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Updates in Interventional Radiology

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24/7 Consultation

Radiofrequency Ablation of Hepatic Tumors

Scope of the Problem

The liver is the most common location for solid organ metastases. Of patients who succumb to any type of cancer, up to 50% will die with from liver metastases. The most common primary tumor with hepatic metastatic involvement is gastrointestinal in general and colorectal specifically. Up to 55% of patients with a primary colorectal cancer (CRC) have hepatic metastases. Mean survival for untreated colorectal metatases is 6-13 months. With the most effective chemotherapy, mean survival climbs to 20 months. Other primary malignancies that frequently metastasize to liver include neuroendocrine, ovarian, pancreas, stomach, liver, breast and melanoma.

For liver-only colorectal metastases, surgical resection increases 5-year survival from 0-1% to 31-71%. A recent study also showed a 10-year survival rate of 60%. Unfortunately, only 5-20% of patients with liver only CRC metastases are candidates for surgical resection due to medical comorbidities or tumor distribution, location and burden. There is also a significant perioperative morbidity for liver resection and 2-10% mortalitiy. Breast cancer with liver only metastases has shown favorable 5-year survival benefit for surgical resection (rates of 18-61%) in carefully selected patients. Focal therapy or resection has not shown an advantage in survival for other hepatic metastases and is reserved for liver-only metastases and for symptomatic relief in the treatment of neuroendocrine tumors.

Hepatocellular carcinoma (HCC) is now the fifth most common cancer worldwide and the third leading cause of cancer deaths with below 10% 5-year survival in the United States and Europe. Hepatic resection is the gold standard for treatment but up to 80% of HCC patients are not candidates usually due to poor hepatic reserve, tumor location or overall tumor burden. Additionally, recurrence rates within 5 years are as range from 70-85%. Liver transplant offers a significant survival advantage but is also limited to a select few due to selection criteria, donor availability, and cost.

Image-guided Therapies

The role of Interventional Radiology in management of primary and metastatic liver disease has grown tremendously over the last decade with the development and refinement of image guided local and locoregional therapies. This subset of therapies require imaging guidance for tumor targeting and response assessment and include both various catheter-based and percutaneous ablative techniques. These techniques are described as minimally invasive and, up until recently, have been used for palliation but are now being increasingly used with the intent to cure. Locoregional therapies are now widely used to supplement the traditional arms of cancer treatment: surgery, radiation oncology, and medical oncology.

Percutaneous ablative techniques, often termed image-guided tumor ablation (IGTA), have been applied to various locations of the body for treating a variety of solid tumors inducing direct tumor death by application of temperature changes or chemicals. IGTA has been applied most commonly to hepatic primary malignancies but also have been shown to be effective in treatment of a variety of other solid primary and metastatic tumors including renal, bone, prostate, lung, breast, and adrenal tumors. (figure 1) IGTA has expanded the pool of patients with primary and metastatic liver tumors that can be safely and effectively treated. IGTA can be used in conjunction with chemotherapy to improve palliation and reduce tumor burden, to bridge a patient to liver transplant and even complement surgical resection. IGTA has also been used to "down-stage" a patient and allow for eventual surgical resection or even transplant.

Radiofrequency Ablation of Hepatic Tumors

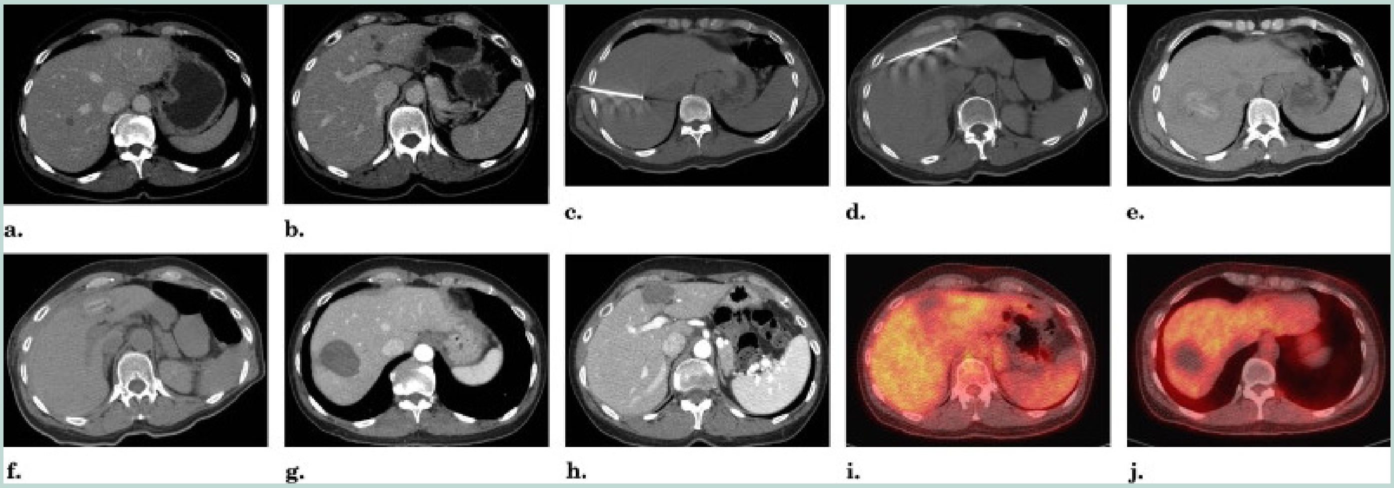

Figure 1 (a,b) Fifty-year-old woman with adenocarcinoma of the sigmoid colon presents with two hepatic metastasis. (c,d) Both lesions were treated with a cluster RF ablation electrode during same session. Immediate postprocedural imaging shows the expected internal hyperattenuation from denatured proteins. (e,f) The area of ablation is much larger than the original metastasis. (g–j) One-year follow-up shows expected hypoattenuating region encompassing the prior metastatic focus with at least 1 cm margin and no FDG avidity, consistent complete treatment. Source: Journal of Vascular and Interventional Radiology 2010; 21:S214-S222 (DOI:10.1016/j.jvir.2010.01.046)

Radiofrequency Ablation (RFA) Image-Guided Tumor Ablation

Radiofrequency has had widespread medical application since the introduction of the Bovie knife. First applied in the treatment of liver tumors in the early 1990's, large numbers (tens of thousands) of liver RF ablations have been reported to date worldwide. Hundreds of journal articles have been published confirming the efficacy of RFA in treating HCC, colorectal metastases, and even other hepatic metastases.

Radiofrequency is the 3 Hz to 300 GHz portion of the electromagnetic spectrum that includes the visible light spectrum, infrared radiation, and x-rays. At the relatively low frequencies (<1MHz) used in RFA, radiofrequency waves cause heating and thermal ablation of a defined volume of tissue depending on local environment and tissue type.

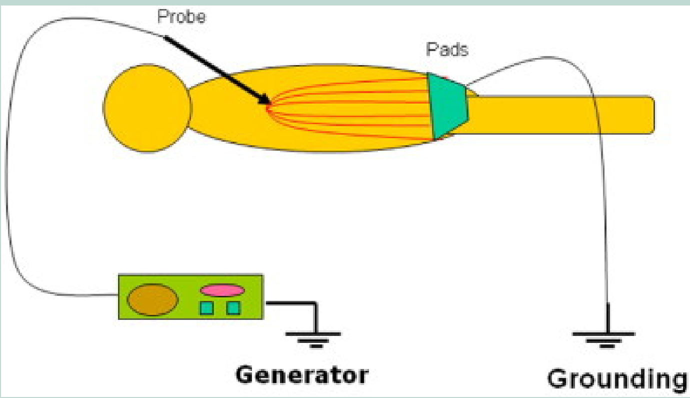

Figure 2 An electrical field is established by inserting the RF probe into tissue parenchyma which acts a cathode and placement of a large grounding (dispersing) pad, usually on the thigh, which then acts as the anode completing the circuit via a RF generator. The patient becomes part of the circuit. (Figure 2) The RF probe itself is insulated with the exception of a variable length of the tip. There is high energy flux around the tip due to a small cross section diameter and tissue damage is limited to the part of the circuit that surrounds the electrode tip. Source: Journal of Vascular and Interventional Radiology 2010; 21:S179-S186 (DOI:10.1016/j.jvir.2010.04.008)

The RF electrode is actually not the source of the heat but rather frictional heat is generated by dipole molecules (mostly water) and ions that surround the tip in an electrical field that oscillates with the RF current. (Figure 2) Heat is generated due to frictional energy loss between adjacent dipoles and ions. Heat is also conducted to surrounding tissue away from the RF probe. The goal of RFA is "thermal coagulation necrosis" in a defined volume of tissue by producing local tissue heating. The goal is to treat the tumor and a surrounding 5-10 mm "surgical" margin of normal tissue. Between 55°C and 100°C, there is near instantaneous protein denaturization and coagulation that irreversibly damages key cytosolic and mitochondrial enzymes and nucleic acid-histone protein complexes. The end result is irreversible thermal damage and most often, although not always, cell death. Cell death occurs within 2 seconds at 55°C. At 100°C, tissue desiccation and charring occurs that acts as an insulating sleeve around the RF probe limiting further transmission of electrical and thermal energy. The objective is to maintain a temperature greater than 60°C but remain below the level that charring and vaporization occurs for at least 4-6 minutes. (figure 3)

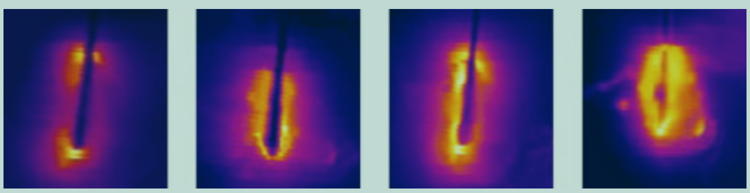

Figure 3 Progression of a radiofrequency ablation shown by color representation of surrounding slow thermal changes without charring. Source: Journal of Vascular and Interventional Radiology 2010; 21:S179-S186 (DOI:10.1016/j.jvir.2010.04.008)

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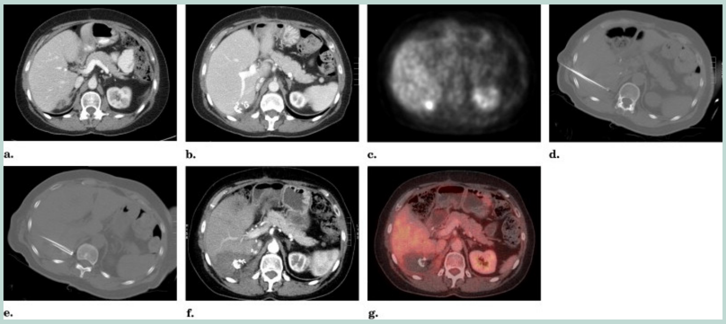

Figure 4 (a) Seventy-year-old woman who presented with a solitary liver metastasis after colon resection for colonrecral carcinoma. (b,c) The patient had this lesion surgically resected, but there was evidence of local progression on follow-up PET/CT. (d,e) This area was treated with multiple overlapping radiofrequency ablations with a cluster probe. (f,g) The 18-month follow-up PET/CT continues to show large hypoattenuating ablation zone without fluorodeoxyglucose avidity, consistent with local treatment response. Source: Journal of Vascular and Interventional Radiology 2010; 21:S214-S222 (DOI:10.1016/j.jvir.2010.01.046)

Does radiofrequency ablation work?

Because surgical resection of colorectal liver metastases has been shown to be so effective, there are no randomized trials comparing RFA to surgery. If a patient can go to surgery, the patient has a liver resection. RFA has largely been evaluated in the subset of patients who are not candidates for surgery. A recent meta-analysis by Mulier et al of 8 independent studies comparing 5 year survival ranged from 14-55%, which approaches that of surgical resection. (figure 4) Number of tumors per patient ranged from 1-5 with a range in diameters from 0.3-17.4 cm.

As would be expected, size and number of the tumors have a significant impact on outcomes. A recent large study of 309 patients published in 2009 looking at 5-year survival following RFA for hepatic colorectal metastases showed a drop from 40% to 34% comparing selection criteria from no more than 3 tumors measuring less than 3.5 cm to no more than five tumors measuring less than 5 cm. Size and number of the tumors were found to be the most important factor following the presence or absence of extrahepatic disease. Other factors found to significantly impact survival included type of chemotherapeutic agents used in conjunction with RFA with bevacizumab and cetuximab having positive survival impact.

There is limited published data evaluating RFA in treating other hepatic metastases. A recent publication documenting 24 patients with hepatic metastases from breast cancer showed local control of 96% of lesions measuring less than 3cm in size and that 63% of patients remained disease free from 4-44 months of follow-up. Overall survival was not impacted.

RFA for the treatment of hepatocellular carcinoma (HCC) has also been strenuously evaluated including two well-done randomized controlled trials comparing RFA to surgical resection of small to medium-sized tumors (up to 5 cm) which both demonstrated equivalent overall or disease free survival rates. Another 3 well-matched cohort retrospective studies showed the same conclusion. (figure 5) Additionally, complication rates and perioperative mortality were significantly higher in the operative groups (11-56% and 2-4%, respectively) compared to the RFA arms (1-10% and 0-0.3%, respectively). Complete ablation is possible in small to medium tumors (up to 5 cm) 80% of the time in one session and 90% of the time in 2 sessions. Local progression rates are low (1-12%) but overall 5-year survival rates remain in the range of 40-58% due to the nature of HCC and the comorbidities of patients suffering with HCC.

Complications and Patient Toleration

The procedure is most frequently done as an outpatient procedure using either CT or ultrasound guidance with 2-4 hours of post-procedure observation. The procedure is usually done with IV sedation but can be done with general anesthesia if required either for pain control or in patients with significant comorbidities. At our institution, preprocedural antibiotics are also administered (Cefazolin 1gm IV). The procedures can be lengthy depending on size and number of lesions but are usually well tolerated with conscious sedation. Most patients go home the same day and recovery time is limited. Most patients are back to normal activities within a few days if not the next day. Usually, chemotherapy is discontinued one week before RF and re-started 2 weeks following the procedure.

RFA has been shown to be safe. Mortality rates of various trials ranges from 0-0.3% compared to surgical resection 2-10%. Major complication rates are reported between 0.5-3%. Bleeding is the most commonly reported complication in most trials followed by abscess formation which is usually seen in patients with diabetes or who have had prior hepatic surgery especially a bilioenteric anastomosis. A trial with 582 patients noted that abscess complicated all procedures in patients with a bilioenteric anastomosis. Other rare but notable major complications include bile duct injury, peritoneal hemorrhage and intestinal perforation. Track seeding is also a known delayed complication but can be limited by indirect tumor puncture (probe traverses normal liver before entering the lesion) and ablating the track as the electrode is removed. Minor complications included persistent pain, pleural effusion, and skin burns at the grounding pad which is becoming more and more uncommon with the latest generation of equipment.

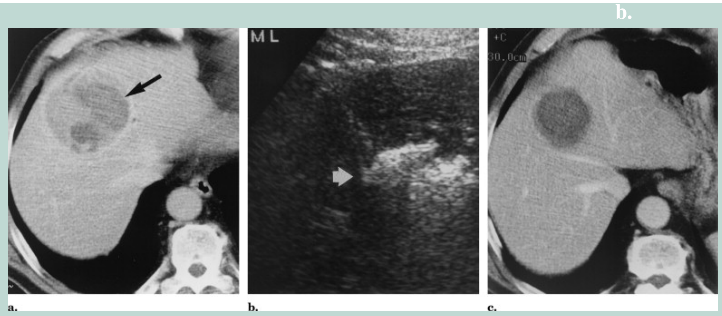

Figure 5 (a) Prepocedural HCC (dark arrow) within the right lobe of the liver with mixed enhancement and density. (b) Intraprocedural ultrasound image with probe placed within the lesion. Echogenic nitrogen bubbles (white arrow) develop within the lesion. (c) 3 month follow-up CT demonstrates lack of enhancement, uniform low density, and decreasing size.

Patient follow-up is performed in conjunction with the primary and referring physicians after discharge. In addition to routine follow-up of any tumor markers, our specific protocol for imaging consists of a dual-phase contrast-enhanced CT scan (or MRI) immediately after ablation to establish a baseline, and then every three months thereafter. PET-CT is used in PET positive tumors such as colon cancer. If the patient has no evidence of recurrent disease at one year, routine surveillance is resumed. Strict follow-up is critical as residual or recurrent tumor should be detected when it remains small. Another simple percutaneous RFA could be performed without much additional risk to the patient.

Conclusion

Radiofrequency ablation in the treatment of hepatocellular carcinoma and select hepatic metastases is a proven addition in the toolbox for treating cancer. It provides options to patients who may otherwise have none. It has been shown to be safe and effective. There is high technical success rates for the procedure and, because it is so minimally invasive, can be repeated to treat residual disease or new tumors as they arise. The procedure itself is well tolerated and patients are quickly back to their normal routine. For additional information, questions or consultation please contact Utah Valley Interventional Associates at 801-701-6581.

Meet Our Interventional Radiologists

Dr. Asay is fellowship-trained and board certified in interventional radiology. His expertise includes treatment of disorders of the arterial and venous circulation and acute stroke intervention. He also performs spine intervention for pain management, including nerve root blocks, facet injections, epidural injections, and treatment of vertebral body compression fractures.

After graduating from medical school at the University of Utah School of Medicine, he completed a residency in diagnostic radiology followed by further training in vascular and interventional radiology at the University of Arizona Health Sciences Center. He then completed a Certificate of Added Qualification in interventional Radiology. In addition to his medical expertise, Dr. Asay holds an MBA from the Brigham Young School of Management.

Dr. Matthew E. Nokes is fellowship trained in interventional radiology. His expertise includes treatment of disorders of the arterial and venous circulation and acute stroke intervention. Dr. Nokes is skilled in such areas as treatment of acute ischemic stroke and DVT therapy.

After graduating from the Medical School of Wisconsin in Milwaukee, Dr. Nokes completed a transitional year of residency, followed by a radiology residency at St. Luke's Medical Center in Milwaukee. He then completed a fellowship in vascular and interventional radiology at Brown University Medical School, Rhode Island Hospital, in Providence. His professional associations include the Radiological Society of North America, the American Roentgen Ray Society, the American College of Radiology, and the Society of Interventional Radiology.

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