The plasmonic photothermal therapy of transplanted tumors in rats using gold nanorods

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Abstract The study of morphological changes in transplanted liver tumors of rats after plasmonic photothermal therapy (PPTT) was conducted. The gold nanorods (GNs) functionalized with polyethylene glycol were injected by one-, two- and three-step intravenous administration. A day after injection tumors were irradiated by the NIR 808-nm diode laser. The most pronounced damage effect of PPTT was observed after triple intravenous injection of GN.

Keywords: plasmonic photothermal therapy, gold nanorods, transplanted liver tumors, morphological changes

The aim of this study was to evaluate the morphological changes in transplanted liver tumors after single, double and triple intravenous administration of gold nanorods (GNs) and plasmonic photothermal therapy (PPTT).

Methodology. 24 male outbred albino rats with transplanted liver cancer PC-1 were used in the experiment. The experimental model of rat liver cancer was reproduced by transplantation of tumor cells suspension of liver cancer (cholangiocarcinoma PC-1). When tumors reached a diameter of 3.0 ± 0.3 cm³ the animals were randomly divided into three groups (6 rats in group): group 1 - without exposure, group 2 - with a single injection of GNs and PPTT, group 3 - with double injections of GNs and PPTT, group 4 - with triple injections of GNs and PPTT. The GNs functionalized with thiolated polyethylene glycol were synthesized in the Laboratory of Nanobiotechnology (Institute of Biochemistry and Physiology of Plants and Microorganisms of RAS) as described previously [1]. Size of the nanorods was 41±8 nm (length) and 10±2 nm (diameter), and concentration of the nanorods in the suspension was 400 μg/ml, which corresponds to optical density of 20 at 808 nm. After one day after injection the tumors were irradiated by the NIR 808-nm diode laser LS-2-N-808-10000 (Laser Systems, Ltd., St.-Petersburg, Russia) during 15 min at power density 2.3 W/cm². Temperature control of the tumor heating was provided by IR imager IR4010 (IRYSYS, UK). Prior medical procedure or treatment, the rats were anaesthetized with Zoletil 50 (Virbac, France) in dose of 0.05 mg/kg. The withdrawal of the animals from the experiment and sampling of tumor tissue for morphological study were performed 24 hours after the PPTT. The standard histological staining was used for morphological study of transplanted tumors. The determination of gold concentration was conducted for 1 g of tumor tissue by atomic absorption spectroscopy on spectrophotometer Dual Atomizer Zeeman AA iCE 3500 (Thermo Scientific Inc., USA).

Results. At PPTT the tumor temperature increased from 35°C up to 42°C in group of the rats with a single GN injection. The atomic absorption spectroscopy showed that gold accumulation in the tumor tissue was insignificant (0.14 ±0.02 μg/g) and the temperature increase was due to only laser radiation hyperthermic action. In tumors the small foci of necrosis were noted, which take 20-30% of slice area, the tumor cells with necrotibiotic changes were noted in a small amount.

In group of the rats with the double GN injection we observed the increase of tumor temperature up to 46°C at PPTT. The gold content in the tumor tissue increased almost 9 times (up to 1.24±0.01 μg/g) compared to group with a single injection. The more pronounced necrotic changes were revealed in the tumor tissue after PPTT, tumor necrosis occupied up to 30-50% of slice area. In group of the rats with 3-fold nanoparticle injection, we observed the increase of tumor temperature up to 70°C at PPTT. The gold content in the tumor tissue significantly increased (up to 10.67±0.39 μg/g) compared to group with a single injection. The most pronounced necrotic changes were revealed in tumor tissue in this group of rats after PPTT, tumor necrosis occupied up to 70-80% of slice area, the tumor cells with necrotibiotic changes were presented only in subcapsular zone.

Conclusion. After triple intravenous injection of gold nanorods PPTT has most pronounced damaging effect in rats with transplanted tumors manifested in necrotibiotic changes of tumor cells.

REFERENCES