NEW ENGINEERING APPROACHES FOR HYPERTHERMIA TREATMENTS

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Abstract

In the field of oncology, hyperthermia (thermotherapy) as one of the methods of treatment is of interest from the engineering point of view as well. For the treatment of a malignant tumor, one of the most important problems is the situation when metastases migrate in the body. Thermal therapeutic (deterministic) effect on metastases is possible by exposure to electromagnetic waves the nanoparticles introduced in them. In our experiments on animals (mouses), the optimal thermal effect for treatment (45 – 55 °C) using Fe_3O_4 nanoparticles was achieved by exposure to electromagnetic waves with frequency of 20 kHz.

1. Relevance of problem

Medical treatment of malignant tumors have been proposed by various methods, including surgical removal, chemotherapy, radiation therapy, hyperthermia treatment, cryogenic therapy, implanted active pellets, sometimes radioactive and other methods. The success of these methods varies widely.

One of the problems often encountered in therapy for malignant tumors is that the cells of the malignant tumor have migrated into the lymphatic systems surrounding the malignant tumor, known as “metastases”.

It is important to understand that the sentinel node will probably be the first one to get cell of the malignant tumor in it the cells have had spread to the lymph nodes at all.

Nano particles placed in the human cancer cells, under proper frequency of the radiowave influence, affects on the cells and causes its death by the thermoeffects [1, 2]. Those approaches are belonging to thermotherapy treatment methods by the high range temperature with 45 – 55 °C. In the current time, approaches in hyperthermia treatments are under investigation and not enough information spread, still researches are continuing.

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Those kinds of methods for cancer treatment are frequently used with combination such as radiotherapy and chemotherapy. After a few hours thermotherapy treatment, cell sensitivity is gained and it is more effective to react for some anticancerogenic agents on the cancer cell then in the treatment without thermotherapy. Also, for some combination treatments research results are not fully successfully achieved.

In the current time there are some types of hyperthermia treatment: 1) local, 2) regional, 3) whole body. Local hyperthermia treatment is subdivided by 1) superficial, which affects locally on skin and subcutaneous tissue.

In local hyperthermia, heat is applied to a small area, such as a tumor, using various techniques that deliver energy to heat the tumor. Different types of energy may be used to apply heat, including microwave, radiofrequency, and ultrasound. Depending on the tumor location, there are several approaches to local hyperthermia:

External approaches are used to treat tumors that are in or just below the skin. External applicators are positioned around or near the appropriate region, and energy is focused on the tumor to raise its temperature.

Intraluminal or endocavitary methods may be used to treat tumors within or near body cavities, such as the esophagus or rectum. Probes are placed inside the cavity and inserted into the tumor to deliver energy and heat the area directly.

Interstitial techniques are used to treat tumors deep within the body, such as brain tumors. This technique allows the tumor to be heated to higher temperatures than external techniques. Under anesthesia, probes or needles are inserted into the tumor. Imaging techniques, such as ultrasound, may be used to make sure the probe is properly positioned within the tumor. The heat source is then inserted into the probe. Radiofrequency ablation (RFA) is a type of interstitial hyperthermia that uses radiowaves to heat and kill cancer cells.

One of the difficulties in the hyperthermia treatment is that magnetic nanoparticles injected in the tumor tissue are not heated homogenously. For example heating starts from patient superficial level faster than inside the tumor tissue. At the same time the treatment process is out of the control. As a conclusion of this process the control of the temperature process is necessary to achieve the high quality treatment.

2. Setup of experiment and related activities

The purpose of an experiment is to achieve optimal geometry and physical specifications of alternative electromagnetic field coil; the optimal radiofrequency wavelength and permittivity of tissue; nanoparticles ablation effects and optimal temperature such as 45 – 55 °C. Results are evaluated by morphologic assays from samples that taken after thermotherapy treatment from the life tissues. The magnitude of the magnetic field is 600 Oe.

Magnetic fluid with Fe_3O_4 nanoparticles (43 – 80 °C Curie temperature) are prepared for experiment (irradiation) which is very sensitive for electromagnetic waves. It is prepared by the Georgian Patent N 6058 (officially permitted by the author). *In vivo* experiments are conducted in rats with 6 series. Experiment was held in the Georgian Scientific Laboratory for “Magnetic Fluids in Medicine and Biology” (LTD “ATT”).

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I-series animals are injected (in the mammary gland) with 43 – 44 °C Curie temperature magnetic fluids.

II-series animals are injected with 45 °C Curie temperature magnetic fluids.

III-series animals are injected with 46 °C Curie temperature magnetic fluids.

IV-series animals are injected with 50 °C Curie temperature magnetic fluids.

V-series animals are injected with 60 °C Curie temperature magnetic fluids.

VI-series animals are injected with 70 °C Curie temperature magnetic fluids.

All those animals are placed under the 20 kHz frequency by alternated electromagnetic field. Temperatures are measured with alcohol thermometers.

3. Research results and data analysis

Experiments has shown that, magnetic nanoparticles with 43 – 45 °C Curie temperature are not proper for treatment in the life tissue. Diagram (on the **Figure 1**) shows that, tissue under the electromagnetic wave for 1 h cannot achieve desire treatment effect. The reason for this difficulty is that, there are capillary network in the life tissue which acts as a natural cooling system that is why above mentioned Curie temperature is not enough.

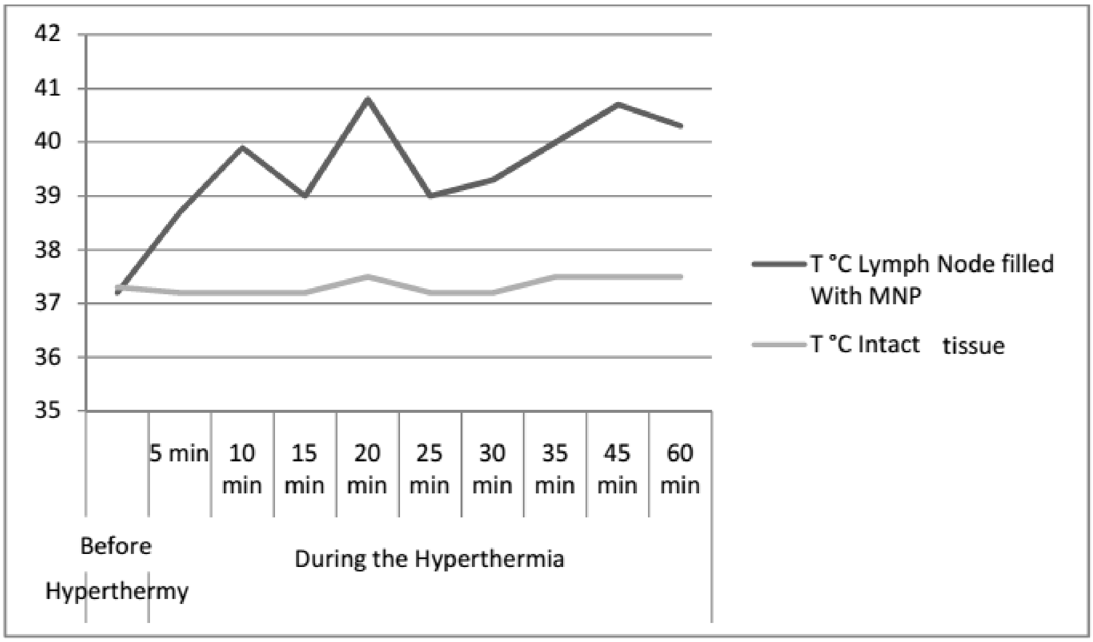

Figure 1. Diagram for magnetic nanoparticles with 43 – 44 °C Curie temperature in life tissue under 60 min exposure of 20 kHz electromagnetic wave.

Experiments with nanoparticles by the Curie temperature of 46 °C and above shows that they are more effective and stable for thermotherapy treatments. Its effectiveness can be achieved after 30 min irradiation for same setup (**Figures 2 – 5**).

For all diagrams vertical line shows temperature in °C and horizontal line shows time in min. Dark line shows the filling level temperature in °C of lymph node bymagnetic nanoparticles (MNP). At the same time light color line shows the temperature in °C of intact tissues. Left side of diagram is the mode before starting the hyperthermia, after that "during the hyperthermia" means that 20 kHz radiofrequency wave is used for tissue exposure.

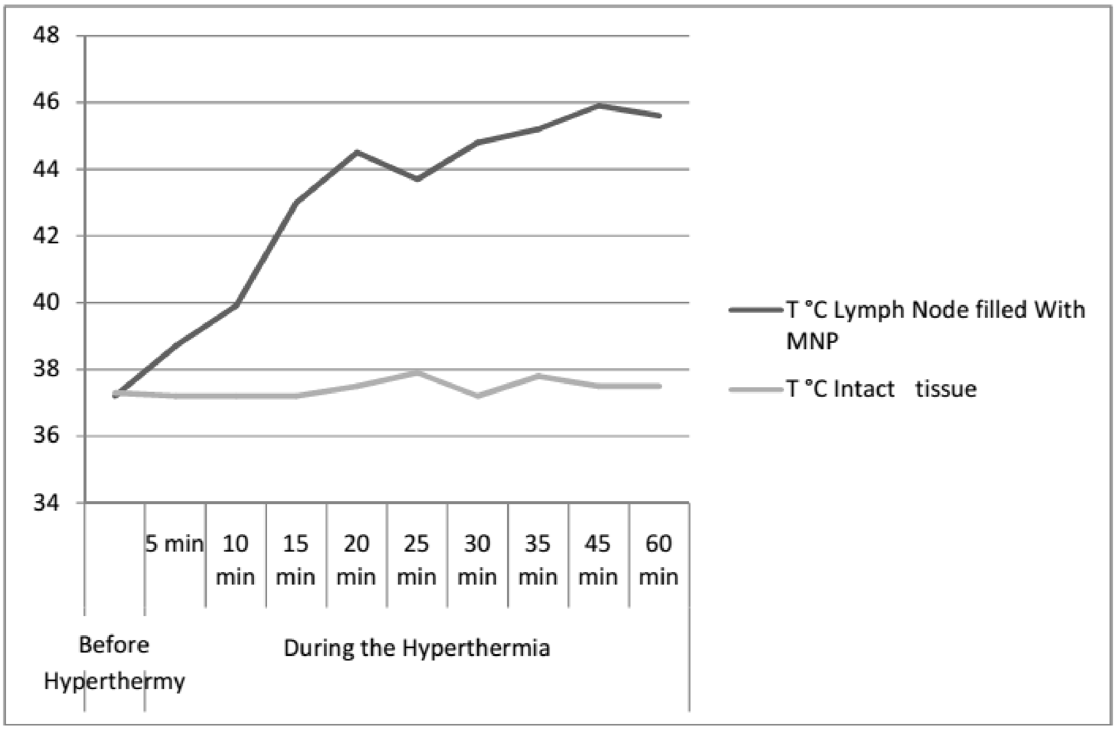

Figure 2. Diagram for magnetic nanoparticles with about 46 °C Curie temperature in life tissue.

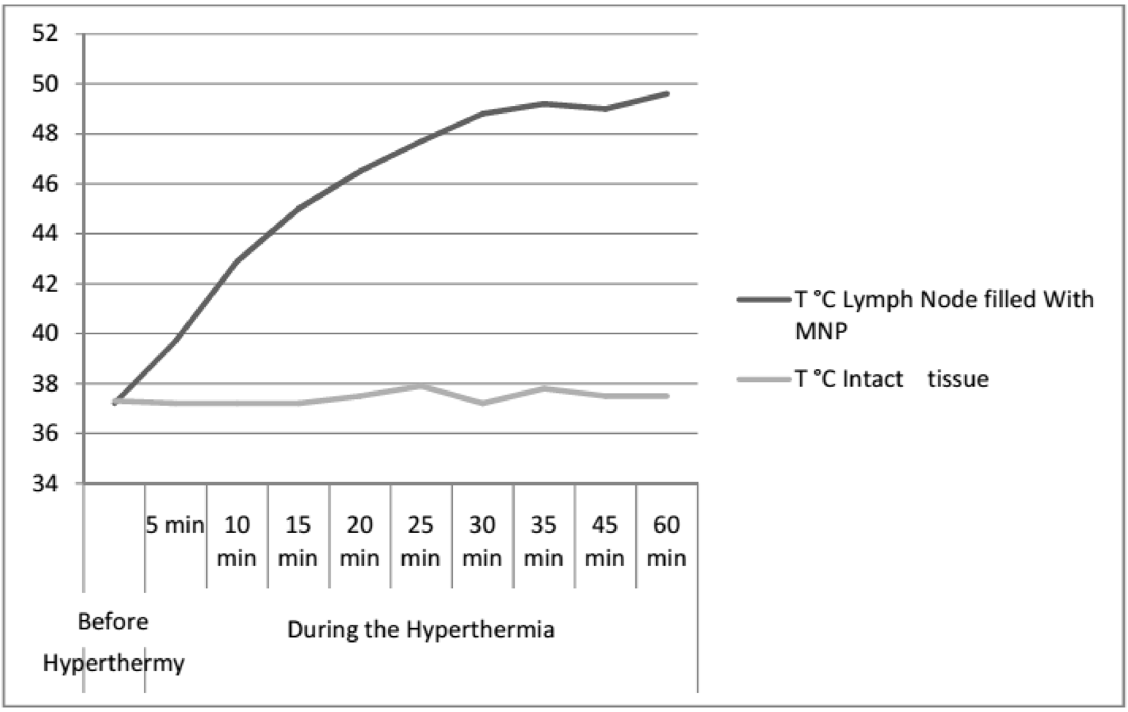

Figure 3. Diagram for magnetic nanoparticles with about 50 °C Curie temperature in life tissue.

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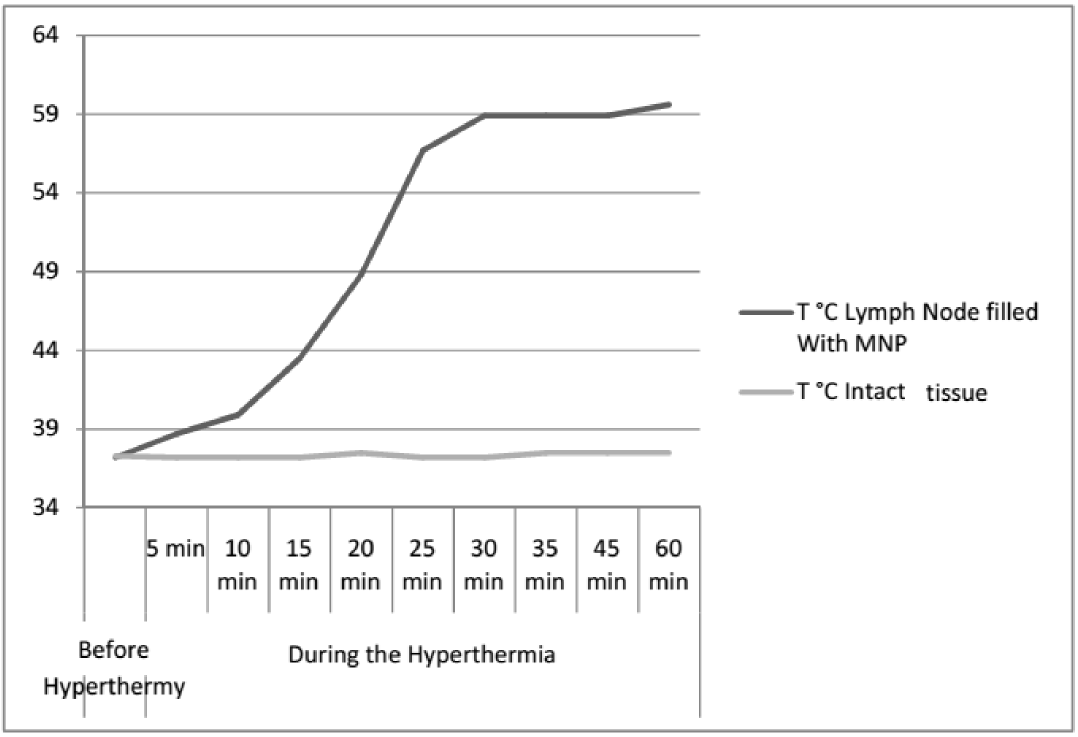

Figure 4. Diagram for magnetic nanoparticles with about 60 °C Curie temperature in life tissue.

Additionally, experiments conducted for magnetic nanoparticles with 80 °C Curie temperature but the effect was the same as 70 °C Curie temperature magnetic nanoparticles. There was no reason to add the diagram for this case.

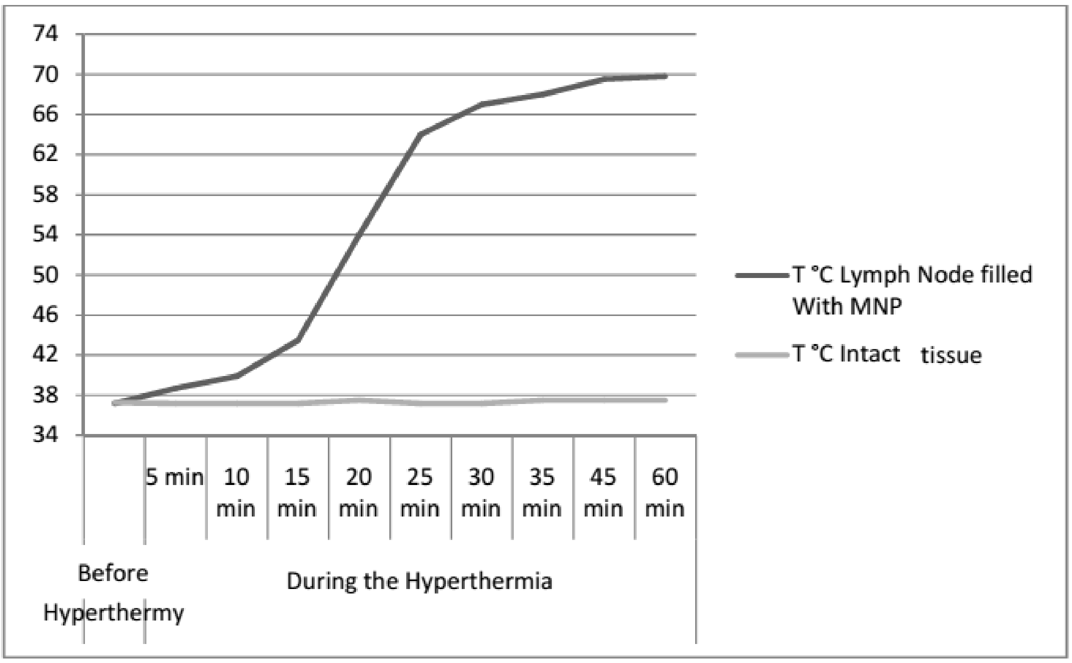

Figure 5. Diagram for magnetic nanoparticles with about 70 °C Curie temperature in life tissue.

Experiment results conclude that, under 20 kHz radiofrequency, 30 – 35 min exposure of magnetic nanoparticles with stable therapeutic effect. Nanoparticles are selected by Curie temperature of 46 – 80 °C. Under or above numbers of Curie temperature range of nanoparticles are not effective.

Nanoparticles above the 80 °C Curie temperature in the soft life tissue is dangerous and not safe because of high temperature biological liquids are evaporating and can distribute in the healthy tissue that can cause undesirable side effects.

References

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[2] M. Allegretti. The Therapeutic Properties of Electromagnetic Waves: From Pulsed Fields to Rifing, 2018, Kdp Print Us.

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