Suppression of Human Cancer Cell Growth In Vitro by Oncothermia

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Purpose
In the present study, we investigated the potential of oncothermia (electro-hyperthermia) for an alternative therapeutic option of pan-human cancer.

Materials and methods
To address this issue, we applied oncothermic heating (42°C 1 hour, three times with a two- or three-day interval) to various human cancer cell lines such as A549 (lung cancer), HepG2 (liver cancer), MDA-MB231 (breast cancer) and A172 & U-87MG (brain cancer), and then examined for cancer cell phenotypic changes. Cell growth was analyzed by an MTT assay or microscopic observation in 3 days of the third oncothermic heating, and apoptosis was estimated in 24 h of the third treatment by ELISA for the detection of denatured ssDNA only formed during apoptotic progression. In addition, the changes in apoptotic cell population was assessed by flow cytometry. The expression of heat shock protein 70 (HSP70), which is known for a typical marker of heat resistance, was determined by quantitative real-time PCR.

Results
As results, oncothermia effectively inhibited the growth of A549, HepG2, MDA-MB231, A172 and U-87MG cells by about 45%, 70%, 47%, 44% and 75%, respectively, accompanying with remarkable morphological changes in cellular level. We also proved that inhibition of U-87MG cell growth was due to increased rate of apoptotic cell death which was about 2-fold higher than in unheated control cells. FACS analysis showed that oncothermic heating (three times with a three-day interval) to U-87MG and A172 glioma cells retards cell cycle progression and increases the apoptotic cell population by about 17% and 7%, respectively. Meanwhile, we observed that the treatment conditions of oncothermia still upregulate the expression of HSP70 by about 84-fold higher in both U-87MG and A172 cells, in 24 h of the third treatment. It may imply that multiple heating could overcome heat-resistance to drive therapeutic outcome in terms of cancer phenotypic changes.

Conclusion
Taken together, these results indicate that oncothermia maybe an attractive alternative for pan-cancer treatment. Further studies should be warranted to investigate the molecular mechanisms underlying the cancer phenotypic changes induced by oncothermia.

Keywords
Oncothermia, lung cancer, liver cancer, breast cancer, brain cancer, growth inhibition, apoptosis, molecular mechanism