Review Article

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High-Frequency Alternating Electrical Current: Selective Electromagnetic Tissue Reaction

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Radiofrequency surgery, also referred to as electrosurgery, utilizes a high-frequency (HF) alternating electrical current to cut or coagulate biological tissues. HF energy—while targeting a particular tissue—can be applied to induce an electrothermal reaction by converting electrical currents into heat energy, depending on the resistance of the tissue and the density of the current. In contrast to the action mechanisms of electrocautery devices, which generate nonselective thermal injury using a heated metallic probe, radiofrequency devices deliver electromagnetic signals—not heat itself—to induce thermal or non-thermal injury to targeted cellular and subcellular structures. Using a radiofrequency device, HF energy can be emitted to tissues via a monopolar or bipolar mode and via minimally invasive or noninvasive electrodes. These differences in the delivery of HF energy to a particular tissue affect the expected type of reaction. A thermo-selective tissue reaction refers to the selective hyperthermic injury achieved by converting an electrical current into heat energy. An electromagnetic-selective tissue reaction refers to non-thermal, selective tissue reactions achieved via a HF-induced electromagnetic field. For minimally invasive bipolar radiofrequency devices, the use of insulated penetrating electrodes, along with longer HF conduction time and continuous type of HF delivery, maximizes thermo-selective tissue reactions. Meanwhile, for minimally invasive bipolar devices equipped with non-insulated penetrating electrodes, application of shorter HF conduction time and/or pulsed type of HF delivery maximizes electromagnetic-selective tissue reactions.

Key words
High frequency; Radiofrequency; Electromagnetic field; Electrothermal reaction

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HIGH-FREQUENCY ALTERNATING ELECTRICAL CURRENT

Radiofrequency surgery, also called electrosurgery, utilizes high-frequency (HF) alternating electrical current to cut or coagulate biological tissues.[1] In medicine, HF typically refers to a radiofrequency between 300 KHz and 30 MHz. In radiofrequency surgery, HF energy is applied to generate an electrothermal reaction in target tissues by converting electrical current into heat energy, depending on the resistance of the tissue and the current density.[1-3] In terms of energy delivery, radiofrequency surgery is quite different from electrocautery surgery. Electrocautery conducts heat to the tissue using a heated metallic probe via a direct electric current.[1,3] Technically, electrocautery is a form of thermocautery, not electrosurgery, as no current actually flows through the patient during the electrocauterization.

By using a radiofrequency device, HF energy can be emitted to tissues via a monopolar or bipolar mode. Monopolar modes employ an active cathode electrode and a grounded anode electrode, whereas bipolar modes utilize two active electrodes. Applied to a patient's body, the monopolar mode comprises the delivery an electron current from the active electrode to the grounded electrode, whereas the bipolar mode generates an electrical circuit between the two active electrodes.[2] The electrical currents derived from the monopolar mode can be delivered deeper to target tissues; however, prediction of the penetration depth is limited.[2,3] The electrical circuit of bipolar mode, however, is limited to superficial areas within the targeted tissue, as the electron current flows through the shortest path between the active electrodes; accordingly, the penetration depth of HF energy in the bipolar mode is predictable.[2,3]

Radiofrequency devices can also be categorized into noninvasive and minimally invasive types according to the composition of their electrodes.[1,4] Noninvasive radiofrequency devices deliver HF energy to target tissues via electrodes in contact with the skin. The depth of energy penetration depends on the radius of the electrode and the HF frequency. Meanwhile, minimally invasive radiofrequency devices utilize microneedle electrodes that penetrate the targeted tissue to deliver electromagnetic energy deeper therewithin.[4-7] For these devices, the depth of energy delivery is controlled by the penetration depth of the microneedles.

MONOPOLAR RADIOFREQUENCY DEVICES

Noninvasive monopolar radiofrequency devices

Noninvasive delivery of monopolar HF energy generates an electromagnetic field of alternating polarity that induces the movement of charged particles.[8] As the electric current tends to conduct through hydrophilic structures, dermal collagen fibers and fibrous septae are better conductors of the current than subcutaneous fat.[8,9] Within the collagenous structures, localized heat is generated by tissue resistance against the flow of the electrical current.[8] For noninvasive monopolar radiofrequency devices, such as the ThermaCool System (Solta Medical, Hayward, California, USA), a homogeneous electric field is emitted across the tips of electrodes that permit the transfer of equal amounts of energy to the skin via a capacitor that is formed between nonconductive layers inside the electrode tips and the skin surface.[9] Immediately after noninvasive monopolar radiofrequency treatment, mild inflammatory cell infiltration is observed in the perivascular and perifollicular areas.[10] Thicker collagen bundles are also found for up to 8 weeks after the treatment.[10] While high-intensity focused ultrasound treatment on *in vivo* human skin has been shown to stimulate neocollagenesis in the mid and deep reticular dermis, noninvasive monopolar radiofrequency treatment has been found to result in neocollagenesis of both the papillary dermis and reticular dermis.[11]

In an *in vivo* experimental setting, use of the monopolar mode, a frequency of 6 MHz, a 15 mm × 15 mm noninvasive grid fractional tip (IntraGen; Jeisys Medical, Inc., Seoul, Korea), and the treatment parameters of 84 W and 200 W for 2 seconds stimulated remarkable tissue coagulation in the papillary and reticular dermal layers of micropig skin, especially at higher HF delivery. After treatment using a noninvasive monopolar, grid fractional radiofrequency device, real-time polymerase chain reaction (PCR) revealed significant increases in the expressions of tumor necrosis factor (TNF)-α, transforming growth factor (TGF)-β, metalloproteinase (MMP)-1, MMP-3, MMP-9, MMP-13, heat shock protein (HSP) 47, and HSP72 throughout the wound healing process. Consequentially, post-treatment histologic features of neocollagenesis and neoelastogenesis were found in the dermis of the micropig skin, along with marked induction of procollagen 1 and 3, tropoelastin, and fibrillin expression.

Invasive monopolar radiofrequency devices

Invasive radiofrequency devices have been applied in scar treatment, skin tightening, and wrinkle reduction by fractional heating of the dermis to induce neocollagenesis and collagen remodeling using penetrating electrodes.[6,7] In treatments utilizing minimally invasive monopolar radiofrequency devices, multiple electrodes penetrate the skin to deliver HF energy directly to targeted areas, inducing thermal injury; the inter-electrode zones are relatively preserved, promoting rapid wound healing.[6] In *ex vivo* bovine liver tissue, use of the monopolar mode, a frequency of 0.4 MHz, and a single non-insulated penetrating electrode stimulated tissue coagulation that started from the distal end of the electrode and propagated upward along the electrode.[6] Applying increasing energy levels, a column of coagulated tissue began to form around entire length of the penetrating electrode.[6] The thickest area of tissue coagulation was found at the distal end of the non-insulated electrode. Thereby, in contrast to ablative fractionated lasers, fractionated invasive radiofrequency devices can be used to effectively destroy target tissues deeper in the skin with greater precision while preserving the epidermis, even with the use of non-insulated microneedle electrodes. One of the main targets of invasive monopolar radiofrequency device is the sebaceous gland. Electrosugery using insulated needles, first proposed by Kobayasi, is currently widely performed in acne patients to control excessive sebum production. Both the original and newer devices (ex. Agnes™; Gowoonsesang Dermatology Clinic, Seoul, Korea) are available.

BIPOLAR RADIOFREQUENCY DEVICES

Noninvasive bipolar radiofrequency devices

When delivering HF energy via noninvasive bipolar radiofrequency devices, the maximal depth of energy penetration is equal to half the distance between the electrodes.[3] Therefore, high energy settings with intensive cooling of the epidermis to prevent burns are required to generate sufficient heat injury at the targeted depth.[1-3] The histologic features of noninvasive bipolar radiofrequency treatment result from selective heating of collagen fibers and fibrotic tissue in the dermis located along the shortest path between the noninvasive electrodes.[1,2]

Invasive bipolar radiofrequency devices

In an *in vivo* experimental setting, use of the bipolar mode, a frequency of 1 MHz, and a 10 mm × 10 mm disposable tip consisting of 49 proximally insulated, penetrating microneedles in a uniform 7 × 7 array (INFINI; Lutronic Corp., Goyang, Korea) generated tissue coagulation that was limited to the distal end of the electrodes without remarkable propagation upward to the proximal end in micropig skin.[7] Water drop- or cocoon-shaped zones of tissue injury formed separately at each tip after HF delivery with the conduction times of 20, 50, 100, and 1000 msec and the signal amplitudes of 5, 10, 20, 25, 37.5, and 50 V. At the same penetration depth and signal amplitude, radiofrequency treatment with longer HF conduction times resulted in larger areas of tissue coagulation; at the same HF conduction time and signal amplitude, deeper penetration of the microneedles created larger areas of coagulation; and at the same penetration depth and conduction time, the delivery of higher signal amplitudes exhibited the greater degrees of tissue injury.[7] Interestingly, no remarkable HF-induced tissue reactions were found in the dermal components between the electrodes, despite the use of bipolar alternating currents.

In an additional *in vivo* micropig skin study, use of the bipolar mode, a frequency of 1 MHz, and a 10 mm × 10 mm disposable tip of 49 proximally insulated, penetrating microneedles (INTRAcel; Jeisys Medical, Inc., Seoul, Korea) demonstrated that invasive bipolar radiofrequency treatment significantly induces the expression of TNF-α, interleukin-1β, TGF-β1, MMP-1, MMP-3, MMP-9, MMP-13, HSP47, HSP72, procollagen 1 and 3, tropoelastin, and fibrillin.[12] Upon further *in vivo* investigation in micropig skin, treatment with a bipolar mode, a frequency of 2 MHz, and a disposable tip of 25 non-insulated, penetrating microneedles in a uniform 5 × 5 array (CELFIRM; Viol, Kyunggi, Korea) formed similar zones of water drop- or cocoon-shaped tissue coagulation at the tip of each penetrating electrode, called the "Na effect," with the conduction times of 120, 200, and 300 msec and signal amplitudes ranging from 25.6 V to 36.6 V.[7,13] Therein, the penetration depth of the non-insulated electrodes and HF conduction time significantly affected the sizes of the areas of tissue coagulation, whereas the signal amplitude was associated with the degrees of tissue injury, as seen in the experiments on insulated electrodes.[13]

In *ex vivo* bovine liver tissue, use of a radiofrequency device with a bipolar mode and non-insulated penetrating electrodes demonstrated that tissue coagulation starts from the distal end of the electrode and propagates upward along the electrode to the proximal end, as seen in the experiments on the monopolar mode and non-insulated penetrating electrodes.[6,13] By increasing the HF conduction time, the convergence of individual zones of HF-induced tissue coagulation began to appear from the tips of neighboring electrodes along the shortest path between the active electrodes.[13] Then, an additional path of electrical current appeared around the middle of the penetrating electrodes that propagated along the entire length of the electrode.

SELECTIVE ELECTROMAGNETIC TISSUE REACTION

In contrast to the action mechanisms of electrocautery devices, which provide nonselective thermal injury using a heated metallic probe, radiofrequency devices deliver electromagnetic signals, not heat itself, to targeted cellular and subcellular structures via invasive or noninvasive manners to stimulate thermal injury. The delivery of electromagnetic signals to the skin stimulates two tissue reactions: a thermo-selective tissue reaction and an electromagnetic-selective tissue reaction. A thermo-selective tissue reaction refers to selective hyperthermic injury achieved by converting electrical current into heat energy.[1-3,14] An electromagnetic-selective tissue reaction refers to non-thermal, selective tissue reactions achieved via a HF-induced electromagnetic field.

As a thermo-selective tissue reaction, electromagnetic signals typically create three zones of thermal injury, comprising a central zone of coagulation necrosis, a peripheral or transitional zone of sublethal tissue damage, and unaffected surrounding normal tissue.[14,15] Temperatures in the central zone, found immediately beyond the active distal tip, can exceed 60°C, at which irreversible changes of cell membrane collapse, rapid protein denaturation, and enzymatic dysfunction occur, leading to coagulation necrosis.[14] In the peripheral zone, which surrounds the central zone, temperatures are estimated at 41-45°C, at which reversible changes of local tissue damage, metabolic dysfunction, and increased blood flow are found.[14] Accordingly, current radiofrequency devices afford clinicians the ability to accurately regulate the extent of thermal reaction and the sizes of the three injury zones.

Applying a bipolar mode, a frequency of 1 MHz, and insulated penetrating microneedles (INFINI; Lutronic Corp.), the delivery of HF energy at a penetration depth of 3.5 mm, 3.0 mm, and 2.5 mm, with a conduction time of 150 msec and a signal amplitude of 25 V, generated significant decreases in hyperhidrosis disease severity, reflected as post-treatment decreases in the numbers and sizes of both apocrine and eccrine glands.[16] Thermo-selective destruction of eccrine and apocrine glands can also be achieved in treatments of hyperhidrosis and bromhidrosis with the settings of a bipolar mode, a frequency of 0.5 MHz, increasing penetration depths of 2.0 mm to 4.5 mm in increments of 0.5 mm, a conduction time of 2,500-3,000 msec, and insulated penetrating microneedles (Onix; Shenb Co., Ltd., Seoul, Korea). As stated above, whether the tissues will be irreversibly destroyed or recovered and regenerated is achieved by controlling the modes of energy delivery, penetration depth, signal amplitude, and HF conduction time in accordance with the desired therapeutic purposes.

Thermo-selective tissue reactions have also been found to effectively eliminate subcutaneous fat tissue, most likely by the induction of apoptosis.[17] The electrical poles of adipocytes rapidly oscillate according to the alternating electromagnetic fields that create HF-induced selective thermal reactions in subcutaneous fat tissue. In *in vivo* pig skin, a radiofrequency applicator (Vanquish; BTL Aesthetics, Prague, CR) at a frequency of 27 MHz was placed 1 cm above the abdominal skin, and tissue temperatures were maintained at 45-46°C in the subcutaneous fat and at 39-42°C in the overlying skin over the total exposure time of 30 minutes.[17] After the radiofrequency treatment, histologic evaluation revealed the disintegration of adipocytes, with the appearance of foamy macrophages; whereas epidermis, dermis, and adnexal structures were preserved.[17] To maintain optimal tissue temperatures for inducing apoptosis of adipocytes, use of a personalized impedance, synchronized application system (enCurve; Lutronic Corp.) that can be used to adjust the power in real time may be helpful.

In *in vivo* micropig skin and *ex vivo* bovine liver tissue, application of a bipolar mode, a frequency of 2 MHz, and 25 non-insulated penetrating microneedles (CELFIRM) induced an electromagnetic-selective tissue reaction just before and during the Na effect.[13] Characteristic histologic changes in microvascular components, ranging from noticeable congestion of small blood vessels to vascular coagulation limited to the tunica adventitia, were found in the non-coagulated inter-electrodes regions of the *in vivo* micropig skin and *ex vivo* bovine liver tissue.[13] Similarly, HF-induced tissue reactions on the vascular components were also found along the fibrous connective tissues and outer root sheaths of hair follicles.[13] These findings resulted from HF-induced tissue reactions along areas with higher current density, particularly in the outer layers of adnexal structures, which exhibit different impedances and permittivity. Moreover, "electric fields sinks," which are associated with distribution of vessel structures in the targeted area, may also contribute electromagnetic-selective tissue reaction patterns.[18] Electromagnetic-selective tissue reactions, however, were not found at non-coagulated inter-electrode regions in skin treated with the experimental settings of a bipolar mode and insulated penetrating microneedle electrodes.[7] In addition to the perifollicular structures and the outer layers of hair follicles, the inner layers of the cortex, medulla, and inner root sheath were also remarkably coagulated.[7] The extension of the electromagnetic field and the electric current density may have been significantly affected by the characteristics of the penetrating electrodes.

PULSED ELECTRIC FIELDS

For decades, continuous radiofrequency irradiation has been used to generate thermal ablative effects for various therapeutic purposes. Clinical applications of pulsed radiofrequency include treatments of cardiac arrhythmia, chronic pain, post-operative pain, melasma, rosacea, electrochemotherapy, gene transfer, and ablating tumors.[18] Pulsed radiofrequency refers to the gated delivery of radiofrequency oscillations at a particular rate of pulses per second. According to the pulse period between the radiofrequency pulse packets and gated pulse width of each packet, the thermal and/or non-thermal effects of pulsed radiofrequency can be achieved. Pulsed electric fields increase cell membrane permeability in a minimally invasive manner, so called electroporation.[18-20] Pulsed irradiation-induced electroporation results in both reversible and irreversible cellular changes, depending on the treatment settings and cellular threshold.[19]

Clinical trials of a bipolar mode, a pulsed radiofrequency, and a disposable tip of 25 non-insulated, penetrating microneedles (SYLFIRM; Viol) have indicated that five to seven sessions of combination therapy with a low-fluence Q-switched Nd:YAG laser and an invasive pulsed radiofrequency device at one-week intervals significantly improves refractory melasma lesions in Asian patients without noticeable side effects.[21] The suggested action mechanisms of the pulsed radiofrequency device in the treatment of acquired pigmentary disorders included pulsed electric fields that were therapeutically effective against the dysfunctional vascular components and pigmentary incontinence by selective electric conductivity.[21] Additionally, pulsed electric fields could potentially regenerate photo-damaged elastic and collagen fibers from the perivascular and peri-adnexal areas.

CONCLUSIONS

For minimally invasive bipolar radiofrequency devices, the use of insulated penetrating electrodes, a longer HF conduction time, and a continuous type of HF delivery maximizes thermo-selective tissue reactions. Meanwhile, for minimally invasive bipolar devices equipped with non-insulated penetrating electrodes, application of a shorter HF conduction time and/or a pulsed type of HF delivery maximizes electromagnetic-selective tissue reactions. Clinicians should consider the mechanism of action for each device and its appropriate applications. Physicians using these techniques must also be aware of the potential complications of electrosurgical procedures and how to prevent them. Electrosurgical complications are relatively common; the two most common hazards are explosion/fire and burns. Radiofrequency devices can also interfere with other electromedical devices or produce a noxious smoke. To improve safety, electrode monitoring, visual inspection of faulty insulation prior surgery, removal of metal objects that are in close proximity to the intended surgical site, and avoidance of electromagnetic interference, which includes cardiac implantable electronic devices (e.g., cardiac pacemakers, implantable cardioverters and defibrillators, etc.), are suggested. In addition, the use of a smoke evacuation system to protect the physician and the operating room staff is recommended. To maximize safety, the US law allows electrosurgery to be performed only by physicians who have received specific training in this field.

Although we have focused mostly on radiofrequency surgery, electrosurgery also includes electrofulguration, electrodessication, electrocoagulation, electrosection and thermocautry which are performed in everyday medical practice (ex. Bleeding control, epidermal tumor and viral wart removal with Ellman^{TM} electrosurgical unit). However simple the procedure may be, all electrosurgery devices carry a hazardous potential. It is nevertheless important that only physicians are permitted on their use.

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