



Tumor Treating Fields—An Emerging Cancer Treatment Modality

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Tumor treating fields (TTFs) are an evolving new anticancer modality. The U.S. Food and Drug Administration has approved the first device, the NovoTTF-100A™, that uses this technology and is indicated for use in progressive glioblastoma multiforme after standard therapies have failed. Promising clinical trial results will likely lead to expanded uses in primary brain tumors and other cancer types. This article will review the concept of TTFs and their mechanism of action, and overview the TTF device and its approved usage.

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The U.S. Food and Drug Administration (2011) approved the NovoTTF-100A™ system as a treatment for recurrent glioblastoma multiforme (GBM) in April 2011. NovoTTF-100A is the first approved device that uses tumor treating fields (TTFs), a novel technology that delivers alternating low-intensity and intermediate-frequency electrical fields to a tumor. NovoTTF-100A was approved for patients with recurrent glioblastoma multiforme as an alternative treatment modality to chemotherapy after surgical and radiation options have been exhausted (Novocure, 2012).

TTFs cause apoptosis (cell death) during mitosis, disrupting the assembly of the spindle apparatus in metaphase, and preventing the parent cell from dividing into two daughter cells during telophase (Kirson et al., 2004). The dividing cells of the hematopoietic system are not affected by TTFs; muscles that surround the bone and marrow act as an effective electrical field shield (Kirson, Giladi, et al., 2009). TTFs do not stimulate nerves or muscles; the frequency is too high to cause mem-

brane depolarization. Also, it does not heat up the tissue because the frequency is too low to cause dielectric (electronic) heating (Pless & Weinberg, 2011). NovoTTF-100A is a portable, battery-operated device that delivers TTFs to patients via electrodes placed on the scalp (see Figures 1 and 2).

Glioblastoma

In 2013, about 23,130 people will be diagnosed with a malignant tumor of the brain or spinal cord, and an estimated 14,080 will die from these tumors (American Cancer Society, 2013). Glioblastoma multiforme is the most common and aggressive primary malignant brain tumor in adults. Median survival is about 15 months from diagnosis, with most tumors reoccurring within nine months of initial treatment (Stupp et al., 2005).

Standard initial therapy for glioblastoma multiforme includes maximal surgical resection and combined temozolomide chemotherapy with radiation, followed by at least six cycles of monthly adjuvant temozolomide (National Comprehensive

Cancer Network [NCCN], 2013). Treatment options are limited for patients with recurrent glioblastoma multiforme. At the time of reoccurrence, re-resection and re-irradiation are options for some patients. Chemotherapy agents have limited effectiveness because of the blood-brain barrier, a tightly woven mesh of endothelial cells, astrocytes, and transmembrane proteins that line the vessels of the central nervous system. The barrier restricts diffusion of bacteria and other large or water-soluble molecules from the bloodstream into the brain. As a result, most chemotherapy agents cannot penetrate the brain. Agents that are used at reoccurrence include temozolomide, the nitrosureas (carmustine and lomustine), carboplatin, irinotecan, and procarbazine. In May 2009, bevacizumab was approved and frequently is incorporated into recurrent glioblastoma multiforme treatment

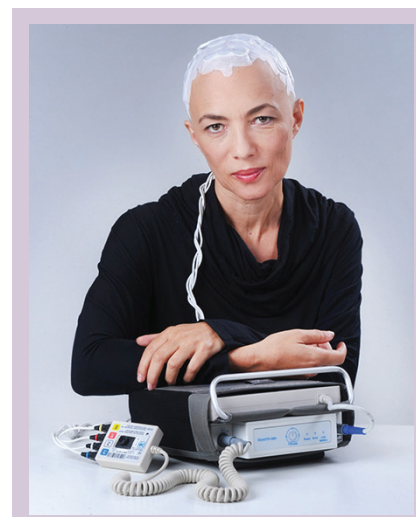


FIGURE 1. Novocure Device

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