International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 5, May 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.5.2025.101

ORIGINAL RESEARCH

Association Between MR Perfusion Parameter And IDH Mutation In Brain Gliomas

[1]Dr. Tushant Kumar, [2]Dr. Satyavrat Verma, [3]Dr. Kaustubh Gupta, [4]Dr. Shamrendra Narayan

[1]Additional Professor, Department of Radiodiagnosis, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
[2] Assistant Professor, Department of Radiodiagnosis, SGPGIMS, Lucknow
[3]Assistant Professor, Department of Radiodiagnosis, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
[4]Additional Professor, Department of Radiodiagnosis, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow

Corresponding Author:
Dr. Tushant Kumar
Additional Professor, Department of Radiodiagnosis, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow

Received: 10 March, 2025 Accepted: 22 April, 2025 Published: 11 May, 2025

Abstract

Introduction: Gliomas are infiltrative primary brain tumours that account for approximately one-third of all central nervous system tumours. The more recent discovery of isocitrate dehydrogenase (IDH) mutations in the gliomas represented major step forward in the molecular characterization of gliomas. IDH mutated glioma have better prognosis and more chemosensitive. MR perfusion is another way of assessment of gliomas which analyse the tumor vascularity. Present study was planned to see any association between MR perfusion parameter (rCBV) and IDH mutation status of gliomas.

Material and methods: This prospective observational was done at a tertiary care hospital. Study included 24 patients of brain glioma. Preoperative MRI brain with MR perfusion done in all cases. Post operative immunohistochemistry for IDH mutation done in all cases gliomas.

Observation and Results: 24 cases of gliomas were assessed preoperatively by MRI brain and MR perfusion. Regional CBV was assessed in all cases of gliomas**.** IDH mutation was also assessed post operatively. Mutated group showed the low rCBV (mean - 1.34) in tumor on as compared to nonmutated group. (rCBV- 1.95) with significant P value. (p value<0.003).

Conclusion: IDH mutant gliomas have favourable prognosis and associated with low tumor vascularity as assessed by MR perfusion. Thus Perfusion MRI can be used as non-invasive means of obtaining functional information about brain tumor vascularity and IDH mutation status. Prediction of IDH mutant status can be done by rCBV values obtained by MR perfusion in future, however more studies with large number of subject needed for further evaluation.

Keywords: rCBV, IDH mutation, MR perfusion, glioma

Introduction

Cancer of the brain is relatively rare, representing only slightly more than 1% of all new cancer cases, it is a disproportionately common cause of cancer-related death and morbidity (1). Gliomas are infiltrative primary brain tumors that account for approximately one-third of all central nervous system tumors (2). Gliomas traditionally have been categorized by the World Health Organization (WHO) grading system into 4 Histopathologic grades, denoted as I to IV, which describes them in terms of histopathologic lineage as either astrocytoma, oligodendroglioma, or oligoastrocytoma (3). The WHO classification provides prognostic information and guidance on treatment, such as radiation therapy and chemotherapy after surgery. However, especially for the diagnosis of grade II and III gliomas, classic histopathologic evaluation is notorious for its interobserver variation (4). Despite the confirmed value of the WHO grading system, accumulating data show that molecular analysis of gliomas is far more informative than is classic histopathologic evaluation. (5-8).

The more recent discovery of isocitrate dehydrogenase (IDH) mutations in the large majority of grade II and III

DOI: 10.69605/ijlbpr_14.5.2025.101

diffuse gliomas represented another major step forward in the molecular characterization of gliomas (9,10). It was shown that IDH-mutated tumors have a much more favorable prognosis than do tumors of similar lineage and grade that express IDH gene wild type (IDHwt) and may even allow identification of chemotherapy sensitive subgroups of patients (11).

IDH is a major enzyme in the citric acid cycle and may also play an important role in the cell's defence against oxidative stress. Both mutant IDH1 and IDH2 result in the production of 2-hydroxyglutarate (2-HG), which is considered an oncometabolite and may serve as a biomarker for assessment of tumor progression and response to treatment (12).

In addition, recent technological advances in diagnostic imaging have paved the way for quantitative, multiparametric assessment of tissue at the cellular and molecular level, with clear potential to further define imaging phenotypes of the various glioma genotypes. It can be expected that techniques that have already been explored, such as the various perfusion (rCBV, K trans) and diffusion parameters, will find increased value and application. Some further implementations of interest include vessel size imaging, tensor decomposition, and chemical exchange saturation transfer imaging. Perfusion MRI provides information about tissue vascularisation, in vivo tumor angioneogenesis, and microcirculation. Perfusion MRI offers information about tissue blood volume, blood flow, and oxygenation of tissues. The signal changes in arteries/veins, which occur with the passage of paramagnetic contrast agent are used to create relative cerebral blood volume (rCBV), mean transit time (MTT), and cerebral blood flow (rCBF) parameters [13, 14]. Perfusion parameters have been correlated with histopathologic measures of micro vascular density, proliferation and hyperplasia [1–5]

MR Perfusion imaging provides a measure of tumour vascularisation and is closely associated with the genetic expression of genes involved in tumor hypoxia and angiogenesis (e.g., vascular endothelial growth factor). The commonly used parameter rCBV is an indirect reflection of these processes, which can be quantified more accurately with vessel size imaging. This is based on the principle that the vascular bed is selectively sensitive to whether a gradient or spin echo sequence is used. Thus MR perfusion parameter can be used to described the glioma genotypes (IDH mutant status). Present study was planned to see any association between MR perfusion parameter (rCBV) and IDH mutation status of gliomas.

Material and Methods

Study design-This prospective observational study included patients of brain glioma who had not received any treatment (surgery, chemo-radiotherapy or both)

Place of study-This study was undertaken at department of Radiodiagnosis DRRMLIMS in collaboration with department of neurosurgery & Pathology.

Study group-Included all the patients suspected with brain glioma coming to DR RMLIMS, Lucknow. Study was approved by institutional ethical committee. Informed consent was taken from all patients.

Inclusion criteria

Treatment naive patients suspected of having brain glioma.

Exclusion criteria:

Patient who had undergone surgical intervention, chemotherapy or radiotherapy prior to imaging
Patients without genotyping of brain glioma

Gold Standard

The results of imaging were compared with histopathology findings which served as gold standard

Statistical Method

STATA 13 software and appropriate statistical methods were employed at the end of the study to analyze the collected data and to extract the results of the study. Level of significance was tested for p-value less than 0.05.

Equipment used:

MRI 3T (GE SIGNA 3.0T HDXT-32 CHANNEL)

IHC Methods

Immunohistochemistry for IDH1 R132H

MR imaging technique

Subjects underwent in MR protocol that included conventional MRI DCE MRI and MRS On a 3T signa OT HDXT 32 channel MRI scanner (general electric, Milwaukee, WI) using a 12 channel head coil which lasted for approximately 40 - 50 minutes. Uncooperative patients underwent the examination under general anaesthesia if clinically appropriate. MR image sequences and parameters used

DCE MRI was performed using a gradient echo planar imaging sequence with TE/TR of approx.20/2000, flip angle of 60°, NEX=1, FOV-28X28cm, 5 mm slice thickness, interslice gap of 1.5mm and number of phases = 42. At the start of the fourth acquisition, Gd - DTPA - BMA 287mg/ml of gadodiamide, OmniScan; GE health care) was administrated through a power injector (spectris solaris EP, medrad, max. pressure 325PSI) timing a injector syringe (Optistar Elite, Mallincarodt) at 5ml/s using a dose of approx.0.4ml/kg body weight, followed by a 30mm saline flush. The relative CBV was then obtained by dividing the mean

DOI: 10.69605/ijlbpr_14.5.2025.101

value of CBV in specified region of interest (ROI) by the value obtained from a ROI placed on a normal contralateral side of the brain. Five ROI of area 40-60mm each were placed within the areas of tumor showing elevated blood flow, with an ROI placed in contralateral hemisphere for comparison. The ROI showing highest CBV was considered. A post contrast FSPGR weighted image was also obtained after DCE MRI.

Observation and Results

Twenty-four patients with various types of intracranial glioma were included in this study. The mean age of patients was 32 years. Minimum age was 16 years and maximum age was 55 years. Out of 24 patients 17 were male and 7 were female

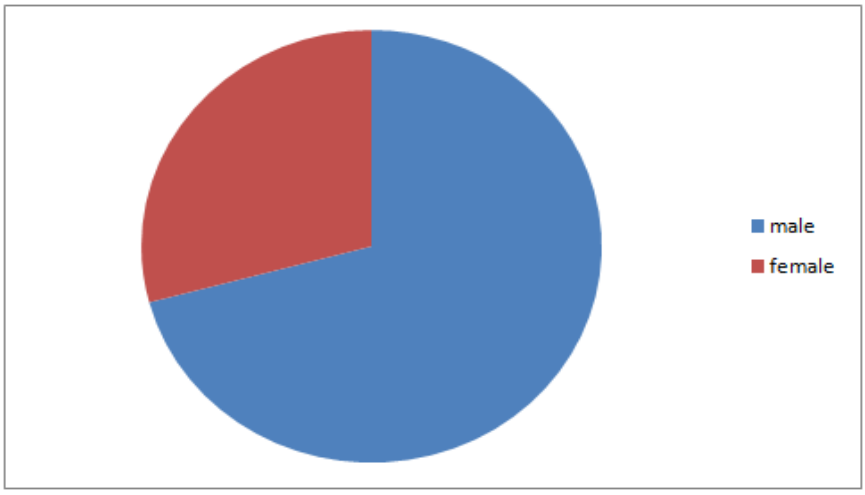

Fig 1- Gender based distribution study population

The most common histological type of intracranial neoplasm noted was diffuse glioma: astrocytoma phenotype and next common ones were diffuse glioma oligodendroglioma phenotype and diffuse anaplastic astrocytoma. The tumors encountered with their respective frequency are represented in the chart below.

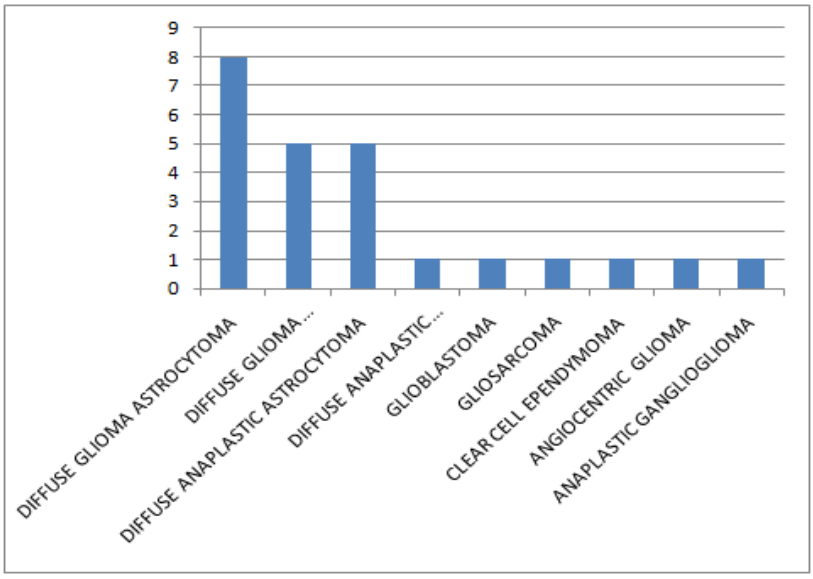

Fig -2 Histological types of gliomas

Regarding the IDH1R132H mutation status it was found that 13 out of 24 patients had the mutation present where 11 out of 24 patients were wild type.

DOI: 10.69605/ijlbpr_14.5.2025.101

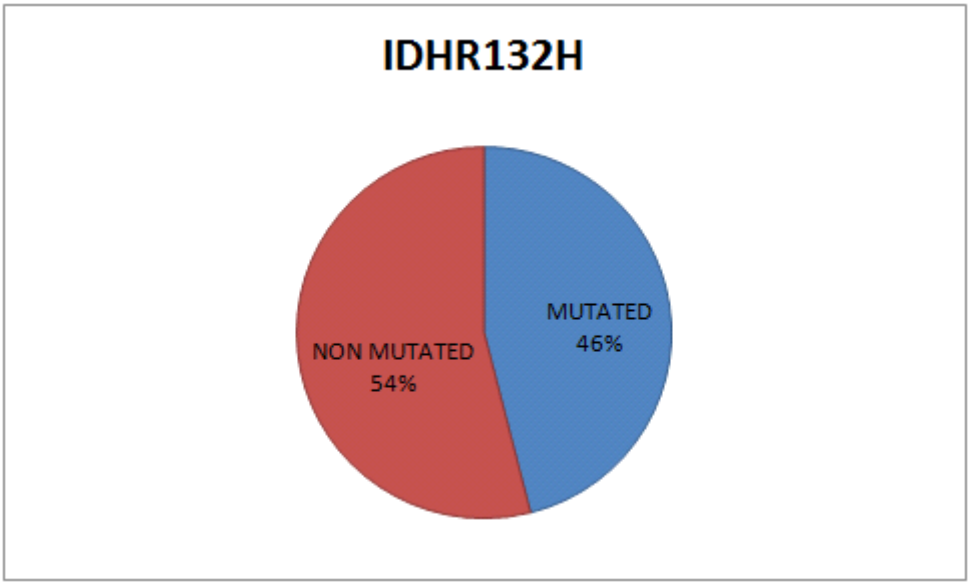

Fig -3 IDH1R132H mutation status in gliomas.

It was noted that the most common WHO grade among all tumor grades was grade II Grade III tumors were next most common in frequency

Table 1- Association between rCBV (measured by MR perfusion) and IDH mutation

T test r CBV by (IDHLR132H) Two-sample t test with equal variance						
Group	Obs	Mean	Std. err	Std dev	[95% conf. Interval]	
Mutated	13	1.338462	0.1211793	0.4369181	1.074435	1.602489
Non mutated	11	1.954545	0.1728708	0.5733474	1.569365	2.339725
Diff=Mean (Mutated) – Mean (Non mutated) Ho: diff =0 Ha: diff <0 Pr (T<t)= 0.0034						

13 patients out of 24 were IDH mutated. Mutated group showed the low rCBV (mean - 1.34) in tumor on MR perfusion as compared to non mutated group. (rCBV-1.95). T test show the significant difference of rCBV between mutated and non mutated group. (p value - < 0.003).

Discussion

Perfusion imaging has proven to be exceptionally useful in the identification of primary CNS gliomas, [15]. Accurate diagnosis, characterization and prognostication with noninvasive imaging is highly desirable. Perfusion techniques are well suited to imaging of primary brain tumors owing to their highly vascular nature [16]. Furthermore, the degree of vascularity has been correlated with glioma grade and genotype[17].

The present study demonstrates that DCE -PWI can be used to evaluate the *IDH* mutational status in gliomas.

At present, genetic and molecular information about tumors comes solely from pathologic results However, given the importance of genetic information for diagnosing and treating glioma, numerous attempts are underway to characterize tumor by means of imaging. This effort to classify genetic information based on imaging findings has been termed radiogenomics. Many studies have evaluated tumor location and size and other imaging features such as degree of enhancement, type of margins, and diffusion characteristics, in an attempt to classify tumors on the basis of MRI appearance.

Twenty-four patients with various types of intracranial glioma were included in this study. The mean age of patients was 32 years. Minimum age was 16 years and maximum age was 55 years. Out of 24 patients 17 were male and 7 were female. The most common histological type of intracranial neoplasm noted was diffuse glioma: astrocytoma phenotype and next common ones were diffuse glioma oligodendroglioma phenotype and diffuse anaplastic astrocytoma.

Regarding the IDHIR132H mutation status it was found

DOI: 10.69605/ijlbpr_14.5.2025.101

that 13 out of 24 patients had the mutation present, where 11 out of 24 patients were wild type. It was noted that the most common WHO grade among all tumor grades was grade II Grade III tumors were next most common in frequency.

IDH mutation has been one of the most thoroughly investigated with respect to imaging features. Commonly cited feature of tumors with IDH mutations include frontal lobe location (15,16-18). In our study too the most common location of the tumor was involving frontal lobe however location of the Tumor or multiple lobe involvement had no association with IDHIR1321 mutation. In a study by Qi et al (13) it was stated that IDH mutated tumors were more frequently confined to a single lobe.

The threshold value of <2.35 for relative maximum CBV in the prediction of *IDH* mutation provided a sensitivity, specificity, positive predictive value, and negative predictive value of 100.0%, 60.9%, 85.6%, and 100.0%, respectively. At perfusion imaging IDH mutants have lower cerebral blood volume than their IDH wild-type counterparts (20,21).

Law et al. (23) reported that DSC-PWI could be used to predict the median time to progression in gliomas and that a lower rCBV corresponds to significantly prolonged progression-free survival. However, these authors did not investigate the rCBV-related molecular mechanisms such as *IDH* mutation. Our data suggest that $rCBV_{max}$ values are significantly associated with the *IDH* mutational status. In our study too similar findings were noted. rCBV had a statistically significant positive condition with IDHIR132H mutation. Similar findings were also seen in a study by Valentini et al (22) Therefore, our findings are in good agreement with prior results and theories. DSC-PWI has the potential to noninvasively provide morphologic, functional & genotype information about gliomas

Conclusion

Perfusion MRI is a convenient, non-invasive means of obtaining functional information about the hemodynamic state of a tissue of interest. This is of particular use in brain tumour imaging where more aggressive lesions typically display greater vascularity. A combination of DSC-PWI techniques produces a high sensitivity, specificity, positive predictive value, and negative predictive value for predicting *IDH* mutations in grade II and III gliomas. The strategy of using advanced, semi quantitative MR imaging techniques may provide an important, non-invasive, surrogate marker that should be studied further in larger, prospective trials.

Reference

1. Surveillance, epidemiology and End Results Program [Internet].SEER. [cited 2019 Sep 3] Available from http://seer.cancer.gov/index.html
2. Ostrom QT, Gittleman H, Fulop J,Liu M, Blanda R, Kromer C,et al CBTRUS Statistical Report: Primary Bran and Central Nervous System Tumors Diagnosed in the United States in 2008-2012 Neuro-Oncol.2015 Oct;17 (Suppl 4):iv 1-62
3. Jain R, Ellika SK, Scarpace L, Schultz LR, Rock JP, Gutierrez J, Patel SC, Ewing J, Mikkelsen T (2008) Quantitative estimation of permeability surface-area product in astroglial brain tumors using perfusion CT and correlation with histopathologic grade. AJNR Am J Neuroradiol 29(4):694–700.
4. Van den Bent MJ. Interobserver variation of the histopathological diagnosis in clinical trials on glioma a clinician's perspective. Acta Neuropathol (Berl). 2010 Sep.120(3),297-304.
5. Cirncross JG, Ueki K. Zlatescu MC, Lisle DK. Finkelstein DM. Hammond RR. et al. Specific genetic predictors of chemotherapeutic response and survival in patients with anaplastic oligodendroglioma. J Natl Cancer Inst. 1998 Oct 7;90(19):1473-9.
6. Van den Bent MJ, Brandes AA, Taphoorn MJB, Kros JM, Kouwenhoven MCM, Delattre JY, et al. Adjuvant procarbazine, lomustine, and vincristine improves progressIon-Free survival but not overall newly diagnosed anaplastic oligodendroglioma and oligoastrocytoma: a randomized European Organisation for Research and Treatment of Cancer phase III trial. J Clin Oncol Off J Am Soc Clin Oncol. 2046 tun 2014(18):2715-22
7. Van den Bent MJ, Brandes AA, Taphoorn MJB, Kros JM, Kouwenhoven MCM, Delattre JY, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC brain tumor group study 26951. J Clin Oncol Off J Am Soc Clin Oncol. 2013 Jan 20:31(3):344-50.
8. Cairncross G, Wang M, Shaw E, Jenkins R, Brachman D, Buckner J, et al. Phase III trial of chemoradiotherapy for anaplastic oligodendroglioma: long-term results of RTOG 9402. J Clin Oncol Off I Am Soc Clin Oncol. 2013 Jan 20;31(3):337-43.
9. Van den Bent MJ, Dubbink HJ, Marie Y, Brandes AA, Taphoorn MIB Wesseling P. et al. IDH1 and IDH2 mutations are prognostic but no predictive for outcome in anaplastic oligodendroglial tumors: a report of the European Organization for Research and Treatment of Cancer Brain Tumor Group. Clin Cancer Res Off J Am Assoc Cancer Res. 2010 Ma 1:16(5):1597-604.
10. Parsons DW, Jones S, Zhang X, Lin JC-H, Leary RJ, Angenendt P, et al. An integrated genomic analysis of human glioblastoma multiforme

DOI: 10.69605/ijlbpr_14.5.2025.101

Science. 2008 Sep 26:321(5897):1807-12.

11. Cairncross JG, Wang M, Jenkins RB, Shaw EG, Giannini C, Brachman DG, et al. Benefit from procarbazine, lomustine, and vincristine in oligodendroglial tumors is associated with mutation of IDH. J Clin Oncol Off J Am Soc Clin Oncol. 2014 Mar 10:32(8):783-90. Cohen AL, 12.Cohen AL, Holmen SL,Colman H. IDH1 and IDH2 mutations in gliomas. Curr Neurol Neurosci Rep. 2013 May 13(5):345..
12. Louis DN, Perry A. Reifenberger G, von Deimling A, Figarella-Branger D. Cavenee WK, et at. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol.(Berl). 2016,131(6):803-20.
13. Law M, Young RJ, Babb JS, Peccerelli N, Chheang S, Gruber ML, Miller DC, Golfinos JG, Zagzag D, Johnson G (2008) Gliomas: predicting time to progression or survival with cerebral blood volume measurements at dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. Radiology 247(2):490–498.
14. Carrillo JA, Lai A, Nghiemphu PL, Kim HJ, Phillips HS. Kharbanda S. et al. Relationship between tumor enhancement, edema, IDHI mutational status, MGMT promoter methylation, and survival in glioblastoma. AJNR Am J Neuroradiol. 2012 Aug;33(7):1349-55.
15. Paldor 1. Pearce FC, Drummond KJ, Kaye AH. Frontal glioblastoma multiforme may be biologically distinct from non-frontal and multilobar tumors. J Clin Neurosci Off Neurosurg Soc Australas. 2016 Dec;34:128-32
16. Sonoda Y. Shibahara L Kawaguchi T. Saito R. Kanamori M. Watin M. et a. Association between molecular alterations and tumor location and MRI characteristics in anaplastic gliomas, Brain Tumor Pathol 2013 Apr 122199-104.
17. Xiong J, Tan W, Wen J, Pan J, Wang Y, Zhang J, et al. Combination of diffusion tensor imaging and conventional MRI correlates with isocitrate dehydrogenase 1/2 mutations but not 1p/194 genotyping in oligodendroglial tumours. Eur Radiol. 2016 Jun;26(6):1705-15.
18. Qi S. Yu L, Li H, Ou Y, Qiu X, Ding Y, et al. Isocitrate dehydrogenase mutation is associated with tumor location and magnetic resonance imaging characteristics in astrocytic neoplasms. Oncol Lett. 2014 Jun:7(6):1895-902.
19. Price SJ. Allinson K. Liu H, Boonzaier NR. Yan J-L Lupson VC, et al. Less Invasive Phenotype Found in Isocitrate Dehydrogenase-mutated Glioblastoma than in Isocitrate Dehydrogenase Wild-Type Glioblastomas: A Diffusion-Tensor Imaging Study. Radiology 2017:283(1):215-21.
20. Kickingereder P. Sahm F, Radbruch A, Wick W. Heiland ST, Deimling A von, et al. IDH mutation status is associated with a distinct hypoxia/angiogenesis transcriptome signature which is non-invasively predictable with rCBV imaging in human glioma. Sci Rep. 2015 Nov 5:5:16238.
21. Law M, Young RJ, Babb JS, Peccerelli N, Chheang S, Gruber ML, Miller DC, Golfinos JG, Zagzag D, Johnson G. Gliomas: predicting time to progression or survival with cerebral blood volume measurements at dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. Radiology. 2008 May;247(2):490-8.
22. Valentini MC, Mellai M, Annovazzi L. Melcarne A. Denysenko T. Cassoni P, et al. Comparison among conventional and advanced MRI, 18F-FDG PET/CT, phenotype and genotype in glioblastoma. Oncotarget. 2017 Oct 4:8(53):91636-53.