Inductive Nano Targeted Electromagnetic Therapy

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ABSTRACT

A Biofunctionalized Nano-scale Electromagnetic Induction Agent (BNEIA) is proposed in this method, capable to attach specifically biologic targets in vivo and in vitro. An External Alternative Magnetic Inductor (EAMI) is designed to create inductive electric, magnetic and thermal effects near the target which can potentially be malignant cell membrane or receptor, a bio-molecule, bacterial cell wall or viral capsid. Since the physical (electric, magnetic and thermal) balance is critical for biologic systems, any irregularity in these factors can potentially cause devastative effects on the target, controllable from dysfunction to destruction.

Keywords: electromagnetic induction, ferromagnetic nano-particle, nano-targeting, cancer detection, cancer treatment

1 INTRODUCTION

One of the greatest obstacles with cancer treatment is the ability to selectively treat only the malignant cells while leaving normal cells unharmed. In the other hand a major challenge in cancer treatment is the ability to destroy the metastatic malignant cells early before detectable large tumor formation. Scientists have focused on detection, targeting and selectively treatment of malignant cells.

Ferromagnetic material is composed of microscopic interacting domains. Once these domains are aligned by a field, they remain oriented and the material is magnetized. As an example for magnetite, Fe_3O_4, the domain size is 15–80 nm (1). Subdomain nanoparticles align and respond to a magnetic field, but when the field is removed, the thermal motion is high enough to randomly reorient them, leaving no residual magnetization (2). They are known as "super paramagnetic particles".

In the year 1957, the first use of magnetic particles to heat tissues is recorded, done by Gilchrist et al, with a 1.2 MHz magnetic field (9). The application of hyperthermia is followed and till now, many studies have been done to find the best way to use this technology for potential clinical applications (10-15). Magnetic nano particles (MNP) are used into drug delivery systems to heat releasing the drug (16-20). Much progress has also been made in developing MNPs. Particles have been developed with higher efficiency (21), heating better (22,23), having different coatings such as polyethylene glycol (24) and gold (25,26).

Direct intratumoral injection was used in the first MNP hyperthermia clinical trial, designed to treat a prostate cancer (27), later another study has reported Safety and some benefits in treating also human glioblastoma using this method (28,29). Heating was done, but complete eradication of malignant cells was not possible because of inhomogeneous MNP distribution.
Since direct intratumoral injection have advantages such as concentrations of MNPs and limiting systemic toxicity, it has some important disadvantages such as invasiveness, not covering the whole tumoral mass (30,31) and not being effective on small metastatic tumors. Later IV injection of MNPs was proposed. Although IV injection has some advantages such as more systemic distribution rather than the local distribution that happens in direct injection (32, 33), it is not effective when a homogeneous loading is needed on the tumor.
IV injection of MNPs followed by induction heating by an Alternative Magnetic Field (AMF) showed some efficacy but was not able to fully ablate tumors, because the required concentration was higher than safe systemic level and could not be reached in the tumors. (34-35).
Tumor to non-tumor concentration ratio is critical in IV MNP injection followed by AMF hyperthermia. Higher tumor to non-tumor ratio and higher concentration in tumors at lower systemic dose leads to get closer to precise tumor ablation (2).
Photodynamic therapy (PDT) combines a drug (photosensitizer or photosensitizing agent) with a specific type of light to kill cancer cells. When photosensitizers are exposed to a specific wavelength of light, they produce activated form of oxygen that kills nearby cells (3-5). In Photodynamic therapy a photo sensitizer is used to cause malignant cell damage by releasing activated form of oxygen (3-5). This method has some limitations such as limited penetration of light in tissues which causes inefficiency of this method for treatment of deep sited tumors. PDT is usually used to treat tumors on or just under the skin or on the lining of internal organs or cavities (5). As the light cannot pass deep into the large tumors, PDT is less effective in treating large tumors, (4,5,8). PDT is a local treatment and generally cannot be used to treat metastasis (8). In the other hand there are some known side effects caused by PDT, as an example Porfimer sodium makes the skin and eyes sensitive to light for approximately 6 weeks after treatment (3,5,8). PDT also can cause burns, swelling, pain, and scarring in nearby healthy tissue (5). Other side effects of PDT are related to the area that is treated. Researchers continue to study ways to improve the effectiveness of PDT and expand it to other cancers. Clinical trials are under way to evaluate the use

of PDT for cancers of the brain, skin, prostate, cervix, and peritoneal cavity. Other research is focused on the development of photosensitizers that are more powerful (3), more specifically target cancer cells (3,5,7) and are activated by light that can penetrate tissues more and treat deeper or larger tumors (4). Researchers are also investigating ways to improve equipment (3) and the delivery of the activating light (7).
As an example Near Infra Red (NIR) light was used to activate the photosensitizer in order to penetrate deeper than PDT (36) but penetration limitation and treating tumors in the shadow of dense tissues like bone is still a severe disadvantage in this method.

Present invention is a novel idea to detect and treat various medical conditions such as cancer. Easy detection, reducing normal cell damage by high selectivity, ability to treat tumors without penetration limitation, effectiveness on metastasis and micro-metastasis and minimal systemic side effects are numbers of advantages in this method. In this method a nano-scale component is proposed which can specifically attach to the target cells or bio-molecules by using agents such as Monoclonal Antibodies. It can be injected Intravenous (IV) to the systemic circulation. The Nano Component travels all over the body but stays in cancer cells longer than it does in normal cells (as an example). When most of the agent has left normal cells but remains in targets, patient is exposed to the AMF. If the exact position of tumor is known, it can also be injected into the vessels that carry blood into the involved organs followed by local exposure to AMF. In the patients with high risk of metastasis, systemic IV injection is recommended followed by general exposure to AMF.

2. MATERIAL AND METHODS

2.1 Biofunctionalized Nano-scale Electromagnetic Induction Agent (BNEIA)

A Biofunctionalized Nano-scale Electromagnetic Induction Agent (BNEIA) is proposed in this method. The BNEIA is an antibody conjugated, PEG coated, ferromagnetic nano particle [figure 1]. The BNEIA is able to attach the targets by using molecules for specific attachment such as monoclonal anti body [figure 2]. Since it contains ferromagnetic nano-particle inside, it is detectable by Magnetic Resonance Imaging (MRI). Magnetic nano-particles have already been used as MRI contrast (37).
An external electromagnetic inductor is proposed to create inductive electric, magnetic and thermal effects around the BNEIA.
Since many of cell activities are depended on cell membrane electric function, electric regularity and balance is necessary to cell normal function. The activated nano component can cause membrane electric dysfunction to the attached target cells. In the other hand thermal effects caused by activated BNEIA causes hyperthermia when attached to the cell membrane. Hyperthermia itself causes cell damage (2,10,11,15,27).

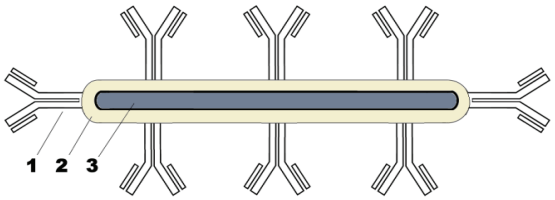

Figure 1: Biofunctionalized Nano-scale Electromagnetic Induction Agent (BNEIA)

1. Monoclonal Antibody
2. P.E.G Coating
3. Ferromagnetic Nano Particle

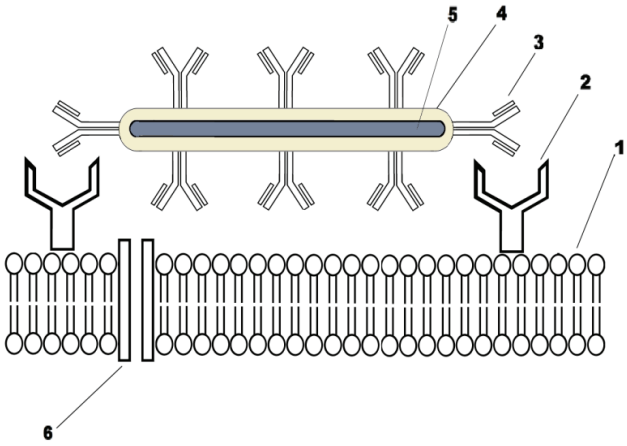

Figure 2: Biofunctionalized Nano-scale Electromagnetic Induction Agent (BNEIA) attached to the target cell membrane

1. Cell membrane
2. Cell Receptor
3. Monoclonal Anti Body
4. P.E.G Coating
5. Ferromagnetic Nanoparticle
6. Membrane Ion Channel

2.2 Closed External Inductor

The external inductor is an electromagnet designed with a closed ferrite core, connected to a high frequency alternative electrical current. Both the current and frequency are adjustable on the system to reach the best effectiveness. In order to reach the maximum induction it is needed to place the tumor area in the center of the inductor. There is a laser lamp provided on the inductor system which shows the center of the inductor and it has no other function [figure 3]. A non metallic bed is designed inside the electromagnet for the patient to lie down on. The bed is also adjustable to place in the optimal position [figure 3].
The external inductor function is to create inductive electric, magnetic and thermal effect in the ferromagnetic nano-particle inside the BNEIA. The electromagnet is rotatable in order to affect the ferromagnetic nano-particles in different space directions to reach the optimal electromagnetic induction efficiency.

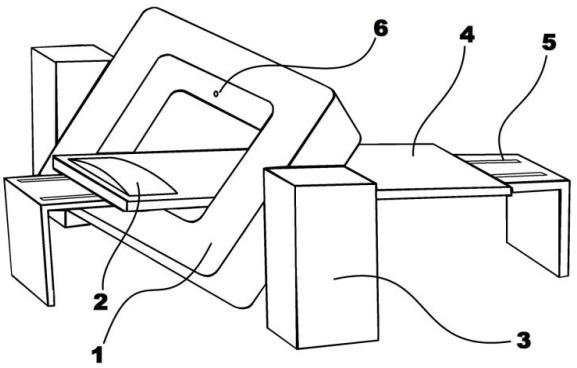

Figure 3: Closed External Inductor System

1. Closed Electromagnet (a coil with closed core)
2. Head Rest
3. The base
4. A non-Conductive Bed
5. Bed Moving Groove
6. Laser Lamp

2.3 Open External Inductor

Open external inductor is an electromagnet connected to a high frequent alternative electric current [figure 4]. It is designed in U-shape as two ends (Poles) of the U-shape electromagnet are placed near the patient's body in the known malignant center. It is proposed for local AMF exposure. When there are known malignant centers with low risk of metastasis, after detection of the tumor exact site, local vascular injection of the BNEIA is recommended followed by local exposure to AMF by open external inductor. The rotation systems are working the same in both closed and open external inductors.

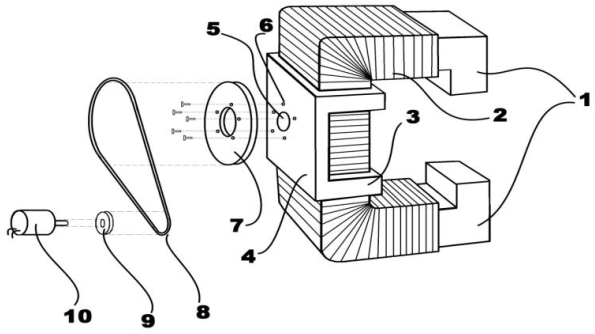

Figure 4: Closed External Inductor System (Exploded View)

1. Two ends (Poles)
2. Coil
3. Basis
4. Basis Plate
5. Rotation Axis
6. Pin Holes
7. Large pulley
8. Belt
9. Small pulley
10. Electromotor

3 CONCLUTION

Since the early detection and specifically treating malignant cells is known as one of the essentials of cancer treatment, in the past few years many of scientists have focused on this issue. The results indicating that despite some advantages in this field, there is still the necessity to find a non-invasive and effective method. The presented invention can lead to the goal of cancer treatment which is maximum effectiveness and minimum invasiveness.

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