Tumor ablation treatment: A review of modalities

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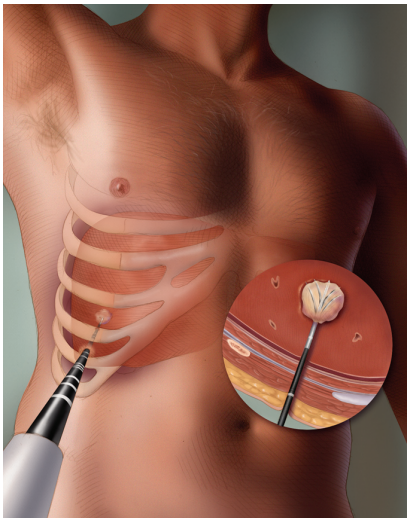
Tumor ablation, the direct local application of chemicals or energy to destroy cancer cells, has undergone rapid development over the past decade and represents an attractive, minimally invasive alternative to surgical resection for liver tumors, colorectal metastatic tumors, and kidney tumors. Energy is delivered directly to tumors to freeze, burn, or chemically destroy cancer cells. Tumor ablation is a promising but young and experimental collection of diverse interventional oncology strategies. Of these modalities, radiofrequency ablation (RFA) is the most widely used; however, even this technique has not been adopted into widespread, routine clinical practice because there have been few high-quality clinical studies of its efficacy.[1]

Ablation has been considered a potential and less expensive, low-morbidity palliative alternative to surgical resection. However, advances in the field have left some authors arguing that ablation, alone or combined with other treatment modalities, may be an established curative strategy for some cancer patients. Ablation is currently used in combination with resection or when complete resection is not feasible.[2]

Ablation may entail open surgical, laparoscopic, or percutaneous procedures, and chemical, thermal, cryo-, radiofrequency, or microwave energy ablation.[2] Although the field is young, potential treatment synergies that may enhance the efficacy of ablation techniques have been identified.[2]



Radiofrequency ablation electrodes focus energy into tumor tissues (insert).

Chemical ablation involving the repeated percutaneous injection of ethanol alcohol or acetic acid appears to be a safe and fairly effective technique for controlling small hepatocellular carcinomas. But the modality is not expected to be adopted as a routine stand-alone clinical practice because other ablative techniques are more effective.[2,3]

Cryoablation is the first ablative modality developed for clinical oncology applications; it involves freezing or inflicting rapid freeze/thaw cycles on tumor cells. Most commonly, liquid nitrogen-cooled cryoprobe rods are placed within a tumor, alternating with rapid tumor tissue thawing via helium or argon gas infusions; the freeze/thaw cycles kill more tumor cells than freezing alone. Cryoablation kills cells directly through cold-protein denaturation and indirectly by absorbing metabolic heat necessary for enzymatic and other cellular functions.[4] Ice crystals form within and between cells, sequestering cellular fluids and rupturing cell membranes; the size of the ice balls that form is determined by the diameter of the cryoprobe needle.[4] *Apoptosis*, or programmed cell death, appears to be triggered among cell populations adjacent to tissues killed by cryoablation.[4]

While thermal ablation (heating tumors to higher than 60°C to denature proteins and DNA) more effectively kills cancer cells, heat gradients near the tumor margins can cause thermal injury to adjacent, noncancerous tissues.[2] Therefore, when tumors occur next to vascular or hepatic biliary anatomies that must be preserved, cryoablation is a superior strategy because the blood stream will remove cold without damaging the local vasculature.[2]

Cryoablation allows real-time monitoring of the ablation zone because iceball formation is readily visualized on ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI).[4] Because nerve cooling is anesthetic, cryoablation is also a less painful procedure than thermal ablation techniques and can be performed without general anesthesia in an outpatient clinic setting.[4] However, cryoablation entails a generally less favorable complication profile than other ablative modalities and is less effective at killing tumor cells; therefore, it is currently under development primarily as a niche modality for tumor ablation near critical vasculature in the liver and renal cell cancers.[2,4,5] Systemic inflammatory cryoshock syndrome is sometimes triggered by extensive cryoablation of large-volume liver tumors and can cause hypotension, multiple organ failure, and bloodstream coagulation.[4] Probes can also cause cracking or fracturing of frozen tumor-adjacent tissue.[4]

Two cryoablation devices are commercially available in the United States: (1) The Percryo System, produced by Healthronics (formerly Endocare) of Austin, Texas, which involves up to eight 17- to 24-mm diameter cryoprobes; and (2) the Galil Medical Cryoablation System, manufactured by Galil Medical in Arden Hills, Minnesota, which uses uniformly-sized 14.7-mm MRI-compatible cryoprobes.

Thermal ablation technologies use focused radiofrequency or, less frequently, microwave energy to burn and kill tumor cells. At 60°C, tissue proteins denature, killing cells. At temperatures higher than 100°C, cells vaporize.[2] However, different tissues conduct heat to different degrees, complicating tumor treatment in heterogenous-tissue organs such as the liver.[2] To ensure the death of all tumor cells, ablated volumes include a margin of presumably healthy tissue around the tumor mass. This heat conduction zone contains a gradient of decreasing temperatures from the 60-degree tumor ablation zone to a marginal 45-degree heat conduction zone.[2]

Radiofrequency ablation involves frictional heat caused by ions released by the conduction of high-frequency currents (460-480 kHz) through target tissue.[2] RFA was first described in the early 1990s for ablation of liver tumors, but tissue temperature effects of radiofrequency energy was first noted in the 1890s. RFA is now the best-studied and most widely used modality for liver tumor ablation.[1] Nevertheless, the technique remains an experimental treatment strategy. Widespread acceptance in clinical practice will require further study via large, high-quality, controlled prospective clinical trials.[1]

Percutaneous RFA electrodes are cathodes that, when combined with dispersing grounding pads carefully positioned on the patient's thighs, create a closed electrical circuit.[1] The cathodic electrodes focus energy in tumor tissue while the large area of grounding pads disperse and dilute current energies delivered to healthy tissues, but skin pad burns can still occur.

Because different tissues conduct electrical currents to different degrees, some tissues—such as blood vessels and bile ducts—disproportionately absorb current, creating heat sinks that can confound planned heating of target ablation zones. This possibility necessitates close follow-up imaging, and in some cases, a repeat RFA with larger treatment volumes—increasing the risk of damage to healthy tissue and resulting patient morbidity. Ablation of tumors larger than 7 cm in diameter is not recommended.[1]

Other challenges, such as the possibility of electrode needle displacement

Continued on page 44

Clinician confidence in RFA exceeds data

Colorectal cancer is the third most common malignancy in the United States and is responsible for 10% of all cancer deaths. Metastatic tumors in the liver occur in half of colorectal cancer cases; however, only 10% to 25% of these tumors are resectable, making metastatic colorectal cancer an attractive application for radiofrequency ablation (RFA).

However, a 2009 American Society of Clinical Oncology (ASCO) review of clinical studies of patients with metastatic colorectal tumors in the liver illustrates the challenge of evidence-based clinical decision-making in a young field such as RFA. Of 468 clinical study articles initially identified by the ASCO team, only 46 were of sufficient quality for inclusion in the ASCO review and represented unique datasets. None of these were randomized, controlled prospective clinical trials. ASCO was therefore unable to develop evidence-based RFA clinical practice guidelines. As is common in clinical trials of cancer treatments, patient reluctance to participate in randomized trials contributes to the paucity of empirical data. Similarly, many clinicians are convinced of ablation's efficacy despite scant evidence and do not consider enrolling patients in randomized clinical trials.

ASCO's limited review of single-arm, retrospective and nonrandomized, uncontrolled prospective trials suggested marked variation in local tumor recurrence and survival rates among patients who underwent RFA. Tumor recurrence rates ranged from 3.6% to 60%, for example, and RFA patients' 5-year survival rates varied from 14% to 55%. The most common major complications of RFA were found to be abscess, hemorrhage, biliary leakage of stricture, pleural effusion, vasculature damage, and grounding pad burns.

Source: Wong SL, Mangu PB, Choti MA, et al. American Society of Clinical Oncology 2009 clinical evidence review on radiofrequency ablation of hepatic metastases from colorectal cancer. *J Clin Oncol.* 2010;28(3):493-508.

and seeding of tumor cells along the insertion path, have not yet been adequately studied. Ultrasound guidance may be compromised by image-disrupting gas bubble formation.

The US Food and Drug Administration (FDA) has approved three commercially-available RFA systems: (1) Valleylab RF Ablation Generator (200W) with Cool-tip Technology (Covidien [formerly Tyco Healthcare Valleylab], Boulder, Colorado), (2) RF 3000 (Boston Scientific, Natick, Massachusetts), and (3) RITA 1500x (Angiodynamics, Mountain View, California).[1]

Microwave ablation aims microwave energy directly into target tissue through interstitial antenna rather than creating a resistive-heating electrical circuit. This modality heats tumor tissue more rapidly than RFA.[6] Microwave is a newer but promising ablation modality. It appears to be less susceptible to heat sink effects, theoretically allowing ablation in tissues not suited for RFA such as lung and bone.[6] Multiapplicator microwave ablation allows simultaneous treatment of multiple tumors. Preliminary clinical studies suggest microwave ablation equals the efficacy and safety of RFA for treatment of hepatocellular carcinomas.[6] Microwave ablation is a new and experimental modality, and only one FDA-approved system is commercially available: the Evident System (Covidien, Boulder, Colorado). ■

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