Reviewing multiple aspects of medicine delivery for brain tumor's, including the recent applications of artificial intelligence to medication and diagnosis

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***Abstract*—In order to improve drug delivery methods for brain tumors, specifically glioblastoma multiforme (GBM), this study investigates the combination of artificial intelligence (AI) with nanomedicine. Because of their rapid growth, resistance to traditional treatments, and the challenge of getting medications over the blood–brain barrier, brain tumors continue to rank among the most complicated and deadly illnesses. The paper emphasizes how AI may be used to predict medication permeability, optimize nanocarrier design, increase diagnostic accuracy, and customize treatment plans. Additionally, it highlights the importance of prognosis monitoring, early biomarker discovery, and innovative computational techniques that improve the accuracy of brain tumor treatment. AI-driven nanomedicine presents new avenues for more efficient, tailored, and minimally invasive treatments, even while traditional therapies like surgery, radiation, and chemotherapy have drawbacks. Additionally, as discussed in future prospects, current innovation uses artificial intelligence for achieving the highest rate of success in medication research.**

Index-Terms— Artificial intelligence in pharmacy, Brain tumor medication, Recent applications in tumor's

I. INTRODUCTION

The brain, which is thought to be the most important organ in the human body, is extremely complex. A brain tumor is an abnormal growth of tissue inside the brain. [1] The aberrant development of brain cells is a characteristic of brain tumors. These tumors may develop in the brain itself (primary brain tumors) or they may spread from another location to the brain (secondary or metastatic brain tumors). There are two types of brain tumors: malignant (cancerous) and benign (noncancerous). In general, malignant brain tumors develop more quickly and are more aggressive. There are many different kinds of brain tumors, such as medulloblastomas, pituitary adenomas, meningiomas, and gliomas. Based on its location, development pace, and accessible treatment choices, each form of tumor is unique. [2] An unnatural and uncontrolled development of brain cells is called a brain tumor. Because the human skull is a volume-limited and hard structure, any unanticipated development may impact a human function based on the specific area of the brain involved; additionally, it may extend to other body organs and impact human functions. [3] About 15% of all brain tumors and 50% of all gliomas are glioblastomas (GBMs), a type of malignant brain tumor that develops from glial cells. glioblastoma multiforme are the most prevalent and dangerous type of primary brain tumors. The World Health Organization's classification system places this condition as a grade IV astrocytoma. It is challenging to totally eradicate with surgery alone due to its diffuse and infiltrative growth style. There is still much to learn about the precise cause of glioblastoma multiforme. Nonetheless, a number of risk factors have been found, such as age, ionising radiation exposure, genetic abnormalities, and specific genetic illnesses. [4]

II. HISTORY

Diagnosis of brain tumors in antiquity

Brain tumors are not mentioned in the Edwin Smith Papyrus, the oldest medical literature, which was written in the 17th century and details 48 head and spine injuries sustained on the battlefield. Brain tumors are likewise not mentioned in the more recent (but still ancient) Ebers Papyrus (1500 BCE). Brain tumors in antiquity caused death and were preceded by chronic headaches, seizures, and coma. In their treatises, Hippocrates, Socrates, Aulus Cornelius Celsus, Galen, and other Byzantine physicians made explicit references to trepanation as a means of reducing intracranial pressure, but they made no mention of brain tumors.

X-rays and the brain

Wilhelm Roentgen announced the discovery of x-rays in 1895. Harvey Cushing, the renowned neurosurgeon, said shortly after that x-rays were useful for diagnosing tumors close to the sella turcica but had little use for diagnosing brain tumors. Around this same period, German neurosurgeon Fedor Krause wrote a book chapter specifically about the use of x-rays for brain tumor localisation. The Transactions of the American Roentgen Ray Society published an article in 1904 about the use of x-rays to identify tumors and brain infarctions. Up until 1949, precise

measuring of the sella turcica on radiographs was the only method to establish the diagnosis of a pituitary tumor.

The living brain and spinal cord are visualized

When neurosurgeon Walter E. Dandy, MD, saw that free intraperitoneal air delineated the abdominal organs in 1918–1919 at Johns Hopkins University (Baltimore, MD), he attempted to apply the same idea to the brain, leading to the development of pneumoencephalography and ventriculography. Dandy was nominated for the Nobel Prize in 1933 for this breakthrough, which was the first method to enable indirect visualisation of the living brain. At the Neurological Institute of New York in New York City, the method was refined in the early 1940s by Leo M. Davidoff, MD, another neurosurgeon, and Cornelius G. Dyke, MD, the first neuroradiologist in America. "Acquired Subtentorial Pressure Diverticulum of a Cerebral Lateral Ventricle" was Dyke's first publication published in Radiology. In 1942, Radiology 39:167–174. The use of radiography and air encephalography as the primary methods for brain tumor imaging was established in 1936 when Radiology published an impressive review on gliomas that addressed their diagnosis. Three papers about the use of "roentgen methods" to locate brain tumors make the August 1943 issue of Radiology noteworthy. In 1952, the first Radiology paper about imaging paediatric brain tumors was published.

Early physiologic tumor neuroimaging

In the late 1940s, George E. Moore, MD, a surgeon in Minneapolis, Minnesota, proposed that some brain tumors could preferentially take up a radiotracer. The era of brain scanning began when he first injected fluorescein, which at the time of operation delineated tumors. He subsequently tagged the fluorescein with radioactive iodine, which made it possible to see the tumors prior to surgery. The authors of a 1954 Radiology article described the use of nuclear scanning on 200 patients and came to the conclusion that 46% of the patients had brain tumors that could be accurately located (the rate of localisation of nontumoral lesions was roughly the same). Nuclear scanning, the first noninvasive technique for locating brain tumors, was already widely used by this point. A Johns Hopkins University study published seven years later contrasted the findings of scintigraphy, pneumoencephalography, and angiography in the detection of 400 brain lesions and discovered that isotope tests had a 73% accuracy rate for tumor diagnosis.

Planar neuroimaging begins

The first feasible transverse, or cross-sectional, isotope imaging technique for brain lesions was developed in the middle of the 1960s, according to a study by Kuhl at exposure index in Radiology. This technique improved the visibility of tumors in the posterior fossa. They provided pictures of astrocytomas and meningiomas in their paper. Neuroradiology saw only modest advancements from the early 1940s and 1970. However, in 1971, a new era of neuroimaging began, particularly in the detection of neoplasias, as our capacity to scan the brain saw a dramatic change. A head-only scanner was first set up in London, England, in 1971. It was then quickly moved to the Mayo

Clinic in the United States. The advent of a new era of imaging-based diagnosis brought about by the rapid publication of numerous studies concerning CT scanning of brain tumors, intra- and extraaxial haematomas, abscesses, and hydrocephalus revolutionised patient examination and the identification of neurologic illnesses.

Advanced physiologic tumor neuroimaging

Michael E. Moseley, MD, demonstrated in 1993 that white matter water diffusion (movement) was anisotropic (directional) and that it was possible to map the direction of white matter tracts in relation to the orientation of the diffusion gradient. Once more, LeBihan and his team (66) demonstrated that diffusion-tensor imaging could generate maps that indicate the orientation of white matter fibres. White matter tractographic images initially surfaced in 1991.

Neuroradiology goes to the operating room

In the past, postoperative magnetic resonance imaging tests were often acquired during the first twenty-four hours following surgery in order to determine whether a tumor remained after resection. This strategy was justified by the belief that the majority of contrast enhancement observed prior to 24 hours was most likely tumor-related rather than reactive inflammation. Beginning in the early 1990s, neurosurgery could be performed under magnetic resonance imaging guidance, allowing for instantaneous determination of the precise biopsy site and the extent of resection, as well as modification as necessary. An report detailing the application of this approach to 200 patients was published in 1999.

Genetics and high-field-strength magnetic resonance imaging of brain tumors

The abundance of genetic data that has lately been available has led to some of the most exciting developments in our knowledge of brain tumors. It should come as no surprise that neuroradiologists are searching for imaging surrogates for several genetic markers. Researchers from the University of California, Los Angeles discovered in 2008 that patients with glioblastomas that were not fully enhancing had higher life times and that there were changes in gene expressions between the two types of tumors. [5]

III. PATHOPHYSIOLOGY

When a lower-grade astrocytoma transforms, secondary glioblastoma results. Numerous genetic and epigenetic changes that are characteristic of contribute to its aggressive behaviour. These changes include mutations in genes related to DNA repair and signalling pathways, tumor suppressor genes, and oncogenes. glioblastoma Glioma stem cells, a subset of glioblastoma cells with the capacity to self-renew and develop into other cell types, are partly responsible for this infiltrative growth pattern. It is believed that glioma stem cells have a role in the development, maintenance, and resistance to treatment of tumors. [6]

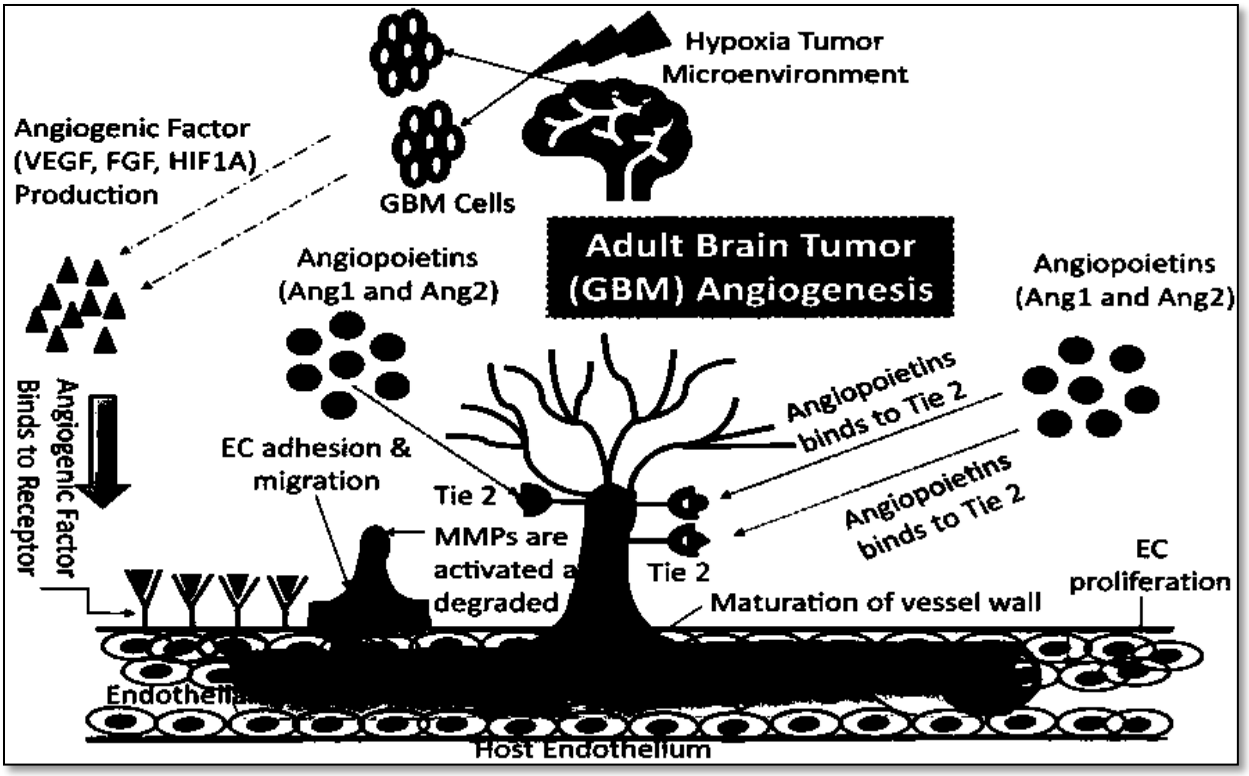

Figure 1 Pathophysiology of brain tumor [7]

Types

Primary and secondary metastatic brain tumors are the two primary categories. Human brain cells are the source of primary brain tumors (BTs), which are often non-cancerous. On the other hand, blood flow from other body areas causes secondary metastatic tumors to spread to the brain. [8] According to WHO, a brain tumor is categorized into grades I–IV. Grades I and II tumors are considered as slow-growing, whereas grades III and IV tumors are more aggressive, and have a poorer prognosis. In this regard, the detail of brain tumor grades is as follow:

Grade I These tumors grow slowly and do not spread rapidly. These are associated with better odds for long-term survival and can be removed almost completely by surgery. An example of such a tumor is grade 1 pilocyticastrocytoma.

Grade II These tumors also grow slowly but can spread to neighboring tissues and become higher grade tumors. These tumors can even come back after surgery. Oligodendroglioma is a case of such a tumor.

Grade III These tumors develop at a faster rate than grade II, and can invade the neighboring tissues. Surgery alone is insufficient for such tumors, and post-surgical radiotherapy or chemotherapy is recommended. An example of such a tumor is anaplastic astrocytoma.

Grade IV These tumors are the most aggressive and are highly spreadable. They may even use blood vessels for rapid growth. Glioblastoma multiforme is such a type of tumors. [9]

Table 1 Types of brain tumor [10]

Types of tumor Based on	Types	Comments
Nature	Benign	Less aggressive and grows slowly.
	Malignant	Life-threatening and rapidly expanding.
Origin	Primary tumor	Originates in the brain directly.
	Secondary tumor	This tumour develops in another area of the body like lung and breast before migrating to the brain.
Grading	Grade I	Basically, regular in shape, and they develop slowly.
	Grade II	Appear strange to the view and grow more slowly.
	Grade III	These grow more quickly than grade II cancers.
	Grade IV	Reproduced with greater rate.
Progression stage	Stage 0	Malignant but do not invade neighbour cells.
	Stage 1 Stage 2 Stage 3	Malignant and quickly spreading.
	Stage 4	The malignancy invades every part of the body.

IV. IMPORTANCE

Biomarker identifications and diagnosis of brain disorders

Early biomarker detection and diagnosis for prompt therapies are essential for the appropriate management of brain diseases. Recent developments in AI-based nanomedicines transform the search for biomarkers, facilitate quick early diagnosis, and allow for individualised treatment of brain illnesses.

Prognosis and disease monitoring

The prognosis and continuous monitoring of the diseases severity are also critical to the management of brain related illnesses. These days, the latest advancement in AI-based nanomaterials are utilised to follow the condition by analysing picture information, releasing neurotransmitters, and tracking the expression level of particular biomarkers.

Therapeutics and drug delivery

This section examines how recent advancement in AI-based nanomedicine have revolutionised drug delivery techniques and approaches to treating brain illnesses. Discuss various deep learning

and machine learning techniques that enhance pattern identification and extraction from various datasets.

Methodological and computational development

The study of additional molecular components at the nanoscale, image processing for tissue analysis, and even molecular interactions are examples of advancement in brain disorders. Researchers are overcoming conventional approaches, obstacles and constraints by fusing AI with nanomedicine to provide more precise and economical solutions. Recent computational developments in molecular sequencing, image analysis, and nanoparticle interactions are examined in this section. [11]

V. CONVENTIONAL METHODS

Surgery techniques and outcomes

The tumor is often removed using traditional surgical methods, such as craniotomy, and a biopsy is taken for histological examination. Reducing the mass effect, maximising the area of resection, and symptom relief are the objectives of surgery for glioblastoma. However, the tumor's infiltrative nature and the proximity to important brain regions, like the language and motor centres, frequently restrict the extent of resection. A number of cutting-edge surgical methods have been created to enhance surgical results for glioblastoma. These methods include awake craniotomy, intraoperative magnetic resonance imaging, and fluorescence-guided surgery. Fluorescent dyes, like 5-aminolevulinic acid, are used in fluorescence-guided surgery because they are selectively absorbed by tumor cells and can be seen under a specialised microscope. This method can lessen the chance of tumor recurrence and increase the extent of excision. Real-time imaging during surgery is made possible by intraoperative magnetic resonance imaging, which uses a specialised magnetic resonance imaging scanner in the operating room. The location and size of the tumor, the degree of resection, and the patient's general condition all affect how well surgery goes for glioblastoma. glioblastoma is still a difficult tumor to treat, and most patients have tumor recurrence and disease progression despite improvements in surgical procedures.

Radiotherapy techniques and outcomes

The usual course of treatment for glioblastoma is radiation, which is usually administered following surgery to target any remaining tumor cells and stop recurrence. glioblastoma is frequently treated using traditional radiotherapy methods, including as external beam radiation therapy. High-energy radiation is delivered to the tumor site from an external source as part of external beam radiation therapy. To optimise tumor management and reduce radiation-induced harm to nearby normal tissues, the radiation is administered in tiny daily fractions over a few weeks. The total radiation dose, the fractionation schedule, and the patient's general health are some of the variables that affect the results of radiotherapy for glioblastoma. Higher radiation dosages are often linked to improved tumor control and survival rates. Higher dosages, however,

may raise the possibility of radiation-related damage, including radiation necrosis, which can result in neurological impairments. To enhance the results of radiation therapy for glioblastoma, sophisticated procedures including intensity-modulated radiation therapy and stereotactic radiosurgery have been developed. Intensity-Modulated Radiation Therapy lowers the risk of radiation-related damage by delivering higher radiation doses to the tumor while preserving healthy tissues. stereotactic radiosurgery uses a highly accurate targeting mechanism to deliver a high dosage of radiation to the tumor in a single fraction. When compared to traditional radiotherapy approaches, several studies have demonstrated better tumor control and survival outcomes, indicating that new radiotherapy techniques have produced encouraging results in glioblastoma. These methods are not risk-free, though, and cautious patient selection and monitoring are necessary to reduce the possibility of radiation-related damage. [12]

Chemotherapy drugs and outcomes:
Usually given in conjunction with surgery and radiation therapy, chemotherapy is a crucial part of the multimodal treatment approach for. glioblastoma chemotherapy medications stop fast dividing cancer cells from proliferating and dividing. The two most often utilised are carmustine and temozolomide. Clinical trials have looked into the use of more recent chemotherapeutic medications, such as temsirolimus and bevacizumab, for the treatment of glioblastoma. Temozolomide glioblastoma is frequently treated with Temozolomide, an alkylating chemotherapeutic medication. It is an oral medication that has demonstrated effectiveness in enhancing glioblastoma patients' chances of survival. Temozolomide is quickly absorbed in the digestive system and has a high oral bioavailability. After surgery, Temozolomide is typically given daily for a few weeks along with radiation therapy. Its elimination half-life is roughly 1.8 hours. Temozolomide causes cytotoxicity in quickly dividing cancer cells by alkylating DNA. The medication is changed into a reactive intermediate that methylates guanine at its O6 position, causing DNA adducts and crosslinks to form. This ultimately causes DNA damage and cell death. Bevacizumab. A monoclonal antibody called bevacizumab has been used to treat glioblastoma. This injectable medication has demonstrated potential in enhancing glioblastoma patients' progression-free survival. Bevacizumab is given intravenously every two to three weeks and has a half-life of about twenty days. Since the medication cannot pass through the blood-brain barrier, it acts by preventing peripheral vascular endothelial growth factor signalling and interfering with angiogenesis inside the tumor microenvironment. By attaching itself to and inhibiting vascular endothelial growth factor, bevacizumab prevents the formation of new blood vessels and lowers the tumor's blood supply. In certain patients, this results in better clinical outcomes and the killing of tumor cells. Hypertension, haemorrhage, thrombosis, gastrointestinal perforation, and slowed wound healing are among the adverse effects linked to bevacizumab. The most frequent adverse effect is hypertension, which antihypertensive drugs can help control. Although less often, bleeding and thromboembolism can be fatal. A rare yet dangerous side effect that can cause fever, infection, and abdominal pain is gastrointestinal perforation. [13]

VI. INNOVATIVE APPLICATIONS

Developments in nanomedicine based on artificial intelligence for the treatment of brain disorders
Nanomedicines provide useful solutions to the above-mentioned issues in the treatment of brain-related diseases. Using nanostructures or nanomaterials, nanomedicine takes advantage of the idea of nanotechnology to manage numerous elements of disease, such as drug delivery, treatment, diagnostics, and disease monitoring. Additionally, the development of highly engineered multifunctional nanomaterials makes it possible to perform a number of tasks with a single smart nanomaterial, including drug delivery at specific locations, detection through protein or antibody conjugation, and tagging with imaging molecules to enable real-time monitoring in both in vitro and in vivo systems. Furthermore, nanocarriers are utilised not only for target drug delivery but to modify the pharmacokinetics of pharmaceuticals, enabling extended slow release of the drug and enhancing the therapeutic response in patients suffering from Alzheimer's and Parkinson's illnesses. [14]

Artificial intelligence integrated nanomedicine for the management of brain disorders
Previous research has shown that typical therapy procedures are ineffective in treating brain disorders. The shortcoming of traditional method may be addressed by recent developments in nanotechnology and AI-based tactics, which could enhance the management of various brain disorders, including multiple sclerosis, Alzheimer’s, Parkinson’s disease and brain cancer. These break throughts are seen in different areas of disease management, such as the discovery of biomarkers for early diagnosis, prognosis and disease monitoring, treatments and medication delivery, and advances in computational technique. The next subsection discusses the wide-ranging applications of AI-based methods to develop nanomedicine and alter the various facets of treating brain disorders. [15]

Artificial intelligence in glioblastoma diagnosis
The tissue samples obtained during tumor removal are essential to the present paradigm for diagnosing glioblastom. AI is improving the pre-operative imaging-based diagnosis accuracy. Radiomics is one of the primary uses of AI in glioblastoma diagnoses. The process of extracting various measurable data features from radiological pictures is known as radiomics. When such traits are extracted, datasets are created that AI can use to enhance glioblastoma treatment.

Artificial intelligence in glioblastoma treatment planning
AI can assist in selecting the best course of therapy and putting customised therapeutic alternatives into practice. Personalised approaches to glioblastoma treatment are desperately needed. CNNs can be used, for instance, to precisely forecast the likelihood of adequate tumor removal.

Artificial intelligence in glioblastoma prognostication

By using more pertinent features, AI can greatly improve glioblastoma patient prognostication and outcomes prediction. Researchers were able to forecast the molecular features of the tumor and the overall survival of the patients under study by using a number of machine learning classifiers and preoperative MRI data. [16]

VII. ADVANTAGES

Overcoming the Blood–Brain Barrier

Artificial intelligence (AI) models can predict which pharmaceutical compounds or nanocarriers have the best chance of passing through the blood-brain barrier by combining imaging biomarkers, physicochemical properties, and omics data. [17]

Reduction in Cost and Time of Development

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Optimization of Nanocarriers and Formulations

Machine learning aids in predicting the optimal nanoparticle size, charge, coating, and medication loading for controlled release and tumor targeting. [19]

VIII. DISADVANTAGES

Regulatory and Accountability Challenges

Absence of uniform standards for evaluating and authorising AI-assisted medication administration systems. It's unclear who is responsible if a patient is harmed by an AI-driven treatment- the clinician, the developer, or the AI system. [20]

Clinical translation gap

Because of the complexities of the blood–brain barrier and tumor heterogeneity, AI predictions may not perform as well in vivo as they do in silico. Premature clinical deployment without adequate validation could result from an over-reliance on AI models. [21]

Black-Box Decision Making (Lack of Explainability)

Clinicians find it difficult to comprehend how a prediction was generated by many AI/ML algorithms, such as deep learning, which operate as "black boxes." Transparency undermines confidence and makes approving AI-driven medication distribution systems more difficult. [22]

IX. FUTURE SCOPE

Diagnostic radiology has changed dramatically as a result of AI technology, however there are still many areas that need improvement. Among these areas is the application of AI to detect, classify, and divide brain tumors, which would enhance patient care. The recent incorporation of an AI system into the clinical workflow demonstrates the potential for AI to improve clinical treatment. AI can be used to identify gliomas early when visual contrast is lacking, but its potential is now constrained by a lack of high-quality image data. Future advancements in AI and image technology will enable the identification of pre-metastatic niches. Early identification of these niches can provide an accurate estimation of a patient's likelihood of acquiring metastatic illness. Upstream applications, which deal with operational analytics, and downstream applications, which focus on the imaging data itself, are the two categories of AI applications. Combining several kinds of annotations makes AI systems more precise and effective. Such a differentiation can be restrictive as it prohibits the combining of different types of annotations. This will bring attention to the oversight of medical image analysis. Artificial intelligence in neurology holds enormous promise for the future because of its ability to categorise brain tumors and predict seizures. On MR Life 2023, the model's capacity to multitask with both local and global annotations significantly improved its capacity to segment brain tumors. The researchers showed that AI systems can accurately partition intracranial haemorrhages on brain CT scans and measure haemorrhage volumes. The instrument can be used to measure and detect head and neck tumors or vascular anomalies. AI has the potential to provide significant improvements in the accurate interpretation of cancer imaging, such as the prediction of clinical outcomes based on the radiographic appearance of a tumors phenotype, volumetric delineation across time, and extrapolation of the tumor genotype. [23]

X. CONCLUSION

Because of the blood–brain barrier, tumor heterogeneity, and resistance to traditional medicines, artificial intelligence has become a game-changing tool in medication administration and treatment planning for brain tumors. Precision medication targeting, early and accurate diagnosis, and enhanced prognostic modeling are made possible by the combination of AI and nanotechnology, opening the door to more individualized treatment plans. In spite of these developments, there are still many obstacles to overcome, including opaque AI models, legal restrictions, and the discrepancy between clinical results and computer projections. Standardized clinical validation frameworks, enhanced multimodal imaging datasets, and improved AI algorithms will be necessary for future advancements. All things considered, AI-driven nanomedicine has enormous potential to transform brain tumor treatment and greatly enhance patient outcomes

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