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Zinc oxide nanocrystals combined with ultrasound for the controlled generation of Reactive Oxygen Species

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OBJECTIVES

Reactive Oxigen Species (ROS) effects on living cells viability and proliferation are numerous. Due to their ability to react with different types of biological molecules, ROS are involved in many cell functions[1]. The ability of maintain the redox homeostasis is crucial and an imbalance can lead to a variety of possible diseases. Controlled generation of ROS can be exploited to generate oxidative stress in cells, leading to cell death, with the aim of developing drug and drug-free therapeutic tools for anticancer treatments. Aminopropyl-functionalized ZnO NCs (ZnO-NH_2 NCs) are proved able to produce ROS in a tunable and reproducible manner, when stimulated by ultrasound (US), using an already approved medical device, LipoZero G39. The generation of hydroxyl radicals is the result of inertial cavitation under the US exposure.

METHODS

Dynamic Light Scattering technique, Field Emission Scanning Electron Microscopy, Transmission Electron Microscopy, X-Ray Diffraction were used to characterize the ZnO-NH_2 NCs previously synthetized via microwave-assisted sol-gel synthesis. A large variety of parameters were evaluated: US frequency and power as well as ZnO-NH_2 NCs concentration. The generation of ROS was evaluated by Passive Cavitation Detection, Electron Paramagnetic Resonance and Ultrasound B-mode imaging.

RESULTS

When ZnO-NH_2 NCs were present in the aqueous solution a significative enhancement of ROS production, and an improved cavitation signal was measured compared with the water alone. The same behavior was verified in PBS, cell culture media and in presence of tissue mimicking materials[2], as ex vivo tissue and phantom.

CONCLUSIONS

It is verified that ZnO-NH_2 NCs are ultrasound responsive nano-agent due to their ability to induce inertial cavitation under pulsed US exposure, which consequently leads to a large ROS production. Controlled ROS production was also assessed in biological media as PBS and cell culture media. This result suggests the applicability of this technology in the biological field, as a possible tool to induce cancer cells death, predicting high potential healthcare applications.

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