P-02 – Dr. Gabor Andocs, et al - Apoptosis induction with modulated radiofrequency (RF) hyperthermia (oncothermia) in immuno-deficient mice xenograft tumors (Review)

Apoptosis induction effect of modulated radiofrequency (RF) hyperthermia (oncothermia) in immuno-deficient mice xenograft tumors

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Introduction: Objective of the work
Oncothermia method is more than twenty years serving the medical practices. It has successful applications either as a complementary therapy with the “gold-standard” modalities either as monotherapy, when no other possibility could be applied. The specialized animal experiments were started five years ago intending to clarify the basic mechanisms by in vivo scientific approaches. The complexity and interdisciplinarity of the in vivo experimental series requested a close cooperation scheme of various respected and honored research institutes and university laboratories. Our objective is to summarize the results of this intensive work and to show the conclusions at the recent phase of the investigations.

Materials and methods
Immuno-deficient nude mice (BalB/c-Web) were used for xenograft and allograft models with HepG2, PC3, HT29, A431; GL261 cell lines. The definite amount of cell line suspension was injected to the flank region of the 8-12 weeks old female mice and 10-20 days later the oncothermia treatment was performed, when the tumors were developed symetrically in both sides on diameter 1.5 cm. The single shot treatment was delivered systematically for all the mice on their right side, the left lesion was kept as untreated individual control to reduce the inaccuracies due to the individual variability of the animals. Treatment were performed by highly specialized laboratory equipment (Lab-EHT, Oncoszter, optronics on mic dimensions, taking into account the physiology of the small animals, creating all the important technical and biological parameters [1]. The influence selection and automatic focusing which is well known in human clinical practices were applied in these experiments too [2]. The temperature of the tumors was controlled by high accuracy infrared thermal camera Extron x-3000, LumaSense.

Results
In its time development we observed the following: 1. A. Oncothermia treatment made significant tumor distortion relative to the control in all the investigated tumors, irrespective its origin.
2. Both the conventional hyperthermia and oncothermia have certain destruction of the malignant cells in the tumors studied cases, but the efficacy of oncothermia is almost three times higher.
3. The documented cell destruction is dominantly apoptotic. This is shown by the upregulation of the p53 protein, involved in the apoptotic control, and also the certain fragmentation of DNA measured by TUNEL reaction.

Conclusion
The applied mice models were suitable to study the effect of oncothermia on molecular level. The dominant role of apoptosis in the oncothermia cell destruction is highly probable. Further investigations are in progress to study the mechanism of apoptotic induction and its connection with the cell cycles as well as the role of the adhesions and other cellular connections.