

1.1 Introduction

Despite tremendous research efforts in recent years, cancer continues to remain the subject of research interest for the scientists and engineers throughout the world. A therapeutic technique that has received increasing attention in recent years is hyperthermia. Hyperthermia is a type of cancer therapy in which body tissue is exposed to high temperature in the range 41–45 °C [Habash *et al.* (2006), Giombini *et al.* (2007)]. It is well established that high temperature in the range 41–45°C can damage and kill cancer cells, while normal cells would survive until over 45°C and the excessive heat formed in normal cells spreads throughout the body via blood circulation [Wang *et al.* (2011)]. Further, heating is not instantaneous. Some time has to be spent before tumor temperature reaches the desired value in the range 41 – 45 °C. Research has shown that by killing cancer cells and damaging proteins and structures within the cells, hyperthermia may shrink tumors, making the cells more sensitive to other anticancer agents like radiation therapy and/or chemotherapy.

The concept of hyperthermia made an appearance through a paper authored by Bush which was first published in 1866 [Bush (1866)]. It was claimed that the sarcoma that occurred on the face of a 43-year old lady was cured when fever was caused by erysipelas (disease caused by bacterial infection). The Busch paper was very significant because it was the first reported case indicating that temperature which normal tissue tolerates, might selectively destroy malignant cells. In the United States, Dr. William Coley began to create bacterial toxins which would induce high fevers. He reported on the results of clinical trials with these toxins in a number of papers starting in 1893 [Coley (1893), Coley-Nauts (1946)] and shown that fever therapy had a major drawback, as each patient responded somewhat differently to a toxin. After the discovery of ionizing radiation in 1895, radiation therapy gave more reproducible results. However, later it was realized that ionizing radiation in radiation therapy will cause normal cells to die.

Worldwide interest in hyperthermia was initiated by the first international congress on hyperthermic oncology in Washington in 1975.

Cancerous cells are hypoxic (deoxygenated), and deficient in nourishing substances. In addition, their environment is acidic with pH value less than 7.4 (i.e. the value for normal tissue). Acidic environment of tumor provides resistance to radiation but favors cell killing due to heat. Poor blood perfusion in the interior of a large tumor volume assists heat accumulation and makes it more sensitive to heat radiation. Moreover, malignant cells have an excess of sodium, which not only affects the membrane potential of cells, but causes malignant tissue to retain more fluid than normal tissue [Joines (1984)]. Additionally, tumor cells have higher water content. The excess sodium, fluid and water content make the dielectric constant and conductivity of tumor slightly higher as compared with normal tissue. Due to higher conductivity of tumor, absorption of electromagnetic energy (EM) rises in the tumor region. The combination of higher sensitivity to heat and higher EM energy absorption by malignant cells increases the efficacy of hyperthermia therapy for treatment of cancer [Short and Turner (1980), Hahn (1984)].

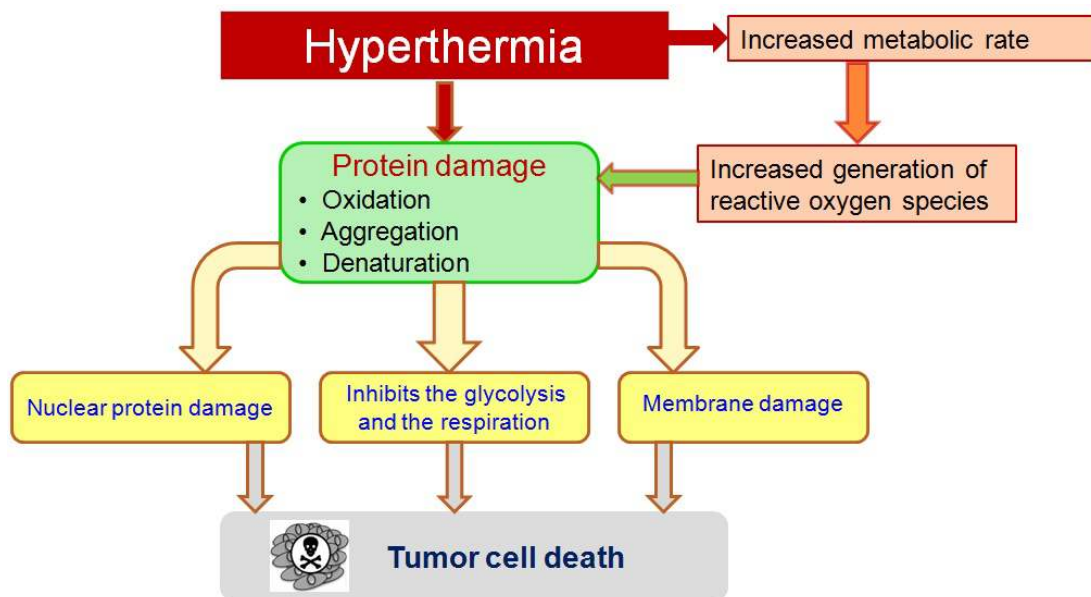


Figure 1.1: Hyperthermia-induced cellular changes that could lead to tumor cell death.

Heat causes numerous subtle changes in tissue physiology, such as increased blood flow, vascular permeability, and metabolic activity. Increased blood flow

registered in the tumor site increases the concentration of the therapeutic chemical drug delivered. Also, increased vascular permeability of tumor allows higher drug penetration rate into the target zone. Elevated temperatures can increase the rate of biochemical reactions. This would increase the generation of reactive oxygen species such as superperoxide and hydrogen peroxide (H_2O_2) which causes increased oxidative stress. Nuclear protein is sensitive to hyperthermia and undergoes aggregation (accumulation of misfolded proteins). The important mechanism of tumor cell death is protein denaturation, observed at temperatures above $40^\circ C$, leading to changes in enzyme complexes for DNA synthesis and repair as well as alterations in structures like cytoskeleton and membranes and inhibition of glycolysis process (Figure 1.1).

For cell division and multiplication, energy is delivered through glucose. This process is realized in the presence of oxygen (aerobic process) for normal cells and as an anaerobic process for cancer cells. In the presence of oxygen, the ability of cancer cells to multiply will decrease [Holt (1980)]. However due to heat, oxygenation in the tumors increases [Song *et al.* (2005)]. This leads to a reduction of the cancer cells' ability to multiply which increases the effectiveness of radiation and chemo-therapies.

Hyperthermia within the tumor can be produced using different types of energy including microwave, radio-frequency and ultrasound. The focussing ability of microwave energy has aroused considerable research interests including hyperthermia [Guy *et al.* (1974)]. Microwave hyperthermia has the advantage of providing rapid heat transfer, volumetric and selective heating, better control and pollution-free heating. It is frequently used in conjunction with chemotherapy and radiotherapy for treatment of cancer.

Interaction of microwave energy with biological tissues is determined by their electrical properties, since the magnetic permeability of biological system is same as that of the free space and magnetic losses are negligible [Hand (1981)]. Biological tissue can be classified into two groups – those with high water content, e.g. skin, muscle, liver, and those with low water content, e.g. fat and bone. At microwave frequencies, biological tissue behaves as an electrolyte (lossy

dielectric material) that contains various salt ions, polar protein molecules, and polar water molecules. When microwave energy is applied to the biological tissue, the polarized molecules rotate and attempt to align with the field, which generates displacement current in the tissue with an associated dielectric loss due to viscosity. Moreover, oscillation of free charges or ions gives rise to conduction currents with an associated energy loss due to electrical resistance of the medium. Heating at microwave frequencies is mainly caused by the rotation of polarized bio-molecules. Hyperthermia is most effective when the area being treated is kept within temperature range 41–45°C for a defined period of time without affecting nearby tissues. This is a challenging task since not all body tissues respond in the same way to heat. Thus, successful microwave hyperthermia therapy requires not only a suitable energy source for heat production but also the ability to reach the target tissue with the required heating modality (or method) without significantly heating the nearby tissues.

Hyperthermia treatments can be categorized into three broad types – local, regional or whole body hyperthermia. Type of hyperthermia which is applied depends upon size, location and the organ involved.

In **local hyperthermia**, heat is applied to a small area, such as a tumor, using various techniques that deliver energy to heat the tumor. It involves the treatment of tumors of 5 to 6 cm size in longest dimension [Chichel *et al.* (2007)]. Moreover, during local hyperthermia, the temperature of tumor tissue should be maintained above that of the surrounding normal tissue. Depending on the applicator positioning, local hyperthermia can be classified into invasive (internal) and non-invasive (external) [Durney (1992)]. Invasive applicators can efficiently heat specific locations but the intrusive nature is not practical for all tumours. Coaxial antennas are inserted into a catheter tube to avoid the contact between the antenna and the tissue, and then located inside the tumour volume [Saito *et al.* (2004), Camart *et al.* (1992)]. The limitation of invasive applicator is that it may cause pain at the site, metastatic cancer, infection, blood clots, bleeding, swelling, burns, and damage to the skin, muscles and nerves near the treated area.

Non-invasive or non-penetrating or external antennas include radiative applicators. Waveguides/horns and microstrip antennas are very common radiative applicators. Waveguides/horns are simple structure and can be loaded with dielectric to improve impedance matching, but microstrip antennas have some fundamental advantages such as their compactness, less weight and conformability.

Regional hyperthermia uses low heat. In regional hyperthermia, a part of the body, such as an organ, limb, or body cavity (a hollow space within the body) is heated. Regional hyperthermia is not hot enough to destroy the cancer cells outright. It is usually combined with chemotherapy or radiation therapy. When regional hyperthermia has to treat deep seated tumors, arrays of antenna can be used.

Whole body hyperthermia is used to treat advanced and widespread malignancies and the heat is applied to the whole body.

Since topic of present thesis pertains to the studies of microwave antennas for hyperthermia applications, the literature survey concerning single antenna applicators in microwave range (300 MHz-30 GHz) only will be covered.

Application of microwave to hyperthermia therapy demands challenging applicator characteristics. External microwave applicators are designed and optimized to non-invasively couple the microwave energy through the skin to kill cancerous cells. Keeping this in mind, engineers and scientists started design and development of efficient applicators for microwave hyperthermia. Designing a microwave antenna for hyperthermia application is somewhat different from that of designing antenna for other applications. For example, some well known parameters of typical antennas, such as the radiation pattern which is defined in the antenna's far field region have minor practical value, while near fields are more important in coupling EM energy into biological systems. Since biological systems have high dielectric constants, the antennas for coupling EM energy into them must be designed differently from those radiating in free space. Another key parameter is impedance at the interfaces between the feed and applicator's input as well as between applicator's aperture and tissue region. This aspect must be

considered in order to transfer maximum power into the biological tissue. Both near field amplitude and impedance matching at the aforesaid interfaces are directly or indirectly influenced by the electrical and geometrical properties of the tissue. Additionally, reflection at the applicator-tissue interface and hence transmission and absorption of EM energy in the tissue depends not only on the specific type of tissue, but also on the frequency, the polarization, and the angle of incidence of the propagating waves. Moreover, leakage radiation originating from the antenna must be minimized to significantly reduce the chances of hazardous effects of EM waves on the operator/medical personnel operating the hyperthermia equipment [Durney and Iskander (1988)].

Microwave-induced hyperthermia is dependent upon specific absorption rate (SAR) in the cancerous tissue. SAR has been used by researchers to characterize energy deposition and heating patterns in tissues/ bio-models. SAR is a dosimetric quantity and is defined as the rate at which microwave energy is absorbed per unit mass of biological tissue [Durney *et al.* (1986), Chou *et al.* (1996)]. SAR is a function of microwave power, frequency, wave polarization, dielectric properties and density of tumor, duration of treatment and blood flow rate. Microwave power fed to specific type of cancerous tissue through the applicator as well as duration of treatment should be optimized for the given frequency and polarization of the wave to obtain adequate cytotoxicity. Additionally, the hyperthermia performance is characterized through the study of temperature distribution in the cancerous tissue. The heat generated by microwave energy absorbed in the tissue is proportional to SAR. The bio-heat equation represents the relationship between the rate of electromagnetic energy absorbed into the tissue and the resulting rise in tissue temperature. The temperature distribution inside the realistic bio-model can be evaluated by using Pennes' bio-heat equation (BHE) [Pennes (1948)]. Thermal optimization can be performed to achieve one or more of the following goals: (i) to achieve a target temperature distribution, (ii) to optimize heating of tumor compared to healthy tissue, (iii) to avoid hot spots, and (iv) to maximize tumor coverage [Paulides *et al.* (2013)]. Various shapes of tumors that are observed in

different regions of the body include spherical, oval and undulating [Agrawal *et al.* (2009)].

Hyperthermia applicator can be designed at a suitable frequency out of allocated frequencies for industrial, scientific and medical (ISM) applications. Microwave ISM frequency bands are centered at 433.92 MHz, 915 MHz, 2.45 GHz, 5.8 GHz, and 24.125 GHz. These frequencies are assigned by the Federal Communications Commission (FCC) to affirm that leakage from devices operating at these frequencies will not interfere with sensitive radio and navigation equipments. Adoption of particular frequency must consider following three factors: (i) The penetration depth (PD) in tissue decreases as frequency increases, (ii) The physical size of antenna decreases as frequency increases, and (iii) Dielectric properties of biological tissues are highly frequency dependent. Therefore, the selection of appropriate frequency is dependent upon PD as well as size and location of tumors. At higher frequencies, applicator's aperture can be electrically large enough to produce good localization with shallow PD to heat smaller size tumors. At lower frequencies, PD is larger but localization of the internal field within smaller area becomes difficult due to smaller electrical aperture size of applicator. It is to be noted that applicator becomes larger in physical size and bulky as frequency is reduced. Thus, there is a fundamental trade-off between depth of penetration and localization of EM field. Based on these results, it is clear that for superficial tumors, single antennas at 915 and 2450 MHz have been used to treat localized tumors extending up to a depth of few centimeters [Johnson and Guy (1972)]. The present thesis describes four non-invasive hyperthermia applicators – three configurations of water-loaded diagonal horns at the operating frequencies of 2450 and 915 MHz and a planar microstrip slot antenna at the operating frequency of 2450 MHz.

1.2 Literature review

Several types of applicators including waveguide/horn and planar applicators are available in the literature for hyperthermia. Waveguide radiators generally provide good coupling of the microwave energy into the tissue and can be loaded

with dielectric to improve the impedance matching and reduce their size. However, waveguide applicators are heavy and have fixed form of aperture. Use of planar applicators may solve most of these problems, because they are small in size, flexible and light in weight. Both waveguide/horn and planar applicators can be designed at the desired frequency in ISM frequency band as discussed earlier. Since the topic of present thesis pertains to the studies of microwave horns and planar antennas for hyperthermia applications. The literature survey concerning these types of applicators in microwave range only is covered in the present chapter.

The literature survey for the applicators available for hyperthermia is divided into two categories: (i) waveguide/horn type of applicators (ii) planar applicators, as presented in the following sections.

1.2.1 Waveguide/Horn applicators

Several types of waveguides/horn antennas terminated in bio-medium and/or layered bio-media have been studied by many researchers and are described in the literature including open-ended waveguide, multimodal-waveguide, horn antenna *etc.* For minimum exposure of electromagnetic wave to the operator as well as normal tissues of patient, direct contact applicators are better to use as compared to spaced applicators because of much reduced leakage (unwanted radiation) in case of direct contact applicators. The choice of applicator depends on wave frequency and polarization, power density, duration of exposure, the desired Specific Absorption Rate (SAR), temperature range and its distribution and the biological target involved.

Waveguide applicator is one of the earliest examples of using microwave energy for therapeutic purposes. Waveguides designed for lower frequency tend to be large and hence bulky, so they have been used mostly at frequencies of 433 MHz and above. Loading the waveguide or applicator with high dielectric constant material having permittivity approximately equal to the permittivity of bio-media improves the matching between the antenna and phantom bio-medium/bio-media, ensures good transmission of microwave energy into the bio-medium/bio-media. Further, it helps in reducing the size of the antenna applicator

considerably. Dielectric-loading also minimizes leakage radiation around the antenna. The effective heating of the bio-medium/bio-media depends strongly on the size of the waveguide/horn aperture and the field distribution across it.

Guy [Guy (1971)] derived the expressions for electromagnetic fields and relative heating pattern inside the bi-layered tissue (fat and muscle) media due to direct contact rectangular aperture source in the frequency range of 433.2 to 2450 MHz. Sorensen and colleagues [Guy *et al.* (1978)] designed and developed a dielectric-loaded (aluminum-oxide-sand-loaded) TE₁₀-mode 13-cm square waveguide source in direct contact with human thigh and measured relative heating pattern and input VSWR for different fat thicknesses at 915 MHz. Lehmann and group [Lehmann *et al.* (1978)] measured temperature distribution in plain parallel-layered phantom tissue model (skin, fat, muscle and bone layers) in direct contact with a 13-cm square waveguide aperture source operating at 915 MHz. Lovissolo *et al.* [Lovissolo *et al.* (1984)] reported horn-shaped waveguide structures operating in the range of 300-1000 MHz with water acting as both a dielectric and a cooling fluid and measured temperature profiles on two young female sheep. Uzunoglu and colleagues [Uzunoglu *et al.* (1987)] developed a water-loaded, indirectly cooled waveguide antenna with a small aperture size ($2.0 \times 5.5 \text{ cm}^2$) operating at 432 MHz and computed the SAR distributions inside the bi-layered tissue (fat and muscle layers) model by evaluating the expressions for induced electric field. Also, they reported that presence of a fat layer between the applicator and muscle tissue modifies the field distributions inside tissues. Nikita and Uzunoglu [Nikita and Uzunoglu (1989)] explored the work by analyzing electric field intensity in a tri-layered tissue model (skin, fat and muscle layers) from water-loaded rectangular-aperture flanged waveguides (carrying TE₁₀-mode) and presented the results at 144 and 432 MHz.

Ho *et al.* [Ho *et al.* (1971)] investigated microwave heating in phantom models of human limbs (tri-layered circular lossy dielectric cylinders consisting of human tissues of fat, muscle and bone) by aperture sources theoretically in the frequency range of 433 to 2450 MHz and experimentally at 918 MHz.

Stuchly *et al.* [Stuchly *et al.* (1980)] reported a design method and experimental results for direct-contact circular aperture applicators operating in S-band (2450 MHz) and X-band (9960 MHz). The aperture is excited in the TE₁₁-mode; a corrugated flange surrounding the aperture of each applicator improves the uniformity of the heating pattern and limits leakage. The performance of circular aperture waveguide has been tested using a short monopole probe and a thermographic camera and determined heating patterns for evaluating the performance of microwave diathermy applicators. Dolzhikov and Serbin [Dolzhikov and Serbin (2004)] determined the expression of the electric field in biological medium in direct contact with a circular aperture waveguide. Circular waveguides having circularly-polarized electromagnetic waves provide relatively symmetrical heating pattern in bio-medium.

Kantor and Cetus [Kantor and Cetas (1977)] perform a comparative study in which large (square aperture horn, circular waveguide, teflon slab-loaded rectangular waveguide, circular aperture horn) and small (emitter and cavity backed spiral antennas) direct-contact applicators were considered. The results show that heating patterns induced in planar and limb phantoms of simulated fat and muscle layers in direct contact with a 2450 MHz circularly polarized circular horn, which has a single feed and a pair of phase shifters for producing circularly polarized TE₁₁-mode fields provide more uniform heating in phantom tissue than linearly polarized fields. There is also an annular choke to control the leakage level within the required 5 mW/cm². Further, Kantor *et al.* [Kantor *et al.* (1978)] designed and developed a direct-contact circular waveguide with a short conical flare horn output section surrounded by an annular choke and two sets of dual posts to generate circular-polarization at ISM frequency of 2450 MHz. Measured heating patterns in phantoms of simulated fat and muscle layers are also provided. In addition, it has been demonstrated that direct contact applicators reduce unwanted radiation.

For uniform power deposition in bio-medium/bio-media multimodal waveguides/horns find potential applications. Multimode waveguides produce relatively uniform heating pattern. Lin *et al.* [Lin *et al.* (1982).] described new

direct-contact applicators which consist of three concentric circular and cylindrical tubes and can propagate TE_{11} and TE_{21} modes. The combination gives relatively uniform, circularly symmetric heating distributions in the tissue.

The uniformity of the field across the aperture of the waveguide can be achieved by TEM-mode of propagation. Cheung *et al.* [Cheung *et al.* (1977)] designed an open-ended rectangular waveguide that is partially loaded with low-loss dielectric slabs, which support TEM mode of propagation. Using a single TEM applicator alone in direct contact with the tissue equivalent phantom, they observed uniform temperature of $42(\pm 0.25)$ °C over the entire tumor phantom but exponentially decaying temperature along the direction of propagation. To compensate this, they used two directly opposed TEM applicators by superimposing the two exponentially decaying temperature profiles to achieve uniformity. Kantor and Witters [Kantor and Witters (1980)] reported a slab-loaded rectangular waveguide at 2450 MHz which is capable to deliver thermally effective absorbed dose to a planar phantom with minimal radiation leakage. Due to excitation of TEM mode in the air space between the Teflon slab results in heating patterns, which are more uniform than the patterns of comparable waveguide applicator without dielectric loading. Additionally, they replaced the waveguide flanges with microwave choke to reduce leakage.

Waterman and Nerlinger [Waterman and Nerlinger (1986)] demonstrated the effect of deionized water ($\epsilon_r' = 81$) and mineral oil ($\epsilon_r' = 2$) coupling medium on the SAR distributions owing to 915-MHz waveguide applicators. Their work confirmed that the coupling material has marked effect on the SAR distribution. Moreover, the distortion in the SAR distributions can also be eliminated by replacing deionized water with mineral oil. SAR profiles for mineral oil coupling are comparable to those obtained for direct contact; however the efficiency of power transfer is slightly less (70%) and the level of microwave leakage is approximately four times greater. Sherar *et al.* [Sherar *et al.* (1993)] measured heating patterns in phantoms of fat and muscle layers with bolus containing saline/gelatin pads at microwave frequencies owing to waveguide applicator. The

results confirm that the area over which therapeutic temperature was achieved increased considerably when absorbing bolus was used.

Van Rhoon *et al.* [Van Rhoon *et al.* (1998)] have investigated that the effective field size (EFS) of a conventional 433 MHz water-filled waveguide has been increased by replacement of the two diverging brass side walls, which are parallel to the direction of the electric field with Lucite walls; and placement of a heterogeneous dielectric in the centre of the aperture. SAR distributions at several depths in layered fat and muscle phantoms are also reported. Samaras *et al.* [Samaras *et al.* (2000)] presented analytical model for a Lucite cone applicator in direct contact with phantom muscle and investigated SAR distribution in phantom muscle theoretically and experimentally at 433 MHz. The theoretical modelling makes use of finite-difference time domain (FDTD) method. Some recent work has been done by Drizdal *et al.* [Drizdal *et al.* (2013)]. They concluded that tuning of waveguide-based Lucite applicators is not required when the applicators are properly designed.

Microwave hyperthermia must have one important characteristic *i.e.* deep localized heating. This can be achieved through the integration of a waveguide with metallic/dielectric lens. Mori and his group [Nikawa *et al.* (1985)] developed a direct-contact convergent lens applicator at 2450 MHz for microwave hyperthermia. They computed theoretically and measured temperature distributions in phantom model of fat and muscle layers. The applicator had a concave-shaped aperture and was designed to contact well with the medium, whose shape was cylindrical like human body. The experimental results showed that the heating power penetration depth increased 40 percent as compared to a single rectangular waveguide of same aperture size. Mori and group [Nikawa *et al.* (1986)] proposed a direct-contact metal-plate converging lens inserted in waveguide at 2450 MHz. They calculated theoretically and measured temperature distribution in phantom muscle and showed that the lens-inserted waveguide operated at 2450 MHz could heat phantom muscle upto twice the depth attained from a conventional waveguide. Further, Mori and group [Nikawa *et al.* (1986)] invented an integrated waveguide array at 430 MHz, which has a convergent

effect on the radiated electromagnetic field in lossy dielectric media with controlled heating pattern for microwave hyperthermia. They reported the measured electric field pattern and temperature distribution in simulated tissue from the integrated waveguide array. Further, Nikawa *et al.* [Nikawa *et al.* (1990)] developed metal plate lens applicator operating at 430 MHz with a computer-controlled heating system. They presented the experimental and theoretical results and concluded that the applicator has the ability to converge microwave energy in the lossy medium. But the lens structure seems somewhat complicated.

Nikawa and Okada [Nikawa and Okada (1991)] developed a dielectric-loaded lens applicator through the integration of a waveguide partially filled with dielectric at 430 MHz. They investigated experimentally that the temperature pattern in simulated muscle of the dielectric-loaded lens integrated waveguide can be controlled by varying the width of the dielectric material with maximum heating depth of over 80 mm from an aperture of $150 \times 100 \text{ mm}^2$. Alexander and colleague [Alexander and Liu (1993)] extended the work of Nikawa and Okada, by analyzing field focusing effect of dielectric-slab-loaded waveguide theoretically and determined field pattern in muscle for different widths of dielectric material at 430 MHz. The lens integrated waveguide has several disadvantages such as complexity in development, narrow bandwidth, larger size, time taking treatment and complicated structure (matching is required with source).

Gupta and Singh [Gupta and Singh (2005), Gupta and Singh (2006)] developed direct contact water-loaded box-horn applicators for therapeutic heating of bio-medium at 915 and 2450 MHz. The theoretical and experimental results showed that the applicators provides more uniform field distribution due to the presence of TE_{10} and TE_{30} modes in conventional box-horns. Further, the conventional box horn has been modified and named it as modified box-horn to increase the heating depth in the bio-medium, while the field uniformity in the tissue is maintained.

1.2.2 Planar applicator design

The disadvantages of waveguide/horn hyperthermia applicators are that they are bulky and have fixed form of aperture. Use of microstrip antenna applicators may solve the said problems associated with waveguide/horn applicators because they are small in size, flexible and light in weight [Montecchia (1992)]. A wide variety of geometrical shapes have been used for the microstrip radiating elements. Some forms of microstrip patch antennas have been investigated by researchers and are reported in the literature for hyperthermia applications.

Bahl *et al.* [Bahl *et al.* (1980)a] developed a slot antenna at 2450 MHz for hyperthermia application. The radiator is well matched with muscle and has a heating pattern comparable to open-ended waveguide aperture [Guy *et al.* (1978)].

Bahl and colleagues [Bahl *et al.* (1980)b] constructed microstrip-ring radiators for hyperthermia at 915 and 2450 MHz. These radiators are well matched when spaced a few millimetres from muscle phantom or when muscle is covered by a layer of fat. However, in these configurations, the heating pattern of the small fundamental-mode radiators is highly non-uniform due to near-field effects. To improve the uniformity of the heating pattern, higher order mode, large-diameter radiators would be required. Further, Bahl and his group [Bahl *et al.* (1982)] extended the work and reported three microstrip loop radiators for hyperthermia application. Two loop radiators were designed at 433 and 915 MHz, while the third one was constructed at 1300 MHz for detection of breast cancer using microwave radiometry. The ring conductor (radiating element) is on one side of a dielectric substrate with a ground plane on the other side. The ring is fed by a coaxial line obtrude through the substrate. A pin shorting the ring to the ground plane through the substrate is located 180° from the feed point. The near-field is not symmetric for microstrip antennas and that causes non-uniform field distribution. To obtain symmetrical heating patterns, distilled water-bolus of various thicknesses were employed.

Tanabe and his group [Tanabe *et al.* (1983)] described the design criteria and experimental results for 915 MHz multi-element microstrip antenna applicators for hyperthermia. Of several antenna designs (patch antenna, the slot antenna, the

multiple radial-arm antenna, the ring antenna, and the spiral antenna) considered, the spiral antenna appears to be the most suitable for use as an applicator element since it produces the most uniform radiation pattern and also has an inherently broad bandwidth. Johnson and group [Johnson *et al.* (1984)] reported patch antennas designed for operation at frequencies from 100–1000 MHz. The applicators are characterized by a good impedance match to tissue, which is reasonably independent of tissue configuration. Ledee *et al.* [Ledee *et al.* (1985)] reported a microstrip slot applicator with a circular aperture for clinical applications in microwave hyperthermia treatment and microwave radiometry for temperature measurement (0.1-2.1 GHz). Beyne and Zutter [Beyne and Zutter (1988)] determined the power deposited in the layered biological tissue using method of moments owing to a microstrip patch antenna designed at 915 MHz. Underwood and group [Underwood *et al.* (1992)] investigated a half wavelength rectangular microstrip patch antenna designed at 915 MHz to radiate in water for hyperthermia heating with an intervening water bolus.

Montecchia [Montecchia (1992)] presented three microstrip antennas of different geometric configurations: a microstrip disk (MDA), a microstrip annular-slot antenna (MASA), and a microstrip spiral patch antenna (MSPA) for hyperthermia (0.5-2 GHz). First two microstrip applicators characterized by single operating frequencies (MDA and MASA). MASA have lower resonance frequency as compared to MDA. The efficiency of the MSPA with a distilled-water bolus is between those of the MDA and MASA, while its heating pattern shape and size are both comparable to those of MASA. Both the MASA and the MSPA are well suited for superficial hyperthermia. The MASA is for treatment at fixed frequency in which higher efficiency is required, while the MSPA is recommended in all other cases. Nikawa *et al.* [Nikawa *et al.* (1992)] developed wide-band spiral antenna for hyperthermia application and presented the results at 145 and 433 MHz. The results illustrated that the applicator has a potential to heat deeper and wider portion of the human body by optimum design.

Andreuccetti *et al.* [Andreuccetti *et al.* (1993)] described a compact, low-profile, high permittivity patch element ($\epsilon_r' = 80$) designed at 434 MHz for

hyperthermia application. The antenna gives effective coupling to the tissues and reliable SAR distribution with good electrical matching over the entire operating frequency band. But the applicator suffers from reduced PD.

Creson and group [Creson *et al.* (1994)] developed a three-dimensional model based on Finite difference Time domain (FDTD) method for the study of external planar applicator for microwave hyperthermia at 434 or 915 MHz.

Michel *et al.* [Michel *et al.* (1996), Michel *et al.* (1997)] presented a theoretical study and experimental verifications concerning microstrip applicators with several patches and apertures at 915 MHz. For both kinds of applicators they showed that the power deposition is more important with these applicators, compared to applicators with a single patch and aperture. Later on Michel *et al.* [Cresson *et al.* (1999)] extended the work and developed a new kind of external applicator called the multi-applicator. They found good agreement between the theoretical (obtained using FDTD method) and experimental results. The results clearly state that the power deposition is improved in multiapplicator case as compared to the previous one.

Jacobsen [Jacobsen (1998)] reported an Archimedean spiral antenna operated in a bandwidth from 1 GHz to at least 3–4 GHz when placed on a high-permittivity and lossy medium. The high gain in the bore-sight direction makes the Archimedean spiral a candidate for sensing weak thermal noise levels at depth in the tissue. Stauffer *et al.* [Stauffer *et al.* (1998), Jacobsen *et al.* (2000)] reported the antenna which has a lightweight structure and consists of a square annular slot dual concentric conductor (DCC) aperture (designed at 915 MHz). It has been demonstrated that it can provide uniform heating to a large area of superficial tissue. Further, the DCC antenna has been combined with an Archimedean spiral element for use as a radiometer.

Carlier and group [Carlier *et al.* (2002)] developed planar applicators with an annular or horseshoe shape for microwave heating at 434 or 915 MHz.

Curto and Ammann [Curto and Ammann (2006)] examined the electromagnetic interaction between a resonant loop antenna in proximity to biological tissue in terms of field, return loss, efficiency, components, wave

impedance and SAR. Various loop orientations were investigated with respect to the tissue, in order to provide the best coupling and power deposition into the body.

Drizdal *et al.* [Drizdal *et al.* (2007)] introduced a shorted circular microstrip antenna at 434 MHz for hyperthermia. They showed that the applicator has the ability for treatment of tumors with approximately 4 cm in diameter. Curto *et al.* [Curto *et al.* (2009)] described the performance of a new compact-patch antenna as hyperthermia applicator for the treatment of superficial cancer cells and compared it with basic loop, dipole and conventional square patch antennas which have been previously used in clinical settings. The results depicted that new compact patch antenna provides efficient coupling, high SAR, frequency detuning stability and a matched input-impedance bandwidth at various distances from the water bolus and layered tissue models. The slotted features in the new compact patch antenna have a 69% area reduction with respect to the conventional square patch design and PD of 63 mm, which exceeds the performance of other waveguides, horn and microstrip designs. Further Curto *et al.* [Curto *et al.* (2011)] extended the work and reported a detailed finite difference time domain (FDTD) anatomical body model to explore simulated radio-frequency (RF) coupling and temperature increments for typical clinical conditions on the same applicator at 434 MHz. The antenna impedance matching, SAR and thermal distribution parameters were evaluated to identify applied performance outcomes. They found that compared with homogeneous and planar-layered models, the heterogeneous anatomical model inform how the clinical treatment setup with surface-cooling waterboluses and the patient features influence the SAR patterns. Additionally, they determined the optimum water-bolus and air-gap dimensions by balancing the impedance matching of the antenna and SAR outcomes. Choi *et al.* [Choi *et al.* (2014)] proposed a symmetrically shaped compact microwave radiator for the treatment of tumor at 434 MHz. Circularly symmetric SAR and temperature distributions are formed in the tissues owing to the applicator.

Stauffer and group [Kok *et al.* (2009)] investigated the performance of contact flexible microstrip applicators (CFMA) operating at 434 MHz for

superficial hyperthermia. Additionally, they compared the simulation results of SAR with the experimental ones. For effective coupling of EM energy to the tissue, most of the applicators have to be conformal with the patient's body. Correia *et al.* [Correia *et al.* (2009)] developed a contact flexible microstrip applicator (CFMA) operated at 434 MHz for hyperthermia. They reported that the behaviour of electromagnetic fields due to flat configurations of antenna is different from that due to curved configuration of the antenna. Smrkovski *et al.* [Smrkovski *et al.* (2013)] evaluated the performance and clinical characteristics of a novel hyperthermia antenna operated at 434 MHz for the treatment of superficial tumors in cats, dogs and horses (Veterinary patients). This antenna provides compact, efficient, focused and favourable electric field as well as deep-penetration in the tissue in comparison to simple flat antenna. Koo *et al.* [Koo *et al.* (2014)] developed a light weight, conformal, flexible, and clinically relevant hyperthermia applicator at 433 MHz for the treatment of cancerous tumors. The design utilizes a half wavelength meander-line to feed a microstrip slot antenna. It is capable of deeper penetration, has a high SAR and adequately matched input-impedance for various tissue loadings. The use of a slot antenna and microstrip feedline improves the bandwidth, EFS and PD. However, slot antenna provides bidirectional radiation, which leads to safety concerns. To limit the back radiation, back shield made of Neoprene has been used. The applicator consists of many layers with embedded feeding which makes the antenna geometry complex, and therefore, it is not easy to handle.

Recently Chakaravarthi and Arunachalam [Chakaravarthi and Arunachalam (2015)] described the design and characterization of a miniaturized cavity backed patch antenna applicator at 434 MHz. They illustrated that the cavity-backed patch has deeper penetration compared to the patch applicators of similar or large size proposed by researchers for microwave hyperthermia treatment of cancer.

1.3 Modelling and simulations

The commercially available electromagnetic simulator developed by computer simulation technology (CST) was used to model the proposed antenna

applicators and the tissue layers. CST microwave studio (CST MWS) software, which is based on finite integration numerical technique (FIT) provides user-friendly computer aided design (CAD) environment to generate different geometries. FIT is used to solve Maxwell equations in time domain whose origins can be traced to the work of Yee in 1966 [Yee (1966)]. The FIT was first proposed by Weiland in 1977 [Weiland (1977)]. In this method, entire computational domain is divided into cells that form the mesh. The equations in integral form are solved using FIT method to calculate the field on the edges of each mesh cell. To improve the accuracy at the boundaries, adaptive automatic meshing is provided in FIT method. CST Multi-physics software is used for thermal analysis which is fully integrated with CST Studio Suite.

MATLAB software was used to numerically solve the theoretical expressions for induced field components in the phantom bio-medium, obtained using plane wave spectral technique.

1.4 Motivation and objective of the thesis

Several simulation/experimental and/or theoretical studies on field and SAR distributions in a bio-medium/bio-media in direct contact/close proximity with different types of hyperthermia applicators at microwave frequencies such as waveguides/horn antennas/conformal antennas are available in the literature. The depth of penetration at microwave frequencies is generally shallow. Researchers are continuing to refine the existing waveguide/horn/conformal antenna applicators and devise better applicators so that these systems can provide enhanced heating depth in the medium to treat tumors at greater depth. Focussing of electromagnetic energy at the target tumor is easily possible through symmetrical high resolution exposure at microwave frequencies.

Diagonal, conical, choke horns and annular cavity antennas may be grouped under the category of antennas providing symmetrical patterns [Love (1976), Balanis (2008), Boriskin *et al.* (2013)]. But significant difference in beamwidths found in the principal planes of conical horn [Balanis (2008)]. Choke horn and annular cavity antennas can provide almost perfect axially symmetrical beam, but

they usually have low gain and provide wide beam [Boriskin *et al.* (2013)]. However, diagonal horn has reasonable gain as well as beamwidth, and its radiation pattern in the far field possesses almost perfect circular symmetry so that the 3, 10 and 20 dB beamwidths are very closely equal, not only in the principal E and H planes, but also in the 45° and 135° planes [Love (1976)]. In other words, the electric field distribution over the aperture of conventional metal diagonal horn is identical in E- and H-planes, resulting in circularly symmetric field distribution. Therefore, the diagonal horn terminated in a bio-medium/bio-media can be one of the promising candidates for the treatment of localized spherical (or near spherical) tumors in superficial abdominal/thoracic/limb region of the body.

The present work is motivated in part by the need to design and develop efficient, practical, non-invasive, direct-contact horn antennas/conformal antennas, which can provide uniform power-absorption at greater depth in bio-medium/bio-media, have the focusing ability and/or remain compatible with the curved portion of the human body. In the present thesis, some antenna applicators in direct-contact/close proximity with bio-medium/bio-media have been analyzed through simulation, experimentally and/or theoretically. These include water-loaded conventional metal diagonal horn, water-loaded improved metal diagonal horn, water-loaded metal-dielectric wall diagonal horn (MDWDH) terminated in a bio-medium/bio-media along with a novel conformal and modified microstrip slot antenna integrated with a novel and compact artificial magnetic conductor (AMC) in close proximity with a bio-medium/bio-media.

The concept of making the aperture field distribution at the aperture of water-loaded improved metal diagonal horn (MDH) more uniform by employing four conducting pins slightly inside its aperture and thereby improving the PD in the bio-medium/bio-media, which is in direct contact with the applicator through better focussing of the beam was borrowed from reference [Silver (1949)] in which two conducting pins inside the aperture of an H-plane horn terminated in free space was used for reducing H-plane beamwidth of the horn.

Aperture field distribution of a water-loaded conventional MDH can be made more uniform by partially replacing the metal walls of the horn through

dielectric (Perspex ($\epsilon_r = 2.59$)) sheets. This partial wall replacement can provide enhanced PD in the bio-medium/bio-media through better beam focussing without generating significant side/back lobes. This concept was used in the design of water-loaded MDWDH applicator. All the proposed diagonal horn applicators provide circularly symmetric SAR distributions in the transverse plane to effectively heat spherical or near spherical tumors.

The characteristics of conventional slot antenna with AMC in free space are described in the literature [Elek *et al.* (2005), Joubert *et al.* (2012), Agarwal *et al.* (2013), EL-Genedy *et al.* (2014)] but its application to hyperthermia has not been explored yet. Hence, a new conformal hyperthermia applicator integrated with AMC is proposed. The person/operator operating this kind of proposed conformal and compact hyperthermia applicator will not get exposed to hazardous level of microwave radiation due to highly suppressed back field response/high front-to-back ratio of the applicator.

The results of research work would find potential applications in hyperthermia and hence provide useful design guidelines for development of prototypes of antenna applicators.

1.5 Organization of the thesis

The present study is divided into six chapters according to the type of antenna applicators under investigation. The systematic investigations made on simulation, experimental and/or theoretical modelling of different types of antennas terminated/close proximity in a bio-medium/bio-media during the course of the research work are described in different chapters of the thesis.

Chapter 1 contains discussion pertaining to general introduction for hyperthermia, properties of cancerous cells, microwave hyperthermia, microwave interaction with biological tissues, antenna applicators used for hyperthermia, selection of frequency for hyperthermia, and literature survey of the work done on different types of direct-contact non-invasive waveguides/horn antennas terminated in a bio-medium/bio-media. Since hyperthermia waveguide/horn applicators are bulky and have fixed form of aperture, use of planar antenna

applicators may solve the aforesaid problems associated with waveguide/horn applicators because these planar applicators are small in size, flexible and light in weight. Literature survey for various planar applicators is also given briefly. Literature survey of waveguide/horn and planar applicators include brief description of all major simulation, experimental and theoretical studies reported so far in this field. It also makes an attempt to track the stages of development in the area to bring out the state-of-the-art. The work presented in this thesis directly stems from the latest trends in the area as described in this chapter.

In chapter 2, water-loaded conventional metal diagonal horns (MDHs) have been investigated through simulation, theoretically and experimentally at 2450 MHz and through simulation and theoretically at 915 MHz for hyperthermia application. Direct-contact water-loaded conventional MDHs were designed using computer simulation technology microwave Studio (CST MWS) 2011 software, which is based on finite integration numerical technique. Further, the horn designed at 2450 MHz was fabricated to demonstrate the technical feasibility of the horn. The experimental study of SAR distributions in a phantom bio-medium of known physical properties was carried out at 2450 MHz with the help of Vidyut Yantra make 50 Ω coaxial L-shaped and straight monopole probes and Agilent make spectrum analyser (Model: E4448A). The simulation results for SAR distributions in the phantom bio-medium (muscle medium) at 2450 and 915 MHz are compared with the corresponding theoretical and/or experimental results. The theoretical investigation of fields in the planar phantom muscle medium due to each water-loaded MDH antenna makes use of plane wave spectral technique for computation of SAR distribution in the medium. The theoretical field components and SAR distributions were numerically evaluated by using MATLAB software. A conventional MDH is a type of multimode horn in which the internal field consists of superposition of the orthogonal TE_{01} and TE_{10} modes in the square waveguide. Therefore, the electric field distribution over the aperture of conventional MDH is identical in E- and H-planes, resulting in circularly symmetric field distribution. The conventional diagonal horn is filled with high dielectric constant material (water). By loading the applicator with water,

matching between the antenna and phantom bio-medium is improved since the effective dielectric permittivity of the bio-medium/bio-media is close to that of water. Also, size of the antenna applicator reduces considerably. Further, simulation study of SAR and/or temperature distributions in realistic tri-layered bio-media without and with embedded tumor due to the water-loaded conventional MDHs designed at 2450 and 915 MHz are also provided.

In chapter 3, water-loaded improved metal diagonal horns (MDHs) have been investigated through simulation, theoretically and experimentally at 2450 MHz and through simulation and theoretically at 915 MHz for hyperthermia application. Improved MDH is a modified version of conventional MDH in which the aperture field is modified by introducing two pairs of conducting pins at appropriate locations near the horn aperture. Direct-contact water-loaded improved MDHs were designed and optimized using CST MWS 2011 software, which is based on finite integration numerical technique. Further, the improved horn designed at 2450 MHz was also fabricated to demonstrate the technical feasibility of the horn for hyperthermia. Simulation study was performed to study the modification of aperture field distributions of water-loaded improved horns designed at 2450 and 915 MHz due to introduction of conducting pins slightly inside the horn apertures, and the resulting SAR distributions in phantom muscle due to these horns. To verify the simulation results for aperture field distributions of the water-loaded improved horns designed at 2450 and 915 MHz, theoretical analysis was carried out which includes the effect of higher order TE_{30} and TE_{03} modes also in addition to TE_{10} and TE_{01} modes. The simulated results for SAR distribution in the phantom bio-medium at 2450 MHz are compared with the corresponding theoretical and experimental results and the simulation results for SAR distribution at 915 MHz are compared with the corresponding theoretical distributions. The simulation of aperture field distributions of both the horn antennas and SAR distributions in phantom muscle due to these antennas was carried out using CST MWS software. The theoretical investigation of fields in the planar phantom muscle medium due to each water-loaded improved diagonal horn antenna makes use of plane wave spectral technique for computation of SAR

distribution in the medium. The theoretical field components aperture field distributions and SAR distributions were numerically evaluated using MATLAB software. Additionally, simulation study of SAR and temperature distributions in a planar realistic tri-layered bio-media without and with embedded tumors due to the two water-loaded improved MDHs are also provided. Each improved MDH is assumed to be filled with water to provide good impedance matching between the horn and bio-medium/bio-media, which ensures good transmission into the bio-medium/bio-media. Results obtained through simulation, theoretical and/or experimental studies indicate that the proposed MDHs give higher PD in the homogeneous biological phantom/tri-layered bio-model as compared with the respective conventional MDHs.

In chapter 4, water-loaded metal-dielectric wall diagonal horns (MDWDHs) have been investigated through simulation and experimentally at 2450 MHz and through simulation at 915 MHz for hyperthermia application. Simulation was performed to study the modification of aperture field distributions of water-loaded MDWDHs designed at 2450 and 915 MHz due to the presence of partial dielectric material on the walls of the horns, and the resulting SAR distributions in phantom muscle due to these horns. In addition, experimental study of SAR distribution in phantom muscle due to the horn designed at 2450 MHz was also carried out. The simulation results for SAR distribution in the phantom bio-medium at 2450 MHz are also compared with the experimental distribution. Additionally, simulation study of SAR and temperature distributions in a planar realistic tri-layered bio-media without and with embedded tumors due to the water-loaded MDWDHs are also provided. Each MDWDH is assumed to be filled with water to provide good impedance matching between the horn and bio-medium/bio-media. Results obtained through simulation, and/or experimental studies indicate that both the proposed MDWDHs give higher PD in the homogeneous biological phantom/tri-layered bio-model as compared with the respective conventional MDHs.

In chapter 5, the simulation and experimental studies of a new conformal and modified microstrip slot antenna integrated with a novel and compact AMC reflector designed at 2.45 GHz for hyperthermia application are presented. The

simulated input characteristics along with near field distribution of the proposed antenna with AMC reflector in presence of phantom bio-medium/multi-layered bio-media and SAR distributions in phantom muscle medium/multi-layered bio-media due to the applicator are investigated. The proposed antenna integrated with the AMC was designed to effectively radiate into the muscle medium/multi-layered bio-media. The AMC structure is utilized to provide in-phase reflection, which significantly enhances the front-to-back ratio and consequently enhances the PD in the muscle medium. Further, the input characteristics and SAR parameters for the proposed antenna without AMC, conventional rectangular patch antenna without AMC and the proposed antenna-AMC and the antenna-conventional perfect electric conductor (PEC) combinations are also compared through simulation. Furthermore, the effect of variations in the dielectric property of bio-medium on the input reflection coefficient-frequency characteristic of the proposed antenna with AMC is also studied through simulation. The reflection coefficient-frequency characteristic of the applicator and normalized SAR distribution in phantom muscle medium due to the applicator with AMC were measured and the experimental results are compared with the respective simulation results. Additionally, the effects of change in the radius of curvature of proposed applicator and bio-model on E-field distribution and SAR distributions/temperature distribution in homogeneous/tri-layered/five-layered bio-models are investigated through simulation. Thermal simulation was also performed for the realistic tri-layered and five-layered bio-models without and with oval-/irregular-shaped tumor, which is in close proximity with the antenna-AMC combination. The unique characteristic features of this new type of applicator include its compactness, relative insensitivity to variations in the dielectric property of bio-medium, availability of enhanced heating depth, the safety of the person/operator operating this kind of hyperthermia applicator who will not get exposed to hazardous level of microwave radiation due to highly suppressed back field response/high front-to-back ratio of the applicator, and its compatibility with the curved surface of human body parts such as abdomen and limbs.

Finally, the major outcomes of the investigations carried out on different types of horn antennas and conformal antenna terminated in a bio-medium/bio-media are presented in chapter 6. The major conclusions drawn on the basis of the study are summarized. The future scopes and extension of the present work are also outlined in this chapter.