. The surgery literature has clearly shown that an adequate tumor-free margin is mandatory to prevent local recurrence of a tumor after hepatic resection. In one of the latest publications on the subject, an adequate tumor-free margin was defined as being preferably 2...
Fig. 9.—64-year-old man with hepatitis C and hepatocellular carcinoma (HCC).
A, CT scan shows 1.5-cm enhancing lesion (arrow) that was biopsy-proven HCC. Patient also had small amount of ascitic fluid surrounding liver.
B, Cooled-tip radiofrequency needle placed via freehand technique directly into hypoechoic HCC lesion (arrow).
C, Immediately after one radiofrequency treatment, echogenic microbubbles are present in area of treatment (arrow).
D, Echogenic response has diminished after approximately 30 min, and well-demarcated lesion measuring 2.8 × 3.8 cm with hyperechoic rim is identified in location of HCC.

cm and no less than 1 cm of normal liver [62]. If the goal of radiofrequency ablation is to duplicate the success rate of hepatic resection, then in all likelihood the same requirements for a tumor-free margin will need to be followed.

Given that most radiofrequency ablation devices produce an approximate 3-cm ablation, the largest tumor that should be treated by a single ablation should be smaller than 2 cm in diameter (Fig. 10A). A 2-cm tumor treated with a 3-cm ablation yields at most a 5-mm tumor-free margin. If error in needle placement is factored in, the margin could be much less. Certainly, 3-cm tumors should not be treated by a single 3-cm ablation. To treat a larger tumor, multiple ablations need to be overlapped to build a composite thermal injury of sufficient size to kill the tumor and to provide the desired tumor-free margin. By strict geometric analysis, six overlapping spherical ablations are necessary to create an intact composite thermal sphere of the next magnitude (Fig. 10B). If six 3-cm thermal spheres are precisely overlapped, with four in the x–y plane and two along the z-axis, the largest intact composite thermal sphere that can be created is just 3.75 cm, or 1.25 times the diameter of a solitary sphere. Thus, the largest tumor...
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Fig. 10.—Artist’s rendition of ablation schemes.
A, Solitary ablation completely envelops small tumor and circumferential rim of healthy liver.
B, Six optimally placed overlapping spheres produce composite spherical thermal injury with diameter equal to 1.25 times diameter of a single ablation sphere.
C, Overlapping thermal cylinders is effective way to treat large tumors. Each cylinder is created by overlapping serial ablations by 50% along a single needle path. Adjacent cylinders are overlapped by 50%.

that should be treated with six 3-cm overlapping ablations should be less than 3.25 cm in diameter. Larger tumors can be treated with radiofrequency ablation, but they require many more ablations or require adjuvant techniques to increase the size of an ablation. A strategy for treating large tumors consists of the creation of thermal cylinders [63] (Fig. 10C).

When performing multiple radiofrequency ablations using sonographic guidance, it is important to plan the order of ablations so that the deepest ablations are performed before the superficial ones (Figs. 8 and 9). This strategy minimizes the possibility that microbubbles might obscure visualization of the deeper portions of the tumor and thus prevent completion of the ablation session.

Follow-Up

Immediate evaluation can consist of sonography performed at the time of treatment. This may be helpful with HCC tumors that are vascular. However, it may not be helpful in metastatic disease. Solbiati et al. [58] found that use of contrast-enhanced sonography may help to detect residual tumor after radiofrequency treatment. This immediate feedback can be used for reapplication of radiofrequency in areas that are untreated.

Most institutions perform CT of the liver within a few hours of the ablation to gauge the completeness of the ablation and to look for any potential complications [61]. However, the accuracy of the completeness assessment on the immediate CT scan is often limited because of the presence of an ablation-induced hyperemic rim around the margin of the ablated tissue (Fig. 11). This hyperemia is difficult to distinguish from residual tumor. Fortunately, the hyperemia is usually resolved by 1 month after the ablation, and a more accurate assessment of the completeness of the ablation can be made at that time (Fig. 12). In some instances, CT is not performed immedi-

ately, but rather 1 month after ablation. If no evidence of residual tumor is seen on the CT scan 1-month after ablation, patients are usually followed up by repeated CT every 3 months. Each follow-up CT scan must be scrutinized for evidence of tumor recurrence in the liver, adjacent to and remote from the ablated site, and outside the liver. Typical sites of extrahepatic tumor recurrence in patients with HCC are the adrenal glands, lungs, bones, and regional lymph nodes along the porta hepatitis, gastrohepatic ligament, celiac axis, and cardiophrenic sulcus. Patients with colorectal carcinoma tend to develop extrahepatic metastases at the primary tumor site, in the peritoneal cavity, and in the lungs. Because of the frequency of extrahepatic metastases in patients with colorectal carcinoma, we usually perform both abdominal and pelvic CT every 3 months and chest CT every 6 months.

The technique used to perform follow-up CT has a significant impact on the early detection of

Fig. 11.—58-year-old man with hepatocellular carcinoma.
A, Arterial phase CT scan of dome of right lobe of liver before ablation shows untreated solitary hypervascular tumor.
B, Arterial phase CT scan immediately after ablation shows normal hyperemic rim (arrows) around ablated tumor. Hyperemic rim may prevent accurate assessment of completeness of ablation.
intrahepatic tumor recurrence. Most early recurrences in patients with HCC are detected only in the arterial phase of good-quality three-phase CT. Likewise, the subtle changes of intrahepatic tumor recurrence in patients with colorectal metastases may be visualized only during a strong portal venous phase contrast-enhanced CT scan [56, 59]. We routinely perform three-phase CT in all patients with HCC and two-phase CT in patients with colorectal metastases. Additionally, we obtain repeated α-fetoprotein and carcinoembryonic antigen levels every 3 months in patients with HCC or colorectal metastases, respectively. We find the levels helpful in assessing subtle changes on the CT scans and in determining if additional evaluation is warranted. Changes in α-fetoprotein or carcinoembryonic antigen values must be assessed on an individual basis for each patient on the basis of their values before treatment and the normal levels used at each medical institution.

Several investigators prefer to use MR imaging to follow up their patients after radiofrequency ablation. One study claims that MR imaging is more sensitive than CT for the detection of early intrahepatic tumor recurrence [61]. The interpretation of MR imaging for tumor recurrence is based primarily on the premise that ablated tissue produces minimal signal on T2-weighted sequences, whereas tumor produces high signal. Dynamic contrast enhancement of suspected tissue is further evidence of tumor recurrence.

Regardless of the technique used to follow up patients after ablation, the primary objective is to detect tumor recurrence as soon as possible so the appropriate therapy can be instituted. If recurrence is limited to the liver, reablation may be effective (Fig. 13). One of the potential benefits of percutaneous radiofrequency ablation over other more invasive forms of treatment, such as surgery, intraoperative cryotherapy, or intraoperative radiofrequency treatment, is that it can be repeated as often as necessary to treat intrahepatic tumor recurrence. In our practices, we have treated individual patients with local tumor recurrences as many as seven times during a 3-year period. Each time the tumor appeared completely destroyed, and the patient had 3–6 months of asymptomatic health between treatments. If a patient develops extrahepatic tumor or extensive intrahepatic tumor, alternative therapies such as systemic chemotherapy or hepatic chemoembolization should be considered.

Results

Long-term results of radiofrequency ablation of either primary or secondary liver neoplasms are scant because this is a fairly new technique. The goal of most of the early reported ablations is complete tumor necrosis and possibly a cure. However, some published results are available on the short-term follow-up of patients treated with radiofrequency ablation. These results are presented by tumor type and method of treatment. Many results are with prototype devices and do not reflect current refined technology. Furthermore, many early results were with conventional needles similar to the original single insulated needle described by McGahan et al. [31] and Rossi et al. [32] (Figs. 1 and 2).

Percutaneous Treatment of HCC

At least four series document the results of percutaneous radiofrequency treatment of HCC. The original study of Rossi et al. [56] used a conventional needle that was insulated to the distal tip. Rossi et al. [55] conducted a later series using an umbrella-type needle (Fig. 3). Livraghi et al. [53] and Francica and Marone [49] published one study each in which they used a cooled needle device. In all studies, near-complete necrosis of 90% of the treated tumors had occurred at 6 months. These results were for tumors smaller than 3 cm. However, for the study by Livraghi et al. [53] with tumors larger than 3 cm (mean, 5.4 cm), the complete necrosis rate was only 47.6%. Complete necrosis was 71% for noninfiltrating tumors that were 3.1–5.0 cm, and only 25% for noninfiltrating tumors greater than 5 cm in diameter. Also, the rate of disease-free survival at follow-up was lower; the first study of Rossi et al. [56] found 64% at 23 months and 71% at 12 months in a subsequent study [55]. Francica and Marone reported 67% of patients to be disease-free at 15 months. Thus, with HCC, although there is a high rate of complete necrosis of ablated tumors, about a third of the patients develop recurrent tumor. Kainuma et al. [50] found it useful to monitor and perform reablation in these patients. These results are summarized in Table 1.

Percutaneous Treatment of Metastatic Liver Tumors

Radiofrequency ablation has also been used to treat tumors that have metastasized to the liver. The results of five series are summarized in Table 2. The original study by
Radiofrequency Ablation of the Liver

Fig. 13.—46-year-old man with metastatic colon cancer. 
A, CT scan before treatment shows 3-cm metastasis (arrow) in posterior right lobe of liver. 
B, CT scan immediately after ablation shows thermal injury (arrow) at site of treated tumor and no definite evidence of residual tumor. 
C, Follow-up CT scan at 3 months after ablation shows recurrent tumor (arrow) at margin of ablated tumor. 
D, CT scan immediately after reablation shows enlarged thermal injury (arrow) at site of treated tumor recurrence and no definite evidence of residual tumor.

<p>| TABLE 1 Percutaneous Radiofrequency Ablation of Hepatocellular Carcinoma |</p>
<table>
<thead>
<tr>
<th>Researchers</th>
<th>No. of Patients</th>
<th>Needle Type</th>
<th>Mean Follow-Up</th>
<th>Percentage of Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossi et al. [56]</td>
<td>39</td>
<td>Conventional</td>
<td>23 months</td>
<td>95% Complete Necrosis</td>
</tr>
<tr>
<td>Rossi et al. [55]</td>
<td>23</td>
<td>Umbrella</td>
<td>12 months</td>
<td>91% Complete Necrosis</td>
</tr>
<tr>
<td>Livraghi et al. [53]</td>
<td>42</td>
<td>Cooled-tip</td>
<td>6 months</td>
<td>47.6% Complete Necrosis</td>
</tr>
<tr>
<td>Francica and Marone [49]</td>
<td>15</td>
<td>Cooled-tip</td>
<td>15 months</td>
<td>90% Complete Necrosis</td>
</tr>
</tbody>
</table>

<p>| TABLE 2 Percutaneous Radiofrequency Ablation of Metastatic Liver Tumors |</p>
<table>
<thead>
<tr>
<th>Researchers</th>
<th>No. of Patients</th>
<th>Needle Type</th>
<th>Mean Follow-Up</th>
<th>Percentage of Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rossi et al. [56]</td>
<td>11</td>
<td>Conventional</td>
<td>11 months</td>
<td>78% Complete Necrosis</td>
</tr>
<tr>
<td>Solbiati et al. [57]</td>
<td>16</td>
<td>Conventional*a</td>
<td>18.1 months</td>
<td>58% Complete Necrosis</td>
</tr>
<tr>
<td>Solbiati et al. [59]</td>
<td>29</td>
<td>Cooled-tip</td>
<td>10.3 months</td>
<td>66% Complete Necrosis</td>
</tr>
<tr>
<td>Livraghi et al. [54]</td>
<td>14</td>
<td>Conventional*a</td>
<td>6 months</td>
<td>52% Complete Necrosis</td>
</tr>
<tr>
<td>Rossi et al. [55]</td>
<td>14</td>
<td>Umbrella</td>
<td>10 months</td>
<td>93% Complete Necrosis</td>
</tr>
<tr>
<td>Lencioni et al. [51]</td>
<td>29</td>
<td>Cooled-tip</td>
<td>6.5 months</td>
<td>88% Complete Necrosis</td>
</tr>
</tbody>
</table>

*aThese two studies also used saline infusion before radiofrequency was applied in hopes of increasing area of tumor necrosis.

Rossi et al. [56] used a conventional needle that was not insulated to the distal tip. Solbiati et al. [57] and Livraghi et al. [54] conducted series with a conventional needle not insulated at the tip combined with saline infusion. Ten to fifteen milliliters of saline was introduced into the tumor before radiofrequency was applied in hopes of increasing the area of tumor necrosis. Rossi et al. [55] performed a series using an umbrella-type needle. Solbiati et al. [59] and Lencioni et al. [51] reported results using a cooled-tip needle in 1997. The rate of complete necrosis in these studies ranged from 52% to 93%. However, few patients remained disease-free; the rates ranged from as low as 11% at 11 months in the series of Rossi et al. [56] to as high as 33% at 18 months in the series of Solbiati et al. [59]. The marked discrepancy between the complete tumor necrosis rate and the percentage of patients who remain disease-free is in part due to the biology of metastatic liver disease and our limited ability to detect the full hepatic tumor burden. Most patients with a few 2- to 3-cm liver metastases also have numerous subcentimeter...
or microscopic tumors that are not detectable with current imaging technology.

Laparoscopic Results

Siperstein et al. [45] described results of laparoscopic radiofrequency ablation of 13 neuroendocrine tumors in the livers of six patients. The tumors ranged in size from 1 to 7 cm. Follow-up CT showed complete necrosis in 11 of 11 lesions in four patients at 3 months. All patients showed improvement in their symptoms after radiofrequency ablation. Cuschieri et al. [46] used laparoscopic sonography to guide treatment of 10 patients, two with hepatoma and eight with metastases. No complications occurred. Patients were discharged within 2 days of intervention. This compares with the usual same-day discharge after percutaneous techniques, but it is a shorter hospitalization than with open techniques. At follow-up ranging from 6 to 20 months, one patient had died of progressive disease, one patient had further metastases, and eight were disease-free.

Intraoperative Results

Elias et al. [64] described the use of combined liver resection and radiofrequency ablation to treat seven patients with liver metastasis. This is an interesting approach in that these were liver metastases that were thought to be unresectable by previous approaches. Radiofrequency was used to ablate those lesions that could not be surgically resected. The Pringle maneuver was performed in all patients, and all seven patients were disease-free up to 10 months of follow-up. Jiao et al. [65] reported a series of eight patients with HCC and 27 patients with metastases in which 30 of the 35 patients underwent intraoperative radiofrequency ablation using the Pringle maneuver. Thirteen of the 30 patients had combined radiofrequency ablation and a surgical resection. At approximately 10 months of follow-up, 24 of the 35 patients were found to have stable disease.

To our knowledge, the largest series to date of intraoperative radiofrequency ablation of hepatic tumors is by Curley et al. [42]. In that study, radiofrequency ablation was used to treat 169 tumors in 123 patients. Of the 123 patients, 92 (75%) were treated with laparotomy and 31 (25%) were treated percutaneously. Forty-eight (39%) patients had HCC and 75 patients (61%) had hepatic metastases. All tumors were treated with an umbrelta-type electrode, and a Pringle maneuver was used on all intraoperative cases. Overall, complete necrosis had occurred in 98% of the ablated tumors at a median follow-up of 15 months, and 72% of the patients remained tumor-free during the same time. In the series of Curley et al., the size of the tumors treated by percutaneous radiofrequency (2.4 cm diameter) was less than the size of tumors treated intraoperatively (3.8 cm). Those authors did not analyze the outcome difference in the percutaneous and the intraoperative groups. However, only three (1.8%) of 169 treated lesions had local recurrence.

Complications

As stated in the section on anesthesia, almost all patients experience pain and nausea during and immediately after ablation. These side effects are usually controllable and transient. Nausea rarely persists longer than 2–3 hr after the procedure. Approximately 25% of patients will have pain that requires continued medication at the time of discharge [66]. In 98% of patients, pain will be gone within 1 week after the procedure [66].

As reported with other types of tumor ablation procedures (chemoembolization and cryoablation), a percentage of patients (in our experience, about 25%) will develop a delayed syndrome after ablation. The frequency, severity, and time to onset appear to be directly related to the amount of tissue ablated. The typical presentation consists of flu-like symptoms (low-grade fever [up to 38.8°C] accompanied by general malaise) that begin 3–5 days after the ablation and persist for approximately 5 days. With large-volume ablations we have seen the syndrome begin almost immediately, cause fever as high as 39.4°C, produce severe lethargy, and last for as long as 2–3 weeks. Several patients have reported night sweats. Appropriate treatment of the syndrome is primarily supportive. We inform patients that they may develop the syndrome after their ablation. Their fever is treated with oral acetaminophen. They are instructed to call us if their fever exceeds 38.8°C or lasts longer than 5 days. If their fever exceeds 38.8°C, a blood sample is drawn and cultured to determine if the patient is septic [66].

Radiofrequency ablation of the liver is considered safe, with an extremely low major complication rate observed by multiple groups. More serious complications have been reported in the literature. Rossi et al. [56] described capsular necrosis, and Solbiati et al. [57, 59] reported intraperitoneal hemorrhage that did not require transfusion. Solbiati et al. [57] also reported one case of fairly severe hypotension that persisted for 3–4 hr after the procedure. Livraghi et al. [53, 54] reported complications in their patients that consisted of two pleural effusions, a perihpatic hematoma, a hemothorax that required surgical repair, self-limited intraperitoneal bleeding, and hemobilia and cholecystitis in one patient each. We have experienced several complications, including three cases of intrahepatic arterial bleeding, with one requiring selective arterial embolization; one burn of the diaphragm that caused pain for 3 months; one 3-cm hepatic abscess that was treated with oral antibiotics; five 1- to 3-cm first- or second-degree burns along the edge of the grounding pads; and three instances of tumor seeding along the needle tract. Additionally, Lees and Gilliams [67] reported hepatic abscesses and a thermal burn of the transverse colon. Livraghi et al. [52] reported a single death (0.8% rate) in their series. This was the result of a Staphylococcus aureus infection that developed 3 days after the procedure. Because of this complication, those authors administer antibiotic prophylaxis of 1000 mg of ceftriaxone sodium (Rocephin; Roche Laboratories) to all patients.

Few reports mention complications occurring after radiofrequency ablation performed via a laparotomy. Of those that have been reported, most consist of fever and pain. Other reported complications include a perihepatic abscess and an intrahepatic hemorrhage that required arterial embolization [42].

Discussion and Future Strategies

Radiofrequency ablation of the liver has been a promising technique. The overall success of radiofrequency ablation of liver tumors has been variable. Differences in reported success rates are no doubt multifactorial and include patient selection, operator experience, and the equipment used. We have learned a great deal in the exploratory phase of radiofrequency ablation of liver tumors. Currently, tumor burden may exceed technologic ability to completely ablate the tumor, and our ability to affect long-term patient survival is thus limited. Much of the future success of radiofrequency ablation will be based on technologic advances in radiofrequency electrode and generator design, and better understanding of methods to ensure adequacy of tumor necrosis. Certainly, compared with the original single uninsulated radiofrequency needle, newer needle designs and more powerful radiofrequency generators have allowed increased tissue necrosis. Further refinements are being investigated. For instance, Goldberg et al. [68] have shown that pulsed radiofrequency current (as compared with continuous application of...
Radiofrequency Ablation of the Liver

Radiofrequency thermal ablation of primary and secondary tumors can be performed safely using percutaneous, laparoscopic, or open surgical techniques. Technologic advances in radiofrequency equipment, methods of altering tissue response to radiofrequency treatment, and combined therapies will likely yield an improvement in the complete ablation rate of small tumors and make the treatment of larger tumors a clinically viable treatment alternative.

References
