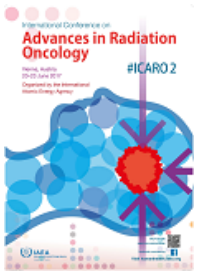

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Abscopal effects with non-ionizing radiation

Wednesday, 21 June 2017 15:50 (5 minutes)

Introduction
Radiation therapy in oncology is in most of the cases local. The malignancy (counting the circulation cancer cells and the micro- and macro-metastases) is systemic, causing controversy with the local actions in curative basis. The abscopal effect of low intensity ionizing radiation is well-known. Our objective is to show the abscopal effect with local non-ionizing radiation, action on blocking the invasion of cells to the blood-stream and together with immune-stimuli extends the local method to systemic therapy.
Method
Non-ionizing modulated RF radiation (mEHT, trade name: oncothermia) is used. This technology is impedance controlled capacitive coupling with amplitude modulation by the time-fractal pattern. mEHT selectively targets the rafts of transmembrane proteins on the cell membrane of malignant cells. The nano-selection is based on the certain deviations of metabolic-processes which enriches the ionic species in the extracellular electrolyte increasing the local conductivity and guiding the RF-flow. The missing or rearranged cellular organizing pattern of malignant cells also makes the selection of the irregular cells possible. Finally the cell-killing energy absorption is connected to the beta and delta absorption in the cell-membranes. There were various in-vitro and in-vivo immune-histochemical studies proving this selection and its effects.
Results
Significant tumor-cell death shown by TUNEL caused by mEHT. Mitochondrial Bax and release of Cytochrome C and nuclear translocation of apoptosis inducing factor AIF are measured [3]. Immunohistochemistry and apoptosis protein array proved elevated hsp70 and hsp90 expression and released them from the cell. Earlier cytoplasmic to cell membrane exposure of calreticulin and later release of HMGB1 protein from cell nuclei were observed. The set of molecules in the measured apoptotic processes form damage associated molecular pattern (DAMP) concluding to immunogenic cell-death (ICD) [4]. The abscopal effect is proven by the in-vivo experiment using an intratumoral dendritic cell (DC) injection together with the mEHT for C3H/He mice inoculated with tumor in femoral region. The non-treated tumor in the abdomen was measured. The whole body antitumor effects are proven, [5]. Furthermore, mEHT plus DC administration significantly inhibits the CT26 tumor growth in BALB/c mice, while even the re-challenging of the tumor inoculation became impossible, [6]. In this case the abscopal effect works like vaccination. The combined mEHT-DC treatment increases the leucocytes and macrophages with increased eosinophils, organizing specific T-cell response.
Together with the experimental research level multiple clinical results show the efficacy of the method and feasibility of the new abscopal approach. The method is combined with most of the major oncotherapies. The main observable indicators of the results are the elongation of the survival time and at the same time improvement the quality of life. There are case-reports, Phase I and Phase II trials that approve the promising technique, including lesions: Bone (metastatic); Breast; Colorectal; Gliomas; Head & neck; Brain (metastatic), Kidney; Liver (metastatic and primary); Lung (NSCLC, and SCLC); Pancreas; Cervix; Ovary; Prostate; Soft-tissue sarcoma; Stomach; Urinary-bladder; Uterus.
Conclusion
Method of mEHT induces tumor cell apoptosis and enhances the release of Hsp70, unlike conventional hyperthermia. The consequence of the selective heating of the membrane rafts induces DAMP and ICD. mEHT can create a favorable tumor microenvironment for an immunological chain reaction that improves the success rate of intratumoral DC immunotherapy inducing abscopal effect by tumor specific immune reaction. The main medical advantages of the method are its personalized targeting together with the effective selec-

tion and distortion of the malignant cells. The new direction of application focuses on the blocking of their dissemination, as well as promoting the bystander (abscopal) effect acting on far distant metastases by local treatment. The method is successfully developed in the direction of the immune-support, pointing an exciting area: cancer-vaccination. These effects are well indicated in clinical practice but due to the proper funding the Phase III clinical trial is missing yet. For further development of the method the Phase III clinical trial is warranted.

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