Basic Science of Radio Frequency

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Background and Historical Perspective

Radiofrequency (RF) therapy had been used in the management of chronic painful conditions since the first documented treatment of trigeminal neuralgia with thermocoagulation of the gasserian ganglion by Kirschner in 1931. Kirschner applied a direct current of 350 mA to the gasserian ganglion utilizing a diathermy apparatus and a needle with an uninsulated tip under x-ray guidance yielding unpredictably sized lesions. The earliest RF lesion generators and electrodes were designed and constructed by B.J. Cosman, S. Aranow, and O.A. Wyss in the 1950s utilizing continuous-wave RF power sources within the frequency range of 0.1–1 MHz. These devices were developed with the purpose of producing RF thermal lesions, and amazingly today's commercial RF generators continue to utilize the same frequency range. Later, in 1965, Rosomoff et al. implemented higher-frequency currents in percutaneous radiofrequency cervical cordotomy procedures for intractable pain from various pathologies, producing more predictable lesion size. Over the years as RF technology has advanced, its clinical implications have grown not only within the realm of pain management but in other specialties as well.

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Physics of Radio Frequency

RF relies on Ohm's law to generate the desired lesion or effect by manipulating current, voltage, impedance, and basic concepts of electromagnetism. Current is the transfer of energy from an electrical source and is measured in Hertz (Hz). Voltage is the force that drives the current and is measured in Volts. Impedance is the resistance to the flow of the current and is measured in Ohms (Ω). These concepts are represented by the following equation: $V = I \times R$, where V is the voltage, I is the current, and R is the impedance. The current in RF is administered as an alternating current within the kilocycle Hz range, as a lower frequency would result in noticeable pain during clinical use.

The setup of the RF circuit consists of a generator, a dispersive pad to return energy to the generator, an insulated introducer needle to prevent dispersal of energy outside of the targeted area, and an electrode with a thermocouple to provide a precise area of therapy with a temperature-regulated lesion. Furthermore, RF setups rely on a system of continuous impedance monitoring to ensure continuity of the electrical current. When the electrode is at the target site, current passes between the pad and the electrode. As current flows through body tissue, which acts as a resistor, ions within the tissue electrolytes are agitated, causing oscillation of molecules and production of friction and heat. Current spreads sideways from the electrode tip, where heat is produced in the tissue. Therefore, the tissue heats up the tip rather than the tip heating the tissue.

The biological changes that occur in tissue exposed to radiofrequency energy are thought to be secondary to the thermal effects, the high intensity electric fields, or a combination of the two. The electric field vector created around an RF electrode within a conductive, dielectric medium, such as human tissue, is governed by the classic Maxwell's Equations on electromagnetism. At the frequencies utilized in RF technology, electrical and magnetic fields are generated, with the magnetic field's effect being thus far clinically negligible. The current density that is responsible for clinical effect is a

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function of tissue electrical conductivity. Structures that readily conduct electrical energy such as nervous tissue and water will have higher current density than those structures with a lower conductivity, such as bone. Also, the coagulated tissue that is produced during continuous RF may serve to affect impedance as the resultant tissue may decrease the flow of energy into tissues.

The resulting temperature is governed by heat production and elimination. Heat production resulting from current flow is related to impedance (resistance to the alternating current) which varies widely from tissue to tissue. Heat elimination can be affected by tissue conductivity and vascularization of the tissue bed as blood flow carries heat away, known as the heat sink effect. Both in vitro and ex vivo models have shown that the presence of vessel simulation leads to smaller volume of tissue ablation. RF lesioning occurs in two phases. The first phase requires a large generator output to build up heat to desired tip temperature. During the second phase, the generator output gradually lowers until a steady level is reached, compensating for heat washout. Temperatures utilized for conventional RF generally range between 80 °C and 90 °C. However, irreversible neuronal disruption can occur above 44 °C, with cell structure destruction found to occur with 20 seconds or more of exposure at 45–50 °C, commonly referred to as the “lethal temperature range.” Tissue exposure to temperature greater than 60 °C causes coagulation as well as protein and collagen denaturation, leading to cell necrosis. Higher temperatures may lead to side effects including hematoma, smoke, and gas formation, along with adherence of tissues to the probe. A temperature gradient exists from the central to the peripheral zone of a lesion. Some RF techniques specifically aim to expose the target structure to lower temperature zones to prevent deafferentation sequelae. Decreased temperature is also thought to have selective effect on small unmyelinated nerve fibers.

By applying radiofrequency to tissue, while controlling for temperature and lesion time, a lesion is produced. The lesion size and tissue injury can be related to the current density, which is current divided by the electrode surface area. For a given constant current, as the electrode surface area decreases in size, a greater current density, tissue heating, and resultant lesioning will occur. The size of the lesion is affected by many factors, which will be elaborated on in a later section.

Types of Radio Frequency

As RF technology has continued to advance, various forms of RF have developed with numerous applications and improving efficacy (see Table 33.1). Continuous RF is the conventional or standard form of RF therapy. It utilizes a current of 100–500 kHz applied in a continuous fashion to the target tissue. The continuous current produces a thermal lesion that interrupts nociceptive signal conduction and blocks pain signal transmission. Continuous RF, similar to other forms of RF, is nonselective and causes destruction in both sensory and motor nerve fibers. Three different types of continuous RF exist: monopolar, bipolar, and cooled. Pulsed radiofrequency will be discussed later in this chapter.

Table 33.1 Advantages and disadvantages based on RF modality

Type of RF	Advantages	Disadvantages
Conventional thermal (monopolar/bipolar)	Less expensive equipment Longer history of clinical utility	Requires parallel placement to target nerve for optimal lesioning
Cooled RF	Larger lesion size generated Parallel or perpendicular approach to nerve may be performed Potentially increased duration of analgesia due to greater tissue coagulation	Increased potential for lesioning adjacent tissue Increased equipment costs
Pulse RF	Less risk of neuro-destruction Reduced risk of deafferentation pain Can potentially be used on peripheral nerves (i.e., intercostal, greater occipital)	Shorter duration of effect Requires repeat procedures more frequently Potential for minimal analgesic benefit

Monopolar RF represents the conventional RF therapy where the current flows between the probe electrode and the dispersive pad. With this technique the current generates heat at the active tip of the electrode and not distal to it. As the lesion is confined to an area at the tip of the electrode, the needle must be placed in a parallel fashion to the direction of the nerve and not perpendicular to it (see Figs. 33.1, 33.2, and 33.3).

In bipolar RF, current flows between two electrode probes without requirement of the dispersive pad. The electrodes are placed across the desired target, usually spaced up to 10–15 mm, resulting in a connecting brick-shaped lesion that spans these adjacent points (see Fig. 33.4). While monopolar RF is able to generate higher maximum ablation temperatures in less time, the volume of tissue ablated by bipolar RF is much larger while causing less vessel damage, possibly due to lower ablative temperature reached. In fact, a bipolar lesion is similar to three closely spaced monopolar lesions produced using the same generator setting and cannula size. Thus, bipolar RF helps to reduce number of lesions and cannula diameter, minimizing patient discomfort. Bipolar RF is also more forgiving toward inevitable operational imperfections as inter-lesion heating is robust to various departures from ideal parallel tip alignment. However, the active tip

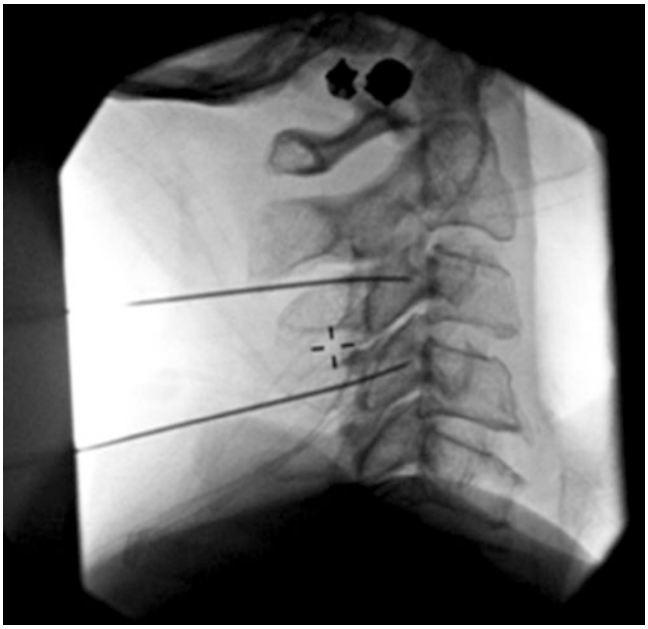

Fig. 33.1 Conventional RFA needle placement in parallel to cervical medial branches, during conduct of cervical medial branch RFA

Fig. 33.2 Image of conventional RFA of cervical medial branches with the patient in prone position

length must be equal; otherwise alterations and less efficacious lesion geometry would result.

Cooled RF is a newer technology that was created with the intent of producing decreased heat at the electrode tip. The electrode is cooled via an internal perfusion system with water, while the RF heat develops around the electrode tip (see Fig. 33.5). Such cooling effect results in decreased impedance around the electrode tip with a theoretical delivery of higher energy, allowing for larger volume of tissue to be heated while avoiding excessive heating of tissue close to the electrode. Temperature at the electrode tip is maintained low, and RF heating takes place beyond the electrode tip and propagates spherically (see Figs. 33.6 and 33.7). Ex vivo studies have demonstrated the ability of cooled RF to achieve suitable temperatures to induce thermal transition of collagen and thermal neurolysis while showing no histologic evidence of damage to neural tissue in safety zones surrounding the targeted area. Cooled RF also generates larger lesions than bipolar RF.

Pulsed radio frequency (PRF) differs from conventional RF in that PRF is suggested to not lead to neural destruction. While heating of tissue does occur with PRF, the clinical effect does not rely on the generation of a heat lesion. Instead, PRF is thought to cause an alteration in the signal transduction of pain fibers. The distinction between PRF and conventional RF lies in the generator setting and the temperature achieved at the active tip. In PRF, pulses of 50 kHz current are delivered for 20 milliseconds at a frequency of 2 Hz (or every 0.5 seconds). The pauses between generated pulses allow for heat to dissipate through adjacent vascular structures, via conduction and convection, producing a lesion less than 42 °C that is insufficient to produce neural coagulation and irreversible tissue damage. Thus the average tissue temperature rise for the same RF voltage and probe electrodes is less in PRF than in conventional RF as the RF duration in PRF constitutes only a small fraction of the time between each pulse. Therefore, larger RF voltages can be used in PRF than in conventional RF without increasing the average tissue temperature around the electrode. In vitro studies have shown that PRF, when compared to conventional RF, leads to less tissue disruption and has a limited or temporary effect on impulse propagation in the nerve tissue. The greatest current density produced in PRF is distal to the active tip, allowing electrodes to be placed perpendicularly to the target nerve, shortening procedure time. PRF is believed to pose a lower risk of developing deafferentation pain than conventional RF. However, its duration of relief is generally much shorter and requires the procedure to be performed more often to obtain similar pain reduction levels as in conventional RF.

The exact mechanism of PRF is yet to be fully elucidated. PRF is believed to cause both short- and long-term changes in several neural markers. C-fos is a proto-oncogene that is expressed rapidly in response to an excitatory stimulus. It has been used as a marker for sensory neuron activation and may play a role in nociceptive transmission. Immunohistochemistry studies demonstrate an increased expression of C-fos in lamina I and II of the spinal cord in animals exposed to PRF vs conventional RF at the same temperature. Such elevated expression is present 7 days after stimulation, suggesting a sustained activation of a pain-inhibiting process. However, c-fos expression is sometimes non-specific in neuronal tissues. ATF3 (activating transcription factor 3) is a marker of neuronal cellular stress, specific to small diameter neurons such as Aδ and C fibers. Application of PRF to dorsal root

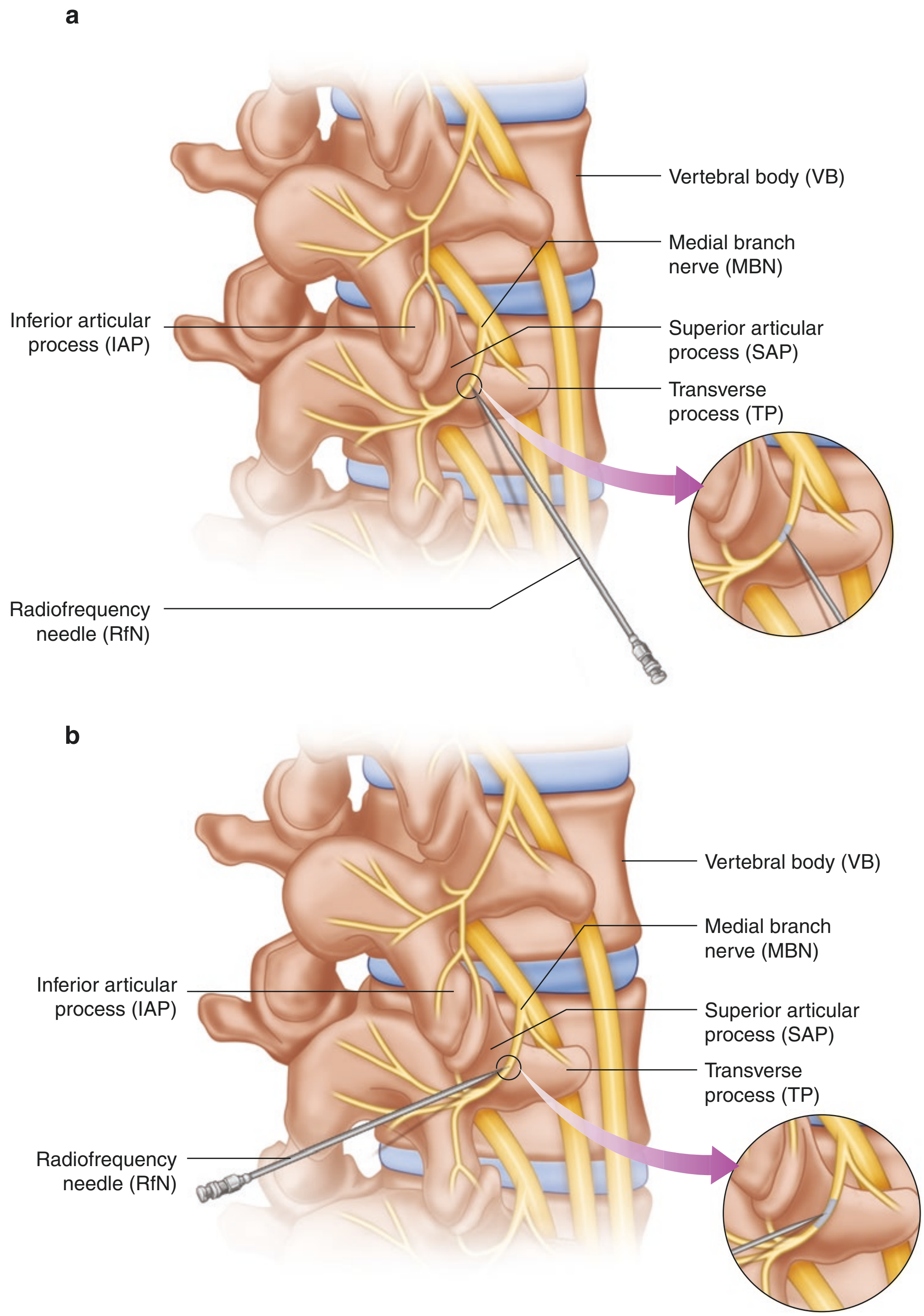

Fig. 33.3 Image (**a**) Needle placement perpendicular to medial branch nerve; Image (**b**) Needle placement parallel to medial branch nerve. With conventional RFA, needle placement parallel to the nerve yields larger surface of ablated tissue

ganglia has been shown to cause both short- and long-term upregulation of ATF3 in small caliber neurons, implicating PRF's role in targeting nociceptive neurons. Limited animal behavioral studies have also shown pain-relieving effect of PRF on mechanical hypersensitivity and thermal allodynia. Increased met-enkephalin level in the spinal cord 24 hours after PRF exposure implies a possible role for endogenous opioids. In addition, PRF effects have been found to be attenuated by α2 antagonists and SSRIs, suggesting PRF analgesic effect may involve descending noradrenergic and serotonergic inhibitory pathways. Lastly, a recent study by Yeh et al. demonstrates that PRF provides neuromodulation with a long-term anti-allodynic effect (up to 28 days) by inhibiting spared nerve injury-induced IGF2 and ERK1/2 activation that is responsible for inflammatory response and mechanical allodynia.

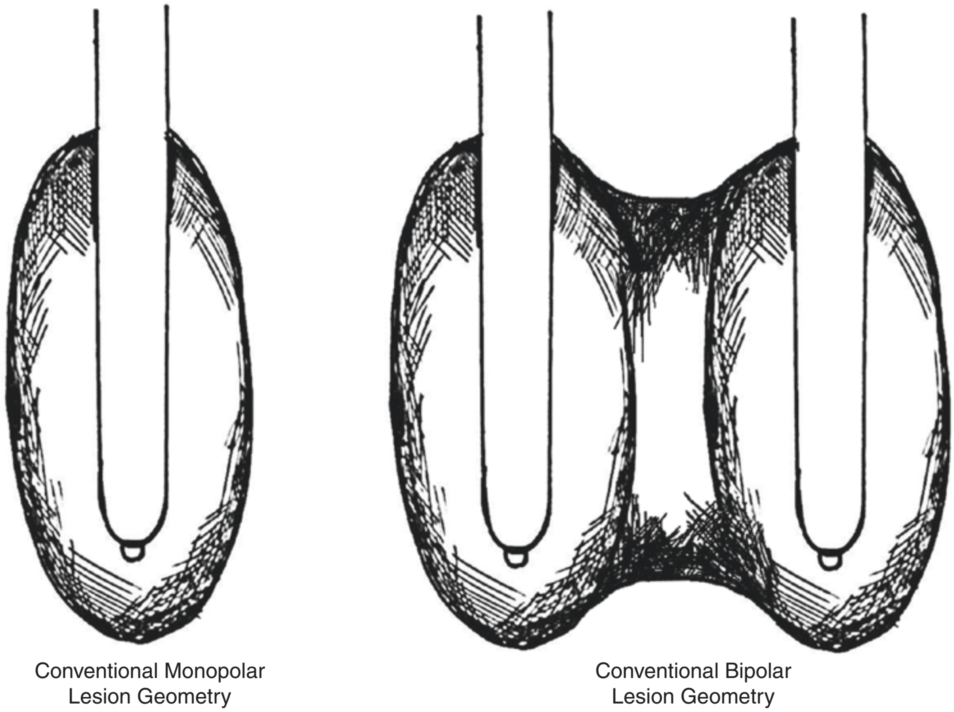

Fig. 33.4 Comparison of conventional monopolar vs bipolar lesion geometry

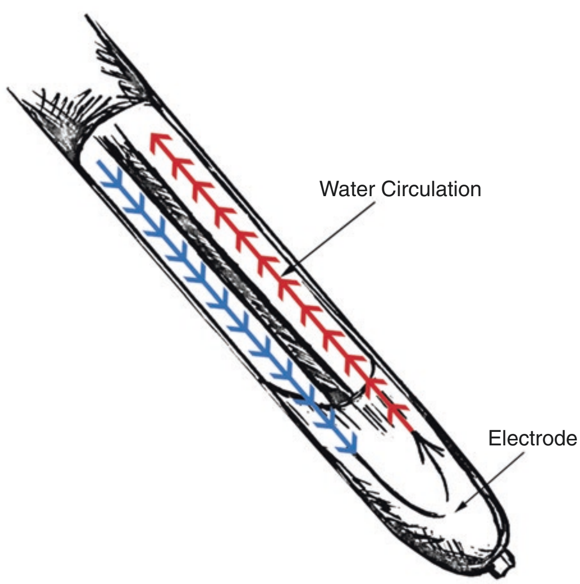

Fig. 33.5 Inner dynamics of a cooled radiofrequency needle, demonstrating flow of water reducing tissue impedance and therefore permitting for larger region of ablated tissue

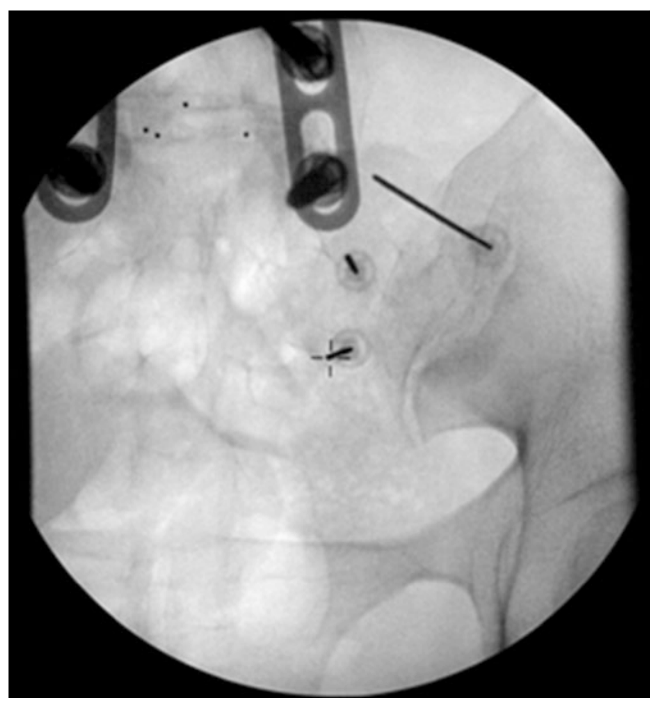

Fig. 33.6 Image of sacroiliac joint (SI joint) RFA with the cooled radiofrequency needles in place lateral to the sacral foramina

Histological Effects of RF

Many animal studies have been performed to evaluate the histological effects of conventional RF and PRF. 42 °C conventional RF lesions in rats result in endoneurial edema in the subperineurial and perivascular areas of the nerve. Light microscopy demonstrates transverse myelin fiber damage along with axoplasma separation, leading to impaired nerve transmission. Electron microscopy also confirms alternation of myelin configuration. Additionally, lamellar separation,

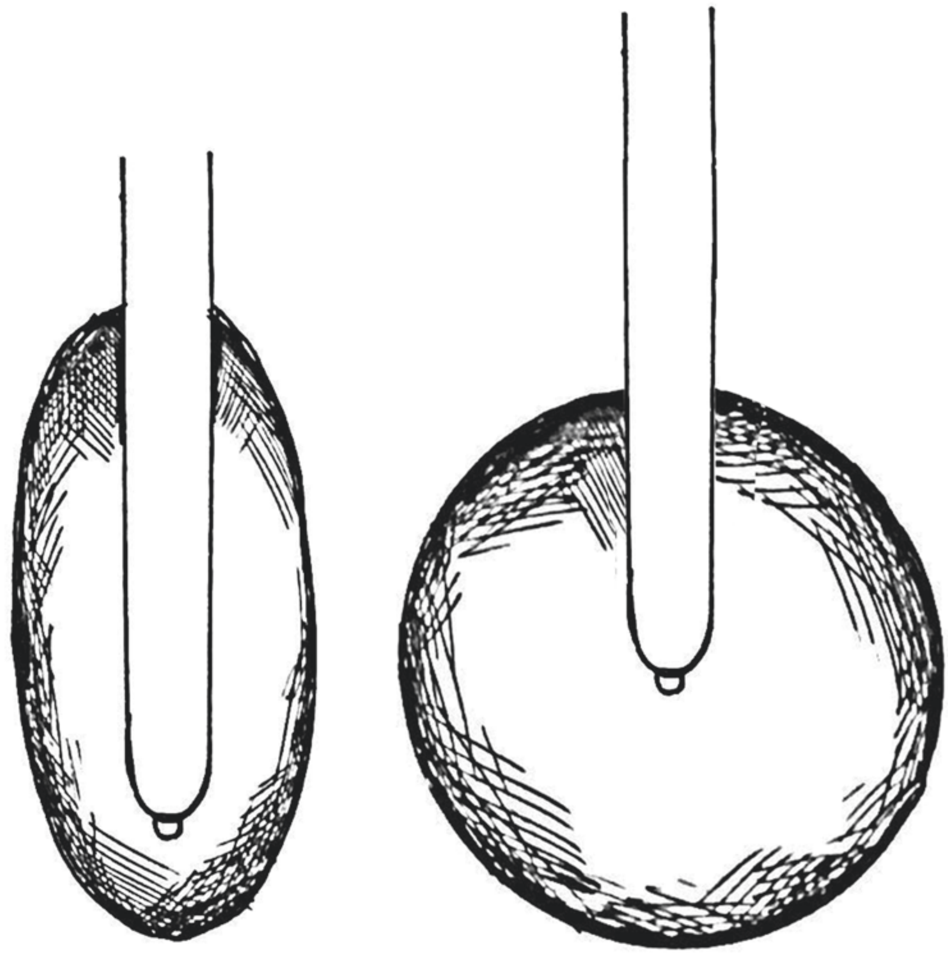

Fig. 33.7 Comparison of conventional monopolar vs cooled RF lesion geometry

protrusion of myelin, and accumulation of neurofilaments were found, pointing to neurodegeneration. However, these changes were transient in nature without progression to overt axonal injury. 80 °C conventional RF lesions caused coagulative necrosis and show significant endoneural edema with progression to Wallerian degeneration. Electron microscopy shows evidence of neurodegeneration, including epineurial thickening, lamellar separation, intra-axonal vacuolization, increased intracellular endoplasmic reticulum, and Schwann cell damage.

PRF only demonstrates relatively minor histological changes, such as the development of large vacuoles throughout the cytoplasm. The changes are restricted to the relatively smaller sized C and Aδ fibers as well, presumably because larger neurons are protected by their myelin sheath. Microscopic examination of PRF lesions has shown morphologic changes of mitochondria with abnormal mitochondrial membranes along with disruption and disorganization of microfilaments and microtubules.

Factors that Affect Lesion Size

Understanding the geometry and size of heat lesions generated with RF is critical for selecting generator settings and probe configuration that will suit patient anatomy and yield favorable clinical objectives. Lesion geometry determines the extent and likelihood of desired and undesired tissue changes based on the active tip's position and orientation with reference to patient anatomy. The lesion size determines the degree and likelihood of interventional success, complications, number of required lesions, methodological difficulty, procedure time, radiation exposure, tissue damage, and intra- or post-procedural pain. The advantage of a large lesion includes a decreased likelihood of missing a target nerve with an increased extent of nerves capture by each lesion. Achieving a large lesion also avoids incomplete neurolysis, improves degree and duration of pain relief, and decreases procedure time, X-ray exposure, and number of lesions required. The disadvantage of a large lesion includes increased likelihood and severity of damage to nontarget nerves, skin burns in thin patients, and post-procedural paresthesia. Side effects are related to the volume of the affected tissue, both target and surrounding structures. Because the target nerve cannot be visualized during the RF procedure with the use of fluoroscopy, successfully ablating it while limiting damage to nontarget structures depends on accurate placement of the electrode and working knowledge of the expected size and variability of the RF-induced lesion.

The size of an RF lesion can be affected by manipulating cannula tip sizes and generator settings. According to Cosman et al., large monopolar RF lesions can be generated by maximizing tip size (16 g/6 mm, 18 g/10 mm, or 16 g/10 mm), heating temperature (80–90 °C), and lesion time (2–3 minutes) within practical limits.

Lesion size can also be further enhanced by fluid injection via the cannulae prior to radiofrequency ablation. Increasing NaCl concentration in the preinjection fluid decreases impedance surrounding RF cannula, increasing power output. Provenzano et al. found that preinjection fluids with >3% NaCl increase lesion growth in all dimensions, most significantly in the horizontal plane with limited growth extension distal to the tip. While most of the lesion growth occurs by 90 seconds regardless of the presence of preinjection fluid, fluid pre-injection with >3% NaCl allows for continued lesion expansion throughout the 180-second cycle, resulting in larger lesions. Lidocaine, which is a standard pre-injectate to prevent procedural pain, when added to NaCl pre-injection fluid, does not significantly alter mean increases in lesion dimensions or modifications in electrical parameters. In bipolar RF, fluid preinjection also increases the inter-electrode distance that can be used to produce an optimal lesion.

Summary

The mechanism of analgesia and treatment after radiofrequency ablation is well-known and founded. As technology has developed from initial monopolar lesions, bipolar and cooled RF have resulted leading to use in various clinical indications. Additionally, the use of pulsed radio frequency, while not commonly used currently in the United States, has received worldwide support for the use in conditions where denervation pain would be a deleterious result. The theory behind RF highlights the conglomeration of electricity and magnetism for clinical care. The monopolar, bipolar, and cooled RF are via a conventional energy approach, with the cooled RF allowing for dissipation of energy to yield a larger lesion size for targeted tissue.

Pulsed RF, while yet to have a fully, elucidated mechanism has shown promise in certain clinical conditions. For more widespread use, the basic, mechanistic science behind PRF needs to be consistently assessed and presented, so that this technology may join the currently utilized approaches for interventional pain procedures.

Recommended Reading

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