LABORATORY MODEL OF THERMORADIOTHERAPY FACILITY: EXPERIMENTAL RESULTS

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Abstract

Hyperthermia and its combination with radiotherapy (thermoradiotherapy) or with chemotherapy is one of promising ways to improve cancer treatment efficiency. The treatment of deep-situated tumors is sufficient problem which can not be solved by means of traditional facilities developed for whole-body or regional hyperthermia because of overheating of healthy tissues and blood. A cylindrical array of independently phased dipoles was proposed to focus electromagnetic energy in deep-situated tumors. Early it was shown by simulations that array of eight independently phased dipoles operating on 100-150 MHz is able to focus energy in an ellipsoid of 30-50 mm in size. Later the laboratory model of thermoradiotherapy facility was developed and constructed and a series of experiments were carried out. Experimental results and its comparison with simulation will discussed in report.

INTRODUCTION

Hyperthermia is an adjuvant method of cancer treatment in which tumor temperature is increased to high values (40-44 °C). Many researches have shown that high temperature can damage and kill tumor cells, thus reduces tumor size. However the main advantage is that hyperthermia is a promising approach to increase efficiency of chemotherapy or radiation therapy. Under hyperthermia some tumor cells become more sensitive to the radiation and anticancer drugs. The effect on surviving fraction depends both on the temperature increase and on the duration of the expose. The main mechanism for cell death is probably protein denaturation at temperatures above 40 °C, which leads to changes in molecular structures such as cytoskeleton and membranes, and changes in enzyme complex for DNA synthesis and repair [1]. Heat also enhances the cytotoxicity of X-rays. Increased cytotoxicity is maximized when radiation and hyperthermia are given simultaneously. The combined effect decreases with time when the treatments are separated by more than one hour [2]. When cells are exposed to increased temperatures to anticancer drugs, their response is often different from the one at normal temperature. Drugs whose rate-limiting reaction is primarily chemical are expected to be more efficient at higher temperatures. Thus the combination of chemotherapy with hyperthermia has high potential in clinical practice [3].

The thermal therapy combined with the radiation (thermoradiotherapy, TRT) has been successfully applied in N.N. Blokhin Russian Oncological Research Center (RORC) since 1980th [4]. More than 1000 patients have been treated to date. Such program allows to sufficient and authoritative reduce of the regional cancer recrudescence and metastases comparatively to the surgery or independently radiotherapy (RT) [5].

One of the major problems of the devices mentioned above is the limited depth of penetration due to the principle of skin-effect. Only tumors located 2-3 cm (7-8 cm for the contact flexible microstrip applicator) from the surface can be heated by these applicators. To increase sufficient specific absorption rate (SAR) value in the tumors situated deeper than 10 cm relative to the surface SAR value it is necessary to focus energy of electric fields produced by an array of applicators. It consists of several antennae surrounding the patient and emitting radio-waves. Single antenna or groups of antennae are fed separately. Thus by proper selection of amplitudes and phases the interference patterns of the produced fields can be focused to create desirable temperature distribution [5]. Significant research successes have been obtained for the deep hyperthermia with the phased array. Simulation and measurements results are presented in [6].

FACILITY FOR TRT BASED ON ANTENNAE ARRAY

The most evident approach is using an antennae array of applicator situated around the patient body. Top view of this structure is shown in Figure 1. Arrays of applicators with variations in frequency, phase, amplitude and orientation in space give more possibilities to control heating pattern during hyperthermia treatment [6]. RF power feeding scheme is presented in [7]. Thus the phased array provides deeper tissue penetration of electromagnetic waves in comparison with single applicator, reduces undesirable heating of healthy tissues situated between applicator and tumour and improve local control for heating area. Also using array of applicators gives ability to control and to plan heating process without changing of patient position. Suggested phased array consists of eight copper dipoles, attached on the inner side of the dielectric cylinder, and surrounds a patient body. The aperture radius is up to 60 cm which can be applied in more cases. Dipoles are fed independently; this approach permits to control wave's phases and amplitudes. Space between dipoles and the patient body is filled by deionised water (conductivity $\sigma \approx 0.001$ S/m and $\varepsilon \approx 80$). Thus applicators are squeezed from the inner side by lossy medium with high permittivity (deionised water), and from the outer side by

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medium with low permittivity (air ε=1). The conducting elements of antenna are isolated from lossy medium by thin layer of an insulator (thickness h≈1 mm). Because of energy density of electrical fields ($\vec{E}\vec{D}/2$) inside the dielectric tank is higher by a factor of ε (the relative dielectric constant of medium), energy is mainly concentrated inside the array. Thus deionised water not only cools body surface and superficial tissues but is also a matching medium. Electric field lines inside the phased array are parallel to the axis of dipoles. That's why heat absorption in the surface and superficial tissues (such as skin and fatty tissue) which is proportional to tissue conductivity (σ, these values for fat and skin are significant lower than for muscle or tumour tissue) will be substantially lower than in deeper tissues. Thus skin and fatty tissue overheating is reduced in comparison with the using capacitive applicators. So E_z (z is direction along of the patient body) is the only component, which may be able to control by shifting the amplitudes and phases of eight dipoles. E_x and E_y components are not under control. E-field generated by each of the dipoles is given by $E_j = A_j E_{j,0}(x, y)\cdot\exp(-i(\omega t - \Phi_j))$, where $E_{j,0}$ – is the complex E-field for A_j=1, Φ_j=0, and A_k=1 for $j \neq k$, A_j – is a scaling factor of amplitude, Φ_j – wave phase, j and k are numbers of dipoles, i is imaginary unit. It is possible to move peak of interference pattern and to focus it into the tumor site with the variation of these two parameters (phase and amplitude). The measure of the rate at which energy is absorbed by the body when exposed to a radio frequency (RF) electromagnetic field is a SAR. It is defined as the power absorbed per mass of tissue and has units of watts per kilogram (W/kg): $SAR = (\sigma\vec{E}^2)/\rho$, ρ – is the density of the tissue (kg/m^3), E – is the root of mean square electric field.

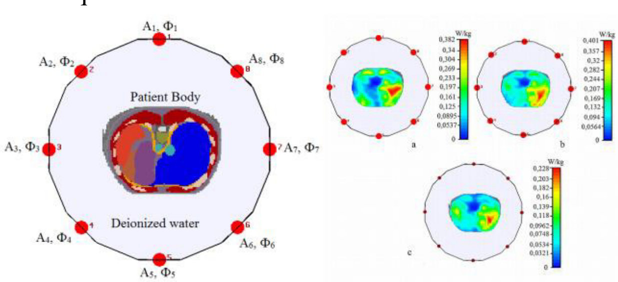

Figure 1: Top view of phased array surrounding patient body (left) and cross-section patterns of the SAR distribution with different operation frequencies (a) 150 MHz; (b) 100 MHz; (c) 80 MHz and with input phases of 50°, 50°, 50°, 50°, 0°, -30°, -40°, -10° applied to channels 1, 2, …, 8 respectively.

It was shown by many sets of simulations that such termoradiotherapy facility and RF power focusing by means of amplitude and phase control for each applicator can provide effective local hyperthermia. For example, the array of dipoles operating on 150 MHz and having aperture diameter of 60 cm can provide RF power focusing wherever of patient body with focusing volume diameter ~30 mm. A 450 MHz system can be used for hyperthermia of head and neck with heated volume size of 15-20 mm.

EXPERIMENTAL RESULTS

Based on previous simulations and RF feeding system design the first experimental prototype was developed and constructed. It consists of two RF dipoles and one feeding system. In such prototype temperature peak can move along the line connecting these dipoles and experiment will demonstrates 2D facility only. Water is used as an absorbing medium because it has dielectric properties and density similar with the muscle tissue. Pictures of laboratory prototype of the TRT facility, RF power feeding device and dipoles array are shown in Figure 2.

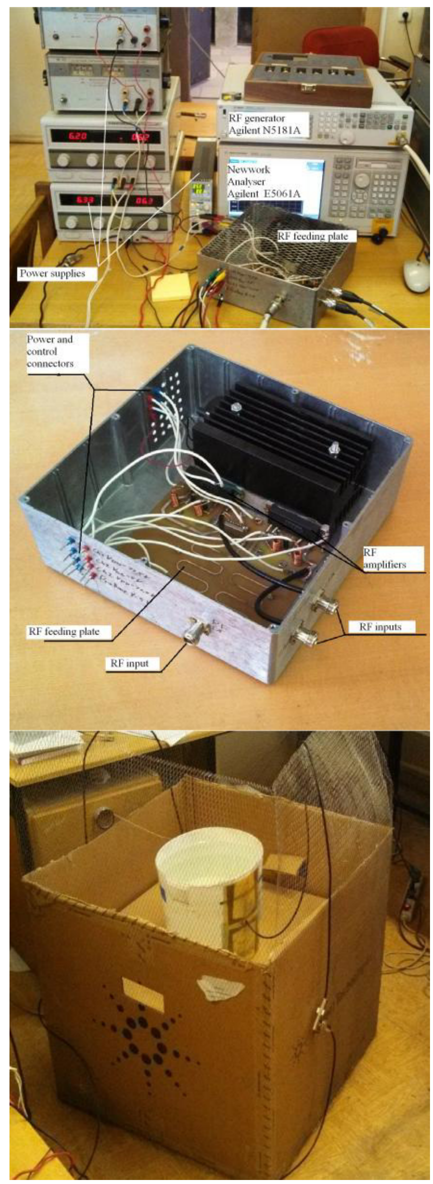

Figure 2: Laboratory prototype of the TRT facility: power feeding and measurement devices (top), RF power feeding device and dipoles array into Faraday cage.

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Series of local heating experiments were done using such prototype. Experimental demonstration of the local energy distribution maximum and its moving versus of phase and amplitudes variation were the main goals of such experiments. Two dipoles were mounted on external side of a dialectical cylinder which was filled by deionised water. The tissue-equivalent phantom was prepared using a number of thin-walled dielectric tubes filled by salt water which permittivity and conductivity are close to human tissues. A number of dielectric tubes were positioned along the line connecting dipoles like it is shown in Figure 3 to prevent water blending during heating. Tubes are made of aluminum oxide (permittivity ε=9.4 and density ρ=3990 kg/m^3). Tubes diameter is 10 mm and wall thick is 2 mm. Tubes were placed on line connects centers of RF dipoles. Such phantom correctly imitates the deep suited tissue and can be easily used in temperature control which was realized by means of a number of thermocouples which were placed into all thin-walled tubes. The initial temperature was constant for all system points. Water starts the energy absorption after RF power on and the temperature in the local heating volume starts growth. Temperature distributions after heating are shown in figure 4 for in-phase dipoles on (a) and for 60 degrees phase shift (b). The heating was provided 20 minutes for in-phase experiments and 12 minutes for experiments with phase-shift. Zero-point on x-axe corresponds to the center of main cylinder. As if follows from figures 50 mm localization can be achieved in hyperthermia system proposed. Experimental heating results are compared with CST Studio Suite simulations (dot curves in Figure 4) and have very good accuracy.

Thermocouple-sensing element ATE-9380 was used to perform temperature measurement. Whereas it has metallic compounds TSE introduce alternations in electric distribution when RF is on. Thus temperature measurement was carried out after switching RF off.

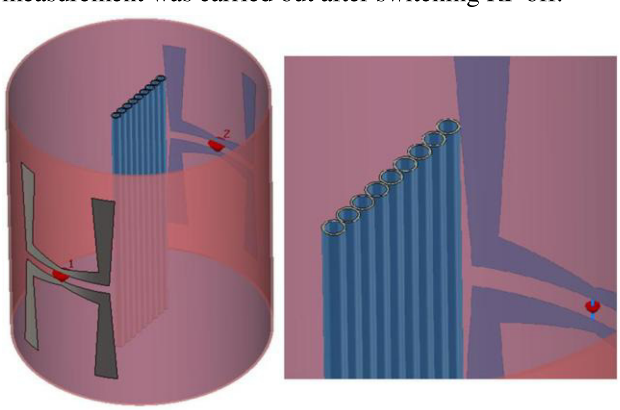

Figure 3: Experimental setup schematic view.

CONCLUSION

It was shown by means of electrodynamics and thermal simulations and experiment that system of a number of independently phased dipoles is suitable for TRT of deep suited tissues and tumors. The first experimental prototype was constructed and numbers of heating localization experiments were carried out. Comparison of simulation and experiments shows that the phased array solves the local heating problem and deep suited tumorous can be successfully heated without overheating of healthy tissues.

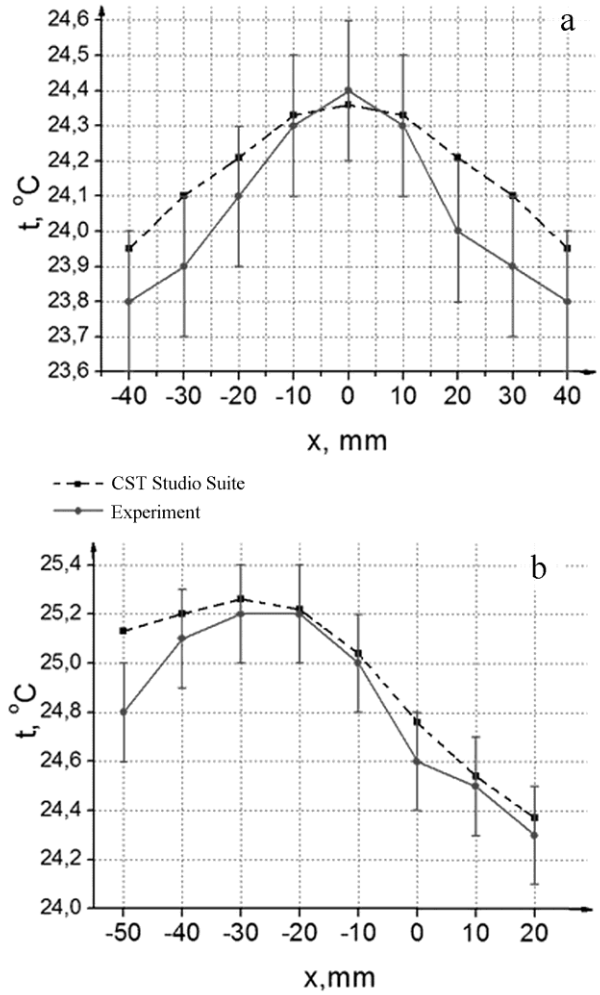

Figure 4: Temperature distributions after heating for in-phase dipoles on (a) and for 60 degrees phase shift (b).

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