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Comparison between Thermal Ablation Techniques for Treatment of Cancer

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Abstract: Thermal ablation is direct application of heat to a specific tumor in order to achieve complete eradication of tumor There are five methods used to produce thermal ablation: cryoablation, radiofrequency (RF), laser, ultrasound and microwave (MW). The thermal ablation received more attention from research community when they realized its potential to become the superior treatment modality with the advancement in technology. In this paper author has compared the entire thermal ablative to treat the cancer in the deep seated organs.

Keywords: Tumor, Ablation, radiofrequency (RF), ultrasound, (microwave MW)

I. INTRODUCTION

Cancer is the most devastating diseases in the present scenario of the world. The foremost question is that: why haven't we found a cure for cancer yet? The main problem is that there are different types of cancers in different organs; hence it is very difficult to find a general cure because the treatments and treatment methods vary with the type of cancer and location.The available treatment modalities are Chemotherapy, Radiation therapy and surgery.

Ablation can be an alternative to risky surgery, and may be an alternative choice for patients with an inoperable tumor. Ablation refers to the direct application of chemical or thermal therapy to a specific organ or tissue in order to achieve complete eradication of tumor. This technique helps in tissue destruction by the formation of a scar tissue (by shrinking) and gradually removing it, sparing the normal tissue. Ablation technologies for hepatic malignancy have developed rapidly in the past decade, with advances in several percutaneous or externally delivered treatment methods including cryoablation, laser ablation, and high-intensity focused ultrasound radiofrequency ablation, microwave ablation. Researchers have focused on increasing the size of the ablation zone and minimizing heat-sink effects.

II. THERMAL ABLATION TECHNIQUES

Human cells can survive up to the 42°C temperatures [25], at 43°C, cells die after 30 min, as temperature is increased, the time to death of cells decreases; at 50°C death occurs in 30sec; at 55°C it occurs at 1s, and above 60°C death of cells is instantaneous. If the cells are cooled to a sufficiently low temperature i.e. < -40°C cell necrosis occurs. The cell response to the temperature changes in the body can be analyzed in Figure 1. An easy way to comply with the conference paper formatting requirements is to use this document as a template and simply type your text into it.

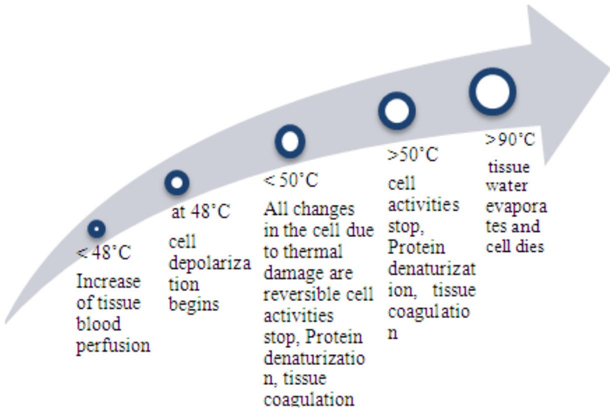

Figure 1 Cell responses to temperature change

The main aim of thermal tumor ablation is to destroy an entire tumor by using heat to kill the malignant cells in a minimally invasive fashion without damaging adjacent vital structures. Ablation has become an important strategy in the treatment of cancer/tumors in different organs. The mechanism of all thermal ablative technologies has been summarized below.

Cryoablation uses extreme cooling to destroy cancer cells. It was the first widely available ablative therapy which came into use in 1955 as slow cooling by liquid Nitrogen [1]. It is performed via open surgical, laproscopic or percutaneous approach. Cell death is due to rapid freezing of intercellular water and subsequent cell lysis [2]. Cryoablation uses repetitive freezing and thawing of tissue to produce necrosis and irreversible tissue destruction will occur between -40°C and - 60°C. Liquid Nitrogen and Argon gas can both be used as coolants and are capable of producing temperatures of at least -60°C [3]. For implementing cryoablation physician will perform a percutaneous procedure, which involves image-guidance assurance to insert cryoprobes or a series of small hollow needles through the skin to the site of the diseased tissue. Once the needles or cryoprobe(s) are in place, the liquid

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nitrogen or argon gas is delivered, due to which an ice ball is created in the target tissue [4-5]. The completeness of cell destruction is directly proportional to the rapidity and duration of freezing and the rate of thawing. The temperature drops faster and to lower temperatures with decreasing distance from the cryoprobe.

Another advantage of cryo energy is that it allows the doctor to freeze tissue to test whether it is responsible for cryomapping, however heat-based therapies don't allow the doctor to do that – once the tissue is burned, it stays burned. In contrast, cryoablation allows re-warming of the frozen tissue to restore its function. The main disadvantage is that, cryoablation can be applied only for small tumors up to 4 cm [6]. Moreover, this technique has fallen out of favor for the treatment of HCC, primarily because the complication rate described are high as 40.7% [7-8] and the risk of "cryoshock," a life-threatening condition resulting in multi-organ failure, severe coagulopathy and disseminated intravascular coagulation following cryoablation. Although cryoablation has been challenged in many cases and replaced by RFA because it is a viable technique for treatment of patients with tumors.

A. Laser Thermal Ablation

Laser is a monochromatic, collimated and coherent radiation with a wavelength of 1024 nm, which concentrates extremely high energy in small focalized areas. It may be transmitted inside the tumor by single or multiple quartz optical fibers inserted through fine needles, thus converting the intense light energy to tissue heating.

As the amount of energy increases interstitial and intracellular water is vaporized and the tissue contracts. At higher energy levels, all cellular material is vaporized and a crater is created in the treated tissue [9]. One of the major disadvantages of laser is its small penetration depth less than 1 mm in the tissue, which restricts its use only for eye and cosmetic surgery.

Further it generates relatively small ablation zone when used for deep seated organs, which generally make its use restricted. Moreover high vascularity or the presence of large vessels near the tumor can result in small or irregular lesions, leading to treatment failure or early recurrence. Laser ablation has been used in the treatment of cancer/tumor, while very few data is available on the treatment of HCC.

B. Ultrasound Ablation

High intensity focused ultrasound (HIFU) functions as a thermal therapy for tumors at a frequency range of 0.8 to 3.5 MHz. In HIFU, the intensity of the US beams is substantially increased by converging the beams within a tight focal zone. It is a truly non-invasive approach as the ultrasound transducer transmits the beams from outside the body. The intensity of the ultrasonic waves is below the threshold to cause damage as they pass through the tissue toward the focal zone [10]. Early clinical results of HIFU promised the local ablation of tumors, although there are time constraints that limit the practicality of current technologies for thermal ablation in many oncology settings. The length of treatment time needed is one of the major limitations for ultrasound ablation.

Although HIFU can reach various locations in the body with insertion depths dependent on the focal length of the transducer, the ability of HIFU to generate a lesion can be limited by air-filled organs such as the lung and the bowel. Focusing the HIFU beam through bone is also a major problem; however, attenuation correction and prediction based upon reference computed tomography (CT) or magnetic resonance (MR) has been performed [11].

C. Radiofrequency Ablation (RFA)

The use of RF alternating current to heat living tissue is credited to d'Arsonval in 1891, which showed that RF waves of high frequencies (> 10 kHz) can pass through living tissue causing an elevation in tissue temperature without causing neuromuscular excitation. These observations eventually led to the development of electrocautery and medical diathermy in the early- to mid-1900s. In the year 1990, both Rossi et al and McGahan et al published papers on ultrasound - guided RFA of hepatic tissue [12-13] . Both groups suggested that RF could be used to create focal coagulative necrosis of hepatic tumors while sparing normal liver tissue.

RFA uses radio-frequency current, usually around 500 kHz to deposit energy over a sizeable region to heat up tissue. The voltage applied is approximately ~100 V, with applied power up to 200 W. RFA works by converting radiofrequency waves into heat through ionic vibration. The ionic friction generates the heat within the tissue only, leading to coagulation necrosis and cell death. The higher the current, the more vigorous is the motion of ions and higher temperature is reached over a certain time. The RFA probe is introduced transcutaneously, in a minimally invasive fashion, into the tumor. The ability to efficiently and predictably create an ablation is based on the energy balance between the heat conduction of localized radiofrequency energy and the heat convection from the circulation of blood, lymph, or extra and intracellular fluid [14].

The performance of RF ablation is hindered by tissue charring which occurs if the temperature reaches nearly 1000C. At this temperature water begins to boil out of the tissue and tissue becomes dehydrated. The current path in dehydrated tissue is depleted. To work out this problem, the driving voltage may be impedance/temperature controlled to be switched off when impedance/temperature rises too high. Due to this reason, a cooling system was introduced in RF ablation to control the temperature at the electrode interface and increasing the ablation zone and keeping zone being too hydrated.

The RF ablation is handicapped in the areas of elevated blood perfusion, especially in liver and kidney and where tissue is desiccated. The major drawbacks encountered are

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that organs and tissues near the liver, such as the gallbladder, bile ducts, diaphragm and bowel loops, are at risk of being injured as the procedure may involve exposure to x-rays. In RFA complete ablation of lesions smaller than 2 cm is possible in more than 90% of patients with local recurrence in less than 1% [15]. In larger tumors five-year survival rates are somewhat lower, at 70-80% for nodules less than 3 cm in diameter, and 50% for tumors between 3 and 5 cm [16], hence it is unacceptable.

D. Microwave Ablation (MWA)

In 1936, Denier reported the use of low – frequency MW therapy to treat a tumor [17]. The basic principle of microwave ablation (MWA) is to apply microwave power to the tumor tissue through the microwave antenna. Microwaves produce effective ablation without islands of viable cells in a rapid and reproducible fashion. The microwave region of the electromagnetic spectrum is well suited to such a role due to the efficient conversation of electromagnetic energy to heat.

This translation of energy is a result of the strong interaction between polar molecules and microwaves that causes oscillation of molecules, which is dissipated as heat. Water is a highly polar molecule, abundant in human body: it is the interaction between the microwaves and water that is principally responsible for the rise in temperature.

The interaction between water and the entire range of frequencies in the microwave bandwidth is particularly strong. Another advantage of microwave ablation is the manner in which the heating occurs. Unlike the alternative ablative devices such as radiofrequency or cryotherapy, the passage of heat is not solely reliant on conduction.

The fundamental reason why microwave energy is unique and efficient is that it is transmitted from a suitable application or probe as a “field” around its tip. Direct heating of water molecules occurs within the whole microwave field, not simply by conduction of heat from the surface of a hot probe. A whole spherical area, perhaps the size of a tennis ball, is heated simultaneously and uniformly within minutes [18].

Microwave-generated heat is used to shrink and/or destroy cancerous tumors. Microwave ablation has generally utilized microwave antennas working at 915 MHz, and 2450 MHz. A hyperthermia system includes the antenna and a non-contacting temperature sensor that scan a predetermined path over the surface of tissue to be treated. The temperature sensor senses the temperature of the tissue, and a controller closes a feedback loop that adjusts the microwave power applied to the antenna in a manner that raises the temperature of the tissue uniformly.

The early systems had the disadvantage of having heating patterns with lateral SAR contours that are significantly smaller than the applicator dimensions, thus causing under-heating problems in early trials when investigators used applicators that covered the tumors visually, but heated only their central region.

Also, at the frequency of operation, these systems have relatively long wavelengths, limiting their ability to focus on tumors. To overcome these limitations, improved antenna-based systems and multiple-applicator systems have been used clinically for large tumors. Szwanowski et al [19] developed implantable coaxial systems that were used to treat deep-seated tumors without affecting the overlying tissue.

In the early 1980s, MW ablation (MWA) was developed as a technique to obtain hemostasis along the hepatic resection plane [20]. In 1983, Coughlin et al were the first to report the use of interstitial MW therapy for the treatment of a brain tumor. However, the electrode was prohibitively large, measuring 1 cm in diameter.

This limitation was overcome in 1986 when Tabuse et al designed a small (2.8- mm diameter) coaxial interstitial MW system [20]. Currently MWA is in clinical use in a number of Asian centers [21-22]. Recently, advances in antenna design have led to a new MWA system in which power feedback is markedly reduced, allowing for longer times of application, greater power deposition, and larger ablation lesion sizes [23].

III. COMPARISON BETWEEN MWA AND OTHER THERAPIES

There is no consensus on the “perfect” local ablation technique. The survival data must be fully elucidated for the different techniques and the growing implementation ablation treatments adds more complexity to the choice of techniques. Survival data should be expected to be similar for similar ablation techniques of local tissue destruction.

If differences exist, it may be due to differing technical aspects such as operator variability, reliability and precision of the device, and specific needle/probe/antenna geometries used. Techniques producing smaller treatment volumes per needle or catheter insertion for laser and cryoablation, or treatment time in ultrasound ablation, may be more susceptible to treatment gaps and treatment failure. Because of this, radiofrequency and microwave may have advantages over laser, cryoablation, and ultrasound ablation, especially in liver tumor ablation where larger volumes of tumor burden are present.

The Image-guided deposition of electromagnetic energy for killing tumor, drug delivery, gene transfection, or enhancement of radiation or immunotherapy will play an emerging role in targeted local and regional oncology, guided by multimodality navigation, automation, and visualization. The comparison between microwave ablation and other therapies as per their advantages and disadvantages is shown in Table 1.

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Table 1Comparison between microwave ablation and other therapies

S. No.	Heating Techniques	Advantages	Disadvantages	Applications
1.	Microwaves	1. Large technology aspects. 2. Heating of large volumes theoretically possible. 3. Multiple applicators, coherent or incoherent, can be used. 4. Specialized antennas for heating from body cavities have been developed. 5. Skin cooling feasible. 6. Interstitial use has been demonstrated.	1. Heating not localized at depth. 2. Limited penetration at high frequencies. 3. Possible adverse effects on personnel. 4. Shielding of treatment rooms required, except at medically reserved frequencies (e.g. 915MHz). 5. Thermometry requires non interacting probes. 6. Temperature distributions subject to variations in local blood flow. 7. Commercial antennas available are of fixed length. 8. Depth of tissue implant alters specific absorption rate pattern.	Surface or near surface lesions, liver cancer treatment, Lesions on breast, chest wall, extremities (external applicators), bladder prostate, esophagus cervix, brain, head and neck with specialized or interstitial applicators.
2.	Radiofrequency (direct current or capacitive coupling)	1. Equipment relatively simple. 2. No special shielding required. Large volumes may be heated. Heating of deep-seated lesions sometimes possible. 3. Interstitial use has been demonstrated. 4. Electrodes not limited in size. 5. Insulation easily accomplished.	1. Fat tissue may heat preferentially. 2. Current flow subject to local electrical tissue characteristics. 3. Temperature distribution additionally subject to blood flow variations. 4. Heating regional with external applicators.	Large surface tumors, lesions in extremities, lung, pancreas, liver, bladder. Interstitial applications, chest wall head and neck, prostate, uterine cervical cancer.
3.	Ultrasound single transducers	1. Readily focuses on tissue. 2. Heating possible to 5-10 cm depth with focused transducers. 3. Dynamic systems have been demonstrated. 4. Shielding not required and no health hazard to. 5. In dynamic systems, effects of the blood flow can be reduced by minimizing focal volume.	1. No penetration of tissue-air interfaces. 2. "Shadowing" by bone. 3. Bone tends to heat preferentially. 4. Patients [illegible] experience pain during tre[illegible]	Surface lesions, head and neck, lesions in extremities.
4.	Laser Ablation	1. Easy to focus 2. Shielding not required 3. Easy to automate 4. Less costly	1. Irregular lesions near blood vessels 2. Small heat generation rate 3. Limited used for abdominal tumors 4. Low penetration depth 5. Time consuming 6. Very costly	Brain, primary and metastatic on the spine, eye and cosmetic surgery.
5.	Cryo-ablation	1. Cryoablation is much safer 2. Does not weaken the tissue 3. Re-warming of the frozen tissue, restore its normal function	1. Complication rates are higher 2. Risk of cryoshock 3. Risk of liver hemorrhage 4. Use repetitive freezing and thawing 5. Applied for small tumors only 6. Large time required to produce a lesion	Kidney, liver, prostate, breast, and musculoskeletal and heart

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Table 2Comparison of microwave ablation versus.radiofrequency ablation

Features	Microwave ablation	Radio frequency ablation
Typical Frequency	915 MHz, 2.45GHz	365-480 KHz
Physics of energy deposition	Induction of oscillation in water molecules by propagating electromagnetic waves	Resistive heating by electrical alternating current
Generator power control	No feedback used	Temperature/impedance
Temperature	Higher	Comparatively lower
Thermal conduction	Less dependent	Dependent
Grounding pad	Not needed	Needed
Duration	Shorter	Long
Lesion Size	Larger lesions with single probe	Less larger lesion
Multiple MWA probes Interference	No interference with each other	Interference with each other
Lesions near blood vessels	Better	Moderate
Multi applicator approach	Possible	Limited
Available Device	No FDA-approved devices (Vivant Medical)	FDA-approved devices (Valley Lab, Boston Scientific, RITA)

MWA offers many benefits over RFA and Ultrasound ablation and has many theoretical advantages that may result in improved performance near blood vessels. Although RF ablation is most widely used thermo-ablative technique worldwide but main limitations of RF ablation are high local recurrence rates, particularly in the treatment of masses larger than 3.0 cm in diameter, the potential for incomplete tumor ablation near blood vessels because of the heat sink effect of local blood flow [24], difficulty in Ultrasound imaging of RF lesions, and evidence of surviving tumorcells even within RF lesions [25]. Ultrasound technique also offer major disadvantages like difficulty in penetration to tissue-air interfaces, shadowing by bone which tends to heat preferentially and patients may experience pain during treatment [26]. The comparison of microwave ablation compared to radiofrequency ablation based upon its important features is shown in Table 2

IV. CONCLUSION

Microwave ablation results in consistently higher intra-tumoral temperatures, larger tumor ablation volumes, faster ablation times, ability to use multiple applicators, improved convection profile, optimal heating of cystic masses, and less procedural pain. In addition, microwave ablation does not require the placement of grounding pads. Because of the drawbacks of other ablative techniques, several groups have successfully proved the efficacious nature of microwave ablation in the treatment of hepatocellular carcinoma.

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BIOGRAPHY

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