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BIODEGRADABLE WAFERS FOR INTRACRANIAL TUMOR THERAPY: A CONVERGENCE OF NANOTECHNOLOGY AND POLYMER SCIENCE

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ABSTRACT

Brain tumors, particularly glioblastoma (GBM) and meningioma, pose significant treatment challenges due to their aggressive progression, high recurrence rates, and resistance to conventional therapies. The blood-brain barrier (BBB) and blood-tumor barrier (BTB) further limit the efficacy of systemic chemotherapy by restricting drug delivery to the tumor site. Despite advancements in surgery, radiation therapy, and chemotherapy, long-term survival rates for malignant brain tumors, especially GBM, remain low.

Biodegradable wafer-based drug delivery systems have emerged as a promising solution to these challenges. Implanted directly into the tumor cavity following surgical resection, these wafers provide localized and sustained drug release, enhancing therapeutic efficacy while minimizing systemic toxicity. Gliadel®, a carmustine (BCNU)- loaded polymer wafer, was the first FDA-approved intracranial chemotherapy implant, demonstrating improved survival outcomes in GBM patients. However, drawbacks such as rapid drug diffusion and systemic clearance have driven the development of advanced polymeric systems, including temozolomide (TMZ)-loaded wafers and

doxorubicin-polymeric wafers, which enable controlled drug release and improved tumor targeting.

Recent advancements in biodegradable electronic devices, such as wireless drug delivery implants and nanomedicine-based multi-drug delivery systems, have further revolutionized localized brain tumor therapy. These innovations show promise in enhancing treatment efficacy, overcoming drug resistance, and reducing tumor recurrence.

This review explores the role of biodegradable wafers in targeted brain tumor therapy, focusing on their mechanisms, benefits, challenges, and future directions. The integration of personalized medicine, advanced imaging techniques, and genetic profiling will be critical for optimizing these therapies. Ongoing research and technological innovations in wafer-based drug delivery systems hold great potential for improving survival rates and quality of life for patients with brain tumors.

Keywords: Brain tumour, Glioblastoma, meningioma, blood -brain barrier, blood - tumor barrier, biodegradable wafers

INTRODUCTION

An Overview of Brain Cancer

Cancer is viewed as genetic illness because the tumor picks up genetic changes along the course of its life, termed as somatic mutations. Such mutation arises in tumor cells and have impacts on all levels of the cancer, including sensitivity to therapy, potential for recurrence, and overall survival of the patient. Such genetic alterations significantly influence the progression and conduct of most solid cancers, such as brain cancers. [4] Brain tumors are abnormal masses of cells in the brain, categorized into benign and malignant. Benign tumors are slow growing and can usually be cured with medication and surgery [1]. Meningiomas are the most frequent benign tumors in adults, usually arising from

the meninges [4]. Malignant tumors, including glioblastoma multiforme (GBM), are very aggressive, invasive, and often recur despite treatment [2]. Malignant tumors are not common accounting for only 1% to 2% of all cancers in adults [4]. According to location tumors can be categorized as-

- Extra-axial tumors: tumors grow outside the brain's parenchyma. For ex: meningiomas, schwannomas, skull base tumors.
- Intra-axial tumors: tumors grow within brain's substance affecting gray and white matter. For ex: glioblastomas, lymphomas, metastatic tumors [3].

Meningiomas are not technically brain tumors, as they are due to meningotheial cells which constitute the external membranous

covering of the brain. Nevertheless, since they occur within the intracranial space and present with neurologic signs and symptoms, they are typically categorized as brain tumors [6]. Glioblastoma is the most aggressive primary brain tumor with fast growth and resistance to traditional treatments. Despite the improvement in surgery, radiotherapy, and chemotherapy, the outlook is not favorable. The median survival time for GBM patients is around 18 months, and few live longer than a few years [2].

Glioblastoma are grade 4 type brain tumor characterized by-

- Microvascular proliferation: abnormal growth of small blood vessels with excessive endothelial cell multiplication.
- Pseudopalisading necrosis: tumor cells surround areas of dead tissue in a layered pattern due to oxygen deprivation [3].

About 75% of all the primary brain tumors are glioblastoma or meningioma; thus, this article focuses primarily on these common tumors [5].

Brain tumors result in generalized symptoms such as headache, nausea, vomiting, and eye problems due to increased pressure. Focal symptoms include weakness, speech difficulty, depending on the location of the tumor. Approximately half of all patients with brain tumors face headaches [6]. The brain's

inherent protective barriers, such as the skull and blood-brain barrier, limit the ability to continuously monitor brain conditions and hinder the efficient delivery of therapeutic agents.

Despite extensive investments in preclinical and clinical research, the survival rate for brain tumor patients has improved only marginally over the past 45 years [9]. A major challenge in drug delivery is bypassing the blood-brain barrier in the central nervous system (CNS). This protective barrier restricts drug entry into brain cells, rendering oral and intravenous delivery methods largely ineffective [8]. brain tumor treatment failure primarily depends on the blood- brain barrier (BBB) and the blood-tumor barrier (BTB), which limit the delivery of therapeutic agents to the brain. The BBB acts as a highly selective filter, preventing the drugs from reaching brain tissue, while the Brain tumor barrier, despite being more permeable, still hinders uniform drug distribution. Consequently, many conventional treatments fail to achieve better therapeutic outcomes [10].

Implantable devices, however, present a promising solution for the accurate diagnosis and treatment of brain disorders [7].

To overcome these challenges, targeted drug delivery is crucial for effectively eliminating

brain tumors. Implantable wafers enable sustained and controlled drug release, minimizing side effects and improving treatment efficiency.

Risk factors

- N-nitroso compounds and dietary factors have been proposed as potential risk factors, but evidence remains inconclusive [6].
- Allergies – Inversely correlated with glioma risk, possibly due to immune system interactions [4].
- Ionizing radiation is the only confirmed risk factor, with cranial irradiation increasing the likelihood of meningiomas by 10-fold and glial tumors by 3- to 7-fold [6].
- Genetic predisposition – Variations in genes such as *TERT*, *CDKN2A/CDKN2B*, *RTEL1*, and *PHLDB1* have been associated with an increased risk of glioma [4].
- Age – Higher incidence of malignant gliomas and CNS lymphomas is observed in older adults [6].
- Radiofrequency electromagnetic fields (EMFs) have been studied for their potential link to brain tumors, but findings remain inconclusive [4].

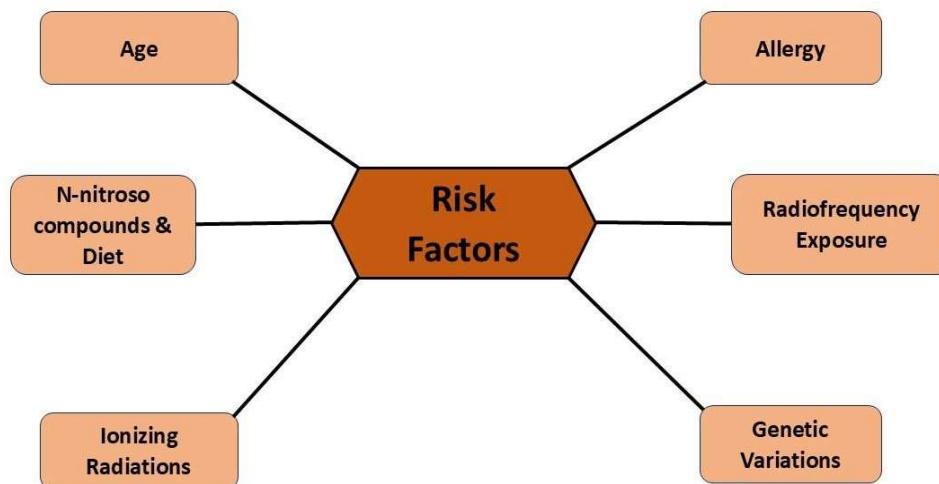


Figure 1: Key Risk Factors Associated with Brain Tumor Development Role of Biodegradable Wafers in Targeted Brain Cancer Therapy

Malignant brain tumors, such as glioblastoma (GBM), are challenging to treat due to their high recurrence rates following surgery and radiation. A major hurdle in chemotherapy is the blood-brain barrier, which restricts drug

delivery to the tumor, reducing the effectiveness of intravenous treatment [1]. Despite significant research efforts, glioblastoma (GBM) remains highly resistant to conventional treatments, including surgery,

radiation, and chemotherapy [10]. Advancements in bioengineering and drug delivery systems have introduced innovative cancer treatment approaches, including nanoparticles, liposomes, and implantable biodegradable devices [12]. Among these, biodegradable wafers provide a promising approach for delivering localized chemotherapy directly to the tumor site. Placed directly in the brain, these wafers hold significant potential for future treatments [10]. These thin, disk-shaped implants, typically measuring 1 mm in thickness and 1 cm in diameter, are placed in the tumor bed after surgical removal, enabling a controlled and sustained release of chemotherapy drugs [2]. Biodegradable wafers are implanted in the tumor bed after surgical removal, enabling controlled and sustained chemotherapy drug release. They provide a local drug concentration up to 100 times higher than systemic chemotherapy, minimizing systemic toxicity [9]. A key advantage of biodegradable wafers is their ability to bypass the blood-brain barrier, allowing for better drug penetration into the tumor while minimizing systemic toxicity. They provide a local drug concentration up to 100 times higher than systemic chemotherapy, improving treatment effectiveness and reducing side effects. Additionally, their biodegradable design

enables gradual dissolution over time, eliminating the need for surgical removal [2]. Wafers can be excreted through body as CO₂ and urine [10]. A maximum of 8 wafers may be placed in the tumor bed following surgical removal. Polymers shield active ingredients from degradation, regulate drug release, and minimize systemic side effects [10]. A biodegradable, soft electronic device is required for wireless drug release in the brain. It operates for a specific duration before dissolving safely, eliminating the need for removal. This innovation could enhance neurological treatment while reducing invasiveness and long-term complications [1]. Intracerebral chemotherapy with polymer implants has been shown to prolong survival in humans with recurrent malignant gliomas and animals with transplanted gliomas. These implants enable targeted drug delivery, enhancing treatment effectiveness while minimizing systemic side effects. The implants enable precise, localized chemotherapy delivery to the tumor, enhancing drug effectiveness while reducing systemic toxicity. They provide controlled drug release, maximizing treatment impact while minimizing side effects [11]. Implantable microdevices provide enhanced control over drug release timing and dosing, potentially leading to improved therapeutic

outcomes. It also enables the simultaneous delivery of multiple therapies while providing precise control over the rate and timing of drug release [14]. Radiological imaging showed the wafer appearing partially degraded after three months and largely vanishing over time [12].

Most widely used wafer to date is Gliadel wafer. Gliadel, a BCNU-loaded polymer wafer, was the first FDA-approved intracranial chemotherapy implant, offering improved survival for GBM patients. However, its efficacy is constrained by rapid drug diffusion and systemic clearance. To address these challenges, we developed a novel PLGA-based wafer designed to co-deliver temozolomide (TMZ) and BCNU. As

a biodegradable and biocompatible polymer, PLGA facilitates sustained drug release for over 30 days, enhancing localized tumor treatment while reducing systemic toxicity [8]. The Gliadel® wafer improved survival with BCNU, but its rapid drug diffusion and systemic clearance led to the development of temozolomide (TMZ)-loaded polymeric wafers. These provide sustained drug release, enhancing tumor control while minimizing systemic toxicity. Studies in rodent glioma models show that intracranial TMZ wafers significantly improve survival, especially with radiation therapy, highlighting their potential as an effective glioma treatment strategy [13].

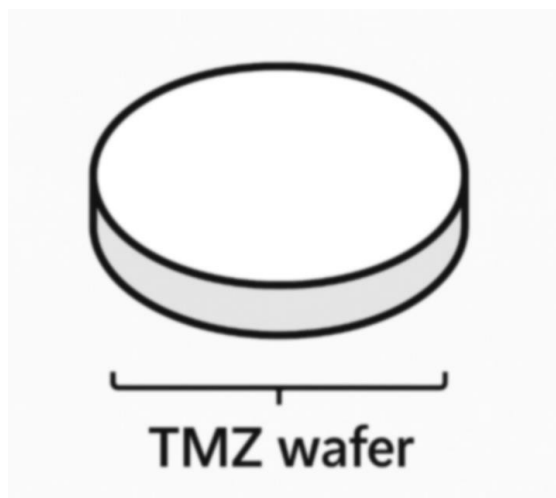


Figure 2: Temozolomide Wafer

Gliadel wafer has two major functions that make it different from other drug delivery methods. First, it delivers a high concentration

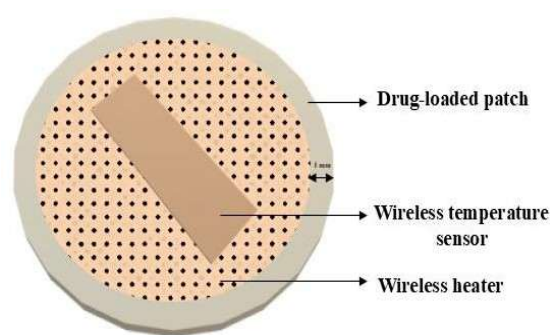


Figure 3: Sustainable Heated Wafer Materials and Composition of Biodegradable Wafers for Brain Cancer

of chemotherapy drugs directly to the tumor area, reducing the side effects typically seen with treatments that affect the whole body.

Second, the wafer is biodegradable and dissolves slowly, allowing the drug to be released in the affected area for a longer period of time.

Gliadel wafer also known as polifeprosan 20

with carmustine implant, is sterile as well as a small device which ranges the size from about 1.45 cm in diameter and 1 mm thick, with an off-white to pale yellow color.

Table 1: Composition of Gliadel Wafer

Ingredient	Quantity	References
Polifeprosan	192.3 mg	[15] and [2]
Carmustine	7.7 mg	[15] and [2]
Biodegradable Polymer	q.s	[15]

• Carmustine

As carmustine is lipophilic (fat-soluble), it is regarded as a very efficient chemotherapy medication, especially when used to treat brain tumors. This characteristic makes it possible for carmustine to readily cross both the blood-brain barrier, a barrier that typically keeps many medications from accessing the brain, and the cell membranes of tumor cells. Since many other chemotherapy drugs cannot effectively reach brain tumors, the ability to cross the blood-brain barrier is a major advantage. Since of this remarkable feature, carmustine is particularly useful in the treatment of brain tumors or cancers since it guarantees that the medication can directly target the diseased cells in this hard-to-reach location.

• Polifeprosan

Drugs are distributed using polifeprosan 20, a biodegradable polymer. In the case of gliadel (carmustine wafers), Polifeprosan 20 encapsulates the chemotherapeutic medication carmustine in a solid, wafer-like structure. This polymer is put straight into the brain during tumor surgery. Polifeprosan 20 releases carmustine to the tumor site gradually as it degrades over time, offering a controlled, targeted chemotherapeutic therapy. This is significant because glioblastoma multiforme, a particularly aggressive type of brain cancer, requires a multimodal treatment strategy, and the blood-brain barrier issue often diminishes the effectiveness of traditional chemotherapy. Carmustine wafers with Polifeprosan 20 may be used as an approach to increase tumoral medication exposure [16, 18].

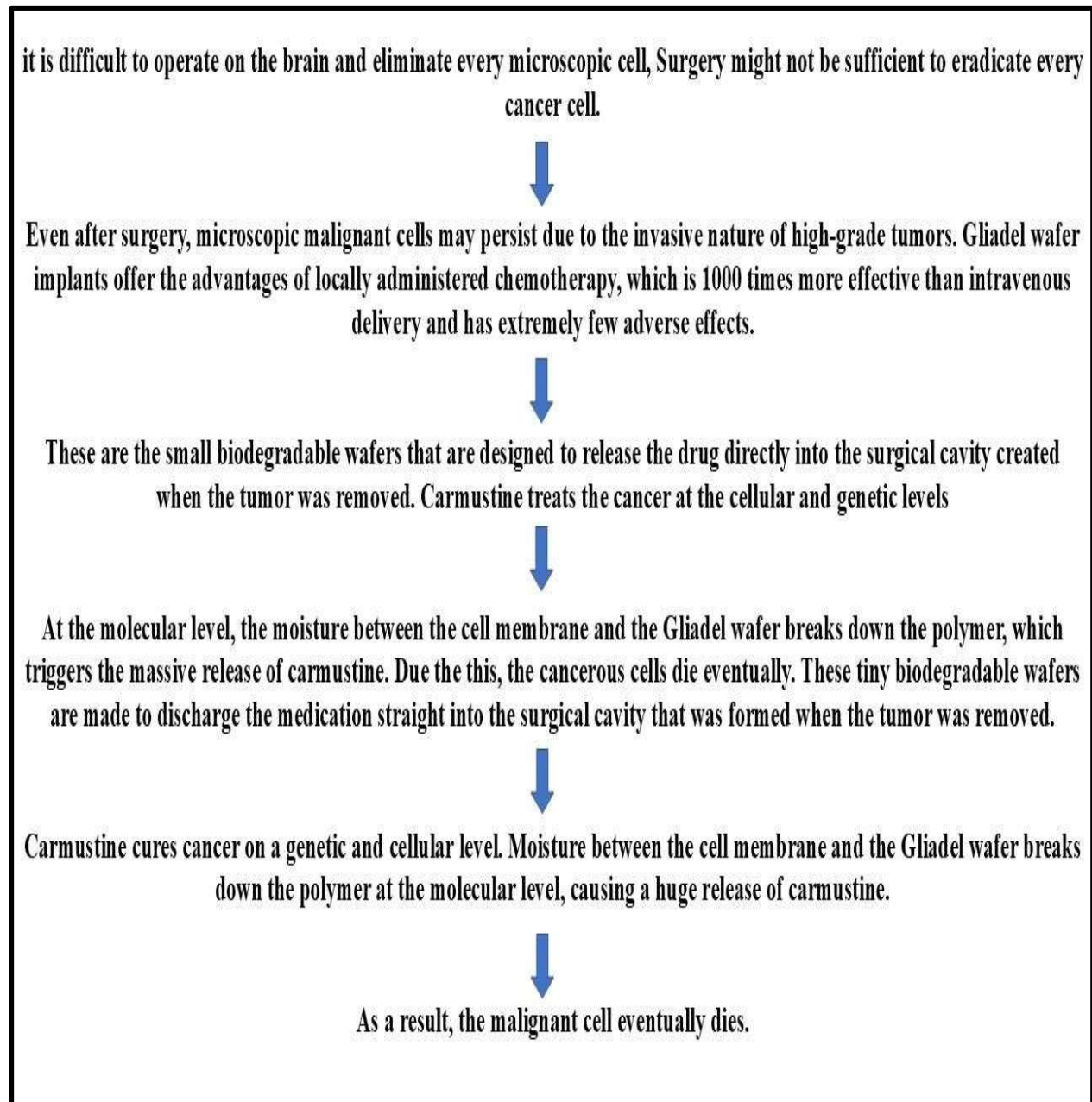


Figure 4: Schematic Flow Chart of Drug Release in Gliadel Wafer

Doxorubicin-Loaded Polymeric Wafers

Delivering chemotherapy medications to the brain tumor itself is one of the most difficult treatment challenges. Many drugs are unable to reach the brain because of the blood-brain barrier. Because they can penetrate this barrier and target both actively dividing and dormant tumor cells, alkylating drugs such as temozolomide and BCNU are frequently employed. Additionally, these medications aid in increasing the tumor cells' radiation sensitivity [19]. But even while they work, they frequently don't increase long-term survival because they can't get to the tumor in high enough [20].

New methods of delivering medications straight to the tumor site are part of recent advancements in treatment. One such is the BCNU-loaded PLGA wafer, a tiny biodegradable instrument that, following

surgery, delivers chemotherapy straight into the tumor. This method may postpone recurrence and aid in targeting remaining tumor tissue [22]. Chemotherapy has a significant drawback, though, in that tumor cells may eventually become resistant. This happens as a result of the cells' production of MGMT, a DNA repair enzyme that can reverse the harm the medications have caused [19].

Alternative medications, such as doxorubicin, are being investigated to get around this. Unlike alkylating agents, doxorubicin does not readily develop resistance. It has been used safely to treat brain malignancies such as lymphoma and leukemia. Researchers intend to give patients new hope by enhancing the efficacy of glioma treatment following surgery by mixing doxorubicin with the PLGA wafer [21-23].

Table 2: Composition of Doxorubicin-Loaded Polymeric Wafers [19]

Material	Quantity
Doxorubicin Hydrochloride	8.4 mg (for 8.4 cm ² surface)
PLGA (50:50 molar ratio, Mw 53114)	318 mg
Solvent (Chloroform)	Not specified
Final Sheet Surface Area	8.4 cm ²

Method-

- Prepare the Doxorubicin sheet.
- Set physiological parameters (pH 7.4, PBS at 37°C).
- Incubate for a specified duration.
- Collect samples at predetermined time intervals.

- Measure drug concentration using a UV-2200A spectrophotometer.
- Calculate the total eluted doxorubicin.
- Analyze data and interpret findings.

Animal Study

The purpose of this study was to investigate the biodegradation of a doxorubicin sheet as

well as its potential for treating cancer in rats and mice.

In the first section, the breakdown of the doxorubicin sheet was evaluated using ICR mice. Weighing the remaining sheet after removal allowed us to determine the biodegradation of a 3x3 mm sheet that had been positioned beneath the skin. To achieve precise results, five mice per group were utilized to compute the rate of degradation as a percentage of the initial weight. In order to create tumors, RT2 glioma cells were injected into Fischer 344 rats during the second phase.

The rats were given two different treatments

four days after it was confirmed that the tumors had grown: [15] applying a sheet of doxorubicin (containing 2.1 mg of the medication) to the tumor, and [16] injecting 8.4 mg of doxorubicin directly into the tumor. After that, tumor growth was tracked to see how well the treatments were working.

Comparing the doxorubicin sheet's disintegration and tumor-treatment effectiveness was the aim of the investigation. A Student's t-test was used to examine the data in order to identify any statistically significant variations between the treatment groups.

The biodegradable doxorubicin-loaded poly(lactic-co-glycolic acid) (PLGA) wafer is placed at the tumor location. Usually, a surgical procedure is used to place this wafer directly in or close to the tumor tissue.[20]



The PLGA wafer gradually starts to break down upon implantation. As it decomposes, it gradually releases the chemotherapeutic medication doxorubicin. This eliminates the need for frequent re-administration by guaranteeing that the medication is continuously supplied to the tumor over a prolonged length of time.



The surrounding tumor cells absorb the doxorubicin that has been released. The medication goes straight to the location where it is most required by passive diffusion or receptor-mediated entry.



Doxorubicin targets and binds to topoisomerase II, an enzyme necessary for DNA replication and repair, once it has entered the tumor cells. Doxorubicin inhibits the enzyme's ability to properly reconnect DNA strands that have been split apart during replication.



Tumor cells accrue DNA strand breaks due to topoisomerase II inhibition. As a result of this disturbance of the regular cell cycle, the cells stop dividing and arrest.[21]



When the tumor cells' cumulative DNA damage becomes irreversible, a series of processes culminate in programmed cell death, or apoptosis. As cells die off, the tumor mass is successfully reduced.[20]

Figure 5: Drug Release Pathway of Doxorubicin-Loaded Polymeric Wafers Temozolomide Plus Rotational Multiagent Chemotherapy

The purpose of the trial is to determine whether giving patients with glioblastoma, a kind of brain cancer, carmustine wafers, radiation, and temozolomide chemotherapy, along with a year of multi-agent chemotherapy, can increase their chances of survival. A group that did not get carmustine wafers, another that had the conventional treatment of surgery, radiation, and temozolomide, and a third that received only surgery and radiation are the three groups that are being compared to this combination treatment. Finding out if this combination of medicines can help patients live longer than those receiving the standard treatments is the aim. Additionally, the study assesses the potential toxicity of each medication. The additional carmustine wafers, radiation, and temozolomide, followed by rotational chemotherapy, are thought to be more effective than the previous therapies at slowing the growth of the tumor and increasing survival [24].

ASSESSMENT OF EXISTING LITERATURE

1. In their 2017 study, Maher *et al.* investigated the creation of 3D-printed titanium (Ti) wafers with a dual micro- and nano-topography designed to improve osseointegration and facilitate localized drug delivery. This process

involved selective laser melting (SLM) to produce titanium wafers, followed by electrochemical anodization to form titanium nanotubes (TNTs) on the surface. This structure was designed to enhance osseointegration and facilitate localized drug delivery. The study specifically invested the loading of anticancer drugs, doxorubicin (DOX) and apoptosis-inducing ligand (Apo2L/TRAIL), with thermogravimetric analysis (TGA) confirming their high drug-loading capacities. The in-vitro drug release studies demonstrated a biphasic release profile, characterized by an initial burst release followed by sustained release, lasting up to 16 days for doxorubicin and 4 days for Apo2L/TRAIL. The prolonged drug release demonstrated potential for localized chemotherapy. The mechanical and biological evaluation confirmed improved fibroblast adhesion, supporting the viability of these wafers for controlled drug delivery and improved cell integration in medical applications. These results suggest the potential of 3D-printed, drug-releasing titanium wafer for osseointegration and advancing cancer treatments [24].

2. Lee, J.*et al.* in the year 2019 conducted

study on the use of biodegradable wafers for targeted drug delivery in glioblastoma treatment. Their study focused on the application of these wafers to enhance brain tumour therapy by enabling localized drug administration. By utilizing a bioresorbable system, the approach aimed to improve drug delivery efficiency while minimizing side effects. The findings emphasize the potential of biodegradable wafers as an innovative strategy for treating glioblastoma. The study highlighted a bioresorbable electronic patch (BEP), which enables controlled intracranial drug delivery via wireless mild-thermic actuation. This wafer-like device features an oxidized starch (OST) drug reservoir and a polylactic acid (PLA) encapsulation layer, ensuring firm adhesion to the brain cavity while reducing unintended drug leakage into cerebrospinal fluid (CSF). The findings revealed that drug release, triggered by alternating radio frequency (RF) magnetic fields, significantly enhanced drug penetration depth, reduced tumour volume, and improved survival rates in both mouse and canine models. The study emphasizes the promise of biodegradable wafers with

electronic activation in advancing brain cancer treatment [1].

3. Perry *et al*, in the year 2007 conducted experiment demonstrating that Biodegradable Gliadel wafers have been extensively studied as a localized chemotherapy treatment for malignant gliomas, offering an innovative solution to the challenges of systemic therapy. Several randomized controlled trials (RCTs) have examined the safety and effectiveness of Gliadel wafers compared to placebo. Notably, two key RCTs demonstrated a significant survival advantage for newly diagnosed patients, showing a median survival increase of two months and a 27% reduction in mortality risk. However, an RCT investigating Gliadel in recurrent malignant glioma showed no significant survival benefit unless prognostic factors were considered, while a prospective cohort study found no advantage compared to historical controls. The wafers contain carmustine (BCNU) within a biodegradable polymer matrix, ensuring controlled and localized drug release at the tumor site after surgical resection. The adverse effects of Gliadel were comparable to those observed in placebo groups, with common

complications including convulsions, brain edema, confusion, and intracranial hypertension. Although Gliadel wafers remain a treatment option for patients with resectable malignant gliomas, their effectiveness compared to systemic chemotherapy remains uncertain, emphasizing the need for further research into their combination with standard therapies like temozolomide [25].

4. Shapira-Furman *et al.* in 2018 studied the development of biodegradable polymer wafers for localized chemotherapy in glioblastoma multiforme (GBM), with the goal of enhancing drug delivery and addressing the limitations of systemic therapy. The study expanded on the success of Gliadel® wafers, which deliver carmustine (BCNU) directly to the tumor site after surgical resection but are limited by rapid drug diffusion and systemic washout. To overcome these challenges, the researchers developed polymeric wafers containing temozolomide (TMZ), a water-soluble alkylating agent, utilizing polylactic acid-glycolic acid (PLGA) to achieve controlled drug release. To overcome these challenges, the researchers developed polymeric wafers containing temozolomide (TMZ), a water-soluble

alkylating agent, utilizing polylactic acid-glycolic acid (PLGA) to achieve controlled drug release. Using a pre-encapsulation technique, TMZ powder was coated with PLGA to create core-shell particles that served as a rate-controlling membrane, enabling a sustained 30-day drug release. Additionally, wafers co-loaded with TMZ and BCNU were developed to enhance therapeutic efficacy. In vivo studies using an intracranial 9L gliosarcoma rat model demonstrated improved survival outcomes with the combination therapy, resulting in a median survival of 28 days and 25% of rats achieving long-term survival, compared to 19 days for TMZ wafers alone and 15 days for BCNU wafers ($p < .0038$ vs. control, $p < .001$ vs. blank polymer). These results underscore the potential of localized TMZ and BCNU delivery via PLGA wafers in enhancing GBM treatment and facilitating the development of novel drug combination strategies for solid tumors [8].

5. Ionov *et al.* in their 2005 study explored the use of stimuli-responsive polymer layers embedded with fluorescent nanocrystals, demonstrating their remarkable sensitivity and photostability

in detecting ions and chemical substances. Recent developments in chemical and biological sensors have increasingly employed fluorescence-based techniques for environmental change detection. Smith *et al.* in 2003 and Johnson & Lee 2004 examined fluorescence quenching in organic dyes, highlighting their instability during prolonged exposure. In 2006, Zhang *et al.* discovered that semiconductor nanocrystals have broad absorption spectra and tunable emission properties, enhancing their effectiveness for environmental sensing. Kim & Wang in 2007 underscored the crucial role of energy transfer in emission spectrum shifts, contributing to improved detection accuracy. Collectively, these findings confirm fluorescence-based nanocrystals as a promising technology for real-time and spatially resolved environmental monitoring [26].

6. Stupp *et al.* in 2005 characterize Glioblastoma multiforme (GBM) as a highly aggressive brain tumor with a poor prognosis, attributed to its invasive nature and the protective role of the blood-brain barrier (BBB). Westphal *et al.* (2003) note that traditional treatments, including Carmustine

(BCNU) and Gliadel wafers, offer limited survival benefits, with BCNU causing systemic toxicity and Gliadel wafers exhibiting only partial tumor penetration. Zhou *et al.* (2018) highlight that retinoids, such as all-trans retinoic acid (ATRA), have been studied for their anti-tumor properties due to their ability to induce differentiation and apoptosis in cancer cells. However, their clinical effectiveness is limited by rapid metabolism and low BBB permeability. Wang *et al.* (2020) introduce ATRA-eluting poly (diol citrate) (POC) wafers as a solution to these challenges, enabling controlled and localized drug release. Studies suggest that these wafers facilitate sustained drug loading and release, improving drug retention at the tumor site while minimizing systemic toxicity. This targeted delivery method shows potential for enhancing GBM treatment efficacy over traditional systemic therapies [27].

LOCALIZED DEPLOYMENT OF BIODEGRADABLE WAFER IN TUMOR SITES

- Materials Selection and Preparation: Relevant research was chosen based on its assessment of polymeric systems, such as wafers, gels, and microchips, in both preclinical and

clinical settings. The study employed biodegradable polymeric materials to create wafers intended for localized drug delivery. The selection of polymers was based on their biocompatibility, controlled degradation rates, and effectiveness in encapsulating Temozolomide (TMZ) and BCNU. The drugs were procured from certified pharmaceutical suppliers and were managed under sterile conditions [8].

- **Polymer Formulation and Drug Incorporation:** Temozolomide (TMZ) was integrated into a biodegradable polyanhydride copolymer made of CPP:SA at weight concentrations of 10%, 20%, and 50%. The polymer-drug blend was shaped into discs, each weighing approximately 10 mg. For in vitro release kinetics and biodistribution studies, tritium-labeled TMZ (3H-TMZ) was included in the formulation [13].
- **Wafer Fabrication:** The polymeric wafers were produced using a solvent casting and compression molding method. This process involved dissolving the polymer in a suitable solvent, combining it with TMZ and BCNU, and casting the resulting mixture into molds. The molds were then subjected to controlled drying and compression to ensure uniform thickness and consistent drug distribution. A comprehensive analysis of implantable polymeric and electronic devices was

conducted, focusing on material selection, fabrication methods, and functionalities [8].

- **Efficacy of Locally Delivered TMZ in Combination with Radiation Therapy:** To explore the synergistic effect of locally delivered TMZ and radiation therapy, tumor-bearing animals received implants of TMZ polymers (50% w/w) followed by a single external beam radiation dose of 20 Gy using a ¹³⁷Cs laboratory irradiator. Control groups included animals that received polymer implants without radiation, those treated with oral TMZ alongside radiation, and untreated tumor-bearing rats [13].
- **Biodegradability and Stability Analysis:** By submerging the polymeric wafers in PBS and tracking weight loss over time, the degradation profile of the wafers was examined. SEM imaging was used to assess structural integrity at different stages of deterioration [8].
- **Clinical Data Analysis:** A retrospective evaluation was conducted on glioblastoma patients treated with or without BCNU wafers who underwent repeat resections when their tumors reappeared. Following surgery, MRI scans were reviewed many times to evaluate wafer deterioration and tumor growth. Immunohistochemical analysis of resected tissue was used to assess immunosuppressive action (FOXP3), immunological weariness

(PD1), macrophage response (CD68), and immune infiltration (CD3, CD4, CD8, and CD20). Digital image analysis was used for quantification, and correlation analysis examined the connections between MRI findings, immune cell infiltration, and the interval between operations. Genetic profiling using The Cancer Genome Atlas (TCGA) improved histological results [12].

- Statistical Analysis: One-way ANOVA and post-hoc Tukey's test were used to assess the experimental data's statistical significance. The median survival rates for each therapy

group were compared using Kaplan-Meier survival curves [10].

Features and attributes of the device: The effectiveness of flexible and biodegradable implants in intracranial sensing—including electrophysiology, temperature, pressure, and pH monitoring—was assessed. We looked at therapeutic uses including electrical/optical stimulation and medication delivery. To compare with Gliadel® experiments, biodegradable polymeric wafers with 50% w/w TMZ and 3.8% w/w BCNU were created [7, 8].

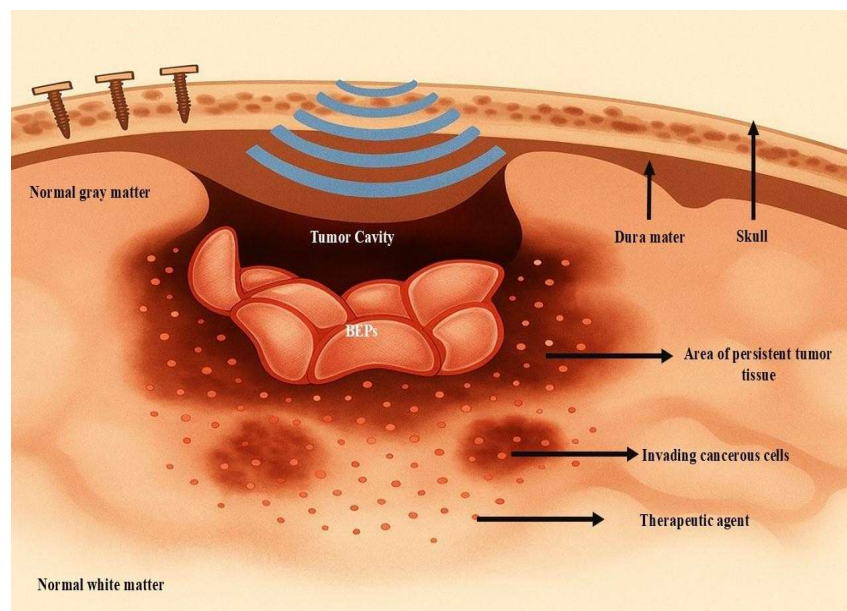


Figure 6: Drug Penetration Through Tumor Bed Facilitated by Mild Thermal Activation Wireless electronic wafers

- The biodegradable wireless electronic wafer was created using bioresorbable materials such as oxidized starch, polylactic acid, and magnesium-based electronic components. This wafer is composed of two distinct layers:
 - Drug-Loaded Layer: This layer features oxidized starch infused with the anticancer agents temozolomide and doxorubicin. The oxidized starch allows for a sustained release of the drug and gradually breaks down into

glucose following the complete diffusion of the medication.

- **Protective Layer:** The outer layer, made of polylactic acid, serves as a barrier to prevent any premature leakage of the drug. As it biodegrades, polylactic acid converts into lactic acid, ensuring compatibility with biological systems.
- A small electronic heater based on magnesium was integrated between these layers. When exposed to external radiofrequency waves, this heater produced mild localized heat, which aided in drug diffusion and allowed for deeper penetration into tumor [1]. The heater was fabricated by depositing a zinc (Zn) film, approximately 500 nm thick, onto a PI film via electron beam evaporation. The Zn layer was then patterned using a lift-off process to form the heater structure. A 1 μ m thick magnesium oxide (MgO) insulating layer was deposited on the regions where the receipt coil and heater overlap, also using electron beam evaporation. This MgO layer was subsequently patterned through the lift-off process to prevent short circuits between the heater and the receipt coil [28].
- **Implantation Procedure:** Following the surgical excision of the tumor, the biodegradable electronic patch (BEP) was directly implanted into the tumor bed. The mechanically disrupted brain tissue improved

the patch's adherence to the affected area, facilitating effective localized drug delivery.

- **Thermal-Triggered Drug Release Mechanism:** The BEP was designed to initiate drug release at physiological temperature (37°C). To further enhance drug penetration, external radiofrequency waves were employed to activate the magnesium heater, resulting in a slight increase in temperature within the patch. This thermal activation expedited drug diffusion and encouraged deeper infiltration into tumor cells.
- **In Vivo Evaluation:** The efficacy of the BEP was assessed in vivo using brain tumor models. The impact of controlled drug release on tumor volume reduction and survival rates was systematically examined. Tumor regression was monitored over time, along with the evaluation of biocompatibility.
- **Data Analysis:** Tumor volume reduction and survival rates were statistically evaluated to determine the therapeutic efficacy of the BEP. Additionally, the biodegradability of the implanted device and any potential side effects were assessed to ensure its safety and feasibility for intracranial applications [1].

Diverse Polymeric Wafers for Targeted Tumor Treatment

1. On-a-Chip Tumor Technology

A tiny gadget called a tumor-on-a-chip is made to mimic the conditions of an actual

tumor. This makes it possible for researchers to examine how cancer spreads and responds to therapies in a laboratory environment without actually utilizing humans.

This method creates a small-scale model of several cancer kinds, enabling researchers to explore how different treatments could function. By learning how a particular tumor reacts to different medications in this virtual environment, the goal is to customize cancer treatments. A useful technique for accelerating drug discovery and guaranteeing that patients receive treatments customized for their particular cancer is tumor-on-a-chip [29].

2. Nanoparticle-Based Wafers

Nanoparticle-based wafers are a novel way to treat cancer by delivering drugs directly to cancer cells using minuscule silicon particles that are small enough to pass through the bloodstream and target specific tumors, making them extremely effective at getting treatment to the right place. Traditional chemotherapy affects the entire body, causing side effects like nausea or hair loss because it can harm both cancer cells and healthy tissues. Using nanoparticles, however, allows the treatment to be more concentrated on the cancer, lowering the likelihood of harming healthy cells and tissues [30].

It is possible to build these nanoparticles to

deliver various cancer therapies. They can provide immunotherapy, which strengthens the body's immune system's ability to identify and combat cancer cells, photodynamic treatment (PDT), which uses light to activate medications to kill tumor cells, and chemotherapy, which targets and kills cancer cells directly [31].

By guaranteeing that the medications reach the cancer cells while avoiding harm to healthy tissues, the use of nanoparticle-based wafers aims to increase the efficacy of treatments. This method not only increases the Effectiveness of the treatment but also lessens the side effects that frequently cause patients to find chemotherapy extremely challenging [30].

3. The Organ-on-a-Chip System

Organ-on-a-chip is a cutting-edge technology that creates a tiny, laboratory-made gadget that mimics the operations of human organs. Compared to conventional studies, it enables researchers to examine the interactions between cancer cells and healthy tissue in a more realistic environment. These platforms assist researchers in assessing the effectiveness of various anti-cancer medications and comprehending metastasis, the process by which cancer spreads to other parts of the body. High-throughput screening is made possible by organ-on-a-chip

technologies, which enable researchers to test several medications simultaneously to determine which ones work best for particular cancer types. This expedites the search for novel treatments and enhances the way we test medications before they are administered to real patients [31, 32].

4. Doxil (Pegylated Liposomal Doxorubicin)

It is a special form of the chemotherapy drug doxorubicin that is encased in small fat particles called liposomes. These liposomes are coated with polyethylene glycol (PEG), which helps the drug stay in the body longer and avoid being broken down too quickly. What makes Doxil unique is its ability to target cancer cells more precisely; by using liposomes, the drug can circulate in the body longer, increasing its chances of reaching the tumor, making it more effective while also minimizing damage to healthy tissues. Doxil is used to treat several cancers, including ovarian cancer, breast cancer, and some types of lymphoma. It demonstrates how sophisticated drug delivery techniques can make chemotherapy more targeted and less harmful overall [32].

Table 3: A Comparative Study of Implantable Wafers vs. Conventional Cancer Treatment

Sr. No	Parameter	Biodegradable Wafers	Chemotherapy	Radiation Therapy	Surgery	References
1	Precision and targeting	Highly targeted with minimal systemic toxicity	Low specificity while affecting both malignant and healthy cells throughout the body	Moderately targeted while affecting cancer cells and the surrounding normal tissues	Offers high precision but is restricted by tumor location and accessibility.	[33] and [34]
2	Mechanism of Action	Provides sustained and localized delivery directly to the tumor site	Delivers cytotoxic agents systemically to destroy rapidly dividing cancer cells	Employs high-energy radiation to destroy or shrink tumor size	Extracts the tumor along with surrounding healthy tissue via surgery	[33] and [34]
3	Duration of Action	Provides prolonged drug release for days to weeks	Demands successive cycles of treatment	Involves repeated treatment sessions over several weeks	Typically involves one surgery, though subsequent procedures might be required	[33]
4	Invasiveness	Minimally invasive; requires implantation via surgery	Administered orally or intravenously	Non-invasive (external beam) or mildly invasive (brachytherapy)	Involves extensive surgery, with tissue extraction and extensive cuts	[33]
5	Patient Compliance	High, requiring just a single procedure	Unpredictable, as adverse effects may hinder compliance	Moderate, involving multiple hospital visits	Generally well-tolerated but demands post-surgical care and recovery	[33] and [34]
6	Side Effects	Lower systemic toxicity; may cause localized irritation or inflammation	Hair loss, nausea, bone marrow suppression, and immune compromise	Skin burns, fatigue, damage to adjacent organs	May cause pain, infection risk, scarring, and potential functional impairment.	[33] and [34]
7	Risk of Recurrence	Lower due to extended localized drug diffusion	Higher, due to possible drug resistance and partial tumor clearance	Moderate, influenced by tumor type and radiation dosage	Recurrence possible, particularly if residual microscopic cancer cells persist.	[33] and [34]
8	Clinical examples	Gliadel® wafer (carmustine) for brain tumor treatment	Doxorubicin and paclitaxel for breast and systemic cancers	External beam radiation and brachytherapy targeting various cancers	Lumpectomy and tumor resection.	[33]

EVALUATING THE PROS AND CONS OF BIODEGRADABLE WAFERS

Favorable aspects:

• Extended Presence and Activity

The wafer remained at the tumor site for up to 421 days, according to radiological and intraoperative findings, and continued to affect the surrounding tumor microenvironment long after it was no longer radiologically detectable. This prolonged presence may contribute to the maintenance of a therapeutic effect over an extended period of time [12].

• Biodegradable Material

The wafer is crafted from a biodegradable material that gradually breaks down at the tumor site, allowing for a steady release of the drug and eliminating the need for removal after treatment [12].

• Increased Survival Potential:

Research has indicated that the BCNU wafer may help patients with high-grade gliomas and glioblastoma by extending their median survival time when used in conjunction with chemotherapy and radiation therapy. All things considered, the BCNU wafer is a viable strategy for the targeted treatment of glioblastoma. It may improve the immune

response and direct drug delivery, and it could serve as a basis for future immunotherapies to be combined with for more effective tumor elimination [12].

- **Minimizes Need for Secondary Surgery**

The biodegradable PLGA wafer gradually decomposes in the body, removing the need for a follow-up surgery for removal. Unlike traditional implantable devices, which require surgical extraction and may lead to complications such as inflammation, this device is absorbed by the body, minimizing risks and streamlining the treatment process [28].

- **Customizable Degradation Time**

The degradation rate of the device can be adjusted by varying the thickness of the material surrounding it. Thicker substrates will take longer to degrade, while thinner ones will break down more quickly. This flexibility allows the treatment to be customized according to the patient's specific needs, such as how long the drug should be released or how fast the device should dissolve in the body, optimizing the therapeutic effect for each individual [28].

- **Compatibility with Biological Tissues and Adaptability**

The device is constructed from materials that replicate the mechanical properties of human tissue, allowing it to function in a similar

manner to natural tissue. Its adaptable design enables it to fit smoothly over complex and uneven surfaces inside the body, promoting seamless integration with adjacent biological tissues. This enhances compatibility and contributes to improved performance and healing [28].

- **Proven Efficacy in Laboratory Studies**

In vitro studies showed that the device effectively inhibited the growth of breast cancer cells (MCF-7). It demonstrated a synergistic effect combining heat-based therapy and drug chemotherapy, leading to improved overall cancer treatment results [28].

- **Minimized Neurological Side Effects**

The bioresorbable patch is intended to gradually break down and be absorbed by the body. After fulfilling its function, it leaves no foreign material in the brain, unlike traditional implants that require surgical removal. This eliminates potential complications, such as infection or inflammation, associated with long-term implants. In essence, the patch offers a safer, more convenient treatment with fewer long-term risks [1].

- **Reduced Systemic Toxicity**

Administering TMZ and BCNU directly to the tumor ensures that the drugs are concentrated on the cancer cells, limiting their spread to other organs. This targeted delivery reduces

the likelihood of side effects typically linked to systemic chemotherapy, such as hematological toxicity (blood cell damage), hepatotoxicity (liver damage), and cardiomyopathy (heart muscle damage), which occur when drugs affect non-target tissues. By directing the treatment specifically to the tumor, overall toxicity is minimized [8].

- **Reduced Need for Systemic Chemotherapy**

Gliadel wafers can reduce the reliance on intravenous chemotherapy, which has a shorter half-life and may require frequent dosing. By providing a sustained release of chemotherapy directly to the tumor site, the need for multiple systemic treatments may be reduced [14].

- **Enhanced Local Control**

The integration of localized drug delivery and the capacity to administer high levels of chemotherapy directly to the tumor may enhance local tumor management, which is vital for treating GBM, a highly aggressive cancer [14].

- **Possibility of Survival Improvement**

Research indicates a slight increase in overall survival (OS) when Gliadel wafers are utilized alongside standard therapies such as surgery, radiation, and chemotherapy. Although the survival advantage may be modest, it offers an extra option in the difficult battle against GBM [14].

Limitations

- **Edema in the Brain**

Brain swelling, or cerebral edema, is one of the most localized adverse effects of Gliadel wafers. These wafers have the potential to cause edema in the afflicted region of the brain by inducing an inflammatory reaction. Neurological deficiencies including motor impairments or issues with cognitive processes like speech or memory may arise from this. Because it can raise intracranial pressure and further harm brain cells, cerebral edema is a dangerous consequence. High dosages of corticosteroids, such dexamethasone, are frequently administered to patients in order to treat this condition by reducing swelling and inflammation [15].

- **Infections and the Healing of Wounds**

A higher chance of infections and slowed wound healing are two other possible risks connected to the usage of Gliadel wafers. when brain tissue is so sensitive, there is a higher chance of intracranial infections when the wafers are surgically inserted into the brain. Complications from infections may include fever, elevated intracranial pressure, or, in extreme situations, sepsis. Furthermore, the wafers' implantation may interfere with the body's natural healing processes, leading to problems like leaks of cerebrospinal fluid or a delayed recovery of

the surgical site. In order to treat the infection, the patient may need to have more surgery or long-term antibiotic treatments, which might prolong their hospital stay [15].

- **Convulsions**

Another possible adverse effect of Gliadel wafers is seizures, which usually start earlier in people using them than in those taking placebos. While the overall rate of seizures in Gliadel wafer-using patients is comparable to that of placebo groups, the number and timing of seizures might vary. Because they can have a major impact on a patient's quality of life and may need continuous medication to manage, seizures are a worrying consequence. In order to prevent further episodes, seizure treatment entails medication modifications and close observation during the post-operative phase. Anti-epileptic medications help manage the majority of seizures, but they can add a level of complication to post-treatment care [15].

- **Limited Effectiveness in Partially Removed Tumors**

The degree of tumor removal following surgery has a significant impact on the efficacy of Gliadel wafers. As little malignant tissue as possible should remain after the tumor has been nearly completely removed. The effectiveness of the wafers is reduced when tumors are not completely removed,

particularly in parts of the brain that are hard to reach. It might be more difficult to reach or completely remove tumors that are situated in "eloquent" brain regions, such as those related to speech, motor function, or vision. In these situations, the medicine delivered by the wafers may not be as effective against any cancer cells that remain, increasing the chance of recurrence [35].

- **Short Time Of Drug Release**

Over the course of two to three weeks, Gliadel wafers release the chemotherapeutic medication carmustine, which is comparatively short for long-term tumor control. This little timeframe may not be sufficient to suppress the tumor in more aggressive forms of gliomas, such as glioblastoma, even if the medication release during this time may be useful in eliminating any residual tumor cells. Given their propensity for rapid growth, aggressive gliomas may need longer-term medication release or other therapies in addition to the wafers' two to three-week timeframe. This little time frame could not have a sufficient therapeutic effect for certain individuals, allowing tumor cells to persist and perhaps causing recurrence [25].

Efficacy And Safety of Gliadel Wafers: Insights From Clinical Trials

There have been some encouraging survival

results in studies comparing Gliadel wafers to a placebo for patients with recently discovered malignant gliomas. Following surgery, individuals who took Gliadel wafers had a somewhat higher

median survival than those who got a placebo in a major, multi-center randomized controlled study (RCT). In particular, the Gliadel group's median survival time was around 13.8 months, whereas the placebo group's median survival was approximately 11.6 months [25].

Gliadel-treated individuals had a 1-year survival rate of 59.2%, whereas placebo-treated patients had a 49.2% rate. This statistically substantial difference in survival rates raises the possibility that Gliadel, as opposed to a placebo, may help prolong life. Gliadel wafer users had higher survival rates even after two years (15.8% against 8.3% in the placebo group).

However, the survival effect of Gliadel was less evident in a subgroup study that was solely focused on patients with glioblastoma multiforme (GBM). The little improvement was not statistically significant, maybe as a result of the limited sample size and variations in patient characteristics. The findings were less evident in a different investigation on recurrent gliomas. Although the initial study did not find a significant overall survival

advantage with Gliadel wafers, a modified analysis that took other parameters into consideration did indicate that Gliadel might increase survival, especially in patients with GBM. The Gliadel group's median survival was almost 31 weeks, whereas the placebo group's was 23 weeks [25].

It's crucial to remember that the majority of Gliadel's recipients had previously had surgery, making them good candidates for wafer therapy. This may restrict the generalizability of the results since individuals with tumors that were not completely resectable or that were situated in difficult-to-reach regions were not included in the studies [25].

In terms of safety, the Gliadel and placebo groups saw comparable side effects, including disorientation, edema, and seizures. Nevertheless, intracranial hypertension, or elevated brain pressure, was a more common consequence among participants in the Gliadel group than in the placebo group. In spite of these adverse effects, Gliadel's overall safety profile was deemed tolerable during the trial.

Key Findings on Gliadel Wafers: Impact and Future Directions

Gliadel wafers may provide some survival advantages for individuals with newly diagnosed malignant gliomas, according to

the results from existing clinical trials. This is especially true if the tumor has been surgically excised almost entirely. More study is needed to determine its effect on glioblastoma patients, especially when combined with other medications like temozolomide. Likewise, it is unclear if Gliadel helps patients with recurrent gliomas, however some people may benefit from it in terms of survival. Future research should examine Gliadel wafers' potential in conjunction with other medicines and compare them to conventional systemic chemotherapy treatments. Additionally, more study is required to determine which patient groups—specifically those based on age, tumor kind, and general health status—may benefit the most from Gliadel.

In order to comprehend how immune responses may affect tumor behavior, this study aims to investigate the relationship between immunological markers and the development of brain tumors. T1-weighted gadolinium-enhanced MRI (T1Gd), which shows regions of active tumor growth, and fluid-attenuated inversion recovery MRI (FLAIR), which shows areas of swelling or edema surrounding the tumor, are the two MRI sequences that researchers specifically use to monitor these changes.

Doctors utilize sophisticated software to determine the size of the tumor and the

surrounding swelling tissue in order to track the evolution of the tumor. They quantify the volumes of the increased regions on the T1Gd scans, which show active tumor tissue, and the high-intensity regions on the FLAIR scans, which show swelling. They calculate a ratio called the F/G ratio by comparing these two volumes, which aids in evaluating the connection between tumor development and alterations in the surrounding tissue. This ratio can provide information about the tumor's potential aggressiveness and the extent to which it has damaged the surrounding tissue. Before the initial operation, when the tumor is originally removed, and before a second surgery, often after the tumor has returned, the scans are obtained. The study monitors the changes in the tumor and surrounding edema over time by comparing the photos from these two time periods [25].

The study also looks at the patients' immunological markers, which show how active their immune systems are, in addition to the imaging. Finding out if these immune markers match the alterations observed in the tumor and surrounding tissue is the aim. This may shed light on how the immune system engages with the tumor and affects its behavior.

In order to assist physicians make better treatment decisions, the study's overall goal is

to provide a clearer understanding of how immune responses may be connected to tumor progression. For therapies like immunotherapy, which strengthens the body's immune system to target and combat cancer, this discovery is especially pertinent. The study hopes to enhance future management and treatment of brain cancers by better understanding and tracking malignancies [25].

ADVANCEMENTS IN BIODEGRADABLE WAFERS: FROM NANOTECHNOLOGY TO PERSONALIZED MEDICINE

- **Customization with 3D Printing and Bio-fabrication** – Innovation in 3D printing and bio fabrication has revolutionized drug delivery systems, allowing more precise control over drug release and degradation kinetics. 3D printing technology enables the design of patient-specific wafers. This ensures precise treatment for tumors, wound healing and infections. Bio fabrication allows the creation of multilayered wafers which can sequentially release the drug, optimizing therapeutic effectiveness. One of the most significant breakthroughs is the development of 3D-printed titanium (Ti) alloy-based drug-releasing implants, which integrate micro-spherical and nano-topographies to enhance cell attachment, drug loading, and localized

chemotherapy for bone cancer treatment. This implant provides high therapeutic concentration directly at the tumor site while also preserving the structural integrity of the implant, making it a promising innovation in personalized medicine [36].

- **Smart and adaptive wafers**- These wafers represent an advancement in biomedical technology utilizing materials that respond to various environmental stimuli such as pH, temperature, light or some specific biomolecules. These wafers ensure the precise release of the therapeutic agent at the optimal time and location in the body. The development a smart wafers incorporating shape-changing polymers enables them to react dynamically to external stimuli, allowing for controlled surface interactions and targeted drug delivery. By integrating multilayered polymeric structures, smart wafers can undergo reversible transformations, optimizing their functionality for various biomedical applications. Their adaptability and precision in releasing therapeutic agents position them as a promising innovation in nano medicine and bioengineering [26].

FUTURE PROSPECTS OF BIODEGRADABLE WAFERS

Biodegradable wafers have significant potential to transform drug delivery, tissue

engineering, and regenerative medicine. Ongoing research is unveiling new possibilities to improve their functionality, precision, and clinical applications.

Biodegradable wafers are emerging as highly versatile platforms for gene and stem cell therapy, offering targeted and sustained delivery with enhanced biocompatibility while also protecting sensitive biomolecules from degradation. In gene therapy, these wafers can be engineered to deliver genetic materials such as DNA, RNA, and CRISPR. These advanced drug delivery platforms hold immense promise in regenerative medicine for treating neurological disorders such as spinal cord injuries, Parkinson's disease, and Alzheimer's by enabling the controlled release of neurotropic factors and CRISPR-based gene-editing tools to promote nerve regeneration and repair. Biodegradable wafers are embedded with gene-silencing agents such as siRNA and mRNA vaccines which can modulate the tumor gene expression precisely, thereby reducing systemic toxicity and increasing treatment efficacy. Moreover, wafers embedded with stem cells facilitate tissue regeneration by progressively releasing growth factors that promote cell differentiation and repair, making them highly effective for wound healing, bone regeneration, and organ transplantation [34].

A key future prospect in the advancement of biodegradable wafers is the development of hybrid and multifunctional designs that integrate nanoparticles, bioactive molecules, and biosensors, transforming them into highly versatile therapeutic platforms. The incorporation of nanoparticles into these wafers can enhance drug stability, precise targeting and more control over drug release while minimizing overall systemic side effects. Additionally, bioactive molecules such as peptides and growth factors can help in tissue regeneration, making wafers valuable for post-surgical healing, wound healing, and orthopedic applications. The integration of biosensors can further augment the capabilities of these wafers by enabling real-time monitoring of various physiological parameters such as pH and glucose levels, facilitating adaptive therapy to individual responses. Moreover, the use of stimuli-responsive materials that react to temperature changes, pH fluctuations and enzymes allows for precise and on-demand release of the drug, enhancing its therapeutic efficacy. Through the convergence of such properties, the hybrid and multifunctional wafers represent groundbreaking innovation in precision medicine. Their ability to provide personalized, controlled, and responsive treatment paves the way for a new era in

biomedical applications [38].

The future advancement of biodegradable wafers focuses on innovating biocompatible polymers such as chitosan, alginate, PGLA, silk fibroin, which provide much greater sustainability, solubility and minimal inflammatory responses. Additionally, the biodegradable materials can serve as an eco-friendly alternative to plastic-based medical films, further reducing biomedical waste and environmental impact [37].

As these technologies advance, the scalability and cost-effectiveness of biodegradable wafers will be key to their widespread adoption. Collaborative efforts between biomedical researchers, material scientists, and healthcare industries will drive innovation, ensuring these wafers meet regulatory standards and patient needs. Biodegradable wafers are poised to revolutionize next-generation medical treatments.

CONCLUSION

Brain tumors present a significant medical challenge due to their complexity, genetic variability, and resistance to treatment. While benign tumors like meningiomas can often be managed with surgery and medication, malignant tumors such as glioblastoma multiforme (GBM) remain aggressive and difficult to treat. Genetic mutations influence

tumor progression, treatment response, and recurrence rates, impacting patient survival.

Wafer-based therapies have emerged as a promising innovation in brain tumor treatment, offering localized and sustained drug delivery directly to the tumor site. Unlike traditional systemic chemotherapy, which struggles to penetrate the blood-brain barrier, wafer implants provide targeted drug administration, reducing systemic toxicity while increasing treatment efficacy.

Despite progress in imaging, surgical techniques, and therapeutics, the prognosis for malignant brain tumors remains poor. Standard treatments—surgery, chemotherapy, and radiation—offer limited success in preventing tumor regrowth. However, new advancements, including immunotherapy, targeted drug therapy, and gene therapy, provide hope for better patient outcomes. Nonetheless, drug resistance, tumor heterogeneity, and drug delivery challenges continue to hinder treatment effectiveness.

Future research must focus on genetic and molecular mechanisms to develop more personalized therapies. Early detection using advanced imaging and biomarker identification is crucial for improving survival rates. A multidisciplinary approach that integrates neurosurgery, oncology, and genetics is essential for driving innovation.

Although wafer-based treatments are a significant advancement, challenges such as drug resistance and diffusion limitations remain. Continued research and innovation in wafer technology, including nanomedicine and multi-drug delivery systems, are vital for improving treatment outcomes and developing more effective, personalized therapies for brain tumor patients.

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