Radiofrequency ablation: technique and clinical applications

REVIEW

Servet Tatlı, Ümit Tapan, Paul R. Morrison, Stuart G. Silverman

ABSTRACT

Radiofrequency ablation is the most commonly used percutaneous ablation technique and well-documented in the literature on focal therapies. It has become the image-guided ablation method of choice because of its efficacy, safety, and ease of use. Radiofrequency ablation has shown promise in treating selected solid tumors, particularly those involving the liver, kidneys, lungs, and the musculoskeletal system. It is a minimally invasive technique often used in inoperable patients with other comorbidities. Radiofrequency ablation requires a minimal hospital stay or can be performed on an outpatient basis. The aim of this article is to review radiofrequency ablation techniques and their clinical applications.

Key words: • radiofrequency catheter ablation • tumor • percutaneous

From the Department of Radiology (S.T. \boxtimes statli@partners.org, P.R.M., S.G.S.), Harvard Medical School, Brigham and Women's Hospital, Boston, Massachusetts, USA; the Department of Internal Medicine (Ü.T.), Tufts University School of Medicine, Steward Carney Hospital, Boston, Massachusetts, USA.

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n last decade, there has been a rapid advancement in the utilization of percutaneous, image-guided tumor ablation methods. Radiofrequency (RF) ablation has become the method of choice because of its safety and efficacy. Image-guided RF ablation is minimally invasive and usually appropriate for inoperable patients with other comorbidities. It requires a minimal hospital stay or can be performed on an outpatient basis. It preserves more normal organ tissue and is less expensive than surgery (1-3). The procedures are generally performed by using 14–21 G, partially insulated electrodes that are placed under guidance (computed tomography [CT], magnetic resonance imaging [MRI], or ultrasonography [US]) into the tumor to be ablated. In most cases, percutaneous RF ablation can be performed in patients under conscious sedation, by using medications similar to those used with any other interventional radiology procedure. In the clinical arena, RF ablation has been used for the treatment of various neoplasms, including metastases from a variety of primary tumors (4, 5), such as hepatocellular carcinoma (HCC) (6, 7), renal cell carcinoma (RCC) (8, 9), non-small cell lung cancer (NSCLC) (10, 11), and osteoid osteoma (12, 13). In this article we review RF ablation techniques and their clinical implications.

The mechanism of RF ablation

Deposition of energy into tumors induces thermal injury resulting in a tumoricidal effect. RF ablation involves flow of electrical alternating current through tissues whereby ionic agitation and resistive heating of the tissues occurs. In order to establish this current, the RF ablation system requires a closed-loop circuit comprised of an electrical generator, a needle electrode, a patient (a resistor), and large dispersive electrodes (or "grounding pads") (Fig. 1). The nature of the thermal damage depends on the tissue temperature and the duration of heating (Table). Effective ablation can only be achieved by optimizing heat production and minimizing heat loss. The difference between the amount of heat produced and heat lost is called heat efficacy. While heat production is correlated with the intensity and duration of the RF energy deposited, heat loss is mainly due to the blood flow within adjacent blood vessels, which is the so-called heat-sink effect (Fig. 2).

Effective RF ablation can be decreased when tissues are heated to greater than 100°C and/or when charring of tissues occur. Rapid loss of heat at a distance from the electrode also limits the size of ablation. An important element of effective ablation is the extent of the ablation zone. In order to assure eradication of microscopic tumoral extensions, the ablation zone needs to include areas beyond the tumor margin. This is called the ablation margin, and safe ablation margins vary depending on the organ being ablated and should preferentially be approximately 1 cm.

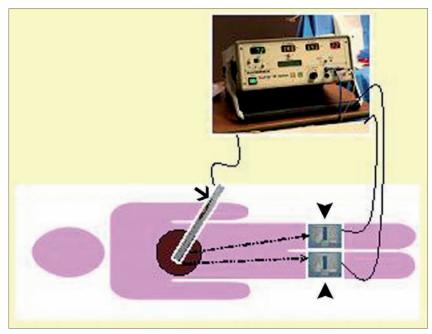


Figure 1. RF ablation circuit. Both the grounding pad (*arrowheads*) and needle electrode (*arrow*) are active, while the patient acts as a resistor, creating an alternating electric field resulting in marked agitation of the ions in the tumor and the surrounding tissue. This ionic agitation creates heat. The marked discrepancy between the surface area of the needle electrode and the grounding pad causes the generated heat to be concentrated around the needle electrode.

Temperature (°C)	Tissue reaction
42	More susceptible to chemotherapy or radiation
45	Irreversible cellular damage in several hours
50–55	Irreversible cellular damage in 4–6 min
60–100	Coagulation of tissue
100–110	Vaporization and carbonization of tissue

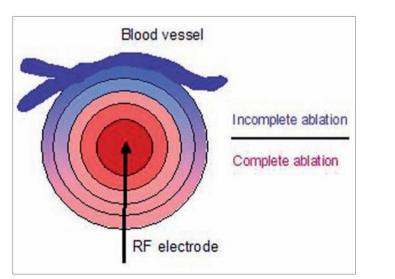


Figure 2. Schematic illustration of the heat-sink effect. Blood flow within adjacent vessels is a major factor for heat loss.

RF ablation systems

Substantial efforts have been made to increase heating efficacy, reduce charring and to achieve larger and more effective tissue damage. New RF ablation devices with more powerful generators (200 watts) are the result of these efforts. Currently, the following three major commercial RF ablation systems are globally available: CooltipTM system (Covidien, Mansfield, Massachusetts, USA) (Fig. 3), RF 3000® (Boston Scientific Corporation, Natick, Massachusetts, USA) (Fig. 4), and Model 1500X RF generator (AngioDynamics, Latham, New York, USA) (Fig. 5). The Cool-tipTM system monitors the impedance (electrical resistance) of the tissue during ablation, automatically adjusting the power output to assure a consistent flow of current to the tissue. Excessive impedance for this device correlates to excessive gas formation in the tissue. RF 3000® also tracks tissue impedance for the user. Here, an increase in tissue impedance is taken as a clinical endpoint, correlating to a thorough coagulation of the tissue around the electrode. Model 1500X RF generator provides direct multi-point temperature measurements throughout the tissue to allow the user to target a pre-selected target temperature for the tumor.

The Cool-tipTM system uses internally cooled electrodes, which minimize charring and permit optimal energy deposition and deeper tissue heating. Multiple probe systems (socalled cluster or switch box system) can achieve greater coagulation necrosis than any individual electrode alone. Expandable, multi-tined electrodes, such as the ones used in the RF 3000[®], permit the deposition of energy over a larger area and decrease the distance between the tissue and the electrode. With the Model 1500X RF generator's perfused RF electrodes, slow infusions of saline from the tines into the tissue around the electrode allow for more thorough heating.

Despite all these advancement, RF ablation techniques still have some limitations regarding ablation size, procedure time, and heat sink effect from adjacent vessels. This resulted in substantial work to develop other tumor ablation technologies such as microwave ablation.

Clinical applications

In the last decade, there has been a rapid advancement in the utilization

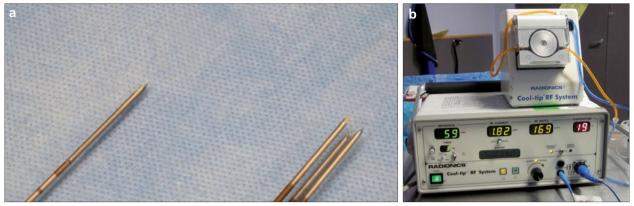


Figure 3. a, b. The internally cooled needle-like electrodes (a) of the Cool-tip[™] system (Covidien, formerly Radionics). An electrode is electrically insulated along its shaft except for the final 1–3 cm, which is the exposed "active" tip. On the left is a "single" 17 G electrode with a 3 cm active tip; on the right is a "cluster" electrode comprised of three 2.5 cm tipped single electrodes incorporated into one handle. The RF generator (Covidien) (b) with a peristaltic pump to drive cooled saline to the electrode prevents charring. The generator provides up to 2 amps of RF electrical current, which is delivered at a power of up to 200 watts. The numeric displays on the front control panel allow the user to observe the electrical impedance in the tissue, the current and power, and the probe temperature as well as the elapsed time.

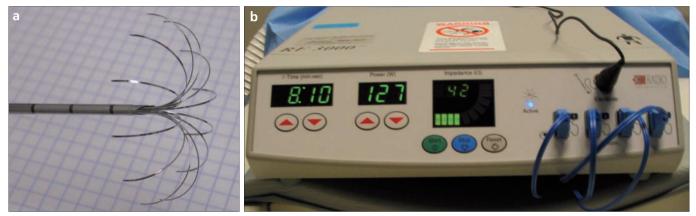


Figure 4. a, b. The LeVeen electrode (Boston Scientific Corporation) (a). This array-type of electrode is expandable and multi-tined. When it is placed in the tumor under image guidance, the non-insulated "tines" of the electrode are deployed and extend from the distal tip of the cannula. The photo shows a deployed electrode. The array diameters are available in a range of 2–5 cm. The RF 3000[®] Generator (b) provides up to 2 amps of current and can provide a power of up to 200 watts, which is typical of currently-used systems. The level of power delivered is controlled by the user. The power level is set low to start and is steadily increased to allow for a gradual heating of the tumor volume. When heating is sufficient to coagulate the target tumor volume, the numeric display in the center of the control panel (reading 42 ohms) shows a marked increase in tissue impedance by an order of magnitude.

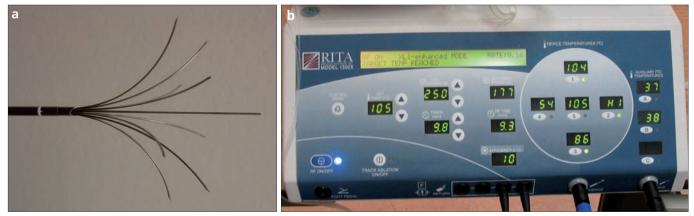
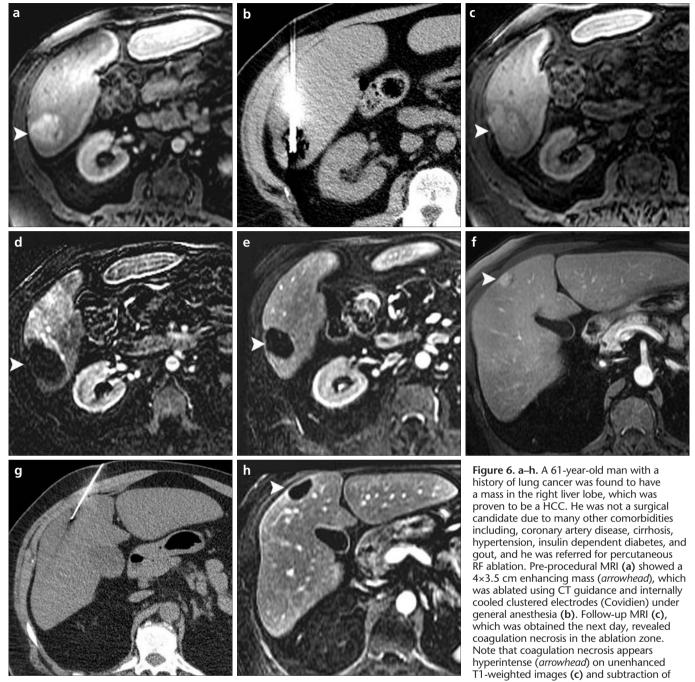


Figure 5. a, b. The Starburst electrode (AngioDynamics, formerly Rita Medical) **(a)**. This is an array-type electrode, which is expandable and multi-tined. After the active tines have been deployed as shown, the array diameters can be adjusted between 2 and 5 cm. Alternating tines of the array have built-in thermal sensors and are able to detect the temperature in the tissue, providing feedback to the generator. The Model 1500X RF generator **(b)** provides up to 2 amps of RF current at up to 200 watts. The operator selects a target temperature for the tissue (such as 105°C seen in the left numeric display). The device then adjusts the power that is delivered to the tissue until the thermocouples "see" that temperature. Temperatures are displayed in the five numeric displays in the circular area on the right. Thereafter, the temperature is held for several minutes to assure tissue necrosis.



post-contrast enhanced T1-weighted images (d) eliminate hyperintense coagulation necrosis and demonstrate the lack of enhancement better (*arrowhead*). The patient had a follow-up MRI every three months. Enhanced MRI on nine month follow-up (e) showed no recurrence of the ablated tumor (*arrowhead*), but there was a new enhancing focus (f, *arrowhead*), which was first proven to be a second HCC and then ablated percutaneously by using an internally cooled RF electrode (Covidien) (g). Enhanced MRI with subtraction (h) which was performed on the next day shows good tumor coverage with no enhancement (*arrowhead*).

of percutaneous, image-guided tumor ablation methods, and RF ablation has been the method of choice because of its availability, safety, efficacy, and cost. In the clinical setting, RF ablation has shown promise for treating solid tumors, particularly those involving the liver (6, 7), kidneys (8, 9), lungs (10, 11, 4, 5), and the musculoskeletal system (12, 13).

RF ablation in liver tumors

Surgery is accepted as the first-line treatment for HCC and colorectal metastases that are limited in number. RF ablation has been shown to be an effective treatment option for patients with primary and metastatic liver tumors, who are not surgical candidates due to tumor location, poor hepatic reserve, other comorbidities, or advanced age (6, 14). Furthermore, RF ablation compares reasonably well with survival rates of surgery in patients with smaller (\leq 3 cm) tumors (7, 15).

RF ablation yields better results for tumors surrounded by nontumor liver parenchyma. Tumors surrounded by cirrhotic parenchyma have the advantage of being insulated and can be coagulated better (Fig. 6). Subcapsular

tumors adjacent to visceral organs and central tumors surrounded by large blood vessels carry the risk of incomplete ablation. Adjacent visceral organs, such as small bowel or colon, can be displaced away from the tumor through patient positioning or hydrodissection (16). Hydrodissection can also be used to displace the diaphragm to prevent diaphragmatic injury during the ablation of tumors in the liver dome (17). Hydrodissection should be performed with sterile water or 5% dextrose rather than saline because the latter conducts electricity. During energy application, the tip of the hydrodissection needle should be placed at least 1 cm away from the tip of the RF applicator.

RF ablation of hepatic tumors is a relatively safe modality with a reported overall complication rate of 7.1% and a very low mortality (0.3%) (6). Immediate major complications include hemorrhage, biliary leakage or obstruction, infection, pneumothorax, and injury to adjacent organs (18, 19). Careful selection of appropriate patients and RF ablation tools, as well as utilization of adjunctive maneuvers are important to prevent complications. In order to decrease the risk of postprocedural bleeding and tumor seeding, exophytic tumors should be avoided, and a transhepatic route rather than a direct route should be selected to approach peripheral tumors (20). Also, the puncture site should be selected as anteriorly and inferiorly as possible, to prevent a pneumothorax because the pleural space extends more inferiorly in the posterior chest. Patients with biliary dilatations have an increased risk of developing a postprocedural abscess or sepsis because of bacterial colonization in the biliary tract. Prophylactic use of antibiotics may be beneficial for these patients who are at higher risk for developing infection (20).

The incidence of HCC is increasing, largely due to infection with the hepatitis B and hepatitis C viruses, and alcoholism (21). For patients with cirrhosis and HCC \leq 3 cm, who are not surgical candidates based on impairment of liver function, the number and distribution of tumors, or cardiopulmonary dysfunction, RF ablation can be used as a first-line treatment method (22). There is substantial data that has demonstrated the safety and efficacy of RF ablation (23, 24). There is increasing

evidence to suggest that percutaneous RF ablation is a safe and effective method to treat larger (3-5 cm) HCCs as well (25). Patients with end-stage cirrhosis (Child-Pugh C) are generally not appropriate candidates for RF ablation because their life expectancy is limited by their hepatic dysfunction rather than cancer (22). Patients with uncorrectable coagulopathies and active alcohol abuse are also not ideal RF ablation candidates (22). RF ablation can also be used as a bridge therapy for patients awaiting transplantation. According to the Milan criteria, patients with a single (≤ 5 cm) or multiple tumors (less than three in number, and ≤3 cm in size) are eligible for transplantation (23). Generally, patients with cirrhosis awaiting transplantation undergo surveillance with enhanced CT or MRI and alpha-feto-protein levels. If a patient develops HCC(s) during this waiting period, RF ablation can be utilized to treat the tumors to keep the patient eligible for transplantation.

Hepatic metastases develop in half of the patients with colorectal cancer and are the most common cause of morbidity and mortality (26). Hepatectomy has been shown to improve survival; however, it is feasible in only a small number of patients. Systemic chemotherapy is the mainstay therapy for those who are not surgical candidates. RF ablation, either alone or in conjunction with chemotherapy, can be used as an alternative local therapy if the size, location, and number of the metastases are appropriate. Berber et al. (27) also showed significant survival benefits of RF ablation in colorectal liver metastasis when lesions were ≤ 3 cm in size. Stang et al. (28) recently published a systematic review of RF ablation for colorectal hepatic metastasis and identified local recurrence rates varying from 5% to 42%. In this review, tumor size was noted to be the dominant factor influencing local failure rates with an increase in relapse rate when ablating tumors ≥ 3 cm. In a prospective study, which involved 167 patients, Gillams and Lees (26), showed that the five-year survival rate for RF ablation and surgical resection are comparable in patients with fewer than five metastases, each ≤ 5 cm in size. Successful use of RF ablation in the treatment of HCC and colorectal metastases led to the utilization of this technique to treat liver metastases

from other primaries. Although metastases from any primary, providing their appropriate number, size and location, can be treated with RF ablation, more experience has been accumulated in metastases from breast carcinoma and neuroendocrine malignancies (29, 30).

RF ablation in lung tumors

Lung cancer is the leading cause of cancer-related death in both men and women, and NSCLC accounts for the majority of the cases. Although surgery provides the best possibility for a cure in early stages (I/II) of NSCLC, the majority of these patients have insufficient cardiopulmonary reserve and thus are not surgical candidates (31, 32). RF ablation, alone or in combination with other treatment modalities such as external beam radiation, is an alternative option for these patients and is currently the most commonly utilized thermal ablation method with promising survival data: 68% for twovear survival (10) and 74% for threeyear survival (11) (Fig. 7).

RF ablation can also be used in patients with metastatic lung disease for eradication of small tumors (<3 cm) limited in number or for palliation of larger tumors that cause symptoms such as cough, hemoptysis, or pain (5). A recent prospective, intent-to-treat multicenter clinical trial studied 106 patients with 183 primary or secondarv lung tumors smaller than 3.5 cm. which had been treated with RF ablation. Cancer-specific survival rates at one and two years were 92% and 73%, respectively, for patients with NSCLC, 91% and 68%, respectively, for patients with colorectal metastases, and 93% and 67%, respectively, for patients with other metastases (4). Crocetti and Lencioni (33) also reported a complete ablation rate of approximately 80% in tumors smaller than 3.5 cm in size.

Pulmonary RF ablation is a safe procedure with a reported mortality of 0.4% (34) and an overall major complication rate ranging between 8% and 12% (35). Pneumothorax is the most common complication (~20%). Small pleural effusions are frequent and generally self-limited. Productive cough with brown sputum occurs in a minority of patients and may last 1–2 weeks. Peripheral, pleural based tumors or tumors surrounded by normal lung parenchyma are best suited for RF ablation. Central tumors located close to

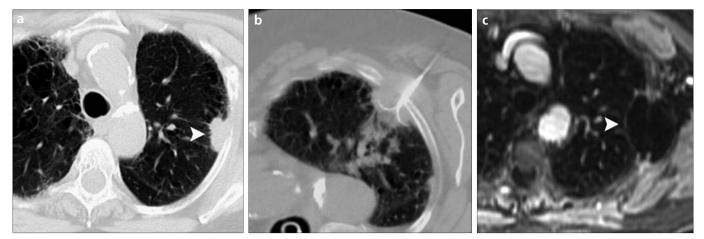


Figure 7. a–c. A 72-year-old woman with a biopsy-proven NSCLC, who was not a surgical candidate due to severe chronic obstructive pulmonary disease, and was referred for percutaneous RF ablation. The mass (*arrowhead*) was 2.5×2 cm in size, pleural-based, and located in the left upper lobe on CT (a). It was ablated using CT guidance and a 3 cm expandable, multi-tined RF ablation electrode (Boston Scientific Corporation) (b). RF energy was applied according to the standard vendor's protocol, starting from 40 watts and gradually increasing up to 150 watts over a total of 22 min. Follow-up MRI (c) obtained the next day showed no residual tumor (*arrowhead*) in the ablation zone. There was no recurrence at 12 months follow-up (not shown here).

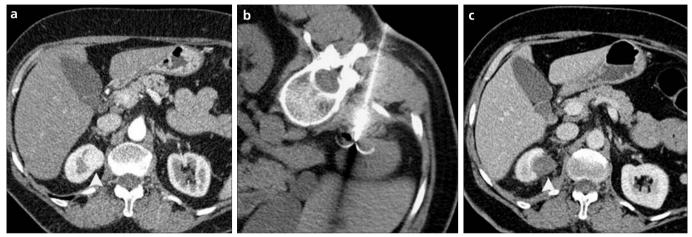


Figure 8. a–**c**. A 65-year-old woman with a 2×2 cm right kidney mass, which was found incidentally. The patient has a pacemaker due to heart block. Axial CT image (**a**) shows an enhancing mass (*arrowhead*) in the medial aspect of the upper pole of the right kidney. Percutaneous RF ablation (**b**) was performed using CT guidance and a 3 cm expandable, multi-tined RF ablation electrode (Boston Scientific Corporation). RF energy was applied starting from 40 watts and gradually increased to 150 watts over 13.5 min, including a booster dose. After the procedure, the patient developed mild hematuria, which subsided spontaneously. Follow-up CT (**c**), which was obtained the next day, showed good tumor coverage with no evidence of suspicious enhancement (*arrowhead*) in the tumor to suggest residue.

the central airway carry a risk of injury of the bronchus, resulting in cavitation, abscess formation, and bronchopleural fistula (5).

RF ablation in kidney tumors

The incidence of RCC has significantly increased in the USA, with an expected incidence of more than 50 000 new cases each year (36). Surgery is the method of choice for localized RCC; however, there are a significant number of patients who are not suitable for surgery because of comorbid illnesses. RF ablation is emerging as a safe and effective alternative for elderly patients with early-stage RCC who are

not surgical candidates (8), and there is increasing evidence that it can be a curative treatment option for these patients, sparing them the risk of mortality and substantial morbidity associated with surgery (9). RF ablation seems to provide the lowest rate of renal impairment compared to extirpative treatment options (37), which is particularly important in patients with a solitary kidney. RF ablation has also been used effectively for treatment of multiple renal cell cancers such as those seen in von Hippel-Lindau patients. Peripheral, exophytic and small (<3 cm) tumors are more suitable for RF ablation (Fig. 8).

Renal RF ablation is a safe procedure with a serious complication rate of <1%(18). The complications depend on the location of the tumor. In peripherally located tumors, there is a potential for thermal injury to adjacent bowel, and in more central or medial lower pole tumors, injury to the collecting system is more common (18). Patient positioning and hydrodissection may help to displace the adjacent bowel to prevent injury. Prophylactic placement of ureteral stents can be considered in patients with a tumor near the ureter, carrying high risk of ureter injury. The stent is placed prior to the ablation and stays in place until 4-6 weeks after the procedure.

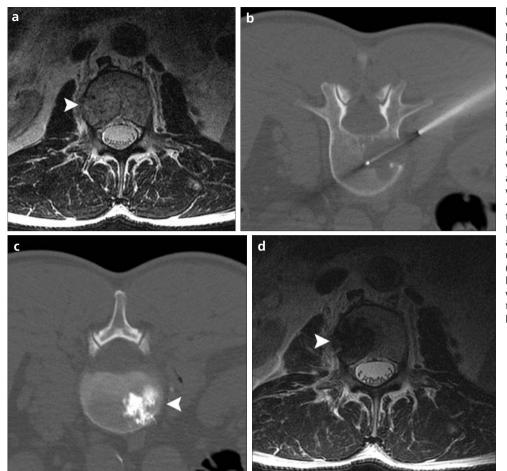


Figure 9. a-d. A 59-year-old man with metastatic RCC was found to have a lytic mass (arrowhead) in the body of the L2 vertebra, which was consistent with a metastasis as shown on T2-weighted MRI (a). The patient was referred for percutaneous RF ablation, followed by vertebroplasty to prevent a potential compression fracture. Following a biopsy, an internally cooled RF ablation electrode (b) with a 2 cm active tip (Covidien) was placed within the mass through a 13 G introducer, and RF energy was applied over 8 min, starting at 40 watts and increasing gradually to 120 watts. After completion of RF ablation, the same introducer and CT fluoroscopy guidance were used and polymethylmethacrylate (arrowhead) was injected into the lytic lesion (c). Follow-up MRI (d), which was obtained the next day, showed that the lytic lesion is filled with T2hypointense cement (arrowhead).

RF ablation in bone tumors

Painful bone metastases are a common cause of morbidity in cancer patients. Metastatic bone disease generally indicates limited life expectancy; therefore, a safe, effective, and tolerable local treatment is essential for providing local pain control and to increase quality of life. Radiation therapy, systemic chemotherapy, hormonal therapy, surgery and pain medications have been used to control pain in these patients (38). RF ablation is a practical alternative to treat painful bone metastases that are not responding to standard measures such as narcotics or radiation therapy (Fig. 9). There is growing evidence on the effectiveness and durability of pain palliation via RF ablation. The recently reported ACRIN (American College of Radiology Imaging Network) trial demonstrated that pain intensity decreased by 26.92 and 14.16 points (on a scale of 0-100 points) in one and three months, respectively (39).

Osteoid osteoma is a benign bone tumor of young adults which typically

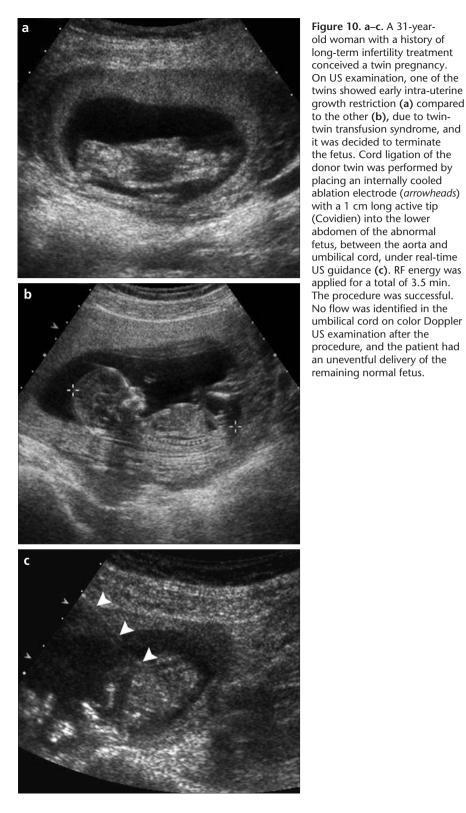
presents with nocturnal pain and responds to anti-inflammatory drugs. Surgical removal has been the established treatment method for many years. Utilization of RF ablation for osteoid osteoma was first reported in 1992 by Rosenthal et al. (40), and several studies have shown effects of RF ablation in treatment of osteoid osteoma since then. In a recent prospective trial by Hoffman et al. (12), 38 patients were successfully treated with RF ablation with only three recurrences during an average follow-up of 32 months, all of which were treated with a second RF ablation. Currently, RF ablation has been shown to be effective in as many as 90% of cases (13). It has replaced surgery in many centers and is now considered a standard of care.

During RF ablation of osteoid osteoma or any other skeletal tumors, RF electrodes can be placed into the tumors with help of a bone biopsy system such as the Binopty (Radi Medical Systems, Uppsala, Sweden). First, a 14 G penetration set of this bone biopsy system is placed into the tumor under CT guidance and then the RF electrode is inserted through the penetration needle. If needed, a biopsy needle can be placed through the penetration needle and specimen can be obtained for histopathological evaluation. The RF electrode should be selected to be long enough so that the penetration needle can be withdrawn by at least a few centimeters from the tip of the RF electrode, to prevent skin burn along the shaft of the needle.

Other clinical applications for RF ablation

A solitary metastasis from a variety of primary tumors to the adrenal gland can be treated with percutaneous ablation (41). Ablation of normal adrenal gland tissue may cause a hypertensive crisis during the procedure and premedication with α and/or β blockers may be helpful.

Although RF ablation is typically used to treat cancer patients with virtually any solid primary and metastatic organ tumors, it can be utilized beyond oncology, such as for ligation of the umbilical cord of fetuses with



twin-twin transfusion (Fig. 10) or selective reduction in complicated monochorionic pregnancies (42).

Imaging follow-up

After an ablation has been performed, long-term follow-up is necessary to

detect residual or recurrent tumor. Although CT or MRI can be used for follow up, MRI provides better demonstration of enhancing tissue within the ablation zone. Coagulation necrosis typically appears hyperintense on T1-weighted images and hypointense

on T2-weighted images. The elimination of previously seen enhancements suggests complete treatment (Fig. 6) (43). Subtracted images may be helpful to differentiate between coagulation necrosis and enhancing viable tumor (44). Ideally, the ablation zone should cover the ablated tumors completely with a 1 cm tumor-free margin (ablation margin) depending on the organ being ablated. Because of increased risk of residual or recurrent tumor, patients with an absent or narrow ablation margin should be followed up more carefully with imaging. Because of inflammation, a thin and even enhancing rim may develop around the ablation margin. A focal, nodular tissue tumor at the ablation margin with similar signal characteristics and the same enhancement pattern as the original may represent residual tumor. Diffusionweighted or perfusion images may be helpful to detect residual or recurrent tumors in addition to signal characteristics and enhancement patterns of ablated tumors (45, 46). Baseline MRI scans should be performed 1-2 weeks prior to the ablation to permit accurate comparison with post ablation images, which should be performed within one week after the RF ablation to detect potential residual viable tumor tissue that requires immediate retreatment. Close imaging follow-up should be performed every three months for one vear after ablation. For fluorodeoxy-Dglucose (FDG)-avid tumors, positronemission CT surveillance scans can also be performed. While elimination of a previously seen FDG-avid tumor with a thin and even activity around the ablation zone, which represents post-ablation inflammation, is an indicator of a complete ablation, presence of persistent asymmetric tracer uptake in the location of previously FDG-avid tumor suggests residual tumor (47).

In conclusion, image-guided RF ablation is a safe and effective method for treatment of a variety of primary, recurrent, and metastatic tumors of many organs, in particular the liver, kidneys, lungs, adrenal glands, and musculoskeletal system. Establishment of ablation procedure rationale, careful selection of appropriate patients and RF ablation systems are important components of a successful ablation.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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