

Cancer

Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2004 Jun;21(3):433-5.

[Effect of steep pulsed electric fields on survival of tumour-bearing mice]

[Article in Chinese]

[Yao C](#), [Sun C](#), [Xiong L](#), [Mi Y](#), [Liao R](#), [Hu L](#), [Hu Y](#).

College of Electrical Engineering, Chongqing University, Chongqing, 400044, China.

To investigate the lethal effect of steep pulsed electric fields (SPEFs) on cancer cells and the life-prolonging effect of SPEFs on the survival of tumour-bearing mice, this study was carried out with the use of SPEFs to treat 40 BALB/C mice inoculated by cervical cancer. The lethal effect on cancer cells and the life-prolonging effect on tumour-bearing mice were examined and compared between the experiment group and control group. The survival periods of the experiment group and control group were 52.05 days and 33.03 days, respectively. There was a significant difference in survival curve between the two groups. The results confirmed the inhibitory effect and lethal effect of SPEFs on cancer cells. SPEFs can prolong the survival period of tumour-bearing mice.

[Physiol Meas](#). 2004 Aug;25(4):1077-93.

Nanosecond pulsed electric fields modulate cell function through intracellular signal transduction mechanisms.

[Beebe SJ](#), [Blackmore PF](#), [White J](#), [Joshi RP](#), [Schoenbach KH](#).

Center for Pediatric Research, Eastern Virginia Medical School, Children's Hospital for The King's Daughters, Norfolk, VA, USA. sbeebe@chkd.com

These studies describe the effects of nanosecond (10-300 ns) pulsed electric fields (nsPEF) on mammalian cell structure and function. As the pulse durations decrease, effects on the plasma membrane (PM) decrease and effects on intracellular signal transduction mechanisms increase. When nsPEF-induced PM electroporation effects occur, they are distinct from classical PM electroporation effects, suggesting unique, nsPEF-induced PM modulations. In HL-60 cells, nsPEF that are well below the threshold for PM electroporation and apoptosis induction induce effects that are similar to purinergic agonist-mediated calcium release from intracellular stores, which secondarily initiate capacitive calcium influx through store-operated calcium channels in the PM.

NsPEF with durations and electric field intensities that do or do not cause PM electroporation, induce apoptosis in mammalian cells with a well-characterized phenotype typified by externalization of phosphatidylserine on the outer PM and activation of caspase proteases. Treatment of mouse fibrosarcoma tumors with nsPEF also results in apoptosis induction. When Jurkat cells were transfected by electroporation and then treated with nsPEF, green fluorescent protein expression was enhanced compared to electroporation alone. The results indicate that nsPEF activate intracellular mechanisms that can determine cell function and fate, providing an important new tool for probing signal transduction mechanisms that modulate cell structure and function and for potential therapeutic applications for cancer and gene therapy.

J Photochem Photobiol B. 2001 Nov 1;64(1):21-6.

Photodynamic effect on cancer cells influenced by electromagnetic fields.

[Pang L](#), [Baciu C](#), [Traitcheva N](#), [Berg H](#).

Institute of Physics, Nankai University, Nankai, PR China.

The synergism of low-frequency electromagnetic field treatment and photodynamic effect on killing of human cancer cells is presented. The weak pulsating electromagnetic field (PEMF) generated by Helmholtz coils in the mT range influences the permeability of cell membranes for photosensitizers. Several types of sensitizers were excited by visible light during incorporation without and with two kinds of PEMF treatment. In the first part suitable photosensitizers were selected in the absorption range between 400 and 700 nm against human myeloid leukaemia K562 and human histiocytic lymphoma U937 cells by treatment of PEMF consisting of rectangular pulse groups. In the second part amplitude and frequency dependencies were measured using sinuous PEMF and white light with the result that after 12 min the PEMF treatment enhanced photodynamic effectivity by more than 40% over the control value. Taking into account the influence of many parameters, an additional optimization will be possible by photodynamic PEMF synergism for an increased drug delivery in general.

[Vopr Onkol](#). 2000;46(4):469-72.

[Use of artificial magnetic field for rehabilitation of children with malignant tumors]

[Article in Russian]

[Kiselev AV](#), [Grushina TI](#).

N.N. Blokhin Center for Oncology Research, Russian Academy of Medical Sciences, Moscow.

Local complications of standard intravenous injections for chemotherapy and due to error of administration were compared in 400 patients (200 of them children) and general wound pathologies described. Treatment for wounds included two modalities: standard medication and alternating or pulsating magnetic field. Magnetic therapy proved highly effective: wound healing was 3-3.5 times faster while duration of treatment--2-3 times shorter than in standard procedure. Clinically-verified partial adhesion-related intestinal obstruction was eliminated by magnetic procedure in 18 children after combined treatment for lymphosarcoma involving the ileum.

Bioelectromagnetics 1996;17(5):358-63.

Exposure to strong static magnetic field slows the growth of human cancer cells in vitro.

[Raylman RR](#), [Clavo AC](#), [Wahl RL](#).

University of Michigan Medical Center, Department of Internal Medicine, Ann Arbor, USA.

Proposals to enhance the amount of radiation dose delivered to small tumors with radioimmunotherapy by constraining emitted electrons with very strong homogeneous static magnetic fields has renewed interest in the cellular effects of prolonged exposures to such fields. Past investigations have not studied the effects on tumor cell growth of lengthy exposures to very high magnetic fields. Three malignant human cell lines, HTB 63 (melanoma), HTB 77 IP3 (ovarian carcinoma), and CCL 86 (lymphoma: Raji cells), were exposed to a 7 Tesla uniform static magnetic field for 64 hours. Following exposure, the number of viable cells in each group was determined. In addition, multicycle flow cytometry was performed on all cell lines, and pulsed-field electrophoresis was performed solely on Raji cells to investigate changes in cell cycle patterns and the possibility of DNA fragmentation induced by the magnetic field. A 64 h exposure to the magnetic field produced a reduction in viable cell number in each of the three cell lines. Reductions of 19.04 +/- 7.32%, 22.06 +/- 6.19%, and 40.68 +/- 8.31% were measured for the melanoma, ovarian carcinoma, and lymphoma cell lines, respectively, vs. control groups not exposed to the magnetic field. Multicycle flow cytometry revealed that the cell cycle was largely unaltered. Pulsed-field electrophoresis analysis revealed no increase in DNA breaks related to magnetic field exposure. In conclusion, prolonged exposure to a very strong magnetic field appeared to inhibit the growth of three human tumor cell lines in vitro. The mechanism underlying this effect has not, as yet, been identified, although alteration of cell growth cycle and gross fragmentation of DNA have been excluded as possible contributory factors. Future investigations of this phenomenon may have a significant impact on the future understanding and treatment of cancer.

In Vivo. 1991 Jan-Feb;5(1):39-40.

Effect of a 9 mT pulsed magnetic field on C3H/Bi female mice with

mammary carcinoma. A comparison between the 12 Hz and the 460 Hz frequencies.

[Bellossi A](#), [Desplaces A](#).

Laboratoire de Biophysique, Faculte de Medecine, Rennes, France.

In a previous experiment, the exposure of tumoral C3H/Bi female mice to a 9 mT, 460 Hz pulsed magnetic field led to an increase in the length of survival in the late period of the disease; this might be due to a hampered metastatic process. In the present study 27 controls and 52 exposed mice were treated with the same protocol (a 10-minute exposure, 3 non-consecutive days a week, from 2-3 weeks after the tumors appeared until death) but with a 12 Hz PMF. In this experiment the 12 Hz PMF appeared to increase length of survival times in the early period of the disease.

[Vopr Onkol.](#) 2003;49(6):748-51.

[Experience with turbulent magnetic field as a component of breast cancer therapy]

[Article in Russian]

[Letiagin VP](#), [Protchenko NV](#), [Rybakov IuL](#), [Dobrynin IaV](#).

N.N. Blokhin Center for Oncology Research, Russian Academy of Medical Sciences, Zdorovje Research Center, Moscow.

No adverse side-effects were reported in an investigation of the antitumor effect of turbulent magnetic field (TMF) carried out as a component of preoperative chemoradiotherapy for breast cancer at the Center's Clinic. The study group included 114 patients with locally advanced tumors(T3, N1-N3, M0). According to the clinical, roentgenological and histological evidence on the end-results, the procedure was highly effective. Also, it was followed by shorter and less extensive postoperative lymphorrhea.

Sov Med. 1991;(7):25-7.

[The assessment of the efficacy of the effect of a rotational magnetic field on the course of the tumor process in patients with generalized breast cancer]

[Article in Russian]

[Bakmutskii NG](#), [Pyleva TA](#), [Frolov VE](#), [Sinitskii DA](#), [Ripa IM](#).

The efficacy of rotational magnetic field generated by a "Magnitoturbotron" unit was evaluated in 51 women with advanced breast cancer. The effect resulted from an action on the patient's body by modulated rotational magnetic field changing in cycles according to induction. A significant response was achieved in 27 of 51 patients. There was no hemopoiesis suppression, negative functional shifts. The unit is recommended for introduction in a combined treatment of breast cancer.

Jpn J Cancer Res. 1990 Sep;81(9):956-61.

Treatment of experimental tumors with a combination of a pulsing magnetic field and an antitumor drug.

[Omote Y](#), [Hosokawa M](#), [Komatsumoto M](#), [Namieno T](#), [Nakajima S](#), [Kubo Y](#), [Kobayashi H](#).

Laboratory of Pathology, Hokkaido University School of Medicine, Sapporo.

We investigated the effects of a combination treatment involving a pulsing magnetic field (PMF) and an antitumor drug, mitomycin C (MMC), on two experimental tumors (fibrosarcoma KMT-17 and hepatocellular carcinoma KDH-8) in WKA rats, paying attention to possible potentiation of the therapeutic effect of the antitumor drug. PMF was obtained using a system generating a pulsed current in a solenoid coil. On day 7 after tumor implantation into the right thighs of rats, the region of the tumor was exposed to PMF (frequency 200 Hz, mean magnetic flux density 40 gauss) for 1 h immediately after iv injection of MMC at a dose of 1 mg/kg. Survival rates at day 90 of KMT-17 implanted rats were 0% (0/10) in the non-treated group, 34% (4/12) in the MMC-treated group, 47% (6/13) in the PMF-treated group and 77% (10/13) in the MMC/PMF combination group. The increase of life span (ILS) of KDH-8-implanted rats in the combination therapy group was significantly prolonged (% ILS 17.6%) compared with that in the MMC-treated (% ILS 3.4%) and PMF-treated (% ILS 7.6%) groups. By using cultured cells of the above two lines of tumor, the therapeutic effects of MMC and PMF were also determined from the cell colony-forming efficiency in soft agar. The colony-forming efficiencies of both cell lines were significantly suppressed in the combination therapy group compared with those in the other single therapy groups. The present results indicate that PMF exhibited a potentiation of the antitumor effect of mitomycin C.

Ann Biomed Eng. 2003 Jan;31(1):80-90.

Viability of cancer cells exposed to pulsed electric fields: the role of pulse charge.

[Krassowska W](#), [Nanda GS](#), [Austin MB](#), [Dev SB](#), [Rabussay DP](#).

Department of Biomedical Engineering, Duke University, Durham, NC 27708-0281, USA. wanda.krassowska@duke.edu

The goal of this study was to collect a comprehensive set of data that related lethal effects of electric fields to the duration of the pulse. Electric pulses of different strengths and durations were applied to a suspension of HEP-2 cells (epidermoid carcinoma of the human larynx) using a six-needle electrode array connected through an autoswitcher to a square wave generator. Pulse durations varied from 50 micros to 16 ms and the ranges of electric field were adjusted for each duration to capture cell viabilities between 0% and 100%. After pulsation, cells were incubated for 44 h at 37 degrees C, and their viability was measured spectrophotometrically using an XTT assay. For each pulse duration (d), viability data were used to determine the electric field that killed half of the cells (E50). When plotted on logarithmic axes, E50 vs. d was a straight line, leading to a hyperbolic relationship: $E50 = \text{const}/d$. This relationship suggests that the total charge delivered by the pulse is the decisive factor in killing HEP-2 cells.

Am J Physiol. 1997 May;272(5 Pt 2):R1677-83.

Electrical fields enhance growth of cancer spheroids by reactive oxygen species and intracellular Ca^{2+} .

[Wartenberg M](#), [Hescheler J](#), [Sauer H](#).

Institute for Neurophysiology, University of Cologne, Germany.

A single electrical field pulse (500 V/m) with a duration of 60 s increased tumor outgrowth over a postpulse period of 24 h. RNA staining with acridine orange showed a rise in RNA content in pulsed spheroids, indicating stimulation of cell cycle activity. The electropulse induced an intracellular Ca^{2+} concentration ($[\text{Ca}^{2+}]_i$) transient that started approximately 40 s after the onset of the electrical field. Neither the presence of extracellular Ni^{2+} (0.5 mM) nor the absence of extracellular Ca^{2+} impeded the $[\text{Ca}^{2+}]_i$ rise. It was, however, totally blocked by thapsigargin (1 microM), indicating that the initial Ca^{2+} response is due to Ca^{2+} release from intracellular stores. The $[\text{Ca}^{2+}]_i$ transient was paralleled by an increase in reactive oxygen species (ROS), as revealed using 2',7'-dichlorofluorescein diacetate as an indicator. The radical scavengers N-acetyl-L-cysteine (NAC)(20 mM) and dehydroascorbate (5 mM) inhibited both ROS production and the $[\text{Ca}^{2+}]_i$ transient during electrical field treatment. The mitogenic activation was dependent on the rise in $[\text{Ca}^{2+}]_i$ because inhibition of Ca^{2+} release during electrical field treatment by addition of either thapsigargin or NAC to the incubation medium abolished the observed effect. We conclude that a single, direct current electrical field pulse induces production of ROS, which in turn mediate Ca^{2+} release from intracellular stores and activate cell cycle activity in multicellular spheroids.

Nippon Geka Gakkai Zasshi. 1988 Aug;89(8):1155-66.

[An experimental attempt to potentiate therapeutic effects of combined use of pulsing magnetic fields and antitumor agents]

[Article in Japanese]

[Omote Y.](#)

First Department of Surgery, Asahikawa Medical College, Japan.

With a view to examining the possible clinical applicability of pulsing magnetic fields (PMF), we investigated the effects of weak, non-heat inducing, PMF on DNA synthesis and sensitivity of cancer cells to antitumor agents. Leukemic T-cells (Molt-4) and a pancreatic ductal adenocarcinoma (solid tumor) transplanted in a Syrian golden hamster were used for the in vitro experiment and in vivo experiment respectively. In order to evaluate the effects of PMF on the DNA synthesis of cancer cells and the incorporation of antitumor agent into cancer cells, cultured cells or solid tumor were exposed to PMF generated by a solenoid coil immediately after 3H-or 14C-thymidine and 3H-methotrexate administration respectively. Thymidine uptake was found to increase by exposure to PMF, as did also 3H-methotrexate uptake by leukemic T-cells. Following exposure to PMF immediately after administration of methotrexate or mitomycin C, antitumor activity in both cells was increased. From these results it appears that the incorporation of antitumor agents into the cells increases by eddy current stimulation induced by PMF, and that the cell cycle shifts from the non-proliferative to proliferative phase, resulting in increased antitumor activity.

Anticancer Res. 1987 May-Jun;7(3 Pt B):391-3.

Tumoricidal cells increased by pulsating magnetic field.

[Malter M](#), [Schriever G](#), [Kuhnlein R](#), [Suss R](#).

Repeated applications of pulsed magnetic fields (right-angle waves, 50 Hz = 135 Gauss, 2 Hz = 262 Gauss) significantly enhanced the number and the tumoricidal activity of nonparenchymal liver cells. The transplantable mouse leukemia L1210 used as a tumor model was not significantly influenced, either directly or during Cyclophosphamide treatment

Vopr Onkol. 1980;26(1):28-34.

[Morphological criteria of lung cancer regression under the effect of magnetotherapy]

[Article in Russian]

[Ogorodnikova LS](#), [Gairabed'iants NG](#), [Ratner ON](#), [Chirvina ED](#), [Sem LD](#).

The complex investigation (histological, histochemical, morphological, electrone microscopy) of lung cancerous tumors from 20 patients, subjected preoperatively to the

action of magnetic fields enhancing the antitumor resistance by developing general nonspecific adaptation reactions: activation and training, has revealed a number of morphological changes which indicate a marked antitumor effect of magnetic fields. These changes were maximum manifest after 20-30 sessions. High-differentiated adenocarcinoma proved to be mostly sensitive to the magnetic field action.

J Cell Biochem. 1993 Apr;51(4):387-93.

Beneficial effects of electromagnetic fields.

Bassett CA.

Bioelectric Research Center, Columbia University, Riverdale, New York 10463.

Selective control of cell function by applying specifically configured, weak, time-varying magnetic fields has added a new, exciting dimension to biology and medicine. Field parameters for therapeutic, pulsed electromagnetic field (PEMFs) were designed to induce voltages similar to those produced, normally, during dynamic mechanical deformation of connective tissues. As a result, a wide variety of challenging musculoskeletal disorders have been treated successfully over the past two decades. More than a quarter million patients with chronically ununited fractures have benefitted, worldwide, from this surgically non-invasive method, without risk, discomfort, or the high costs of operative repair. Many of the athermal bioresponses, at the cellular and subcellular levels, have been identified and found appropriate to correct or modify the pathologic processes for which PEMFs have been used. Not only is efficacy supported by these basic studies but by a number of double-blind trials. As understanding of mechanisms expands, specific requirements for field energetics are being defined and the range of treatable ills broadened. These include nerve regeneration, wound healing, graft behavior, diabetes, and myocardial and cerebral ischemia (heart attack and stroke), among other conditions. Preliminary data even suggest possible benefits in controlling malignancy.