ENERGY-BASED THERAPIES FOR CANCER TREATMENT

This Guide had been provided by the Anticancer Fund as a service to patients, to help patients and their relatives better understand the possible use of energy-based therapies for cancer treatment. We recommend patients to consult their doctor. The information described in this document is based on scientific research and has informative purposes only.

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For words marked with an asterisk, a definition is provided at the end of the document.*

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1. INTRODUCTION

Energy Medicine is a term generally used for holistic healing therapies that are focused on manipulating the human body's energies to bring about balance and well-being. Energy medicine is a domain in Complementary and Alternative Medicine (CAM) that deals with the putative and veritable energy fields as defined by the National Center for Complementary and Alternative Medicine (NCCAM). Practices based on putative energy fields (also called biofields) generally reflect the concept that humans are infused with subtle forms of energy. Reiki*, therapeutic touch*, and qigong* are examples of such practices which are discussed in another section of this guidance booklet (see mind-body interventions and body-based & manipulative therapies).

Here we would like to focus on practices that use 'instrument-generated' energy fields to either directly kill malignant cells or stimulate the body with the purpose of curing people of cancer. This more restricted concept of energy medicine (here denoted as energy-based therapies) encompasses all therapeutic cancer treatments based on the transfer of energy into the body. These energies employ electricity, ultrasound waves and electromagnetic* (EM) forces, including radio waves, monochromatic* radiation* (such as laser* beams), magnetism, and rays from other parts of the EM spectrum. They involve the use of specific, measurable wavelengths* and/or frequencies* to treat patients with cancer. Most energy-based therapies that are used in combination with other therapeutic modalities may improve the efficacy of conventional treatments.

There is a growing appreciation that energy-based medicine may hold the key to the future of medicine. The majority of the therapies, however, are still at clinical trial, preclinical experimental or purely experimental stage. Much remains to be learned about their mechanisms of action and efficacy. This preliminary, brief outline of energy-based therapies should not be viewed as comprehensive or definitive. Rather, it is intended to provide you with a sense of the possibilities offered by energy-based approaches generally unknown to the broader public. In-depth reviews of the therapies mentioned hereafter will be made available on the Anticancer Fund website.

2. OVERVIEW OF ENERGY-BASED THERAPIES

A major obstacle to providing an overview of energy-based therapies is stymied by the fact that the field is very broad and developing rapidly. The literature dealing with electrical, magnetic and electromagnetic* field stimuli is full of a bewildering array of model systems, clinical investigations, signal configurations and stimulation devices. The different therapies will be categorized for the sake of simplicity and guidance into those that are gaining clinical acceptance and those that are experimental. The subdivisions used under these two broad categories do not reflect the vast array of therapeutic modalities nor do they represent the potential they may have for treating cancer patients.

2.1 Energy-based therapies in clinical practice

Most energy-based therapies which have entered clinical practice or which are regarded as legitimate belong to the group of thermal therapies. They are divided into hyperthermia, thermal ablation* and cryoablation according to the temperature range being used. Photodynamic therapy and electrotherapy and their various derived technologies may be classified within this subdivision as well. The vast majority of these therapies, however, are limited in availability depending on geographic location.

- **Hyperthermia**

The goal of hyperthermia is to raise the temperature of a tumor to about 41-43°C through the application of electromagnetic* energy for a defined period of time to damage and kill the cancer cells. Above this temperature, heat has a direct cytotoxic effect on both normal and tumor cells and will be referred to as thermal ablation* (see the next section on thermal ablation). An increase in temperature due to hyperthermia would change the blood microcirculation of the tumor, inhibit cellular repair mechanisms, induce heat-shock proteins*, denature proteins, induce apoptosis, and inhibit angiogenesis. Hyperthermia has also been shown to stimulate the immune system* with observed increases in natural killer cell* activity. All of these events can significantly disrupt a tumor cell's capacity to divide and may ultimately lead to shrinkage of tumors.

Hyperthermia can be applied using several methods. The most common method is to apply hyperthermia locally to various parts of the body where the tumor is located. Local hyperthermia has been used extensively for superficial lymph nodes, recurrent or advanced breast cancer, and cutaneous or subcutaneous melanoma* metastasis*. Regional hyperthermia has been used primarily for advanced pelvic tumors and for sarcomas* of the trunk or extremities. At the moment, most advances are being made in improving heating technology, thermometry*, the development of hyperthermia treatment planning models and, most recently, drug targeting using thermosensitive drug-carriers such as nanoparticles* and liposomes*.

Thousands of patients have been treated with hyperthermia and many research and clinical studies have been reported in the literature. It has been shown to be an effective modality of cancer treatment, showing significant improvements in clinical responses for a subset of patients when used alone or in combination with established cancer treatment modalities such as radiotherapy* and chemotherapy*. Depending on their endpoints and the investigated malignancy, the results are

generally positive and may provide useful local supportive or palliative (non-curative) effects. However, today hyperthermia is generally still treated with some skepticism in mainstream medicine, probably because of a lack of adequate treatment experience and long-range, comprehensive statistics. The positive results of most of the recent studies may explain the renewed enthusiasm for hyperthermia, which is reflected in the growing number of clinics interested in its application.

- **Thermal ablation**

Thermal ablation* uses very high temperatures (above 45°C) to destroy cells within a localized section of a tumor in a minimally invasive fashion without damaging adjacent vital structures. Multiple energy sources are used to provide the heat necessary to induce coagulation* necrosis*. Electromagnetic* energy has been used in the form of both radiofrequency* and microwaves*, photocoagulation* uses intense pulses of light produced by a laser* as the energy source, high-intensity focused ultrasound uses sound energy to produce heat, injection of heated fluids and contrast material have been used to induce coagulation by direct thermal contact. Thermal ablation can be used in various organs such as the breast, liver, lungs and prostate. Clinical trial results to date have demonstrated thermal ablation to be safe and in some cases clinically effective.

- **Photodynamic therapy**

Photodynamic therapy (PDT) is a minimally invasive therapeutic procedure involving administration of a photosensitizing* agent followed by irradiation of the tumor at a particular wavelength*. In the presence of oxygen, a series of events lead to direct tumor cell death, damage to the microvasculature*, and induction of a local inflammatory reaction. PDT has received increased attention since regulatory approval was granted to several photosensitizing* drugs and light applicators worldwide. PDT offers various treatment options in cancer management and has been used for localized, superficial or endoluminal malignant and pre-malignant conditions. There have been over 200 clinical trials for PDT. Recent systematic reviews revealed that PDT can be considered as an option in the treatment of malignant and premalignant non-melanoma* skin lesions. However, its effectiveness in the management of other types of tumors has not yet been unequivocally proven.

- **Electrotherapy**

Electrotherapy employs electrical stimulation to treat cancer. The cancer cells are destroyed using relatively high currents by electrolysis* in that at least two electrodes* (needles) are placed close to the tumor between which a direct current field is generated. The currents penetrate directly into tumors (invasive electrotherapy) or from the skin above the tumor (non-invasive electrotherapy). These therapies have been largely practiced in Asia. Electrotherapy is used most often as an adjuvant with other therapies, such as in combination with chemotherapeutic cancer drugs with an intracellular target. This type of electrochemotherapy has been used for the treatment of easily accessible superficial tumor nodules. Few experimental studies have been conducted to treat deep-seated tumors. Electrochemotherapy today can be considered as a palliative option for cancers where surgery or radio*/chemotherapy * treatment is not a possibility.

More recently, research has been conducted on pulsed electrical fields applied around or within the tumor. It has been shown that drugs actually may not be always necessary, since the impact of certain strong electric field* pulses that cause electroporation* itself is sufficient to trigger cellular mechanisms that lead to cellular death. One of the methods being commercialized is the NanoKnife® system (AngioDynamics®). This system employs irreversible electroporation* that uses a series of microsecond* electrical pulses to permanently open cell membranes in soft tissue tumors causing them to die naturally and be routinely discarded by the body. This could be particularly useful in the liver in which case cells regenerate more easily where tumor cells have been removed. A group of researchers at the Frank Reidy Center for Bioelectrics (Norfolk, USA) have discovered that pulsed electrical fields of ultrashort duration (nanoseconds*) and high field strengths can also be used as an electrical cancer therapy to kill tumors without hyperthermia or drugs. They reported that when melanoma* tumors in mice are treated with nanosecond*-pulsed electrical fields, tumors can be completely ablated* with a single treatment. This technology is now being developed for medical applications by BioElectroMed Corp. The first clinical trials will target basal cell carcinoma* and are scheduled for the end of 2011.

2.2 Energy-based therapies in experimental stage

Several academic institutions and companies are currently conducting valuable research exploring the curable effects of low- to high-level EM radiation* in cancer. The different types of experimental therapies using either electrical, magnetic or electromagnetic* fields are beyond the scope of this brief outline. For the time being, preliminary information is given here regarding some of these therapies for information purposes only. They illustrate the variety of cancer research in using externally delivered energy sources. Examples of these systems are in pre-clinical investigation and/or under examination by the European Medicines Agency (EMA) or the USA Food and Drug Administration (FDA).

- **Nanoparticle*-mediated thermal therapies**

The major problem with currently applied hyperthermia treatments is achieving a homogenous heat distribution in the treated tissue. The currently available modalities of hyperthermia are often limited by their inability to selectively target tumor tissue and, hence, they carry a risk of collateral* organ damage or they deposit heat in a localized manner, which can result in undertreatment of a tumor. Nanotechnology*-based cancer therapy is a special form of interstitial* thermotherapy* with the advantage of selective heat deposition to the tumor cells. This new therapy is one of the first applications of nanotechnology* in medicine and is based on heating of nanoparticles* or quantum dots* in an external electromagnetic* field. Depending on the duration of treatment and the achieved intratumoral temperatures, the tumor cells are either directly destroyed (thermal ablation*) or sensitized for concomitant chemo*- or radiotherapy*. The nanoparticles* would remain in place at the treatment area, allowing for repeated treatments and the integration of multimodal therapy concepts.

Nanoparticle*-mediated thermal therapies are being studied worldwide by using either a radiofrequency* field, an alternating magnetic field*, or near-infrared* light as a source of delivering energy. Research teams funded by the Kanzius Cancer Research Foundation have previously reported on the use of noninvasive radiofrequency* fields to induce thermal cytotoxicity in human and mammalian cancer cells exposed to targeted solid gold nanoparticles*. The surfaces of these nanoparticles* are conjugated with specific antibodies* that would be recognized by the cell-surface receptors of cancer cells. Cancer cells would endocytosis* these nanoparticles with subsequent intracellular heat release during shortwave radiofrequency* field treatment sufficient to produce cellular cytotoxicity. Initial studies have validated the efficacy, consistency and safety in *in vitro* research. Work is underway to seek FDA approval and to begin with the phase I human trials.

A similar technique for local treatment of solid tumors has been developed by MagForce Nanotechnologies* and given the name NanoTherm® therapy. The principle of the therapy is the use of nanoparticles* containing iron-oxide, which are injected into tumors in a procedure similar to a biopsy. The patient is then placed in a magnetic field* applicator, a machine that produces an alternating magnetic field*. Through this high frequency* magnetic field, the nanoparticles begin to oscillate and warmth is produced from directly within the tumor tissue. The method is also known as magnetic fluid hyperthermia (MFH). Depending on the temperature reached and length of treatment, the tumor cells are either directly destroyed or sensitized for the accompanying chemotherapy* or radiation*. Phase I clinical trials have been terminated for glioblastoma* and prostate carcinoma* in which they have observed longer periods of survival.

Another company (Nanospectra Biosciences) has developed the AuroLase® therapy which is based on using gold nanoparticles* (AuroShell®) currently for investigational use only. These particles are administered intravenously and would enter the tumor through its leaky vasculature*. After the particles accumulate in the tumor, the area is illuminated with a near-infrared* laser*. The AuroShell® particles are specifically designed to absorb this wavelength* and convert the laser* light into heat. This would result in the ablation* of the tumor. The efficacy of this technology has been evaluated pre-clinically for eradicating prostate cancer in a subcutaneous tumor model and one clinical trial in patients with refractory and/or recurrent tumors of the head and neck is ongoing.

Particle-based thermal therapy is thus a growing domain in cancer research. Different designs of nanoparticle* structures or thermosensitive liposomes* are in development as carriers for drug delivery.

- **Laser immunotherapy**

Immunotherapy, designed to stimulate a patient's immune system* to attack and destroy the tumors, has been considered as a cancer treatment modality for quite some time. Many novel strategies have been proposed including Laser* Immunotherapy (LIT) otherwise named *in situ* photoimmunotherapy. LIT combines photothermal therapy with an active immunological stimulation to induce systemic immune responses. It consists of three major components: a near-infrared* laser*, a light-absorbing agent, and an immunological stimulant. The light-absorbing agent is injected into the patient's body followed by directed, non-invasive laser* radiation* onto the area where the tumor is located. The interaction between the two heats up the target tissue causing the tumor cells

to swell and lyse, allowing for the release of tumor-associated antigens which can induce a specific antitumor immune response. Subsequently, an immunoadjuvant is injected into the center of the tumor, which enhances the immune response.

LIT is designed specifically for the treatment of late-stage cancer patients, who have not had success with conventional treatment modalities and face severely limited options. The method is made available through Immunophotonics® named inCVAX to treat metastatic* cancers. Initial results of a pre-clinical study on metastatic* breast cancer have shown that LIT can reduce primary tumors and metastases*. Also, preliminary clinical outcomes of patients with advanced melanoma* treated with LIT have been reported. The results generally show LIT to be a safe and useful palliative modality with a favorable toxicity profile compared to current methods of treatment.

- **Therapies using weak electromagnetic* fields**

A bewildering variety of therapies based on devices using low EM frequencies exist in private practice. Practitioners of these therapies affirm that this would bring about changes in the physical body and beneficially influence health. In contrast to the wide range of electromagnetic* energy methods that have been proven for standard medical treatment, many of the alternative electronic devices promoted to cure cancer have not been scientifically proven to be effective. These approaches are among the most controversial of energy-based practices because neither the energy fields nor their biological effects have been demonstrated convincingly by any biophysical or medical means. Clinical trial data concerning the efficacy of the majority of these therapies have not been evaluated using a systematic, evidence-based approach. It should be noted however that many of these devices were not initially developed for the treatment of cancer but obtained anecdotal testimonials later on. Lack of regulation and the widespread use of false or unproven marketing claims persist. Patients should always seek advice from a qualified medical practitioner if they have any questions about these devices.

This particular type of electromagnetic* therapy has a multitude of other common names such as bioenergy and bioresonance* therapy. The use of weak EM fields has a long history and its term is frequently being used to summarize the whole field of electrical, magnetic and combined electromagnetic* effects on cells. Many EM instruments and devices are based on high voltage Tesla coils*, which are claimed to bring beneficial health improvements to humans. The Tesla coil class of therapy devices generally comprises pulsed electromagnetic* fields (PEMF) that deliver broadband, wide spectrum, nonthermal photons* and electrons deep into biological tissue. Bioresonance therapy uses low-frequency* electromagnetic waves to diagnose and treat patients assisting the return to a normal range of cellular activity, promoting the healing process, and relieving pain. The method is based on the notion that electromagnetic oscillations emitted by cancer cells and diseased organs are different from those emitted by healthy cells. The electromagnetic differences are supposedly detected by an electrical device (such as MORA or BICOM) via electrodes* placed on certain parts of the body, which in some cases is said to determine which organs are involved and be able to cancel out unhealthy signals. The underlying theory behind this is that all matter has a resonant frequency* and every cell in the body resonates at a particular frequency*. This takes the form of an EM field and groups of cells in an organ or system have multiple frequency* patterns which are unique. Hence, the whole body has a complex frequency* make-up which can change or

become distorted when affected by illness. The stimulation may be delivered through electrodes* in contact with the skin, or by pulsed magnetic fields* that penetrate the body, inducing electrical potentials deep into the tissues. Examples of devices based on bioresonance* are Rife, Tesla, Multiwave oscillator, BICOM, Zappers, MORA, VIBE, etc. Many of these devices currently on the market claim to use bioresonance*-type methods but do not provide adequate engineering descriptions of the systems to confirm their assertions. Signal processing methods are treated as proprietary design secrets and only anecdotal testimonials support the efficacy of these therapies. Very little evidence-based data gained through scientific methods or clinical investigation is available.

Recent developments in research have shown other ways in which weak EM fields can be used to control tumor growth. *In vitro* and *in vivo* research has already extensively shown that low levels of exogenous electromagnetic* fields may modify cell growth. An interesting proposal was recently made by the research group of Barbault et al. (2009) claiming to have identified cancer-related frequencies. They suggested that treatment with amplitude-modulated electromagnetic* fields may block cancer cell growth. So far, a single clinical study has been performed to investigate the safety and feasibility of treating patients with certain advanced cancers with low level amplitude-modulated electromagnetic* fields but further results of their research are awaited.

Another development is seen in the Tumor Treating Fields (TTF) therapy (NovoCure) which is designed to slow and reverse tumor cell proliferation by inhibiting mitosis*, the process by which cells divide and replicate themselves. This is accomplished by using an instrument which generates low-intensity, intermediate frequency* (100 - 200 kHz) alternating electric fields* by insulated electrodes* applied to the skin surface. This field exerts physical forces on electrically charged cellular components within the underlying tumor, which would prevent the normal mitotic process and causes cancer cell death prior to division. A phase III clinical trial in patients with recurrent glioblastoma* multiforma has been conducted to evaluate the efficacy of TTF. The results showed that TTF as a monotherapy* are at least as effective as the best available chemotherapy*. TTFields were also explored in a phase I/II study in combination with pemetrexed for advanced non-small cell lung cancer and found that TTF was well tolerated as a second-line treatment and resulted in better time to progression and survival.

3. CONCLUDING REMARKS

This brief outline has illustrated the potential of energy-based therapies to deliver added value to the existing treatments either as a monotherapy* or in combination with other modalities. The delivery of energy in treating cancer has shown to be most successful when the tumor cells are rapidly killed by locally induced thermal energy. More pragmatic solutions with better outcomes for treating cancer may be expected from bioelectromagnetic medicine. Particularly electrotherapy and possibly weak electromagnetic* fields, currently of unknown characteristics, may hold promise for the near future. RCT will closely monitor developments in energy-based medicine and will report on its website when considerable clinical trial progress has been made.

4. REFERENCES

Agostinis P, Berg K, Cengel Ka, Foster Th, Girotti Aw, Gollnick So, Hahn Sm, Hamblin Mr, Juzeniene A, Kessel D, Korbelik M, Moan J, Mroz P, Nowis D, Piette J, Wilson Bc, Golab J. Photodynamic Therapy Of Cancer: An Update. Ca Cancer J Clin. 2011;61(4):250-81.

Barbault A, Costa Fp, Bottger B, Munden Rf, 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; 14,28:51.

Cherukuri P, Glazer Es, And Curley Sa, Targeted Hyperthermia Using Metal Nanoparticles. Adv Drug Deliv Rev. 2010;8;62(3):339-345.

Dayanc Be, Beachy Sh, Ostberg Jr, Repasky Ea. Dissecting The Role Of Hyperthermia In Natural Killer Cell Mediated Anti-Tumor Responses. Int J Hyperthermia, 2008;24(1):41-56.

Dieing A, Ahlers O, Hildebrandt B, Kerner T, Tamm I, Possinger K, Wust P, The Effect Of Induced Hyperthermia On The Immune System. Prog Brain Res, 2007;162:137-52.

Fayter D, Corbett M, Heirs M, Fox D, Eastwood A. A Systematic Review Of Photodynamic Therapy In The Treatment Of Pre-Cancerous Skin Conditions, Barrett's Oesophagus And Cancers Of The Biliary Tract, Brain, Head And Neck, Lung, Oesophagus And Skin. Health Technol Assess. 2010;14(37):1-288.

Franckena M, Van Der Zee J. Use Of Combined Radiation And Hyperthermia For Gynecological Cancer. Curr Opin Obstet Gynecol. 2010;22(1):9-14.

Gao F, Bai Y, Ma Sr, Liu F, Li Zs. Systematic Review: Photodynamic Therapy For Unresectable Cholangiocarcinoma. J Hepatobiliary Pancreat Sci. 2010;17(2):125-31.

Glazer Es, Zhu C, Massey Kl, Thompson Cs, Kaluarachchi Wd, Hamir An, Curley Sa. Noninvasive Radiofrequency Field Destruction Of Pancreatic Adenocarcinoma Xenografts Treated With Targeted Gold Nanoparticles. Clin Cancer Res. 2010;16(23):5712-21.

Huang Hc, Barua S, Sharma G, Dey Sk, Rege K. Inorganic Nanoparticles For Cancer Imaging And Therapy. J Control Release. 2011 Jun 22. [Epub Ahead Of Print]

Issels Rd, Lindner Lh, Verweij J, Wust P, Reichardt P, Schem Bc, Abdel-Rahman S, Daugaard S, Salat C, Wendtner Cm, Vujaskovic Z, Wessalowski R, Jauch Kw, Dürr Hr, Ploner F, Baur-Melnyk A, Mansmann U, Hiddemann W, Blay Jy, Hohenberger P. Neo-Adjuvant Chemotherapy Alone Or With Regional Hyperthermia For Localised High-Risk Soft-Tissue Sarcoma: A Randomised Phase 3 Multicentre Study. Lancet Oncol. 2010;11(6):561-70.

Jolescha A, Elmera K, Bendzb H, Issels Rd, Noessner E, Hsp70, A Messenger From Hyperthermia For The Immune System. Eur J Cell Biol. 2011 Mar 30. [Epub Ahead Of Print]

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(24):10152-157.

Koning Ga, Eggermont Am, Lindner Lh, Ten Hagen Tl. Hyperthermia And Thermosensitive Liposomes For Improved Delivery Of Chemotherapeutic Drugs To Solid Tumors. Pharm Res. 2010;27(8):1750-4.

Krawczyk Pm, Eppink B, Essers J, Stap J, Rodermond H, Odijk H, Zelensky A, Van Bree C, Stalpers Lj, Buist Mr, Soullié T, Rens J, Verhagen Hj, O'connor Mj, Franken Na, Ten Hagen Tl, Kanaar R, Aten Ja. Mild Hyperthermia Inhibits Homologous Recombination, Induces Brca2 Degradation, And Sensitizes Cancer Cells To Poly (Adp-Ribose) Polymerase-1 Inhibition. Proc Natl Acad Sci Usa. 2011;108(24):9851-9856.

Krishnan S, Diagaradjane P, Cho Sh. Nanoparticle-Mediated Thermal Therapy: Evolving Strategies For Prostate Cancer Therapy. Int J Hyperthermia. 2010;26(8):775-89.

Landon Cd, Park J-Y, Needham D And Dewhirst Mw, Nanoscale Drug Delivery And Hyperthermia: The Materials Design And Preclinical And Clinical Testing Of Low Temperature-Sensitive Liposomes Used In Combination With Mild Hyperthermia In The Treatment Of Local Cancer. The Open Nanomedicine Journal, 2011;3:38-64.

Li X, Naylor Mf, Le H, Nordquist Re, Teague Tk, Howard Ca, Murray C, Chen Wr. Clinical Effects Of In Situ Photoimmunotherapy On Late-Stage Melanoma Patients: A Preliminary Study. Cancer Biol Ther. 2010;10(11):1081-7.

Li X, Ferrel Gl, Guerra Mc, Hode T, Lunn Ja, Adalsteinsson O, Nordquist Re, Liu H, Chen Wr. Preliminary Safety And Efficacy Results Of Laser Immunotherapy For The Treatment Of Metastatic Breast Cancer Patients. Photochem Photobiol Sci. 2011;1;10(5):817-21.

Maier-Hauff K, Ulrich F, Nestler D, Niehoff H, Wust P, Thiesen B, Orawa H, Budach V, Jordan A. Efficacy And Safety Of Intratumoral Thermotherapy Using Magnetic Iron-Oxide Nanoparticles Combined With External Beam Radiotherapy On Patients With Recurrent Glioblastoma Multiforme. J Neurooncol. 2011;103(2):317-24.

Mccaig Cd, Rajnicek Am, Song B, Zhao M. Controlling Cell Behavior Electrically: Current Views And Future Potential. Physiol Rev. 2005;85(3):943-78.

Naylor Mf, Chen Wr, Teague Tk, Perry La, Nordquist Re. In Situ Photoimmunotherapy: A Tumour-Directed Treatment For Melanoma. Br J Dermatol. 2006;155(6):1287-92.

Nuccitelli R, Chen X, Pakhomov Ag, Baldwin Wh, Sheikh S, Pomicter Jl, Ren W, Osgood C, Swanson Rj, Kolb Jf, Beebe Sj, Schoenbach Kh. A New Pulsed Electric Field Therapy For Melanoma Disrupts The Tumor's Blood Supply And Causes Complete Remission Without Recurrence. Int J Cancer. 2009;15;125(2):438-45.

Nuccitelli R, Tran K, Sheikh S, Athos B, Kreis M, Nuccitelli P. Optimized Nanosecond Pulsed Electric Field Therapy Can Cause Murine Malignant Melanomas To Self-Destruct With A Single Treatment. Int J Cancer. 2010;127(7):1727-36.

Pless M, Betticher Dc, Buess M, Von Moos R, Weinberg U, Kirson E, Palti Y. A Phase Ii Study Of Tumor Treating Fields (Ttfields) In Combination With Pemetrexed For Advanced Non Small Cell Lung Cancer (Nsclc). [Abstract 371pd]. Esmo; 2010

Pless M, Weinberg U. Tumor Treating Fields: Concept, Evidence And Future. Expert Opin Investig Drugs. 2011;20(8):1099-106.

Pokorný J, Vedruccio C, Cifra M, Kučera O. Cancer Physics: Diagnostics Based On Damped Cellular Elastoelectrical Vibrations In Microtubules. Eur Biophys J. 2011;40(6):747-59.

Privalov Va, Lappa Av, Seliverstova Ov, Faizrakhmanova Ab, Yarovoya Nn, Kochnevaa Ev, Evnevichb Mv, Anikinab As, Reshetnicovc Av, Zalevskyd Id, Kemovc Yv, Clinical Trials Of A New Chlorin Photosensitizer For Photodynamic Therapy Of Malignant Tumors. Proceedings Of Spie 2002;4612:178-189

Rosch Pj And Markov Ms (Editors) Bioelectromagnetic Medicine. Infrma-Hc; 1 Edition (December 2004).

Sadadcharam M, Soden Dm, O'sullivan Gc. Electrochemotherapy: An Emerging Cancer Treatment. Int J Hyperthermia. 2008; 24(3):263-723.

Salzberg M, Kirson E, Palti Y, Rochlitz C. A Pilot Study With Very Low-Intensity, Intermediate-Frequency Electric Fields In Patients With Locally Advanced And/Or Metastatic Solid Tumors. Onkologie 2008;31(7):362-65.

Stern Jm, Stanfield J, Kabbani W, Hsieh Jt, Cadeddu Ja. Selective Prostate Cancer Thermal Ablation With Laser Activated Gold Nanoshells. J Urol. 2008;179(2):748-53.

Stupp R, Kanner A, Engelhard H, Heidecke V, Taillibert S, Lieberman Fs, Dbalý V, Kirson Ed, Palti Y, Gutin Ph. A Prospective, Randomized, Open-Label, Phase Iii Clinical Trial Of Novottf-100a Versus Best Standard Of Care Chemotherapy In Patients With Recurrent Glioblastoma. J Clin Oncol 2010;28(18s): Abstract Lba2007.

Van Sonnenberg E, Mcmullen Wn, Solbiati L (Eds). Ablation: Principles And Practice. Springer 2005 Edition.

5. GLOSSARY

Ablation
The removal of abnormal tissue growth by surgery or other medical interventions.

Antibody
Specialized proteins produced by white blood cells that circulate in the blood recognizing and binding to foreign proteins, microorganisms or toxins in order to neutralize them. They are a critical part of the immune response. Also called immunoglobulins.

Bioresonance
Is a term used in the Bioresonance therapy, an alternative medicine which states that each cell or organ has a specific vibration frequency* of electromagnetic* nature.

Carcinoma
Cancer that begins in the skin or in tissues that line or cover internal organs.

Chemotherapy
A type of cancer treatment using drugs that kill cancer cells and/or limit their growth. These drugs are usually administered to the patient by slow infusion into a vein but can also be administered orally, by direct infusion to the limb or by infusion to the liver, according to cancer location.

Coagulation
The disruption of tissue by physical means to form an amorphous residuum.

Collateral damage
Damage that is unintended or incidental to the intended outcome.

Electric field
That which surrounds electrically charged particles and time-varying magnetic fields*. This electric field exerts a force on other electrically charged objects.

Electrode
An electrical conductor used to make contact with a nonmetallic part of a circuit (e.g. a semiconductor or an electrolyte).

Electrolysis
Chemical change, especially decomposition, produced in an electrolyte (a substance containing free ions) by an electric current.

Electromagnetic
Refers to radiation such as light, microwaves*, x-rays, gamma rays, or radio waves.

Electroporation
A technique to create holes in the cell membrane by means of short voltage pulses.

Endocytosis

The process by which cells absorb molecules (such as proteins) by engulfing them. It is used by all cells of the body because most substances important to them are large polar molecules that cannot pass through the hydrophobic plasma or cell membrane. The opposite process of endocytosis is exocytosis.

Frequency
The number of cycles of a periodic quantity, such as alternating current, that occur in a period of 1 second. Electromagnetic frequencies, formerly expressed in cycles per second (cps), are now expressed in hertz (Hz).

Glioblastoma
A general term that refers to malignant astrocytoma, a type of brain tumor.

Heat shock protein
Any of a group of cellular proteins that are produced under conditions of heat stress and help to stabilize other cellular proteins exposed to high temperatures.

Immune system
The immune system is a biological system of structures and processes that protects the body from diseases by identifying and killing tumor cells and foreign invaders such as viruses and bacteria.

Infrared
Electromagnetic radiation with a wavelength* of between 0.7 and 300 micrometers, which equates to a frequency range of between approximately 1 and 430 THz

Interstitial thermotherapy
Thermotherapy* in which electrodes* or antennas to induce heat are implanted directly into tumor areas.

Laser
A device that emits light (electromagnetic radiation) through a process of optical amplification based on the stimulated emission of photons*. The term “laser” originated as an acronym for Light Amplification by Stimulated Emission of Radiation. The emitted laser light has a high degree of spatial and temporal coherence.

Liposome
An artificial microscopic vesicle consisting of an aqueous core enclosed in one or more phospholipid layers, used to convey vaccines, drugs, enzymes, or other substances to target cells or organs.

Magnetic field
Is a field of force produced by moving electric charges, by electric fields that vary across time, and by the 'intrinsic' magnetic field of elementary particles associated with the spin of the particle.

Melanoma
A darkly-pigmented, malignant, frequently widely metastasizing tumor arising from a melanocyte and occurring most commonly in the skin.

Metastasis
The spread of cancer from one part of the body to another. A tumor formed by cells that have spread is called a metastatic tumor or a metastasis. The metastatic tumor contains cells that are like those in the original tumor.

Microsecond
One millionth (10^{-6}) of a second.

Microwave
A high-frequency electromagnetic wave of one millimeter to one meter in wavelength*, intermediate between infrared and shortwave radio wavelengths*.

Mitosis
The process by which a single parent cell divides to make two new daughter cells. Each daughter cell receives a complete set of chromosomes from the parent cell. This process allows the body to grow and replace cells.

Monochromatic
Relating to a pure spectral color of a single wavelength*.

Monotherapy
Treatment of a disorder with a single therapy.

Nanoparticle
A microscopic particle with at least one dimension less than 100 nm.

Nanosecond
One billionth of a second.

Nanotechnology
The study of manipulating matter on an atomic and molecular scale. Generally nanotechnology deals with structures sized between 1 to 100 nanometers on at least one dimension, and involves developing materials or devices within that size.

Natural killer cell
A lymphocyte that acts as a primary immune defense against infection

Necrosis
Refers to the death of living tissues.

Photocoagulation
Condensation of protein material by the controlled use of an intense beam of light (e.g., diode laser*) used e.g. in the destruction of tumor masses.

Photon

A particle representing a quantum of light or other electromagnetic radiation.

Photosensitivity
Photosensitivity is sensitivity to light or radiation*. Photosensitivity of the skin comes in various degrees.

Qigong
A system of breathing and exercise designed to benefit both physical and mental health.

Quantum dots
Tiny nanocrystals that glow when stimulated by an external source such as ultraviolet (UV) light.

Radiation
Can be defined as energy travelling through space. Examples of radiation include UV, and x-rays which are commonly used in medicine.

Radiofrequency
The part of the electromagnetic spectrum with frequencies lower than about 10^{10} Hz, used to produce magnetic resonance images for example.

Radiotherapy
A therapy in which radiation is used in the treatment of cancer always oriented to the specific area of the cancer.

Reiki
A form of therapy in which the practitioner is believed to channel energy into the patient in order to encourage healing or restore wellbeing.

Sarcoma
A cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.

Tesla coil
A step-up transformer with an air core used to produce high voltages at high frequencies.

Therapeutic touch
A technique where human energy is redirected using the hands, usually without actual physical contact. Harmful energy is said to create blockages; therapeutic touch proponents claim to remove these blockages. It is generally promoted as a complementary therapy, to be used along with other remedies.

Thermometry
The technology of temperature measurement.

Thermotherapy
Medical therapy involving the application of heat.

Tissue

A group or layer of cells that work together to perform a specific function.

Vasculature
The arrangement of blood vessels in an organ or body part.

Wavelength
The spatial period of the wave or the distance over which the wave's shape repeats.