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Mini Review

An Epitome Review of Radiofrequency Ablation for Cancer Treatment

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Abstract

In comparison to traditional cancer treatment methods, such as surgery and chemotherapy, the radiofrequency ablation (RFA) provides great advantages of minimally invasive and cost-effective therapy with a short hospital stay. In addition, RFA also can be used for patients inoperable for surgery or chemotherapy. In the last century, scientists have dedicated themselves to enlarging the ablation size by designing various electrode shapes and combining conventional treatments. This mini-review aims to illustrate the history of RFA technology, the structural design of the electrode geometries, the auxiliary method to enhance the ablation lesion size and minimize cancer reoccurrence, and the current challenges to RFA and their potential solutions.

Keywords: Radiofrequency ablation; Tumor/Cancer ablation

Introduction

Cancer is one of the dominant diseases causing death before the age of 70, based on the World Health Organization (WHO) mortality data in 2019 [1]. In 2020, the estimated new cancer cases, including 27 major cancers, were about 19.3 million, and the predicted new cancer patients will reach 28.4 million by 2040 in the world [2,3]. The cancer-related mortality population possibly reaches 13 million by 2030 [4], which is going to be a heavy burden for many developing countries. Radiofrequency ablation (RFA) provides significant advantages of minimally invasive and cost-effective therapy with a short hospital stay and low morbidity [5,6]. In addition to all the advantages above, RFA is capable of killing tumors in undesired resection locations or poor surgery candidates. The RFA history can be traced back to the early 19th century when English physicist Michael Faraday proposed the principle of alternative current (AC). Then, the RFA technique benefited from the English physicist James C. Maxwell and the German physicist Heinrich Hertz, who proved the existence of electromagnetism and developed Maxwell's equations. In 1881, the radiofrequency heating phenomenon was first reported by D' Arsonval. However, a wide medical application of RF had not occurred until 1928 when Harvey Cushing and William T Bovie [7] innovated their novel RF generator and Bovie knife [7,8]. Unlike the current RFA technique, the Bovie knife was a monopolar electrode mainly used to cut tissue or cauterization by applying RF current. Organ [8] first illustrated the mechanism and experiment setup of RFA in 1976 [8,9]. In 1990, McGahan [10] replaced the Bovie knife with the specifically designed electrode with insulated material to the distal tip [10]. He further evaluated the RF hepatic ablation in an animal model with ultrasound guidance in electrode placement and echogenic response [11], resulting in a liver lesion with a size of 1x2cm. Since then, the RFA was developed into commercial products, applied to humans, monitoring and guiding through ultrasound, computed tomography, and magnetic resonance imaging (MRI) [12-15]. To now, the new RFA technique is still under development.

The following section will introduce the RFA mechanism, RFA probe structure design, auxiliary methods for lesion size enhancements, as well as the current challenges and their potential solutions.

Mechanism of RFA

The malignant tumors are eliminated by heating in RFA therapy. After the placement of the electrode and grounding pad on the patient body, a certain power from the RF generator is applied to the electrode, and the ion flow tends to follow in the direction of AC current. With a high frequency of AC current, the target tissues, not the electrode, produce frictional heating and induce coagulation and cellular necrosis in the tumor when the temperature reaches a certain level, typically above 70 °C [6,16]. Regarding frictional heating (Joule effect), Organ [8] proposed a principle of RF lesion making with serval parameters such as the distance from the probe tip, RF current intensity, heating duration, and heat loss. In general, the lesion size depends on the heat generated and the heat lost. The heat generation is positively proportioned to the 1/(distance) [4], (current intensity) [2], and duration time of the heating, while the heat loss presents a negative influence on lesion size due to heat conduction, convection (especially in perfusion organ), and low heat resistance shunting [8,17,18]. The frequency of RFA is another critical factor, which typically is about 300 to 500kHz in clinical devices, whereas a lower frequency (<20kHz) may result in stimulating neuromuscular reaction and electrolysis, and a higher frequency (>20MHz) has the potential risk of uncontrolled lesion volume by excessive heat generation [19,20]. Carbonization and evaporation are two undesired conditions, which both undermine the lesion size by rapidly increasing impedance [6,8,21,22]. Carbonization usually results from the sudden increment of the current intensity and charred tissue around the electrode tip, inhibiting the current flow. Evaporation is a double-edged sword in RFA treatment. On the one hand, it limits the lesion size because of the existing gas in the interstice with low electrical conductivity. On the other hand, it serves as a security system to avoid the ablation temperature higher than 100 °C under improper operation.

RFA electrode/probe structure type and design

A. Monopolar electrode: Monopolar RFA electrode is the most primitive design with one electrode and one grounding pad developed from Bovie knife [10].

B. Bipolar electrode: Unlike monopolar, bipolar RFA replaces the grounding pad with a neutral electrode [12,23]. Therefore, the electrical field gradient is generated, and heating takes place between the two parallel electrodes.

C. Multiple electrodes: With the demand for larger lesion sizes, the multiple electrodes usually contain two to five electrodes under treatment [24].

D. Expandable electrode: One main electrode with multiple deployable prongs with hollow electrode tips now serves as the most vital one in clinical trials. All prongs are uninsulated and function as RF antenna [25-27]. In this design, there are serval available geometries with different prong tip lengths and diameters, with umbrella, inverted umbrella, and spring shapes [28]. Overall, in addition to the geometry difference, multiple-step placements are also applied to enhance the lesion size. Although the current advanced imaging-guide technique is helpful, it still faces difficulty in the accuracy of the electrode placement inside the tumor.

Auxiliary methods

a) Wet electrode: By combing saline solution infusion, either isotonic or hypertonic, with the RFA, the coagulation size can increase, resulting from hydration and increased concentration of ions. However, an inadequate infusion rate may cause an unexpected lesion size. Therefore, a precise flow rate and concentration of saline solution are desired [29-33]. The wet electrode is available for monopolar and expandable electrode [32,34].

b) Cooled electrode: With a closed hollow channel in the electrode, the cooling fluid, typically water or saline, circulates between the inner lumen and outer lumen of the electrode. The cooling fluid brings an advantage in avoiding carbonization and evaporation around the tip and further enlarges the lesion size. However, because of the cooling effect nearby the tip, it potentially leads to not fully killing the adjacent tumor and the risk of seeding tumor cells in the electrode withdrawal pathway [35].

c) Cooled wet electrode: By combining the wet electrode and cooled electrode, scientists invented a cooled-wet electrode to further enhance the lesion size [36-38].

d) Chemo-combination probe: Combining the benefit of chemotherapy and RFA started in 1999 [39]. To minimize the cancer reoccurrence and unintended damage to normal tissues, a peripheral 1cm "surgical margin" of ablated lesions is necessary [39-41]. Unlike the saline infusion, the chemo-combination RFA probe delivers the anti-tumor agent during the RFA treatment. The hyperthermia condition in peripheral tissue facilitates the entry of therapeutic agents into tumor cells and the destruction of the tumor tissue [42,43].

e) Others: Besides the methods described above, the RFA is also capable of combing with resection or ethanol injection treatments [6,22,26,44-46].

Applications of RFA

RFA is widely applied to the treatment of tumors, including hepatic, kidney, bone, lung, breast, adrenal, prostate, head, neck, thyroid, parathyroid, pancreas, lymph nodes, brain and bladder cancers [47]. Hepatic tumor treatment is one major RFA application. The hepatic tumor is one of the most common solid tumors. Only 10-20% of hepatic cancer patients can be treated by traditional surgical resection [48]. Since McGaha and Rossi first utilized the RFA technology for liver cancer treatments, there are numerous experiments and clinical trials have been conducted [14,19,41,46].

Recently, Glassberg provided a systematic review and meta-analysis of liver cancer treatment [49]. Kidney cancer treatment is another primary RFA application with very promising results [50,51] with a successful rate of about 98.5% [52]. The most effective ablation size of kidney tumors is less than 3cm in diameter. Due to the heat sink effect, the ablation performance is weakened when the probe is close to large renal blood vessels. In addition, the RFA is also active in hematuria control. which does not require the surgical margin depending on whether nephron-sparing is a priority [47]. RFA technique is also common in treating lung cancer [6,32,43]. Brace further discussed the difference in RFA treatment strategies among liver, kidney, lung, and bone cancers [16]. Recently, RFA has been used for new applications in thyroid cancer treatments [53]. The moving shot technique is recommended for treating thyroid nodules because the thyroid nodules typically are elliptical and exophytic from the thyroid gland [53]. Scientists keep investigating the possibility of RFA and trying to deliver this minimally invasive method to more different types of cancer patients.

Challenges

Although the interventional RFA for cancer treatment has been developed for over a century, there are still challenges for both doctors and patients. First of all, since most of the tumors have irregular and unique shapes in different patients [27,54,55], there is an urgent need to develop RF electrodes that fit various shapes of the tumor. An adjustable electrode fit various patients is needed, which coverage big enough to kill all tumor tissue and small enough to prevent unnecessary damage for normal tissue. Secondly, the current temperature or impedance-based monitoring system is only available to detect the profile of areas surrounding the probe tip. The detailed temperature distribution inside the tumor and surrounding normal tissues are unknown during the treatment [55-59]. With lack of temperature distribution profile, the treatment performance and time face huge challenge to be optimal. Thirdly, the blood-flow heat sink effect plays a critical role in the performance of RFA treatments by undermining the ablation temperature near a large blood vessel or perfusion organ [60,61]. Heat dissipation phenomenon should be considered as heat loss term during the experiment or calculation, which brings the temperature uneven around the electrode. Fourthly, the method for the accurate placement of the electrode is needed to enhance the success rate in cancer coagulation [19,57,62]. Lastly, RFA has advantage in short hospital stay and minimize invasive, however, it still cannot be extend its application or has poor results for medium and large size tumor. Lesion size is still limited to 3cm. For a medium (3cm to 5cm) or large (5cm to 7cm) size tumor, RFA often leads to an incomplete treatment and a high recurrence rate [55-63].

Potential solutions

Considering the challenges of the irregular shape of a tumor and the need for temperature profile control during the RFA treatment, a computer simulation model with pre-programmed algorithms is possibly helpful to facilitate the doctors before the treatment [64,65]. With the given ultrasound or MRI imaging, the simulation model with temperature distribution assists the doctor in determining the optimal placement locations of electrodes, the ablation time, and other operation settings [66,67]. In addition, a novel 3D multi-modal spherical perfused electrode could enlarge the lesion size and coagulate with the irregular and unique tumors [68-70]. Furthermore, a new principle of high power and short duration heating approach may lead to a more significant size of tissue necrosis [71]. Moreover. a robotic operated electrode has more precise control in location and expandable electrode.

Conclusion

Overall, the RFA is one of the most promising methods of cancer treatment, which eliminates the tumor by depositing lethal thermal energy from Joule heating. Relying on the massive experiments and clinical research in the past century, the RFA undergoes huge progress in structural design of the electrodes, leading to enhancing the lesion size and reducing cancer reoccurrence. In addition, some assisted and combined approaches have been developed with wet, cool, wet-cool electrodes, and chemo-RFA combination approaches. However, the RFA technology still has some limitation in treatment, such as irregular shape tumor, heat sink effect, medium or large size tumors. Therefore, researchers are continuously working on further improving the RFA technology for more cancer treatments. With novel imaging and computational techniques, RFA has a great opportunity to improve its lesion size and treatment performance with it original advantages, minimal invasive and short hospital stay, and cost effective.

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