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Application of laser-synthesized boron nanoparticles for boron neutron capture therapy

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Boron neutron capture therapy (BNCT) is a binary form of radiation therapy based on the selective destruction of cells of malignant tumors. The basic principle of BNCT is in the high ability of the non-radioactive ^{10}B nucleus to absorb a thermal neutron, resulting in the reaction $^{10}B(n,\alpha)^7Li$, the products of which have a high deceleration rate and a short path length, thus the released energy of 2.79 MeV is limited by the size of one cell [1].

An important aspect of the successful implementation of BNCT in clinical practice is the development of targeted boron delivery drugs [2]. We investigated elemental boron nanoparticles (BNPs) fabricated using the methods of pulsed laser ablation in liquids as potential boron-containing agents for BNCT. Depending on the conditions (nanosecond and femtosecond pulses) of laser-ablative synthesis, the NPs were amorphous (a-BNPs) or partially crystallized (pc-BNPs) with a mean size of 20 nm or 50 nm, respectively, both coated with polyethylene glycol to improve their colloidal stability [3,4].

In *in vitro* experiments human tumor cell lines U87 (glioblastoma) and SW-620 (colorectal adenocarcinoma) were used. MTT-test and clonogenic assay did not show any cytotoxicity effects of BNPs up to ^{10}B concentrations of 100 μg/mL. The cells were preliminarily incubated with BNPs at a ^{10}B concentration of 40 μg/mL and were then irradiated with a thermal neutron beam at the accelerator-based neutron source at the Budker Institute of Nuclear Physics [5] for 30 min, providing the equivalent calculated dose of 8 Gy-Eq. Colony forming capacity of SW-620 cells dropped down to 12.6% for BNCT group previously incubated with a-BNPs and 1.6% for pc-BNPs BNCT group. Colony-forming capacity for U87 cells dropped down to 17%. The data is confirmed by MTT results.

For future BNCT *in vivo*, the boron biodistribution study was performed. Intratumoral administration of BNPs in immunodeficient SCID mice with subcutaneous U87 tumors demonstrated highest accumulation of boron in the tumor of 56 μg/g and 82 μg/g at 30 and 90 min after BNPs administration, respectively. The concentration of boron in the blood and in the surrounding normal tissue (skin and muscle) was statistically significantly lower, close to background values. Therefore, laser ablation of elemental boron powders and targets leads to the formation of spherical nanoparticles with a size of 20-50 nm. This technique provides the achieved boron content in the tumor, and the tumor/blood, tumor/ normal tissue boron concentration ratios is sufficient for successful BNCT in the case of boron enrichment with the therapeutically suitable isotope boron-10.

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