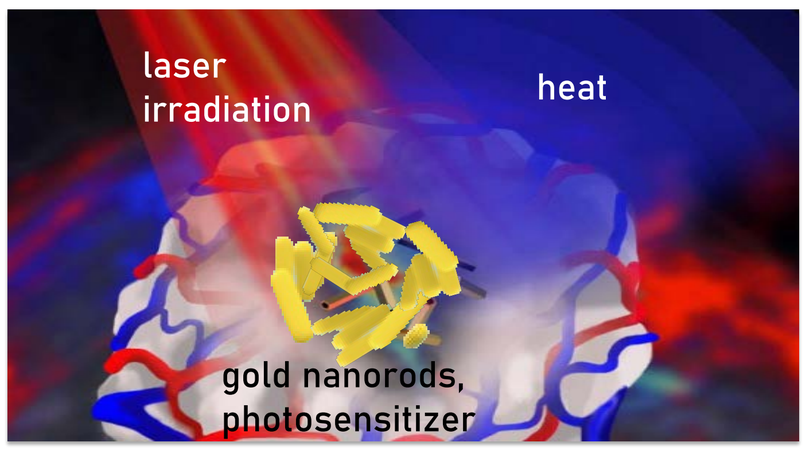
Treatment of rat model tumor with combined photodynamic/photothermal therapy

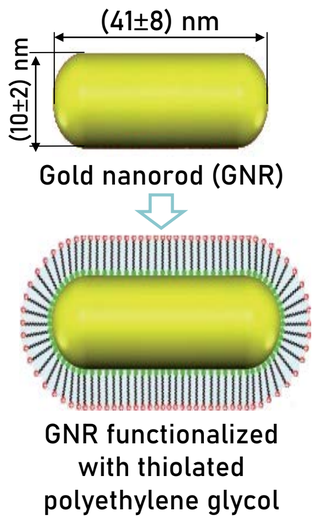
Vadim D. Genin[1,2], Alla B. Bucharskaya[1,2,3], Nikita A. Navolokin[1,3], Georgy S. Terentyuk[3], Boris N. Khlebtsov[4], Nikolai G. Khlebtsov[1,4], Valery V. Tuchin[1,2,5], Elina A. Genina[1,2]

[1] Saratov State University, Saratov, Russia; [2] Tomsk State University, Tomsk, Russia;
[3] Saratov State Medical University, Saratov, Russia;
[4] Institute of Biochemistry and Physiology of Plants and Microorganisms, FRC «Saratov Scientific Center of the RAS», Saratov, Russia

Motivation

The growth of a number of oncological diseases stimulates extensive development of both early tumor diagnostics and therapy methods. The relevance of the development of innovative methods of therapy in oncology based on combined technologies of photodynamic therapy (PDT) and plasmonic photothermal therapy (PPT) is due to the insufficient effectiveness of standard types of therapy for the treatment of tumors in hard-to-reach localizations. PDT and PPT are promising methods of tumor treatment that provides more heating locality than the traditional hyperthermia, which allows damage reduction in surrounding healthy tissues. The purpose of the study was to develop a combined technology of PPT and PDT in rats with model tumors





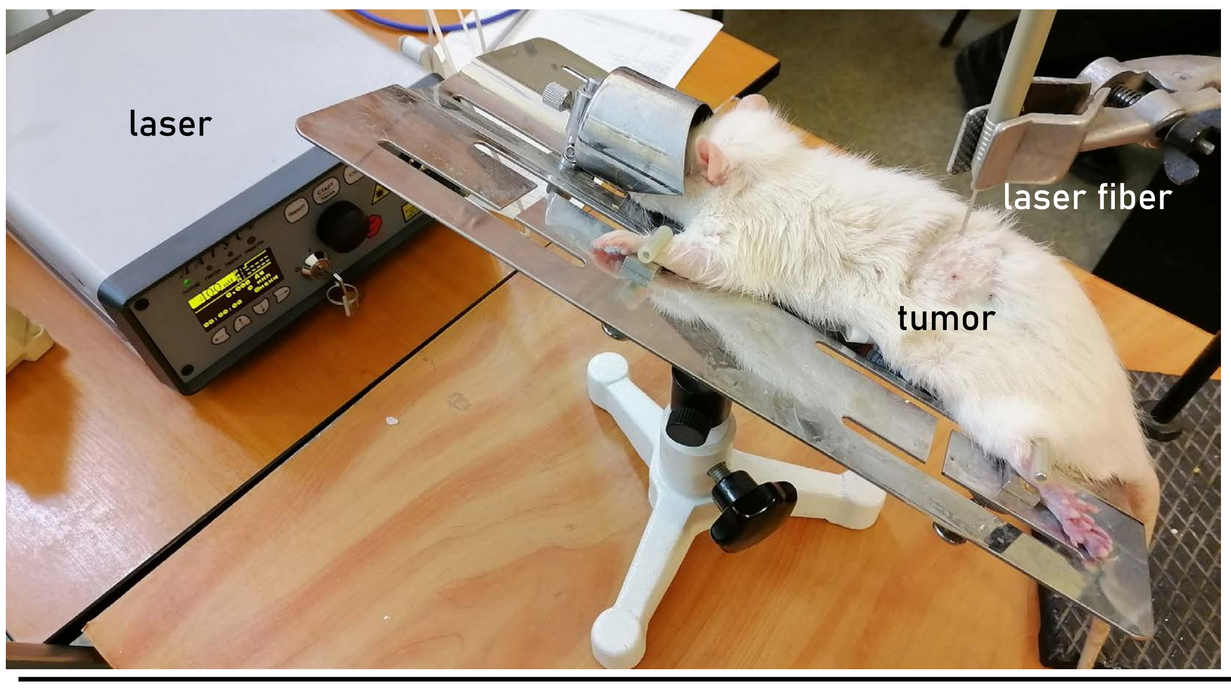
Materials and Methods

- 3 outbreed albino male rats with a subcutaneously grafted experimental model tumors of liver bile ducts cancer (cholangiocarcinoma of the PC-1 line)
- Irradiation for PDT (rats 1, 2): laser 660 nm, 0.4 W, ~0.5 W/cm^2, 15 min
- Irradiation for PPT (rats 1, 2): laser 808 nm, 2 W, ~2.5 W/cm^2, 15 min
- Irradiation for PPT+PDT (rat 3): laser 808 nm, 2 W, ~2.5 W/cm^2, 15 min
- Optical parameters: reflectance spectra before laser irradiation, after PDT and after PPT in ranges 400-900 and 900-2150 nm

Experimental animals

rat No.	tumor volume	photosensitizer injected intratumorally for PDT	volume of photosensitizer solution in physiological saline	photosensitizer concentration in the solution	volume of GNR suspension in PEG-300	GNR concentration in the suspension
rat 1	~3.8 cm^3	Photosens	0.30 ml	2 mg/ml	1.25 ml	400 mg/ml
rat 2	~8.2 cm^3		0.45 ml	2 mg/ml	2 ml	400 mg/ml
rat 3	~4.7 cm^3	indocyanine green	0.20 ml	10 mg/ml	1.57 ml	400 mg/ml

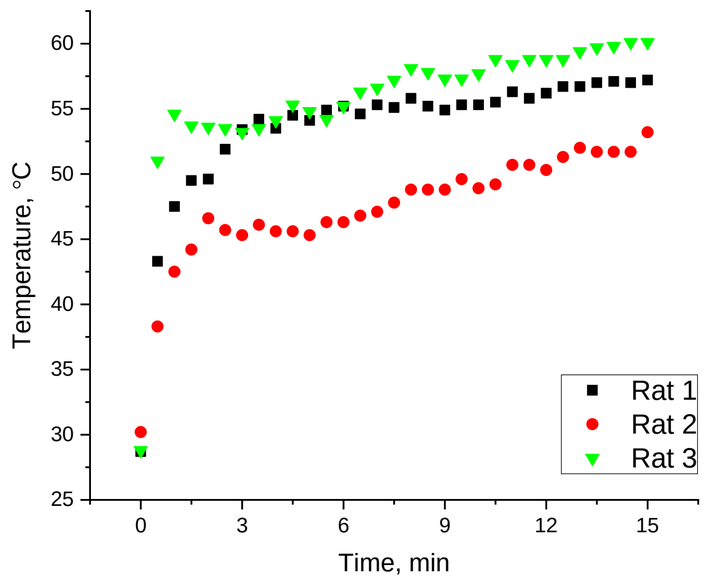
Design of the experiment



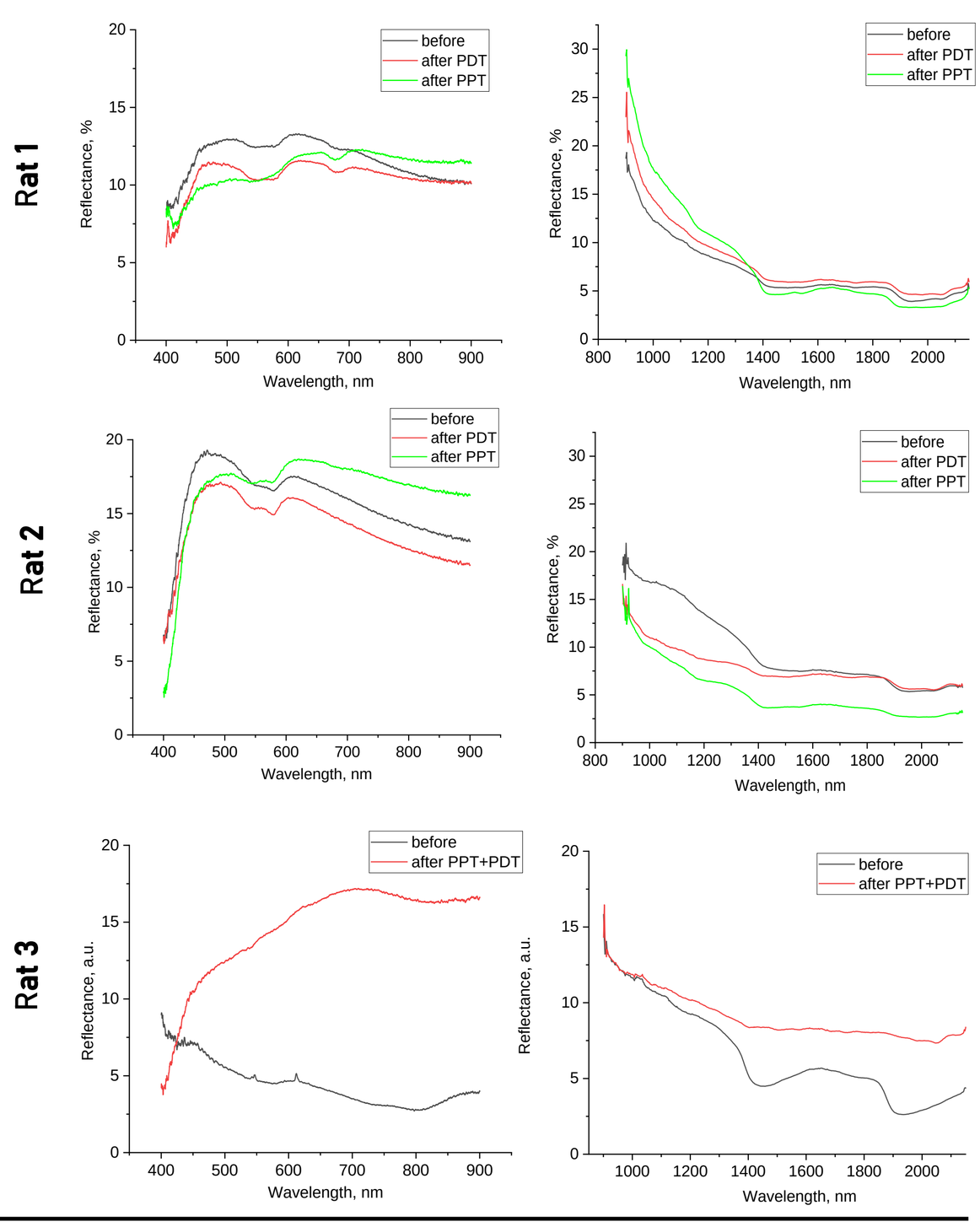
Results

Photos of rat 2 tumor

Kinetics of skin surface heating over tumors



Reflectance spectra of rat tumors at different stages of the experiment



Conclusion

The combined photodynamic/photothermal therapy of model rat tumors *in vivo* with the introduction of a photosensitizer (Photosens or indocyanine green) for PDT and gold nanorods for PPT was studied. Analysis of the data obtained showed that with approximately the same heating of the surface of the skin above the tumor, in the case of using indocyanine green in the NIR range, a significant change in the reflection spectra of the skin above the tumor occurs, which may be due to dehydration. A strong change in the spectrum in the visible range may be due to the optical properties of the indocyanine green itself.

The work was supported by RSF grant 23-14-00287