

Саратовский государственный
медицинский университет
имени В. И. Разумовского



Photodynamic therapy of tumors in mice with colorectal cancer

Bucharskaya A.B.1,2*, Genin V.D.2, Navolokin N.A.1,2, Chekhonatskaya M.L.1,
Shushunova N.A.1,2, Guslyakova O.I.2, Lomova M.V.2, Genina E.A.2, Tuchin V.V.2.

1Saratov State Medical University, Saratov, Russia;

2Saratov State University, Saratov, Russia



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Background

- The relevance of research is due to the sharp increase in morbidity and mortality from cancer: according to the International Agency for Research on Cancer (IARC), in 2020, 19.3 million new cases of cancer were diagnosed worldwide, and about 10 million people died (<https://gco.iarc.fr/today/fact-sheets-cancers>);
- search for new treatment methods: traditional chemotherapy and radiotherapy are not effective enough due to the development of drug resistance in tumor cells (Alfarouk KO et al, 2015).

Globally

1 OUT OF **6** **DEATHS**
 is due to **cancer**

Materials and methods

Test-object:
Balb/c mice 30±3 g weight

Tumor cell culture: 20 µl of CT-26 colorectal cancer cell suspension was inoculated to mice intramuscularly ($2,5 \cdot 10^6$ cells)

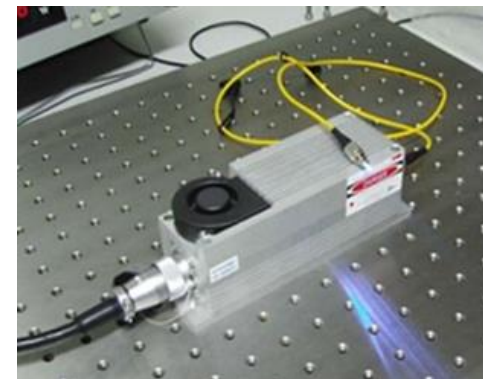
Indocyanine green (ICG) (Pulsion Medical Inc) was used as a photosensitizer, which was diluted in polyethylene glycol at a ratio of 1:100 and administered to mice intratumorally or intravenously at a dose of 2 mg/kg

Visualization of indocyanine green distribution using Fluor i In Vivo Fluorescence Imaging System before PDT

1 hour after ICG injection
Diode infrared laser 808 nm LS-2-N-808-10000 with a power density of 2.3 W/cm² for PDT

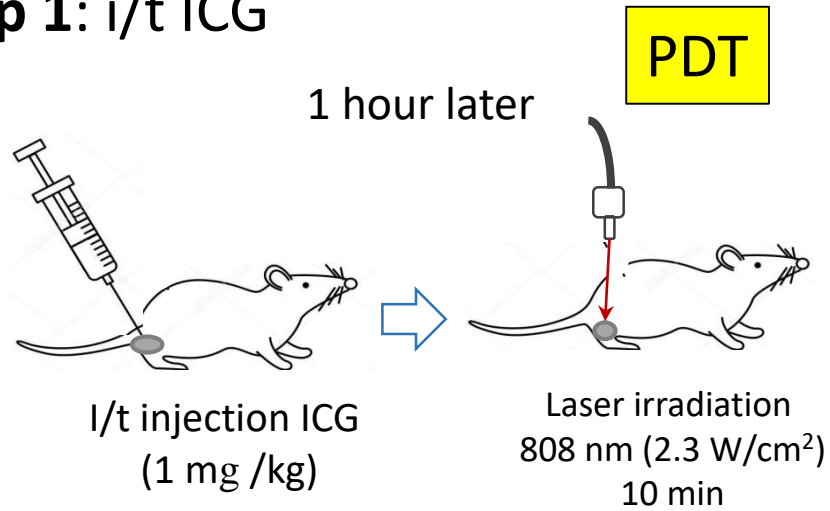
GE Healthcare Voluson S8 ultrasound diagnostic system – for assesment of tumor vascularization before PDT

The temperature of local tumor heating was measured by IRYSYS 4010 thermal imager

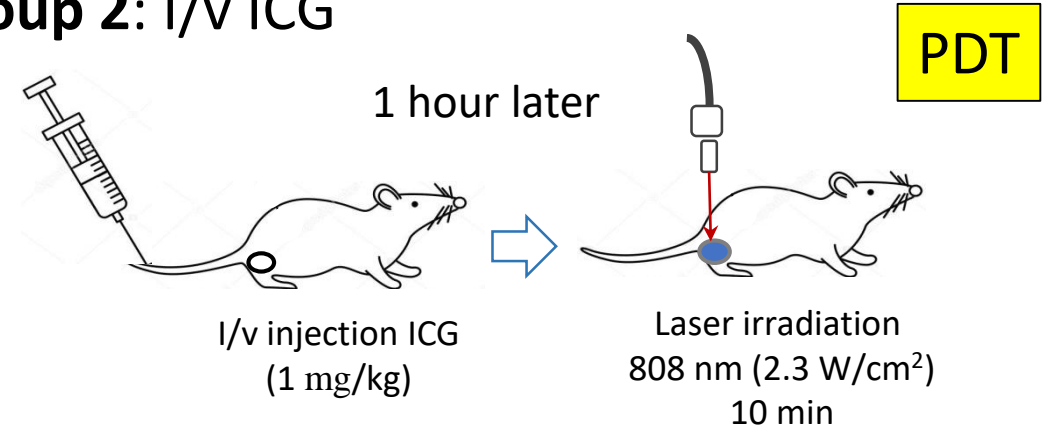


Study design

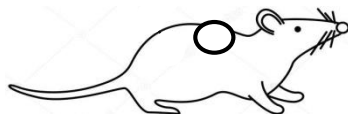
Group 1: i/t ICG



Group 2: I/v ICG

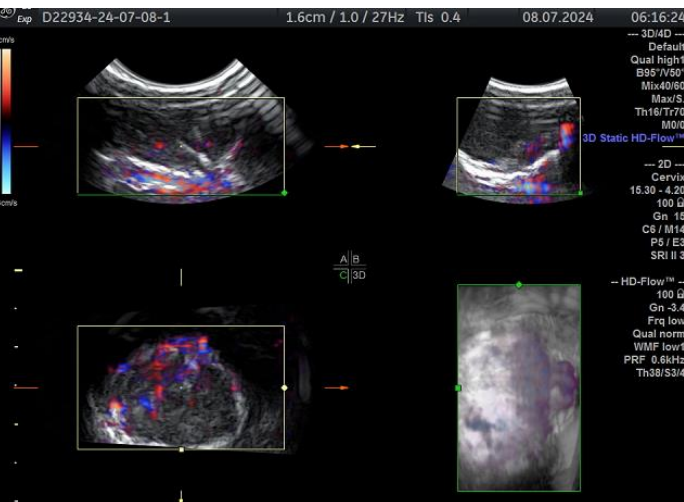
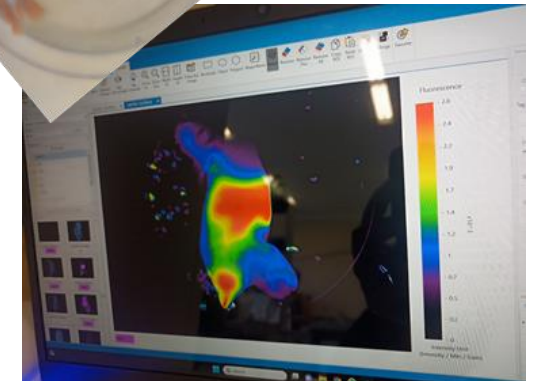
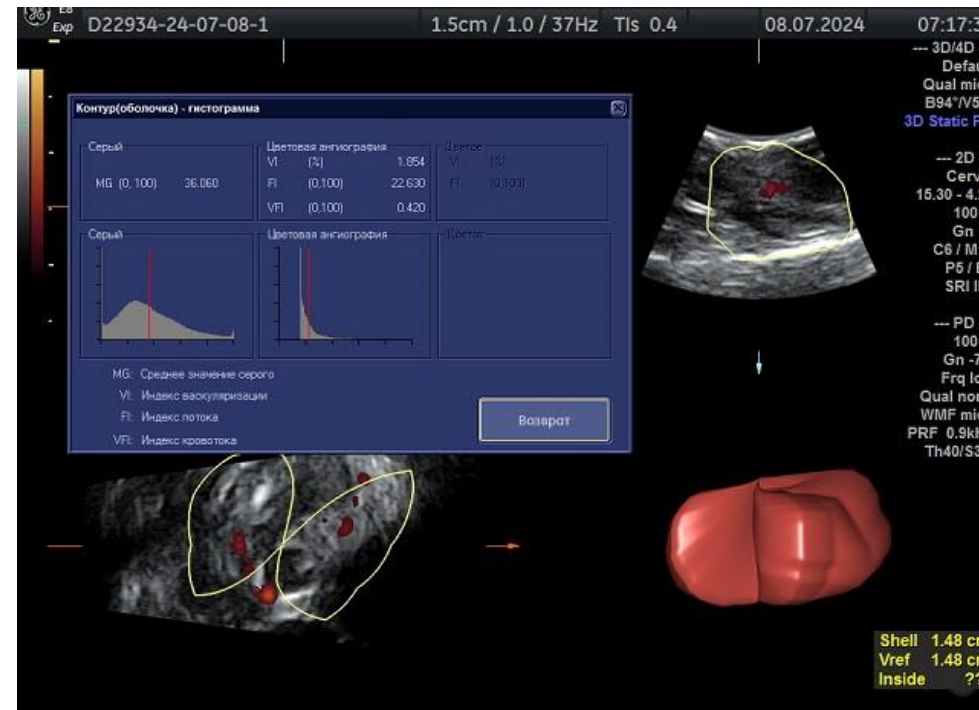


Group 3: without treatment



Animal withdrawal and sampling of tumor tissues for morphological examination were performed 72 h after therapy

Doppler and Fluor in Vivo investigation of tumors



Prior to intravenous injection of indocyanine green, mice underwent Doppler examination of tumors to determine the vascularization index before PDT: in the presence of a formed vascular network in the tumor, mice were injected with ICG

The Fluor i In Vivo imaging system was used to analyze the biodistribution of ICG after IV injection: PDT was performed when ICG accumulated in the tumor

PDT caused significant damage to tumor tissue



Group 1: i/t ICG

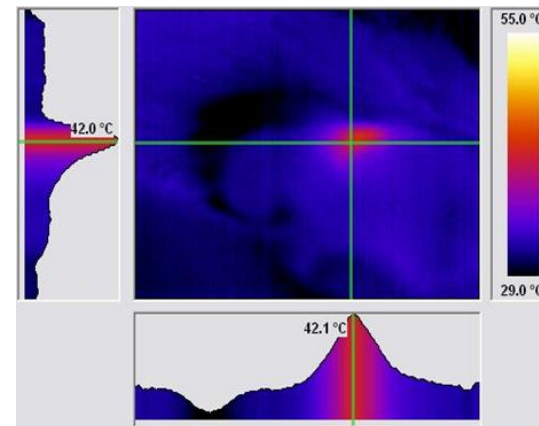


Group 2: I/v ICG



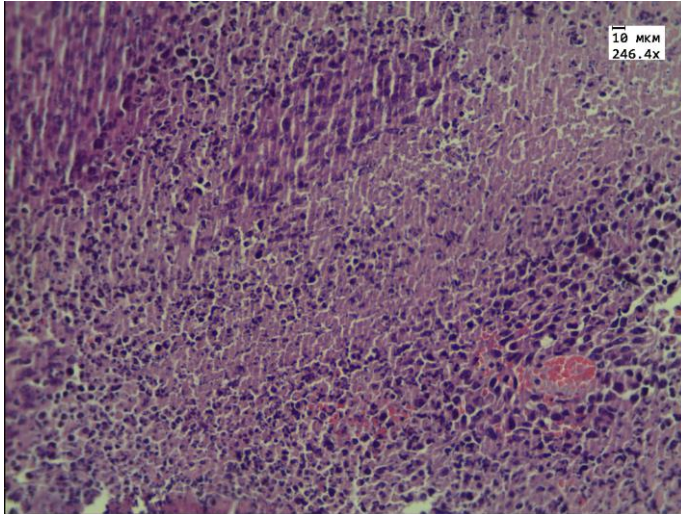
Group 3: without treatment

During PDT therapy, a slight rise in local tumor heating temperature (up to $40 \pm 5^\circ\text{C}$) due to IR laser exposure, 72 h after PDT the pronounced damage of tumor tissue were observed



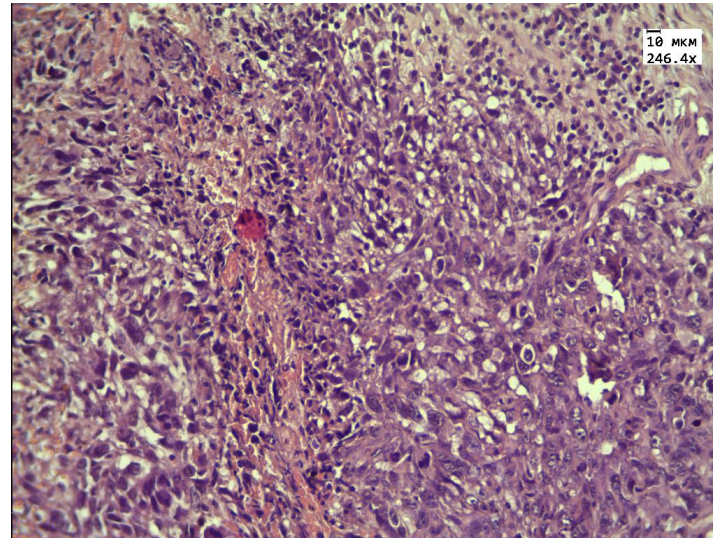
Tumor pathomorphosis 72 h after PDT

I/t ICG+PDT



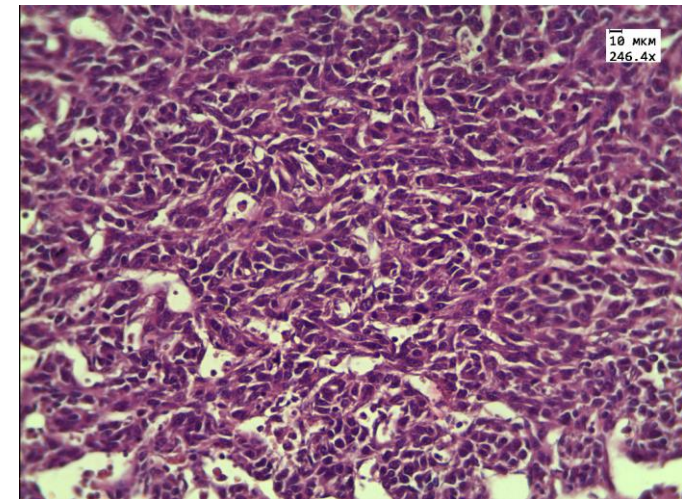
Tumor with pronounced necrotic changes

I/v ICG+PDT



Tumor with necrotic changes and inflammatory infiltration

The most pronounced necrotic changes in the tumor were observed after PDT in the group with intratumoral injection of ICG, moderate necrotic changes and inflammatory infiltration in the tumor were observed in the group of animals with intravenous injection of ICG.



Tumor without treatment

Conclusion

- **The proposed protocol of PDT therapy causes pronounced damage to tumor tissue, but further studies of safety and long-term effects of PDT are needed**
- **A promising direction for further research is the development of multifunctional nanocomposites containing gold nanoparticles and photosensitizer for use in combined therapeutic technologies**