Revealing the mechanism of action of modulated electro-hyperthermia experimentally in animal model

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Objective. Modulated radiofrequency (RF) electro-hyperthermia (mEHT) is an emerging technique for oncology. Modeling it in vivo conditions is rather complex task. Experimentally proven extra effect (three times higher cell killing rate) of mEHT in addition to the temperature induced hyperthermia actions was presented earlier (STM2009). Our present investigation is focused on revealing the mechanism of action of mEHT experimentally in vivo.

Method. The in vivo studies were performed using a BalbC/nu/nu mice xenografted with HT29 human colorectal carcinoma cell line. To reveal the process how the cell destruction is developing a time-course study was designed. Animals had two tumors in the left and right femoral regions, and their right tumor had been treated by mEHT with single shot (30min) and its effects were studied immediate and 0.5, 1, 2, 4, 8, 12, 24, 48, 72 hours after the treatment. Comparison to the untreated control was made histomorphologically and immunohistochemical (IHCH)detection of β-catenin and p53 protein was performed.

Results. Morfologically the first significant sign of cell destruction was seen 8h after the treatment and it was expanded to 24h. Completely destructed tumor tissue was observed 48h after the treatment with picnotic cell nuclei, tissue debris and significantly large number of apoptotic body in the treated tumor compared to the control one. The large amount of leukocyte invasion to the tumor core was observed 72h after the treatment. According to the IHCH analysis a special relocalization of β-catenin from the cell-membrane to the nuclei was detected at mEHT after 24 and 72 hours. Immediate activation of p53 after mEHT and its active state during the study period (72 h) was measured also.

Conclusion: Tumor-distortion effect of mEHT is not immediate, the treatment activates mechanisms (observed by β-catenin and p53 protein) to disintegrate the tumor and malignant cells. Further experimental support and repeating control by independent laboratories are desired.