



Effect of Electrical Capacitance-Based Therapy on the Viability of U87 and T98-G Glioblastoma Cell Lines

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ABSTRACT

AIM: To examine the selective cytotoxic effects of Electro-Capacitive Cancer Therapy (ECCT) on human glioblastoma (GBM) cell lines (U87-MG and T98-G) and to evaluate its impact on normal epithelial cells.

MATERIAL and METHODS: U87-MG and T98-G glioblastoma cells, along with Beas-2B normal epithelial cells, were exposed to ECCT at 100 kHz frequency and 20 V for 24 hours. Cell viability was determined using the MTT assay, while morphological changes were assessed through phase-contrast microscopy. Statistical analyses were conducted using one-way ANOVA and Student's t-test, with statistical significance defined as $p < 0.05$.

RESULTS: ECCT exposure caused a time-dependent reduction in the viability of both GBM cell lines. U87-MG cells showed significant inhibition at all exposure durations, whereas T98-G cells exhibited a marked decrease only after 24 hours ($p < 0.0001$). In contrast, Beas-2B cells maintained their morphology and viability, suggesting that ECCT selectively targets malignant cells while sparing normal epithelial cells.

CONCLUSION: ECCT significantly inhibits glioblastoma cell proliferation without adversely affecting normal cells, highlighting its promise as a non-invasive adjunctive treatment option for GBM. Further preclinical and clinical studies are warranted to clarify its underlying mechanisms, optimize exposure parameters, and determine its potential integration into multimodal glioblastoma therapy.

KEYWORDS: Glioblastoma, Electro-capacitive cancer therapy, Electric field therapy, Cell viability, Apoptosis

INTRODUCTION

Glioblastoma (GBM) is among the most aggressive and fatal primary tumors of the central nervous system (CNS), accounting for roughly 60% of all gliomas (19). Classified as a World Health Organization (WHO) grade IV malignancy, GBM exhibits rapid cellular proliferation, diffuse infiltration, and marked resistance to conventional therapies, which together contribute to its poor clinical outcome (23).

Despite advances in multimodal management, the median overall survival for affected patients remains approximately 12–15 months (8). The disease most commonly affects individuals between 60 and 75 years of age and occurs more frequently in men (15).

At the molecular level, GBM is distinct from lower-grade gliomas. Its histopathological hallmarks include extensive necrosis, microvascular proliferation, and a high mitotic index (16).

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Frequent genetic alterations such as PTEN deletions, EGFR amplifications, and TERT promoter mutations are key drivers of tumor aggressiveness (31). The 2021 WHO classification further emphasizes the importance of IDH mutation status, which has major prognostic and therapeutic implications (3).

Standard treatment for GBM consists of maximal safe resection followed by radiotherapy and adjuvant temozolomide chemotherapy (30). Nonetheless, recurrence remains nearly universal, and the improvement in survival is limited. Consequently, attention has shifted toward exploring novel, non-pharmacological treatment modalities. Among these, Tumor Treating Fields (TTFields) and Electro-Capacitive Cancer Therapy (ECCT) have attracted increasing interest as innovative therapeutic approaches (14).

TTFields apply low-intensity, intermediate-frequency alternating electric fields via adhesive scalp electrodes, which disrupt mitotic spindle formation and interfere with cell division, thereby restraining tumor growth (21). The U.S. Food and Drug Administration (FDA) has approved TTFields for use alongside temozolomide in both newly diagnosed and recurrent GBM (4,12).

ECCT, by contrast, employs contactless capacitive electrodes to generate alternating electric fields, offering a non-invasive and patient-friendly alternative that does not require direct scalp contact. Mechanistically, ECCT induces microtubule disorganization and ionic imbalance across the tumor cell membrane, leading to apoptosis or necrosis while sparing normal cells (13,22,25,34). This selective cytotoxicity may provide a therapeutic advantage with minimal side effects (1). Early experimental studies indicate that ECCT interferes with the mitotic spindle, triggers apoptosis, and decelerates tumor progression (24,26). However, the precise molecular pathways underlying ECCT-mediated cytotoxicity remain incompletely understood.

Within this framework, the present study aims to evaluate the potential antitumor effects of ECCT in glioblastoma, focusing on its selective cytotoxicity in GBM cell lines and its possible role as an adjunctive therapeutic modality.

MATERIAL and METHODS

Cell Lines and Culture Conditions

Human glioblastoma cell lines T98-G (ATCC® CRL-1690™) and U87 MG (ATCC® HTB-14™) were obtained from the American Type Culture Collection (ATCC, USA). Cells were cultured in Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 (DMEM/F12) supplemented with 10% fetal bovine serum (FBS; Sigma-Aldrich, USA) and 1% penicillin-streptomycin (Sigma-Aldrich, USA). Cultures were maintained at 37°C in a humidified 5% CO₂ atmosphere and subcultured at 80–90% confluence to ensure logarithmic growth.

ECCT System and Electric Field Application

Cells were seeded into sterile 6-well plates at a density of 2,500 cells per well and incubated overnight. The plates were then placed in a custom-built ECCT device featuring con-

tactless capacitive electrodes (Figure 1). A 5 mm gap between the electrodes and the monolayers was maintained to ensure homogeneous field distribution. Preliminary tests were conducted to optimize the voltage and frequency parameters (100 kHz, 20 V) before the main experiments.

Alternating electric fields were generated using an oscillating high-capacitance voltage source. The system was calibrated before each trial to maintain field uniformity and reproducibility. The final experimental parameters included a 100 kHz frequency, 20 V amplitude, and 24-hour exposure period.

Cell Viability Assessment (MTT Assay)

Following ECCT exposure, cell viability was determined by MTT assay. After the exposure period, 20 µL of MTT solution (5 mg/mL in phosphate-buffered saline; Sigma-Aldrich, USA) was added to each well and incubated for 4 hours at 37°C. Without removing the medium, 100 µL of solubilization solution (10% sodium dodecyl sulfate in 0.1 M HCl) was added to dissolve formazan crystals.

Absorbance was read at 570 nm using a microplate reader (BioTek Synergy HTX, USA). Viability was expressed as a percentage relative to untreated control cells (defined as 100%). Beas-2B human bronchial epithelial cells were used as a non-malignant control to evaluate selective cytotoxicity.

Statistical Analysis

Data are presented as mean ± standard deviation (SD) from at least three independent experiments (n = 12 per group, representing biological replicates). Statistical analyses were conducted using GraphPad Prism 9.0 (GraphPad Software, USA). One-way ANOVA followed by Tukey's post hoc test was used for multiple comparisons, and unpaired two-tailed Student's t-tests were applied for pairwise comparisons. Differences with p < 0.05 were considered statistically significant.

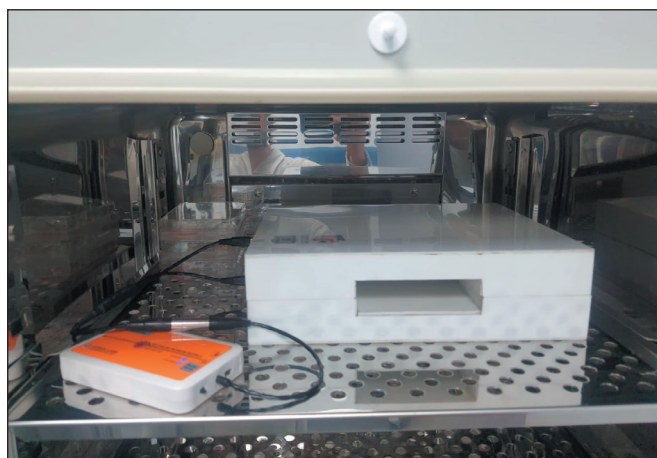


Figure 1: Setup of the ECCT system. Glioblastoma cells seeded in culture plates were exposed to alternating electric fields generated by a contactless capacitive electrode system. A uniform distance was maintained between the electrodes and cell layers to ensure homogeneous field distribution throughout the exposure period.

RESULTS

Effects of ECCT on T98-G Glioblastoma Cells

Exposure of T98-G cells to ECCT (100 kHz, 20 V) produced a gradual, time-dependent reduction in cell viability. Morphological evaluation revealed early apoptotic changes at 6 hours, including rounding, shrinkage, membrane blebbing, and partial detachment (Figure 2).

Quantitative MTT analysis demonstrated a progressive decline in viability (Figure 2). Decreases observed at 6 and 12 hours were not statistically significant ($p > 0.05$), whereas a marked reduction became evident after 24 hours ($p < 0.0001$). Corresponding mean absorbance values at 570 nm declined from 0.83 ± 0.04 in controls to 0.54 ± 0.03 , 0.42 ± 0.02 , and 0.29 ± 0.02 at 6, 12, and 24 hours, respectively. These findings indicate that ECCT exerts significant cytotoxic effects on T98-G glioblastoma cells after prolonged exposure.

Effects of ECCT on U87-MG Glioblastoma Cells

U87-MG cells showed more pronounced morphological and functional alterations following ECCT treatment. Early chan-

ges such as cytoplasmic condensation, vesicle formation, and detachment from the substrate appeared within 6 hours (Figure 3).

MTT assays revealed greater sensitivity compared to T98-G cells (Figure 3). Cell viability decreased by 39.6% at 6 hours ($p < 0.0001$), 59.3% at 12 hours ($p < 0.0001$), and 74.8% at 24 hours ($p < 0.0001$). Corresponding absorbance readings dropped from 0.89 ± 0.05 in controls to 0.54 ± 0.04 , 0.36 ± 0.03 , and 0.22 ± 0.02 . Thus, U87-MG cells were more susceptible to ECCT-induced cytotoxicity than T98-G cells.

Effects of ECCT on Beas-2B Normal Epithelial Cells

In contrast, Beas-2B normal human bronchial epithelial cells showed minimal morphological alterations under identical ECCT conditions. Phase-contrast microscopy confirmed that the cells retained their polygonal shape and firm attachment, without membrane blebbing or detachment.

MTT results were consistent with these observations: cell viability remained stable ($p > 0.05$) across all time points (Figure 4), with absorbance values around 0.81 ± 0.04 . These results

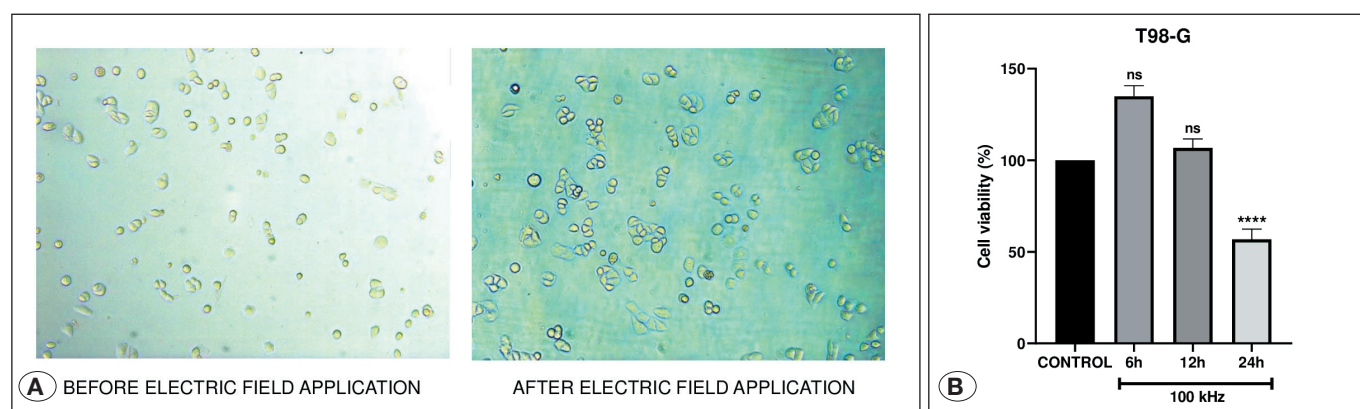


Figure 2: Effects of ECCT exposure on T98-G glioblastoma cells. **A)** Representative phase-contrast images show morphological changes before and after treatment. **B)** Quantitative MTT assay results illustrate a gradual, time-dependent reduction in cell viability at 6, 12, and 24 hours compared to control cells, with statistical significance observed only at 24 hours ($p < 0.0001$). Data are expressed as mean $\pm$ SD ($n = 12$). Statistical significance: **** $p < 0.0001$; ns: non-significant.

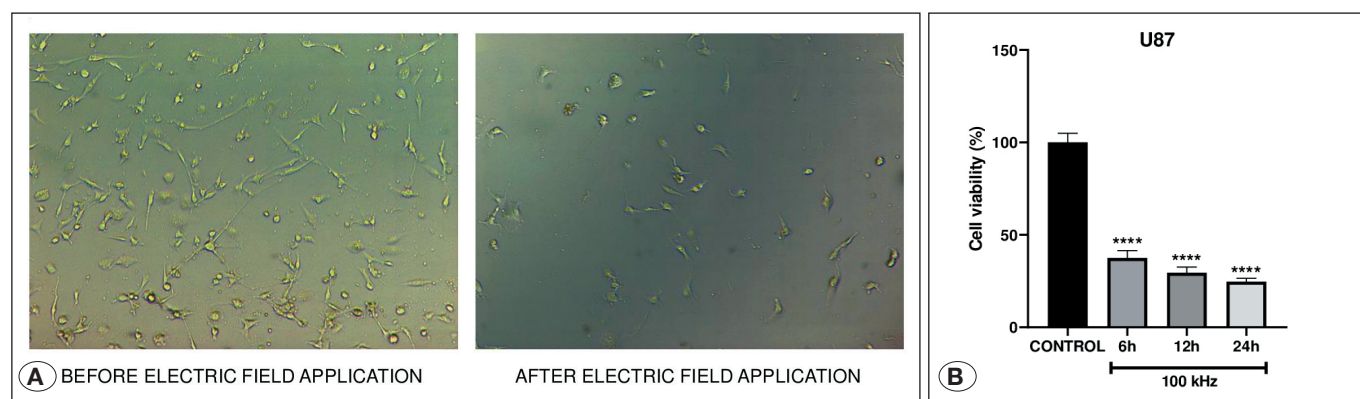


Figure 3: Effects of ECCT exposure on U87-MG glioblastoma cells. **A)** Representative phase-contrast images depict morphological alterations following ECCT application. **B)** MTT assay results indicate a significant, progressive decrease in viability across 6, 12, and 24 hours compared to controls. Data are expressed as mean $\pm$ SD ($n=12$). Statistical significance: **** $p < 0.0001$.

suggest that ECCT selectively targets malignant glioblastoma cells while sparing non-cancerous epithelial cells, supporting its potential therapeutic selectivity.

DISCUSSION

GBM remains one of the most malignant and treatment-resistant brain tumors, characterized by rapid recurrence and poor clinical outcomes (7,18). Despite improvements in surgical resection, radiotherapy, and chemotherapy, gains in patient survival have been modest (29). The tumor's high proliferation rate, molecular heterogeneity, and infiltrative behavior continue to limit the effectiveness of conventional interventions (6).

Recently, ECCT has emerged as a potential adjunctive therapy for GBM. Electric field-based therapies interfere with mitotic spindle formation and disrupt cellular architecture, thereby reducing cancer cell proliferation (5,20). Experimental data in other malignancies have demonstrated that ECCT can suppress chemokine expression, reduce tumor growth, and induce apoptosis. For example, Pratiwi et al. reported that ECCT inhibited breast tumor progression (27), and Alamsyah et al. found that ECCT reduced MCF-7 breast cancer cell proliferation by 28–39% and tumor volume by approximately 67% (2). Similarly, studies involving MG-63 osteosarcoma cells demonstrated apoptosis induction via intrinsic pathways following exposure to non-contact electric fields (10).

Comparable outcomes have been observed with TTFields therapy. Wu et al. reported a significant reduction in GBM cell proliferation and delayed tumor growth in both in vitro and in vivo models (32). Compared with TTFields, ECCT offers distinct advantages such as contactless application, minimal dermatologic complications, and improved patient comfort. In the current study, ECCT applied via capacitive coupling significantly inhibited proliferation in both U87-MG and T98-G gli-

oblastoma cell lines. These findings support earlier suggestions that combining ECCT with chemotherapy or radiotherapy may enhance treatment efficacy (9,32,33). Supporting this concept, Stupp et al. demonstrated that TTFields combined with temozolomide improved both progression-free and overall survival in GBM patients (28), and Jo et al. observed synergistic effects when TTFields were combined with radiotherapy in pancreatic cancer models (11).

Nonetheless, several limitations should be acknowledged. The current work was limited to in vitro experiments, precluding assessment of systemic or microenvironmental interactions. Only two well-established GBM cell lines were used, without patient-derived or primary tumor models. Combination studies with temozolomide or radiation were also beyond the current scope. Future research should therefore include in vivo and patient-derived systems to validate the translational relevance of ECCT. Recent developments in directionally controlled, implant-based electric field systems have shown encouraging results in GBM models (17). Moreover, mechanistic studies should explore how ECCT influences molecular signaling pathways and genetic biomarkers. In particular, findings by Mujib et al. implicating p53-mediated apoptosis suggest that ECCT may engage key tumor suppressor pathways (20).

CONCLUSION

In summary, ECCT administered at low to medium frequencies effectively inhibits GBM cell proliferation while exerting minimal effects on normal epithelial cells. Although the existing evidence remains limited, this technique shows promise as a non-invasive, patient-tolerant therapeutic option. Further well-designed preclinical and clinical investigations are warranted to elucidate its mechanisms, optimize its parameters, and determine its integration within multimodal GBM management strategies.

Declarations

Funding: No financial support was received for this research.

Availability of data and materials: The datasets generated and/or analyzed during the current study are available from the corresponding author by reasonable request.

Disclosure: The authors declare no competing interests.

Ethics approval and consent to participate: Not applicable. This in vitro study was conducted using commercially available established cell lines and did not involve human participants or experimental animals; therefore, ethics committee approval and consent to participate were not required.

AUTHORSHIP CONTRIBUTION

Study conception and design: EA, HB, MBY

Data collection: AS, SA, EA

Analysis and interpretation of results: SO, EA

Draft manuscript preparation: NAD

Critical revision of the article: AK, HU

Other (study supervision, fundings, materials, etc.): n/a

All authors (EA, HB, MBY, NAD, AS, SA, SO, AK, HU) reviewed the results and approved the final version of the manuscript.

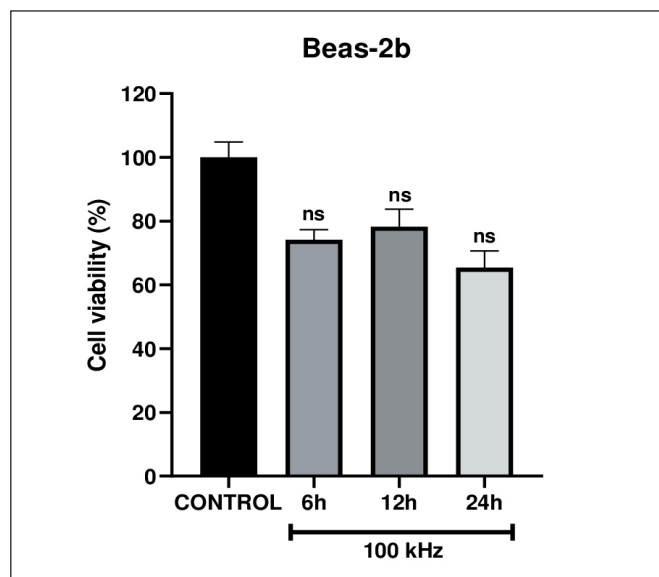


Figure 4: Effects of ECCT exposure on Beas-2B normal epithelial cells. Quantitative MTT assay results show cell viability at 6, 12, and 24 hours compared with control cells. ns: non-significant.

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