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ACCEPTED MANUSCRIPT

An innovative therapeutic approach for malignant mesothelioma treatment based on the use of Gd/Boron multimodal probes for MRI guided BNCT

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ABSTRACT The aim of this study is to develop an innovative imaging guided approach based on Boron Neutron Capture Therapy, for the treatment of mesothelioma, assisted by the quantification of the *in vivo* boron distribution by MRI. The herein reported results demonstrate that overexpressed Low Density Lipoproteins receptors can be successfully exploited to deliver to mesothelioma cells a therapeutic dose of boron (26μg/g), significantly higher than in the surrounding tissue (3.5μg/g). Boron and Gd cells uptake was assessed by ICP-MS and MRI on two mesothelioma (ZL34, AE17) and two healthy (MRC-5 and NMuMg) cell lines. An *in vivo* model was prepared by subcutaneous injection of ZL34 cells in Nu/Nu mice. After irradiation with thermal neutrons, tumor growth was evaluated for 40 days by MRI. Tumor masses of boron

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