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About the Interstitial Microwave Cancer Ablation: Principles, Advantages and Challenges

EMAD TAMMAM¹, ASHRAF M. SAID², AHMED A. IBRAHIM¹, (Member, IEEE),
AND AHMED I. A. GALAL¹

¹Electrical Engineering Department, Faculty of Engineering, Minia University, Minia 61511, Egypt

²Biomedical Engineering Department, Faculty of Engineering, Minia University, Minia 61511, Egypt

Corresponding author: Emad Tammam (emad.tammam@mu.edu.eg)

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ABSTRACT This article presents a review of the interstitial microwave cancer ablation. Microwave cancer ablation is an effective technique for the cancer therapy using the electromagnetic radiations in the microwave range. The idea behind using the microwave electromagnetic radiations in cancer therapy is basically based on dielectric heating of the cancerous tissues until the death of the infected cells. This article reviews the theory of operation of the microwave cancer ablation technique with overview of the electrical properties of the biological tissues as they are key parameters to study the behavior of the cancer ablation process. Advantages of microwave cancer ablation technique over the other techniques especially its most related one, i.e., the radiofrequency cancer ablation are highlighted. Although the microwave cancer ablation has attained high attention by the researchers, many of challenges which degrade its performance still exist. The paper discusses the challenges of the microwave cancer ablation and highlights the efforts done by the researchers to tackle them. Different antenna structures utilized for microwave cancer ablation are presented with mention of their behavior, advantages and disadvantages. Moreover, some of the most recent progresses in the microwave cancer ablation field are presented.

INDEX TERMS Coaxial antenna, dielectric heating, microwave cancer ablation, radiofrequency ablation, SAR distribution.

I. INTRODUCTION

One of the most challenging diseases nowadays is the cancer. Cancer is uncontrolled overgrowth of abnormal cells that spread rapidly to form malignant tumors that invades neighboring parts of the body. Recently, the World Health Organization (WHO) has estimated a number of 9.6 million people worldwide are to die from cancer in 2018 [1]. According to 2012 statistics of WHO, the most common types of cancer over the world are lung, liver, colon, stomach, and rectum cancers, in addition to the prostate in men and the breast in women [2].

Enormous efforts have been done in the past years to find a successful therapy for cancer. Several types of therapy are used nowadays to destroy or ablate the cancerous tumors such as the surgery, chemotherapy, and hormone therapy, etc. Recently, thermal therapy using electromagnetic (EM) fields

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has been presented as an alternative therapy for different types of cancerous tumors. In fact, the treatment by heat has been used since the early ages of humanity [3], [4]. It has been used by the physicians, since the beginning of the twentieth century, in the treatment of various forms of tumors. It was found that tumor cells are more affected by the heat than normal cells [5]. Nowadays, thermal tumor ablation became an important candidate in the treatment of many types of cancerous tumors such as the liver, lung, kidney and breast [6], [7]. Due to its simplicity, it is a preferable choice for the ablation of unresectable tumors whether benign or malignant ones especially those of small sizes. Also, It is more suitable for many patients particularly those with surgery intolerance.

Thermal ablation using EM fields is conducted through the placement of an applicator inside the tumor. The applicator delivers the thermal energy to the surrounding tissues to rise the temperature to at least 50 – 60 °C. The rise of temperature leads to the cellular death of the heated cancerous

cells. Ablation of the tumors can be done at open surgery, laparoscopy, or percutaneously using image-guidance and monitoring [8], [9].

There are many techniques nowadays that are based on the idea of treatment using heat such as radiofrequency (RF), microwave (MW), laser, and high-intensity ultrasound waves [7]. Each one of these techniques is used for the same objective, i.e., to deliver amount of heat to the tissues and raise the temperature to more than 50 °C in order to destroy the infected cells of tumor [6]. Microwave ablation (MWA) came into view as an attractive technique for cancer therapy within a short period of time. It is relatively safe and efficient treatment method and is suitable for the treatment of different types of tumors such as liver, kidney, lung, pancreas, adrenal glands and more rarely to bone [10]. The published work in the literature in addition to the field use of the MWA show that it can be used as an effective alternative to the other ablation techniques. However, further investigations are required to confirm the effectiveness of MWA technique and its benefits with respect to the other known ablation techniques, especially radiofrequency ablation (RFA) [11].

In this article, we are concerned about the MWA as an efficient technique for cancer ablation. The operation of the MWA, its advantages and challenges are discussed in Section 2. The operation of the MWA is related basically to the electrical characteristics of the biological tissues. An overview of the electrical properties of the biological tissues is provided also in Section 2. Section 3 discusses the advantages of the MWA and the challenges which face its progress. One of the most challenging requirements for the MWA is to control the resulted heat pattern to protect the normal tissues which lie in the surrounding area of the tumor. The heating pattern depends mainly on the specific absorption rate (SAR) distribution, which in turn depends on the structure of the used antenna [12]. Section 4 overviews the main antenna structures used for MWA. Then, a discussion about the heat distribution control is presented in Section 5. Finally, the main points of the article are concluded.

II. MICROWAVE CANCER ABLATION

Microwave ablation is a minimally invasive technique for ablation of the tumor through the coagulative necrosis of the cancerous cells due to the rise of temperature resulted from the deposition of the EM energy [13], [14]. It has been reported that the temperatures from 50 °C to 60 °C result in the death of the cells through denaturing its protein structure, while instantaneous death of the cells can be obtained at temperatures in excess of 60 °C [6], [15].

The basic microwave ablation system, as shown in Fig. 1, consists of three main components: a microwave generator, a coaxial cable terminated by the antenna, and a cooling system. The generator is responsible of the feeding by the microwave signal which is transferred to the antenna through the coaxial cable. The antenna is the most important component in the MWA system as it is the responsible of the microwave energy distribution during tissue ablation.

Microwave antennas utilized for cancer ablation are mostly implemented as a thin coaxial cable with diameters in the range of 1.5 to 2.5 mm. It can take different forms such as monopole, dipole, double slot, helical, triaxial, choked, and sleeved. Due to the high temperatures exist along the antenna shaft during the heating of the infected tissues, a cooling system is used to cool the antenna. The cooling process includes passing a cold liquid such as saline through the antenna shaft as shown in figure.

Microwave ablation systems operate in the microwave frequency ranges and the operating frequency is an important issue that differentiates the performance of different systems. It has been reported that the frequencies in the range from 900 MHz to 18 GHz are used in cancer ablation [16]. The most commonly available MWA systems work either at 915 MHz or 2.45 GHz [17], [18]. As it is allowed by the Federal Communications Commission (FCC), frequencies in the range of 900 MHz are most commonly used in the USA, while the frequency of 2.45 GHz is the most popular in Europe and Asia [13]. There is no conclusion about which frequency is more effective for MWA procedures; however, a comparison between the most commonly used frequencies, i.e., 915 MHz and 2.45 GHz, has suggested that the 915 MHz frequency may generate larger ablation zones than those obtained at 2.45 GHz frequency [19], [18]. Ablation zones of the 915 MHz ablation systems were characterized by its more elongated shape compared to those of the 2.45 GHz ablation systems and this put some restrictions on the anatomic areas in which they can be used [18]. In spite of the investigations which outbalance the 915 MHz regarding the size of the ablation area, it has been demonstrated that, adequately powered 915 MHz and 2.45 GHz, or even 10 GHz, ablation systems can be used to create large ablation zones, but still the 915 MHz frequency results in a longer ablation zone due to the longer wavelength [20], [21].

Some studies suggest more advantageous performance for the higher frequencies over the lower ones [13]. The higher frequency MWA antenna guarantees shorter radiating part which leads to localized SAR patterns and less invasiveness [22]. Moreover, operation at high frequencies results in spherical heating pattern which is one of the most preferable requirements of MWA system [23]. On the other hand, the high frequencies have the drawback of larger ohmic losses. Therefore, the choice of an intermediate frequency can offer a good compromise between the advantages and drawbacks. For example, the 7 GHz frequency is presented in [13] as a good choice for operating frequency that enforces the production of large ablation zone with localized distribution [24], [25].

A. THEORY OF OPERATION OF MW CANCER ABLATION

Operation of microwave ablation is basically based on the dielectric heating under the effect of applied EM field. The dielectric material here is the biological tissue. Dielectric heating phenomenon involves the continuous rotation of the polar molecules, e.g., water molecules, to realign with the

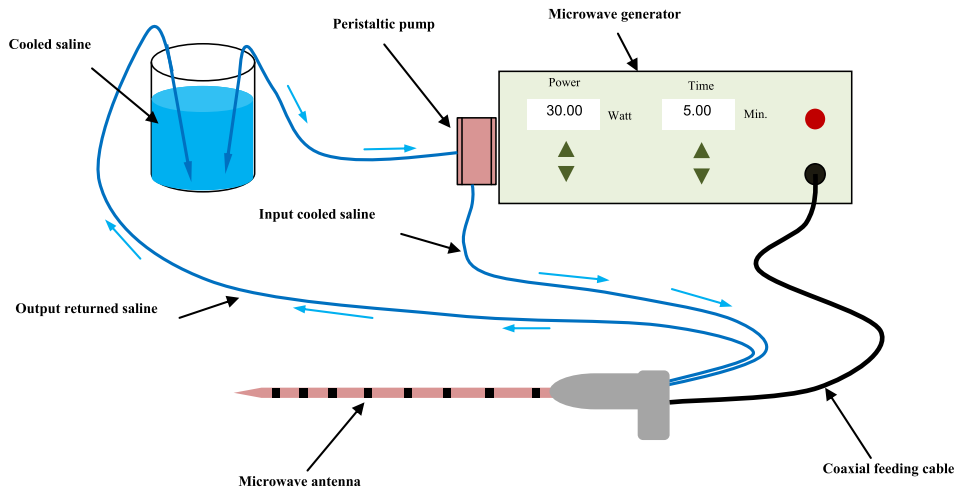


FIGURE 1. Microwave ablation system.

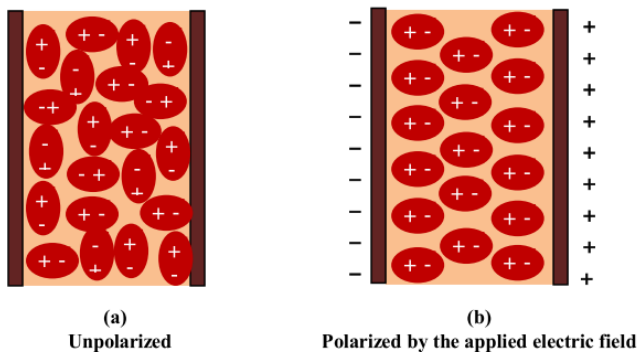


FIGURE 2. Polarization of polar molecules due to EM fields which is the basis of the dielectric heating.

direction of the applied EM field as shown in Fig. 2. Due to the high frequency of the applied EM field, the polarity of the molecules alternates billions of times per second. The polar molecules are unable to keep up with the fluctuations of the EM field under the friction effects leading to the damping effect of the rotating dipoles, then, the excess energy applied is deposited on the tissue as heat [11], [26]. In other words, the bonded water molecules try to rotate out of phase with the applied fields; as a result some of the EM energy is converted to heat. Microwave energy penetrates through all biological tissues while the rate of EM energy deposition within tissue is directly proportional to the water content of the tissue. If low water content such as in fat, less heating occurs. The electrical properties of the material such as conductivity (σ) and relative permittivity (ϵ_r) are the factors that determines the EM absorption efficiency. At the range of MW frequencies, heating is more efficient in materials of high conductivity and permittivity [9], [6], [18], [27].

In addition to the properties of the material and frequency of the applied field, the period of exposure is an important factor that determines the heating rate. Regarding the biological

tissues, the rise of the temperatures to 46 °C for a time period of 60 minutes leads to irreversible cellular damage. However, only about 5 minutes are required for the cellular damage at temperature of about 52 °C. Above 52 °C, the cells of the tumor tissue will be killed immediately [16]. If the temperature goes greater than 105°C, tissue boiling, vaporization, and carbonization will result. This in turn decreases the energy transmission rate, leading to the increase of the time period required for complete ablation of the infected area. Thus, it is important for ablative therapies to maintain the temperature in the range of 50–100°C within the volume under ablation [3].

B. ELECTRICAL PROPERTIES OF BIOLOGICAL TISSUES IN MICROWAVE FREQUENCIES

Thermal ablation of the infected biological tissues is a dynamic process, i.e., it induces changes in tissue's electrical, thermal, and mechanical properties. Tissue's electrical properties determine the interaction between tissue and EM wave, however, both electric and thermal properties dictate the size and shape of the ablation zone [9]. Electric and thermal properties of biological tissues are directly related to its water content. During the ablation process, tissues properties change under the effect of temperature rise leading to slowing down the heat conduction rate within tissue and consequently the location of energy deposition [28], [29]. This behavior of the tissues under the heating effect poses additional load on the MWA antenna designer to take this dynamic behavior into account.

Exposure of the biological tissues that have a sensible value of electrical conductivity to the electric field (E) will induce a conduction current inside that material according to the relation:

$$J = \sigma E \quad (1)$$

where J is the induced conduction current density in A/m^2 . The induced current leads to a conduction loss due the high

TABLE 1. Dielectric properties of some biological tissues.

Material	Relative Permittivity	Conductivity	Tangent loss
Blood	60	2.04	0.27
Liver	44	1.79	0.288
Kidney	50	2.63	0.338
Fat	12	0.82	0.21
Muscle	49.6	2.56	0.242

electrical resistivity of the biological materials. The electromagnetic wave energy is then dissipated as a heat which rises the temperature of the tissues. Generally, the electrical conductivity of the biological tissues lies within limited values. On the other hand, the dielectric properties of biological tissues are responsible of the higher part of EM wave dissipation due to the dielectric polarization effect. The amount of loss inside the dielectric material depends on its complex permittivity which can be expressed as [30]:

$$\varepsilon^* = \varepsilon' - j\varepsilon'' \quad (2)$$

The real part of the complex permittivity ε accounts for the energy storing and the imaginary part accounts for the loss due to the damping of the vibrating dipole moments. The total loss inside the material can be characterized by the value of the tangent loss ($\tan\delta$) which is given by [31]:

$$\tan \delta = (\omega\varepsilon'' + \sigma)/\omega\varepsilon' \quad (3)$$

where ω is the angular frequency of the applied electric field. The nominator of Equation (3) represents the total conductivity of the material which is a combination of a frequency-independent ionic conductivity and a frequency-dependent damping effect of the vibrating dipole moments. Some values of the electrical conductivity, relative permittivity, and tangent loss of some biological tissues are shown in Table (1) [30], [32].

III. ADVANTAGES AND CHALLENGES OF MW CANCER ABLATION

Generally, thermal cancer ablation has many advantages compared to the other cancer therapy techniques. Thermal ablation is simple and has a short time, high degree of safety, and limited side effects. So, it is the best choice for the patients of small cancerous tumors. Microwave ablation can be considered as an extension to the radiofrequency ablation. Here, we are meant by the advantages of the MWA over its most related technique, i.e., the RFA. Operation of MWA mechanism is based on the continuous realignment of the polar molecules with the oscillating microwave field, increasing the kinetic energy and, consequently, the tissue temperature [33]. On the other hand, The heating mechanism in the case of the RFA is different while a thin needle-like electrode is placed into the tumor under the imaging guidance. The RF electrode

is of an insulated metal shaft terminated by conductive tip which is placed in direct electrical contact with the biological tissue volume under process. The RF power is supplied by a generator to the tissue through the shaft electrode while the other port of the RF generator is connected to a reference electrode, i.e., a large conductive pad placed in contact to the skin surface of the patient. Due to the voltage drop between the two electrodes, electric field lines are established in the patient's body. The ions within the tissue will oscillate at the same frequency of the applied electric field with a velocity that is directly related to the field intensity. The mechanism of RFA is based on the resistive energy loss resulted due to the ionic current [3], [34]. Mechanisms of the RFA and MWA are shown in Fig. 3.

A. ADVANTAGES OF MWA OVER THE RFA

Microwave ablation has many advantages over the other ablation techniques, in particular RFA [35]– [38]. Advantages of MWA can be summarized in the following points [8], [11], [39], [40]:

- Microwave ablation is characterized by the rapid temperature progress which speeds up the tissue coagulation and necrosis. Faster ablation property of the MWA increases the chance of achieving larger ablation volume and this is of particular interest, as incomplete ablation of the infected cells within the tissue is associated with high recurrence probability [13], [41], [42].
- Microwave frequencies are capable of propagating through all types of biological tissues [43], even those of low electrical and thermal conductivities. For example, bone and lung are two types of tissues that have low conductivity and permittivity, so, the MWA is more suitable than the RFA which has been associated with suboptimal performance when be used with such types of tissues [13], [20].
- Compared to the RF and laser, microwaves have the ability to easily penetrate through the charred or desiccated tissues that surrounds the ablation applicator which result in limited power delivery for non-microwave energy systems [18].
- Microwave ablation has the ability to use simultaneously multiple applicators as an array in small area. This property enables larger ablation area in addition to the control of the heating pattern [8].
- Microwave ablation is a suitable choice in the case of tumors that lies in closure to blood vessels. Moreover, MWA has less procedural pain compared to the other ablation techniques [11].

As the mechanism of heating in the case of MWA differs substantially from RFA, MW heating mitigates the problems related to the RF heating such as the need to an electrically conductive path, the limited heating efficiency in the areas of low electrical conductivity, and the concentration of heating only at the areas directly adjacent to the electrode [18].

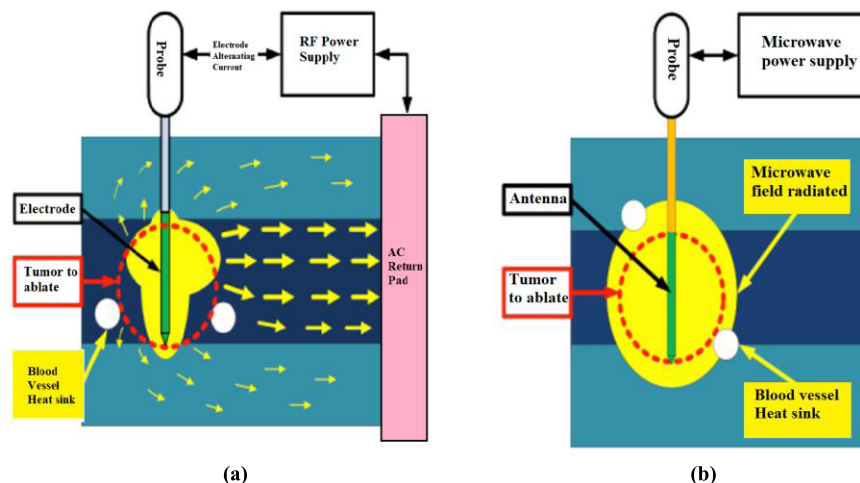


FIGURE 3. Mechanisms of; (a) radio frequency ablation (RFA), (b) microwave ablation (MWA) [33].

B. CHALLENGES OF MW CANCER ABLATION

Although the MWA provides a distinguish performance compared to the other techniques of cancer therapy, it has some challenges that have attracted the attention of the researchers. In this section we are concerned about the challenges related to the MWA antenna from the engineering point of view. The main requirement of the MWA antenna is to be properly impedance matched to the biological tissues under ablation, i.e., the output impedance of the antenna has the same value of the input impedance of the biological tissues. This condition is required to ensure maximum power transfer from the antenna to the tissues. The impedance of the biological tissues is a function in its dielectric properties.

Unfortunately, the accumulation of the power in the tissues does not follow the same rate during the whole ablation process. As the temperature of the tissues increases, their dielectric properties change and consequently their input impedance, leading to mismatching between the antenna and the tissues [6]. Fig. 4 shows how the properties of a biological tissue, i.e., the bovine liver, changes with temperature at 2.45 GHz operating frequency [44], [45]. It is clearly shown in the figure that the dielectric permittivity conductivity of the liver tissues decreases with the increase of the temperature. This scenario has two different challenging problems; the first one is that the enlargement of the ablated area stops after a short period of time, and the second one is that a high reflection of the electromagnetic wave exists, leading to a large standing wave over the length of the antenna. The power of the standing wave is consumed as heat causing the back heating of the antenna. The back heating of the antenna is an important issue because it causes the overheating of the antenna which can destroy the antenna itself, and on the other hand it harms the normal tissues through which the antenna penetrate to reach the tumor. Antennas used for MWA have to be designed with minimum reflection coefficient to minimize the backward overheating of the antenna shaft [9].

Another requirement of the MWA antenna is the control of the heating pattern [19]. The MWA is used in the treatment of several types of organs with different shapes of tumors. Most of the used MWA antennas provide elongated or elliptical ablation shapes whereas the spherical shape is more preferable in many cases. Typical elongated and localized patterns are shown in Fig. 5(a) and Fig. 5(b), respectively. There are many factors that are responsible of temperature increase along the antenna shaft, and then creating elongated heating patterns, such as the impedance mismatching between antenna and tissues, the conductivity of the material from which the antenna is made, and the leakage current along the outer conductor of the antenna [26]. Many antenna designs in the literature have been proposed to achieve localized ablation zone, while the need for a reconfigurable pattern antenna still one of the challenging requirements.

IV. ANTENNA STRUCTURES USED FOR CANCER ABLATION

The main requirements of the ideal interstitial cancer ablation antenna include a small diameter to minimize the invasiveness effect, a low input reflection coefficient, a localized SAR pattern at the operating frequency, and most importantly, a localized heating zone [17]. However, the choice of an antenna for MWA depends on clinical indications such as tumor size, location, and adjacent organs [43]. The most common antenna structure used for interstitial MWA is the coaxial antenna. Till now many researchers have presented several coaxial antennas such as monopole antenna, dipole antenna, choked antenna, slot antenna, and floating sleeve antenna [5]–[48], [9], [49]. Each one of the stated antenna designs has its characterizing performance regarding the heating pattern, backward heating, and the transient behavior under heating [5].

Monopole and slot antennas are the basis of most clinical MWA antennas and are constructed in the form of basic

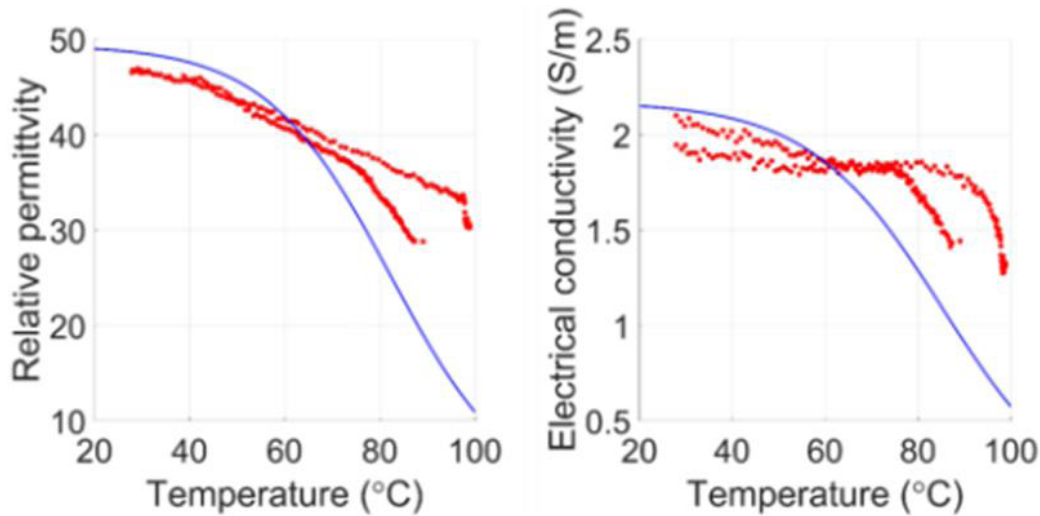


FIGURE 4. Change of biological tissues' properties with temperature. (a) Change of relative permittivity, (b) change of electrical conductivity. Red dots show the experimental data obtained in [44], and the blue solid line is shows the results of [43].

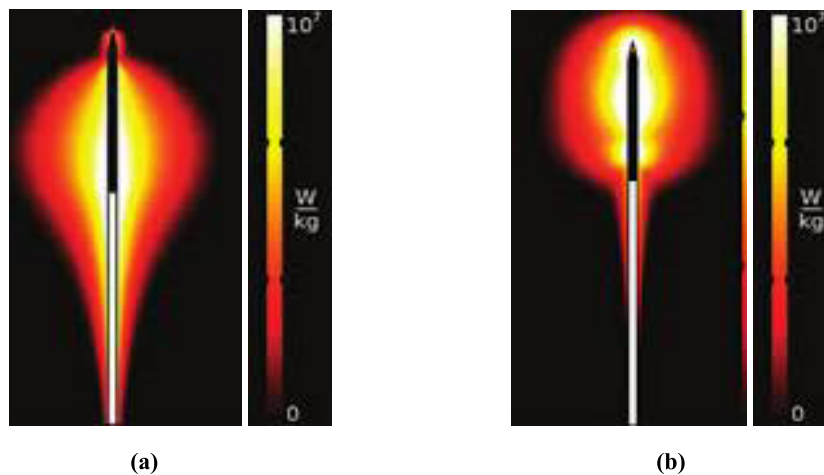


FIGURE 5. Examples of SAR distribution of MWA antennas; (a) elongated distribution with high back heating of the antenna, (b) near spherical distribution with localized heat deposition.

coaxial structure. Configuration of the coaxial monopole antenna is shown in Fig. 6(a), and it is characterized by its elongated ablation zone which is a result of the backward heating [6]. The elongated ablation might be undesirable in several clinical applications [13]. The main advantage of the coaxial monopole antenna is its simplicity and ease of fabrication [43].

Single slot antenna, as shown in Fig. 6(b), is a coaxial shaped structure of short-circuited tip. A small ring cut is etched from the outer conductor near the tip of the antenna. Like monopole, single slot MWA antenna has elongated ablation and suffers from backward heating. It has ability to deliver more energy to the tissue than the monopole.

To overcome the drawbacks of coaxial monopole and single slot antennas, dual slot antenna has been introduced [50]. As shown in Fig. 6(c), it is a coaxial antenna with two slots

designed to work simultaneously to minimize both reflected power and ablation length. Dual slot coaxial antenna is more efficient than the monopole and single slot antennas regarding the power localization around the tip, although the backward heating is not completely removed [9], [43], [13].

V. SAR DISTRIBUTION AND CONTROL OF ABLATION AREA

The rise of temperature is required for destroying the malignant cells; however, the rise of temperature inside the healthy tissues has to be mitigated. For example, temperature of about 41°C has little effect on most malignant cells, while at temperatures of about 45°C, thermal damage of normal cells can take place. So that, precise temperature control is important such that the heating is totally confined to the harmed tissue

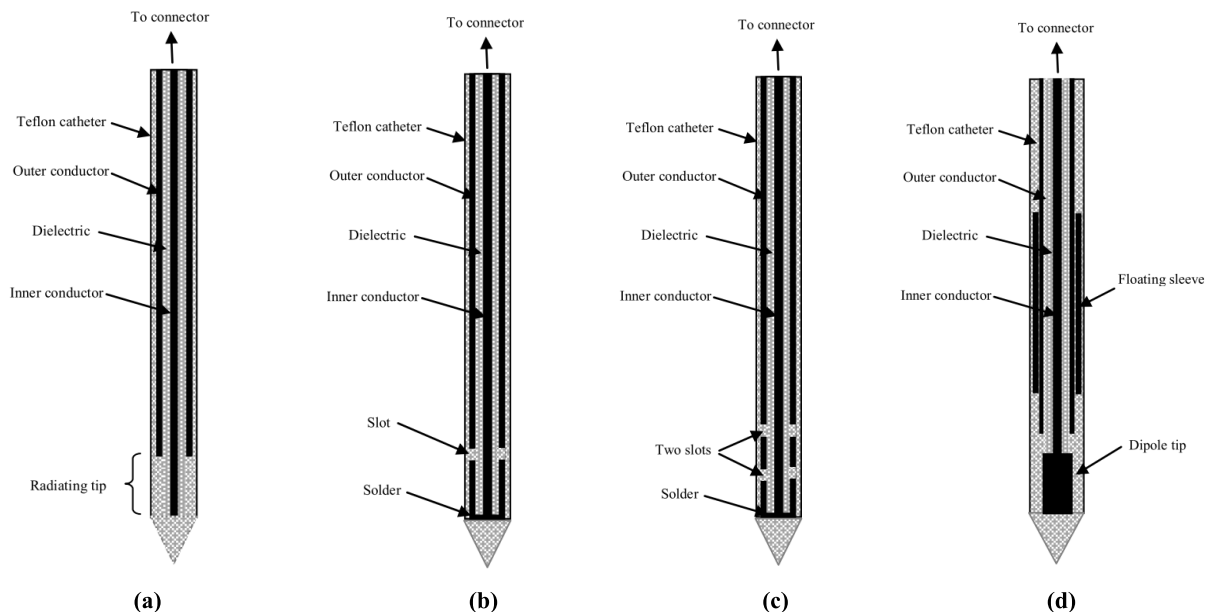


FIGURE 6. Microwave ablation antenna configurations; (a) monopole coaxial antenna, (b) single slot coaxial antenna, (c) dual slot coaxial antenna, (d) floating sleeve dipole antenna.

under treatment and mitigate the damage of the surrounding healthy tissues.

Most tumors of the liver, kidney, and lung indicated for thermal ablation are focal and exhibit a relatively spherical morphology [8], [16]. Unfortunately, the majority of MWA antennas have axisymmetric heating patterns which cause elongated ablation zones. In some of the MWA scenarios, the elongated ablation zone may not be ideal. For example, If a vital healthy organ exists in the proximity of the targeted ablation zone and the center region of the tumor is not easily accessible, using of a MWA antenna with elongated ablation zone will cause damage in the adjacent healthy organ [24]. For these reasons, matching of the antenna’s ablation zone with the tumor’s shape may prevent the expected damage of the adjacent healthy tissues [8]. Therefore, the interstitial MWA antenna has to be developed with the objective of delivering and focusing energy to the infected tissue effectively. Design of the MWA antenna is a critical factor that decides the size and shape of the ablation zone. Many of researches concerned by MWA antenna development have recently focused on controlling the shape and size of the antenna’s ablation zone [9].

Some studies have proposed the choked antennas as a solution, as they produce a concentrated pattern and prevents backward heating of the antenna [26], [51], [52]. Operation of the choked antenna is based on choking the excited currents on the outer surface of the outer conductor of the coaxial antenna. One of the most common techniques used to choke such unwanted currents is to use a coaxial balun [53]. The coaxial balun is realized by encircling the coaxial antenna with a hollow conducting tube which is electrically isolated from the surface of the coaxial antenna by a dielectric

material. The hollow conducting tube, the dielectric material, and the outer surface of the antenna constitute a new transmission line that guides the antenna’s outer surface currents toward a short circuit or an open circuit termination in order to be suppressed. The microwave energy localization abilities of such a type of designs make it the best choice for tumors ablation [43]. Structure of a balun-equipped coaxial antenna, i.e., floating sleeved antenna, is shown in Fig. 6(d). As shown in figure, the antenna is enclosed within a teflon catheter to facilitate the extraction of the antenna from the hard ablated tissue. Although the choked designs have the advantage of heating pattern confinement to the distal aspect of the antenna, they have the drawbacks of complex geometrical configuration that complicates its fabrication procedures and they increase the antenna diameter and potentially increase power reflections from the antenna [8], [54].

Some of new variations were proposed in the literature to provide high levels of control on the resulted heating pattern. In [24], a directional interstitial MWA antenna was introduced. As shown in Fig. 7, the antenna is a monopole with extended outer conductor which acts as a reflector that directs the radiated fields toward the opposite direction. A half ring slot cut is etched in the outer conductor to provide directional fields away from the reflector. The reflector with the slot removes the parasitic currents along the antenna’s shaft and eliminates the need to baluns which increases the overall antenna size [55].

In the cases where the tumor’s volume is large, array of applicators may be used instead of single applicator [56], [57]–[59]. In this case more than one applicator are applied simultaneously to the infected area with specific configuration to provide a central large heating area as shown

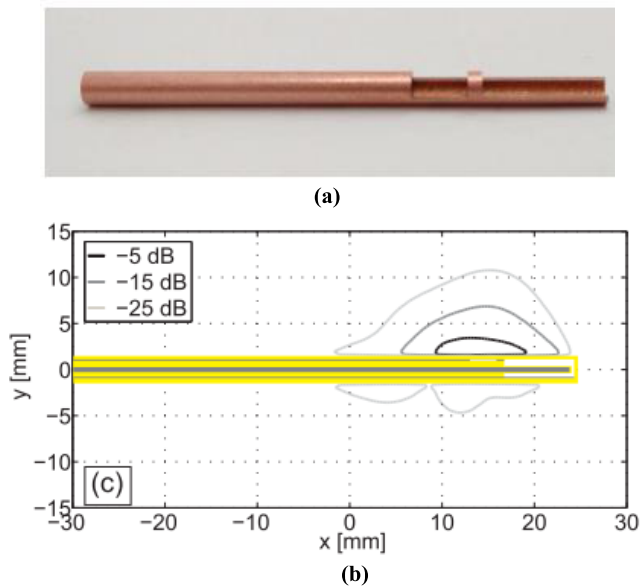


FIGURE 7. Side directional MWA antenna; (a) fabricated outer conductor reflector, (b) SAR distribution.

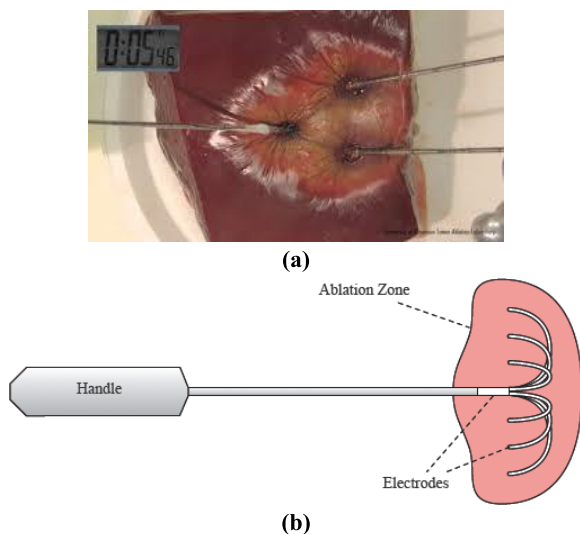


FIGURE 8. MWA antenna arrays; (a) array of three applicators, (b) tip-split applicator.

in Fig. 8(a). Triangular array configuration can produce a spherical ablation zone, while square configurations result in flatter ones [13]. In spite of the effectiveness of using the MWA arrays, it is accompanied with increased invasiveness as multiple applicators are used within a limited area simultaneously [24]. In a trial to reduce the invasiveness of the array, tip-split array applicator has been introduced [60], [61]. The tip-split array applicator is composed of two or more coaxial-slot antennas which split only inside the tumor. The tip of the applicator splits inside the tumor to take the umbrella shape as shown in Fig. 8(b). In addition to its reduced invasiveness, the tip-split array applicator has the ability to achieve large ablation area. For more focusing and high degree of

controllability, adaptive microwave phased array has been utilized for cancer ablation [59]. Operation of the adaptive phased array is based on using an array of antennas together with an adaptive processor to direct the combined radiation of the array toward the infected area and introduce nulls in the directions of the healthy areas. Performance of the microwave phase array has been investigated in many of published studies [62], [63]. Although the published results have revealed good performance in the cases of surface and near surface tumors, more investigations still are required about the use of adaptive microwave phased array for the ablation of the deeply located tumors.

VI. CONCLUSION

A review about the microwave cancer ablation is presented in this article. Principle of operation, advantages, and challenges of the MWA technique are discussed. Microwave ablation is an effective minimally invasive technique for cancer therapy. It has many advantages over the other cancer ablation techniques, and therefore it seems to be promising for cancer therapy in the future. In spite of the large number of published researches about MWA and its performance enhancement, there are many of the MWA challenges still need for more investigations.

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ASHRAF M. SAID received the B.Sc. degree in biomedical engineering, the M.Sc. degree in optimum design of MRI gradient and RF coils, and the Ph.D. degree in statistical analysis of brain connectivity using bold images of fMRI on human vision system from Cairo University, in 2000, 2005, and 2011, respectively. He is currently an Associate Professor with the Biomedical Engineering Department, Faculty of Engineering, Minia University. His scope of research interests include bio signal processing, recognition in biometric, image processing, biotechnology, and biomedical application of nanotechnology



AHMED A. IBRAHIM (Member, IEEE) was born in 1986. He received the B.Sc. degree and the M.Sc. and Ph.D. degrees in electrical engineering from the Electronic and Communication Engineering Department, Minia University, Minya, Egypt, in 2007, 2011, and 2014, respectively. He is currently an Associate Professor with the Electrical Engineering Department, Faculty of Engineering, Minia University. He has been a Visiting Professor with University Pierre and Marie Curie, Sorbonne University, Paris VI, France, for seven months, and Otto-von-Guericke-Universität Magdeburg-Germany, for six months. He has published more than 70 peer-reviewed journal articles and conference papers. His research has focused on miniaturized multiband antennas/wideband, microwave/millimeter components, and MIMO antennas and energy harvesting systems. He is a Senior Member of URSI and a member of the National Committee of Radio Science, Egypt. He is also a Reviewer of the IEEE ANTENNAS AND WIRELESS PROPAGATION LETTERS, the IEEE MICROWAVE AND WIRELESS COMPONENTS LETTERS, IEEE ACCESS, *IET Microwaves, Antennas & Propagation*, *Electronics Letters* (IET), MOTL, and many other journal and conferences.



EMAD TAMMAM was born in Qena, Egypt, in 1978. He received the B.Sc. and M.Sc. degrees in electrical engineering from Minia University, Egypt, in 2001 and 2007, respectively, and the Ph.D. degree in electronics and communications engineering from the Egypt-Japan University of Science and Technology (E-JUST), Alexandria, Egypt, in 2013. He is currently an Assistant Professor with the Electrical Engineering Department, Minia University. His current research interests are the design of antenna for biomedical applications, RF energy harvesting, UWB antennas for different wireless communications applications, and miniaturization of antenna.



AHMED I. A. GALAL received the B.Sc. and M.Sc. degrees from the Electrical Engineering Department, Minia University, Egypt, in 1995 and 2003, respectively, and the Ph.D. degree from the Electronic Engineering Department, Kyushu University, Japan, in 2011. He was a Visiting Researcher with Kyushu University, from February 2016 to August 2016. Since 2011, he has been working as an Assistant Professor with the Faculty of Engineering, Minia University, Egypt. His research interest is in analog RF front end transceiver for ultrawide band systems.

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