Ionizing radiation improves glioma-specific targeting of superparamagnetic iron oxide nanoparticles conjugated with cmHsp70.1 monoclonal antibodies (SPION-cmHsp70.1).

Abstract:

The stress-inducible 72 kDa heat shock protein Hsp70 is known to be expressed on the membrane of highly aggressive tumor cells including high-grade gliomas, but not on the corresponding normal cells. Membrane Hsp70 (mHsp70) is rapidly internalized into tumor cells and thus targeting of mHsp70 might provide a promising strategy for theranostics. Superparamagnetic iron oxide nanoparticles (SPIONs) are contrast negative agents that are used for the detection of tumors with MRI. Herein, we conjugated the Hsp70-specific antibody (cmHsp70.1) which is known to recognize mHsp70 to superparamagnetic iron nanoparticles to assess tumor-specific targeting before and after ionizing irradiation. In vitro experiments demonstrated the selectivity of SPION-cmHsp70.1 conjugates to free and mHsp70 in different tumor cell types (C6 glioblastoma, K562 leukemia, HeLa cervix carcinoma) in a dose-dependent manner. High-resolution MRI (11 T) on T2-weighted images showed the retention of the conjugates in the C6 glioma model. Accumulation of SPION-cmHsp70.1 nanoparticles in the glioma resulted in a nearly 2-fold
drop of values in comparison to non-conjugated SPIONs. Biodistribution analysis using NLR-M2 measurements showed a 7-fold increase in the tumor-to-background (normal brain) uptake ratio of SPION-cmHsp70.1 conjugates in glioma-bearing rats in comparison to SPIONs. This accumulation within Hsp70-positive glioma was further enhanced after a single dose (10 Gy) of ionizing radiation. Elevated accumulation of the magnetic conjugates in the tumor due to radiosensitization proves the combination of radiotherapy and application of Hsp70-targeted agents in brain tumors.