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LOW-INTENSITY LF EM TUMOR TREATING FIELDS: COMMENTS AND IMPLICATIONS FOR INTEGRATIVE MEDICINE \*

SLABA LF EM POLJA ZA TRETMAN MALIG-NIH TUMORA: KOMENTARI I IMPLIKACIJE ZA INTEGRATIVNU MEDICINU \*

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#### Key words

cancer treatment, LF EM tumor treating fields, integrative medicine implications.

#### Ključne reči

tretman kancera, LF EM tumor tretirajuæa polja, implikacije za integrativnu medicinu.

#### Abstract

In past several years a team of scientists from Israel reported of their usage of low-intensity low frequency (LF) electromagnetic (EM) Tumor Treating Fields (TTFs) to cell cultures, animal cancer models, as well as to patients suffering from locally advanced and/or metastatic solid tumors. In April 2011 the U.S. Food and Drug Administration (FDA) approved the NovoTTF-100A System, a new device to treat adults with glioblastoma multiforme (GBM) that recurs or progresses after receiving chemotherapy and radiation therapy. Shortly afterwards, in December 2011 it was announced that the University of Illinois Hospital was the first center in North America to prescribe this treatment for patients GBM. In this communication we provide some information on the TTFs approach, and consider wider implications for integrative medicine.

# Low-Intensity LF EM Tumor Treating Fields

Low-intensity low frequency (LF) electromagnetic (EM) Tumor Treating Fields (TTFs) are a new physical cancer treatment modality that has recently been demonstrated to be highly effective when applied to cell cultures, animal cancer models, as well as patients suffering from locally advanced and/or metastatic solid tumors <sup>[1-6]</sup>. TTFs are alternating electric fields of low intensity (1-3 V/cm) and intermediate frequency (100 - 300 kHz) that are generated by special insulated electrodes applied to the skin surface.

These specially tuned fields have no effect on quiescent cells while having an anti-proliferation and destructive effect on mitotic cells, according to two proposed mechanisms [1-2]: (i) during cytokinesis, TTFs exert forces that move charged or polar macromolecules and organelles towards the narrow neck, separating the newly forming daughter cells, by a process termed dielectrophoresis; (ii) during cell divi-

sion, TTFs also interfere with the polymerization processes of the microtubule spindle. Thus, TTFs disrupt the cell structure, inhibit cell division and result in cell death. In contrast to most anti-cancer agents, TTFs are not associated with any meaningful systemic toxicity [2-6]. Furthermore, it was recently shown that TTFs may be used clinically, not only as an anti-proliferation agent, but also as effective adjuvant to currently used chemotherapeutic agents [2-6].

In April 2011 the U.S. Food and Drug Administration (FDA) approved the NovoTTF-100A System, a new device to treat adults with glioblastoma multiforme (GBM) that recurs or progresses after receiving chemotherapy and radiation therapy. "Recurrent glioblastoma multiforme is a devastating form of brain cancer that often eludes standard treatments," said Jeffrey Shuren, M.D., J.D., director of the FDA's Center for Devices and Radiological Health. "The agency's approval of the NovoTTF-100A System shows FDA's commitment to innovative new devices that provide patients with other treatment options." [7]

<sup>\*</sup>Invited paper /Rad po pozivu

The FDA based its approval of the NovoTTF-100A System on results from a single international clinical study in 237 patients with recurrent GBM or with GBM that hadn't responded to traditional therapy. Patients in the study were randomly assigned to receive either the NovoTTF device or chemotherapy treatment. The study showed comparable overall survival rates between patients treated with the NovoTTF device and those who underwent chemotherapy. The NovoTTF device is not intended to be used in combination with other cancer treatment, and should only be used after other treatments have failed.

"The FDA approval of the NovoTTF device is the culmination of ten years of research, development and clinical trials conducted by an exceptional team of scientists, engineers, and clinicians and built on the original insights of our founder and CTO Yoram Palti, M.D., Ph.D.," said William F. Doyle, Novocure's executive chairman. "We look forward to bringing this device to recurrent GBM patients and their families, and we look forward to developing NovoTTF therapy for a range of additional solid tumor cancers." [8] The NovoTTF portable device is designed for continuous use throughout the day by the patient and has U.S. and European marketing approvals.

In December 2011 it was announced that the University of Illinois Hospital was the first center in North America to prescribe this treatment for patients GBM [9].

### Implications for Integrative Medicine

The above U.S. FDA permitted low-intensity LF EM TTFs anti-tumor complementary therapy of intermediate frequency (100 - 300 kHz) might have wider implications for trends in integrative medicine, which

focuses on the least invasive, least toxic, and least costly methods to help facilitate health by integrating both allopathic and complementary therapies.

On these lines, recently reported usage of low-intensity amplitude modulated RF EM fields at precise modulation frequencies (from 0.1 Hz to 114 kHz) [10-14] might also lead to the development of a new type of complementary anti-tumor therapy, after U.S. FDA permitted trials on large groups of patients.

Some other trials with different types of electric fields were reported to inhibit cancer cell proliferation and cause cancer cell destruction, for example: exposure of cancer cells to low amplitude DC currents [15], low intensity low frequency 50 Hz [16] and 120 Hz [17] AC currents – with continuing controversy of EM phenomena and health [18-19].

Also, acupuncture-based and consciousness-based approaches and techniques of quantum-informational medicine [20], via (MW/ULF-modulated or RF/LF-modulated [21-24] balancing of psychosomatically disordered (acupuncture palpatory-painful or psychologically traumatic) state, might provide valuable complementary procedure in removing stress-induced EM quantum-informational origin of cancers [14].

Finally, it should be mentioned that quantum-informational origins of Resonant Recognition Model (RRM) of biomolecular recognition (in the EM optical range [25-27]) provided advances and novel approaches in experimental and computational drug discovery and design, including potential therapeutic agents for future cancer treatment [28,29].

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#### **Apstrakt**

U poslednjih nekoliko godina tim naučnika iz Izraela je objavio rezultate korišćenja slabih nisko frekventnih (LF) elektromagnetnih (EM) tumor tretirajućih polja (TTFs) na ćelijskim kulturama, životinjskim modelima kancera, kao i na pacijentima koji pate od lokalno uznapredovalih i/ili metastatskih čvrstih tumora. U aprilu 2011. godine američka Administracija za hranu i lekove (FDA) je odobrila NovoTTF-100A sistem, novi uređaj za tretman odraslih sa glioblastomom multiforme (GBM) koji se vraća ili progredira posle primanja hemoterapije i radioterapije. Ubrzo potom, u decembru 2011. godine objavljeno je da je Univerzitetska bolnica UIC u Čikagu prvi centar u Severnoj Americi koji propisuje ovaj tretman za pacijente sa GBM. U ovom saopštenju dajemo neke informacije o TTFs pristupu, i razmatramo šire implikacije za integrativnu medicinu.

#### **REFERENCES**

- 1. Kirson ED, Gurvich Z, Schneiderman R, Dekel E, Itzhaki A, Wasserman Y, Schatzberger R, Palti Y. Disruption of cancer cell replication by alternating electric fields. Cancer Res 2004; 64: 3288-95.
- 2. Kirson ED, Schneiderman RS, Dbaly V, Tovarys F, Vymazal J, Itzhaki A, Mordechovich D, Gurvich Z, Shmueli E, Goldsher D, Wasserman Y, Palti Y. Chemotherapeutic treatment efficacy and sensitivity are increased by adjuvant alternating electric fields (TTFields). BMC Med Phys 2009; 9: 1-13.
- 3. Salzberg M, Kirson E, Palti Y, Rochlitz C. A pilot study with very lowintensity, intermediate-frequency electric fields in patients with locally advanced and/or metastatic solid tumors. Onkologie 2008; 31: 362-5.
- 4. Kirson ED, Dbaly V, Tovarys F, Vymazal J, Soustiel JF, Itzhaki A, Mordechovich D, Steinberg-Shapira S, Gurvich Z, Schneiderman R, Wasserman Y, Salzberg M, Ryffel B, Goldsher D, Dekel E, Palti Y. Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors. Proc Natl Acad Sci USA 2007; 104: 10152-7.
- 5. Kirson ED, Giladi M, Gurvich Z, Itzhaki A, Mordechovich D, Schneiderman RS, Wasserman Y, Ryffel B, Goldsher D, Palti Y. Alternating electric fields (TTFields) inhibit metastatic spread of solid tumors to the lungs. Clin Exp Metastasis 2009; 26(7): 633-40.
- 6. Schneiderman RS, Shmueli E, Kirson ED, Palti Y. TTFields alone and in combination with chemotherapeutic agents effectively reduce the viability of MDR cell sub-lines that over-express ABC transporters. BMC Cancer 2010; 10: 229.

7.

- http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm251669.htm,,medicaldevice
- 8. http://www.prnewswire.com/news-releases/fda-approves-the-novottf-100a-system-forthe-treatment-of-patients-with-recurrentglioblastoma-multiforme-gbm-brain-tumors-119924919.html
  - 9.
- http://chicago.medicine.uic.edu/UserFiles/Servers/Server\_442934/File/Neurosurgery\_Chicago/Documents/NEWS%20Articles/UICNews\_Dec\_2\_2011.pdf

- 10. Barbault A, Costa F, Bottger B, Munden R, Bomholt F, Kuster N, Pasche B. Amplitude-modulated electromagnetic fields for the treatment of cancer: discovery of tumor-specific frequencies and assessment of a novel therapeutic approach. J Exp Clin Cancer Res 2009; 28(1):
- 11. Costa FP, de Oliveira AC, Meirelles R, Machado MCC, Zanesco T, Surjan R, Chammas MC, de Souza Rocha M, Morgan D, Cantor A, Zimmerman J, Brezovich I, Kuster N, Barbault A, Pasche B. Treatment of advanced hepatocellular carcinoma with very low levels of amplitude-modulated electromagnetic fields. British J Cancer 2011; 105: 640–648.
- 12. Zimmerman JW, Pennison MJ, Brezovich I, Yi N, Yang CT, Ramaker R, Absher D, Myers RM, Kuster N, Costa FP, Barbault A, Pasche B. Cancer cell proliferation is inhibited by specific modulation frequencies. British J Cancer 2012; 106: 307–313.
- 13. http://www.guardian.co.uk/science/2012/jan/08/electromagnetic-fields-could-stop-cancer
- 14. Raković D, Djordjević D. Weak amplitude-modulated RF EM fields for cancer treatment: Comments and implications from the viewpoint of quantum-informational medicine. Med Data Rev 2012; 4(1): 89-92, and references therein
- 15. Gottesman MM, Fojo T, Bates SE. Multidrug resistance in cancer: Role of ATP-dependent transporters. Nat Rev Cancer 2002; 2: 48-58.
- 16. Wartenberg M, Wirtz N, Grob A, Niedermeier W, Hescheler J, Peters SC, Sauer H. Direct current electrical fields induce apoptosis in oral mucosa cancer cells by NADPH oxidase-derived reactive oxygen species. Bioelectromagnetics 2008; 29:47-54.
- 17. Jiménez-García MN, Arellanes-Robledo J, Aparicio-Bautista DI, Rodríguez-Segura MÁ, Villa-Treviño S, Godina-Nava JJ. Anti-proliferative effect of extremely low frequency electromagnetic field on preneoplastic lesions formation in the rat liver. BMC Cancer 2010; 10: 159.
- 18. Adey WR. Biological effects of electromagnetic fields. J Cell Biochem 1993; 51: 410-416.
- 19. Lai HC, Singh NP. Medical applications of electromagnetic fields. In: Electromagnetic Phenomena and Health A Continuing Controversy? IOP Conf. Series: Earth and Environmental Science 2010; 10(1): 012006.

- 20. Raković D, Arandjelović S, Miæović M, eds. Symp. Proc. Quantum-Informational Medicine QIM 2011: Acupuncture-Based and Consciousness-Based Holistic Approaches & Techniques. Belgrade: QUANTTES & HF & DRF, 2011, http://qim2011.org
- 21. Zhang Y. ECIWO Biology and Medicine: A New Theory of Conquering Cancer and Completely New Acupuncture Therapy. Beijing: Neimenggu People Press, 1987.
- 22. Grubnik BP, Sitko SP, Shalimov AA. Experience of using Sit'ko-MRT technology for rehabilitation of III-IV stage oncologic patients. Physics of the Alive 1998; 6: 97-115.
- 23. Chopra D. Quantum Healing: Exploring the Frontiers of Mind/Body Medicine. New York: Bantam, 1989.
- 24. http://www.energy-medicine.info; Inergetix website with contemporary critical review of technologies in the wider field of quantum-informational medicine, including information on Rife's early research in the field of bioresonance cancer treatments in 1930ies, which was not recognized at that time.
- 25. Cosic I. Macromolecular bioactivity: Is it resonant interaction between macro-molecules? Theory and applications. IEEE Trans Biomed Eng 1994; 41(12): 1101-1114.
- 26. Cosic I. The Resonant Recognition Model of Macromolecular Bioactivity: Theory and Applications. Birkhauser Verlag, Basel, 1997
- 27. Vojisavljevic V, Pirogova E, Cosic I. The effect of electromagnetic radiation (550 – 850 nm) on l-lactatedehydrogenase kinetics. Int. J. Rad. Biol. 2007; 83(4): 221-230.
- 28. Pirogova E, Istivan T, Gan E, Cosic I. Advances in methods for therapeutic peptide discovery, design and development. Curr Pharm Biotechnol 2011; 12: 1117-1127.
- 29.Istivan TS, Pirogova E, Gan E, Almansour NM, Coloe PJ, Cosic I. Biological effects of a de novo designed myxoma virus peptide analogue: Evaluation of cytotoxicity on tumor cells. PLoS ONE 2011; 6(9): e24809.