Research lines in Hyperthermia at the Bioinstrumentation Laboratory of the Centre for Biomedical Technology

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The Bioinstrumentation Laboratory belongs to the Centre for Biomedical Technology (CTB) of the Technical University of Madrid and its main objective is to provide the scientific community with devices and techniques for the characterization of micro and nanostructures and consequently finding their best biomedical applications.

Hyperthermia (greek word for “overheating”) is defined as the phenomenon that occurs when a body is exposed to an energy generating source that can produce a rise in temperature (42-45ºC) for a given time [1]. Specifically, the aim of the hyperthermia methods used in The Bioinstrumentation Laboratory is the development of thermal therapies, some of these using different kinds of nanoparticles, to kill cancer cells and reduce the damage on healthy tissues.

The optical hyperthermia is based on noble metal nanoparticles and laser irradiation. This kind of nanoparticles has an immense potential associated to the development of therapies for cancer on account of their Surface Plasmon Resonance (SPR) enhanced light scattering and absorption. In a short period of time, the absorbed light is converted into localized heat, so we can take advantage of these characteristics to heat up tumor cells in order to obtain the cellular death [2].

In this case, the laboratory has an optical hyperthermia device based on a continuous wave laser used to kill glioblastoma cell lines (1321N1) in the presence of gold nanorods (Figure 1a). The wavelength of the laser light is 808 nm because the penetration of the light in the tissue is deeper in the Near Infrared Region. The first optical hyperthermia results show that the laser irradiation produces cellular death in the experimental samples of glioblastoma cell lines using gold nanorods but is not able to decrease the cellular viability of cancer cells in samples without the suitable nanorods (Figure 1b) [3].

The generation of magnetic hyperthermia is performed through changes of the magnetic induction in magnetic nanoparticles (MNPs) that are embedded in viscous medium. The Figure 2 shows a schematic design of the AC induction hyperthermia device in magnetic fluids. The equipment has been manufactured at The Bioinstrumentation Laboratory. The first block implies two steps: the signal selection with frequency manipulation option from 9 KHz to 2MHz, and a linear output up to 1500W. The second block is where magnetic field is generated (∅ 5mm, 10 turns). Finally, the third block is a software control where the user can establish initial parameters, and also shows the temperature response of MNPs due to the magnetic field applied [4-8].

The Bioinstrumentation Laboratory in collaboration with the Mexican company MRI-DT have recently implemented a new research line on Nuclear Magnetic Resonance Hyperthermia, which is sustained on the patent US 7,423,429B2 owned by this company. This investigation is based on the use of clinical MRI equipment not only for diagnosis but for therapy [9]. This idea consists of two main facts: Magnetic Resonance Imaging can cause focal heating [10], and the differentiation in resonant frequency between healthy and cancer cells [11]. To produce only heating in cancer cells when the whole body is irradiated, it is necessary to determine the specific resonant frequency of the target, using the information contained in the spectra of the area of interest. Then, special RF pulse sequence is applied to produce fast excitation and relaxation mechanism that generates temperature increase of the tumor, causing cellular death or metabolism malfunction that stops cellular division.

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Figures

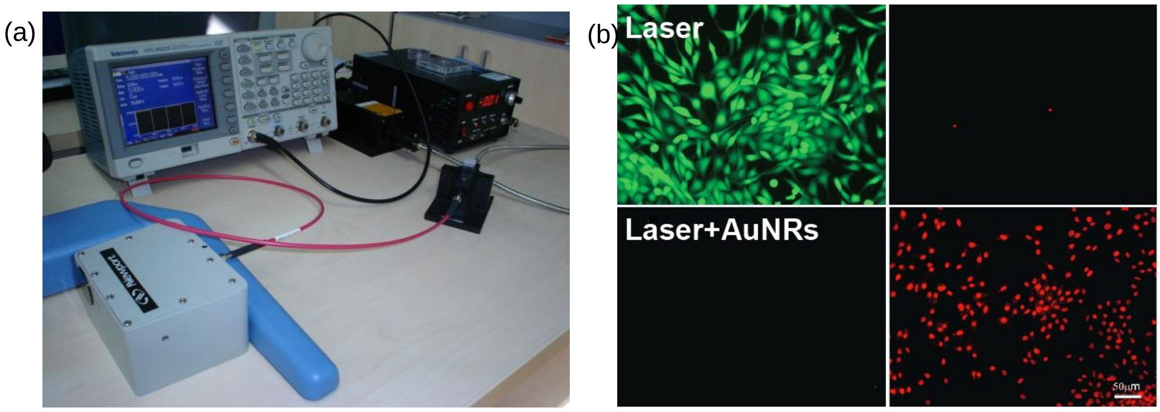

Figure 1. a) Optical Hyperthermia device, b) IP/Calcein essay in samples of glioblastoma cell lines and gold nanorods (24 h after the irradiation).

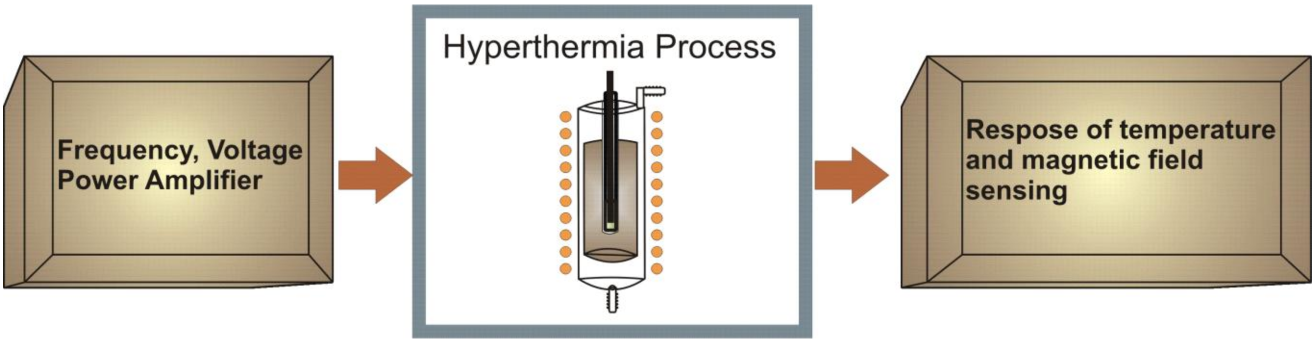

Figure 2. Schematic of the Magnetic Hyperthermia device