Ultrasound microbubbles functionalized with photodithazine for photodynamic therapy in an experimental orthotopic renal cancer model

Daria A. Terentyeva[1], Olga A. Sindeeva[1], Olga I. Gusliakova[2], Polina G. Rudakovskaya[1], Dmitry A. Gorin[1]

[1] Skolkovo Institute of Science and Technology, 3 Nobel Str., 143005 Moscow, Russia;

[2] Saratov State University, 83 Astrakhanskaya Str., 410012 Saratov, Russia.

E-mail: Daria.Terentyeva@skoltech.ru

Abstract

Albumin-based microbubbles have been widely used as ultrasound contrast agents over the decades, and recent attention has been paid to their use as drug delivery systems. Recently, it was shown that photosensitizers can be efficiently loaded into the microbubble shell, and the resulting platform may enhance the photodynamic activity. In our study, PDT was carried out using a constant laser with a wavelength of 660 nm, selected optimally for photodithazine. In a series of preliminary experiments on small groups of animals, conditions (laser time and power) that did not lead to irreversible changes in renal tissue due to excessive exposure to laser radiation during the local injection of microbubbles with a photodynamic agent through the renal artery. Thus, the range of photodynamic therapy parameters was narrowed: volume of injected bubbles/conjugate - 24 μl (15 μg of photoditazine per mouse), as in the biodistribution experiments; laser irradiation power of 50 mW (100 mW led to total disruption of renal blood flow already 0.5 minutes after laser exposure, 25 and 10 mW did not cause photodynamic therapy of the tumor even with prolonged (30 min) exposure to laser irradiation); exposure times of 10 and 20 min were studied in more detail (5 min exposure was not sufficient to show the effect of photodynamic therapy). The results of this study demonstrated the efficacy of the developed approach in the case of vesicle administration and, to some extent, in the case of conjugate administration. However, additional large-scale studies with larger animal groups, histologic analysis for all individuals on day 10, and assessment of survival time are needed to confirm the reliability of the developed concept more confidently.

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Keywords: photodynamic therapy, microbubbles, photosensitizer, bovine serum albumin, Photodithazine.