Rotating Magnetic Fields

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8631329/ Baskin

Rotating Magnetic Fields Inhibit Mitochondrial Respiration, Promote Oxidative Stress and Produce Loss of Mitochondrial Integrity in Cancer Cells 2021 Electromagnetic fields (EMF) raise intracellular levels of reactive oxygen species (ROS) that can be toxic to cancer cells. Because weak magnetic fields influence spin state pairing in redox-active radical electron pairs, we hypothesize that they disrupt electron flow in the mitochondrial electron transport chain (ETC). We tested this hypothesis by studying the effects of oscillating magnetic fields (sOMF) produced by a new noninvasive device involving permanent magnets spinning with specific frequency and timing patterns.

Pairing of electrons in bimolecular reactions and electron transfer processes with free radical intermediates, termed as the radical pair mechanism (RPM), is perturbed by magnetic fields in the milliTesla (mT) and microTesla (μ T) ranges (<u>3–6</u>). This perturbation is due to a quantum mechanical phenomenon in which the spin of an electron tends to align itself with the axis of a magnet.

Here, we explore the effects of mT range sOMF produced by rapidly spinning permanent magnets on the electron transport occurring in these complexes. We achieve this by using a sOMF producing component called an oncoscillator of a newly developed potentially therapeutic noninvasive anticancer device called an Oncomagnetic device. This component is comprised of a high field strength neodymium permanent magnet attached to the shaft of a battery-operated electric motor.

The range of potential magnet rotation frequencies and acceleration/deceleration of the resulting waveforms is vast, and we have only explored a limited range of the options available. The peak nominal sOMF frequency used was \approx 280 Hz (wave duration of \approx 3 ms), although we have explored a wide range of frequencies between 50 and 350 Hz. The oncoscillator was turned on for 250 ms and then turned off for 250 ms, allowing the oscillations to slow down. During this on/off power cycle the oncoscillator performs a rapid sweep through increasing frequencies (during acceleration) and a slower sweep through decreasing frequencies (during deceleration). The frequency sweeps quite possibly span the cycling rates of electron fluxes associated with different mitochondrial states (26, 27). Short 5 to 15 min runs of on-off cycles were separated by pauses of similar durations.



A half-rotation, numbered from (1) to (7), begins from an initial field parallel position, and proceeds into the perpendicular ($\underline{4}$), and returns to parallel orientation, but with the field having an opposing polarity ($\underline{7}$). This field rotation will allow all spins in the x-y orientation to find themselves aligned with the external field.

To conclude, in this study we provide evidence that specific on and off patterns of sOMF cycles generated by rapid rotation of a strong permanent magnet perturb mitochondrial electron transport as measured by sOMF-induced changes in the time course of O_2 consumption. This mechanism is likely responsible for sOMF-induced cytotoxicity in DIPG, GBM and meningioma tumor cells. Ongoing experiments are investigating further the utility of this mechanism in producing anticancer effects in mouse xenograft models and end-stage recurrent GBM patients under an FDA-approved expanded access program (<u>18</u>).

https://pubmed.ncbi.nlm.nih.gov/34367992/ Baskin

Case Report: End-Stage Recurrent Glioblastoma Treated With a New Noninvasive Non-Contact Oncomagnetic Device 2021

Alternating electric field therapy has been approved for glioblastoma (GBM). We have preclinical evidence for anticancer effects in GBM cell cultures and mouse xenografts with an oscillating magnetic field (OMF) generating device. Here we report OMF treatment of end-stage recurrent glioblastoma in a 53-year-old man who had undergone radical surgical excision and chemoradiotherapy, and experimental gene therapy for a left frontal tumor. He experienced tumor recurrence and progressive enlargement with leptomeningeal involvement. OMF for 5 weeks was well tolerated, with 31% reduction of contrast-enhanced tumor volume and reduction in abnormal T2-weighted Fluid-Attenuated Inversion Recovery volume. Tumor shrinkage appeared to correlate with treatment dose. These findings suggest a powerful new noninvasive therapy for glioblastoma.

Selective induction of rapid cytotoxic effect in glioblastoma cells by oscillating magnetic fields 2021

Purpose: The mechanisms underlying anticancer effects of electromagnetic fields are poorly understood. An alternating electric field-generating therapeutic device called Optune[™] device has been approved for the treatment of glioblastoma (GBM). We have developed a new device that generates oscillating magnetic fields (OMF) by rapid rotation of strong permanent magnets in specially designed patterns of frequency and timing and have used it to treat an end-stage recurrent GBM patient under an expanded access/compassionate use treatment protocol. Here, we ask whether OMF causes selective cytotoxic effects in GBM and whether it is through generation of reactive oxygen species (ROS).

Methods: We stimulated patient derived GBM cells, lung cancer cells, normal human cortical neurons, astrocytes, and bronchial epithelial cells using OMF generators (oncoscillators) of our Oncomagnetic Device and compared the results to those obtained under unstimulated or sham-stimulated control conditions. Quantitative fluorescence microscopy was used to assess cell morphology, viability, and ROS production mechanisms.

Results: We find that OMF induces highly selective cell death of patient derived GBM cells associated with activation of caspase 3, while leaving normal tissue cells undamaged. The cytotoxic effect of OMF is also seen in pulmonary cancer cells. The underlying mechanism is a marked increase in ROS in the mitochondria, possibly in part through perturbation of the electron flow in the respiratory chain.

Conclusion: Rotating magnetic fields produced by a new noninvasive device selectively kill cultured human glioblastoma and non-small cell lung cancer cells by raising intracellular reactive oxygen species, but not normal human tissue cells.

https://www.houstonmethodist.org/leading-medicine-blog/articles/2023/mar/oncomagnetic-device-a-promising-non-invasive-weapon-against-deadly-brain-cancercells/

Oncomagnetic Device a Promising Non-Invasive Weapon Against Deadly Brain Cancer Cells 2023

https://pubmed.ncbi.nlm.nih.gov/36154345/

Method for noninvasive whole-body stimulation with spinning oscillating magnetic fields and its safety in mice 2022

We recently reported shrinkage of untreatable recurrent glioblastoma (GBM) in an end-stage patient using noninvasive brain stimulation with a spinning oscillating magnetic field (sOMF)-generating device called the Oncomagnetic device. Our *in vitro* experiments demonstrated selective cancer cell death while sparing normal cells by sOMF-induced increase in intracellular reactive oxygen species (ROS) levels due to magnetic perturbation of mitochondrial electron transport. Here, we describe the results of an *in vivo* study assessing the toxicity of chronic sOMF stimulation in mice using a newly constructed apparatus comprised of the sOMF-generating active components of the Oncomagnetic device. We chronically stimulated 10 normal 60-day old female C57BL/6 mice in their housing cages for 2 h 3 times a day, as in the patient treatment protocol, over 4 months. We also studied the effects of 2-h acute sOMF stimulation. Our observations and those of blinded independent veterinary staff observers, indicated no significant adverse effects of chronic or acute sOMF stimulation on the health, behavior, electrocardiographic activities, hematologic profile, and brain and other tissue and organ morphology of treated mice compared to age-matched untreated control mice. These findings suggest that short- and long-term therapies with the Oncomagnetic device are safe and well tolerated.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10630398/pdf/41598_2023_Article_46758.pdf

Spinning magnetic field patterns that cause oncolysis by oxidative stress in glioma cells 2023

The intermittent sOMF stimuli generated by an oncoscillator with a spinning magnet had a peak frequency (PF) of \sim 272 Hz, and on time (Ton) and off time (Toff) of 250 ms each (Fig. 1B). The oncoscillators did not produce an increase of temperature much beyond 37 °C at the location of stimulated cell culture dishes (Fig. 1C). The stimulation was carried out for 4 h. We observed that in both GBM and DIPG cells ROS generated by sOMF (1Dsp) was significantly higher than that generated by both 1Dst and 3Dst static magnetic fields at 2 h (during stimulation), 4 h (at the end of stimulation) and 6 h (2 h post-stimulation) (Fig. 2). While the increased effectiveness of a spinning magnetic field compared to a static field along one dimension confirms a prediction of the MEP hypothesis, the lack of a significant ROS-inducing effect of static fields oriented in all three dimensions suggests that the field oscillations themselves are essential for this effect. Magnetic field oscillations induced by a rotating magnet are characterized by two distinct components – the sinusoidal waves of the magnetic field and the cyclically changing angles of the axis of the field. The above results indicate that field oscillations play a critical role in inducing ROS. To test whether oscillations are sufficient to produce the ROS effect we compared the effect of magnetic field oscillations produced by a Helmholtz coil, whose axis remains fixed in one orientation, with those produced by the rotating magnet of an oncoscillator. The current passing through the coil alternated at ~ 137 Hz and was large enough to generate a peak-to-peak amplitude (PPA) of ~ 5 mT, values that were comparable to those produced by the spinning magnet of an oncoscillator for 4 h. We observed that Helmholtz coil did not produce any significant increase in ROS at 2 and 4 h during stimulation or 2 h post-stimulation in GBM and DIPG cells (Fig. 2D). In contrast, the oncoscillator significantly raised the ROS levels at all three time points in both cancer cell types

Magnet rotation along three axes

Because repeated changing of the angle of the magnetic field axis in all three dimensions may have a greaterimpact on ETC complexes oriented in all directions in space, we then investigated whether rotating magnetsalong all three orthogonal axes in three-dimensional space potentiates further the increase in ROS produced by magnet rotation along only one axis. We positioned three oncoscillators (3DSeq, Fig. 3A) at right angles to each other and activated them in repeating sequential or alternating cycles compared to intermittent stimulation with a single oncoscillator (1DSp). This experiment showed a greater increase in ROS at 2 h in both GBM and DIPG cells with 3DSeq compared to 1DSp stimulation; however, this difference was not statistically significant (Fig. 3B, C). The significant increases in ROS levels over control seen at 4 h and 2 h post-stimulation are also not significantly different between 3DSeq and 1DSp (Fig. 3B, C). This suggests that 1DSp stimulation might be sufficient to produce maximal ROS enhancement given that one activated oncoscillator sweeps through all angles in a two-dimensional plane.

Variation in stimulus parameters

Stimulation with an oncoscillator has four physical parameters that can be varied along a continuous scale. They are Ton, Toff, strength of the magnetic field or PPA of the stimulus, and the stimulus PF. We kept Ton constant at 250 ms and determined the effects of varying the values of each of the other three parameters to at least three different levels. Comparing three different Toff values (250, 750 and 2750 ms) while keeping Ton at 250 ms (Fig. 3D, E) showed that in GBM cells 250 and 750 ms Toff produced slightly better effect than 2,750 ms on ROS generation

(Fig. 3D). In contrast, in DIPG cells maximum ROS was generated by 2,750 ms Toff (Fig. 3E). We studied the effect of changing the PPA to ~ 0.42 mT, ~ 1.2 mT, ~ 5.5 mT and ~ 58.3 mT by positioning the cell culture dishes at distances of 7 cm, 5 cm, 3 cm, and 1.4 cm, respectively, from the oncoscillator (Fig. 4A–C and Supplementary Fig. S1C). All field strengths tested showed significant increases in ROS levels at the 4-h time point in GBM and DIPG cells (Fig. 4B, C). In terms of variation of PF between ~ 77, ~ 135 and ~ 277 Hz, the latter two frequencies

were significantly more effective than ~ 77 Hz (Fig. 4D, E).

Static and oscillating magnetic field exposure

Oncoscillators were positioned at different distances from the cell culture plates to change the PPA of the sOMF felt by the cells to ~ 0.4 , ~ 1 , ~ 5 mT and ~ 58 mT using an apparatus specially constructed in house for this purpose (Fig. 1A). The values of magnetic flux density at the various distances from the axis of the axially magnetized cylindrical neodymium (N52) magnets used in the oncoscillators were measured using a Homend handheld digital WT10A gauss meter. Three different values of PF of rotation of the magnet (sOMF oscillation frequency) were used— ~ 77 Hz, ~ 135 Hz and ~ 277 Hz. For intermittent stimulation, the Ton or sOMF pulse train duration was kept constant at 250 ms. The Toff times were set at 250, 750 or 2,750 ms. All frequency and timing values were programmed into the microprocessor controlling the oncoscillators. sOMF effects produced by each set of parameters were compared with the other two sets and with unstimulated controls. Comparisons were also made with exposure to static magnetic field of one non-rotated magnet and three orthogonally oriented non-rotated magnets, as well as with the sOMF produced by rotating the latter three magnets. Stimulation with sOMF produced by a non-rotating Helmholtz coil was also carried out by passing a sinusoidal current of a strength sufficient to produce a PPA of ~ 5 mT in between its two solenoids where the cell culture dish was placed. The sinusoidal current was generated by a function generator (Wavetek, San Diego, CA) and amplified to the desired current amplitude by a high current amplifier (Taidacent, Shenzhen Taida Century Technology Co., Ltd., China).

Cells were stimulated once for a total duration of 2 h or 4 h in each experiment. In one experiment they were stimulated for 2 h thrice with two 2-h intervals between the three stimulation periods to test for effects of repeated stimulations. Intermittent stimulation for 4 h was also compared with continuous stimulation for the same duration at the same PF and PPA



https://pubs.rsc.org/en/content/articlehtml/2020/na/d0na00187b

Cancer treatment by magneto-mechanical effect of particles, a review 2020

Simplified diagrams of the mainly used magnetic field application devices. (a) Magnetic stirrer composed of two magnets at the end of a rotating rod (top view). (b) A coil powered by an alternating current that creates an alternating magnetic field inside or above the coil. The arrows in loops represent the magnetic flux line. (c) Ferrite core surrounded by a copper coil through which a sinusoidal alternating current flows. (d) System composed of 4 coils powered by an alternating sinusoidal current. The amplitude, phase shift and frequency of the applied current can be chosen to create an alternating or rotating field in the center of the 4 coils. (e) Halbach cylinder composed in this example of 8 permanent magnets creating an homogeneous field in the hollow of the cylinder. The rotating field is obtained by rotating the cylinder. (f) System composed of two magnets allowing to create a relatively homogeneous constant field.



The first method of field application was to use commercial or homemade magnetic stirrers, traditionally used for stirring mixtures with a magnetic bar.19,30,31,38 They are composed of two oppositely magnetized magnets located at each end of a rotating rod with the rotation speed up to 2000 rpm depending on the model (Fig. 3(a)). Advantage of these devices is that they are cheap and already present in most chemistry or biology laboratories. The major disadvantage is the inhomogeneity of the applied magnetic field. Indeed, a field mapping carried out on a commercial magnetic stirrer shows that right above the magnets, the field is perpendicular to the plane of the stirrer and has a value of 30 mT.84 Although the term "rotating magnetic field" is generally used to refer to this type of device, the field acting on the particles located above the circular trajectory of the rotating magnets is actually pulsed up and down during the rotation of the magnets. Moving away from the trajectory by 1 cm outwards, the field strength decreases and an in-plane component appears, of about 5 mT. In the center of the agitator, the field is parallel to the plane and has a value of 15 mT, which is indeed a rotating field. In the rest of the literature, the field strength values applied with magnetic stirrer are given between 30 and 240 mT but the location of the measurement (center or above the trajectory of the magnets) is not indicated.19.31,38,41.85 This device can only be used in vitro, taking care to distribute the cells to be treated over the path of the magnets for a pulsed vertical field, or in the center of the agitator for a rotating horizontal field. In both cases, the inhomogeneity of the field and the induced field gradient must be considered. Similarly, a system also based on the rotation of two magnets is used by Li et al.50 In this case, the sample was placed between the ends of two rotating rods. The two rods were aligned and a magnet was placed at the end of each rod in opposite directions. The applied field was adjusted by varying the distance between the two rods with a maximum of 50 mT. Wo et al.45 developed a more complex system using four permanent magnets placed on a disk under the culture plate producing a 45 mT field on the cells. During magnetic field exposure, the disk rotates and can also move on axial and radial direction.45 Moreover, Maniotis et al.26 recently developed a versatile system for TMMEP, configured with two to eight permanent magnets inserted in a rotating turntable, leading to field amplitudes of 200 mT and mean field gradient of 45 T m-1.

A method widely used to apply an alternating magnetic field to cells consists in using coils or electromagnets (Fig. 3(b)–(d)). The field can be applied with an iron stick placed between the wells of a culture plate, itself wound with copper wire, to apply a 90 Oe (=9 mT) field.22 Alternatively, the culture plate can be directly placed above a coil (Fig. 3(b)).33,46,49,51 Kilinc et al.34 used a Fe–Co–V tip wound with a copper coil to apply the magnetic field (the amplitude is not indicated).34 In the latter case, the magnetic field was applied very locally (500 µm from the tip). Magnetic fields produced by these three methods are highly inhomogeneous and decrease sharply as a function of the distance from the field source. Another method consists in placing the sample in the air gap of a U or C-shaped ferrite core subjected to alternating current (Fig. 3(c)). This technique was chosen by D. Cheng et al.32 and used at very high frequency (35 kHz) on cells detached from the support and placed in a tube; and by Martínez-Banderas et al.35 to apply a 1 mT field at 10 Hz. With this method, the magnetic field is homogenous in the air gap but limitations come from the size of the device compared to the field amplitude. In a different approach, cells or mouse are placed directly in the center of the solenoid to apply a 100 Oe (=10 mT) field.40 Here again, the field amplitude is very limited. Several commercial devices composed of an induction system with a ferromagnetic core or several coils have also been used.21,43,44 The field produced by these three systems creates a gradient that is either used by some authors or avoided by positioning the cells with respect to the field source geometry. The use of coils of identical size and even number, placed around the area of interest, creates a fairly homogeneous field around the symmetry plane separating them. This is referred to as Helmholtz coils (Fig. 3(d)). This configuration was used to apply a 140 Oe (=14 mT) uni- or bi-axial pulsed field.36 The disadvantage of this me

In order to produce a homogeneous field of larger amplitude, a Halbach cylinder can be used (Fig. 3(e)). This cylinder is composed of several permanent magnets (usually 8, 12 or 16) suitably oriented to produce a uniform magnetic field in the hollow of the cylinder. Using a rotation system, this cylinder was used to apply a rotating field in its center of about 1 T on cells, but also on mice.25,27,37,39 This device allows stronger fields to be applied in a limited space. The field rotation frequency is determined by the cylinder rotating speed which can be adjusted as required and is only limited by mechanical constrains (motor, generator, mechanical and magnetic forces, magnets weight).

In an innovative approach, a preclinical MRI system was used to apply a pulsed gradient.48 The main advantage of this method is its compatibility for subsequent clinical use, as MRI imaging systems are already widely used in hospitals. The field strength applied here is 9.4 T at a frequency of 5.4 kHz.

As mentioned above, while most of the studies discussed here focus on an oscillating or rotational motion of particles, some studies aimed solely at creating static forces pulling on the cell-membrane-bound particles, through the application of a static magnetic field gradient.42,47 In this case, static magnetic field gradients are applied using two permanent magnets placed on either side of cells or mouse (Fig. 3(f)). The maximum field created is between 0.2 and 0.66 T. However, in a study comparing the effects of an oscillating field and a field gradient, the oscillating field showed a better efficacy.29 The magnetic field of amplitude 160 kA m-1 (i.e.B \sim 200 mT) was here applied by a magnet moved alternatively away or closer to the sample to produce the oscillating field and field gradient.

https://pubmed.ncbi.nlm.nih.gov/32238091/

The efficacy and safety of low-frequency rotating static magnetic field therapy combined with chemotherapy on advanced lung cancer patients: a randomized, double-blinded, controlled clinical trial 2020

Results: 77 patients were enrolled and 60 finished the study. Comparing to CON group, more patients in MF group (66.7% vs 25.9%) were experiencing life quality improvement on day 21. Besides, MF group patients had higher concentrations of IP-10 and GM-CSF, and lower concentration of sTREM-1 in plasma. However, the two groups were having similar ORR, DCR and PFS after treatment. Moreover, MF treatment did not increase adverse events in MF group. **Conclusions:** MF therapy could improve life quality and modulate blood cytokine concentration in advanced lung cancer patients. Hence, it might be applied as an adjuvant therapy along with chemotherapy.

https://pubmed.ncbi.nlm.nih.gov/27061713/

Early exposure of rotating magnetic fields promotes central nervous regeneration in planarian Girardia sinensis 2016

Magnetic field exposure is an accepted safe and effective modality for nerve injury. However, it is clinically used only as a supplement or salvage therapy at the later stage of treatment. Here, we used a planarian Girardia sinensis decapitated model to investigate beneficial effects of early rotary non-uniform magnetic fields (RMFs) exposure on central nervous regeneration. Our results clearly indicated that magnetic stimulation induced from early RMFs exposure significantly promoted neural regeneration of planarians. This stimulating effect is frequency and intensity dependent. Optimum effects were obtained when decapitated planarians were cultured at 20 °C, starved for 3 days before head-cutting, and treated with <u>6 Hz 0.02 T RMFs</u>. At early regeneration stage, RMFs exposure eliminated edema around the wound and facilitated subsequent formation of blastema. It also accelerated cell proliferation and recovery of neuron functionality. Early RMFs exposure up-regulated expression of neural regeneration related proteins, EGR4 and Netrin 2, and mature nerve cell marker proteins, NSE and NPY. These results suggest that RMFs therapy produced early and significant benefit in central nervous regeneration, and should be clinically used at the early stage of neural regeneration, with appropriate optimal frequency and intensity.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5090029/

The use of magnetic fields in treatment of patients with rheumatoid arthritis. Review of the literature 2016

According Cieślińska-Świder [14], magnetic intensity of 2 mT and frequency of 12 Hz are used in arthritis. The recommended treatment time is from 15 to 30 minutes, and the treatments are performed 1–2 times per day for several weeks [14].

The aim of the research carried out by Kumar et al. [41] was to evaluate the effect of pulsed electromagnetic fields (PEMF) on experimentally induced inflammation in rats. A sinusoidal unipolar magnetic field was applied with different parameters. The activity of lysosomal enzymes, inflammatory cell infiltration as well as swelling were assessed. Optimal field parameters were 4 mT, 5 Hz and exposure time of 90 min in that case [41]. In studies by Dortch and Johnson [42] rats with experimentally induced rheumatoid arthritis were subjected daily to AC magnetic field with the parameters 10 mT and 5–50 Hz. It has been shown that PEMF may be a useful therapeutic agent in the treatment of chronic inflammatory diseases such as rheumatoid arthritis [

https://pubmed.ncbi.nlm.nih.gov/37048045/

Rotating Magnetic Field Mitigates Ankylosing Spondylitis Targeting Osteocytes and Chondrocytes via Ameliorating Immune Dysfunctions 2023

In this study, the effects of a rotating magnetic field (RMF; 0.2 T, 4 Hz) on an AS-like mouse model were investigated. The RMF treatment (2 h/d, 0.2 T, 4 Hz) was performed on AS mice from two months after birth until the day before sampling. The murine specimens were subjected to transcriptomics, immunomics, and metabolomics analyses, combined with molecular and pathological experiments. The results demonstrated that the mitigation of inflammatory deterioration resulted in an increase in functional osteogenesis and a decrease in dysfunctional osteolysis due to the maintenance of bone homeostasis via the RANKL/RANK/OPG signaling pathway. Additionally, by regulating the ratio of CD4+ and CD8+ T-cells, RMF treatment rebalanced the immune microenvironment in skeletal tissue. It has been observed that RMF interventions have the potential to alleviate AS, including by decreasing pathogenicity and preventing disease initiation. Consequently, RMF, as a moderately physical therapeutic strategy, could be considered to alleviate the degradation of cartilage and bone tissue in AS and as a potential option to halt the progression of AS.

https://www.frontiersin.org/articles/10.3389/fmolb.2021.742596/full

Electromagnetic Field as a Treatment for Cerebral Ischemic Stroke 2021

Many studies indicate that neurons in this zone remain functionally inactive but structurally intact and that they maintain membrane potential for several hours or more after the onset of a stroke (<u>Strandgaard and Paulson, 1990; Xing et al., 2012; Guruswamy and ElAli, 2017</u>). However, the longer the ischemic period lasts, the more these cells are at risk of dying. As a result, many treatments have been developed that aim to prevent the death of these neurons in the penumbra, such as recanalization therapies which recover the blood flow (<u>Rha and Saver, 2007; Amki and Wegener, 2017</u>).

Among the investigated treatment options for ischemic stroke, electromagnetic field (EMF) has been studied, first as a rehabilitation agent but later on also in the acute phase of the disease as a neuroprotective agent (<u>Rauš et al., 2014</u>; <u>Cichoń et al., 2017a</u>; <u>Cichoń et al., 2018c</u>). EMF is a magnetic field produced by moving electrically charged particles and can be viewed as a combination of electrical and magnetic fields. EMF can be divided into stationary magnetic fields (SMF) and time-varying magnetic fields. SMF has the same direction and magnitude with time because the electrical component is suppressed or has a 0 Hz frequency. Permanent magnets or electromagnetic coils with direct current are the most common sources of SMF. In time-varying magnetic fields, the intensity and direction of the electrical component and as a consequence the magnetic field varies over time (frequency different from 0 Hz) (Figure 1).



FIGURE 1. Representation of different types of EMFs used for stroke treatment. **(A)** EMF classification used in this article based on waveform and frequency (inverse of the signal period). SMF does not change its magnitude and direction in time (f = 0 Hz). Time-varying EMFs are divided into PEMF and SEMF. PEMFs include non-sinusoidal EMFs. This category includes monophasic square (like the carrying and burst signals), biphasic square, and burst-modulated signals. Burst-modulated signals consist of a carrying signal with a higher frequency modulated by a burst signal with a burst width and burst wait interval at a lower frequency. In this representation, $f_S > f_P > f_B$. **(B)** Three of the EMF waveforms used in the consulted literature. In red (<u>Cichorí et al., 2017a</u>), with a 7 mT/40 Hz biphasic square PEMF. In blue (<u>Duong and Kim, 2016</u>), with a 1 mT/50 Hz SEMF. In green (<u>Luo and Xu, 2017</u>), using a burst-modulated PEMF with a burst

frequency of 15 Hz (burst width, 5 ms; burst wait, 60 ms) and 4.5 MHz carrying monophasic square signal. SMF: stationary magnetic field; PEMF: pulsed electromagnetic field; SEMF: sinusoidal electromagnetic field; MF: magnetic field; *f*: frequency; f_P : pulse frequency; T_P : pulse period; f_C : carrying signal period; B_{Wd} : burst width; B_{Wt} : burst wait interval; T_B : burst period; f_B : burst frequency; f_S : sinusoid frequency; T_S : sinusoid period. As can be appreciated from this review, there is increasing evidence that supports the idea that therapeutic effects can be achieved from EMF in ischemic stroke. However, except for application to orthopedics (i.e., non-union fractures), there is a long way to go before this promising treatment can be accepted as a conventional medical practice.

https://www.nature.com/articles/s41598-017-18557-7

Application of Rotating Magnetic Fields Increase the Activity of Antimicrobials Against Wound Biofilm Pathogens 2018

Infective complications are a major factor contributing to wound chronicity and can be associated with significant morbidity or mortality. Wound bacteria are protected in biofilm communities and are highly resistant to immune system components and to antimicrobials used in wound therapy. There is an urgent medical need to more effectively eradicate wound biofilm pathogens. In the present work, we tested the impact of such commonly used antibiotics and antiseptics as gentamycin, ciprofloxacin, octenidine, chlorhexidine, polihexanidine, and ethacridine lactate delivered to *Staphylococcus aureus* and *Pseudomonas aeruginosa* biofilms in the presence of rotating magnetic fields (RMFs) of 10–50 Hz frequency and produced by a customized RMF generator. Fifty percent greater reduction in biofilm growth and biomass was observed after exposure to RMF as compared to biofilms not exposed to RMF. Our results suggest that RMF as an adjunct to antiseptic wound care can significantly improve antibiofilm activity, which has important translational potential for clinical applications. RMF of 10–50 Hz for 1 h

The frequencies of the RMF (*f*) were changed by a transistorized inverter. In the experimental procedure, this frequency was changed in the range from 10 to 50 Hz. The values of magnetic induction, *B*, were detected by using a Hall probe and a personal computer. The measurement of magnetic induction at the selected RMF frequency was repeated several times and mean values of magnetic induction were calculated. Basing on the records of the magnetic induction random signals the mean values of the parameter, *B*, at each sampling point were calculated. As follows from the analysis of the calculated data, the maximal values of the magnetic induction were obtained ($t = 10 \text{ Hz} - B_{\text{ max}} = 23 \text{ mT}$; $t = 25 \text{ Hz} - B_{\text{ max}} = 29 \text{ mT}$; $t = 50 \text{ Hz} - B_{\text{ max}} = 34 \text{ mT}$).

https://pubmed.ncbi.nlm.nih.gov/33170636/

Oscillating Magnetic Field Regulates Cell Adherence and Endothelialization Based on Magnetic Nanoparticle-Modified Bacterial Cellulose 2020 In our study, we demonstrated a new strategy to remotely regulate the adhesion of endothelial cells based on an oscillating magnetic field and achieve successful endothelialization on the modified BC membranes. In details, we synthesized bacterial cellulose (BC), magnetic BC (MBC), and RGD peptide-grafted magnetic BC (RMBC), modified with the HOOC-PEG-COOH-coated iron oxide nanoparticles (PEG-IONs). The endothelial cells were cultured on the three materials under different frequencies of an oscillating magnetic field, including "stationary" (0 Hz), "slow" (0.1 Hz), and "fast" (2 Hz) groups. Compared to BC and MBC membranes, the cells on RMBC membranes generally show better adhesion and proliferation. Meanwhile, the "slow" frequency of a magnetic field promotes this phenomenon on RMBC and achieves endothelialization after culture for 4 days, whereas "fast" inhibits the cellular attachment. Overall, we demonstrate a noninvasive and convenient method to regulate the endothelialization process, with promising applications in vascular tissue engineering.

https://pubmed.ncbi.nlm.nih.gov/28841803/

Tumor treating fields: a novel and effective therapy for glioblastoma: mechanism, efficacy, safety and future perspectives 2017 Tumor treating fields (TTF, Optune®), one of the low-intensity alternating electric fields, have been demonstrated to disrupt mitosis and inhibit tumor growth with antimitotic properties in a variety of tumor types. The Food and Drug Administration (FDA) of the United States approved TTF for recurrent GBM and newly diagnosed GBM in 2011 and 2015, respectively.

The advantages of TTF in GBM treatment, including non-invasive antitumor effect, superior therapeutic benefit in combination with chemotherapy, and minimal systematic toxicity, have been demonstrated in pre-clinical data and randomized phased III clinical trials. Future investigations will be needed to explore combinations of chemotherapy, radiation therapy, targeted therapy, as well as immunotherapy with this novel anti-tumor treatment modality to achieve additive or synergistic therapeutic benefit for GBM and other solid tumors.

Tumor treating fields (TTF) are low-intensity alternating electric fields, which have been demonstrated to disrupt mitosis, induce cell cycle arrest, and induce apoptosis with antimitotic properties in a variety of tumor types (4-7). An external and transportable TTF therapeutic medical device, Optune® (Novocure Ltd., Haifa, Israel), was developed to deliver 200 KHz alternating electric fields via two pairs of flexible transducer array panels. Each panel has nine insulated electrodes placed on the shaved scalp and is connected to a portable electric field generator in a non-invasive and continuous administration (Figure 1

https://pubmed.ncbi.nlm.nih.gov/28497056/

Direction-Dependent Effects of Combined Static and ELF Magnetic Fields on Cell Proliferation and Superoxide Radical Production 2017

Proliferation of human umbilical vein endothelial cells was stimulated by a nearly vertical 60 or 120 μ T static magnetic field (MF) in comparison to cells that were shielded against MFs. When the static field was combined with an extremely low frequency (ELF) MF (18 Hz, 30 μ T), proliferation was suppressed by a horizontal but not by a vertical ELF field. As these results suggested that the effects of an ELF MF depend on its direction in relation to the static MF, independent experiments were carried out to confirm such dependence using 50 Hz MFs and a different experimental model. Cytosolic superoxide level in rat glioma C6 cells exposed in the presence of a nearly vertical 33 μ T static MF was increased by a horizontal 50 Hz, 30 μ T MF, but not affected by a vertical 50 Hz MF. The results suggest that a weak ELF MF may interact with the static geomagnetic field in producing biological effects, but the effect depends on the relative directions of the static and ELF MFs.

https://pubmed.ncbi.nlm.nih.gov/12379225/

Mechanism for action of electromagnetic fields on cells 2002

A biophysical model for the action of oscillating electric fields on cells, presented by us before [Biochem. Biophys. Res. Commun. 272(3) (2000) 634-640], is extended now to include oscillating magnetic fields as well, extended to include the most active biological conditions, and also to explain why pulsed electromagnetic fields can be more active biologically than continuous ones. According to the present theory, the low frequency fields are the most bioactive ones. The basic mechanism is the forced-vibration of all the free ions on the surface of a cell's plasma membrane, caused by an external oscillating field. We have shown that this coherent vibration of electric charge is able to irregularly gate electrosensitive channels on the plasma membrane and thus cause disruption of the cell's electrochemical balance and function [Biochem. Biophys. Res. Commun. 272(3) (2000) 634-640]. It seems that this simple idea can be easily extended now and looks very likely to be able to give a realistic basis for the explanation of a wide range of electromagnetic field bioeffects

https://pubmed.ncbi.nlm.nih.gov/10860806/

A mechanism for action of oscillating electric fields on cells 2000

The biological effects of electromagnetic fields have seriously concerned the scientific community and the public as well in the past decades as more and more

evidence has accumulated about the hazardous consequences of so-called "electromagnetic pollution." This theoretical model is based on the simple hypothesis that an oscillating external electric field will exert an oscillating force to each of the free ions that exist on both sides of all plasma membranes and that can move across the membranes through transmembrane proteins. This external oscillating force will cause a forced vibration of each free ion. When the amplitude of the ions' forced vibration transcends some critical value, the oscillating ions can give a false signal for opening or closing channels that are voltage gated (or even mechanically gated), in this way disordering the electrochemical balance of the plasma membrane and consequently the whole cell function.

https://pubmed.ncbi.nlm.nih.gov/36574882/

Biological effects of rotating magnetic field: A review from 1969 to 2021 (2023)

As one of the common variable magnetic fields, rotating magnetic field (RMF) plays a crucial role in modern human society. The biological effects of RMF have been studied for over half a century, and various results have been discovered. Several reports have shown that RMF can inhibit the growth of various types of cancer cells in vitro and in vivo and improve clinical symptoms of patients with advanced cancer. It can also affect endogenous opioid systems and rhythm in central nerve systems, promote nerve regeneration and regulate neural electrophysiological activity in the human brain. In addition, RMF can influence the growth and metabolic activity of some microorganisms, alter the properties of fermentation products, inhibit the growth of some harmful bacteria and increase the susceptibility of antibiotic-resistant bacteria to common antibiotics. Besides, there are other biological effects of RMF on blood, bone, prenatal exposure, enzyme activity, immune function, aging, parasite, endocrine, wound healing, and plants. These discoveries demonstrate that RMF have great application potential in health care, medical treatment, fermentation engineering, and even agriculture. However, in some cases like pregnancy, RMF exposure may need to be avoided. Finally, the specific mechanisms of RMF's biological effects remain unrevealed, despite various hypotheses and theories. It does not prevent us from using it for our good.

In 2012, there was a clinical study in which 0.4T, 7Hz RMF was applied to treat 13 advanced non-small cell lung cancer patients (2 h/day, 5 days per week, for 6– 10 weeks).Decreased pleural effusion (2 patients, 15.4%), remission of shortness of breath (5 patients, 38.5%), relief of cancer pain (5 patients, 38.5%), increased appetite (6 patients, 46.2%), improved physical strength (9 patients, 69.2%), regular bowel movement (1 patient, 7.7%), and better sleep quality (2 patients, 15.4%)

https://pubmed.ncbi.nlm.nih.gov/34071384/

Modulation of Cellular Response to Different Parameters of the Rotating Magnetic Field (RMF)-An In Vitro Wound Healing Study 2021

The presented study was conducted to determine whether a low-frequency RMF (rotating magnetic field) with different field parameters could evoke the cellular response in vitro and is possible to modulate the cellular response. The cellular metabolic activity, ROS and Ca²⁺ concentration levels, wound healing assay, and gene expression analyses were conducted to evaluate the effect of RMF. It was shown that different values of magnetic induction (B) and frequency (f) of RMF evoke a different response of cells, e.g., increase in the general metabolic activity may be associated with the increasing of ROS levels. The lower intracellular Ca²⁺ concentration (for 50 Hz) evoked the inability of cells to wound closure. It can be stated that the subtle balance in the ROS level is crucial in the wound for the effective healing process, and it is possible to modulate the cellular response to the RMF in the context of an in vitro wound healing.

https://pubmed.ncbi.nlm.nih.gov/24460420/

Effects of rotating magnetic field exposure on the functional parameters of different species of bacteria 2015

The aim of the present study was to determine the effect of the rotating magnetic field (RMF) on the growth, cell metabolic activity and biofilm formation by S. aureus, E. coli, A. baumannii, P. aeruginosa, S. marcescens, S. mutans, C. sakazakii, K. oxytoca and S. xylosus. Bacteria were exposed to the RMF (RMF magnetic induction B = 25-34 mT, RMF frequency f = 5-50 Hz, time of exposure t = 60 min, temperature of incubation 37 °C). The persistence of the effect of exposure (B = 34 mT, f = 50 Hz, t = 60 min) on bacteria after further incubation (t = 300 min) was also studied. The work showed that exposure to RMF stimulated the investigated parameters of S. aureus, E. coli, S. marcescens, S. mutans, C. sakazakii, K. oxytoca and S. xylosus, however inhibited cell metabolic activity and biofilm formation by A. baumannii and P. aeruginosa. The results obtained in this study proved, that the RMF, depending on its magnetic induction and frequency can modulate functional parameters of different species of bacteria.

https://pubmed.ncbi.nlm.nih.gov/29317719/

Application of Rotating Magnetic Fields Increase the Activity of Antimicrobials Against Wound Biofilm Pathogens 2018

In the present work, we tested the impact of such commonly used antibiotics and antiseptics as gentamycin, ciprofloxacin, octenidine, chlorhexidine, polihexanidine, and ethacridine lactate delivered to Staphylococcus aureus and Pseudomonas aeruginosa biofilms in the presence of rotating magnetic fields (RMFs) of 10-50 Hz frequency and produced by a customized RMF generator. Fifty percent greater reduction in biofilm growth and biomass was observed after exposure to RMF as compared to biofilms not exposed to RMF. Our results suggest that RMF as an adjunct to antiseptic wound care can significantly improve antibiofilm activity, which has important translational potential for clinical applications.

(f = 10 Hz - Bmax = 23 mT; f = 25 Hz - Bmax = 29 mT; f = 50 Hz - Bmax = 34 mT).

https://pubmed.ncbi.nlm.nih.gov/35690675/

Effect of pine essential oil and rotating magnetic field on antimicrobial performance 2022

This work presents the results of a study which concerns the influence of rotating magnetic field (RMF) on the antibacterial performance of commercial pine essential oil. A suspension of essential oil in saline solution and Escherichia coli were exposed to the rotating magnetic Afield (the frequency of electrical current supplied by a RMF generator f = 1-50 Hz; the averaged values of magnetic induction in the cross-section of the RMF generator $B = \frac{13.13 \text{ to} - 19.92 \text{ mT}}{13.03 \text{ to} - 19.92 \text{ mT}}$, time of exposure t = 160 min, temperature of incubation 37 °C)

The present study indicates the exposition to the RMF, as compared to the unexposed controls causing an increase in the efficacy of antibacterial properties of pine oil. We have shown that rotating magnetic fields (RMF) at a frequency, f, between 25 Hz to and 50 Hz increased the antimicrobial efficiency of oil a concentration lower than 50%

https://pubmed.ncbi.nlm.nih.gov/36905969/

Exposure to a rotating magnetic field as a method of increasing the skin permeability of active pharmaceutical ingredients 2023

The paper presents a method of increasing the permeability of various active substances through the skin by means of a rotating magnetic field. The study used 50 Hz RMF and various active pharmaceutical ingredients (APIs) such as caffeine, ibuprofen, naproxen, ketoprofen, and paracetamol. Various concentrations of active substance solutions in ethanol were used in the research, corresponding to those in commercial preparations. Each experiment was conducted for 24 h. It was shown that, regardless of the active compound used, an increase in drug transport through the skin was observed with RMF exposure. Furthermore, the release profiles depended on the active substance used. Exposure to a rotating magnetic field has been shown to effectively increase the permeability of an active substance through the skin.

Rotating magnetic field delays human umbilical vein endothelial cell aging and prolongs the lifespan of Caenorhabditis elegans 2019

The biological effects of magnetic fields are a research hotspot in the field of biomedical engineering. In this study, we further investigated the effects of a rotating magnetic field (RMF; 0.2 T, 4 Hz) on the growth of human umbilical vein endothelial cells (HUVECs) and *Caenorhabditis elegans*. The results showed that RMF exposure prolonged the lifespan of *C. elegans* and slowed the aging of HUVECs. RMF treatment of HUVECs showed that activation of adenosine 5'- monophosphate (AMP)-activated protein kinase (AMPK) was associated with decreased mitochondrial membrane potential (MMP) due to increased intracellular Ca²⁺ concentrations induced by endoplasmic reticulum stress in anti-aging mechanisms. RMF also promoted the health status of *C. elegans* by improving activity, reducing age-related pigment accumulation, delaying Aβ-induced paralysis and increasing resistance to heat and oxidative stress. The prolonged lifespan of *C. elegans* was associated with decreased levels of daf-16 which related to the insulin/insulin-like growth factor signaling pathway (IIS) activity and reactive oxygen species (ROS), whereas the heat shock transcription factor-1 (hsf-1) pathway was not involved. Moreover, the level of autophagy was increased after RMF treatment. These findings expand our understanding of the potential mechanisms by which RMF treatment prolongs lifespan. The entire experimental equipment consisted mainly of natural magnets (Figure 1A). The experimental material was placed 6 cm (0.2 T) from the motor-driven rotating magnet, which produced a 4 Hz magnetic field change frequency. The frequency of the magnet rotation and the

timing of the changes in the magnetic field direction were constant and the entire experimental setup provided an environment for culturing the cells (Figure 1B, 1C).

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10187713/pdf/ad-14-3-825.pdf

Which Factors Influence Healthy Aging? A Lesson from the Longevity Village of Bama in China 2023

Hence, the geomagnetic intensities of the villages in limestone rocky mountain areas are generally higher than those of the villages in hilly sandstone areas. This pattern is roughly consistent with the spatial distribution of the long-lived population in Bama [131]. A "power window" curve describes the relationship between geomagnetic field intensity and longevity in Bama villages [131]. Nevertheless, few studies to date have investigated this association in Bama. An appropriate geomagnetic field promotes cell growth [144], activates cells [145], balances endocrine disorders [146], promotes blood circulation [144, 147], promotes inflammation regression [148], reduces swelling and pain [149], and regulates blood pressure [150].

https://pubmed.ncbi.nlm.nih.gov/9084869/

Action of a 50 Hz magnetic field on proliferation of cells in culture 1997

Proliferation of SV40-3T3 mouse fibroblasts and human HL-60 promyelocytes was studied after treatment with a sinusoidal **2 mT 50 Hz** magnetic field. A single exposure of 60 minutes caused quasicyclic changes in the number of SV40-3T3 cultures as function of time after treatment, which was interpreted to be due to the induction of chronobiological mechanisms by the field. Moreover, small variations in cell cycle distribution were measured during postexposure incubation for both cell lines. To discriminate between the effect of the magnetic vector and the induced electric field, HL-60 cell exposure was also performed on organ culture dishes. These dishes consist of two coaxially centered, isolated compartments in which different electric field levels are induced in the medium during treatment. Cell growth was affected in the outer compartment only where the induced electric field ranged from 8 to 12 mVpeak/meter at 2 mT, but it was not affected in the inner compartment (field range 0-4 mVpeak/meter). This suggests that the effects on cell growth are due to the induced electric field and are expressed only above a threshold of between 4 and 8 mVpeak/meter.

Notes: 2mT at 50Hz(20ms), means 1 cycle takes 20ms (since electromagnet then distance independant)

https://www.physicscurriculum.com/magnetism3d \$79usd

https://pubmed.ncbi.nlm.nih.gov/23594452/

The use of magnetic field for the reduction of inflammation: a review of the history and therapeutic results 2013

Immunological studies show that MF therapy, even low-intensity MF, interacts with cells and tissues, and the use of MF as an alternative or complement to currently prescribed therapies could lead to a faster reduction in the inflammatory response.

https://pubmed.ncbi.nlm.nih.gov/20329696/

Low frequency pulsed electromagnetic field--a viable alternative therapy for arthritis 2009

Optimization of the physical window comprising the electromagnetic field generator and signal properties (frequency, intensity, duration, waveform) with the biological window, inclusive of the experimental model, age and stimulus has helped in achieving consistent beneficial results. Low frequency pulsed electromagnetic field (PEMF) can provide noninvasive, safe and easy to apply method to treat pain, inflammation and dysfunctions associated with rheumatoid arthritis (RA) and osteoarthritis (OA) and PEMF has a long term record of safety. This review focusses on the therapeutic application of PEMF in the treatment of these forms of arthritis. The analysis of various studies (animal models of arthritis, cell culture systems and clinical trials) reporting the use of PEMF for arthritis cure has conclusively shown that PEMF not only alleviates the pain in the arthritis condition but it also affords chondroprotection, exerts antiinflammatory action and helps in bone remodeling and this could be developed as a viable alternative for arthritis therapy.

https://pubmed.ncbi.nlm.nih.gov/37510998/

Pulsed Electromagnetic Fields (PEMF)-Physiological Response and Its Potential in Trauma Treatment 2023

In this review, we give a birds-eye view of the vast landscape of studies that have been published on PEMF, presenting the reader with a scaffolded summary of relevant literature starting from categorical literature reviews down to individual studies for future research studies and clinical use. We also highlight discrepancies within the many diverse study setups to find common reporting parameters that can lead to a better universal understanding of PEMF effects.

https://pubmed.ncbi.nlm.nih.gov/36574882/

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susceptibility of antibiotic-resistant bacteria to common antibiotics. Besides, there are other biological effects of RMF on blood, bone, prenatal exposure, enzyme activity, immune function, aging, parasite, endocrine, wound healing, and plants. These discoveries demonstrate that RMF have great application potential in health care, medical treatment, fermentation engineering, and even agriculture. However, in some cases like pregnancy, RMF exposure may need to be avoided. Finally, the specific mechanisms of RMF's biological effects remain unrevealed, despite various hypotheses and theories. It does not prevent us from using it for our good.

https://pubmed.ncbi.nlm.nih.gov/16304694/

Effects of 0.4 T rotating magnetic field exposure on density, strength, calcium and metabolism of rat thigh bones 2006

Synergy of daily RMF exposure (30 min a day for 30 days using an 8 Hz rotary 0.4 T MF) with calcium supplement tended to increase the indexes of thigh bone density, energy absorption, maximum load, maximum flexibility, and elastic deformation as compared to those of untreated OVX control group. The study indicated that RMF exposure to both male and OVX female rats for 120 min a day over 15 day period should effectively promote increase of bone calcium contents (BCC) and bone-specific alkaline phosphatase (BAP) in rats thigh bone as well as a corresponding decrease in deoxypyridinoline crosslinks (DPD).

https://pubmed.ncbi.nlm.nih.gov/38612456/

The Effect of a Rotating Magnetic Field on the Regenerative Potential of Platelets 2024

Platelets are actively involved in tissue injury site regeneration by producing a wide spectrum of platelet-derived growth factors such as PDGF (platelet-derived growth factor), IGF-1 (insulin-like growth factor), TGF- β 1 (transforming growth factor β), FGF (fibroblast growth factor), etc. A rotating magnetic field (RMF) can regulate biological functions, including reduction or induction regarding inflammatory processes, cell differentiation, and gene expression, to determine the effect of an RMF on the regenerative potential of platelets. The study group consisted of 30 healthy female and male volunteers (n = 15), from which plasma was collected. A portion of the plasma was extracted and treated as an internal control group. Subsequent doses of plasma were exposed to RMF at different frequencies (25 and 50 Hz) for 1 and 3 h. Then, the concentrations of growth factors (IGF-1, PDGF-BB, TGF- β 1, and FGF-1) were determined in the obtained material by the ELISA method. There were statistically significant differences in the PDGF-BB, TGF- β 1, IGF-1, and FGF-1 concentrations between the analyzed groups. The highest concentration of PDGF-BB was observed in the samples placed in RMF for 1 h at 25 Hz. For TGF- β 1, the highest concentrations were obtained in the samples exposed to RMF for 3 h at 25 Hz and 1 h at 50 Hz. The highest concentrations of IGF-1 and FGF-1 were shown in plasma placed in RMF for 3 h at 25 Hz. An RMF may increase the regenerative potential of platelets. It was noted that female platelets may respond more strongly to RMF than male platelets.

https://pubmed.ncbi.nlm.nih.gov/39057024/

Safety of Exposure to 0.2 T and 4 Hz Rotating Magnetic Field: A Ten-Month Study on C57BL/6 Mice 2024

Amidst the burgeoning interest in rotating magnetic fields (RMF) within biological research, there remains a notable gap in the scientific evidence concerning the long-term safety of RMF. Thus, this study aimed to investigate the safety of protracted exposure to a 0.2 T, 4 Hz RMF over 10 months in mice. Two-month-old female C57BL/6 mice were randomly allocated to either the RMF group (exposed to 0.2 T, 4 Hz real RMF) or the SHAM group (exposed to 0 T, 4 Hz sham RMF). Throughout the experiment, the murine weekly body weights were recorded, and their behavioral traits were assessed via open field tests. In the final month, a comprehensive evaluation of the murine overall health was conducted, encompassing analyses of blood parameters, histomorphological examination of major organs, and skeletal assessments using X-ray and micro-CT imaging. The murine immune system and lipid metabolism were evaluated through immunochip analysis and metabolomics. Notably, no discernible adverse effects with RMF exposure were observed. Murine body weight, locomotor behavior, organ histomorphology, and skeletal health remained unaffected by RMF. Blood analysis revealed subtle changes in hormone and lipid levels between the SHAM and RMF groups, yet these differences did not reach statistical significance. Moreover, RMF led to elevated serum interleukin-28 (IL-28) levels, albeit within the normal range, and modest alterations in serum lipid metabolites. Conclusively, mice exposed to the 0.2 T, 4 Hz RMF for 10 months displayed no significant signs of chronic toxicity, indicating its potential clinical application as a physical therapy.

https://pubmed.ncbi.nlm.nih.gov/30142006/

Moderate intensity low frequency rotating magnetic field inhibits breast cancer growth in mice 2018

Moderate intensity low frequency rotating magnetic field (LF-RMF) has been shown to inhibit melanoma, liver and lung cancer growth in mice. However, its effects on other types of cancers have not been investigated in vivo. Here, we show that 0-0.15T moderate intensity 4.2 Hz LF-RMF can inhibit tumor growth in mice bearing MDA-MB231 and MCF7 human breast cancer cells by over 30%. In contrast, the human gastrointestinal stromal tumor GIST-T1 growth was not inhibited by LF-RMF. In all RMF treatments, there were no apparent adverse effects on mice organs, body weight or water/food consumptions. However, the alanine aminotransferase (ALT) level was decreased in LF-RMF-treated mice bearing MCF7 and GIST-T1 cells, which indicated alleviated liver damage. Therefore, our study shows that moderate intensity LF-RMF might be a safe physical method that has clinical potentials to be used to inhibit breast cancer growth in the future.

https://pubmed.ncbi.nlm.nih.gov/38420580/

Gradient Rotating Magnetic Fields Impairing F-Actin-Related Gene CCDC150 to Inhibit Triple-Negative Breast Cancer Metastasis by Inactivating TGFβ1/SMAD3 Signaling Pathway 2024

Triple-negative breast cancer (TNBC) is the most aggressive and lethal malignancy in women, with a lack of effective targeted drugs and treatment techniques. Gradient rotating magnetic field (RMF) is a new technology used in oncology physiotherapy, showing promising clinical applications due to its satisfactory biosafety and the abundant mechanical force stimuli it provides. However, its antitumor effects and underlying molecular mechanisms are not yet clear. We designed two sets of gradient RMF devices for cell culture and animal handling. Gradient RMF exposure had a notable impact on the F-actin arrangement of MDA-MB-231, BT-549, and MDA-MB-468 cells, inhibiting cell migration and invasion. A potential cytoskeleton F-actin-associated gene, CCDC150, was found to be enriched in clinical TNBC tumors and cells. CCDC150 negatively correlated with the overall survival rate of TNBC patients. CCDC150 promoted TNBC migration and invasion via activation of the transforming growth factor $\beta 1$ (TGF- $\beta 1$)/SMAD3 signaling pathway in vitro and in vivo. CCDC150 was also identified as a magnetic field response gene, and it was marked down-regulated after gradient RMF exposure. CCDC150 silencing and gradient RMF exposure both suppressed TNBC tumor growth and liver metastasis. Therefore, gradient RMF exposure may be an effective TNBC treatment, and CCDC150 may emerge as a potential target for TNBC therapy.

https://pubmed.ncbi.nlm.nih.gov/38801615/

Systematic simulation of tumor cell invasion and migration in response to time-varying rotating magnetic field 2024

Cancer invasion and migration play a pivotal role in tumor malignancy, which is a major cause of most cancer deaths. Rotating magnetic field (RMF), one of the typical dynamic magnetic fields, can exert substantial mechanical influence on cells. However, studying the effects of RMF on cell is challenging due to its complex parameters, such as variation of magnetic field intensity and direction. Here, we developed a systematic simulation method to explore the influence of

RMF on tumor invasion and migration, including a finite element method (FEM) model and a cell-based hybrid numerical model. Coupling with the data of magnetic field from FEM, the cell-based hybrid numerical model was established to simulate the tumor cell invasion and migration. This model employed partial differential equations (PDEs) and finite difference method to depict cellular activities and solve these equations in a discrete system. PDEs were used to depict cell activities, and finite difference method was used to solve the equations in discrete system. As a result, this study provides valuable insights into the potential applications of RMF in tumor treatment, and a series of in vitro experiments were performed to verify the simulation results, demonstrating the model's reliability and its capacity to predict experimental outcomes and identify pertinent factors. Furthermore, these findings shed new light on the mechanical and chemical interplay between cells and the ECM, offering new insights and providing a novel foundation for both experimental and theoretical advancements in tumor treatment by using RMF.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4724455/

Rotating Magnetic Field Induced Oscillation of Magnetic Particles for in vivo Mechanical Destruction of Malignant Glioma 2016

Magnetic particles that can be precisely controlled under a magnetic field and transduce energy from the applied field open the way for innovative cancer treatment. Although these particles represent an area of active development for drug delivery and magnetic hyperthermia, the *in vivo* anti-tumor effect under a low-frequency magnetic field using magnetic particles has not yet been demonstrated. To-date, induced cancer cell death via the oscillation of nanoparticles under a low frequency magnetic field has only been observed *in-vitro*. In this report, we demonstrate the successful use of spin-vortex, disk-shaped permalloy magnetic particles in a low-frequency, rotating magnetic field for the *in vitro* and *in vivo* destruction of glioma cells. The internalized nanomagnets align themselves to the plane of the rotating magnetic field, creating a strong mechanical force which damages the cancer cell structure inducing programmed cell death. *In vivo*, the magnetic field treatment successfully reduces the brain tumor size and increases the survival rate of mice bearing intracranial glioma xenografts, without adverse side effects. This study demonstrates the novel approach of controlling magnetic particles for treating malignant glioma that should be applicable to treat a wide range of cancers.

The rotating magnetic field station used an NdFeB Halbach Array magnet (Bunting Magnetics Europe Ltd., Hertfordshire, UK), which produces a uniform 1 Tesla magnetic field diametrically across the central air gap. The magnet was mounted on a motor to control its rotation and the head of the mice was placed inside the central air gap.

https://pubmed.ncbi.nlm.nih.gov/38904930/

Rotating magnetic field improved cognitive and memory impairments in a sporadic ad model of mice by regulating microglial polarization 2024 Neuroinflammation, triggered by aberrantly activated microglia, is widely recognized as a key contributor to the initiation and progression of Alzheimer's disease (AD). Microglial activation in the central nervous system (CNS) can be classified into two distinct phenotypes: the pro-inflammatory M1 phenotype and the antiinflammatory M2 phenotype. In this study, we investigated the effects of a non-invasive rotating magnetic field (RMF) (0.2T, 4Hz) on cognitive and memory impairments in a sporadic AD model of female Kunming mice induced by AlCl₃ and D-gal. Our findings revealed significant improvements in cognitive and memory impairments following RMF treatment. Furthermore, RMF treatment led to reduced amyloid-beta (Aβ) deposition, mitigated damage to hippocampal morphology, prevented synaptic and neuronal loss, and alleviated cell apoptosis in the hippocampus and cortex of AD mice. Notably, RMF treatment resulted in reduced aluminum deposition in the brains of AD mice. In cellular experiments, RMF promoted the M1-M2 polarization transition and enhanced amyloid phagocytosis in cultured BV2 cells while inhibiting the TLR4/NF-κB/MAPK pathway. Collectively, these results demonstrate that RMF improves memory and cognitive impairments in a sporadic AD model, potentially by promoting the M1 to M2 transition of microglial polarization through inhibition of the NF-κB/MAPK signaling pathway. These findings suggest the promising therapeutic applications of RMF in the clinical treatment of AD.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10017101/

Intermittent F-actin Perturbations by Magnetic Fields Inhibit Breast Cancer Metastasis 2023

Here, we show that 0.1/0.4-T 4.2-Hz moderate-intensity low-frequency rotating magnetic field-induced electric field could directly decrease F-actin formation in vitro and in vivo, which results in decreased breast cancer cell migration, invasion, and attachment. Moreover, low-frequency rotating magnetic fields generated significantly different effects on F-actin in breast cancer vs. noncancerous cells, including F-actin number and their recovery after magnetic field retrieval. Using an intermittent treatment modality, low-frequency rotating magnetic fields could significantly reduce mouse breast cancer metastasis, prolong mouse survival by 31.5 to 46.0% (*P* < 0.0001), and improve their overall physical condition.

A pair of permanent magnets (rare-earth permanent magnet N42M) were equipped on a rotor with opposite poles facing up, which rotate at 4.2 Hz (the maximum speed of the instrument) clockwise

https://pubmed.ncbi.nlm.nih.gov/38622314/

The effect of a rotating magnetic field on the antioxidant system in healthy volunteers - preliminary study 2024

Oxidative stress is characterized by an excessive concentration of reactive oxygen species (ROS) resulting from a disturbance in the balance between ROS production and their removal by antioxidant systems (SOD, CAT, GPx). Prolonged and intense oxidative stress can cause various forms of damage to cells, which markers are total antioxidant capacity (TAC), reactive oxygen species modulator (ROMO1), and malondialdehyde (MDA). It has been demonstrated that magnetic fields can positively affect human health, for example, by reducing oxidative stress. Determination of the effect of a rotating magnetic field (RMF) on the activity/concentration of selected oxidative stress markers. A group of 30 healthy volunteers (15 women and 15 men) (mean age 24.8 ± 5.1) in the study classified into the following groups: internal control group (CG);1 h 25 Hz (samples placed in the field for one hour at 25 Hz); 3 h 25 Hz (samples placed in the field for 3 h at 25 Hz), the 1 h 50 Hz group (placed in RMF for an hour at 50 Hz), and a group of 3 h 50 Hz (samples placed in the field for 3 h at 50 Hz). Serum samples were collected in K₂EDTA tubes. The magnetic induction value obtained for RMF is **37.06 mT and 42.64 mT**. Activity/concentration of selected oxidative stress markers was analyzed by ELISA. The influence of an RMF on the activity/concentration of SOD, MDA, TAC, and ROMO1 was demonstrated (p < 0.001; p = 0.0013; p < 0.001; p = 0.003). The RFM can reduce oxidative stress, as evidenced by higher SOD and CAT activities in the CG than in samples placed in the RFM. Prolonged exposure to the RFM at 50 Hz increased the TAC level, indicating an **intensification of oxidative stress** in these samples. The optimal conditions for staying in the RFM (reducing oxidative stress) are 1 h 50 Hz for SOD and MDA; 3 h 25 Hz for CAT and TAC. In the case of ROMO1, it is stated that 1 h 25 Hz are the optimal conditions for no increased production of ROS.

https://pubmed.ncbi.nlm.nih.gov/39021081/

Rotating magnetic field inhibits Aß protein aggregation and alleviates cognitive impairment in Alzheimer's disease mice 2024

In this study, we examined the effects of a moderate-intensity rotating magnetic field (RMF) on Aβ aggregation and AD pathogenesis. Results indicated that the RMF directly inhibited Aβ amyloid fibril formation and reduced Aβ-induced cytotoxicity in neural cells *in vitro*. Using the AD mouse model APP/PS1, RMF restored motor abilities to healthy control levels and significantly alleviated cognitive impairments, including exploration and spatial and non-spatial memory abilities. Tissue examinations demonstrated that RMF reduced amyloid plaque accumulation, attenuated microglial activation, and reduced oxidative stress in the APP/PS1 mouse brain. These findings suggest that RMF holds considerable potential as a non-invasive, high-penetration physical approach for AD treatment.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8947294/

Rotating Magnetic Field-Assisted Reactor Enhances Mechanisms of Phage Adsorption on Bacterial Cell Surface 2022

The rotating magnetic field (RMF) is a promising biotechnological method for process intensification, especially for the intensification of micromixing and mass transfer. This study evaluates the use of RMF to enhance the infection process by influencing bacteriophage adsorption rate. 5. Conclusions

Present studies indicated that the adsorption process of T4 bacteriophage on the bacteria host's surface could be improved by RMF exposition. It has been proved previously that the RMF system can act as an active micro-mixer in water solution systems such as bioliquids. The culture medium contains many magnetically vulnerable particles (e.g., ions), which are forced to move under the action of the external magnetic field, thus also creating a movement of liquid particles causing the micro-mixing phenomenon. It is well known that the mixing process can affect the adsorption process, which was observed during these studies. Moreover, the electromagnetic field may charge surfaces and an induced electric field. Due to the increased charges on the host cell surface and bacteriophage tail (see Figure 3), the adsorption of bacteriophage may be more accessible thanks to the stronger electrostatic forces and RMF-forced movement of the phage near the surface of the host cell, compared to the conditions without the RMF. Forthcoming works should concentrate on the influence of RMF on bacteriophages lytic activity and therapeutic effectiveness.

https://www.sciencedirect.com/science/article/abs/pii/S0009250911001084?via%3Dihub

Studies of a mixing process induced by a transverse rotating magnetic field 2011

This study reports on research results in the field of a mixing process under the action of a transverse rotating <u>magnetic field</u> (TRMF). The main objective of this paper is to present the effect of this type of a magnetic field on the mixing time.

The possibility of using the magnetic particles (Fe₃O₄) as active micro-stirrers under the influence of a TRMF for active enhancement of a mixing process was considered.

In addition, the homogeneity of a system is dependent on the stirred tank configuration, the fluid properties as well as the performance characteristics of the employed agitator.

The use of magnetic particles as active micro-stirrers has attractive applications in the various areas of the chemical engineering.

The TRMF induces a time-averaged azimuthal force (Lorentz force), which drives the flow of the electrically conducting fluid in a circumferential direction.

https://www.sciencedirect.com/science/article/abs/pii/S0255270113000263?via%3Dihub

Mixing energy investigations in a liquid vessel that is mixed by using a rotating magnetic field 2013 he purpose of the present report is, first, to develop the basic equations and similarity criteria governing the mixing system with the magnetic particles under the

effect of a <u>rotating magnetic field</u> (RMF);

The data obtained for mixing efficiency was correlated in terms of the <u>modified Reynolds number</u> which can be used for predictions of mixing process in systems with the magnetic particles. The <u>magnetic particle may be treated as a miniaturized mixer</u> and it may offer a unique alternative approach to mixing. Static magnetic fields (SMFs) are used as electromagnetic brakes and transverse rotating magnetic fields (TRMFs) are commonly used as electromagnetic stirrers [1].

https://pubmed.ncbi.nlm.nih.gov/26344254/

Modification of bacterial cellulose through exposure to the rotating magnetic field 2015

The aim of the study was to assess the influence of rotating magnetic field (RMF) on production rate and quality parameters of bacterial cellulose synthetized by Glucanacetobacter xylinus. Bacterial cultures were exposed to RMF (frequency f=50Hz, magnetic induction B=34mT) for 72h at 28°C. The study revealed that cellulose obtained under RMF influence displayed higher water absorption, lower density and less interassociated microfibrils comparing to unexposed control. The application of RMF significantly increased the amount of obtained wet cellulose pellicles but decreased the weight and thickness of dry cellulose. Summarizing, the exposure of cellulose-synthesizing G. xylinus to RMF alters cellulose biogenesis and may offer a new biotechnological tool to control this process. As RMF-modified cellulose displays better absorbing properties comparing to non-modified cellulose, our finding, if developed, may find application in the production of dressings for highly exudative wounds.

https://aiche.onlinelibrary.wiley.com/doi/abs/10.1002/aic.15456

Enhancing liquid micromixing using low-frequency rotating nanoparticles 2016

Magnetic nanofluid actuation by rotating magnetic fields was proposed as a high-performance tool for liquid mixing with enhanced micromixing features. A comparative study was conducted to evaluate the mixing index in T-type mixers of magnetic and nonmagnetic fluids subject to static (SMF), oscillating (OMF), and rotating (RMF) magnetic fields. RMF excitation unveiled superior mixing indices with strong dependences to magnetic field frequency and content of magnetic nanoparticles.

https://pubs.aip.org/aip/pof/article/31/6/063603/1068267/Modeling-of-mass-transfer-enhancement-in-a

Modeling of mass transfer enhancement in a magnetofluidic micromixer 2019

Mixing efficiency may reach 90%, which is significantly higher than that of molecular diffusion. <u>Zhu and Nguyen (2012b)</u> reported the mixing phenomena caused by the interaction between a uniform magnetic field and a ferrofluid in a circular microfluidic chamber. Both studies used an electromagnet to generate the magnetic field. The authors showed that a mixing efficiency as high as 90% can be achieved instantaneously at a relatively low magnetic field of less than 10 mT. <u>Feng et al. (2016)</u>

https://pubmed.ncbi.nlm.nih.gov/36132704/

Magneto-mechanical destruction of cancer-associated fibroblasts using ultra-small iron oxide nanoparticles and low frequency rotating magnetic fields 2022

The destruction of cells using the mechanical activation of magnetic nanoparticles with low-frequency magnetic fields constitutes a recent and interesting approach in cancer therapy. Here, we showed that superparamagnetic iron oxide nanoparticles as small as 6 nm were able to induce the death of pancreatic cancer-associated fibroblasts, chosen as a model. An exhaustive screening of the amplitude, frequency, and type (alternating vs. rotating) of magnetic field demonstrated that the best efficacy was obtained for a rotating low-amplitude low-frequency magnetic field (**1 Hz and 40 mT**), reaching a 34% ratio in cell death induction; interestingly, the cell death was not maximized for the largest amplitudes of the magnetic field.

This study established a proof-of-concept that ultra-small nanoparticles can disrupt the tumor microenvironment through mechanical forces generated by mechanical activation of magnetic nanoparticles upon low-frequency rotating magnetic field exposure, opening new opportunities for cancer therapy.

Elongated Nanoparticle Aggregates in Cancer Cells for Mechanical Destruction with Low Frequency Rotating Magnetic Field 2017

Magnetic nanoparticles (MNPs) functionalized with targeting moieties can recognize specific cell components and induce mechanical actuation under magnetic field. Their size is adequate for reaching tumors and targeting cancer cells. However, due to the nanometric size, the force generated by MNPs is smaller than the force required for largely disrupting key components of cells. Here, we show the magnetic assembly process of the nanoparticles inside the cells, to form elongated aggregates with the size required to produce elevated mechanical forces. We synthesized iron oxide nanoparticles doped with zinc, to obtain high magnetization, and functionalized with the epidermal growth factor (EGF) peptide for targeting cancer cells. Under a low frequency rotating magnetic field at **15 Hz** and 40 mT, the internalized EGF-MNPs formed elongated aggregates and generated hundreds of pN to dramatically damage the plasma and lysosomal membranes. The physical disruption, including leakage of lysosomal hydrolases into the cytosol, led to programmed cell death and necrosis. Our work provides a novel strategy of designing magnetic nanomedicines for mechanical destruction of cancer cells.

https://pubmed.ncbi.nlm.nih.gov/20625540/

Simulating Magnetic Nanoparticle Behavior in Low-field MRI under Transverse Rotating Fields and Imposed Fluid Flow 2010

In the presence of alternating-sinusoidal or rotating magnetic fields, magnetic nanoparticles will act to realign their magnetic moment with the applied magnetic field. The realignment is characterized by the nanoparticle's time constant, τ . As the magnetic field frequency is increased, the nanoparticle's magnetic moment lags the applied magnetic field at a constant angle for a given frequency, Ω , in rad/s. Associated with this misalignment is a power dissipation that increases the bulk magnetic fluid's temperature which has been utilized as a method of magnetic nanoparticle hyperthermia, particularly suited for cancer in low-perfusion tissue (e.g., breast) where temperature increases of between 4°C and 7°C above the ambient in vivo temperature cause tumor hyperthermia.

https://pubmed.ncbi.nlm.nih.gov/29970658/

Effect of low-frequency rotary magnetic fields on advanced gastric cancer: Survival and palliation of general symptoms 2018 In this study, we investigated 21 patients with advanced gastric cancer (AGC) treated with 420 r/min, 0.4-T low-frequency rotary MFs. The treatment area encompassed the primary tumor sites, metastatic sites, and metastatic lymph nodes. In addition, the patients were treated 2 h per day, 5 days per week for 6-12 weeks.

Results: Our results demonstrated that low-frequency rotary MFs improved abdominal pain in 9/21 (42.9%), nausea/vomiting in 4/21 (19.0%), weight loss in 11/21 (52.4%), ongoing blood loss in 2/21 (9.5%), physical strength in 5/21 (23.8%), and sleep quality in 4/21 (19.0%) patients. No severe toxicity and side effect were observed in our trial. The median survival time was 8.0 months (95% confidence interval, 5.190-10.810). The 1-year survival rate was 25.8%. Conclusion: Low-frequency rotary MFs may prolong survival and improve general symptom of AGC patients, as an effective, well-tolerated, and safe treatment choice.

https://www.nature.com/articles/s41598-019-39198-y

Rotating magnetic field as tool for enhancing enzymes properties - laccase case study 2019

The aim of this study was to analyse the effect of rotating magnetic field (RMF) exposition on the fungal laccase catalytic properties. The results obtained in the study revealed that RMF may positively alter the laccase activity. A significant increase in activities of 11%, 11%, and 9% were observed at 10 Hz, 40 Hz and 50 Hz, respectively. Exposure of laccase to the rotating magnetic field resulted in its increased activity at broader pH range and a slight shift in optimum pH from 4.0 to 4.5 at RMF with frequency 20 Hz. The results show that the enzyme activity, stability, and optimum pH can be significantly altered depending on the characteristic of the applied RMF. Application of rotating magnetic field opens a new way for controlling and directions of enzyme-based bioprocessing.

https://pubmed.ncbi.nlm.nih.gov/27786558/

Increased water content in bacterial cellulose synthesized under rotating magnetic fields 2017

The current study describes properties of bacterial cellulose (BC) obtained from Komagataeibacter xylinus cultures exposed to the rotating magnetic field (RMF) of 50 Hz frequency and magnetic induction of 34 mT for controlled time during 6 days of cultivation.

The obtained BC displayed an altered micro-structure, degree of porosity, and water-related parameters in comparison to the non-treated, control BC samples.

https://pubmed.ncbi.nlm.nih.gov/29729595/

Decrease of motor cortex excitability following exposure to a 20 Hz magnetic field as generated by a rotating permanent magnet 2018 Fourteen healthy volunteers received 20 Hz tAMF stimulation over the MC, over the vertex, and 20 Hz tACS over the MC, each with a duration of 15 min. Conclusions: The recorded single and paired pulse MEPs indicate a general decrease of MC excitability following 15 min of tAMF stimulation. Significance: The effects demonstrate that devices based on rotating magnets are potentially suited to become a novel brain stimulation tool in clinical neurophysiology.

https://pubmed.ncbi.nlm.nih.gov/25196555/

Extremely low frequency magnetic fields inhibit adipogenesis of human mesenchymal stem cells 2014 In the present study, we investigated the effects of 7.5 Hz, 0.4 T ELF-MF on differentiation of human umbilical cord MSCs. We found that ELF-MF inhibited adipogenic differentiation (exposed 2 h/day for 15 days) of MSCs but had no effect on osteogenic differentiation (exposed 2 h/day for 21 days).

https://www.semanticscholar.org/paper/The-hemoprotective-effects-of-a-rotary-magnetic-in-Xie-Qi/e39cd1191f5dc087d298977871cea29f76dec0c1 The hemoprotective effects of a rotary magnetic field in mice exposed to irradiation 2008

Conclusion The RMF treatment had an obvious protective effect against the effects of irradiation and it accelerated the recovery of hematopeiesis and the hematopoietic microenvironment in mouse bone marrow

https://pubmed.ncbi.nlm.nih.gov/18821389/

The expression and intranuclear distribution of nucleolin in HL-60 and K-562 cells after repeated, short-term exposition to rotating magnetic fields 2008

The aim of the study was to analyze the influence of rotating magnetic fields (RMF) on the expression and intranuclear distribution of nucleolin, protein involved in ribosome biosynthesis, in HL-60 (acute promyelocytic leukemia) and K-562 (chronic myelogenous leukemia) established human cell lines. Conclusion: The nucleolin is responsive to RMF in HL-60 and K-562. The increase of its expression may indicate a reaction of cells to RMF and it may influence their other biological properties.

https://pubmed.ncbi.nlm.nih.gov/23713419/

Effects of 50 Hz rotating magnetic field on the viability of Escherichia coli and Staphylococcus aureus 2014

The obtained results prove that RMF (B = 30 mT, f = 50 Hz) has a stimulatory effect on the growth and metabolic activity of E. coli and S. aureus. Furthermore,

taking into account the time of exposure, stronger influence of RMF on the viability was observed in S. aureus cultures, which may indicate that this effect depends on the shape of the exposed cells.

https://pubmed.ncbi.nlm.nih.gov/24314291/

Effect of low frequency magnetic fields on melanoma: tumor inhibition and immune modulation 2013

The mice were then exposed to an LF-MF (0.4 T, 7.5 Hz) for 43 days. Survival rate, tumor markers and the innate and adaptive immune parameters were measured.

LF-MF inhibited the growth and metastasis of melanoma cancer cells and improved immune function of tumor-bearing mice.

https://pubmed.ncbi.nlm.nih.gov/24278103/

Low frequency magnetic fields enhance antitumor immune response against mouse H22 hepatocellular carcinoma 2013

The mice were then exposed to a low frequency MF (D.4 T, 7.5 Hz) for 30 days. Survival rate, tumor growth and the innate and adaptive immune parameters were measured.

Conclusion: The inhibitory effect of MF on tumor growth was related to the improvement of immune function in the tumor-bearing mice.

https://pubmed.ncbi.nlm.nih.gov/18204839/

Study of rotating permanent magnetic field to treat steroid-induced osteonecrosis of femoral head 2009

Sixty New Zealand rabbit models with steroid-induced necrosis of femoral head were exposed to a rotating permanent magnetic field (RPMF) RPMF could affect various critical aspects in the course of femoral head necrosis, which will be a promising measure in the prevention and treatment of steroidinduced necrosis of femoral head, especially in the early stage

https://pubmed.ncbi.nlm.nih.gov/28389657/

LF-MF inhibits iron metabolism and suppresses lung cancer through activation of P53-miR-34a-E2F1/E2F3 pathway 2017

In this study, Tumor- bearing mice subcutaneously inoculated with Lewis lung cancer cells were exposed to a LF-MF (0.4T, 7.5 Hz) for 35 days and Survival rate, tumor growth and the tumor markers were measured. Results showed that tumor growth was obviously inhibited with a prolonged survival of tumor- bearing mice by LF-MF exposure.

Taken together, these observations imply that LF-MF suppressed lung cancer via inhibiting cell iron metabolism, stabilizing p53 protein and activation P53- miR-34a-E2F1/E2F3 pathway.

https://pubmed.ncbi.nlm.nih.gov/8353767/

[The effect of rotating magnetic fields on the growth of Deal's guinea pig sarcoma transplanted subcutaneously in guinea pigs] 1993

Over a period of 24 days the animals were daily two times exposed to RMF for 3 hours. The animals were sacrificed in chloroform anesthesia, the inguinal tumors, lungs and hearts were removed and weighed. The following findings were recorded: 1. RMF inhibited the growth of DGPS cells in experimental guinea pigs compared to control animals (p < 0.001); 2. In the experimental animals DGPS cells did not metastasize into the lung parenchyma; 3. The pathological characteristics of the tumors in the experimental and control group of guinea pigs tended to be different. (Tab. 3, Ref. 14.)

https://pubmed.ncbi.nlm.nih.gov/16027840/

Regulation of proteolytic activity of pepsin in rats [correction of mice] by rotating electromagnetic field 2005

In experiments on Wistar rats we studied the effect of low-frequency electromagnetic field rotating in either right-handed or a left-handed sense on proteolytic activity of pepsin. The right-handed rotating field increased, while left-handed rotating field decreased pepsin activity. Possible mechanisms of these changes in pepsin activity are discussed.

https://pubmed.ncbi.nlm.nih.gov/23162666/

A pilot study of extremely low-frequency magnetic fields in advanced non-small cell lung cancer: Effects on survival and palliation of general symptoms 2012

We investigated the effects of 420 r/min, 0.4-T extremely low-frequency MFs (ELF-MFs) on the survival and palliation of general symptoms in 13 advanced nonsmall cell lung cancer (NSCLC) patients.

Additionally, the patients were treated 2 h per day, 5 days per week for 6-10 weeks.

Our results demonstrated that decreased pleural effusion, remission of shortness of breath, relief of cancer pain, increased appetite, improved physical strength, regular bowel movement and better sleep quality was detected in 2 (15.4%), 5 (38.5%), 5 (38.5%), 6 (46.2%), 9 (69.2%), 1 (7.7%) and 2 (15.4%) patients, respectively.

No severe toxicity or side-effects were detected in our trial. The median survival was 6.0 months (95% CI, 1.0-11.0). The 1- and 2-year survival rates were 31.7 and 15.9%, respectively. This study is the first to describe survival and palliation of general symptoms in advanced NSCLC patients treated with ELF-MFs. As an effective, well-tolerated and safe treatment choice, ELF-MFs may prolong survival and improve general symptoms of advanced NSCLC patients.

https://pubmed.ncbi.nlm.nih.gov/26807660/

Extremely low frequency magnetic fields regulate differentiation of regulatory T cells: Potential role for ROS-mediated inhibition on AKT 2016 Tumor-bearing mice were exposed to sham ELF-MFs and ELF-MFs (0.4 T, 7.5 Hz) 2 h/day for 27 days.

Furthermore, reactive oxygen species (ROS) was increased and phospho-serine/threonine protein kinase (p-AKT) was inhibited in both T cells and Jurkat cells. Taken together, our data show that ELF-MF exposure promoted the inhibitory effect of ROS on AKT pathway and decreased Foxp3 expression, which provides an explanation for why ELF-MF exposure can inhibit differentiation of Treg cells and enhance antitumor effect in metastatic melanoma mouse model.

https://pubmed.ncbi.nlm.nih.gov/135992/

Effect of prolonged exposure to a magnetic field on the haematopoietic stem cell 1976

The authors studied the effect of prolonged exposure (3, 4 and 5 months) to the action of a magnetic field of **180-200 gauss** formed by the poles of a rotating permanent magnet on the haematopoietic stem cells of mouse bone marrow donors. The effect of the field was evaluated from the ability of the donors' bone marrow cells to form haematopoietic colonies in the spleen of lethally irradiated mice. It was found that the number of stem cells was not reduced by the action of the above magnetic field and that proliferative capacity was likewide unimpaired.

https://pubmed.ncbi.nlm.nih.gov/21360556/

Involvement of midkine expression in the inhibitory effects of low-frequency magnetic fields on cancer cells 2011

Results showed that exposure to a 0.4-T, 7.5 Hz MF inhibited the proliferation of BGC-823, MKN-28, A549, and LOVO cells, but not MKN-45 and SPC-A1 cells. Moreover, the inhibitory effect of the MF on BGC-MK cells was lower (12.3%) than that of BGC-823 cells (20.3%). Analysis of the cell cycle showed that exposure to the MF led to a significant increase in the S phase in BGC-823 cells, but not in BGC-MK cells. In addition, organelle morphology was modified in BGC-823 cells exposed to the MF. These results suggest that exposure to a 0.4-T, 7.5 Hz MF could inhibit tumor cell proliferation and disturb the cell cycle. The alteration of MK expression in cancer cells may be related to the inhibitory effect of the MF on these cells.

https://pubmed.ncbi.nlm.nih.gov/26661902/

Nerve-muscle activation by rotating permanent magnet configurations 2016

Here we report a new technique for nerve activation using high speed rotation of permanent magnet configurations, generating a sustained sinusoidal electric field using very low power (of order 10 W). A high ratio of the electric field gradient divided by frequency is shown to be the key indicator for nerve activation at high frequencies. Activation of the cane toad sciatic nerve and attached gastrocnemius muscle was observed at frequencies as low as 180 Hz for activation of the muscle directly and 230 Hz for curved nerves, but probably not in straight sections of nerve.

In contrast, moving permanent magnets can provide a time-varying magnetic field without any heating. The latest high-strength neodymium iron boron (NdFeB) magnets have magnetic remanence of 1.45 T and are equivalent to a 1.1 kA surface current density loop for every millimetre of magnet thickness (Watterson, 2000).

https://pubmed.ncbi.nlm.nih.gov/28924214/

Low Frequency Magnetic Fields Induce Autophagy-associated Cell Death in Lung Cancer through miR-486-mediated Inhibition of Akt/mTOR Signaling Pathway 2017

Our previous studies showed that LF-MFs (0.4 T, 7.5 Hz) can inhibit hepatocellular tumor and metastatic lung cancer *in vivo* 14,15. Of note, compared with chemotherapy and radiotherapy, safety is an advantage of LF-MFs. In a toxicity human study, patients with advanced cancer treated with LF-MFs showed no toxicity and adverse side effects.

We previously reported that LF-MFs prevent lung metastasis of melanoma. Here, the anti-tumor effect of LF-MFs was further confirmed on a Lewis lung carcinoma (LLC) subcutaneous injection mouse model. Cisplatin was used as a positive control. As shown in Fig. <u>1A–C</u>, mice treated with LF-MFs (0.4 T, 7.5 Hz, 4 h/day) for 35 days had reduced tumor weight and tumor volume, which is comparable with mice treated with cisplatin. More importantly, no body weight loss was observed in LF-MFs-treated mice (Fig. <u>1D</u>).

https://pubmed.ncbi.nlm.nih.gov/32265343/

Rotating magnetic field ameliorates experimental autoimmune encephalomyelitis by promoting T cell peripheral accumulation and regulating the balance of Treg and Th1/Th17 2020

Multiple sclerosis (MS) is an autoimmune disease characterized by T cell infiltration and demyelination of the central nervous system (CNS). Experimental autoimmune encephalomyelitis (EAE) is a classical preclinical animal model of MS. In this study, we found that rotating magnetic field (RMF) treatment exerts potential preventive effects on the discovery of EAE, including reducing the severity of the disease and delaying the onset of the disease. The results indicated that RMF (0.2 T, 4 Hz) treatment increases the accumulation of CD4⁺ cells in the spleen and lymph nodes by downregulating the expression of CCL-2, CCL-3 and CCL-5, but has no significant effect on myelin oligodendrocyte glycoprotein (MOG) specific T cell responses.

https://pubmed.ncbi.nlm.nih.gov/18726401/

Molecular mechanism of effect of rotating constant magnetic field on organisms 2001

The effect of RCMF-magnetic therapy apparatus on signal substances was studied. The radioimmunoassay (RIA) suggested that the magnetic field increased beta-endorphin markedly in plasma. ELISA indicated that the magnetic field inhibited vomiting reaction induced by chemotherapy drug, with reversible decrease of serotonin (5-HT) level in brains, small intestine tissue and serum.

The coexistence of NO and AVP may play an important role in the regulation of endocrine and neuroendocrine by the magnetic field. And our data also confirmed that the magnetic field increased the content of NO so strongly that high NO level lasted for 3 hours, also made neuropeptide Y (NPY) cell in medulla stained heavily.

https://www.researchgate.net/publication/341242877_Study_on_the_Effect_of_Rotating_Magnetic_Field_on_Cellular_Response_of_Mammalian_Cells

Study on the Effect of Rotating Magnetic Field on Cellular Response of Mammalian Cells 2020 Thus, the aim of the study was to evaluate the cellular response of L929 fibroblast cell line to a rotating magnetic field (

Thus, the aim of the study was to evaluate the cellular response of L929 fibroblast cell line to a rotating magnetic field (RMF) for 8-h exposure incubation period. We conclude that the exposure of L929 fibroblasts to the rotating magnetic field (RMF) in tested magnetic flux density range alerted the cellular dehydrogenases metabolism in a dose-dependent manner, with the highest values in dehydrogenases activity for cells incubated at 10.06 mT and lowest incubated at 1.23 mT of RMF.

https://pubmed.ncbi.nlm.nih.gov/26809700/

Effect of GO-Fe3O4 and rotating magnetic field on cellular metabolic activity of mammalian cells 2016

The effect of hybrid material-graphene flakes with Fe3O4 nanospheres (GO-Fe3O4), graphene oxide (GO) and magnetite nanospheres (Fe3O4) in rotating magnetic field on mammalian cells metabolism has been studied. Several reports shown that exposure to magnetic field may have influence on cellular membrane permeability. Thus, the aim of presented study was to determine the cellular response of L929 fibroblast cells to nanomaterials and rotating magnetic field for 8-h exposure experiment. The GO had tendency to adsorb proteins, thus cell metabolism was decreased and the effect of that mechanism was enhanced by impact of nanospheres and rotating magnetic field. The highest reduction of cellular metabolism was recorded for WST-1 and NR assays at concentration 100 µg/mL of all tested nanomaterials and magnetic induction value 10.06 mT. The lactate dehydrogenase leakage assay has shown significant changes in membrane permeability. Further studies need to be carried out to precisely determine the mechanism of that process.

https://pubmed.ncbi.nlm.nih.gov/37446167/

Molecular Biological Effects of Weak Low-Frequency Magnetic Fields: Frequency-Amplitude Efficiency Windows and Possible Mechanisms 2023 This review covers the phenomenon of resonance-like responses of biological systems to low-frequency magnetic fields (LFMF). The historical development of this branch of magnetobiology, including the most notable biophysical models that explain the resonance-like responses of biological systems to LFMF with a specific frequency and amplitude, is given. Two groups can be distinguished among these models: one considers ion-cofactors of proteins as the primary targets for the LFMF influence, and the other regards the magnetic moments of particles in biomolecules. Attention is paid to the dependence of resonance-like LFMF effects on the cell type. A radical-pair mechanism of the magnetic field's influence on biochemical processes is described with the example of cryptochrome. Conditions for this mechanism's applicability to explain the biological effects of LFMF are given. A model of the influence of LFMF on radical pairs in biochemical oscillators, which can explain the frequency-amplitude efficiency windows of LFMF, is proposed.