

Percutaneous Image-Guided Electrochemotherapy of Spine Metastases: Initial Experience

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Abstract Two patients underwent percutaneous image-guided electrochemotherapy on blastic spine metastases involving posterior walls of the lumbar vertebral bodies with epidural extension. These treatments were performed safely under cone beam computed tomography. Local tumor control was obtained on the subsequent follow-up as well as pain relief and disability improvement. Electrochemotherapy might be considered for patients with thus far no other alternative in order to obtain tumor control and improvement in patients' quality of life.

Keywords Electrochemotherapy · Bone · Metastasis · CBCT · Interventional oncology

Introduction

Image-guided percutaneous ablation for treatment of spinal metastases is determined by tumor location, size, and composition (osteolytic, osteoblastic, or mixed) [1]. Thus far, osteoblastic lesions are treated with radiofrequency ablation, cryoablation, or microwave ablation. However, important potential complications of these thermal ablations are myelopathic and radicular symptoms related to injuries to spinal cord and nerve roots [1]. Irreversible electroporation (IRE) is a nonthermal ablation technique allowing the disruption of cell membranes and homeostatic mechanisms after the passage of electric current through tissue [2–4]. However, potential injury to the nerve roots remains a concern for the use of IRE in the epidural space [4]. Electrochemotherapy is a tissue-sparing procedure allowing a highly selective destruction of tumors cells [5–7]. It uses ultra-short but strong electrical fields to create, unlike IRE, reversible nanopores in the cell membrane facilitating delivery of a chemotherapeutic drug, such as bleomycin, to cells [5, 6].

Although electrochemotherapy was mainly tested for primary and secondary liver tumors [8–10], a study demonstrated clinically its feasibility and safety in bone [11]. Hence, it might be an option to treat tumors in challenging location or to further avoid injuries on sensitive tissue such as nerve roots. Only one case description was reported in spine performed during a surgical procedure [7]. The purpose of this case report was therefore to demonstrate the feasibility of electrochemotherapy performed percutaneously in spine under imaging guidance and to report its tolerance and short-term efficacy.

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Cases Description

Two successive patients underwent two percutaneous image-guided electrochemotherapies of blastic spine metastases (Figs. 1A, 2A). The first patient was a 59-year-old woman who had a metastatic breast carcinoma, and the second patient was a 60-year-old man who had a metastatic lung carcinoma. Both had previously undergone chemotherapy.

Both patients received radiation therapy on bone metastases due to severe back pain. Tumors presented with epidural extension located on L2 and L1 vertebra, respectively (Figs. 1B, C, 2B, C). As the patients were still symptomatic 3 months after, the patients were referred to the interventional oncology department for further treatment. Pain was quantified at 65 mm on the visual analogue scale (VAS, which consists of a straight 10 cm line with the end points defining extreme limits such as 'no pain at all' and 'pain as bad as it could be') for the first patient and 90 mm for the second patient. Electrochemotherapy was offered as a local palliative treatment option to obtain pain relief and prevent rapid disease progression. Electrochemotherapy was intended to spare the patients from any intolerable morbidity coming from extended surgical resection. Conventional ablation techniques such as

radiofrequency ablation, microwave ablation, or cryoablation were not considered as an option due to the location of the tumor involving the posterior wall of vertebral bodies [12]. The patients agreed with this option discussed in multidisciplinary team meeting and gave their informed consent.

Under general anesthesia, the patients were placed in the prone position. In order to obtain an adequate insertion of electrodes to cover the whole tumor, cone beam CT-guided procedure was planned. For each patient, a total of six 20-cm-long needle electrodes were inserted after drilling each pedicle and vertebral body of the vertebrae targeted as well as the vertebrae located above and below (Figs. 1D, 2D). The needles had a 3-cm non-isolated tip length and were all carefully placed parallelly. This disposition allowed to produce a sufficiently intensive electric field encompassing the tumor according to the individualized treatment plan (Figs. 1E, 2E). Electric pulses, generated by Cliniporator Vitae (IGEA, Italy) not synchronized with ECG, were delivered 8 min after the intravenous administration of bleomycin in a bolus of 60 s (15,000 IU/m², Sanofi, France). The settings were fixed to produce a 1000 V/cm electric field within the targeted area, and 8 pulses of 100 μ s were delivered at a voltage ranging

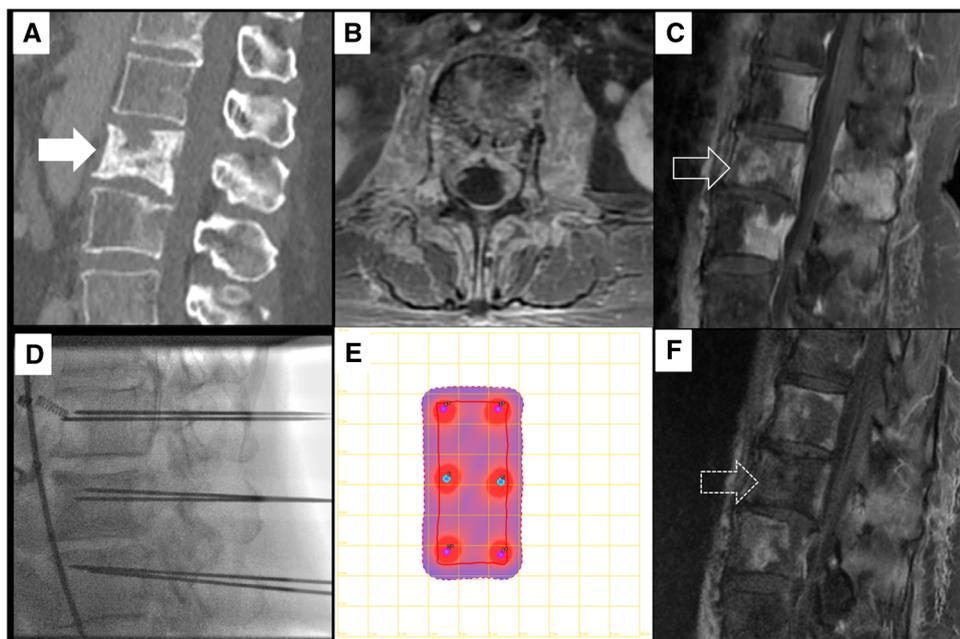


Fig. 1 A 59-year-old woman who underwent percutaneous image-guided electrochemotherapy of spine metastases from breast carcinoma (patient 1). **A** Preprocedural computed tomography reconstructed in the sagittal plane showing a blastic tumor on L2 (white arrow). **B** Preprocedural axial post-contrast T1-weighted MR image confirms the epidural extension of the tumor in L2. **C** Preprocedural sagittal post-contrast T1-weighted MR image shows the metastases located on L1, L2, and L3 (arrow). **D** Six needles were inserted under

imaging guidance under cone beam CT to cover the whole tumor following the individualized treatment plan. **E** Individualized treatment plan, coronal reconstruction. This disposition allowed to produce a sufficiently intensive electric field encompassing the tumors. **F** Enhancement decreased on the sagittal post-contrast T1-weighted MR image performed the day after the procedure (dashed arrow)

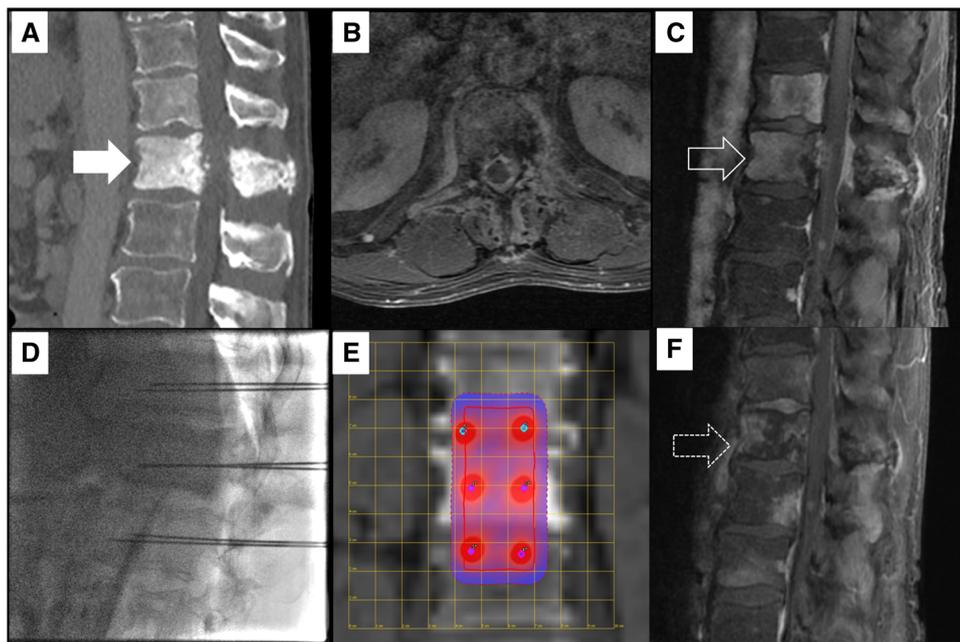


Fig. 2 A 60-year-old man who underwent percutaneous image-guided electrochemotherapy of spine metastases from lung carcinoma (patient 2). **A** Preprocedural computed tomography reconstructed in the sagittal plane showing a blastic tumor on L1 (white arrow). **B** Preprocedural axial post-contrast T1-weighted MR image confirms the epidural extension of the tumor in L1. **C** Preprocedural sagittal post-contrast T1-weighted MR image shows the metastases located on

T12 and L1 (arrow). **D** Six needles were inserted under imaging guidance under cone beam CT to cover the whole tumor following the individualized treatment plan. **E** Individualized treatment plan, coronal reconstruction. This disposition allowed to produce a sufficiently intensive electric field encompassing the tumors. **F** Enhancement decreased on the sagittal post-contrast T1-weighted MR image performed 2 weeks after the procedure (dashed arrow)

from 2100 to 3000 V for each combination of needles, the distance between the probes ranging from 21 to 35 mm.

The tolerance was excellent, and the post-treatment period was uneventful without reported side effects according to the CIRSE classification of complications [13]. Hospital stay was 3 days after the treatment. On contrast-enhanced MR imaging performed 24 h after treatment, enhancement of metastases decreased (Fig. 1F). At discharge, the VAS was 0 mm for the first patient and 10 mm for the second. The length of follow-up was 6 months for patient 1 and 2 months for patient 2. In addition of pain relief, local tumor response was confirmed on all follow-up imaging (Fig. 2F). No adverse effect was reported. Both patients reduced pain medication after the procedures.

Discussion

Our observations illustrate that percutaneous electrochemotherapy of bone metastases can be performed safely and effectively under CBCT guidance even in challenging locations such as spine. Preclinical studies demonstrated preservation of both bone osteogenic activity and bone hardness after electrochemotherapy [14]. In a clinical trial, electrochemotherapy was considered to be

safe and feasible in the treatment of painful bone metastases located in the appendicular skeleton [11]. In this study, pain relief and disease progression control were achieved in the majority of the patients, with consequent improvement of quality of life. Moreover, a case report demonstrated regressive histopathological changes [7]. A > 95% necrosis in the biopsy specimen at 3 months follow-up period was observed.

Electrochemotherapy induces cell death as any other ablation methods such as radiofrequency ablation, microwave ablation, or cryoablation [15–17]. However, electrochemotherapy is not an ablation method. Contrary to these, other percutaneous image-guided techniques producing cell death based on the effects of physical agents only, the effect of electrochemotherapy is based solely on the toxicity of the chemoagent itself, i.e., the bleomycin, on the dividing cells within the targeted area. Bleomycin local toxicity is increased up to 10.000 times by the electric field produced between the needles [5, 18]. It is hence a tissue-sparing procedure that maintains the functionality of the tissues while allowing a highly selective destruction of the tumors cells within 24 h [19–21]. Immune responses and modification of tumor blood flow may also be observed. Systemic immunity is induced because of the generation of an immunogenic cell death [22], which suggests that

further improvements could be reached by the combination of electrochemotherapy and immunotherapy [23].

In conclusion, local control in spine metastases was obtained after percutaneous image-guided electrochemotherapy. In spine, percutaneous image-guided electrochemotherapy seems an option potentially limiting the occurrence of adverse effects even when the posterior wall is involved. This minimal invasive treatment should be considered for patients with thus far no other alternative in order to obtain tumor control and improvement in patients' quality of life. Further larger evaluation is mandatory before drawing definitive treatment decision tree to guide physicians managing patients under this setting.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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