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Clinical hyperthermia by resonant selective tumor destruction tuned by hyperfine interaction: I. Basic model

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Abstract

We suggest here a method for clinical hyperthermia treating by selective tumor destruction tuned by hyperfine interaction between the magnetic ions, introduced selectively in malignant cells and the nuclear spin surrounding. As a carrier for a microscopic magnetic moments the 2-deoxyglucose can be used, on which the standard by now imaging by PET (Positron Emission Tomography) is based. Influence of external frequency radiation may heat the tumor cells selectively above it basal temperature and kill the cell. Clusterization of magnetic atoms into magnetic nanoparticles within the tumor and its mechanical vibrations under external EM fields could be used to destroy the malignant cell. A new model of the hyperfine interaction between the atom spins and nuclear spins of surrounding atoms tuned by nonlinear focusing of local magnetic fields is introduced.

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1 Introduction

Interaction of electromagnetic fields with magnetoactive media is well studied and widely employed in various fields of science and medicine [1, 2]. The most powerful methods are connected with the spin degrees of matter and are called magnetic resonances both electron and nuclear[3, 4]. Recent enormous progress in nanotechnology results in fastly growing applications of hyperfine interactions in creating unprecedented advances in nano electronics, quantum information processing etc. [5-9]. Here we address some implications of these new methods of the Nuclear Spintronics in the certain fields of oncological research.

2 Definition of medical problem

There are two known methods in oncology to manage a malignant tumor – apoptosis, means induction of "normal" cell death by chemotherapy, and necrosis, means direct destruction of malignant cell by physical or chemical event. Hyperthermia is one of physical events that come be popular last decade [10-13].

Radiofrequency ablation of malignant tumors is promising, but controversial in modern oncology [14-18]. The problem is that RF need to be used locally to the tumor bed by using invasive technique and special devices [14, 16, 17]. Very often malignant disease is disseminated in several organs and systems that local control can not be used for management of it.

Using of magnetic particles to heat the tumor and destroy it is the new development of hyperthermia [19]. The idea is to introduce into malignant tumor magnetic particles and to rise up the interstitial temperature of it by alternating magnetic field to eliminate the tumor [20-22]. The technique means injection to the tumor suspension of nanoparticles interstitially, and actually is the modification of local hyperthermia treatment and can not be used for disseminated malignancy. Heating is not selective for malignant cell because it is extracellular.

There are several agents that may accumulate selectively in malignant cells . One of them is 2-[18F] fluoro-2-dexy-D- glucose (FDG). Cancer cells show increased metabolism of both glucose and amino acids, which can be monitored with FDG, a glucose analogue, and 11C-L-methionine (Met), respectively. FDG uptake is higher in fast-growing than in slow-growing tumors. FDG uptake is considered to be a good marker of the grade of malignancy. The FDG accumulates in the malignant tumor cell with atoms

of radioactive isotope F^{18} and can be used for imaging purpose [29-33] by PET-CT: positron electron annigilation techniques.

The F^{18} is radiolabelling the FDG molecule in such a way that the positrons emitted by the F^{18} nuclear annihilate with an electron and irradiate. This radiation is registered by counters thus showing where the malignant cells, which absorbed the FDG are located PET-CT.

We suggest here that once the FDG enters into malignant cell we can transform it using modern chemistry and physics methods into active heating or cutting body which may destroy the malignant cell.

Influence of external radiofrequency radiation may heat the tumor cells selectively without using of local irradiation (see physical aspects below). It is well known that heating the biological cell by 5 centigrade above it basal temperature will kill the cell [10, 19]. So we may selectively destroy any malignant tumor cell in the body even in disseminated malignancy by using physical factor – hyperthermia, that may be very promising.

There is no similar technique in modern medicine and using of combination of active magnetic entities in 2-deoxyglucose as carrier and surrounding nuclear spins for tuning the resonant frequencies and redistributing the heat is revolutionary here.

3 Physical part

3.1 Electron spin resonance

An electron placed in a magnetic field is described by the spin Hamiltonian:

$$H_{ESR} = g_e \mu_B \overrightarrow{B} \cdot \overrightarrow{S} \tag{1}$$

In Eq. (1) $g_e \simeq 2$ is the g-value for a free electron, $\mu_B \simeq 10^{-20}$erg/g is the Bohr magneton, $\overrightarrow{B}$ is the magnetic field strength, and $\overrightarrow{S}$ is the spin vector. For a field B_o in z-direction: $\overrightarrow{B} \parallel \widehat{z}$ the electron spin energy is splitted in two (spin up -spin down) levels.

A resonant photon can change the electron spin direction thus forcing the electron to cross this energy gap

$$\hbar\omega_{res} = g_e \mu_B B_o S \tag{2}$$

thus storing its energy to the electron spin system. This stored electromagnetic energy will be thus leading to heating of the chosen cells.

The effectiveness of this process depends on the physical mechanisms connecting the magnetic entity (say magnetic atom or magnetic nanoparticle) absorbing the electromagnetic wave, we will call it Internal Heating Unit (IHU), with the different degrees of freedom of the surrounding atoms and molecules.

The effectiveness of the heating during the ESR is an old and widely studied subject and is treated in details in text books [3, 4].

3.2 Hyperfine interactions

Among the most important mechanisms defining the rate of the external RF energy absorbtion in magnetic resonance are the molecular vibrations, phonons in the nanoparticles and the dynamic nuclear spin polarization which arises due to the hyperfine interaction between nuclear and electron spins [3, 4]. The phonon vibration is difficult to localize especially in a non-latice (soft) media.

We will concentrate here on the dynamic nuclear polarization by the atomic spins of huge numbers of nearby nuclei. Due to the different kinds of nuclear spin diffusion the nuclear polarization, obtained from a magnetic center, will cover a large, compared to external MI radius, thus being in contact with huge number of underlying atoms.

In most cases nuclear spin relaxation is due to the contact hyperfine interaction between the nuclear and conduction electron spins. For a given nucleus in the point $\mathbf{R}$ with the spin $\mathbf{J}$, the interaction is described by the Hamiltonian:

$$\mathcal{H} = -\frac{8\pi}{3}\gamma_n g\mu_B\hbar(\mathbf{J}\cdot\mathbf{s})\sum_e \delta(\mathbf{r}_e - \mathbf{R}). \tag{3}$$

Here γ_n is the nuclear gyromagnetic ratio, μ_B is the Bohr magneton, g, [34]$\mathbf{s}$ and $\mathbf{r}_e$ are the effective g-factor, spin operator and radius-vectors of electrons.

By interaction (3) the excitaton of the electron spin of a MI is transferred to the nuclear spin of the surrounding sell. Due to complicated atomic and nuclear structures the parameters of such systems may vary by many orders of magnitude. The practical estimates of necessary power and technicalities will be considered in the follow up publication [35].

Yet another aspect of the problem is clusterization of magnetic particles introduced into tumor cells by multiple 2-deoxyglucose molecules. While out of resonance this magnetic clusters could be used for selective mechanical destruction of tumors using the methods of forced detected nuclear magnetic resonance [34].

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