

## Overview and Case Observation of Electric Field Treatment (TTF) of Glioblastoma

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### 1. Abstract

Glioblastoma (GBM) belong to the central nervous system of the common tumors, the incidence of about 50% of primary malignant tumor in the brain, and high malignant degree and poor prognosis, it is a kind of highly invasive tumors, show the invasive growth, complete resection is very difficult, as the intraoperative neural navigation, intraoperative ultrasound, intraoperative MRI techniques such as the development of glioma safe resection scope expands unceasingly, at present, the standard treatment for the resection of large area, combined radiotherapy and

Chemotherapy for mo thiazole amine again, but the median survival of these GBM patients was only 14 ~ 17 months, 5-year survival rate was 9.8%. In order to prolong the OS of GBM patients, TTF was applied to treat GBM patients for the first time in the United States in 2004. We used one patient to get better results, as reported below.

### 2. Article

Glioblastoma (GBM) is a common tumor of the central nervous system, with an incidence of about 50% of the primary malignant tumors in the brain, with a high degree of malignancy and a poor prognosis [1]. It is a highly invasive tumor with invasive growth and complete resection is very difficult. With the continuous development of intraoperative neuronavigation, intraoperative ultrasound, intraoperative MRI and other technologies, the scope of safe resection of gliomas Continuous expansion. At present, the standard treatment plan is the largest resection,

combined with radiotherapy and temozolomide chemotherapy, but the median survival time of GBM patients is still only 14-17 months, and the 5-year survival rate is 9.8% [2].

With the rapid development of molecular biology, there are also many studies on targeted therapy of glioblastoma. The vascular endothelial growth factor (EGFR) antibody bevacizumab can

prolong disease-free survival, but it cannot extend the overall survival [3]. Targets at phosphatidylinositol 3-kinase (pi3k)/ protein kinase b (AKT) mammalian rapamycin target (MTOR) signaling pathway [4,5], p53 [6] And retinoblastoma (RB) pathway [7] And epidermal growth factor (EGFR) [8,9] No positive results were obtained in studies, and special types of glioblastomas also targeted high tumor mutation load (TMB) and BRAF gene mutations [10]. N neurotrophic tyrosine receptor kinase (NTRK) [3] Fibroblast growth factor receptor (FGFR) gene fusion [11] And met gene amplification or fusion [12,13] In terms of exploration, in addition, there are still many studies targeting tumor immune microenvironment, and no breakthrough has been achieved [14,15].

After so much research, the current treatments are very limited to improve the overall survival of patients. Since temozolomide was launched in 2005 and the US Food and Drug Administration (FDA) approved bevacizumab for relapsed glioblastoma cells in

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2009 After tumor patients, no other drug therapy is available [16] Moreover, no matter whether traditional surgery, radiotherapy, chemotherapy or emerging targeted therapy, immunotherapy have a certain impact on the quality of life of patients [17] We need to find a treatment that is both effective and tolerable.

Tumor Therapeutic Electric Field (TTF) is an alternating electric field with specific parameters (field strength range 1~3V / cm, frequency range 100kHz ~ 300kHz). It acts on the spindle formed during the mitosis of the cell, thereby preventing cancers that divide rapidly. The proliferation of cells is harmless to normal cells. At the same time, a strong electric field is mainly concentrated in the dividing groove of cancer cells, which can cause the intracellular material to accumulate in the middle and eventually cause the cancer cells to disintegrate [18] In 2004, the first paper on TTF was published [19] And soon its effectiveness was proven in gliomas [20]. 2013 National Comprehensive Cancer Network (NCCN) guidelines include electric field therapy in recommendations [21] with the continuous accumulation of clinical data, the recommendation level has been continuously improved in recent years. In 2018, the NCCN guidelines have made "routine radiotherapy + synchronous and adjuvant temozolomide chemotherapy + electric field therapy" as a type 1 recommendation for the treatment of glioblastoma [22]. In December 2018, the National Health and Medical Commission's Specifications for the Diagnosis and Treatment of Glioma " (2018 edition) also specifically recommended tumor electric field therapy for new-type glioblastomas and recurrent high-grade gliomas [23].

At the end of 2018, electric field therapy entered Hong Kong, and Chinese patients began to have the opportunity to receive this advanced treatment method. At present, inland areas of mainland China, due to various factors, there are not many users, and it is difficult for us to collect a case of glioblastoma diagnosed by West China Hospital of Sichuan University and undergoing conventional surgery and postoperative adjuvant chemoradiotherapy. The patient went to Hong Kong on May 6, 2019 to start using electric field treatment. After more than 8 months of follow-up, the following initially report the recent efficacy and adverse reactions of this case.

A female patient, 47 years old, was admitted to the hospital in October 2018 due to "a sudden disturbance of consciousness, limb twitching for 26 days, headache and vomiting for 20 days, and aggravation for 3 days". At the time of admission, she was lethargic, her pupils were different, her light reflection was dull, and her limbs Muscle

Strength decreased, left upper limb muscle strength was 4th

grade, remaining limb muscle strength was 2nd grade, bilateral pathological signs were negative, and meningeal stimulation signs were negative. Head enhanced MRI examination showed multiple left temporoparietal occipital lobe occupancies. November 2018 Surgical treatment was performed on the 22nd. Postoperative treatments such as nutritional nerves, dehydration, antihypertensive, and rehabilitation training were recovered well (Figure 1). The postoperative pathological diagnosis was: glioblastoma. The patient received conventional radiation therapy (Figure 1,2) and temozolomide chemotherapy, the condition is stable, on May 6, 2019, the patient began to receive electric field therapy and temozolomide adjuvant chemotherapy, the patient's use time was relatively fixed, the usage rate reached 92%, and the compliance was good (Figure 3). The scalp is scattered with an allergic rash, slight itching, no ulceration and infection, and he recovered quickly after applying anti-allergic drugs for several days. The temperature of the patch has been too high for several times, considering

The reasons: 1.the ambient temperature used is high (Such as hot weather, direct sunlight, etc.), 2.The contact between the patch and the skin is not good, guidance the person adjusted the indoor temperature to about 24°C, strengthened the loose patch with a headgear or adhesive tape, used a headgear when sleeping at night, and paid

Attention to cleaning the scalp hair every time, and observed the presence of hydrogel when changing the patch. The phenomenon of melting, if the hair grows too fast or the hydrocolloid melts, changing the patch in time, the situation has improved significantly. During the review of the cranial MR0049, the condition is stable (Figure 4). During follow-up to 2020.1.18, the patient did not

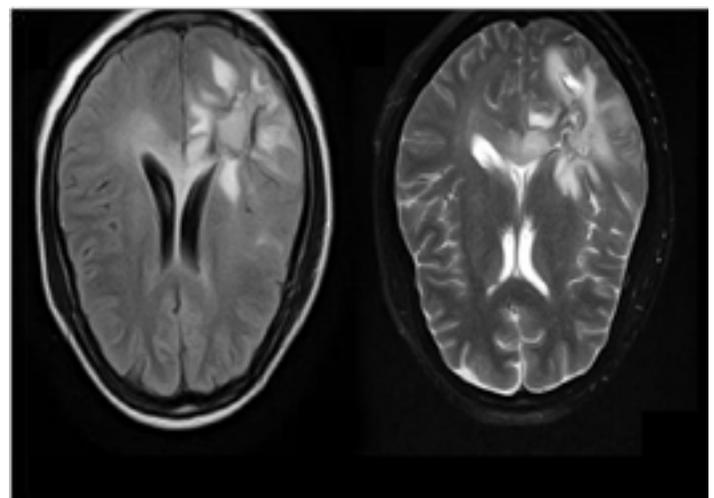


Figure 1

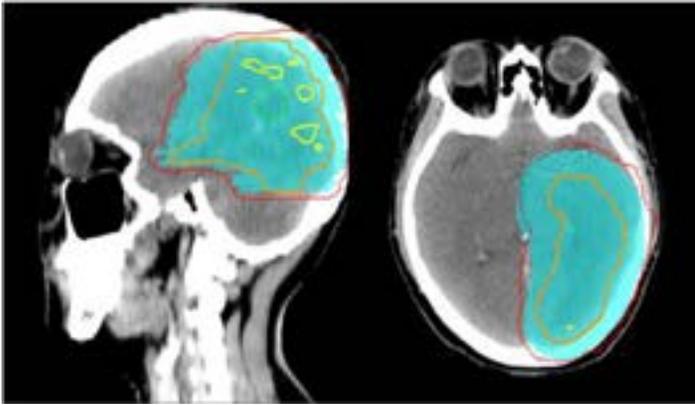


Figure 2

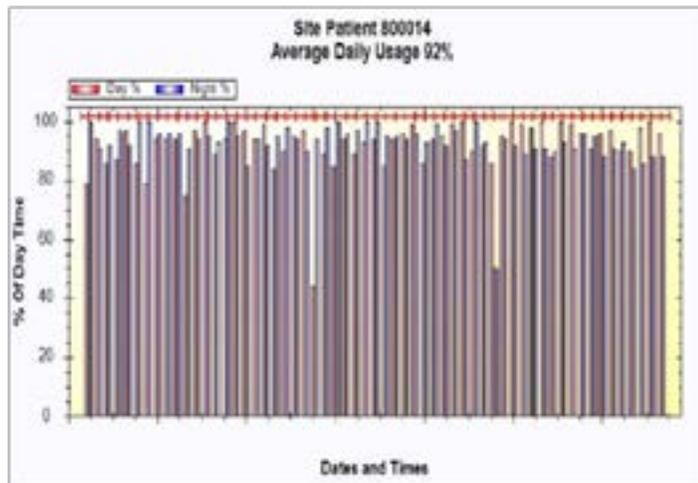


Figure 3

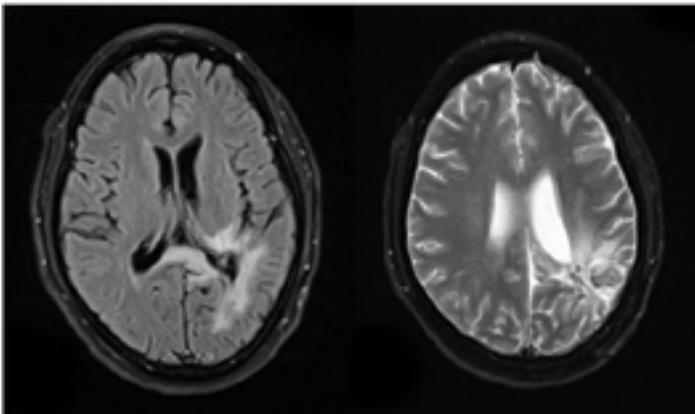


Figure 4

experience discomfort symptom.

Electric field treatment has no side effects such as hair loss, vomiting, fatigue, anemia, cognitive function and neurological damage caused by traditional radiotherapy and chemotherapy, and it has a good effect. It can not only improve the patient's progression-free survival time (PFS), but also extend it. Overall survival (OS) can be said to have both excellent effectiveness and tolerance. Electric field therapy, as a new anti-tumor treatment,

has not been developed for a long time, and further research is needed to further improve the clinical value of TTF. At present, many studies are actively looking for the optimal intensity and frequency of treatment, as well as the mode of use of electric field therapy combined with immune checkpoint inhibitors or targeted therapeutic drugs, and determine the best efficacy and safety of this combined mode. These issues still need to be studied with large sample clinical Trials. At present, electric field therapy has come to mainland China, and it is expected that with all efforts, electric field therapy can be as feasible as traditional radiotherapy and chemotherapy, and benefit more Chinese patients.

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