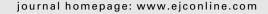


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Introduction

Why a supplemental issue on electrochemotherapy and why now?

Electrochemotherapy (ECT) is a non-thermal tumour ablation modality, safe and effective on any type of solid tumour. Its use is presently standardized to skin and subcutaneous localisations, whatever the tumour histological origin. ECT is based on the local delivery of electric pulses that permeabilize the cell membrane, allowing non-permeant or low-permeant anticancer drugs, such as bleomycin or cisplatin, to enter the cell, thus magnifying their cytotoxicity by orders of magnitude. Treatment is safe, very well tolerated by the patients, and efficacy is very high on the treated nodules.

The term electrochemotherapy was coined in 1987, when the concept was elaborated by my team at the Institute Gustave-Roussy, in the laboratory, on cells in culture, and soon after, in preclinical experiments. The procedure was rapidly translated in clinical studies. These initial studies showed feasibility and already good antitumour effectiveness in treatment of tumours in cancer patients. However, up to now ECT has not been utilised regularly in the clinical practice for two main reasons. The initial clinical trials were performed with equipments used in the laboratory, they required the assistance of specialised personnel (e.g. researchers, etc.), electrodes were customised by each centre, and, overall, the safety and quality of products used did not meet the criteria required for routine application. Human trials with devices for clinical use were only reported with Medpulser, but these treatments were exclusively performed using intratumor injection of bleomycin and one type of electrodes. Secondly, no standardization of the ECT had been reached: the procedures were based on individual experience often directly derived from preclinical trials on animals, and no direct comparison among the different ECT modalities had been performed to specify their use in different clinical conditions, i.e. number, size, type and localisation of the nodules.

In fact the development of the electrochemotherapy has been a very good example of translational research that is also reviewed in this issue. The biological and physiological bases of the electrochemotherapy (L.M. Mir, this issue), as well as the constraints for effective delivery of electric fields to the tumours (D. Miklavcic, this issue) have been explored in the last 15 years, for a science-based, efficient and safe application of the new concepts at the clinical stage. Numerous clinical experiences (summarised in this issue by G. Sersa) were reported in the late 90s, all reinforcing the evidence of the ECT efficacy and of the need for adequate equipment and validated standard operational procedures.

Nowadays, electrochemotherapy has thus reached the stage to leave the restricted circle of the clinical groups involved in translational research to become a routinely used treatment modality thanks to the work supported by EU Commission during the last 6 years. Within the 5th FP, the EU Commission funded first the Cliniporator (QLK3-1999-00484) project that led to the development of a new device, the Cliniporator[™], which is now available to all oncologists and can be used in the clinical practice. As presented in this issue this device incorporates a number of features that make the ECT simpler, faster and safer. Then the use of this device has been validated within a second project (QLK3-2002-02003) that was also funded by the EU Commission within the 5th FP: the ESOPE project, acronym of European Standard Operating Procedures of the Electrochemotherapy (and of the Electrogenetherapy, another biomedical application of the electric pulses delivery in vivo, not discussed in this

Within the frame of the ESOPE EU project, performed by three clinical groups with previous preclinical and clinical experience on ECT and one group without such a previous experience, SOP of the electrochemotherapy were prepared and then internally validated in a clinical study reported in this issue by M. Marty, G. Sersa, and the ESOPE colleagues. The SOP are also published here. These two main papers are followed by short case reports that provide several examples of difficult cases that could be treated by ECT. Finally, the supplemental issue is completed by the three short review papers, presented here above, that address the bases and rationale for the treatment, and summarise all the clinical experience on ECT present in the literature.

The content of this issue should thus allow physicians to fully understand the potential of ECT, and, through the SOP, provide the information required for ECT application. To help the dissemination of ECT the partners of the EU projects have defined training programmes to demonstrate the methodology. The physicians that had just one day training now treat by ECT their own patients at their institutions.

As shown in this issue, ECT is bringing high benefit to patients even, in the worst of the cases, on inoperable tumours, located in pre-irradiated areas and resistant to chemotherapy. ECT, in most of the patients, can be applied under outpatient bases, and cost benefit ratio is very favourable, since bleomycin and cisplatin are inexpensive drugs and the equipment necessary for ECT is much less costly that any ionising radiation device, or other devices, like those necessary for cryosurgery.

Electrochemotherapy is still restricted to the treatment of cutaneous and subcutaneous metastasis localisations. In the future, with further technological development of the electrodes, internal tumours will also be accessible to treatment with ECT.

The combined efforts of the partners gathered by the EU Commission (researchers, clinicians and industry) has made available to oncologists a new very efficient treatment modality that with limited investment can be adopted by many centres both in developed and underdeveloped countries. I am confident that the information contained in this issue will be convincing to the readers and provide the support for the dissemination of the electrochemotherapy methodology.

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