



Review Article

Emerging Trends in Diagnosis and Treatment of Brain Tumor

Rashida Perveen^{1*}, Muhammad Naveed Babur¹, Noor-Ul-Ain Shah¹, Muhammad Adnan Hafeez¹, Sadia Sabir¹, Tahreem Fatima¹, Rai Shahzad Ali¹ and Aiman Faizan¹

¹Department of Allied Health Sciences, Superior University, Lahore, Pakistan

ARTICLE INFO

Key Words:

MRI, PET, Imaging Biomarker, Nanoparticles, Response Assessment, Brain Tumors

How to Cite:

Perveen, R., Naveed Babur, M. ., Shah, N. U. A. ., Hafeez, A. ., Sabir, S. ., Fatima, T. ., Shahzad Ali, R., & Faizan, A. . (2022). Emerging trends in Diagnosis and Treatment of Brain Tumor: Emerging Trends in Brain Tumor. *Pakistan BioMedical Journal*, 5(5). <https://doi.org/10.54393/pbmj.v5i5.478>

***Corresponding Author:**

Rashida Perveen,
 Department of Allied Health Sciences, Superior
 University, Lahore, Pakistan
rashida.perveen@superior.edu.pk

Received Date: 11th May, 2022

Acceptance Date: 20th May, 2022

Published Date: 31st May, 2022

ABSTRACT

Brain tumors are rare but have high mortality rate among children and young adults. The purpose of this report is to portray the situation of imaging strategies and advancements for distinguishing reaction of cerebrum tumors to remedy within the placing of multicenter medical trials. Inside as of now utilized advances, usage of institutionalized image procurement and the usage of volumetric appraisals and subtraction maps are likely going to decorate tumor notion, depiction, and dimension. Throughout the subsequent couple of years, new innovations, for instance, 23Na MRI and CEST imaging improvements may be investigated for their usage in growing the ability to quantitatively photo tumor response in order to provide remedies in a scientific trial placing. The combination of poor visualization and absence of remedial choices urge the need to enhance clinical results for patients experiencing CNS malignancies.

INTRODUCTION

A brain tumor occurs when abnormal cell production starts to form in the brain. There are two types of tumors: one of them is benign, while the other one is malignant or cancerous. Typically, our body produces cells that usually die after aging or complete their cycle. The production of abnormal cells by the body and their accumulation in any part of the body leads to the formation of a tumor. Like other cells, the cancerous cells do not die, instead they multiply and cause the formulation of tumors in the body parts. Cancerous tumors are of two types: primary tumors are the ones that start within the brain, this one is the most common type of brain tumor in the adult stage and it develops in the cerebrum which is the main part of the brain. About a quarter of tumors (24%) develop in the

meninges. These two membranes protect the spinal cord. Around 1 in 10 (10%) tumors start in the glands of the brain such as the pituitary gland or pineal gland [1]. The primary stage of tumors is named regarding the type of cells they affect and in which part of the brain they start their production. Gliomas, for example, are brain tumors that begin in the glial cells. Primary brain tumors are usually located in the brain's glial cells [2]. The formation of gliomas begins in the glial cells of the brain that are found in the supportive tissue of the brain. Various types of gliomas are classified according to the place they are found in the brain and how the formation of tumors started to occur. Various types of gliomas are as follows:

Astrocytoma: this tumor occurs in the shaped of star glial

cells known as astrocytes. This may be of any grade, and it arises at the cerebrum part of the brain, that is usually occurred in adults.

Grade I or II astrocytoma: these are known as the low-grade gliomas.

Grade III astrocytoma: it is known as the high-grade glioma or in the other term it is anaplastic astrocytoma.

Grade IV astrocytoma: this type known as glioblastoma or in another term it is called astrocytic glioma [3].

Oligodendroglioma: this tumor could be found in the cells that make fatty substance and covers the nerves through that fatty substance. It could be found in the cerebrum part of the brain and it could affect middle-aged adults [4].

Meningiomas: such type of tumor is slow-growing, and meningiomas are usually found in the outer coverings of the brain, under the skull. This tumor type is very less common and affects one-third of adults worldwide. It is slow-growing and often found in the benign tumor and it could be of grade I, II, or III [5].

Common types of tumors among children are as follows:

Medulloblastoma: such tumor type found in the cerebellum part of the brain. The tumor arises from cerebellum and often called as neuroectodermal tumor. It could be of grade IV. **Grade I or II astrocytoma:** such tumors could occur anywhere in the brain. They are low grade tumors and the most common type of astrocytoma in children is "juvenile pilocytic astrocytoma". It could be of grade I among children [5,6].

Ependymoma: this type of tumor occurs in the ependyma tissues, these tissues are present in the CNS. It could be of grade I, II and III and could affect both adults and children.

Brainstem glioma: as its name shows that it will affect the lowest part of the brain that is known as its stem. Brainstem glioma's most common type is diffuse intrinsic pontine glioma. There is a slight difference among children around 6 out of 10 tumors start in the cerebellum and brain stem part of the brain. Only 40% start in the cerebrum [7]. Secondary tumors are those that have spread from other parts of the body, known as brain metastasis tumors [8] (Figure 1).

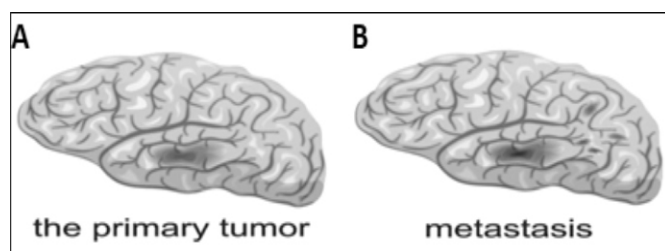


Figure 1: Difference between primary and secondary tumor. In (A) Tumor is shown in one part of brain where as in (B) tumor is in spread form

Every type of tumor causes different symptoms in human beings, symptoms depend on the type of tumor. Common symptoms of brain tumors are changes in mental habits and vision problems. Types of tumors that could be found in adults are meningiomas and astrocytomas e.g; glioblastomas. A common tumor type of brain in children is medulloblastoma, it is malignant. Upon medical examination, diagnosis is done through computed tomography or MRI. These are the most common techniques that are used to diagnose cancer. After diagnosis, it is decided that biopsy treatment, radiation therapy, chemotherapy, or surgery should be done [9,10].

Detection and Diagnosis: Brain tumors are diagnosed when the patient consults a doctor about the symptoms he is experiencing. If the symptoms show the possibility of brain tumor then different tests are performed like MRI, CT scan and sometimes biopsy is also useful for identification [11].

Symptoms: The symptoms of the brain tumor depend upon its or what is its size and location. Symptoms may appear when a tumor presses on a nerve or affects the activity of brain parts. It may also cause blockage and brain swelling because of increased fluid. People will experience those symptoms and it does not matter whether the tumor is benign or malignant. Primary or secondary brain tumors often show the same sign and symptoms. The most common symptoms of brain tumor are as follows: headaches, blurred vision, or inability to see properly, nausea, vomiting, hearing and speech problems, changes in the mood and other personality disorders, inability to walk properly, inability to focus or concentrate for the longest period of time, short term or long term memory loss in some cases occur, seizures and convulsions of the muscle and feeling of numbness and tingling sensations in the body or mostly in the arms and legs [12,13].

Diagnosis: If anyone has one of the above discussed symptoms then consultant will do physical examination and will ask about the family history regarding cancer. Following test will be performed for the confirmation of the tumor.

Neurologic exam: to examine the activities that your brain usually does, this test is performed to examine the attentiveness, concentration, vision, hearing, muscle coordination of the brain. Eyes are also examined to check the activity and swelling around the eyes that may be caused by the tumor, pressing the nerves [14].

Magnetic Resonance Imaging (MRI): MRI is performed by the machine to which the strong magnet is attached and it takes the images inside the brain to see the areas of the brain. Sometimes a dye is injected into the vessels through arm, so that it can show the colorful images so that the

differentiation would be easy in the tissues of the brain. Identification of tumor is done through images taken by MRI machine [15].

CT scan: it is an X-ray machine that scans the head and take images of the parts of the brain. A dyed material injected so that it would be easy to find out the abnormal areas of the brain [16].

Angiogram: Angiogram is taken through injecting dye into the bloodstream through the vessels that reach the vessels of the brain and show the abnormal areas by highlighting them in the x-ray [17].

Spinal tap: in this test, sample of the cerebrospinal fluid is taken. Moreover, surgeon takes a thin needle to take the sample from the lowest part of spinal column. This procedure taking around 30 minutes. Spinal tap is performed through local anesthesia. After that sample is sent to the laboratory to find out if the cancer cells are present in it or not [18].

Biopsy: In biopsy, main purpose is to extract the tissue where tumor exists. The tissue examined under the microscope to check any sort of abnormality. Biopsy will help to identify changes in the cells that may results into the formation of cancerous cells. It is the only sure way through which we know the level or severity of it and can plan treatment according to it [19,20].

Advanced techniques for Diagnosis and Treatment:

Computational diagnosis: Propelled MRI strategies for example, attractive reverberation spectroscopy (MRS), attractive reverberation perfusion (MRP), dispersion Weighted imaging (DWI). Furthermore, dispersion tensor imaging (DTI) are utilized to their specificity. DTI, which hinges upon dissemination of water atoms along axons, is supportive with access the integument from claiming White matter (WM), and in addition those area and introduction from claiming WM tracts. Concerning illustration assistance with other imaging, this strategy needs supplemented pre-surgical arranging, also characterization from claiming intra-axial lesions with observe metastases starting with GBM. DWI and MPR have ability in differentiating metastatic tumors starting with cerebral abscesses [21-23]. Stimulated Raman Scattering (SRS) is used to observe the inner areas of brain tissue to identify tumor cells and to differentiate healthy brain tissue from the tumor in mice. After this experimentation they saw that it is possible to remove tumor like glioblastoma multiforme (most deadly brain tumor) in humans [24]. In the SRS technique, weak light signals can be detected that comes out from the material when it hit with the light of non-invasive laser. Analyzing the colors of spectrum in the light signal is really helpful for the researchers to understand the chemical makeup of the sample. By

amplifying the weak Raman signal by more than 10,000 times scientist has advanced the technique it's not impossible to make multicolor SRS images of living tissue. Biopsy is a good method for detecting and removing tumor [25].

The goal of cerebrum tumor surgery is to promote tumor rapture while preserving the underlying structure of the brain. This goal is tough to achieve since distinguishing tumor from non-tumor tissue is challenging. However, while routine histopathology provides information that can aid tumor depiction, it cannot be conducted repeatedly during surgery due to the time required to harden, segment, and recolor the tissue. Invigorated Raman dissipating (SRS) microscopy is a chemical compound imaging technology that allows for quick mapping of lipids and proteins within a single sample. This information can be transformed into pathology-like images. Despite the fact that SRS imaging has been utilized to quantify glioma cell thickness in murine orthotopic xenograft models and human cerebrum tumors, tissue heterogeneity in clinical mind cancers has yet to be fully quantified [26,27].

The Role of Focused Ultrasound in the Disruption of the Blood-Brain Barrier:

The use of focused ultrasound to disrupt the blood brain barrier (BBB) significantly, enhances the entry of BCNU through the barrier. Furthermore, using focused ultrasound before administering BCNU to tumor-embedded rats inhibited tumor migration and improved creature survival. This study expands on the utility and practicality of non-invasive focused ultrasound in improving the outcome of cerebrum tumor chemotherapy. Centered ultrasound disturbance of the BBB can likewise be utilized for additional top to bottom examinations on the advantages of locally expanding chemotherapeutic medication fixations, which at last could enhance the general nature of clinical treatment and watch over patients with mind tumors [28,29].

Magnetic nanoparticles: an advanced technology for malignant brain tumor imaging and therapy:

Attractive nanoparticles (MNPs) focused on treatment and imaging of threatening cerebrum tumors. Usually conjugation of peptides or antibodies to the surface of MNPs permits focusing on the tumor cell surface and potential disturbance of dynamic flagging pathways show in tumor cells. Conveyance of nanoparticles to dangerous mind tumors speaks to an impressive test because of the nearness of the blood-cerebrum obstruction and invading disease cells in the ordinary mind. More up to date procedures allow better conveyance of MNPs fundamentally and by guide convection-upgraded conveyance to the mind. Consummation of a human clinical

trial including direct infusion of MNPs into intermittent dangerous mind tumors for thermotherapy has built up their attainability, security and viability in patients. Future investigations are required to comprehend the promising effect of MNPs in the treatment of dangerous cerebrum tumors[30].

Correlated magnetic resonance imaging and Ultra-microscopy: (MRI-UM): Neo angiogenesis is important remedial focus in glioblastoma. Tumor imaging techniques are required to evaluate treatment impacts and malady movement. The tumor vasculature has been difficult to trace up to this point. To think about neo angiogenesis in glioma models, we've built together a combined appealing reverberation and optical toolbox. To study neovascularization, *in vivo* attractive reverberation imaging (MRI) and correlative ultra-microscopy (UM) of *ex vivo* cleansed whole brains are combined. T2* imaging allows for the identification of single vessels in glioma progression and the subsequent quantification of neo vessels. Incomplete vascular standardization occurs as a result of pharmacological VEGF inhibition, with decreased vessel bore, thickness, and penetrability. Connected UM of fluorescently identified micro vessels in cleansed brains to resolve tumor microvasculature are used. UM settled run of the mill highlights of neo angiogenesis and tumor cell attack with a spatial determination of ~5 µm. MR-UM can be utilized as a stage for three-dimensional mapping and high-determination measurement of tumor angiogenesis [31,32].

CONCLUSION

With passing time and advancement new techniques are being introduced by the medical teams doing research all over the world. The advancement and new trends have shown that how new methods of diagnosis and treatment of cancers helped to explore new ways of treatment for the brain tumor. New diagnostic methods helped a lot to diagnose tumors quickly and at early stages. Advances in the field of cancer by the scientist have made it easy to diagnose cancer and its location.

REFERENCES

- [1] Lauko A, Lo A, Ahluwalia MS, Lathia JD. Cancer cell heterogeneity & plasticity in glioblastoma and brain tumors. *Semin Cancer Biol.* 2022 Jul;82:162-175. doi: 10.1016/j.semcancer.2021.02.014.
- [2] Yu Y, Hong H, Wang Y, Fu T, Chen Y, Zhao J et al. Clinical Evidence for Locoregional Surgery of the Primary Tumor in Patients with De Novo Stage IV Breast Cancer. *Ann Surg Oncol.* 2021 Sep;28(9):5059-5070. doi: 10.1245/s10434-021-09650-3.
- [3] Dasari A, Shen C, Devabhaktuni A, Nighot R, Sorbye H. Survival According to Primary Tumor Location, Stage, and Treatment Patterns in Locoregional Gastroenteropancreatic High-grade Neuroendocrine Carcinomas. *Oncologist.* 2022 Apr 5;27(4):299-306. doi: 10.1093/oncolo/oyab039.
- [4] Brandner S, McAleenan A, Jones HE, Kernohan A, Robinson T, Schmidt L et al. Diagnostic accuracy of 1p/19q codeletion tests in oligodendroglioma: A comprehensive meta-analysis based on a Cochrane systematic review. *Neuropathol Appl Neurobiol.* 2022 Jun;48(4):e12790. doi: 10.1111/nan.12790.
- [5] Buerki RA, Horbinski CM, Kruser T, Horowitz PM, James CD, Lukas RV. An overview of meningiomas. *Future Oncol.* 2018 Sep;14(21):2161-2177. doi: 10.2217/fon-2018-0006.
- [6] Brastianos PK, Galanis E, Butowski N, Chan JW, Dunn IF, Goldbrunner R et al. Advances in multidisciplinary therapy for meningiomas. *Neuro Oncol.* 2019 Jan 14;21(Suppl1):i18-i31. doi: 10.1093/neuonc/noy136.
- [7] Tubiana M, Feinendegen LE, Yang C, Kaminski JM. The linear no-threshold relationship is inconsistent with radiation biologic and experimental data. *Radiology.* 2009 Apr;251(1):13-22. doi: 10.1148/radiol.2511080671.
- [8] Mustafa M, JamalulAzizi AR, Illzam EL, Nazirah A, Sharifa AM, Abbas SA. Lung cancer: risk factors, management, and prognosis. *IOSR Journal of Dental and Medical Sciences.* 2016;15(10):94-101.
- [9] Prakash J, de Jong E, Post E, Gouw AS, Beljaars L, Poelstra K. A novel approach to deliver anticancer drugs to key cell types in tumors using a PDGF receptor-binding cyclic peptide containing carrier. *J Control Release.* 2010 Jul 14;145(2):91-101. doi: 10.1016/j.jconrel.2010.03.018.
- [10] Frolkis M, Fischer MB, Wang Z, Lebkowski JS, Chiu CP, Majumdar AS. Dendritic cells reconstituted with human telomerase gene induce potent cytotoxic T-cell response against different types of tumors. *Cancer Gene Therapy.* 2003 Mar;10(3):239-49. doi.org/10.1038/sj.cgt.7700563.
- [11] Mallidi S, Luke GP, Emelianov S. Photoacoustic imaging in cancer detection, diagnosis, and treatment guidance. *Trends Biotechnol.* 2011 May;29(5):213-21. doi: 10.1016/j.tibtech.2011.01.006.
- [12] Madhusoodanan S, Ting MB, Farah T, Ugur U. Psychiatric aspects of brain tumors: A review. *World J Psychiatry.* 2015 Sep 22;5(3):273-85. doi: 10.5498/wjp.v5.i3.273.
- [13] Reulecke BC, Erker CG, Fiedler BJ, Niederstadt TU, Kurlemann G. Brain tumors in children: initial

- symptoms and their influence on the time span between symptom onset and diagnosis. *J Child Neurol*. 2008 Feb;23(2):178-83. doi: 10.1177/0883073807308692.
- [14] Schroeder SR, Salomon MM, Galanter WL, Schiff GD, Vaida AJ, Gaunt MJ et al. Cognitive tests predict real-world errors: the relationship between drug name confusion rates in laboratory-based memory and perception tests and corresponding error rates in large pharmacy chains. *BMJ Qual Saf*. 2017 May;26(5):395-407. doi: 10.1136/bmjqs-2015-005099.
- [15] Van den Berg PJ, Daoudi K, Steenbergen W. Review of photoacoustic flow imaging: its current state and its promises. *Photoacoustics*. 2015 Sep 1;3(3):89-99. doi.org/10.1016/j.pacs.2015.08.001.
- [16] Brenner DJ, Hall EJ. Cancer risks from CT scans: now we have data, what next? *Radiology*. 2012 Nov;265(2):330-1. doi: 10.1148/radiol.12121248.
- [17] Lee KW, Lo CP. Acute Cerebral Infarction Masked by a Brain Tumor. *Case Reports in Neurology*. 2011;3(2):179-84. doi.org/10.1159/000330302.
- [18] De Mattos-Arruda L, Bottai G, Nuciforo PG, Di Tommaso L, Giovannetti E, Peg V et al. MicroRNA-21 links epithelial-to-mesenchymal transition and inflammatory signals to confer resistance to neoadjuvant trastuzumab and chemotherapy in HER2-positive breast cancer patients. *Oncotarget*. 2015 Nov 10;6(35):37269-80. doi: 10.18632/oncotarget.5495.
- [19] Vaidyanathan R, Soon RH, Zhang P, Jiang K, Lim CT. Cancer diagnosis: from tumor to liquid biopsy and beyond. *Lab on a Chip*. 2019;19(1):11-34. doi: 10.1039/C8LC00684A.
- [20] Simmons C, Miller N, Geddie W, Gianfelice D, Oldfield M, Dranitsaris G et al. Does confirmatory tumor biopsy alter the management of breast cancer patients with distant metastases? *Ann Oncol*. 2009 Sep;20(9):1499-1504. doi: 10.1093/annonc/mdp028.
- [21] Noreen N, Palaniappan S, Qayyum A, Ahmad I, Imran M, Shoaib M. A deep learning model based on concatenation approach for the diagnosis of brain tumor. *IEEE Access*. 2020 Mar 5;8:55135-44. doi: 10.1109/access.2020.2978629.
- [22] Dong H, Yang G, Liu F, Mo Y, Guo Y. Automatic brain tumor detection and segmentation using U-Net based fully convolutional networks. In annual conference on medical image understanding and analysis 2017 Jul 11: 506-517. Springer, Cham. doi.org/10.1007/978-3-319-60964-5_44.
- [23] Cao S, Strong MJ, Wang X, Moss WN, Concha M, Lin Z et al. High-throughput RNA sequencing-based virome analysis of 50 lymphoma cell lines from the Cancer Cell Line Encyclopedia project. *J Virol*. 2015 Jan;89(1):713-29. doi: 10.1128/JVI.02570-14.
- [24] Yang W. Biomedical Applications of Stimulated Raman Scattering Microscopy (Doctoral dissertation). 2017.
- [25] Ji M, Orringer DA, Freudiger CW, Ramkissoon S, Liu X, Lau D et al. Rapid, label-free detection of brain tumors with stimulated Raman scattering microscopy. *Sci Transl Med*. 2013 Sep 4;5(201):201ra119. doi: 10.1126/scitranslmed.3005954.
- [26] Petersen KD, Landsfeldt U, Cold GE, Petersen CB, Mau S, Hauerberg J et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. *Anesthesiology*. 2003 Feb;98(2):329-36. doi: 10.1097/00000542-200302000-00010.
- [27] Duffau H. The huge plastic potential of adult brain and the role of connectomics: new insights provided by serial mappings in glioma surgery. *Cortex*. 2014 Sep 1;58:325-37. doi.org/10.1016/j.cortex.2013.08.005.
- [28] Liu HL, Hua MY, Yang HW, Huang CY, Chu PC, Wu JS et al. Magnetic resonance monitoring of focused ultrasound/magnetic nanoparticle targeting delivery of therapeutic agents to the brain. *Proc Natl Acad Sci U S A*. 2010 Aug 24;107(34):15205-10. doi: 10.1073/pnas.1003388107.
- [29] Daneman R, Prat A. The blood-brain barrier. *Cold Spring Harb Perspect Biol*. 2015 Jan 5;7(1):a020412. doi: 10.1101/cshperspect.a020412.
- [30] Wankhede M, Bouras A, Kaluzova M, Hadjipanayis CG. Magnetic nanoparticles: an emerging technology for malignant brain tumor imaging and therapy. *Expert Rev Clin Pharmacol*. 2012 Mar;5(2):173-86. doi: 10.1586/ecp.12.1.
- [31] Kirschbaum K, Sonner JK, Zeller MW, Deumelandt K, Bode J, Sharma R et al. In vivo nanoparticle imaging of innate immune cells can serve as a marker of disease severity in a model of multiple sclerosis. *Proc Natl Acad Sci U S A*. 2016 Nov 15;113(46):13227-13232. doi: 10.1073/pnas.1609397113.
- [32] Breckwoldt MO, Bode J, Kurz FT, Hoffmann A, Ochs K, Ott M et al. Correlated magnetic resonance imaging and ultramicroscopy (MR-UM) is a tool kit to assess the dynamics of glioma angiogenesis. *Elife*. 2016 Feb 2;5:e11712. doi: 10.7554/eLife.11712