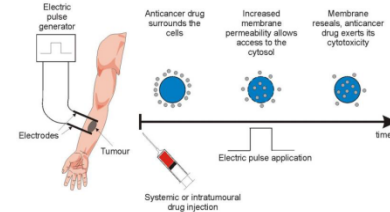


ELEKTROKEMOTERAPİ

Dr Canfeza Sezgin
İstinye ÜTF, Tıbbi Onkoloji BD, İstanbul

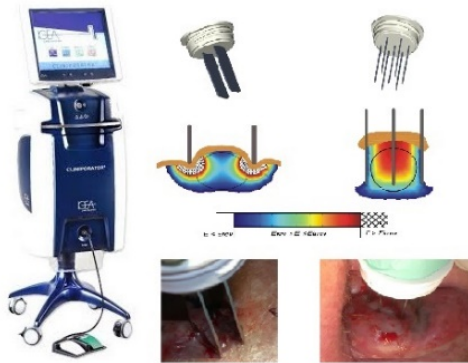
Elektrokemoterapi nedir ?

- Elektrokemoterapi, kemoterapi ilacının doğrudan kanser hücrelerinin içine alınmasını kolaylaştıran tıbbi tedavi yöntemidir



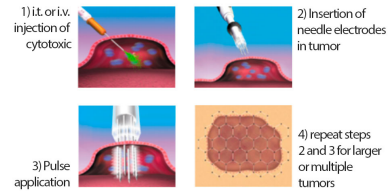
Probst U. Electrochemotherapy as a New Modality in Interventional Oncology: A Review. Technol Cancer Res Treat. 2018;17:1533033818785329.

Elektrokemoterapi



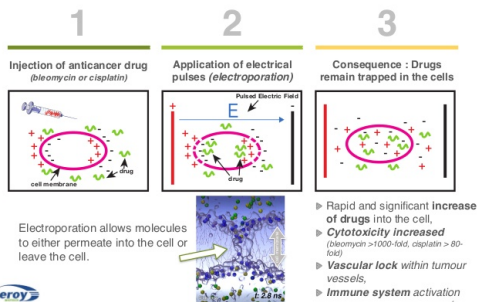
Elektrokemoterapi uygulaması nasıl yapılır?

- Önce intratümöral veya intravenöz kemoterapi ilacı uygulanır
- Sonrasında kanser hücrelerinin kemoterapi ilacını içlerine almasını kolaylaştırmak için elektrotlarla tümöre elektrik uyarısı verilir



Nasıl etki gösterir ?

01 Principles of electrochemotherapy

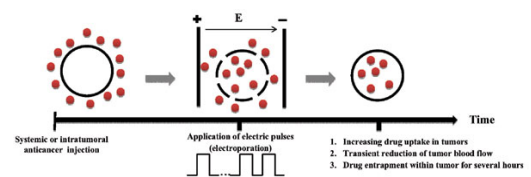


Hani ilaçlar kullanılmaktadır

- Bleomisin

hücrelerin elektrik akımına maruz kalması bleomisin toksisitesini 10,000 kat ↑

- Sisplatin



Elektrokemoterapi hangi kanserlerin tedavisinde yardımcı olur?

- Elektrokemoterapi özellikle deriyi veya deri altındaki yumuşak dokuyu tutan palyasyon gerektiren **cerrahi inoperabl & radyoterapiye uygun olmayan** metastatik veya nonmetastatik kanser tedavisinde kullanılır



Hangi kanser tedavilerinde yardımcıdır?

- Anjiyosarkom, Kaposi sarkomu, Merkel hücreli kanser
- Bazal hücreli ve skuamöz hücre deri kanseri
- Cilt metastazı yapmış meme kanseri
- Cilt / ciltaltı tutulumlu baş ve boyun kanserleri
- Dermatofibrosarkom protuberans & desmoid tümörler
- Dil ve ağız bölgesi kanserleri
- Malign melanom tipi saldırgan deri kanseri
- Karaciğer metastazı
- Kseroderma pigmentozum
- Kütanöz B Hücreli Lenfoma
- Perianal & Anorektal kanserler
- Penil kanserler
- Özefagus kanseri
- Stoma ağzında tümör nüksü
- Vulva kanserleri
- Yüzeysel yerleşimli yumuşak doku sarkomları
- **Kanser aşılari ve immunoterapinin etkisinin artırılması**
- **Radyoterapi etkinliğinin artırılması**

Kontrendikasyonları nelerdir ?

- Gebelik
- Emzirme
- Cisplatin veya bleomisin alerjisi
- Bleomisin kümülatif dozu < 400,000 IU olmalı
- Akciğer fibrozisi – Bleomisin kullanılmamalı

Tedavi öncesi değerlendirme

- Lokal / genel anesteziyle ilişkili önceki sorunlar
- Akciğer fonksiyonu: şart değil; sorunlu hastalarda test
- Renal fonksiyon: gerekirse bleomisin dozu azaltılır
- Koagülasyon testleri
- Karaciğer hastalığı engel değil
- EKG: genel anestezi veya riskli hastalık varsa
- Pace-maker kontrendike değil; yakınında kullanılmamalı
- Ağrı: işleme bağlı ağrı olabilir, riskli hastalarda premed.
- RT veya antiöstrojen tedaviyle emniyetli kullanım; sistemik KT ile arasında birkaç hafta olmalı; immunoterapiyle araştırılıyor

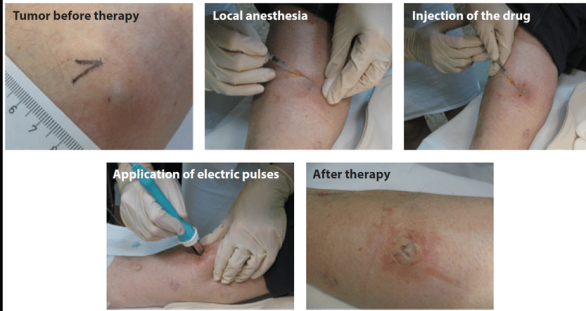
Tedavi seçimi kriterleri

- Tümörün sayısı
- Çapı
- İşlemden 40 dakikalık zamana göre planlama

Anestezi seçimi

	Consider local anesthesia / local drug injection	Consider general anesthesia / intravenous drug injection
Tumour size	≤ 3 cm	> 3 cm
Tumour count	≤ 7	> 7
Region suitable for local anesthesia	yes	no

Lokal elektrokemoterapi uygulaması



İşleme bağlı hangi yan etkiler olabilir ?

İşlem iyi tolere edilirken ciddi yan etki azdır

- Kanama
- Sızıntı
- Ağrı
- Koku
- Ödematöz genişleme
- Tümör nekrozuna bağlı geçici renk değişikliği

İşlem sonrası takip-1

- Bleomisin' e bağlı hiperpigmentasyon
- Pansuman yapışmayan malzeme kullanılmalı
- Ülsere lezyonlar --- medikal bal & gümüş preparat
- Nekrotik dokular debrite edilmeli & Plastik Cerrahi
- Tedavi sonrası banyo yapılabilir
- Profilaktik penisilin / kinolon AB terapi
- Ağrı tedavisi

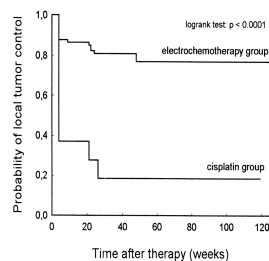


İşlem sonrası takip-2

- 2 haftada bir klinik takibi veya telefon izlemi ile başlanır; 1, 2, 4 ve 6. aylarda kontrolleri yapılır
- Tümör çapı ölçümü, fotoğraf çekimi
- Büyük lezyonlarda daha uzun süreli takip
- **EKT tekrarlanabilir mi?**
4-6 haftalık değerlendirme sonrasında yanıt yetersiz olur ise tekrarlanabilir

Elektrokemoterapinin başarı oranı nedir?

- 376 hastalık çalışmada 60 gün sonunda hastaların yarısında kanser kitlelerinde tam yanıt, hastaların % 88' inde kısmi & tam yanıt elde edilmiş



Campana LG, et al. Treatment efficacy with electrochemotherapy: A multi-institutional prospective observational study on 376 patients with superficial tumors. *European Journal of Surgical Oncology* 2016; 42(12): 1914-1923.

Elektrokemoterapi – baş & boyun kanseri

Head Neck. 2019 Feb;41(2):329-339. The DAHANCA 32 study: Electrochemotherapy for recurrent mucosal head and neck cancer.

Abstract

BACKGROUND: Electrochemotherapy is an established treatment for cutaneous tumors. This study aimed at determining efficacy of electrochemotherapy in recurrent head and neck cancer.

METHODS: Phase II clinical trial in patients with recurrent head and neck carcinomas with no curative treatment options. Electrochemotherapy was performed under general anesthesia. Primary endpoint was tumor response (CT scanning) evaluated at week 8. Secondary endpoints included biopsy results, MRI and fluorodeoxyglucose-positron emission tomography scanning, safety, toxicity, pain score, and quality-of-life questionnaires.

RESULTS: Of 26 patients treated, 5 (19%) achieved complete response, 10 (39%) partial response, resulting in an objective response of 58%. Two responders remain without recurrence. No serious adverse events occurred during treatment. Four events occurred posttreatment: one bleeding episode, two episodes with mucosal swelling, and one patient died due to disease progression.

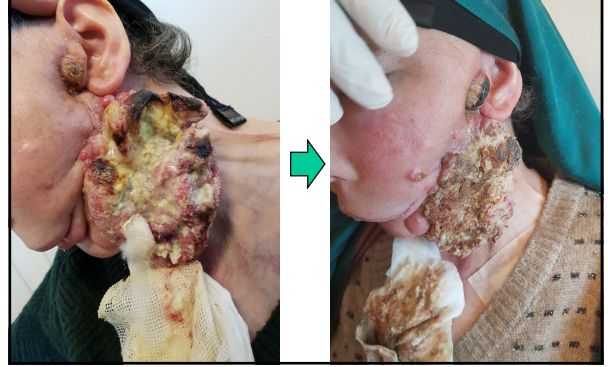
CONCLUSION: Electrochemotherapy is efficient against local recurrence of head and neck cancer with an overall response rate of 58%.

Elektrokemoterapi – baş & boyun kanseri



Benazzo M. Electrochemotherapy of Head and Neck Cancer. 2016

Baş boyun kanseri vakamız: 0 – 1. ay



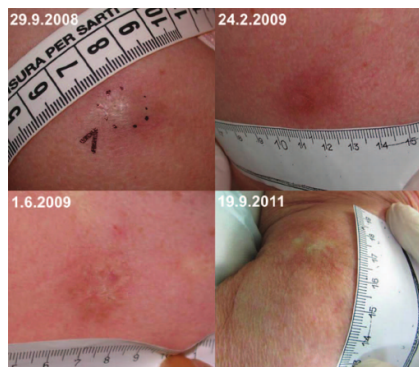
Baş boyun kanseri vakamız: 0 – 2 – 3. ay



Elektrokemoterapi – melanom



Elektrokemoterapi – melanom



Anorektal melanom vakamız: 0 – 4. ay



Elektrokemoterapi - deri

Response of tumor in the cheek after combined treatment with electrochemotherapy and external beam radiation therapy. A 78-year-old female patient with a huge tumor in the right cheek. The patient was treated with one application of electrochemotherapy using N-20-HG needle electrodes with hexagonal configuration, with intravenous administration of bleomycin under local anesthesia, subsequently followed by a single dose of radiation therapy (10 Gy). After three months, two additional applications of electrochemotherapy were performed with a one-month interval. The patient was in complete response for two years, until her death due to disease (St. Savvas Anticancer Hospital of Athens, March 2008).



Elektrokemoterapi - deri

Electrochemotherapy for Non-melanoma Skin Cancer in a Child with Xeroderma Pigmentosum

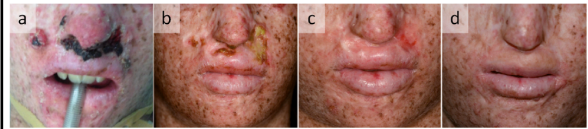
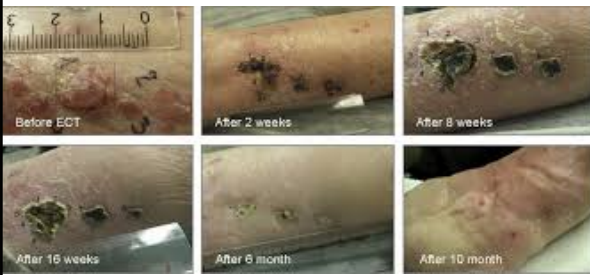


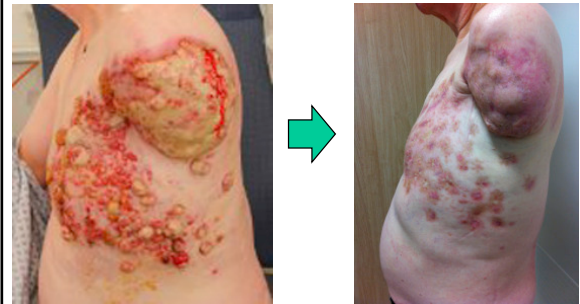
Fig. 1. (a) Squamous cell carcinoma and basal cell carcinomas before treatment, (b) 8 weeks after the first session of electrochemotherapy (ECT), (c) 2 weeks and (d) 15 months after the second session of ECT. Baltas E. Acta Derm Venereol. 2017 Aug 31;97(8):962-964.

Elektrokemoterapi- deri metastazi



Marty M. E J C SUPPLEMENTS, 4 (2006) 3-13

Elektrokemoterapi- Merkel CC



Holdsworth R, JPRAS Open 6 (2015) 49e52

Electrochemotherapy for Breast Cancer-Results From the INSPECT Database.

Matthiessen LW¹, Keshtgar M², Curatolo P³. Clin Breast Cancer 2018 Oct;18(5):e909-e917.

Abstract

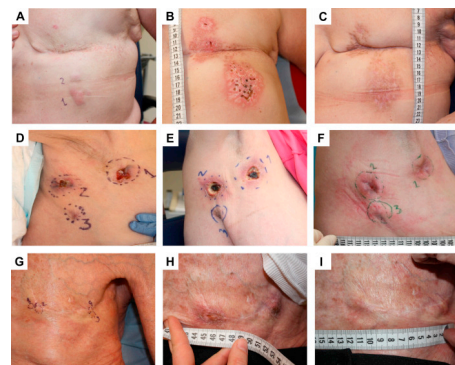
BACKGROUND: Cutaneous recurrence from breast cancer can pose a clinical challenge. It might be the only disease site, or could be part of disseminated disease, and often profoundly affects quality of life. Electrochemotherapy is a palliative treatment using electric pulses to locally permeabilize tumor cells and thereby significantly increase bleomycin cytotoxicity. Collaborating with the International Network for Sharing Practice on ElectroChemoTherapy (INSPECT), we consecutively and prospectively accrued data on patients treated with electrochemotherapy for cutaneous metastases from breast cancer.

PATIENTS AND METHODS: Patients were treated with electrochemotherapy at 10 European centers. Under either local or general anaesthesia patients were treated with either local injection (1000 IU/mL intratumoral) or systemic infusion (15,000 IU/m²) of bleomycin.

RESULTS: One hundred nineteen patients were included at 10 institutions in the INSPECT network. The primary location was the chest (89%), the median diameter of the cutaneous metastases was 25 mm. Ninety patients were available for response evaluation after 2 months. **Complete response was observed in 45 patients (50%), partial response in 19 (21%), stable disease in 16 (18%), and progressive disease in 7 (8%).** Three patients were not evaluable. Common side effects were ulceration, long-lasting hyperpigmentation, and low-grade pain. No serious adverse events were observed.

CONCLUSION: Electrochemotherapy showed high response rates after a single treatment. Electrochemotherapy has few side effects and can be used as an adjunct to systemic therapies or as a solo treatment. We therefore recommend considering electrochemotherapy for patients with cutaneous metastases.

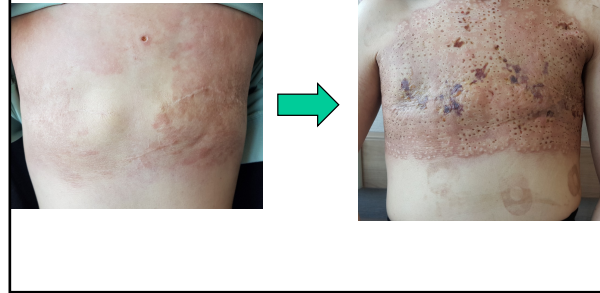
Elektrokemoterapi - meme kanseri



Meme kanseri vakamız - 0 – 2 – 10. ay



Meme kanseri sırt / göğüs yaygın cilt metastazı vakamız: 0 – 1. ay



Elektrokemoterapi – vulva kanseri

J Surg Oncol. 2015 Oct;112(5):529-32. doi: 10.1002/jso.24036. Epub 2015 Sep 8.

Palliative electro-chemotherapy in elderly patients with vulvar cancer: A phase II trial.

Abstract

OBJECTIVE: The primary endpoint of this trial was to assess clinical response (cCR) of squamocellular vulvar cancer (V-SCC) in elderly patients treated with electro-chemotherapy (ECT). Secondary endpoints were symptoms relief and local tumor control.

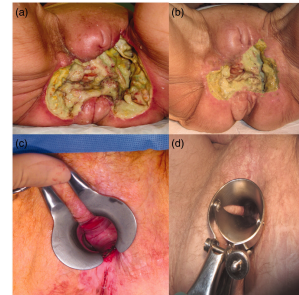
METHODS: A phase II study was designed and elderly patients with V-SCC unfit for other treatments were treated. Response Evaluation Criteria in Solid Tumors (RECIST criteria) were applied to evaluate tumor response. Quality of life (QoL) was evaluated by visual analogue score (VAS) for pain and four items of vulvar cancer subscale (VCS), of functional assessment of vulvar cancer therapy (FACT-V) [16], before, one month after the procedure and during follow-up.

RESULTS: Median age was 85 years (range 66-96 years). **One month after treatment complete response was observed in 13 patients (52%), partial response in 7 (28%), stable disease in 3 (12%), and progressive disease in 2 (8%). Local tumor control at 1 and 6 months was 91% and 53%, respectively.** Symptom free survival at 1 and 6 months was 78% and 40%, respectively, with significant reduction of pain ($P < 0.01$). One-year overall survival was 34%.

CONCLUSIONS: Our study showed that ECT produces high response rate with significant reduction of pain and improvement of local symptoms.

Elektrokemoterapi – vulva kanseri

Figure 2. Pre- and post-palliative treatment for ulcerated peritoneum (STAGE IIB) (a, b) and complete response for Paget (c; d).



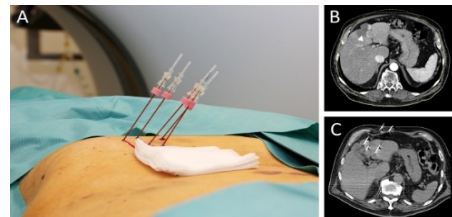
Bizzeri N. Cutaneous metastasis from vulvar squamous cell carcinoma: a rare occurrence that should not be forgotten. *Journal of Obstetrics and Gynaecology* 37:8, pages 975-981.

Elektrokemoterapi – Vajina metastazı vakamız

- 72 yaş kadın
- Endometrium ca, opere- RT almış
- Vajina metastazı (kanama – ağrı) – akciğer metastazı
- Cerrahi – morbid – hasta kabul etmemiş
- RT – ek doz önerilmiyor
- Metronomik kemoterapi – vajina metastazına EKT
- 12 aydır tam yanıtli izlemde

Electrochemotherapy as a New Modality in Interventional Oncology: A Review

The aim of this article is to review the recent published clinical experiences of electrochemotherapy use in deep-seated tumors with particular focus on liver cases. The principle of electrochemotherapy as well as the application to cutaneous metastases is briefly described. A short insight in the treatment of bone metastases, unresectable pancreas cancer, and soft tissue sarcoma will be given. Preclinical and clinical studies on treatment efficacy with electrochemotherapy of hepatic lesions and safety of the procedure adopted are discussed. **Probst U, Technol Cancer Res Treat. 2018; 17: 1533033818785329.**



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Original research
Electrochemotherapy in locally advanced pancreatic cancer: Preliminary results

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^e IRCCS Ospedale Civile, Via S. Maria del Carmine, 66012, Sulmona, Italy

• Termal ablasyon: riskli – çevre doku hasarı

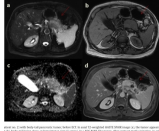
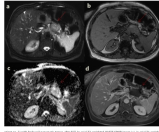
• Lokal ileri pankreas kanserinde hegzagonal EKT emniyetli ve ciddi yan etki risk düşük

• BT / USG RECIST kriteri – Stabil yanıt

• Dinamik MRI – kontrast tutan canlı hücre oranında yüksek oranda azalma

• MRI ile 5/7 kısmi yanıt; 2/7 stabil yanıt

• Metalik stent olanlarda EKT riskli

Sonuç olarak EKT:

- İnoperabl / RT' ye uygun olmayan yüzeysel doku kanser ve metastazlarının palyatif tedavisinde iyi bir alternatiftir
- Sistemik veya lokal tedavilerle kombine edilebilir
- Onkolojik Cerrahi branşlarla işbirliği başarısını arttırmaktadır
- İletişim: canfezsezgin@gmail.com