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Comparison of induced biological effects of modulated electrohyperthermia to conventional capacitive hyperthermia

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Introduction: Capacitive coupling is a popular technical solution of hyperthermia realization in oncology. Modulated electrohyperthermia (mEHT) is an emerging new loco-regional radiofrequency (RF) method. Several technical innovations implemented in mEHT producing certain differences in its biological effects compared to the conventional hyperthermia (HT) methods. Our objective is to point the major differences of biological effects.

Methods: The mEHT method has particular basic concept among conventional hyperthermia solutions. The RF energy by mEHT selectively targets the clusters of transmembrane proteins (rafts) of the malignant cells. Heating the rafts on high temperature does not heat up the entire tumour mass to the thermal cytotoxic level, but excites special signal transduction pathways producing damage associated molecular pattern induced from the extracellular side. We measured the differences with various immunohistochemical methods, as well as by flow cytometry and Western-blot.

Results: Despite the same temperature we observed earlier definite differences in the biological response in vivo [1], and also contrary to the similar capacitive coupling the efficacy of the absorbed power observed very different in vivo. Despite the same electromagnetic phenomena of the RF current the differences between mEHT and HT are characteristic, and well-shown in vitro [2]. The mEHT was able to induce significant apoptotic cell death process in vitro and immunogenic cancer cell death in vivo in mild temperature range (≤42oC) where conventional HT did not induce significant cell destruction. Effect of HT was identical with the water-bath heating at 42oC. Compared to HT, mEHT in vitro produced significant enhancement of ROS, Caspases 3, 8 and 9, calreticulin, and extracellular HSP70 expression, as well as the E-cadherin and beta-catenin expression showed re-established adherent connections by mEHT, which was not observed by HT treatment on the same temperature. Furthermore, significant differences were observed in comparison of GeneChip heat-maps between the HT and mEHT on the same temperature both in vitro [3] and in vivo [4].

Conclusions: mEHT applies non-equilibrium, non-homogeneous membrane-heating feature to improve the effects of conventional heating by HT. It is a new kind of hyperthermia therapy extending with feasible advantages the conventional capacitive coupled HT method.

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3. Andocs et.al. (2016) Cell Death Discovery (Nature Publishing Group), 2, 16039
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