ELECTRO CHEMOTHERAPY
AND ELECTRO IMMUNOTHERAPY

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Executive Summary

In 1987, Okino and Mohri showed for the first time that electro-permeabilization can be applied *in vivo* to increase the concentration of anticancer agents in solid tumours. *In vivo* electropermeabilization used to augment the chemotherapeutic efficiency in cancer treatment has been termed *electro chemotherapy*. This novel mode of tumour treatment has been employed mostly for subcutaneous and coetaneous malignancies but the treatment of orthotopic tumours, e.g. mammary tumours, melanoma, hepatic tumours from colorectal cancer, hepatomas, subcutaneous and orthotopic pancreatic adenocarcinomas , soft tissue sarcomas , bladder cancer, subcutaneous and intracerebral gliomas.

In electro chemotherapy treatment, only the cells exposed to a sufficiently strong electric field will respond immediately. Permeabilized cells become much more accessible to hydrophilic molecules, which normally are rejected by the membrane barrier. Bleomycin, a very toxic anticancer agent, has proven to be the most potent drug in electro chemotherapy and is by far the one most often used, but Cisplatin, another anticancer agent has also been found to be effective.

Reports on efficient *electro chemotherapy* on orthotopic tumours are truly encouraging. Using a high voltage pulse supply and an obsolete anticancer agent (Bleomycin or Cisplatin) to achieve complete eradication of highly malignant tumours within a few days without side effects may appear almost too good to be true.

Mir and colleagues in France performed the first clinical trial with electro chemotherapy on head and neck tumours, 1991. Since then head and neck squamous cell carcinoma has been treated clinically using electro chemotherapy be several groups . Some of these studies report very high rates of complete response with few or no recurrences.

A response-rate greater than 90% in electro chemotherapy of skin cancers, including basal cell carcinoma and coetaneous melanoma with intralesional bleomycin and electric voltage pulses has been demonstrated in clinical trials. Clinical experience from treatment of malignant melanoma patients with electro chemo-therapy and bleomycin has been reported by.

Besides high treatment efficiency and lack of side effects *electro chemotherapy* is performed in a short time compared to other therapeutic regimes. Due to these beneficial properties clinical applications of *electro chemotherapy* are continuously growing and gaining increasing interest in the medical community.

Several studies have suggested that the host's immune system is activated after tumour treatment with electropermeabilization. In one study systemic, antimetastatic immune responses were achieved by delivering histoincompatible cells secreting interleukin-2 (IL-2) in combination with electro chemotherapy.

In an attempt to achieve immunoreactions against implanted brain tumours, rats with N29 glioma tumours were delivered with electric pulses followed by injections of IL-18 and IFN-γ secreting cells. This treatment resulted in a prolonged survival (the time for the contralateral tumour to reach the predetermined limit volume), by 50%.

These results show that a systemic response of the host's immune system can been achieved against the tumour, using *syngeneic* tumour cells. This may be an important step towards development of *electro immunotherapy* to an effective tumour treatment modality.

The pulse shape, amplitude and pulse length used in the mostly used protocols are not necessarily the most efficient in all conditions. Therefore there is a great need for a method to verify and control the degree of electroporation that is achieved after each pulse in order to optimise the outcome of the treatment.
This important aspect can be handled by using a computerised arbitrary pulse generator that is able to design, in principle, any pulse form or pulse train. Such equipment, which is integrated with an impedance spectrometry device, has been developed and built by Aditus in Lund. This instrument will be used to refine and optimise the pulse protocols governing the optimal efficiency in electro chemo-therapy applications. Although the equipment for controlled electro chemo-therapy is and advanced highly computerized device, it is easy to move around and can be operated from a movable power source. Thus this gives makes it possible to perform electro chemotherapy in regions where radiation therapy and operation theatre for advanced surgery are not accessible.

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