Electro-Pulse-Enhanced Cancer Therapy

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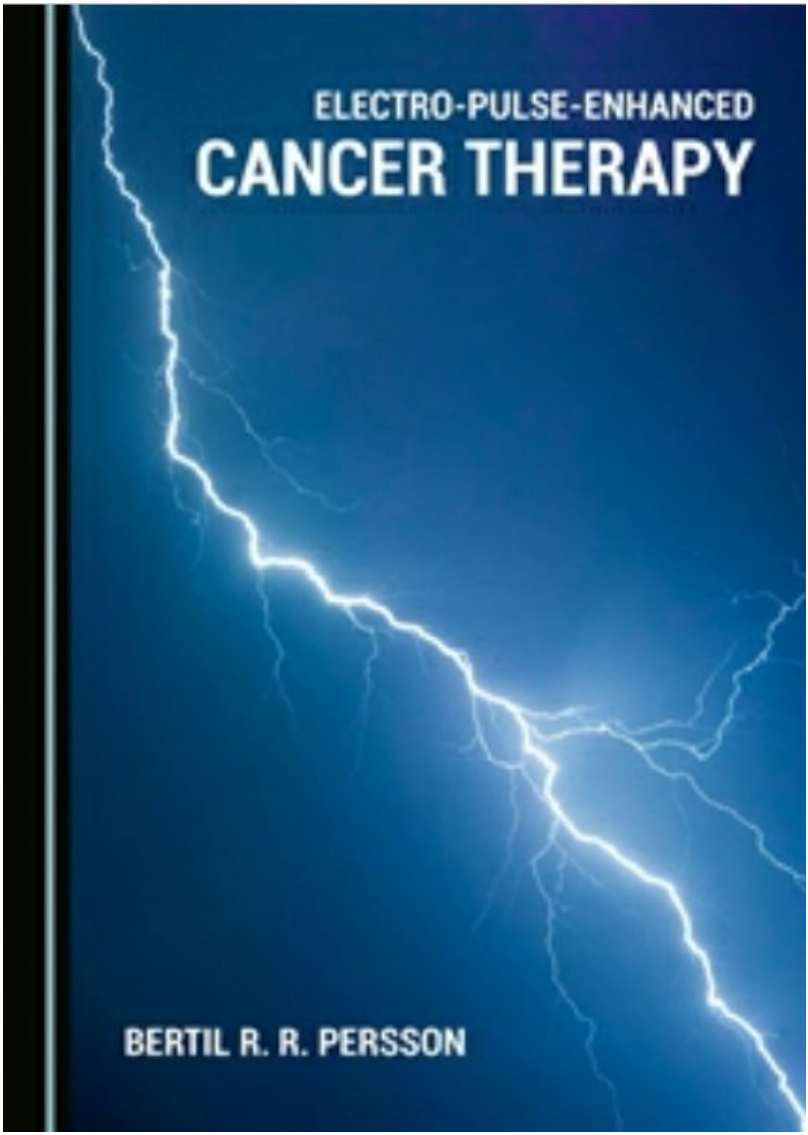
ELECTRO-PULSE-ENHANCED
CANCER THERAPY
BERTIL R. R. PERSSON

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ABSTRACT

This book is a summary of my 30 years' experience of electro-pulse-enhanced-therapy in the treatment of malignant tumours.

The first chapter is a short history of the discoveries that led to the clinical use of electro-pulse-enhanced cancer therapy (EpECT). In the late 1960s, Sale found that the action of inducing short electric pulses upon biological cell membranes made them transiently permeable without damaging the membrane structures. In the 1970s, Zimmermann observed that red blood cells began to lose haemoglobin after exposure to a pulsed electric field that exceeded a certain threshold. Exposure to short electrical pulses with amplitudes between 4 and 6 kV/cm resulted in the cells melting together into larger cells containing several nuclei. In the 1980s, Neumann and Wong demonstrated that electrical field-mediated transfer of DNA into cells is a handy technique, simple and easy to apply for DNA transfection. Okino and Mohri reported in 1987 the possibility of using the electroporation effect for enhanced transport of the anticancer drug Bleomycin across the cell membrane. The first clinical trial with EECT was performed on head and neck tumours by L. Mir and colleagues in France, 1991.

The second chapter describes the electrochemical and biophysical principles of the action of high voltage electrical pulses applied to human cells and tissues. The creation of channels in the cell-membrane, usually called electroporation, is the main phenomenon considered in electro-enhanced chemotherapy. However, electrochemical processes may also be involved.

My profession is in medical radiation physics, where radiation dosimetry is the most critical issue in radiation therapy. Thus, I considered it essential to know for certain the amount of energy delivered to the patient in electro-pulse enhanced cancer therapy as well.

The third chapter describes the measurement of the change in the electrical impedance of the tissue as an excellent way to estimate the energy delivered to the tissue through exposure to electrical high voltage pulses.

Another branch of my profession is the use of radio-pharmaceuticals to study the morphology and function of various human organs. As such, the fourth chapter describes the use of radioactive labelled drugs and gamma-camera recording to explore the enhanced uptake of drugs after exposure to electric pulses. Multivariate statistical methods are used to predict the

dependence of drug uptake in the exposed and non-exposed tissue on several variables

The fifth chapter summarizes the results of numerous preclinical studies of electro-pulse enhanced cancer therapy. Bleomycin and Cis-platinum are the drugs mainly used in clinical applications of such therapy. The results of extensive preclinical studies are shown to indicate promising combinations of electro-pulse chemotherapy with established immune therapy and radiation therapy regimes.

As mentioned above, the first clinical trial using Bleomycin and electric pulse treatment (called “electro-chemotherapy” (ECT)) was performed on head and neck tumours by Mir and colleagues in France in 1991. In the following years (up until 2018), clinical trials have treated more than 1500 patients with malignant melanoma, Kaposi´s sarcoma, breast cancer, squamous cell carcinoma, and basal cell carcinoma. The sixth chapter reviews and analyses the clinical results of these trials.

The seventh section discusses the safety concerns that must be taken into account when treating patients with high voltage electrical pulses.

The eighth, and final, part of the book presents a summary of potential new dimensions in electro-pulse enhanced Cancer therapy.

ACKNOWLEDGEMENTS

This book is dedicated to my collaborators in the field of electro-pulse-enhanced cancer therapy (EpECT) over the past 30 years: Leif G. Salford, MD, Professor of Neuro Surgery at Lund University, who opened his laboratory for the first experiments with malignant glioma implanted in rat brains; Louis Mir who supported us with a French electroporation device for animal experiments which led to the publication of "A new brain tumour therapy with EpECT"; Per Henriksson for the "Zero Weed" adventure; Maria Danfelter MSc, for her dedicated pioneering work with cell survival; Per Engström, PhD, for his eminent pre-clinical pioneering work, a strong thesis, and for conducting the first clinical operations with EpECT; Catrin Bauréus-Koch, PhD, for her dedicated work in the extensive rat experiments using radiation and immune therapy combinations, and her exquisite thesis; Gustaf Grafström, PhD, for his skilful operations in the extensive rat experiments; Susanne Strömblad and Catarina Blennow, for their skilful technical assistance in the animal experiments and histology preparations; Bernt Böhmer, engineer and entrepreneur, for his skilful constructions and manufacturing of our various electro-pulse devices; Anders Johnsson, for promoting the gamma camera experiments, and Mohan Frick for bringing electro-pulse-enhanced cancer therapy to the market.

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