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## Tumor Treating Fields - Behind and Beyond Inhibiting the Cancer Cell Cycle

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## Abstract

The unmet need for a safe treatment that significantly improves the overall survival, as well as the quality of life of patients with brain tumors, has urged researchers to work out new treatment modalities. About 15 years ago, it was shown that alternating electric fields significantly impair the growth of cancer cells. Recently, this potentially revolutionary approach called Tumor Treating Fields (TTFs) has been FDA-approved for the treatment of glioblastoma as well as mesothelioma. However, despite the promising reports on the potential of TTFs, the precise knowledge of the mechanisms of action is still lacking. The purpose of this review is, thus, to present the current state of research and to highlight the variety of ultrastructural effects of TTFs. Moreover, the aim is to bring to the foreground less discussed mechanisms of action of TTFs, which might develop into novel therapeutic approaches. Therefore, a systematic literature search in Ovid Medline and Embase was performed on clinical and preclinical data concerning TTFs. The alternating electric fields force cellular components to aberrant dynamics, among which the most evident is the inhibition of the mitotic spindle assembly leading to impaired cancer cell division and cell death. However, a variety of other microstructural events induced by TTFs, such as inhibition of DNA repair and cell migration, as well as an enhancement of anti- tumor immune response and membrane permeability, have been reported. In addition, apart from a suggested interference with angiogenesis, no TTF-induced effects on normal cells have been described so far.

**Keywords:** Tumor Treating Fields (TTF); brain neoplasms; cancer treatment; cell cycle; central nervous system; glioblastoma.

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