Applications of Microwave radiations in the Diagnosis and Treatment of Cancer: A brief Review

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Radio frequency MWs (RFM) exert various effects on biological system and possess a great impact in medical applications for instance by heating, altering chemical reactions or inducing electrical current in tissues and cells. The knowledge of temperature-dependent electrical properties of biological tissues is important to calculate the deposition of electromagnetic energy in a variety of diagnostic procedures and treatments. Every single molecule of biological system is continuously generating electromagnetic field due to thermal agitation of charged particles that is directly proportional to its frequency, so the higher frequency indicates higher energy. The current advancement in the research technology, especially telecommunication, has raised great concerns regarding possible effects of excessive RF/MW exposure. Biological system when exposed to RF radiations they can be reflected, transmitted, refracted or absorbed (1). Based on the amount of absorbed energy within the biosystem, effects can be divided into thermal and non-thermal and the mechanism of RF interaction with the body is the increase tissue or body temperature which is responsible for to cellular and intracellular changes. The amount of heat depends on the intensity of radiation, electrical properties of exposed tissue and body′s thermoregulatory mechanism (2).

According to Dodge and Glaser,1977 (3), the exposure level established in the United States adheres to a level of 10 mW/cm^2 averaged over 0.1 h. It is reported that minimum energy required for these processes should exceed 26 meV, the average energy of thermal noise measured at body temperature. These effects could only be observed if certain biological structures had the same vibration frequencies as the applied electromagnetic field (EM). For example, microtubule reassembly was related with the peak of cellular EM field emission during replication suggesting the crucial role in their generation. Interestingly microtubules can vibrate in kHz to GHz frequency region (4). Adey reported that RF/MW radiation seems to induce electric oscillations that disturb cell membrane proteins, activating enzyme cascades that may transfer cell surface signals to the intracellular system (5). Foster et al in 2016 (6) performed a study on RF-induced increase in skin temperature in the frequency range from 3GHz through the millimeter frequency range (30-300 GHz). They developed a model based on Pennes ‘Bioheat equation (BHTE) and the parameter analysis showed mall irradiated areas (less than about 0.5-1 cm in radius) the temperature increase at the skin surface is chiefly limited by conduction of heat into deeper tissue layers, while for larger irradiated areas, the steady-state temperature increase is limited by convective cooling by blood perfusion. The study supported the use and limitations for using MW radiations in biological system.

Based on these findings scientists investigated the involvement of MW in the diagnosis and treatment of cancer and other related diseases. Researchers have proposed the biophysical mechanism of a novel diagnostic methods based on MW radiation technology for cancer detection. These methods are related to the frequency-based absorption of electromagnetic waves emitted by the malignant tumors.
This review presents the literature survey of recent progress in MW technology for early detection and treatment of cancer based on scientific research. These MW techniques will bring new paradigms for cancer imaging and therapy may emerge soon that challenge conventional methods for diagnosing, staging and treating cancer and metastatic diseases.

Dielectric Properties of Normal and Malignant Human Tissues

Every cell and tissue of human body possess different electric environment and behave differently when exposed to MWs. At MW frequencies, dielectric properties are determined by water content and thus less affected by tissue removal than at RF frequencies. The application of temperatures greater 50-60°C likely causes irreversible changes in the electrical properties as result of dehydration, shutdown of perfusion, and other cellular and molecular changes and can be responsible for malignant tissue or cell (7).

Table 1: Temperature-dependent electrical properties of normal and malignant human tissues studied by the researchers.

Reference	k [W/m/K]	k Coeff. [%/°C]	α [m^2/s]	alpha Coeff. [%/°C]	c [W/m/K]	c Coeff. [%/°C]	Tissue type	Temperature range [°C]	Tissue state
Choi,2013	0.550	0.257	-	-	-	-	Kidney human	3–45	Not specified
Choi,2013	0.503	0.092	-	-	3499*	0.2*	Liver human	25–80	> 12–24 h postmortem
Choi,2013	0.396	0.603	-	-	-	-	Lung human	3–45	Not specified
Valvano,1985	0.493	0.120	1.474 E-07	0.339	3212	-	Myocardium human	3–45	1–2 days after biopsy
Valvano,1985	0.415	0.004	1.436 E-07	−0.341	2726	-	Adenocarcinoma of the breast human	3–45	within 24hrs
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Valvano,1985	0.545	0.080	1.134 E-07	-	4533	-	Colon cancer human	-	within 24hrs
Valvano,1985	0.540	0.204	1.482 E-07	0.371	3505	-	Renal medulla human	3–45	1–2 days after biopsy
Valvano,1985	0.540	0.204	1.482 E-07	0.371	3505	-	Renal medulla Zuman	3–45	1–2 days after biopsy
Valvano,1985	0.539	0.241	1.444 E-07	0.326	3592	-	Spleen human	3–45	1–2 days after biopsy

+c calculated via k/alpha/rho
*The values and the coefficient were calculated for the temperature range 20 to 70°C.
The presented conductivity and diffusivity were calculated for 37°C; original values were presented temperatures different from 37°C. Data taken from Rossmann et al., 2014 (7).

1. Ultra-wide band (UWB) antenna sensor Base MW Imaging:

MW imaging is defined by Fear et al. in 2003 (8) as "seeing the internal structure of an object by means of electromagnetic fields at MW frequencies of 300 MHz to 30 GHz". MW imaging techniques have been intensely studied as a promising diagnostic tool for rapid and cost-effective early-stage cancer detection.

Ultra-wideband (UWB) antenna imaging technology began since last decade and used mainly for the detection of breast cancer. The antenna acts as a transmitting and receiving sensor. The breast tissues are exposed to MW signals from transmitting sensor and the back-scattered signals from the breast tissues are collected from receiving sensors. The changes in the back-scattered signal are analyzed and used to identify tumor cells inside the breast, which exhibit higher dielectric constants than normal cells (9). Recent studies show that the antenna sensor should have high gain, the ability to transmit a wide range of frequencies with higher efficiency, directive radiation of power, small size and model simplicity, compatible penetration of human tissue and the ability to operate at both low and high frequencies (10, 11) Ultra-wideband (UWB) antenna technology has some useful features, like high-speed data rates, very small interference, simple low-cost designs and low power spectrum density and it is reported that high gain and wideband of approximately 8 GHz has shown quite good results. Since 2002, the Federal Communications Commissions (FCC) has allowed UWB bands of 7.5 GHz (from 3.1 to 10.6 GHz) for commercial usage (12). Recently MW tomography and ultra-wideband (UWB) radar imaging for breast cancer detection is also gaining importance and UWB radar imaging is important for histological procedures.

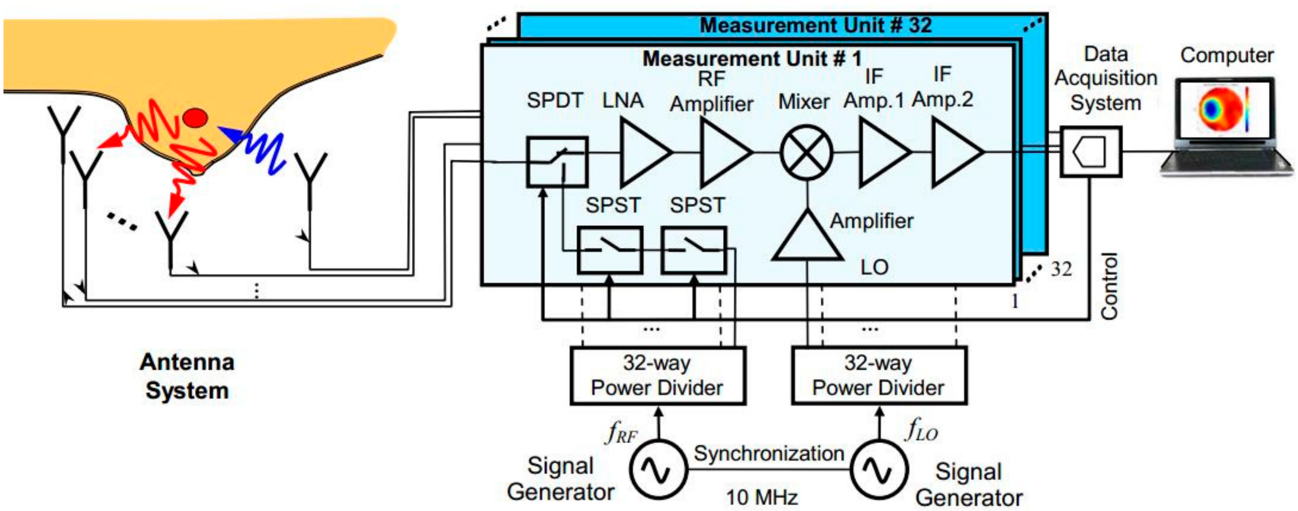

Figure 1: Schematic block diagram of MW imaging using UWB antenna sensor (13).

2. **MW-induced thermoacoustic imaging (TAI)**:

TAI uses the same physical principal as PAI, except that short electromagnetic pulses between 0.3 and 3 GHz are used as the source for excitation and images are proportional to the absorbed MW energy. Because tumors with higher water content differentially absorb MWs compared to surrounding tissue (e.g., adipose), TAI has been proposed as a novel approach for diagnostic breast imaging, and a pilot study at 434 MHz revealed 3D in vivo images of the human breast with excellent sensitivity for detecting tumors. However, limitations in MW and ultrasound hardware in these early studies prevented high resolution characterization and accurate classification of suspicious lesions (14). Because resolution in TAI depends on the duration of the excitation pulse, the long MW pulse of 1 μs contributed to poor spatial resolution (> 1 mm) (14). To overcome this drawback, two research teams recently tested a novel broadband transmitter for TAI with ultrashort impulse excitation. Instead of a traditional tube-based amplifier, the low-cost excitation source exploited a high-voltage triggered spark gap for generating short electromagnetic impulses (10 ns duration) with high peak power (up to 40 MW).

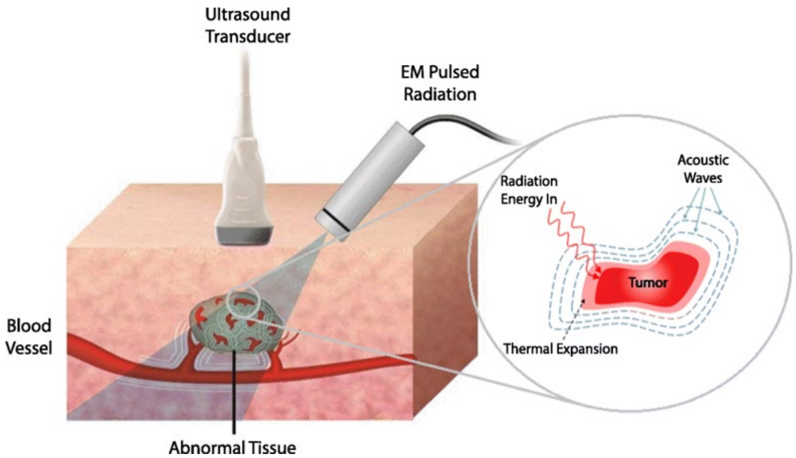

Figure3: Schematic representation of MW-induced thermoacoustic imaging system (14).

3. MW Ablation (MWA):

Radiofrequency ablation (RFA) and MW ablation (MWA) are the two percutaneous thermal ablative techniques for the treatment of unresectable tumors and for MW ablation the important properties are relative permittivity and effective conductivity. In comparison with surgical resection, percutaneous image-guided ablation delivers a minimally invasive treatment source, ideal for nonoperative candidates but the rate of blood perfusion in each tissue is important for both RF and MW ablation. RF MWs in low frequencies are also reported to kill cancer cells thereby reported as cytotoxic and can be a promising tool for the treatment of cancer of various origin. In addition, percutaneous radio-frequency ablation has been widely accepted as the first-line treatment of early-stage hepatocellular carcinoma (HHC) and many randomized controlled trials have shown significant differences between these local ablation techniques. MW technology is a new thermal ablation technique for different types of tumors, providing all the benefits of radiofrequency and substantial advantages. MW ablation has been applied to liver, lung, kidney and more rarely to bone, pancreas and adrenal glands (15). One study shows that MWA is a preferable treatment modality for benign thyroid nodules with less complications. Hyperthermia has found very effective in the treatment of cancer patients in addition to chemotherapy, hormone therapy surgical resection and radiation therapy with minimal toxicity. MWA offers potentially better local control in larger and perivascular tumors.

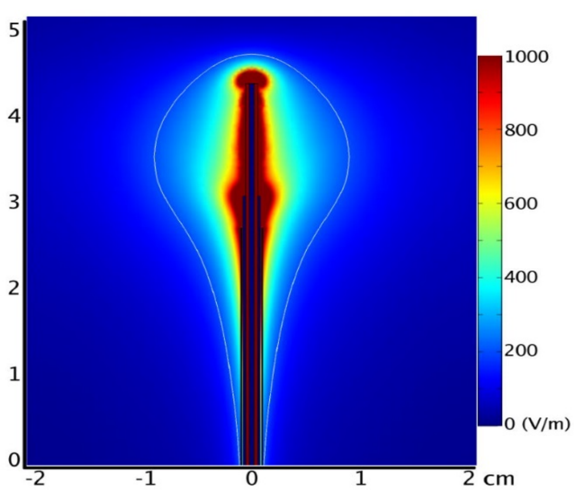

Figure 2: Heating pattern around a triaxial MW ablation antenna. Note that the zone of active heating is nearly 2 cm in diameter and no ground pads are needed. This larger zone of heating results in better performance near blood vessels and improved multiple-antenna capabilities (16).

Mechanism of MW-induced Hyperthermia in Cancer Cell Death

The mechanism of MW induced cell death is still unclear and under investigation. However, some of the recent studies show that MWs induced anti-cancer effect is due to various cellular changes such as increased cellular permeability, disassembly of cytoskeleton, enlarge tumor pores, protein denaturation, DNA fragmentation or strand breakage that contribute to apoptosis (17). Researcher have studied MW-induced apoptosis in bladder cancer, lung cancer and prostatic adenomas.

Conclusion: Based on the published literature on the involvement of MW radiations in the clinical and medical industry gained a great importance for the scientists. Further investigations need to be carried out to study the effect of MW on in-vitro and in-vivo experiments for the treatment of cancer.

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