Saratov Fall Meeting
SFM'21

9th International Symposium “Optics and Biophotonics”

25th International School for Junior Scientists and Students on Optics, Laser Physics &Biophotonics

BRICS Workshop on Biophotonics-2021

Analysis of the sono-photodynamic effects using Protoporphyrin IX (PpIX): in vitro and in vivo studies

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Abstract

Sono-photodynamic therapy (SPDT) is a relatively new and promising approach to cancer treatment, based on the combination of photodynamic therapy (PDT) and sonodynamic therapy (SDT). This study aims to analyze the mechanisms and effects of the sonophotodynamic (SPD) activity using Protoporphyrin IX (PpIX) as a sono-photosensitizer. In vitro, a series of 5 μM PpIX solutions were irradiated with red light (635 nm, 30-50 mW/cm2), ultrasound (1 MHz, 1-2 W/cm2, 50%) and both sources simultaneously. The PpIX absorption spectra recorded during each process, showed that the PpIX decay rate (k) induced by the irradiation of both sources was approximately the sum of those induced by the irradiation of light and ultrasound (k_"SPD" ≈ k_"SD" + k_"PD"). In vivo, rats were intraperitoneal injected with 5-ALA at dose of 500 mg/kg body weight. At 3 hours after injection, livers were irradiated with red light (635 nm, 180±10 J/cm2), ultrasound (1.0 MHz, 1.5 W/cm2, 50%) and both sources simultaneously. For these procedures, it was built a single probe capable of irradiating both light and ultrasound. After 30 hours, animals were sacrificed, the livers were surgically removed and histologically processed. Scanned histological slides showed that the SPD activity induced greater depth and area of necrosis than photodynamic (PD) activity alone. These results suggest that SPD activity could generate a greater amount of ROS than either PD or sonodynamic activity alone, which results in the increment of the drug decay rate, as well as the activity scope in a homogeneous biological tissue.