

Review Articles

Radiofrequency Ablation: Mechanism of Action and Devices

Kelvin Hong, MD, and Christos Georgiades, MD, PhD

Since the first radiofrequency (RF) ablation description in early 1990's for percutaneous tumor ablation, there has been considerable published data on the subject worldwide. An understanding of RF ablation equipment, mechanism of action and its interactions with tissue is critical to avoid complications and improve patient outcomes. There is considerable variability in the way that RF ablation may be performed, and there is a variety of equipment choices. Despite the accumulated data, the desire to more quickly obtain larger zones of ablation has quickly spurred the introduction of several new ablation modalities. However, RF ablation remains the prototypical thermal ablation technique.

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Abbreviations: EM = electromagnetic, RF = radiofrequency

THE application of radiofrequency (RF) energy and its thermal effects on tissue were described in 1891 by d'Arsonval (1), who reported how RF waves passing through tissue were observed to cause increased local tissue temperature. RF energy became incorporated into mainstream modern medicine via the advent, at first, of the Bovie knife (1928), used for both cauterization and cutting tissue by varying the RF current. A pulsed current would cause cauterization of tissue, whereas a more continuous current caused cutting of tissue. The first generation Bovie knife was in fact a crude monopolar RF electrode with surface adhesive skin pads closing off the circuit. McGahan et al (2) and Rossi et al (3) independently reported in 1992 the use of RF energy for liver tu-

mor ablation. Early tissue ablation was performed with a modified Bovie knife, with the insulated portion up to the tip.

Since the early RF description, large numbers of liver RF ablations have been reported to date worldwide. Acceptance into mainstream medicine has been encouraging, although widespread use and acceptance as standard of care remains elusive and will hinge on production of high-quality clinical data. On the technical front, RF ablation will need to deliver larger tumor ablation volumes in a timely manner. The options for percutaneous tumor ablation has considerably evolved, with the introduction of several other thermal modalities, including microwave, cryoablation, high intensity-focused ultrasound scan, irreversible electroporation, and interstitial laser. These new ablative techniques hold great appeal, and it is natural to consider investigating "new" thermal treatment options. However, to date, the evidence suggests that RF ablation should remain the prototypical ablation device, particularly for lesions < 3 cm and should still be the cornerstone of any ablation practice. It is the most frequently used ablative technique and it has the longest track record. Familiarity with RF ablation mechanism of action, clinical rationale, and techniques re-

mains critical to any successful ablation practice.

PHYSICS AND PRINCIPLES

RF refers to the part of the electromagnetic (EM) spectrum bounded by the frequencies of 3 Hz and 300 GHz (Fig 1). EM radiation includes (in addition to radio waves), infrared radiation, the visible spectrum, ultraviolet radiation, x-rays and γ -rays, in increasing frequency. Although the EM radiation spectrum has been divided into many other subtypes (for example, ultra high-frequency radio waves [UHF]), these divisions are arbitrary and they differ only in the frequency of particle oscillation.

Even though all EM radiation subtypes have the same basic physical properties, their interactions with matter can be very different and depend on their frequency and the type of matter. Radiofrequency waves as applied in medicine cause thermal ablation of a defined volume of tissue. The RF ablation electrode acts as the cathode of an electrical circuit, which is closed by the application of dispersing pads on the patient's thighs (Fig 2). Because of the small cross-sectional area of the electrode tip, there is a very high energy flux around it. On the other hand, the large cross-sectional area of the ground-

From the Division of Interventional Radiology, Johns Hopkins Medical Institutions, 600 N Wolfe St, Blalock 544, Baltimore Maryland. Received November 26, 2009; final revision received April 19, 2010; accepted April 29, 2010. **Address correspondence to** K. H.; E-mail: Khong1@jhmi.edu

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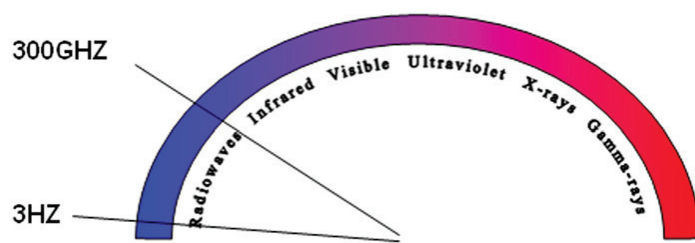


Figure 1. The EM spectrum is modeled as a continuous frequency spectrum of vibrating massless energy quanta. The EM radiation is composed of both an electric and a magnetic field oriented at 90° to each other. The EM radiation, whose frequency is between 3 HZ and 300 GHz, is defined as radio waves.

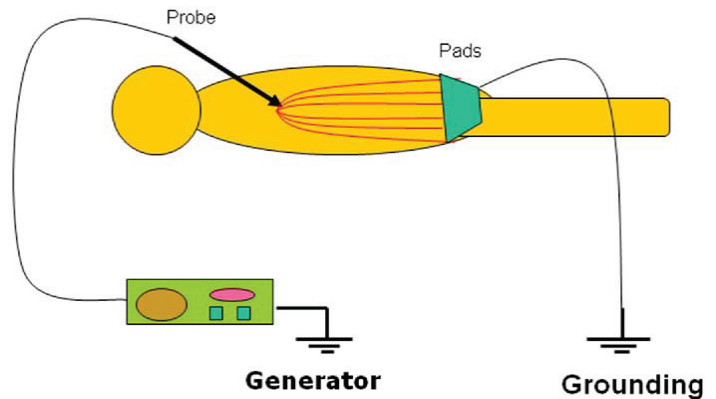


Figure 2. The RF ablation "circuit." The electrode acts as the cathode, and the pads as the anode. The patient is actually part of the circuit, and tissue conductivity is important in achieving adequate ablation zone.

ing pads disperses the energy, thus minimizing the energy flux. As a result, tissue damage is limited to the part of the circuit that surrounds the electrode tip.

RF ablation results in coagulative necrosis of tissue from high temperatures. The dipole molecules (mostly water) immediately next to the tip of the RF electrode attempt to remain aligned in the direction of the current and are forced to vibrate as rapidly as alternating current is applied. Molecules that are farther away from the electrode are set into motion by other vibrating molecules near them. The frictional energy losses between adjacent molecules result in local energy deposition and temperature increase (4). With greater distance from the electrode, the resultant energy and generated temperature drops exponentially (Fig 3). The RF electrode itself is not the source of heat and is not hot to the touch. It generates an alternating EM field that sets adjacent molecules into motion causing intense agitation. These molecules immediate next to the electrode are the source of the heat, which is transmitted farther by tissue conductivity (4).

One of the limitations of RF ablation is that it is heavily dependent on good electrical and thermal tissue conductivity. If one pushes the generator's power too high too quickly, the tissue around the electrode becomes desiccated (charred). The desiccated tissue acts as an insulating "sleeve" around the electrode, which limits the transmission of further electrical or thermal energy (Fig 4) and limits any further extension of desired tissue destruction (4). It is instructive to note that time is just as cru-

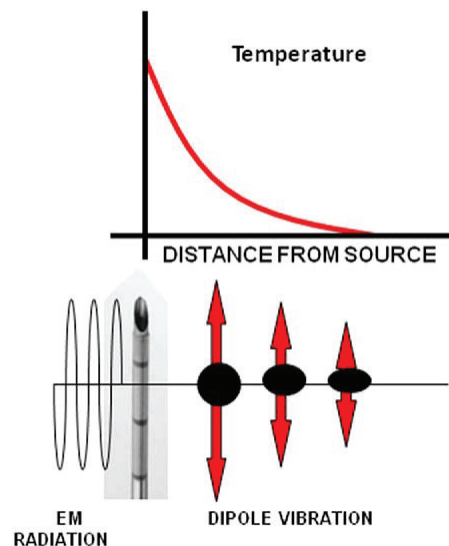


Figure 3. The RF electrode itself is not the source of heat. It generates an alternating EM field that sets adjacent molecules into motion. The molecules adjacent to the electrode are the source of the heat, which is transmitted farther by tissue conductivity.

cial in achieving a large ablation zone as the maximum temperature reached. Figure 5 shows the approximate time needed for tissue death at various temperatures. Mammalian tissue is very sensitive to temperature changes. At 55°C, for example, tissue death results within 2 seconds. At 100°C, death is instantaneous as evaporation occurs. Micro bubbles primarily containing nitrogen are produced and released from the cells. This, however, is not desired in RF ablation because of the insulating effect of charred tissue. Thus, a slow, methodical energy deposition is more effective

than a quick temperature rise for purposes of enlarging intentional tissue ablation (Fig 6) (6). The objective is to heat tissues to 50°–100°C for 4–6 minutes without causing charring or vaporization. If temperatures greater than 105°C are reached rapidly, boiling, vaporization, and carbonization result, all of which decrease energy transmission and consequently limit larger ablation sizes.

Extrapolated from surgical data, the goal of RF ablation technique is to intentionally ablate a zone of healthy tissue analogous to a "surgical margin" around the target tumor (Fig 7). This margin should be 0.5–1.0 cm of ablated normal tissue, based on the difficulty in truly identifying exact tumor margins and the concerns for microscopic tumor extension beyond those confines (6). This means that for a 2-cm tumor, one would need to produce an ablation of approximately 3–4 cm.

There is considerable heterogeneity of heat deposition through any RF ablation tissue volume. The extent of coagulation necrosis is dependent on the energy deposited and local tissue interaction minus the heat lost from cooling effects, such as the "heat sink" of adjacent blood vessels (5). The heat sink effect is a phenomenon that limits the effectiveness of all thermal ablation methods. When the target lesion abuts a blood vessel 3 mm or larger, the flowing blood prevents large temperature variations in the part of the tumor near the lesion, thereby keeping the tissue "cooler" (Fig 8). This phenomenon potentially leaves behind re-

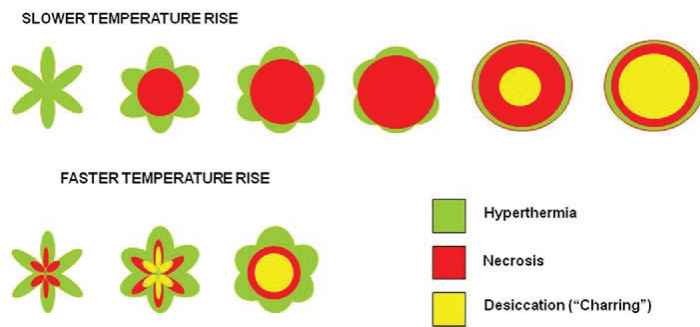


Figure 4. A “thought” experiment using an umbrella-type RF electrode seen in cross section. The top row shows an eventual larger zone of ablation compared with the bottom row. This is because the faster increase in energy input (bottom row) resulted in a faster temperature increase in the tissue immediately around the electrode. This tissue charred before the maximum ablation zone was achieved. Once charring occurs, further energy deposition is impossible because resistance is too high.

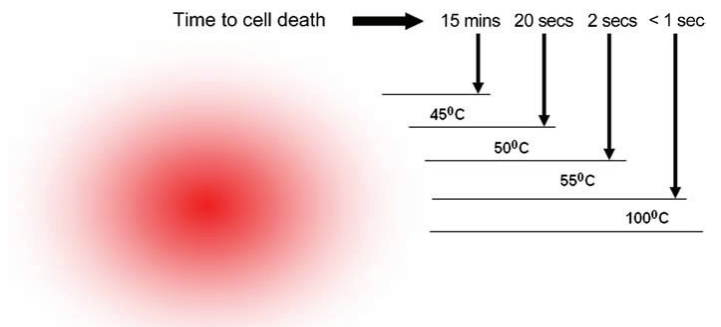


Figure 5. Time needed for tissue death at various temperatures. Mammalian tissue is very sensitive to temperature changes. At 55°C, for example, tissue death results within 2 seconds. At 100°C, instantaneous cell death occurs. However, this is not preferred because the charred tissue that results prevents the deposition of RF energy away from the active electrode. Therefore, a gradual elevation of energy deposition is associated with better outcomes.

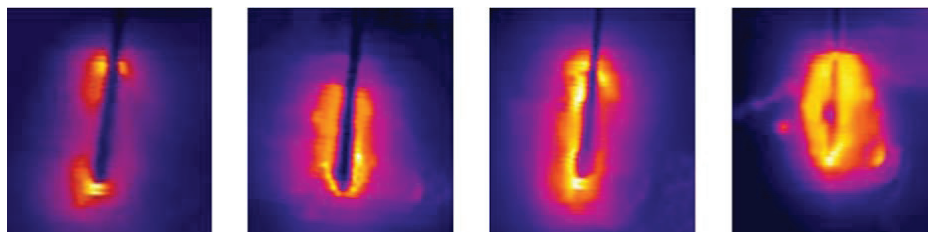


Figure 6. Progression of a radiofrequency ablation shown by color representation of surrounding slow thermal changes without charring.

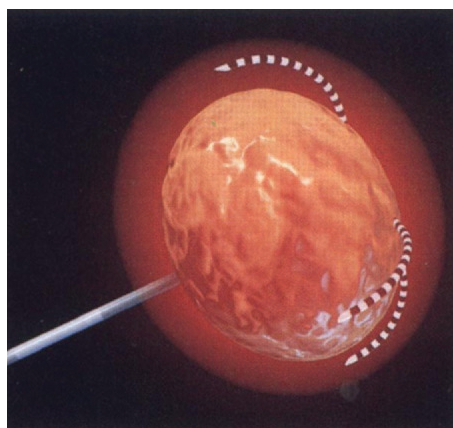


Figure 7. RF ablation zone of 1 cm “surgical margin” beyond the visible tumor confines.

sidual unablated tumor near the vessel wall, increasing the chance of local tumor progression. Factors that influence local tumor progression after RF ablation include tumor-related factors (size, site, orientation, organ, histology, biology) and technical factors

(electrodes, generator power, heat sink, time).

Data from RF ablation of liver primary tumors have shown that 3 cm or less is the optimal size, and there is a persistent effort to improve and enlarge ablation size with improvement of RF ablation techniques (7). Goldberg et al (8) described the following relationship regarding development of a thermal lesion: induced coagulation necrosis = (energy deposited $\times$ local tissue interactions) – heat loss. Investigators have taken different approaches to solve these physical constraints by modulating tissue characteristics, increasing RF energy deposition, or modifying blood flow.

ADVANTAGES AND DISADVANTAGES OF RF ABLATION

Given the fact that the majority of experimental and clinical data for tumor ablation has been reported for RF ablation-based systems, RF ablation will remain relevant for the foresee-

able future, as data are accumulating with novel ablation techniques. Much of oncologic practice is driven by evidence-based medicine. Nonetheless, RF ablation certainly has relative strengths and weaknesses, particularly when compared with other developing thermal modalities (Tables 1 and 2). Overall, RF ablation has the advantage of being the first commercially viable ablation device and is currently available widely. It is relatively cost effective compared with other newer devices, such as microwave ablation and high-intensity-focused ultrasound scan. However, its main limitation is the lack of consistency when attempting to obtain larger homogenous tumor ablations ($> 5\text{--}7\text{ cm}$) as well as the time needed to deposit sufficient energy with RF ablation. There has been considerable interest in combining RF ablation with adjuvant cytotoxic therapies, chemoembolization, intravenous liposomal Doxorubicin, and radiation therapy (15–17).

GENERATORS

Early RF generators for percutaneous application produced modest outputs of 50 W. Current generators manufactured in the United States are capable of 200- to 250-W outputs, delivering high frequency (460–500 kHz) alternating current via RF electrodes (usually 14–17 gauge) of varying configurations. The three systems have distinctly different electrode designs as well as varying algorithms and methods to deposit energy. They also

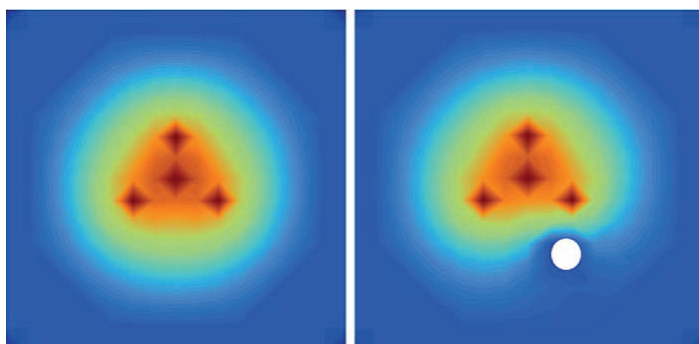


Figure 8. The heat sink effect is a phenomenon that limits the effectiveness of all thermal ablation methods. When the target lesion abuts a blood vessel 3 mm or larger, the flowing blood prevents large temperature variations in the part of the tumor near the lesion, thereby keeping the tissue “cooler.” Color simulation of a cross section of an RF ablation local temperature effect during multitined electrode RF ablation; the left image simulates lack of adjacent blood vessel “heat sink” effect; the right image simulates the temperature disturbance caused by the cooling effect of the blood vessel.

Table 1
Advantages of RF Ablation

- Long track record of accumulated data
- Considerable RF ablation awareness among oncologists; historical perspective
- Other RF ablation roles in medicine: cardiac EP ablations, electrocautery
- Wide availability
- Cost: relatively cheaper compared with “new” ablation modalities
- Small electrode size (14–17 gauge)
- Multiorgan experience: RF ablation data in multiple organs
- Acceptable safety profile; slow gentle burns inherent in technique
- Hemostasis effect: helpful in periprocedural bleeding
- Magnetic resonance imaging-compatible devices available
- Typically single procedure

use different end points as a measure of clinical success. No definitive data have shown one system to be superior over another. Despite the company-suggested algorithms, there is great variability among users. Personal preference and familiarity still play a distinct role in the varying achievable patient outcomes.

ELECTRODE MODIFICATIONS

Given the limited ablation zone with solitary electrodes such as the Bovie knife, a clear need was identified to increase the zone of necrosis by elongating the active areas in any given system. Modifications included developing expandable electrodes or using several straight electrodes in a cluster. These designs resulted in cylindrical ablation zones, which did not uniformly conform to and cover the typical spherical nature of most small malignancies. As a further modification, the ability to place up to three single

electrodes individually, has been used as well to increase ablation size. With this technique, it is crucial to keep the active tips parallel and approximately 1 cm apart. With increasing interelectrode distance, the area of coagulation can have a “dog bone” or “dumbbell shape,” with the potential for leaving remaining viable tumor between the electrodes. This illustration is particularly important when building compound ablation areas (overlapping ablations) for large tumors (> 5 cm) (Fig 9).

MULTITINED EXPANDABLE ARRAYS

Improving on the original single monopolar needle, LeVeen (9) described a novel approach by having multiple curved uninsulated prongs deployed from the needle tip central cannula, creating the shape of an umbrella. Each prong caused a separate area of coagulation necrosis, which slowly coalesced by gradually admin-

Table 2
Disadvantages of RF Ablation

- Concerns for needle tract seeding
- Skin pad burns
- Heat sink: RF ablation susceptible to vessel “heat sink”
- Size limitation: RF ablation of larger lesions difficult (from 5–7 cm)
- Speed: ablations are relatively slow
- RF ablation monitoring of therapy: during ultrasound image guidance, gas formation limits visualization
- Operator-dependant technique
- Dependant on additional imaging guidance

istering increasing amounts of RF energy in a stepwise fashion. This approach resulted in a larger, more reproducible volume (Fig 10). Currently, this type of system is represented commercially by the LeVeen device (Boston Scientific, Nantucket, Massachusetts) (Fig 11). Others pursued a stepwise deployment in a forward orientating electrode, for example, the Starburst Xli electrode (Angiodynamics, Queensbury, New York) (Figure 11).

INTERNALLY COOLED ELECTRODES

Goldberg (10) described in 1996 an innovative approach whereby chilled saline is pumped through the chamber shaft of the needle, with the resultant reduction in charring, impedance, and increased tumor volume ablation. Cool-Tip electrode (Covidien, Boulder, Colorado) is the commercial prototype for this concept, which was then modified further by clustering three electrodes together (Fig 12) for a synergistic coalescence of each thermal ablation.

PERFUSION ELECTRODES

Perfusion electrodes were developed whereby saline or hypertonic saline is injected or infused into target ablation tissue, capitalizing on the concept that high local sodium chloride ion concentration can expand volume of tumor ablation by altering tissue electrical conductivity (11–12). Examples of this commercially are the XLi-Enhanced and Talon electrodes (AngioDynamics, Queensbury, New York), which are multitined devices

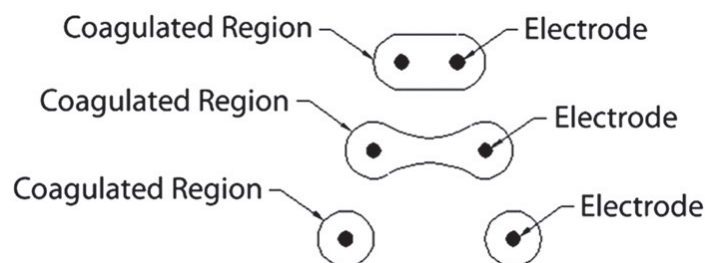


Figure 9. Effects of electrode spacing. If the electrode placement is separated by an excessively large distance (>1 cm), the resulting overlapping area of effected tissue would change shape. As distance between electrodes increases, the area of coagulation would have a “dog bone” or “dumbbell” shape. As the electrodes are further separated, this shape would evolve into distinct and separate areas immediately around each electrode, leaving viable tumor/tissue in between. This is particularly important when building compound ablation areas (overlapping ablations) for large tumors > 5 cm.

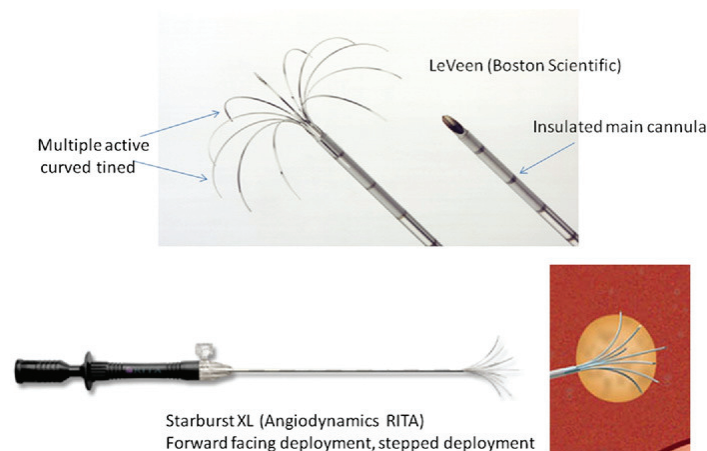


Figure 11. Multitined RF electrodes. Diagram shows various examples of commercially available multitined RF electrodes.

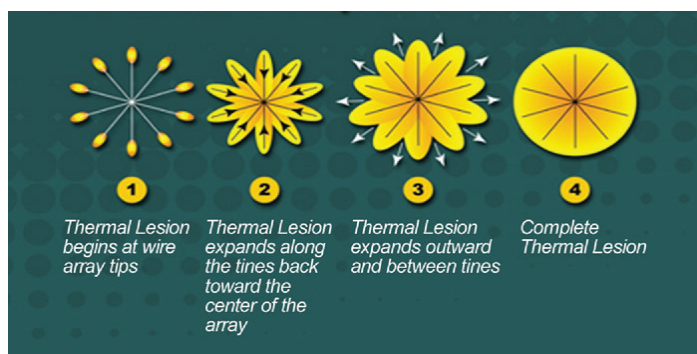


Figure 10. Multitined electrode. Concept diagram shows multiple coalescing areas of coagulation necrosis from multitined electrode.

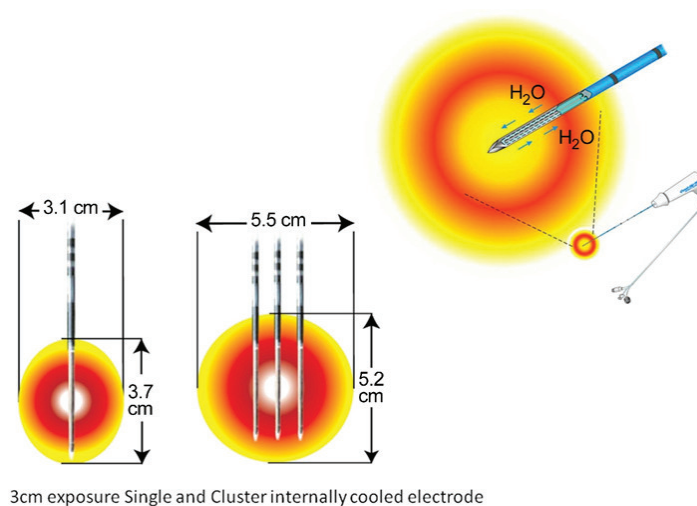


Figure 12. Internally cooled electrodes. Concept diagram shows internally cooled electrode design and additive ablation coagulation zone by clustering electrode design.

with saline pump perfusion enhancement creating ablation diameter volumes of up to 7 cm.

BIPOLAR RF ABLATION ELECTRODES

Most commonly available systems in the United States are monopolar devices, whereby the RF current travels from generator to electrode in tumor, through the patient toward the skin pads, and back to the generator to complete the full circuit. A recent advent has been the development of bipolar systems, whereby two or more bipolar electrodes are placed into the tumor, and the applied RF current runs from one electrode to another

without the need for grounding pads. This essentially ensures that all electrodes within the tumor are active with minimal energy loss allowing greater ablation volumes more efficiently. Bipolar systems also do not require grounding pads and avoid the risks of skin pad burns. InCircle bipolar device (RFA Medical, Freemont, California) is a US Food and Drug Administration (FDA)-approved system that is compatible with most available generators from other manufacturers. The InCircle electrode is unusual in that two electrodes are placed on each side of the tumor, without penetrating the integrity of the lesion, and surround the lesion (**Fig 13**). This may be helpful in circumstances in which

mobile or fibrotic tumors are challenging to direct penetration. In early reports this bipolar system attained quick large burns and may show promise for larger ablation volume, compared with that of monopolar RF ablation (13–14). Several other systems are available in Europe and Asia.

COMMERCIALLY AVAILABLE RF ABLATION SYSTEMS

In clinical practice, three major manufacturers of mono-polar RF devices are on the market in the United States that are FDA approved. All three systems reflect the key design modifications in the development of

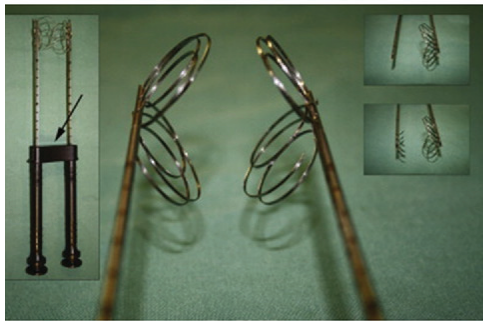


Figure 13. Bipolar InCircle electrode. Two electrodes are placed parallel around the tumor, each probe acting as an active energy pole. Arrow denotes a guiding spacer to optimize the distance between poles of the circuit.

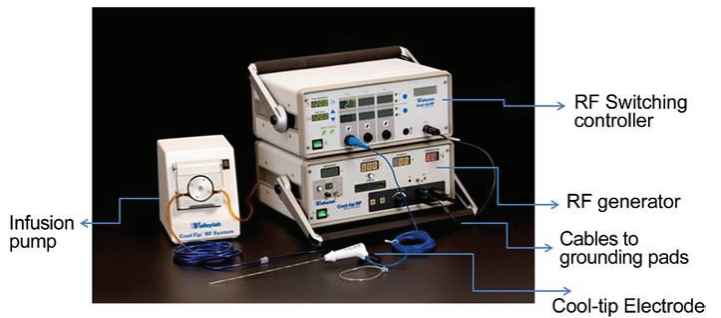


Figure 14. Covidien Cool-Tip RF ablation system.

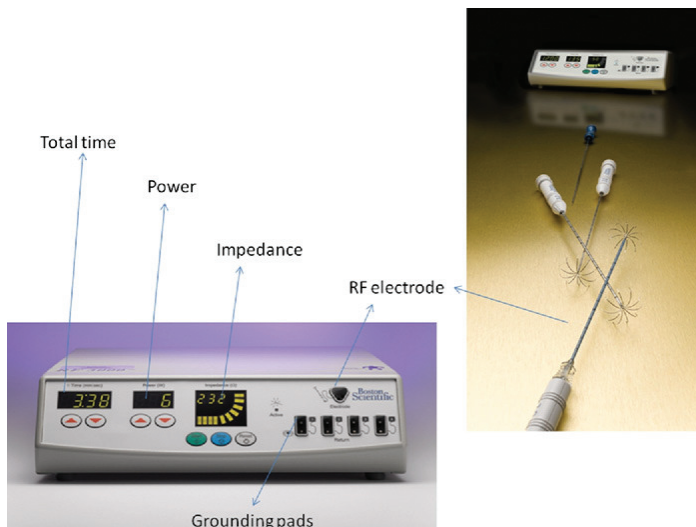


Figure 15. Boston Scientific "LeVeen" RF ablation system.

the RF electrodes in their product line and intellectual property, all initially spurred by the desire to overcome the physical constraints of RF energy deposition in tumor tissue. They differ in the end points of the generator, the technique used to maximize treatment volumes, the size of the electrodes, and the electrical parameters monitored to maximize energy deposition. Although temperature and impedance are measured in several of the systems, each uses one parameter to maximize treatment diameter, and each system has a specific algorithm for treatment, which requires varying degrees of operator input. Each system with its generator and electrode range has strengths and drawbacks, and ide-

ally, operators should have access to more than one system.

Covidien

Covidien (Boulder, Colorado), (formerly Tyco Healthcare Valleylab) features monopolar single straight electrodes that are cooled internally to enhance slow heating of adjacent tissue (Fig 12). In turn, this reduces charring and vaporization, and thus increases ablation volume and shortens ablation time. The Valleylab RF Ablation Generator (200W) with Cool-tip Technology features a feedback algorithm that continually monitors tissue impedance and adjusts to achieve the appropriate energy output for each electrode, based on tissue impedance

and tip exposure (Fig 14). The pulsed ablation system also allows tissue to rehydrate during the ablation cycle, reducing tissue impedance increases that could limit RF output. Covidien also offers a cluster electrode comprised of three electrodes all contained within one handle. The cluster electrode has up to a 4 cm exposure. Covidien offers four electrode lengths and four tip exposures for customized ablation sizes. Larger ablation zones can also be created with the Valleylab RF Ablation Switching Controller with Cool-tip Technology, which allows the use of three separate single electrodes placed simultaneously. Also, the needle gauge for the Valleylab RF Ablation Electrodes is 17 gauge, and the desired electrode tip is placed optimally to the end and slightly beyond the distal margin of the target lesion. Tract ablation is possible with the depression of the tract ablate button on the generator coupled with a slow withdrawal of the electrode.

Boston Scientific

Power is derived from a 480-kHz generator (RF 3000, Boston Scientific, Natick, Massachusetts) capable of producing a maximum power of 200 W (Fig 15). The Boston Scientific system also features an impedance-based feedback algorithm that continually monitors tissue impedance and adjusts to achieve the appropriate energy output for each electrode, based on tissue impedance and tip of electrode. The Boston Scientific radiofrequency procedures are performed with a monopolar array-type electrode with an

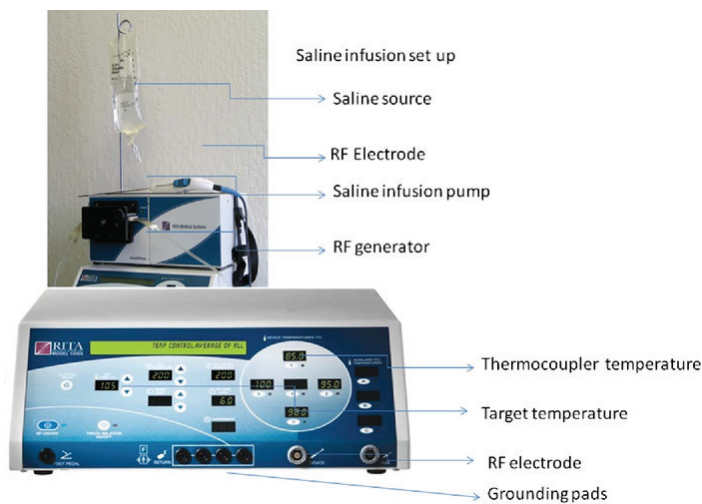


Figure 16. Angiodynamics RITA RF ablation system.

umbrella-like deployment configuration (LeVein; Boston Scientific) with diameters of 2–5 cm in increments of 0.5 cm in various lengths (15 gauge), with 2-cm and 3-cm electrodes also available in a smaller gauge size (17 gauge), useful in high-risk access sites. All electrode tips are active and give impedance feedback. The umbrella-shaped LeVein electrode is expanded (single step, except 5-cm electrode staged deployment) once the electrode is placed under guidance in the center to the target lesion and umbrella-like tines deployed; imaging verification of the position of the tines is done before commencing the ablation. A single straight electrode is also available for small lesions (Soloist electrode), in 17-gauge size. Boston Scientific has an introducer coaxial system that allows computed tomography scanning with needles in place (without bulky hubs) and also multiple needle placement for treatment planning and convenient pre-RF ablation biopsy without re-access.

Power from the radiofrequency generator (RF 3000, Boston Scientific) is delivered in a stepwise algorithm that provides starting powers of 20–80 W and increased 5–10 W/min to maximum values of 55–200 W. End point of ablation is a dramatic increase in impedance (termed *roll-off* by the manufacturer) with the Boston Scientific device. Standard algorithm suggests a second “burn” starting at 70% of maximum roll-off power (W). At the end of the procedure, tract ablation (to reduce needle tract seeding) is possible

by retracting the prongs and the electrode is pulled back slowly by continuously applying 30 W if needed.

Angiodynamics RITA Medical Systems

AngioDynamics RITA uses a temperature-controlled 460-kHz generator (Model 1500X, RITA Medical Systems, Mountain View, California) capable of producing maximum output of 250W (Fig 16). RITA has several electrode options with the Starburst XL electrode as the mainstay capable of ablations from 3–5 cm, 15-gauge, which contains nine deployable curved tines. When fully extended, the maximum diameter is 5 cm and mimics the configuration of a Christmas tree. The tips of the RITA hooks have thermocouples that report realtime temperature at the treatment volume margin, as the tissue heats up, which automatically maximizes treatment volume. Realtime temperature readings are displayed on the generator console, measured at the five electrode tips. This manufacturer has a versatile range of flexible electrodes (SB Flex, SB Semi-Flex) to mitigate computed tomography gantry constraints and has the only FDA-approved magnetic resonance imaging device (SM MRI) and a smaller SB SDE for small ablations (2 cm). RITA has an additional saline infusion system (Intelliflow Pump, Angiodynamics), which infuses saline into the ablation zone for the purposes of enhancing ablation by reducing charring (SB XLi-enhanced, for up to 7

cm) and SB Talon with side deployment tines, for difficult access lesions. Coaxial access is possible with their soft and hard introducer. At the end of the procedure, tract ablation is possible with the RITA system by retracting the prongs and pulling the electrode back slowly while maintaining a 70°C reading. Ideally, the electrodes should be placed at the proximal portion of the target lesion, allowing the tines’ tips to be deployed in a Christmas tree shape forward (except for the SB Talon with distal lesion placement and side deployment).

CONCLUSION

Percutaneous tumor ablation was introduced almost 20 years ago for the treatment of liver tumors. There has been considerably more awareness of this therapy option as well as greater application in other organs and disease states. Overall, there is growing interest in the adaptation of tumor ablation to interventional practices. A strong understanding of the principles and mechanism of action behind RF ablation and its interactions with tissue is required to avoid complications and improve patient outcomes. There is considerable variability in the way that RF ablation may be performed. Successful tumor ablation requires a balance between maximizing tumor kill while minimizing injury to surrounding normal tissue, requiring operator skill and familiarity with available RF ablation equipment. Although RF ablation has the longest history and accumulated data, the limitation of RF ablation to acquire uniform larger ablation in a timely manner has spurred the advent of several new ablation modalities. Because of the accumulated experience, equipment availability, and cost, RF ablation is likely to remain the mainstay of ablations for small tumors < 3 cm (or in combination with other techniques) until sufficient experience emerges for the widespread acceptance for alternative ablative modalities.

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