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Electrotherapy & Cancer

Dangers and Contraindications for Electrotherapy in Cancer Care

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Electrotherapy & Cancer

- What is the problem?
- Is it real, imagined, evidenced . . . ?
- Are there guidelines that can help?
- How can we interpret the grey areas?
- How can we be safe, and effective and provide benefit for the patient?

What is the Problem?

- The problem, as widely viewed, is that the application of electrotherapy modalities to a patient who has 'cancer' could have a detrimental effect on the disease progress and hence constitutes a contraindication or at the very least, a 'danger'

What is the Problem? . . .

- Some modalities are generally considered to be more of a problem than others
 - » e.g. ultrasound, laser, pulsed shortwave
- Many practitioners are unsure whether it is OK to apply or not and therefore tend to shy away

What is the Problem? . . .

- If it is a problem, then clearly we should not be applying the modalities
- If it is not a problem, yet we treat it as such, then the patient could miss out on a potentially beneficial treatment / modality
- There will always be some grey areas, but should be able to have some sound guidelines

Is it real, imagined, evidenced ?

- Is there a known adverse effect of some or all electrotherapy modalities on some or all cancers?
- Is this proposed, considered or directly evidenced?
- Absence of evidence vs evidence of absence

Can electrotherapy influence cancer?

- Useful point at which to start
- If electrotherapy modalities are not able to influence cancers (in general terms) then how could they constitute a danger?
- Growing body of evidence to strongly support the fact that electrotherapy **can** have an influence

Effects of electrotherapy on cancer

- If one considers electrotherapy in its widest context (i.e. the delivery of electrophysical agents to the body tissues) and you leave out the ionising radiations, is electrotherapy used as a treatment?
- Avoiding the topics already covered, worth a brief exploration

Quick search of the literature . . .

- If you do a quick lit search on a limited number of databases and seek a specific combination of **ELECTROTHERAPY** and **CANCER** you come up with a significant number of references
- Over 600 without any trouble at all

Snapshot of Electrotherapy and Cancer related references from Database

Author	Year	Title
Ochiara	2000	Potential of effects of anticancer agents by local electric pulses in murine bladder cancer
Shen	2000	Electroacupuncture for control of myeloblastic chemotherapy-induced emesis. A randomized controlled
Tortolici	2000	Laser and electromagnetic fields in the treatment of cancer
Wojcicki	2000	Antitumor effect of electrochemical therapy on transplantable mouse cancers
Cabrales	2001	Electrochemical treatment of mouse Ehrlich tumor with direct electric current
Cummings	2001	Electroacupuncture is effective for control of myeloblastic chemotherapy-induced emesis (m104)
Engstrom	2001	Electrically mediated drug delivery for treatment of an adenocarcinoma transplanted into rat liver
Engstrom	2001	A new antitumor treatment combining radiation and electric pulses
Harris	2001	Upper extremity rehabilitation in women with breast cancer after axillary dissection. Clinical practice guide
Itô	2001	Newly developed drug delivery system in cancer chemotherapy using direct electric current
Kuriyama	2001	A potential approach for electrochemotherapy against colorectal carcinoma using a clinically available at
Ozgur Tan	2001	Combination of transcutaneous electrical nerve stimulation and ondansetron in preventing cisplatin-induc
Ren	2001	Variations of dose and electrode spacing for rat breast cancer electrochemical treatment
Williams	2001	Therapeutic electromagnetic field effects on angiogenesis and tumor growth
Benjamin	2002	Pulsed electrostatic fields (ETG) to reduce hair loss in women undergoing chemotherapy for breast canci
Clavo	2002	Increase of brain tumor oxygenation during cervical spinal cord stimulation. Report of three cases
Piang	2002	EM-electromagnetic fields inhibit the proliferation of human cancer cells and induce apoptosis
Rabussay	2002	Enhancing the effectiveness of drug-based cancer therapy by electroporation (electroporomeabilization)
Ye	2002	Effects of electro-acupuncture on immune function after chemotherapy in 28 cases
Jarm	2003	Perturbation of blood flow as a mechanism of anti-tumour action of direct current electrotherapy
Marinco	2003	Unrelievable pain resulting from abdominal cancer: new hope from biophysics?
Yu	2004	A review of research into the uses of low level ultrasound in cancer therapy

- Some of the literature is more directly relevant than others, but to be able to find 800+ refs and when sorted to find 500+ particularly relevant ones, is not bad going
- Some relate to electrodiagnosis and some to therapy
- Some are experimental and others review

Examples of Published Research that Identifies Definite Link between Electrotherapy Modalities and Cancer / Tumour / Malignancy

O' Clock, G. (1997).

The effects of in vitro electrical stimulation on eukaryotic cells: suppression of malignant cell proliferation

J Orthomol Med 12(3): 173-81

- This technique offers a relatively comfortable, low cost and minimally toxic approach towards the treatment of cancer, and it also provides an alternative treatment for malignancies that have developed a resistance to conventional therapeutic approaches.
- The in vitro results reported in this paper strongly indicate that some of the mechanisms associated with electrotherapy may also be occurring at the cellular level.

Vodovnik, L. et al. (1992). Modified cell proliferation due to electrical currents. Med Biol Eng Comput 30(4): CE21-8.

- It is known that non-dividing cells, e.g. mature neurons, have high transmembrane potential (TMP) whereas fast-dividing cells, e.g. cancerous cells, have low TMP.
- When a cell is exposed to an electrical field, one side of the cell becomes hyperpolarised while the opposite side is depolarised.
- It can be shown that in non-dividing cells their high TMP is lowered; whereas in cells with a high division rate, their low TMP is raised due to cell exposure to the external electrical field.
- These alterations in transmembrane potential could contribute to the normalisation of abnormal cell proliferation.

Habal, M. B. (1980). Effect of applied dc currents on experimental tumor growth in rats. J Biomed Mater Res 14(6): 789-801.

- An experimental tumour in rats is treated with small anodal direct current.
- There was major retardation in tumour growth when the treatment was started early.
- There was enhancement of tumour growth when the treatment was started early and then was discontinued.

Taylor, T. et al. (1994). Ablation of neoplasia by direct current. Br J Cancer 70(2): 342-5.

- In humans, the application of low voltage direct current to two patients with benign anal condyloma acuminata, three patients with inoperable obstructing oesophageal cancer and one patient with disseminated Kaposi sarcoma resulted in striking necrosis of tumour tissue that was confirmed by macroscopic and microscopic studies.
- These initial findings imply promising therapeutic potential for the use of direct current as a simple, effective, safe, low-cost alternative for ablation of neoplasia.

Mir, L. et al. (1998). Effective treatment of cutaneous and subcutaneous malignant tumours by electrochemotherapy. Br J Cancer 77(12): 2336-42.

- Electrochemotherapy (ECT) enhances the effectiveness of chemotherapeutic agents by administering the drug in combination with short intense electric pulses.
- ECT is effective because electric pulses permeabilize tumour cell membranes and allow non-permeant drugs, such as bleomycin, to enter the cells.
- The aim of this study was to demonstrate the anti-tumour effectiveness of ECT with bleomycin on cutaneous and subcutaneous tumours.
- This article summarizes results obtained in independent clinical trials performed by five cancer centres.

Mir et al 1998 (contd)

- A total of 291 cutaneous or subcutaneous tumours of basal cell carcinoma (32), malignant melanoma (142), adenocarcinoma (30) and head and neck squamous cell carcinoma (87) were treated in 50 patients.
- Short and intense electric pulses were applied to tumours percutaneously after intravenous or intratumour administration of bleomycin.
- The tumours were measured and the response to the treatment evaluated 30 days after the treatment.

Mir et al (1998) Contd

- Objective responses were obtained in 233 (85.3%) of the 273 evaluable tumours that were treated with ECT. Clinical complete responses were achieved in 154 (56.4%) tumours, and partial responses were observed in 79 (28.9%) tumours.
- The application of electric pulses to the patients was safe and well tolerated.
- Minimal adverse side-effects were observed.
- ECT was shown to be an effective local treatment.
- ECT was effective regardless of the histological type of the tumour.

Ye, F. et al. (2002). Effects of electroacupuncture on immune function after chemotherapy in 28 cases.

J Tradit Chin Med 22(1): 21-3.

- **PURPOSE:** To observe the effects of electroacupuncture therapy on T cells and activity of NK cell in the patient of Chemotherapy.
- **METHOD:** Electro-acupuncture therapy was simultaneously applied during chemotherapy.
- **RESULTS:** Before chemotherapy, CD3 was low within the normal range, CD4 was much lower than the normal range, and CD8, CD4/CD8 and activity of NK cell were within the normal range. After one month of chemotherapy combined with electro-acupuncture, no decline of all the indices was found ($P > 0.05$).
- **CONCLUSION:** Electro-acupuncture can really increase the immune function of patients of chemotherapy.

Various heat related therapies

- Aleksandrov, N. et al. (1973). "Use of thermal effects in the compound treatment of malignant tumors." Vopr Onkol 19(4): 78-88.
- Babbs, C. F. and D. P. DeWitt (1981). "Physical principles of local heat therapy for cancer." Med Instrum 15(6): 367-73.
- Dickson, J. A. et al. (1977). "Tumor eradication in the rabbit by radiofrequency heating." Cancer Res 37(7 Pt 1): 2162-9.
- Israel, L. et al. (1982). "Localized hyperthermia by radiofrequency waves in the treatment of cancer." Prog Clin Biol Res 107: 721-9.

New areas . . .

- New work includes for example the use of ultrasound as a tumour ablation method
- High Intensity Focussed Ultrasound (HIFU)
- WELL above the levels that we would employ in the clinical environment
- BUT very effective for some tumour types

Wu, F. et al. (2004). Extracorporeal high intensity focused ultrasound ablation in the treatment of 1038 patients with solid carcinomas in China: an overview. Ultrason. Sonochem. 11:149-154.

- The ideal treatment of localized cancer should directly cause an irreversible and complete death of tumor cells without damage to surrounding normal tissue. High intensity focused ultrasound (HIFU) is such a potential treatment, which induces a complete coagulative necrosis of a tumor at depth through the intact skin.
- The idea that using an extracorporeal source of therapeutic ultrasound was introduced more than 50 years ago. Up to now, most of the studies on HIFU have been dealing with animal experiments because this extracorporeal technique is very complicated in clinical applications.
- The purpose of this study is to introduce Chinese clinical experience of using extracorporeal HIFU for the treatment of patients with various kinds of solid tumor. From December 1997 to October 2001, a total of 1038 patients with solid tumors underwent HIFU ablation in China.

Wu et al (2004) Contd

Pathological examination showed that the target region presented clear evidence of cellular destruction.

Small blood vessels less than 2 mm in diameter were severely damaged.

Follow-up diagnostic imaging revealed that there was no, or reduced, blood supply, and no uptake of radioisotope in the treated tumor after HIFU, both indicating a positive therapeutic response and an absence of viable tumor.

Imaging at 6-12 months showed obvious regression of the lesion.

Four-year follow-up data were significantly observed in patients with hepatocellular carcinoma, osteosarcoma, and breast cancer.

An extremely low major complication rate was noted.

It is concluded that HIFU ablation is a safe, effective, and feasible modality for the ablation of carcinomas.

Other Recent HIFU Papers

- Kratzik, C. et al. (2006). Transcutaneous high-intensity focused ultrasonography can cure testicular cancer in solitary testis. *Urology* **67**(6): 1269-73.
- Lynch, J. H. and S. Loeb (2007). The Role of High-intensity Focused Ultrasound in Prostate Cancer. *Curr Oncol Rep* **9**(3): 222-5.
- Ren, X. L. et al. (2007). Extracorporeal ablation of uterine fibroids with high-intensity focused ultrasound: imaging and histopathologic evaluation. *J Ultrasound Med* **26**(2): 201-12.
- Wu, F. et al. (2007). Wide local ablation of localized breast cancer using high intensity focused ultrasound. *J Surg Oncol*.

Effects of electrotherapy

- It would seem from the published literature that various forms of electrotherapy, including electrical stimulation thermal therapies and ultrasound can have a direct and real effect on 'cancer'

Effects of electrotherapy

- Assuming that several hundred references are not all wrong, then if 'electrotherapy' has the capacity to influence abnormal growth at a physiological / biochemical / cellular level, then an electrotherapy modality applied for therapeutic reasons **COULD** also have such an effect

Good or Bad . . . ?

- Most of the examples cited from the literature have shown a positive (beneficial) effect in relation to cancer therapy
- There are examples which demonstrate less positive effects in that the rate of tumour growth increases following exposure

Positive and Negative Effects of the Same Modality

-  Worthington, A. E. et al. (1997). Mechanism of ultrasound enhanced porphyrin cytotoxicity. Part I: A search for free radical effects. *Ultrasound Med Biol* **23**(7): 1095-105.
-  Sicard-Rosenbaum, L. et al. (1995). Effects of continuous therapeutic ultrasound on growth and metastasis of subcutaneous murine tumours. *Physical Therapy* **75**(1): 3-13.

Electrotherapy Contraindications

- As previously identified, generally held belief that electrotherapy modalities are contraindicated in relation to cancer, tumours, active TB
- Difficult to find any definitive lists to which everybody agrees
- Some in books, articles and manufacturers guidelines

CSP Guidelines

STANDARDS FOR THE USE OF ELECTROPHYSICAL MODALITIES



THE CHARTERED SOCIETY OF PHYSIOTHERAPY
14 BEDFORD ROW, LONDON WC1R 4ED TEL: 071 242 1941

- CSP Standards published in 1991
- Do not identify contraindications for the individual modalities

STANDARD 4

The selection and application of the modality ensures efficacy and patient safety.

CRITERIA

- 4.1. Assessment includes the identification of any drugs the patient is taking which may sensitise them to electrotherapy or mask their condition and/or response, e.g. anti-inflammatory drugs and analgesia.
- 4.2. All contra indications to treatment are checked.
- 4.3. Treatment is not given to those unable to comprehend information, warnings and instructions.
- 4.4. The physiotherapist minimises the exposure of the patient to any undesirable effects of the modality.
- 4.5. The modality is applied in a way which ensures the maximum therapeutic effect.
- 4.6. The part of the body to be treated is exposed as necessary.
- 4.7. The type of sensation to be experienced is explained to the patient.

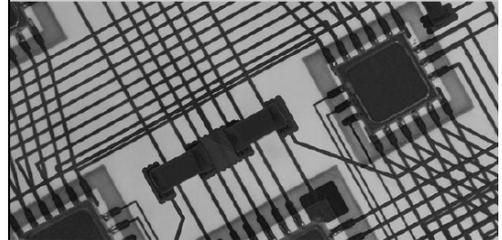


- Identifies that you need to check the contraindications, but not what they are
- Also states that you need to minimise the exposure to undesirable effects

Current Guidance

- More recent series of meetings and discussion with 'group of experts' who tried to identify a set of good practice guidelines and standards for all commonly applied modalities
- Started in 1997, completed in 1999
- Updated in 2002 and again in 2006
- Now actually published (launched Feb 2007)

2006 Guidance for the Clinical use of Electrotherapy Agents



Guidelines . . . the process . . .

- Considerable controversy with regards what IS and what IS NOT an EVIDENCED contraindication and / or precaution and / or danger for specific modalities
- Had to combine published evidence where it existed and use expert opinion and clinical norms where not

Generic Guidance

During the selection and application of any electrophysical agents (EPA's), the following measures should be taken to ensure safety and good practise.	Reference
Contraindications for all agents	
those who are unable to comprehend instructions, or who are unable to co-operate	CSP Core Standards (2005)
the application of electrophysical agents over the abdomen, lower back or pelvis is normally contraindicated during the first 35-weeks of pregnancy. Refer to specific information for each agent.	Expert Opinion
In the area of a tumour where there is active or suspected malignancy, except for palliative care	001*002*003*004*005*006*007*008*009*
areas of recent bleeding tissue or haemorrhage.	Expert Opinion
active tuberculosis in treatment area	Expert Opinion

Reference Support

References – All agents – Contraindications

- *001 Auda, S. P. G. Hall, et al. (1979). 'Selective tumor heating and growth retardation by shortwave radiofrequency.' *Surg Forum* 30:154-6.
- *002 Auda, S. P. H. R. Steiner, et al. (1980). 'Selective tumor heating by shortwave radiofrequency (RF).' *Cancer* 46(9): 1962-8.
- *003 Habal, M. B. (1980). 'Effect of applied dc currents on experimental tumor growth in rats.' *J Biomed Mater Res* 14(6): 789-801.
- *004 Jarm, T. Y. A. Wickramasinghe, et al. (1999). 'Blood perfusion of subcutaneous tumours in mice following the application of low-level direct electric current.' *Adv Exp Med Biol* 471: 497-506.
- *005 Lejbkovicz, F. M. Zviran, et al. (1993). 'The response of normal and malignant cells to ultrasound in vitro.' *Ultrasound Med Biol* 19(1): 75-82.
- *006 Marino, A. (1993). 'Electromagnetic fields, cancer and the theory of neuroendocrine related promotion.' *Bioelectrochemistry and Bioenergetics* 29(3): 255-276.
- *007 Miyagi, N., K. Sato, et al. (2000). 'Effects of PEMF on a murine osteosarcoma cell line: Drug-resistant (P-Glycoprotein-positive) and non-resistant cells.' *Bioelectromagnetics* 21: 112-121.
- *008 Sicard-Rosenbaum, L. D. Lord, et al. (1995). 'Effects of continuous therapeutic ultrasound on growth and metastasis of subcutaneous murine tumors.' *Physical Therapy* 75(1): 3-13.
- *009 Verschaeve, L. (1995). 'Can nonionising radiation induce cancer.' *Cancer Journal* 8(5): 237-249.

General Precautions and Health / Safety

Precautions for all agent	Reference
Treatment should not normally be carried out over the anterior aspect of the neck	Expert Opinion
where there is significant impairment in the circulation/sensory loss of the area to be treated.	Expert Opinion
where there is devitalised tissue e.g. after recent radiotherapy.	Expert Opinion
where there is local acute skin conditions e.g. eczema, dermatitis.	Expert Opinion

6.1 Health and Safety Considerations	
treatment is carried out in compliance with local regulations.	Norm
the surrounding environment is safe for treatment	Expert Opinion
there is a warning sign relating to patients with internal stimulators where high frequency equipment is used.	Expert Opinion

Contraindications Grid

- It was identified that there was a considerable overlap between numerous modalities in terms of CI's and Precautions
- The GRID solution was a way to resolve the common issues and also to provide a quick reference for clinical practice

6.1 Quick reference grid

CONTRAINDICATION PRECAUTION	Pregnancy (in fetal regard)	Pregnancy (in breast)	Malignancy	Spontaneous tissue	Active implants - i.e. Pacemaker	Active Epilepsy	Metast. implants	Local circulation insufficiency	Epilepsy	Chest related tissue	Bleeding tissue	Thermal skin test	Metabolic skin test
Agent													
Electrical stimulation													
generic			E, T									?	?
interferential			E, T									?	?
low frequency			E, T									?	?
tens			E, T									?	?
Non thermal													
laser			E, T									?	?
pulsed shortwave			E, T									?	?
ultrasound			E, T									?	?
Thermal													
hot pack			E									?	?
ultrasound			E									?	?
microwaves			E, T									?	?
shortwave (continuous)			E, T									?	?
ultrasound			E, T									?	?
wave			E									?	?
Others													
biofeedback (no stimulation)												?	?
cold therapy			E									?	?
ultra violet												?	?
			E = eyes									N = neck	
			T = teeth										
			contraindication									necessary	?
			local contraindication									not required	?
			precaution										
			no known adverse effects										
			see specific agent										

Malignancy on the contraindication lists

- Still some debate, especially with regards some of the electrical stimulation modalities
- The GRID is a summary for the 'general' therapist
- 'Play it safe' - conservative - for the most part

How can we interpret the grey areas?

- Still some difficulty in terms of the list
- ??what counts as malignant tissue
- ??is it malignant post surgery
- ??how long after Rx does it no longer count
- ??what about palliative / terminal / hospice care

Suggestions

- Some modalities present a higher risk
- E.g. ultrasound, laser and pulsed shortwave
- But still only in the local area
- Although this may be quite extensive for 'large field' modalities such as shortwave / pulsed shortwave

Suggestions II

- If the cancer / tumour is being actively treated, best to avoid electrotherapy
- If it is being monitored, but not 'treated' as such, have to make a clinical judgement
- If in doubt best avoid the LOCAL area

Suggestions III

- There is LEAST evidence for an adverse effect with regards the electrical stimulation modalities
- DC type stimulation is still best avoided as it has the greatest capacity to influence tumour growth and development
- TENS, IFT and NMES are not DC in nature and therefore present a minimal (if any) risk

Palliative / Hospice Care

- Suggest that quality of life is the main issue
- If (??) electrotherapy has an adverse effect on progress of cancer / tumour, which is the worse option - leave the patient in pain / discomfort or run the potential risk of increased division rate

Palliative / Hospice Care

- 'Informed consent' applies as it would to any intervention
- Outline the options and relative benefits
- Follow normal clinical practice in such circumstances

Summary

- Cancer / malignancy / tumour widely considered to be a contraindication for all forms of electrotherapy
- Some evidence base, but not as categorical as once thought
- Potential treatment in the not too distant future???

Summary II

- Electrotherapy has the same potential benefit as it would for other patients
- Best avoided in the local region of the rapidly dividing tissue
- Can apply elsewhere (especially 'localised' treatments)

Summary III

- OK to use in palliative etc care
- OK to use if tumour is not being actively treated
- Need consent in the normal way
- If in doubt think '***DIVIDING TISSUE EXPOSURE***'
- If still in doubt, then don't!