In vivo MRI follow-up of murine tumors treated by electrochemotherapy with bleomycin.

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INTRODUCTION: Electrochemotherapy (ECT) using electroporation (EP) to deliver an anticancer drug (usually bleomycin) to tumor cells, it makes possible to treat animal and human superficial tumors without the adverse effects of the anti-cancer drugs. Several MR indexes are known to reflect the efficiency of chemotherapies at a short time interval after drug delivery to tumor. This study aims to detect tumor modifications linked to ECT, done with normal and high dose of bleomycin known to produce different cellular effects (mitotic cells death or rapid pseudoapoptosis respectively).

MATERIALS & METHODS: Sixteen C57 Bl/6 mice, that had undergone a graft of LPB fibrosarcoma cells and developed a tumor of 4 to 7 mm diameter, were divided in 4 groups. The electrical pulses were delivered with flat electrodes laid at each side of the tumor, as described in [1]. In the EP group (E) 5 mice underwent EP twenty minutes after an IP Dotarem injection to test the extent of efficient electric field in the tumor [2] and two mice received only electrical pulses. In the treated group (B) 6 mice underwent EP 4 minutes after bleomycin injection at a dose of 4 µg/kg in 100 µL injected in the retroorbital sinus. In the group treated with a high dose of bleomycin and EP (HB) 3 mice were treated identically at a dose 800 µg/kg. Mice were anesthetized with 1.5 % isoflurane in 1 L/min oxygen during electric pulse delivery and imaging. For groups E and B, MRI examinations were performed before and 24 and 48 hrs after the treatment, and for group HB, before and at 3, 6, 10 and 24 hrs after the treatment. ADC measurements were done also at 3 hrs for 2 mice of group E. MRI studies were performed on an in-house developed 4.7 T scanner. The mice were laid prone inside a 42 mm diameter bird cage. Tumor was surrounded with alginate in order to increase the magnetic field homogeneity.

RESULTS: In the 5 animals that received EP and Dotarem, the tumor signal enhancement was homogeneous with mean value 38 ± 10 % at 48 hrs, confirming the homogeneity of the electric field applied to the tumor under our treatment conditions (Fig. 1a. and b.). Mean values and standard deviations of all parameters related to tumor evolution are given in Table 1. All the animals of group E could be pooled altogether since no differences in parameters were found between the mice that received Dotarem or not, resulting in a larger control group.

CONCLUSION: Though a more detailed study during the time after ECT is needed, our results suggest that T2 values are very sensitive to osmotic edema, and that ADC values rather reflect apoptosis and tumor death, and the accompanying loss of structural integrity that would lead to longer T2 values.