Thermal and mechanical effects of different excitation modes based on low frequency laser modulation in optical hyperthermia

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Abstract

Recently, gold nanoparticles, in combination with laser light, have been used successfully to achieve controlled thermal damage in tumor tissue [1] [2]. Gold nanostructures show a unique optical property, ie, they efficiently absorb light due to the surface plasmon resonance phenomenon and then convert the absorbed light into localized heat [3].

Our first work was aimed at obtaining a proof of concept of an optical hyperthermia system [4]. The instrument was similar to others currently being used [5] [6], but with the possibility of using different excitation methods by changing the light exposure pattern from continuous wave light to pulsed light. The system was developed to evaluate the effectiveness of gold nanorods designed to work in the optimal tissue window for light absorbance (808 nm) used to produce cellular death in glioblastoma cell lines (1321N1). The obtained results showed that the use of gold nanorods in hyperthermia therapy is very effective (Figure 1) but in order to develop an optimal treatment, many parameters still need to be optimized, concerning both laser irradiation and gold nanorods characteristics.

After these first results, our work is focused on the development of new excitation methods with the aim of increasing the effectiveness of the hyperthermic treatment thanks to the well known thermal effects and to other mechanical effects that are being studied and could influence the cell death process.

The low frequency modulation of the laser source (<30KHz) allows the generation of a pulsed signal that intermittently excites the gold nanorods. The temperature curves obtained for different frequencies and duty cycles of modulation but with equal average power and identical laser parameters, show that the thermal behavior in continuous wave and modulation modes are the same (Figure 2). However, the cell death experiments suggest that the percentage of death is higher in the cases of modulation (Figure 3). This observation allows us to conclude that there are other effects in addition to temperature that contribute to the cellular death.

The mechanical effects like sound or pressure waves are expected to be generated from thermal expansion of gold nanorods. In order to study the behavior and magnitude of these processes we have developed a measure device based on ultrasound piezoelectric receivers (25KHz) and a lock-in amplifier that is able to detect the sound waves generated in samples of gold nanorods during laser irradiation providing us a voltage level proportional to the pressure signal.

The first results (Figure 4) show that the pressure measurements are directly proportional to the concentration of gold nanorods and the laser power, therefore, our present work is focused on determine the real influence of these effects in the cell death process.

References

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Figures

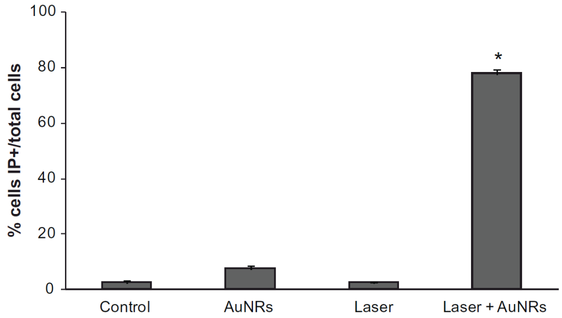

Figure 1. Photothermal treatment of 1321N1. The cells were stained with propidium iodide and then fixed and analyzed on a flow cytometer. The graph shows the percentages of dead cells (IP+-cells) over total cells, calculated for each condition. Control: 1321N1 basal cell death rate. AuNRs: 1321N1 cells incubated with gold nanorods. Laser: 1321N1 cells subjected to laser irradiation. Laser + AuNRs: 1321N1 cells subjected to laser irradiation in the presence of gold nanorods.

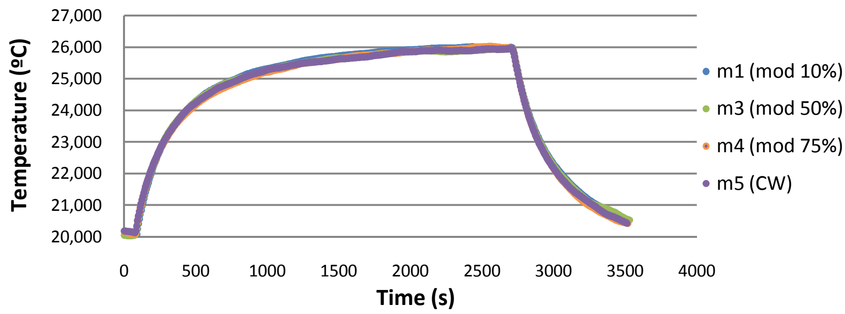

Figure 2. Temperature curves of gold nanorods suspension for different duty cycles of modulation in comparison to the continuous wave mode (CW). The parameters of the laser are fixed in an average power of 381 mW and a frequency of modulation of 5KHz.

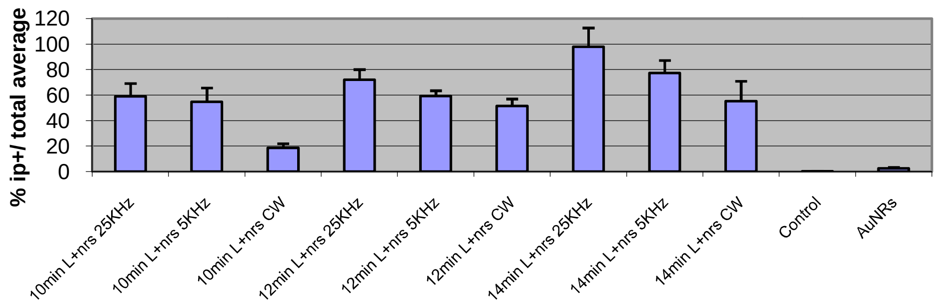

Figure 3. IP/calcein essay 24h after irradiation: Comparison between different times and excitation modes (modulation and CW).

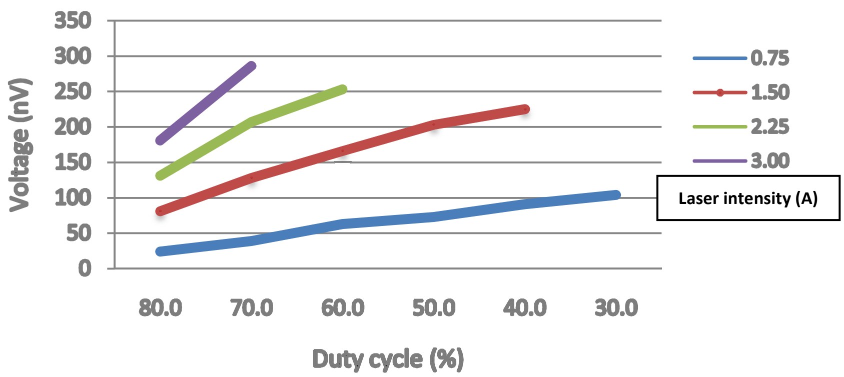

Figure 4. Voltage levels for different laser intensitiy values (linearly proportional to the power source) in a duty cycle sweep.