Microwave Ablation of Hepatic Malignancy

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Abstract

Microwave ablation is an extremely promising heat-based thermal ablation modality that has particular applicability in treating hepatic malignancies. Microwaves can generate very high temperatures in very short time periods, potentially leading to improved treatment efficiency and larger ablation zones. As the available technology continues to improve, microwave ablation is emerging as a valuable alternative to radiofrequency ablation in the treatment of hepatic malignancies. This article reviews the current state of microwave ablation including technical and clinical considerations.

Keywords

- ► interventional radiology
- ► microwave
- ► ablation
- ► liver tumors

Objectives: Upon completion of this article, the reader will be able to discuss the technical aspects of microwave ablation that differentiate it from other forms of thermal ablation, and identify the clinical utility and limitations of the technology.

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Microwave ablation is an extremely promising heat-based thermal ablation modality that has particular applicability in treating hepatic malignancies. Microwaves can generate very high temperatures in very short time periods, potentially leading to improved treatment efficiency and larger ablation zones. As the available technology continues to improve, microwave ablation is emerging as a valuable alternative to radiofrequency ablation in the treatment of hepatic malignancies.

How Microwave Ablation Works

Microwave ablation utilizes dielectric hysteresis to produce heat. Polar molecules in tissue (primarily water [H_2O]) are forced to continuously realign with the oscillating electric field (typically at 900 to 2500 MHz), increasing their kinetic energy and hence the temperature of the tissue. Tissues with a high percentage of H_2O (such as solid organs and tumors) are most conducive to this type of heating.[1–8]

Microwave energy radiates into the tissue through an interstitial antenna that allows for direct heating of a volume of tissue around the antenna. This mechanism of heating differs substantially from radiofrequency (RF) ablation, which creates heat via resistive heating when electrical current passes through the ionic tissue medium. Whereas RF heating requires an electrically conductive path, microwaves are capable of propagating through and effectively heating many types of tissue, even those with low electrical conductivity, high impedance, or low thermal conductivity.[3,9,10] Unlike RF and laser energy, microwaves can readily penetrate through the charred or desiccated tissues that tend to build up around all hyperthermic ablation applicators, limiting power delivery for nonmicrowave energy systems.[11]

Multiple microwave antennas can be powered simultaneously to take advantage of thermal synergy when placed in close proximity or widely spaced to ablate several tumors

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simultaneously.[12–15] Multiple-applicator ablation is possible with other power sources, but unlike RF, microwave energy can be powered continuously without switching from one applicator to another. Another feature unique to microwave ablation is the ability for antennas to be positioned and phased to exploit overlap of the electromagnetic field energy.[12–20]

Microwave technology has continued to evolve and improve. Early-generation microwave systems had fairly large noncooled applicators. Due to reflected power and shaft heating, short relatively low-power ablation cycles had to be utilized to prevent skin burns. Subsequently, water-cooled relatively low-power systems emerged, followed by water-cooled higher power systems, some with phased multiple probes. More recently, systems with more advanced cooling mechanisms have been able to decrease the applicator size and deliver higher power. These also can power multiple applicators in a phased fashion. This improved technology has finally begun to harness the theoretical potential of microwave energy.

Advantages of Microwave Ablation

Global

Microwave has many theoretical advantages over current technologies: Microwave energy has the potential to produce faster heating over larger volumes of tissue with less susceptibility to heat-sink effects; it can be effective in tissues with high impedance such as charred desiccated tissue; it is capable of generating very high temperatures, often in excess of 100°C; it is highly conducive to the use of multiple applicators; and it does not require grounding pads or other ancillary components.[12,13,15]

Liver

The liver is a vascular solid organ with an abundance of large vessels creating the potential for a heat-sink effect. Microwaves appear to be more able to overcome perfusion and large heat sinks than other heat-based ablation modalities (►**Fig. 1**).[5,10,21–23] Microwave energy has been shown to ablate tissue up to and around large hepatic vessels (measuring up to 10 mm), and it creates large zones of ablation in high perfusion areas.[5,22,23] High perfusion rates in hepatic vessels >3 mm limit the effectiveness of RF and has been shown to be an independent predictor of incomplete tumor destruction.[24] Recently, Fan et al compared paired microwave antennas and radiofrequency probes in in vivo porcine liver, demonstrating that the long and short axis diameters for all power settings of microwave were larger than RF and the rates of temperature rise to 60°C was significantly faster for microwave.[25]

The decreased susceptibility to vascular cooling has been studied and confirmed in preclinical studies. Bhardwaj et al performed microwave ablation in rat livers and showed

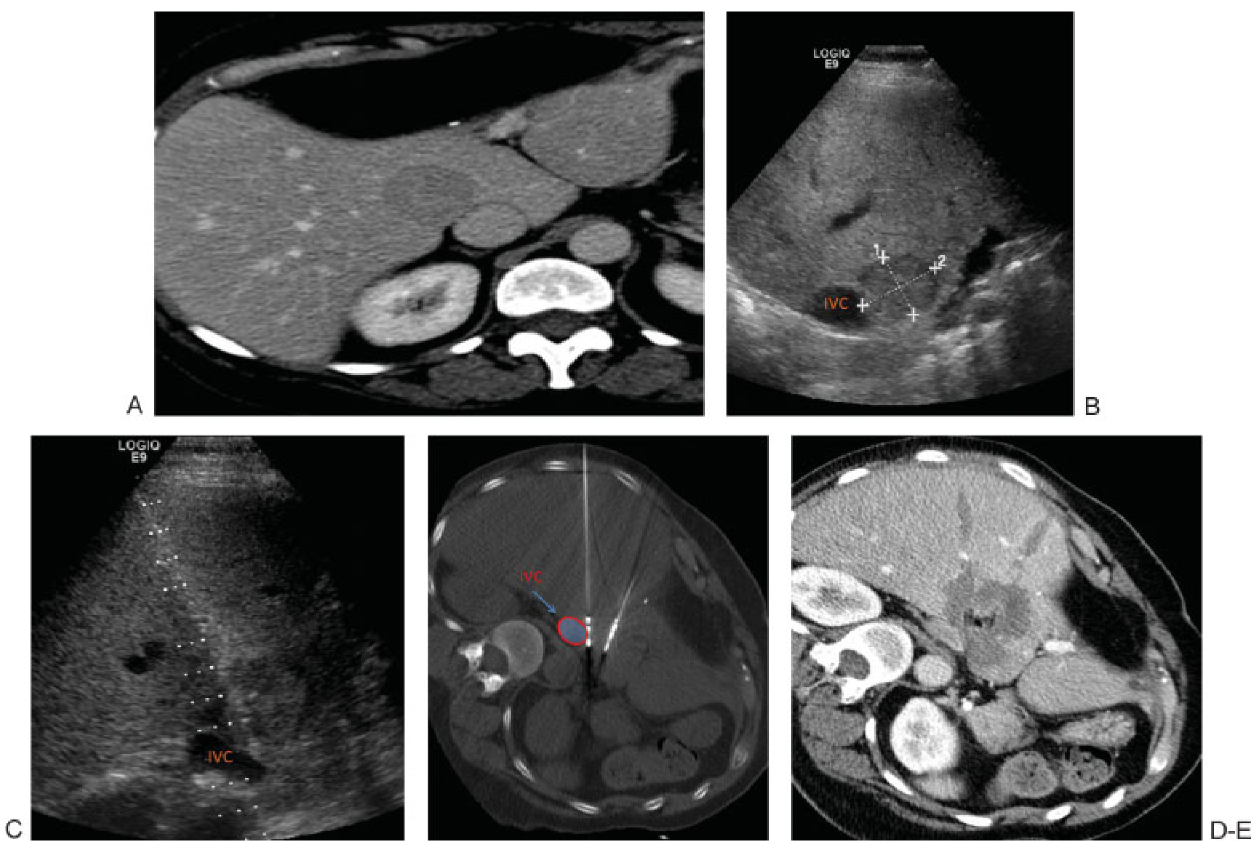

Figure 1 (A) Contrast-enhanced computed tomography (CT) demonstrates a single low attenuation lesion adjacent to the inferior vena cava (IVC) consistent with metastatic disease in this patient with breast cancer. (B) Ultrasound (US) image redemonstrates the proximity of this lesion to the IVC. (C, D) US and CT images obtained during treatment demonstrate applicator placement in the tumor just adjacent to the IVC. A second antenna was placed more laterally in the tumor (D). (E) Immediate postablation contrast-enhanced CT demonstrates an ablation zone measuring 4.8 × 5.5 cm, encompassing the tumor and extending to directly about the IVC, overcoming the expected heat-sink effects.

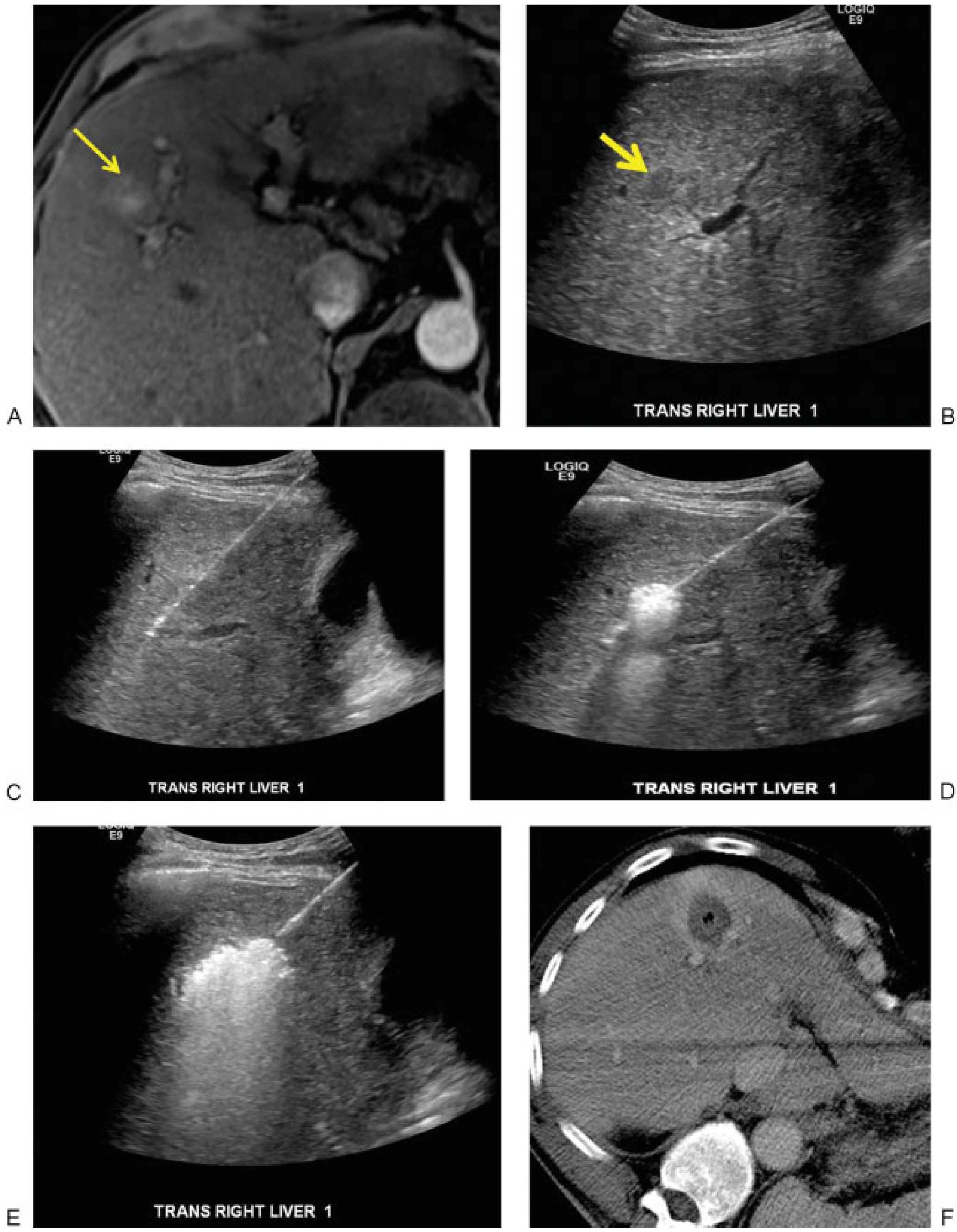

Figure 2 (A) Contrast-enhanced T1-weighted magnetic resonance (MR) image demonstrates an arterially enhancing lesion (arrow) in segment VIII measuring 2.0 × 1.8 cm. (B) This vaguely hypoechoic lesion is redemonstrated (arrow) on gray scale ultrasound. Following placement of a single antenna (C), and commencement of the ablation cycle, there is rapid early generation of gas after ~20 seconds (D), which rapidly grows to encompass the lesion at 5 minutes (E). (F) On postprocedural contrast-enhanced computed tomography, the final ablation zone generated with a single antenna at 100 W for 5 minutes measures 3.9 × 3.0 cm.

complete coagulative necrosis in ablation zones with no evidence of influence from surrounding blood vessels.[26] Awad et al demonstrated large and consistent zones of ablation in shorter times than would normally be seen with RF ablation, and proximity to hepatic vasculature and inflow did not significantly change the ablation zone size or shape with microwave ablation.[23] In an in vivo porcine liver model, Brace et al created circular ablation zones with minimal effects related to even large intrahepatic vessels, suggesting that there is minimal heat-sink effect near vessels.[5]

Most authors report shorter ablation times in the liver, particularly with large lesions, with microwave than with RF; ablation times are frequently <10 minutes, with many ranging from 2 to 5 minutes depending on number of applicators, lesion size, and power output (►**Fig. 2**). From a practical standpoint, decreased time needed for microwave ablation translates to more efficient use of equipment and personnel and decreased time for patients under general anesthesia, if it is used. In addition, the speed of treatment gives microwaves an advantage for treating multiple lesions during one ablation session.[27]

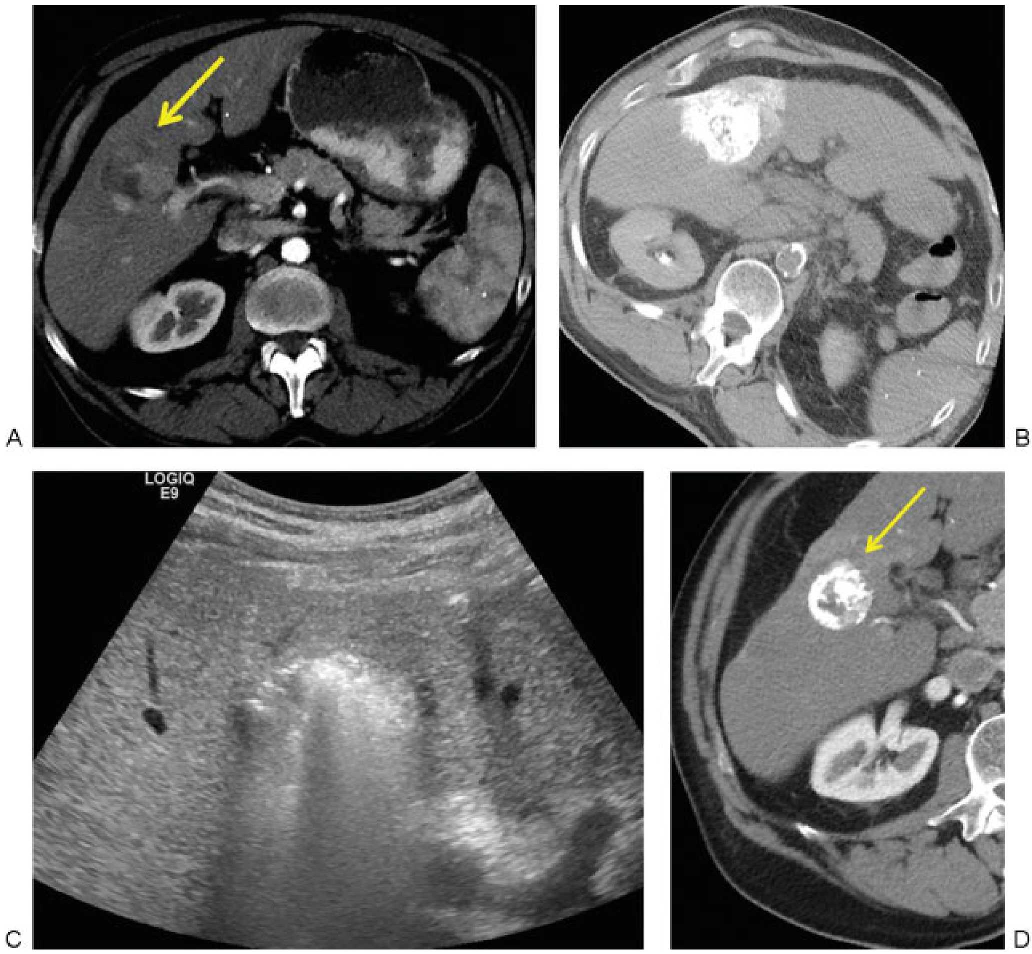

Figure 3 (A) Contrast-enhanced computed tomography (CT) demonstrates a heterogeneously enhancing lesion (arrow) measuring 4.2 × 4.7 cm in the central liver, near the portal venous bifurcation, compatible with hepatocellular carcinoma in this patient with hepatitis C cirrhosis. Given the size, the lesion was treated with combination therapy using (B) transarterial chemoembolization immediately followed by (C) microwave ablation. No evidence of residual tumor was seen on contrast-enhanced CT performed 4 months afterward. In (D) note the residual lipiodol staining (arrow), although the patient did ultimately require repeat combination therapy ~1 year later.

Treatment of Hepatocellular Carcinoma

Clinically, even with early-generation microwave ablation systems, microwave ablation was demonstrated in several studies to have equal effectiveness, safety, and survival with shorter ablation times when compared with RF ablation for the treatment of small hepatocellular carcinomas (HCCs).[8,28,29] Dong et al looked at 234 patients who underwent percutaneous microwave ablation, and they demonstrated favorable survival rates without severe complications.[29] Shibata et al performed a randomized prospective comparison of microwave and RF in the treatment of HCC and found no significant difference in the rates of residual or untreated disease.[28] Lu et al retrospectively compared 102 patients who underwent treatment with either microwave or RF ablation, with no significant difference in survival or complication rates between the two groups.[8] This equivalence was seen using early-generation microwave systems, even prior to the availability of more advanced technology.

More recent studies with newer microwave systems have impressively demonstrated the efficacy of microwave ablation in the liver.[8,30–34] Shiomi et al compared percutaneous and laparoscopic-assisted magnetic resonance (MR)-guided microwave ablation in patients with HCC and metastatic disease. The 3-year survival rates of almost 90% were obtained in both groups for patients with HCC (median follow-up: 21 months).[30] Iannitti et al treated 87 patients with both HCC and metastatic disease and found an overall survival rate of 47% (all tumor types) at 19 months.[31] Qian et al prospectively compared microwave and RF ablations in treating 42 patients with small HCCs, and they found that microwave ablation produced significantly larger ablation zones with complete ablation rates and local tumor progression rates similar to RF ablation.[35] Takami et al compared intraoperative microwave ablation with hepatic resection and found no difference in overall survival rates, disease-free survival, or local recurrence rates in patients with fewer than three lesions, all <3 cm.[36] Jiao et al treated 60 patients with 96 tumors (mean size: 3.2 cm) with complete ablation of 96% of tumors <3 cm and local tumor progression in 5% of cases.[37]

Preclinical data have suggested that microwave ablation, particularly with the use of multiple applicators, may be effective in the treatment of larger tumors (>3 cm).[12,13,38,39] Tumors >3 cm have historically been problematic for RF

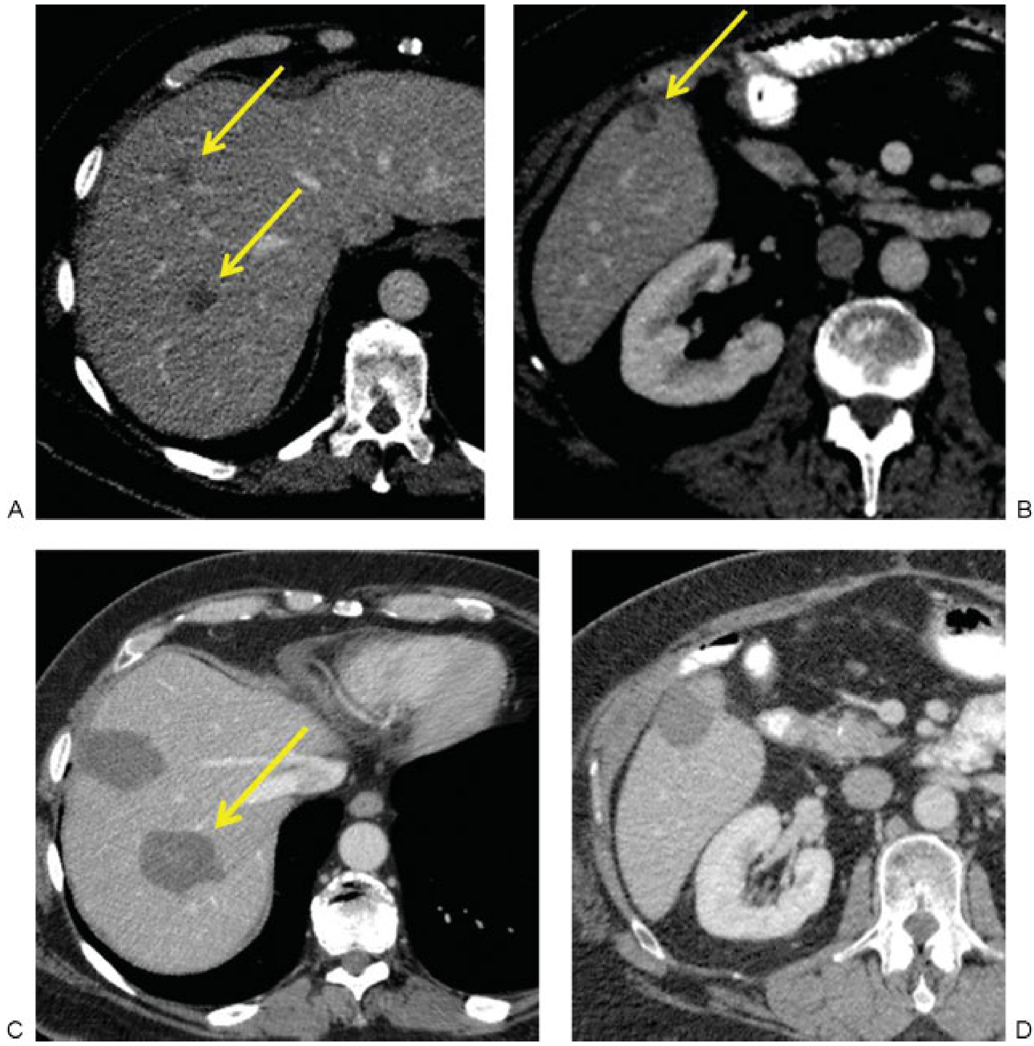

Figure 4 (A, B) Contrast-enhanced computed tomography images demonstrate three small low attenuation hepatic lesions compatible with metastatic colorectal cancer (arrows), with the largest measuring 14 × 17 mm (posterior lesion, A). (C, D) Postablation images demonstrate ablation zones encompassing the lesions with the largest ablation zone (arrow, C) measuring 5.2 × 3.6 cm.

ablation, with a significantly increased risk of local tumor progression.[40–42] However, the larger ablation zones obtainable with microwave ablation could potentially make these tumors more consistently treatable. For example, Brace et al demonstrated ablation zones with mean diameters up to 6.5 cm using three 17-gauge microwave antennas spaced 3 cm apart in an in vivo porcine model.[12] Strickland et al used variable times and power outputs ranging from 36 to 200 W in an in vivo porcine liver model, and they demonstrated ablation zones ranging from 3 to 6 cm in diameter. Ablation zones were produced very rapidly, (i.e., within 3 minutes).[38]

Early clinical data, again with first- or second-generation microwave technology, has supported the hypothesis that microwaves may be more effective against larger tumors than other ablation techniques.[27,39,43–45] For example, Yu et al treated four patients with HCCs >6 cm in diameter, and in two to three sessions achieved complete ablation of three of the four lesions.[43] Yin et al treated patients with medium and large hepatic tumors. Although microwave showed a trend toward less local recurrence and larger ablation than for a similarly sized HCC (96% microwave, 90% RF; $p = 0.288$), the differences were not statistically significant.[46] However, larger tumors still show higher rates of treatment failure in some series. Veltri et al treated 19 lesions in 15 patients with a mean diameter of 47 mm and had treatment failures in 60% of cases, with lesion diameter inversely associated with complete ablation.[47] In many cases, combination therapy including intra-arterial treatment followed by ablation may improve efficacy and survival for larger tumors (►**Fig. 3**).[48]

Treatment of Metastatic Disease

Early clinical studies have suggested microwaves are effective in the treatment of colorectal hepatic metastatic disease, which requires a larger ablation margin and, therefore, a larger ablation zone than for HCC (►**Fig. 4**).[49,50] Shibata et al prospectively randomized 30 patients with multiple metastatic colorectal tumors to microwave ablation or surgical resection and identified no significant difference between the 1-, 2-, and 3-year survival rates, with less blood loss in the microwave group.[50] Ogata et al treated 102 unresectable

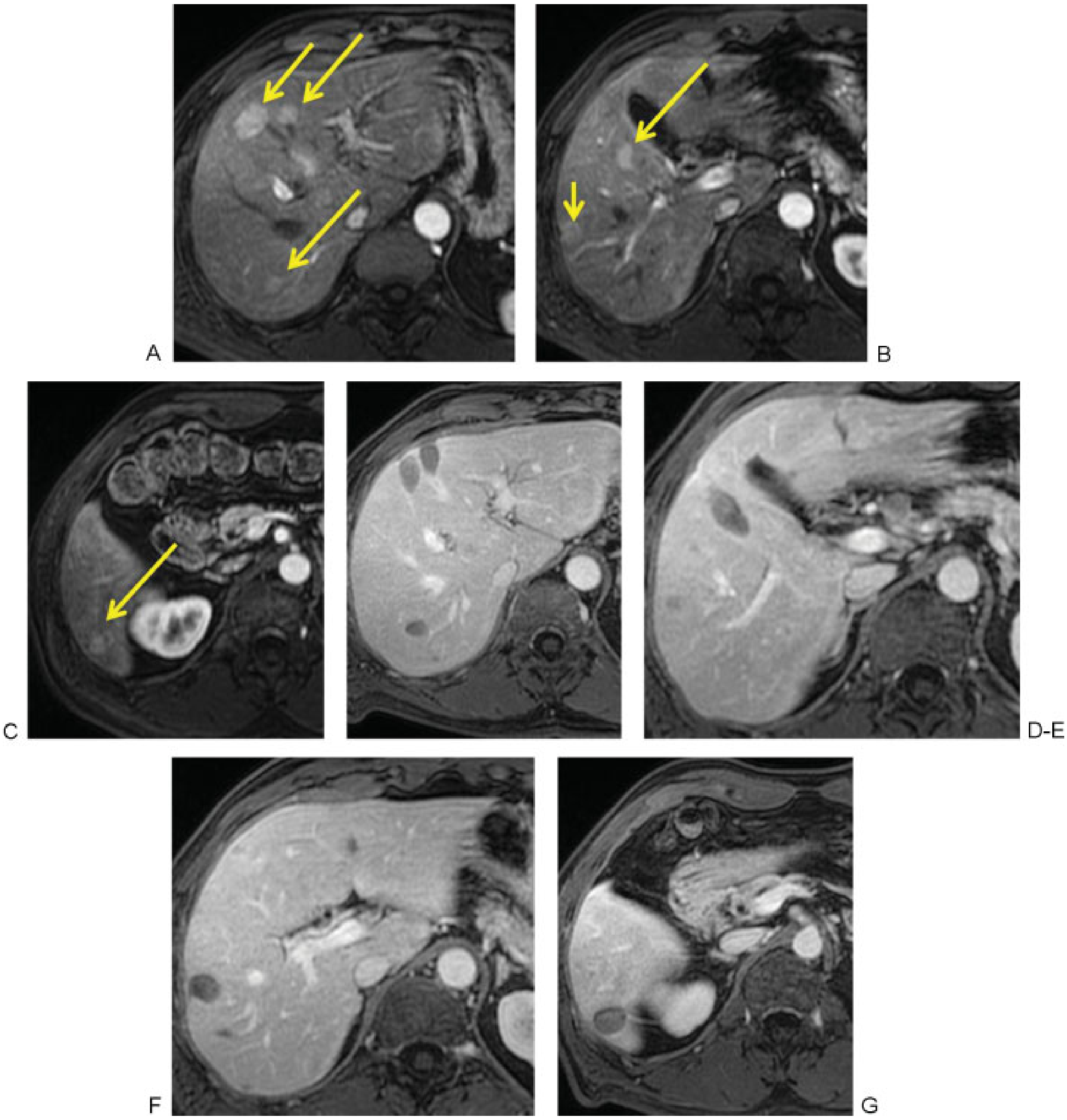

Figure 5 (A–C) Contrast-enhanced T1-weighted magnetic resonance images demonstrate multiple arterially enhancing lesions throughout the liver (arrows) in this patient with metastatic carcinoid and symptoms of refractory diarrhea. (D–G) Contrast-enhanced images obtained 6 months after microwave ablation of multiple lesions demonstrate corresponding low signal intensity ablation zones at sites of prior tumor without residual enhancement. The patient's symptoms improved dramatically postablation.

Figure 6 Contrast-enhanced (A) transverse and (B) coronal computed tomography images following ablation demonstrate a large and long ablation zone extending into the body wall (arrow, A) and abutting the gallbladder (arrow, B). (C) Follow-up image demonstrates hepatic abscess containing gallstones (arrow) due to gallbladder injury with gas seen in the gallbladder lumen (star) and tracking into the body wall. Case courtesy of Franca Meloni, MD, Ospedale Valduce Radiology Department, Como, Italy.

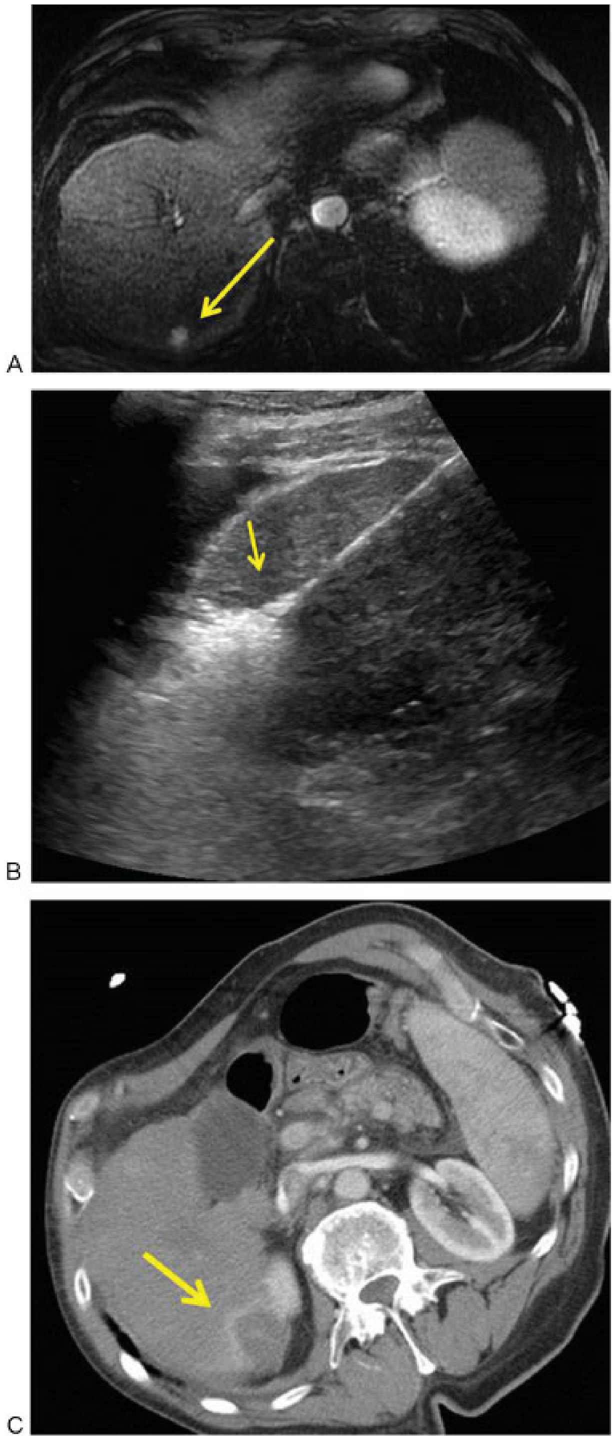

Figure 7 (A) Preablation magnetic resonance imaging demonstrates a small focal lesion along the posterior right lobe (arrow). Given the small size of the lesion and the position abutting the hepatic capsule, an applicator producing shorter, rounder ablation zones was selected (Precision probe, NeuWave Medical, Madison, WI). (B) The lesion was treated with a single applicator for 2 minutes and 30 seconds at 65 W, with steam cloud seen on ultrasound (arrow). (C) Postablation contrast-enhanced computed tomography demonstrates a very round ablation zone (arrow).

colorectal metastatic lesions, with a high local control rate of 95% over a median follow-up of 33 months.[51] However, new hepatic lesions or extrahepatic recurrence occurred in 78% of patients, and median survival time was 43 months. Although, as with RF, there are limited data regarding microwave ablation for other types of metastatic disease, it could be applicable to selected patients with: metastatic neuroendocrine tumors, particularly those in need of symptom control (►**Fig. 5**); selected patients with oligometastatic disease from primary tumors such as breast cancer; and selected patients with oligometastatic disease from other primary tumors with limited systemic treatment options. Further study of microwave treatment of metastatic lesions is needed.

Disadvantages of Microwave

Microwave power is inherently more difficult to generate and deliver safely and efficiently when compared with RF. This is primarily due to the fact that microwave energy is transmitted in coaxial cables that are larger in diameter, more cumbersome, and more prone to heating than the simple wires used in RF ablation. Decreased cable surface area leads to increased power loss and cable heating. Because one of the primary advantages of microwave is the ability to deliver large amounts of power, the technical hurdles to distribute this power to tissues without significant cable and shaft heating must be overcome before this advantage can be fully realized. A robust active shaft cooling mechanism can mitigate many of these risks and is imperative to high-power delivery. A large clinical study comparing cooled with noncooled antennas in a cohort of 1136 patients showed that use of the cooled-shaft antenna led to fewer treatment sessions and fewer major procedural complications.[52]

Although the technology has continued to improve, some currently available microwave systems continue to face technical limitations. Major limitations of some systems include low power, shaft heating, large diameter probes (13 to 14 gauge), and long (up to 8 cm in some cases) and relatively thin (1- to 2-cm) ablation zones that have limited clinical application (especially in small bone lesions such as osteoid osteomas and solid organ surface lesions) (►**Fig. 6**). Similarly, there is still some unpredictability regarding the size and shape of the zone of ablation that may be related to technical factors. However, several very promising new systems have emerged in recent years, and overall microwave ablation complication rates have compared favorably with other ablative techniques (RF, percutaneous ethanol ablation) as shown in a large meta-analysis by Bertot et al.[53] One microwave system has created an applicator that creates shorter, rounder ablation zones to help combat these technical limitations (►**Fig. 7**).

The University of Wisconsin Experience

Between December 2010 and March 2012, our ablation group at the University of Wisconsin treated 58 patients with 96 hepatic malignant lesions utilizing microwave ablation. This included 62 HCCs and 34 metastatic lesions (13 carcinoid, 5 colorectal, 5 sarcoma, 4 choroidal melanoma, 3 endometrial, 2 renal cell carcinoma, 1 melanoma, and 1 squamous cell carcinoma). A total of 62 HCCs were treated in 44 patients in 47 sessions with an average tumor diameter of 2.3 cm (range: 0.5

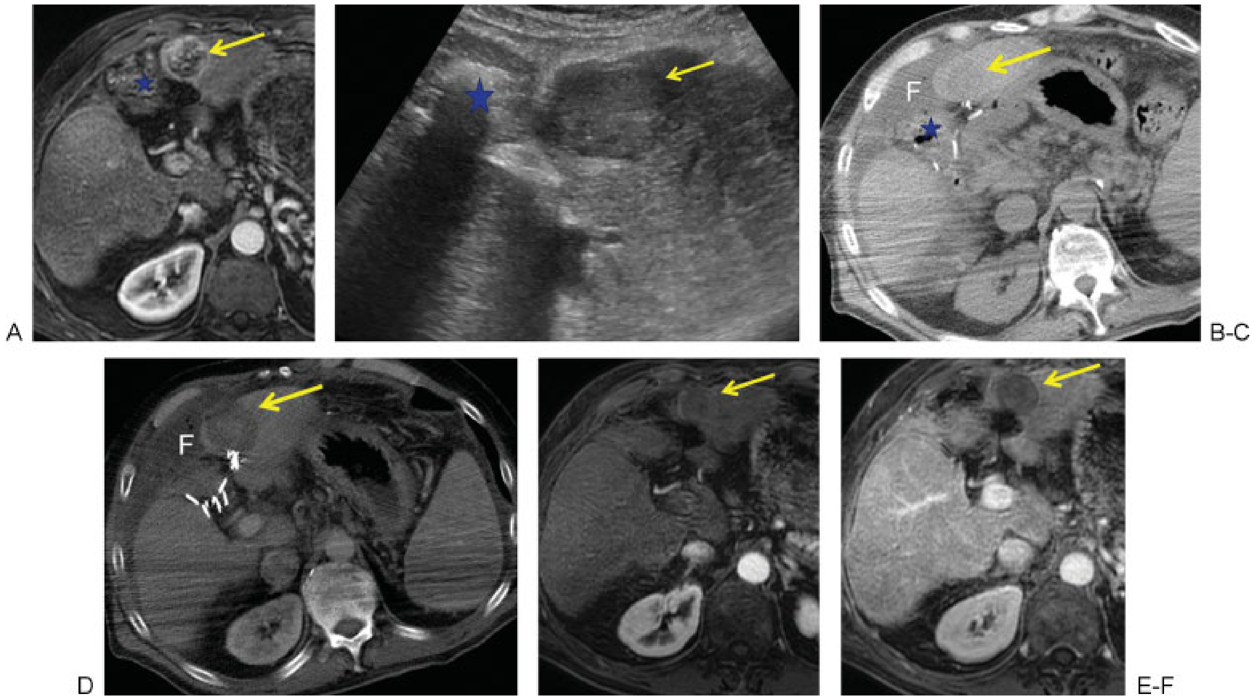

Figure 8 (A) Contrast-enhanced T1-weighted magnetic resonance (MR) image demonstrates an arterially enhancing lesion (arrow) in a cirrhotic liver consistent with hepatocellular carcinoma that closely abuts the colon (star). (B) Gray scale ultrasound image redemonstrates the proximity of the tumor (arrow) to the colon (star). (C) Noncontrast intraprocedural computed tomography (CT) image following infusion of 5% dextrose in water (F) demonstrates displacement of the colon (star) away from the vaguely seen tumor (arrow). (D) Immediate postablation contrast-enhanced CT demonstrates a buffer of fluid (F) around the ablation zone (arrow). Six-month follow-up contrast-enhanced (E) arterial and (F) portal venous phase MR images demonstrate the ablation zone with no residual enhancement (arrows).

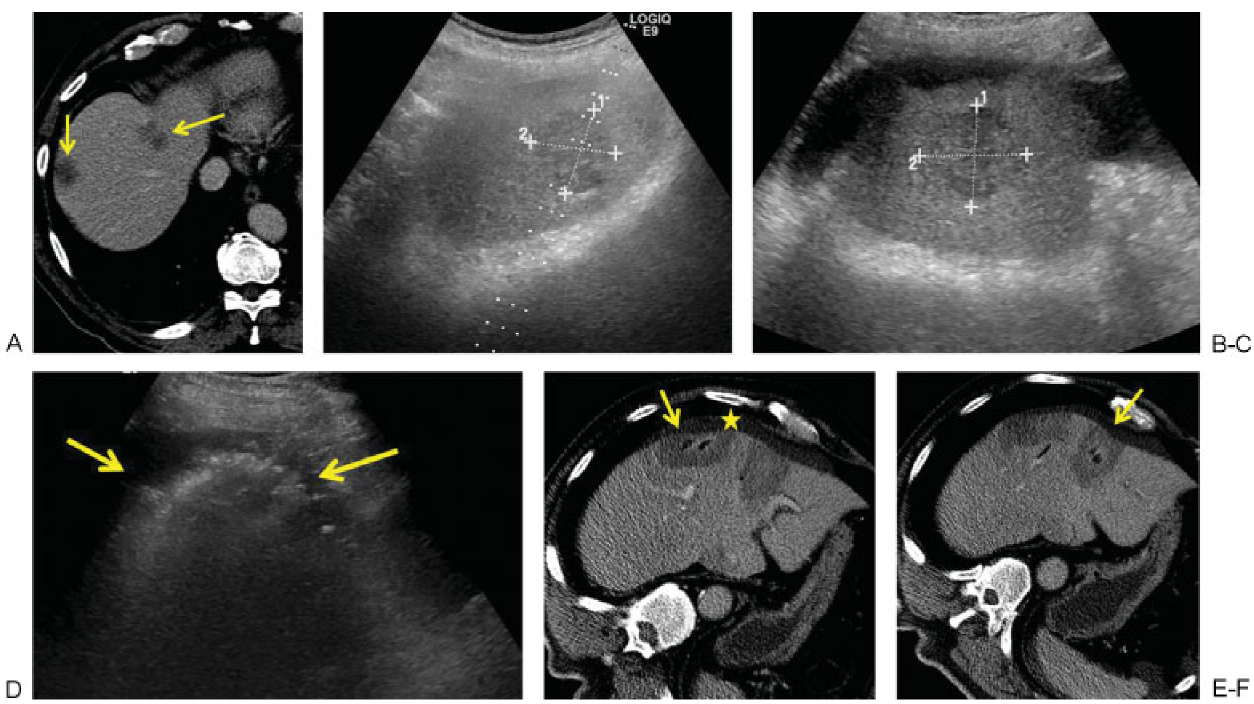

Figure 9 (A) Contrast-enhanced computed tomography (CT) image demonstrates two low attenuation lesions (arrows) abutting the diaphragm near the hepatic dome in this patient with metastatic colorectal cancer. (B) Initial grayscale image of the more lateral and superior lesion is somewhat limited, but there is improved visualization on (C) ultrasound following infusion of 5% dextrose in water (D5W) around the liver. The D5W also serves to protect the diaphragm from the growing ablation zone (arrows, D). (E, F) Postablation CT images demonstrate the ablation zones (arrows) encompassing the tumors, with D5W (star) surrounding the liver protecting the diaphragm. This 82-year-old patient had no postprocedure pain and was discharged the following day.

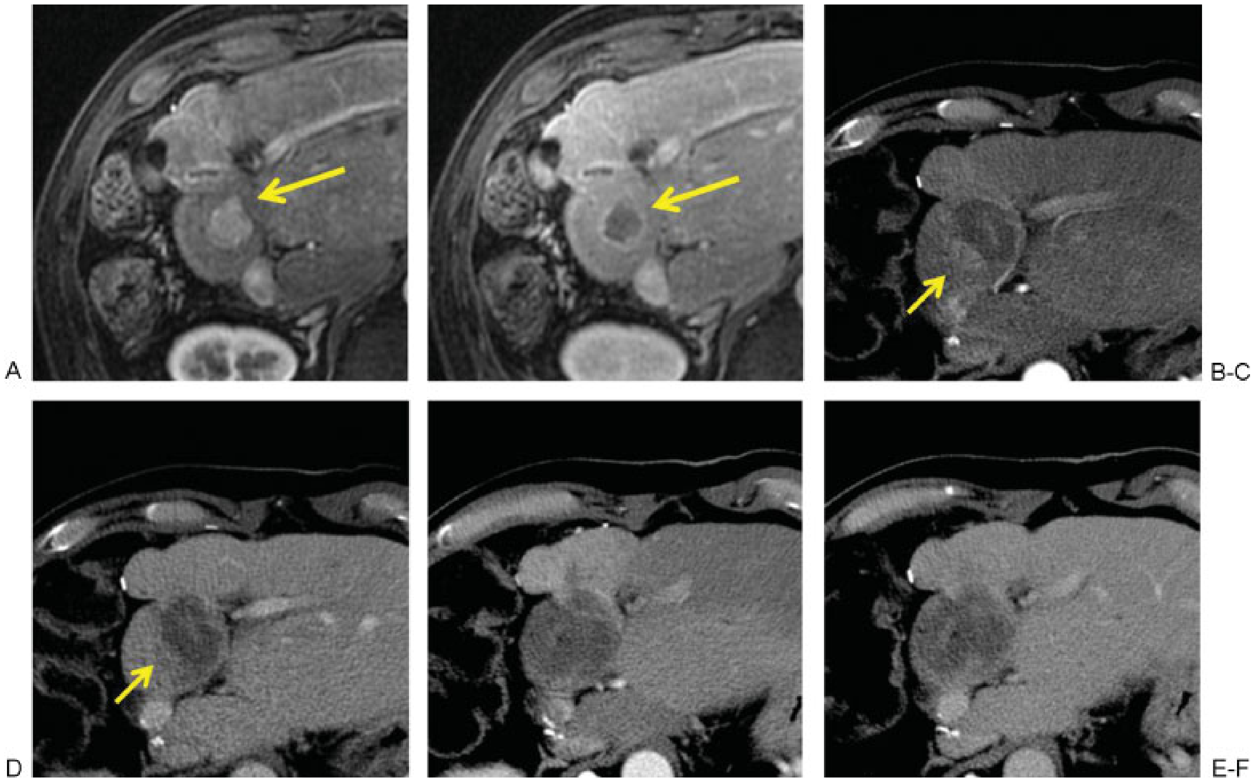

Figure 10 Preprocedure T1-weighted postcontrast magnetic resonance (MR) images in the (A) arterial and (B) portal venous phases demonstrate an isolated arterially enhancing lesion with washout, compatible with hepatocellular carcinoma (HCC) (arrows) in a patient with a history of hepatitis B virus, HCC, and prior resection, ablation, and transarterial chemoembolization. Immediate postablation (C) arterial and (D) portal venous computed tomography (CT) images demonstrate residual enhancement with washout (arrows) along the right margin of the ablation zone. This allowed the opportunity of additional ablation along this margin, with repeat contrast-enhanced biphasic CT (E, F) demonstrating subsequent coverage of this site.

to 6 cm). Local tumor progression at a median 6-month follow-up occurred in four cases (6.5%), with three only noted at explant pathology and one noted on 1-month follow-up imaging. Overall, 34 metastatic lesions were treated in 14 patients in 14 sessions with an average diameter of 2.5 cm (range: 0.8 to 6 cm). In this population, there was no local tumor progression at 5-month median follow-up (Ziemlewicz et al, oral presentation, World Conference Interventional Oncology 2012).

The University of Wisconsin Approach

Most of the referrals originate from one of two multidisciplinary conferences that include cases of either primary hepatic malignancy or metastatic disease. We also receive direct referrals from oncologists and oncologic surgeons. A nurse dedicated to the ablation program coordinates the preprocedure work-up that includes a planning ultrasound used to identify the lesion(s), determines the approach and need for adjunctive maneuvers, and explains the procedure in detail and obtains informed consent for the procedure. All procedures are performed by one of four abdominal imaging radiologists. A weekly meeting involving available radiologists, trainees, nurses, and technologists is utilized to preview cases for the upcoming week to ensure that appropriate equipment is available and to problem-solve potentially difficult cases in consensus.

Our standard is to perform percutaneous microwave ablations in a dedicated interventional computed tomography (CT) suite with the patient under general anesthesia. Although not all groups use this approach, we use it to optimize patient comfort during prolonged procedures in which very hot temperatures are generated and to enable more controlled breath holding, which decreases movement of the target during probe placement and ablation. Ultrasound is used for antenna placement, with the rare lesion not visualized with ultrasound targeted by CT fluoroscopy. When necessary, a dedicated noncontrast CT is performed to confirm antenna placement or evaluate proximity to nontarget structures (predominantly bowel). The ablation is monitored in real time with ultrasound, allowing determination of appropriate coverage in the near field and monitoring for extension of ablation to nontarget structures. For lesions in proximity to nontarget structures, hydrodissection is utilized to create a buffer (►**Fig. 8**). For lesions abutting the diaphragm, hydrodissection is also used as a buffer to prevent postprocedural pain for diaphragmatic burn as well as improve visualization of the lesion (►**Fig. 9**). At the completion of the procedure, a contrast-enhanced CT is performed while the patient is still under anesthesia so any incompletely treated tumor can be retreated in the same session (►**Fig. 10**). Following the procedure, all patients are admitted overnight by the referring physician or our hospitalist service for observation.

For selected HCCs that are large (>4 to 5 cm), ill defined, or not well visualized with ultrasound, patients undergo combination transarterial chemoembolization (TACE) followed by ablation. At our institution the chemoembolization is performed by a vascular interventional radiologist and the ablation by an abdominal radiologist. Although we have performed these procedures in the same session, our preference is to have the patient undergo TACE initially and return for percutaneous ablation 2 to 3 weeks later. This limits procedure time, provides recovery time for each procedure, and allows washout of Ethiodol from noninvolved liver, improving ablation targeting (►**Fig. 3**).

Our standard follow-up imaging sequence for hepatic malignancy ablation is contrast-enhanced CT or magnetic resonance (MR) imaging at 1, 3, 6, 9, 12, 18, and 24 months following ablation. If local progression or new lesions are noted at follow-up, the case is discussed at one of our interdisciplinary conferences, where the determination is made for retreatment with ablation versus another treatment modality.

Conclusion

Continued improvement in microwave ablation technology has made this modality increasingly applicable in the clinical setting. It has a variety of advantages over other heat-based treatment modalities, such as RFA, including shorter ablation times and generation of larger ablation zones, with comparable efficacy and complication rates.

Disclosures

Fred T. Lee, Jr., Chris Brace, and J. Louis Hinshaw are stockholders at NeuWave Medical, Madison, WI. Fred Lee is also a board director at NeuWave Medical. Meghan Lubner receives grant funding from GE Medical.

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