

It's electric: Boogie woogie, woogie those tumors away!! An overview of treating skin tumors with electrochemotherapy

Introduction:

Treatment for cancer in veterinary medicine entails many different modalities. Oncologists will often refer to cancer therapy in two broad categories. These include local disease control and systemic disease control. Local disease treatment often includes surgery and/or radiation therapy for the treatment of the primary tumor, while systemic disease control is achieved with chemotherapy for the treatment of metastatic disease.

In some patients, the tumor may not be amenable to surgical removal or complete margins may not be obtainable given the anatomical location. If tumor cells are left behind, the tumor can recur; therefore, radiation therapy is effective for treatment of residual disease. While effective, radiation therapy can be cost prohibitive for some pet owners and requires multiple anesthetic events over a period of a few weeks. An alternative therapy for such cases is electrochemotherapy (ECT). This is an additional treatment modality that has come into favor in veterinary medicine over the past several years and is now gaining recognition as a viable treatment option for cancer.

What is electrochemotherapy (ECT)?

ECT is the local treatment of cancer using a combination of chemotherapy drugs and electrical pulses.¹⁻¹⁰ Electric pulses are created by a generator and delivered to the target tissue using electrodes to achieve "electroporation" of the tumor cells.¹

Mechanism of action:

Electroporation is a physical method that uses electrical pulse to create temporary pores in cell membranes through which substances like chemotherapy can pass into the cells and target the DNA directly.^{6,7,10} There are three major reported mechanisms of action for ECT: electroporation (electroporation), vascular effects and the induction of systemic immunity.^{1,9}

The cell membrane is the major obstacle to be overcome by chemotherapy agents to reach their biological targets. The principal mechanism of ECT is electroporation of the tumor cells leading to increased intracellular drug accumulation by exposure of the tumor cells to an electric field.¹⁻³

ECT also has vascular effects in the tumor microenvironment and these include vascular disruption and vasoconstriction. Vascular disruption involves endothelial cell death leading to decreased local blood flow to the surrounding tissues.^{1,4} The vasoconstriction effect induces prolonged entrapment of the chemotherapy drug within the tumor.^{1,4}

The last mechanism of action occurs from induction of systemic immunity by antigen shedding from the tumor cells after they are destroyed by ECT.¹ Eradication of the tumor occurs once the immune system has been triggered.⁸

Which drugs are used for treatment?

The two chemotherapeutics that have shown the most promise are bleomycin and cisplatin.¹⁻¹⁰ These drugs have limited transport through the cell membrane but are extremely cytotoxic once bound to DNA inside the cell. Bleomycin, an antitumor antibiotic, has efficacy that appears to be potentiated 1,000-fold with electroporation of cells.^{2,4} Cisplatin, a platinum containing chemotherapeutic, has increased cytotoxicity up to 80-fold.^{2,4}

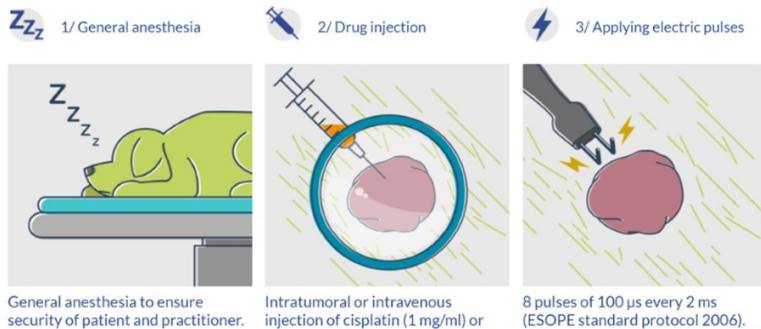
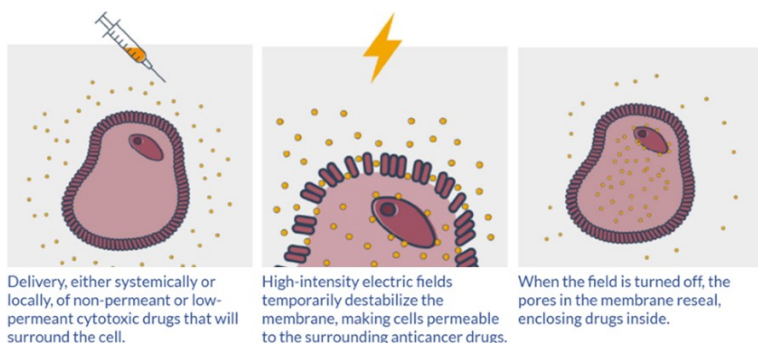
What tumors can be treated with electrochemotherapy?

In veterinary medicine, ECT is used for dermal, cutaneous, or subcutaneous tumors. A few examples include (but are not limited to):

- Melanoma
- Squamous cell carcinoma (SCC)
- Soft tissue sarcomas
- Feline injection-site sarcoma
- Localized cutaneous lymphoma
- Plasmacytic tumors
- Low to intermediate grade mast cell tumors
- Some oral tumors
- Perianal and rectal tumors
- Sarcoids and SCC in horses
- Superficial tumors on exotics

Procedure:

1. General anesthesia of the patient
2. Injection of the chemotherapy either intratumorally and/or intravenously
3. Waiting the appropriate amount of time and then applying the electric pulse. The procedure uses the application of permeabilizing short high voltage electric pulses with appropriate amplitude and waveforms generated with an electric pulse generator machine^{1,3,5}



Photos courtesy of Leroy biotech

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Most patients typically need one to three treatments, and each treatment under general anesthesia typically takes about 20 minutes. Depending on response or size, tumors often require 1-3 treatments given once every 2-4 weeks.^{1,3,4} This technique can be used for incompletely excised tumors and/or tumors that cannot be excised without significant complication/deformity to the patient.⁴ The treatment can be performed on an outpatient basis, it is safe, and shows good long-lasting objective responses in approximately 80% of patients.^{3,4,7,10}

What are the side effects of electrochemotherapy?

- **Immediate:** involuntary, temporary contractions/spasms of the underlying muscle in the treated area, minor irritation locally
- **Delayed:** erythema, edema, and possible necrosis of the tumor

Supportive care, such as bandage changes, anti-inflammatories, and antibiotics, are utilized until the treated wound has healed.⁴ Over a period of a few weeks, healthy scar tissue will replace damaged tissue.³ Patients will sometimes develop permanent hair loss over the treatment site.

Summary:

ECT is a viable treatment option for local disease control of cancer in veterinary patients. It is safe, efficacious, and not cost prohibitive for most pet owners. ECT can be done on an outpatient basis and does not have significant long term side effects. It is a great novel therapy in veterinary oncology and should be considered for patients that fit the appropriate criteria.

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 11. Photos courtesy of Leroy biotech: <https://www.leroybiotech.com/electrochemotherapy/what-is-electrochemotherapy/>

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