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Kumaran, B. and T. Watson (2018). "Skin thermophysiological effects of 448 kHz capacitive resistive monopolar radiofrequency in healthy adults: A randomised crossover study and comparison with pulsed shortwave therapy." Electromagn Biol Med: 1-12.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Thermal+build-up%2C+decay+and+retention+responses+to+local+therapeutic+application+of+448+kHz+capacitive+resistive+monopolar+radiofrequency%3A+A+prospective+randomised+crossover+study+in+healthy+adults

Radiofrequency-based electrophysical agents (EPA) have been used in therapy practice over several decades (e.g., shortwave therapies). Currently, there is insufficient evidence supporting such devices operating below shortwave frequencies. This laboratory-based study investigated the skin physiological effects of 448 kHz capacitive resistive monopolar radiofrequency (CRMRF) and compared them to pulsed shortwave therapy (PSWT). In a randomised crossover study, seventeen healthy volunteers received four treatment conditions - High, Low and Placebo dose conditions receiving 15-min CRMRF treatment and a Control condition receiving no intervention. Fifteen participants also received high dose PSWT for comparison. Treatment was applied to the right lower medial thigh. Pre, post and 20-min follow-up measurements of skin temperature (SKT), skin blood flow (SBF) and nerve conduction velocity (NCV) were obtained using Biopac MP150 system. Group data were compared using the ANOVA model. Statistical significance was set at p </= 0.05 (0.8P, 95%CI). Significant increase and sustenance of SKT with both high and low dose CRMRF was demonstrated over the other groups ($p < 0.001$). PSWT increased SKT significantly ($p < 0.001$) but failed to sustain it over the follow-up. However, among the five conditions, only high dose CRMRF significantly increased and sustained SBF ($p < 0.001$). Overall, the CRMRF physiological responses were significantly more pronounced than that of PSWT. No significant changes in NCV were noted for any condition. Physiological changes associated with CRMRF were more pronounced when compared to PSWT, placebo or control. Any potential stronger therapeutic benefits of CRMRF need to be confirmed by comparative clinical studies.

Janczewska, K., et al. (2017). "[New physical methods in osteoarthritis treatment]." Wiad Lek 70(3 pt 2): 644-648. (Article in Polish)

https://www.ncbi.nlm.nih.gov/pubmed/?term=Janczewska+New+physical+methods+in+osteoarthritis+treatment

Osteoarthritis is a chronic disease in which the pathological processes start from the catabolism of cartilage extracellular matrix and next extend on the whole joint. Therefore, it is important to diagnose the disease and determining treatment, selecting individually for each patient. The main health problems presents by every patients is pain, which decreases the everyday functioning and quality of life. The paper presents the definition of the disease and new therapeutic methods which improve the quality of life, as well as reduce intensity of pain.

Spottorno, J., et al. (2017). "Influence of electrodes on the 448 kHz electric currents created by radiofrequency: A finite element study." Electromagn Biol Med 36(3): 306-314.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Influence+of+electrodes+on+the+448+kHz+electric+currents+created+by+radiofrequency%3A+A+finite+element+study

Radiofrequency is a technology used in physical rehabilitation by physicians and physiotherapists for more than fifteen years, although there exist doubts on how it works. Indiba is a particular method that applies a voltage difference of 448 KHz between two electrodes, creating an electric current between them. These electrodes are an active one that is placed on different areas of the body and a passive one that is left on the same position during the treatment. There are two different types of active electrodes: the capacitive one and the resistive one. In this paper, it has been studied how the different electrodes affect the current density inside the body and thus how they affect the efficacy of the treatment. It shows how finite element calculations should help physicians in order to better understand its behavior and improve the treatments.

Tashiro, Y., et al. (2017). "Effect of Capacitive and Resistive electric transfer on haemoglobin saturation and tissue temperature." Int J Hyperthermia: 1-7.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+Capacitive+and+Resistive+electric+transfer+on+haemoglobin+saturation+and+tissue+temperature

PURPOSE: This study aims to evaluate the effects of Capacitive and Resistive electric transfer (CRet) and hotpack (HP) on haemoglobin saturation and tissue temperature. MATERIALS AND METHODS: The participants were 13 healthy males (mean age 24.5 +/- 3.0). They underwent three interventions on different days: (1) CRet (CRet group), (2) HP (HP group) and (3) CRet without power (sham group). The intervention and measurement were applied at the lower paraspinal muscle. Indiba(R) active ProRecovery HCR902 was used in the CRet group, and the moist heat method was used in the HP group. Oxygenated, deoxygenated and total haemoglobin (oxy-Hb, deoxy-Hb, total-Hb) counts were measured before and after the 15-min interventions, together with the temperature at the skin surface, and at depths of 10 mm and 20 mm (ST, 10mmDT and 20mmDT, respectively). The haemoglobin saturation and tissue temperature were measured until 30 min after the intervention and were collected at 5-min intervals. Statistical analysis was performed for each index by using the Mann-Whitney U test for comparisons between all groups at each time point. RESULTS: Total-Hb and oxy-Hb were significantly higher in the CRet group than in the HP group continuously for 30 min after the intervention. The 10mmDT and 20mmDT were significantly higher in the CRet group than in the HP group from 10- to 30 min after intervention. CONCLUSIONS: The effect on haemoglobin saturation was higher in the CRet group than in the HP group. In addition, the CRet intervention warmed deep tissue more effectively than HP intervention.

Hernández-Bule, M. L., et al. (2016). "Antiadipogenic effects of subthermal electric stimulation at 448 kHz on differentiating human mesenchymal stem cells." Mol Med Rep 13(5): 3895-3903.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Antiadipogenic+effects+of+subthermal+electric+stimulation+at+448+kHz+on+differentiating+human+mesenchymal+stem+cells

The 448 kHz capacitiveresistive electric transfer (CRET) is an electrothermal therapy currently applied in anticellulite and antiobesity treatments. The aim of the present study was to determine whether exposure to the CRET electric signal at subthermal doses affected early adipogenic processes in adiposederived stem cells (ADSC) from human donors. ADSC were incubated for 2 or 9 days in the presence of adipogenic medium, and exposed or shamexposed to 5 min pulses of 448 kHz electric signal at 50 microA/mm2 during the last 48 h of the incubation. Colorimetric, immunofluorescence, western blotting and reverse transcriptionquantitative polymerase chain reaction assays were performed to assess adipogenic differentiation of the ADSC. Electric stimulation significantly decreased cytoplasmic lipid content, after both 2 and 9 days of differentiation. The antiadipogenic response in the 9 day samples was accompanied by activation of mitogenactivated protein kinase kinase 1/2, decreased expression and partial inactivation of peroxisome proliferatoractivated receptor (PPAR) gamma, which was translocated from the nucleus to the cytoplasm, together with a significant decrease in the expression levels of the PPARG1 gene, perilipin, angiopoietinlike protein 4 and fatty acid synthase. These results demonstrated that subthermal stimulation with CRET interferes with the early adipogenic differentiation in ADSC, indicating that the electric stimulus itself can modulate processes controlling the synthesis and mobilization of fat, even in the absence of the concomitant thermal and mechanical components of the thermoelectric therapy CRET.

Kumaran, B. and T. Watson (2015). "Thermal build-up, decay and retention responses to local therapeutic application of 448 kHz capacitive resistive monopolar radiofrequency: A prospective randomised crossover study in healthy adults." Int J Hyperthermia 31(8): 883-895.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Thermal+build-up%2C+decay+and+retention+responses+to+local+therapeutic+application+of+448+kHz+capacitive+resistive+monopolar+radiofrequency%3A+A+prospective+randomised+crossover+study+in+healthy+adults

PURPOSE: Radiofrequency-based electrophysical agents are widely used in therapy-related clinical practice for their thermal effects, mainly relieving pain and inflammation and improving tissue extensibility. The most commonly used and researched are shortwave therapies that operate at 27.12 MHz. Although relatively new, electrophysical agents employing much lower frequencies have also emerged. Capacitive resistive monopolar radiofrequency employing 448 kHz is one such therapy. This laboratory-based study was aimed to investigate the skin thermal responses to 448 kHz radiofrequency-based therapy in healthy adults. METHODS: In a two-group randomised crossover study, 15 volunteers attended two modes (capacitive and resistive) of 448 kHz radiofrequency-based therapy (using 'Indiba Activ 902') administered locally to the lower thigh region. Starting at minimum, the intensity was increased incrementally until thermal discomfort was felt. Participants reported three time points: thermal onset, definite thermal sensation, and onset of thermal discomfort. Local skin temperature was measured before, immediately post-treatment and up to 45 min post-treatment. RESULTS: Both capacitive and resistive modes of therapy significantly increased the skin temperature and sustained it over the 45-min follow-up. There was statistically significant difference between the thermal response patterns produced by the two modes. Peak post-treatment temperatures attained were not significantly different between the two; however, the retention rate at follow-up was significantly higher for the resistive mode. CONCLUSIONS:

This study confirms that radiofrequency-based therapy at 448 kHz can significantly increase and sustain skin temperature. The study also provides useful baseline data for further research in the low frequency ranges of radiofrequency-based therapy that remain largely unexplored.

Saitoh, Y., et al. (2015). "Synergic carcinostatic effects of ascorbic acid and hyperthermia on Ehrlich ascites tumor cell." Exp Oncol 37(2): 94-99.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Synergic+carcinostatic+effects+of+ascorbic+acid+and+hyperthermia+on+Ehrlich+ascites+tumor+cell.

AIM: In this study, we evaluated the carcinostatic effects of combined ascorbic acid (AsA) and a capacitive-resistive electric transfer (CRet) hyperthermic apparatus-induced hyperthermic treatment on Ehrlich ascites tumor (EAT) cells. MATERIALS AND METHODS: EAT cells were exposed to various AsA (0-10 mM) concentrations for 1 h; they subsequently underwent CRet treatment for 15 min at 42 degrees C. Cell viability was assessed by the WST-8 assay 24 h after the combined treatment. Reactive oxygen species involvement was evaluated using catalase and tempol; caspase-3/7 activation was determined by their fluorescent substrates; cell proliferation were estimated by time-lapse observation. The effect on the cell cycle was analyzed by flow cytometry. RESULTS: Combined AsA and CRet treatment synergistically suppressed cell viability compared with either treatment alone, and these synergistically carcinostatic effects were evident even at noncytotoxic concentrations of AsA alone (</= 2 mM). The carcinostatic effects of combined AsA and CRet treatment were attenuated in a dose-dependent manner by catalase addition, but not by the superoxide anion radical scavenger tempol. Time-lapse observation revealed that combined AsA and CRet treatment activated caspase-3/7 at 10-24 h after treatment, accompanied by significant cell growth suppression. Cell cycle analysis revealed that the rate of sub-G1-phase (apoptotic) cells was drastically increased at 12 h and 24 h, and that the G2/M-phase cells gradually increased at 6-24 h after treatment. CONCLUSION: These results indicate that combined AsA and CRet treatment synergistically inhibits EAT cell growth through G2/M arrest and apoptosis induction via H2O2 generation at lower AsA concentrations; this carcinostatic effect cannot be exerted by AsA alone.

Gutiérrez-Martínez J, N.-G. M., Carrillo-Mora P. (2014). "[Technological advances in neurorehabilitation]". Rev Invest Clin. 66(sup.1): 8-23. (Article inSpanish)

https://www.ncbi.nlm.nih.gov/pubmed/25264802

Hernández-Bule, M. L., et al. (2014). "Molecular mechanisms underlying antiproliferative and differentiating responses of hepatocarcinoma cells to subthermal electric stimulation." PLoS One 9(1): e84636.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Molecular+mechanisms+underlying+antiproliferative+and+differentiating+responses+of+hepatocarcinoma+cells+to+subthermal+electric+stimulation

Capacitive Resistive Electric Transfer (CRET) therapy applies currents of 0.4-0.6 MHz to treatment of inflammatory and musculoskeletal injuries. Previous studies have shown that intermittent exposure to CRET currents at subthermal doses exert cytotoxic or antiproliferative

effects in human neuroblastoma or hepatocarcinoma cells, respectively. It has been proposed that such effects would be mediated by cell cycle arrest and by changes in the expression of cyclins and cyclin-dependent kinase inhibitors. The present work focuses on the study of the molecular mechanisms involved in CRET-induced cytostasis and investigates the possibility that the cellular response to the treatment extends to other phenomena, including induction of apoptosis and/or of changes in the differentiation stage of hepatocarcinoma cells. The obtained results show that the reported antiproliferative action of intermittent stimulation (5 m On/4 h Off) with 0.57 MHz, sine wave signal at a current density of 50 microA/mm(2), could be mediated by significant increase of the apoptotic rate as well as significant changes in the expression of proteins p53 and Bcl-2. The results also revealed a significantly decreased expression of alpha-fetoprotein in the treated samples, which, together with an increased concentration of albumin released into the medium by the stimulated cells, can be interpreted as evidence of a transient cytodifferentiating response elicited by the current. The fact that this type of electrical stimulation is capable of promoting both, differentiation and cell cycle arrest in human cancer cells, is of potential interest for a possible extension of the applications of CRET therapy towards the field of oncology.

Kato, S., et al. (2013). "Repressive effects of a capacitive-resistive electric transfer (CRet) hyperthermic apparatus combined with provitamin C on intracellular lipid-droplets formation in adipocytes." Int J Hyperthermia 29(1): 30-37.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Repressive+effects+of+a+capacitive-resistive+electric+transfer+(CRet)+hyperthermic+apparatus+combined+with+provitamin+C+on+intracellular+lipid-droplets+formation+in+adipocytes

PURPOSE: The aim of this study was to evaluate inhibitory effects of L-ascorbic acid-2-O-phosphate-Na(2) (APS), a pro-vitamin C, combined with hyperthermia on adipogenic differentiation of mouse stromal cells, OP9. MATERIALS AND METHODS: OP9 preadipocytes were differentiated with serum replacement, administered with APS, and simultaneously treated with hyperthermia using a capacitive-resistive electric transfer (CRet) apparatus, which was conducted repeatedly twice a day. After 2 days, intracellular lipid droplets were stained with Oil Red O, then observed by microscopy and assessed spectrophotometrically. RESULTS: After stimulation by serum replacement for 2 days, lipid droplets were accumulated surrounding nucleus of OP9 cells. When APS of 0.15-0.6 mM was administered without hyperthermia, the amount of lipid droplets was markedly suppressed to 50.5% approximately -11.3% versus the undifferentiated control, and diminished huge aggregates of lipid droplets. In OP9 cells treated by hyperthermia at 42 degrees C for 0.5 min, 1 min or 3 min in the absence of APS, adipogenesis was suppressed abruptly in a time-dependent manner to 95.4%, 18.7% or -5.5%, respectively. Whereas, the percentage of adipogenesis was 96.8% in OP9 cells treated by mild hyperthermia alone at 41 degrees C for 1 min. The simultaneous application of APS and hyperthermia at 41 degrees C for 1 min markedly suppressed the accumulation of lipid droplets to 25.7% approximately -66.2%. By scanning electron microscopy (SEM) observation, the surface of OP9 cells treated with APS and hyperthermia appeared to have the morphological property of undifferentiated OP9 cells. CONCLUSION: Combined treatment of APS and mild hyperthermia suppresses adipogenesis in OP9 cells, particularly in lipid droplets accumulation during spontaneous differentiation of OP9 preadipocytes.

Pavone, C., et al. (2013). "TECAR therapy for Peyronie's disease: a phase-one prospective study. Great evidence in patients with erectile dysfunction." Urologia 80(2): 148-153.

https://www.ncbi.nlm.nih.gov/pubmed/?term=TECAR+therapy+for+Peyronie's+disease%3A+a+phase-one+prospective+study.+Great+evidence+in+patients+with+erectile+dysfunction.

Our phase-one prospective study wants to evaluate the safety and tolerability of TECAR therapy in the treatment of Peyronie's disease. From June 2011 to September 2012 we enrolled 70 patients. Each patient had been previously subjected to andrological examination, to a questionnaire for the evaluation of IPP and ED, and the SF-36 (V1) for the evaluation of the general state of health. The evaluation of pain was made using the VAS scale of pain. Every patient was subjected to TECAR treatment of the fibrotic plaque (both in resistive mode and in capacitive mode) for a total of three sessions carried out on consecutive days. We recorded a good compliance by patients; none of them reported side effects. Pain was decreased by the technique in 80% of the cases.The whole sample completed the study. Surprisingly enough those patients who complained also of erectile dysfunction, reported an improvement in sexual potency.

Hernandez-Bule, M. L., et al. (2012). "Radiofrequency currents exert cytotoxic effects in NB69 human neuroblastoma cells but not in peripheral blood mononuclear cells." Int J Oncol 41(4): 1251-1259.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Radiofrequency+currents+exert+cytotoxic+effects+in+NB69+human+neuroblastoma+cells+but+not+in+peripheral+blood+mononuclear+cells

Recently, a number of electric and electrothermal therapies have been applied to the treatment of specific cancer types. However, the cellular and molecular mechanisms involved in the response to such therapies have not been well characterized yet. Capacitive-resistive electric transfer (CRET) therapy uses electric currents at frequencies within the 0.45-0.6 MHz range to induce hyperthermia in target tissues. Preliminary trials in cancer patients have shown consistent signs that CRET could slow down growth of tumor tissues in brain gliomas, without inducing detectable damage in the surrounding healthy tissue. Previous studies by our group have shown that subthermal treatment with 0.57-MHz electric currents can induce a cytostatic, not cytotoxic response in HepG2 human hepatocarcinoma cells; such effect being mediated by cell cycle alterations. In contrast, the study of the response of NB69 human neuroblastoma cells to the same electric treatment revealed consistent indications of cytotoxic effects. The present study extends the knowledge on the response of NB69 cells to the subthermal stimulus, comparing it to that of primary cultures of human peripheral blood mononuclear cells (PBMC) exposed to the same treatment. The results showed no sensitivity of PBMC to the 0.57 MHz subthermal currents and confirmed that the treatment exerts a cytotoxic action in NB69 cells. The data also revealed a previously undetected cytostatic response of the neuroblastoma cell line. CRET currents affected NB69 cell proliferation by significantly reducing the fraction of cells in the phase G2/M of the cell cycle at 12 h of exposure. These data provide new information on the mechanisms of response to CRET therapy, and are consistent with a cytotoxic and/or cytostatic action of the electric treatment, which would affect human cells of tumor origin but not normal cells with a low proliferation rate.

Kato, S., et al. (2011). "Anticancer effects of 6-o-palmitoyl-ascorbate combined with a capacitive-resistive electric transfer hyperthermic apparatus as compared with ascorbate in relation to ascorbyl radical generation." Cytotechnology 63(4): 425-435.

https://www.ncbi.nlm.nih.gov/pubmed/?term=Anticancer+effects+of+6-o-palmitoyl-ascorbate+combined+with+a+capacitive-resistive+electric+transfer+hyperthermic+apparatus+as+compared+with+ascorbate+in+relation+to+ascorbyl+radical+generation

The aim of the present study is to determine the anti-proliferative activity of 6-o-palmitoyl-L: -ascorbic acid (Asc6Palm) that is a lipophilic derivative of L: -ascorbic acid (Asc), on human tongue squamous carcinoma HSC-4 cells by combined use of hyperthermia in comparison to Asc. Asc6Palm or Asc were administered to HSC-4 cells for 1 h, to which hyperthermia at 42 degrees C was applied for initial 15 min. After further 1-72 h incubation at 37 degrees C, cell proliferation was determined with Crystal Violet staining. Ascorbyl radical (AscR) in HSC-4 cell suspension was measured by electron spin resonance (ESR), and cell morphology was observed with scanning electron microscopy (SEM). At 37 degrees C, 4 mM Asc or 0.35 mM Asc6Palm were enough to suppress proliferation of HSC-4 cells. By combined use of hyperthermia at 42 degrees C, cell proliferation was decreased when compared to 37 degrees C. After Asc of 4 mM was incubated with HSC-4 cell suspensions at 37 degrees C or 42 degrees C for 0-180 min, the signal intensity of ascorbyl radical (AscR) by ESR was not different regardless of the presence or absence of cells at 37 degrees C, whereas AscR signal was enlarged in the presence of HSC-4 cells at 42 degrees C. It was suggested that oxidation of Asc occurred rapidly in HSC-4 cells by hyperthermia, and thereby enhanced the anti-proliferative activity. By SEM observation, the surface of HSC-4 cells treated with Asc6Palm revealed distinct morphological changes. Thus, the combined regimen of Asc6Palm and hyperthermia is expected to exert a marked antitumor activity.

Hernández-Bule, M. L., et al. (2010). "Cytostatic response of HepG2 to 0.57 MHz electric currents mediated by changes in cell cycle control proteins." International Journal of Oncology 37(6).

https://www.ncbi.nlm.nih.gov/pubmed/?term=Cytostatic+response+of+HepG2+to+0.57+MHz+electric+currents+mediated+by+changes+in+cell+cycle+control+proteins

The capacitive-resistive electric transfer (CRet) therapy is a non-invasive technique that applies electrical currents of 0.4-0.6 MHz to the treatment of musculoskeletal injuries. Although this therapy has proved effective in clinical studies, its interaction mechanisms at the cellular level still are insufficiently investigated. Results from previous studies have shown that the application of CRet currents at subthermal doses causes alterations in cell cycle progression and decreased proliferation in hepatocarcinoma (HepG2) and neuroblastoma (NB69) human cell lines. The aim of the present study was to investigate the antiproliferative response of HepG2 to CRet currents. The results showed that 24-h intermittent treatment with 50 μA/mm2current density induced in HepG2 statistically significant changes in expression and activation of cell cycle control proteins p27Kip1 and cyclins D1, A and B1. The chronology of these changes is coherent with that of the alterations reported in the cell cycle of HepG2 when exposed to the same electric treatment. We propose that the antiproliferative effect exerted by the electric stimulus would be primarily mediated by changes in the expression and activation of proteins intervening in cell cycle regulation, which are among the targets of

emerging chemical therapies. The capability to arrest the cell cycle through electrically-induced changes in cell cycle control proteins might open new possibilities in the field of oncology.

Hernandez-Bule, M. L., et al. (2007). "In vitro exposure to 0.57-MHz electric currents exerts cytostatic effects in HepG2 human hepatocarcinoma cells." Int J Oncol 30(3): 583-592.

https://www.ncbi.nlm.nih.gov/pubmed/?term=In+vitro+exposure+to+0.57-MHz+electric+currents+exerts+cytostatic+effects+in+HepG2+human+hepatocarcinoma+cells

Capacitive-resistive electric transfer (CRET) therapy is a non-invasive technique currently applied to the treatment of skin, muscle and tendon injuries that uses 0.45-0.6 MHz electric currents to transdermically and focally increase the internal temperature of targeted tissues. Because CRET electrothermal treatment has been reported to be more effective than other thermal therapies, it has been proposed that the electric stimulus could induce responses in exposed tissues that are cooperative or synergic with the thermal effects of the treatment. Previous studies by our group, investigating the nature of the alleged electric response, have shown that short, repeated stimuli with 0.57-MHz currents at subthermal levels could provoke partial, cytotoxic effects on human neuroblastoma cells in vitro. The aim of the present study was to investigate the response from another human cell type, the human hepatocarcinoma HepG2 line, during and after the exposure to 0.57-MHz CRET currents at subthermal densities. The electric stimuli provoked a decrease in the proliferation rate of the cultures, possibly due to an electrically-induced blocking of the cell cycle in a fraction of the cellular population.

Hernandez-Bule, M. L., et al. (2004). "[Nonthermal levels of electric currents applied in capacitive electric transfer therapy provokes partial cytotoxic effects in human neuroblastoma cultures]." Neurocirugia (Astur) 15(4): 366-371; discussion 371. (Article inSpanish)

https://www.ncbi.nlm.nih.gov/pubmed/?term=Nonthermal+levels+of+electric+currents+applied+in+capacitive+electric+transfer+therapy+provokes+partial+cytotoxic+effects+in+human+neuroblastoma+cultures

The present study investigates the cellular response to weak, sine wave, 0.5-MHz electric currents. The experimental exposure to identical signals at an intensity high enough as to significantly increase the temperature in target tissues, has provided positive responses in clinical treatments of tumors with capacitive electric transfer (CET) thermal therapy. The present results show that the in vitro exposure to CET signals at athermal doses causes cytotoxic effects in human neuroblastoma cells. Such a response seems to be due to signal-induced alterations in the cell cycle. As a whole, the results suggest that the potential therapeutic effects of the CET strategy could be due to the thermal response of the tissues to the currents, added to an athermal response of the cells to the electric current itself.