COMPARATIVE STUDY OF Tc-99m GHA SPECT-CT, F-18-FDG PET-CT AND MRI IN IMAGING OF PRIMARY BRAIN TUMORS

THESIS

Submitted to

All India Institute of Medical Sciences, Jodhpur

In partial fulfilment of the requirement for the degree of

Doctor of Medicine (MD)

(Nuclear Medicine)

JULY, 2020 **DR. RAVICHANDRAN T**

AIIMS, JODHPUR

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, JODHPUR

CERTIFICATE

This is to certify that the thesis titled **"Comparative study of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and MRI in imaging of primary brain tumors"** is an original work of **Dr. Ravichandran T,** carried out under guidance and supervision, in the Department of Nuclear Medicine, All India Institute of Medical Sciences, Jodhpur.

GUIDE

Dr. Rajesh Kumar
Professor and Head
Department of Nuclear Medicine
All India Institute of Medical Sciences
Jodhpur, Rajasthan

CO-GUIDES

Dr. Sameer K Taywade
Associate Professor
Department of Nuclear Medicine
AIIMS, Jodhpur

Dr. Poonam Elhence,
Professor and Head
Department of Pathology & Lab Medicine, AIIMS, Jodhpur

Dr. Mayank Garg
Additional Professor
Department of Neurosurgery,
AIIMS, Jodhpur

Dr. Sarbesh Tiwari,
Associate Professor
Department of Diagnostic & Interventional Radiology,
AIIMS, Jodhpur

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, JODHPUR

DECLARATION

I, hereby declare that the work reported in the thesis entitled **"Comparative study of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI in imaging of primary brain tumors"** embodies the result of original research work carried out by me in the Department of Nuclear Medicine, All India Institute of Medical Sciences, Jodhpur.

I further state that no part of the thesis has been submitted either in part or in full for any other degree of All India Institute of Medical Sciences or any other institution/University.

DR. RAVICHANDRAN T

Junior Resident

Department of Nuclear Medicine,

All India Institute of Medical Sciences, Jodhpur.

ACKNOWLEDGEMENT

I wish to express my sincere appreciation to those who have contributed to this thesis and supported me in one way or the other during this amazing journey.

I owe it to every patient, for entrusting their faith and belief in medical professionals and modern medical science. I'm grateful for their altruistic effort throughout their difficult illness to take part in research that would add to the knowledge of medical science and will prove to be beneficial in providing care to many.

I want to express my gratitude to my guide, **Dr. Rajesh Kumar**, who served as my study mentor, for his advice and unwavering support. He has been very generous and patient while suggesting the structure of this study. This dissertation would not have been possible without his assistance.

I sincerely thank my co-guide, **Dr. Sameer K. Taywade**, for his encouragement and efforts in making this study possible. He has consistently assisted me in my patient selection, was always available to clear my doubts and has motivated me on every step along the road.

I also owe a great part of this project to my Co-Guides, **Dr. Mayank Garg,** Additional professor, Department of Neurosurgery, **Dr. Poonam Elhence,** Professor & Head, Department of Pathology & Lab medicine, and **Dr. Sarbesh Tiwari**, Department of Diagnostic and Interventional Radiology, AIIMS, Jodhpur**.** Their in-depth knowledge and willingness to help me at any time to complete my thesis in time bound manner were tremendous. I am fortunate to be influenced by their vision and leadership. My vocabulary would never encompass enough words to express my gratitude toward them as teachers.

I'm thankful to our Nuclear physicists **Mr. Mahesh and Mr. Pankaj** for their important role in assisting this study, extending their helping hands & round clock availability at all times. I express my gratitude to my senior **Dr. Althaf**, for his support and valuable help in doing the statistical analysis. I would like to thank my seniors **Dr. Deepanksha Datta, and Dr. Navin** for their guidance.

I'm very thankful to my co-pg **Dr. Rakesh Pandey**, this dissertation would not have been possible without his valuable moral support.

My heartfelt thanks to my junior **Dr. Santhosh,** for the vibrant & exuberant ideas and inputs provided, which helped me to carry on in the hard times, **Dr.Tanisha** for meaningful suggestions and valuable support during my study. I'm thankful to **Dr. Nitish, Dr. Tanvi, Dr. Alok, Dr. Priyank,** and **Dr. Siddharth**, for their support and constant help in patient management**.** My sincere thanks to the nuclear physicists **Ms. Ruchi, Mr. Praveen,** and **Ms. Arushri** for helping in the scan acquisition. I'm overwhelmed by the selfless help extended by the staff of the Department of Nuclear Medicine, AIIMS Jodhpur.

I would like to thank my family, **Mrs. Prema, Mr. Thirupathi, Mrs. Punitha,** and **Mr. Sampath** for their perpetual love and blessings during this endeavor. Their understanding, cooperation, and everlasting patience deserve a salute for which my expression of thanks would not suffice.

I'm very thankful to my friends **Dr. Pravin Kumar, Dr. Praveen Raj, Dr. Bharatwaj,** and **Dr. Mohan Kumar** for their continued support and encouragement during this endeavor.

I would like to offer my sincerest gratitude to my institute; **All India Institute of Medical Sciences, Jodhpur** which provided a platform to carry out this research work.

DR. RAVICHANDRAN T

INDEX

S. No.	Content	Page No.
1.	**Summary**	**1**
2.	**Introduction**	**3**
3.	**Review of Literature**	**12**
4.	**Aims and Objectives**	**16**
5.	**Materials and Methods**	**17**
6.	**Results**	**24**
7.	**Discussion**	**52**
8.	**Conclusion**	**58**
9.	**Colour plates**	**60**
10.	**References**	**62**
11.	**Annexures**	**68**
	Annexure-1: Ethical Clearance Certificate	68
	Annexure-2: Clinical Sheet	69
	Annexure-3: Informed Consent - English	71
	Annexure-4: Informed Consent – Hindi	72
	Annexure-5: Patient Information Sheet – English	73
	Annexure-6: Patient Information Sheet – Hindi	74
	Annexure-7: Correlation coefficients of Glial tumors	75

LIST OF TABLES

S. No.	Title	Page No.
1.	F-18-FDG PET-CT in brain tumor —International societies' recommendations	9
2.	Demographic characteristics	24
3.	Dose & other characteristics	27
4.	Comparison of MRI diagnosis with HPE diagnosis	28
5.	Comparison Tc-99m GHA SPECT diagnosis with HPE diagnosis	28
6.	Comparison Tc-99m GHA SPECT-CT diagnosis with HPE diagnosis	28
7.	Comparison F-18-FDG PET diagnosis with HPE diagnosis	29
8.	Comparison F-18-FDG PET-CT diagnosis with HPE diagnosis	29
9.	Comparison of CT diagnosis with HPE diagnosis	29
10.	Diagnosis of all modalities for tumors	30
11.	Diagnostic accuracies	30
12.	Statistical analysis for the difference in diagnostic accuracies pairwise	31
13.	Median & Mean values of quantitative parameters from the Tc-99m GHA SPECT-CT	33
14.	Median & Mean values of various ratios of quantitative parameters from the Tc-99m GHA SPECT	34
15.	Correlation coefficient of different quantitative parameters and various parameters ratios of Tc-99m GHA SPECT-CT for WHO Grades (I-IV)	35
16.	Correlation coefficients of different quantitative parameters and various parameter ratios on Tc-99m GHA SPECT-CT for Subgroups Low vs high grades.	36
17.	Correlation coefficients of different quantitative parameters and various parameter ratios on Tc-99m GHA SPECT-CT for Tumor types.	37

18.	Median & Mean values of quantitative parameters from the F-18-FDG PET-CT	40
19.	Median values of ratios of quantitative parameters from the F-18-FDG PET-CT	41
20.	Median values of quantitative parameters for the whole tumor from the F-18-FDG PET-CT	43
21.	Correlation coefficients of different quantitative parameters and various parameter ratios on F-18-FDG PET-CT for WHO grades.	44
22.	Correlation coefficients of different quantitative parameters and various parameter ratios on F-18-FDG PET-CT with Subgroups high vs low grades.	46
23.	Correlation coefficients of different quantitative parameters and various parameter ratios on F-18-FDG PET-CT with tumor types.	48
24	Correlation of MRI Grades with HPE Grades	51
25.	Correlation coefficients of different quantitative parameters and various parameter ratios on F-18-FDG PET-CT in glial tumors.	75

LIST OF FIGURES

S. No.	Legends	Page No.
1.	Technetium-99m glucoheptonate molecular structure	5
2.	Flow chart for Research methodology	22
3.	Histopathological results of study participants	26
4.	Distribution of Grades of Brain Tumors	26
5.	Diagnostic accuracies of all imaging modalities	31
6.	Quantitative image analysis of Tc99m GHA- SPECT-CT	32
7.	Quantitative image analysis of F-18-FDG PET-CT by fixed VOI	38
8.	Quantitative image analysis of F-18-FDG PET-CT by manual segmentation method for whole tumor parameters	42
9.	Case of oligodendroglial Hamartoma	60
10.	Case of meningioma	61

LIST OF ABBREVIATIONS

1.	ICRP	International Commission on Radiological Protection
2.	BBB	Blood-Brain Barrier
3.	TLG	Total Lesional Glycolysis
4.	GHA	Glucoheptonate
5.	Tc99m	Technetium-99m
6.	mCi	Milli Curie
7.	MBq	Mega Becquerel
8.	mGy	Milli Gray
9.	mSv	Milli Sievert
10.	SPECT	Single Photon Emission Computed Tomography
11.	MRI	Magnetic Resonance Imaging
12.	PET	Positron Emission Tomography
13.	GLUT	Glucose transporters
14.	FDG	2-Fluoro 2- Deoxy Glucose
15.	F18	Fluorine -18
16.	EANM	European Association of Nuclear Medicine
17.	SNMMI	Society of Nuclear Medicine and Molecular Imaging
18.	IAEA	International Atomic Energy Agency
19.	DOPA	Dihydroxy phenylalanine (DOPA)
20.	MET	Methyl-methionine
21.	FET	Fluoro ethyl tyrosine
22.	FLAIR	Fluid Attenuation Inversion Recovery
23.	mpMRI	multiparametric Magnetic Resonance Imaging
24.	CT	Computed Tomography
25.	WHO	World Health Organisation
26.	cMRI	conventional MRI
27.	DWI	Diffusion-weighted imaging
28.	ASL	Arterial spin labelling
29.	DKI	Diffusion kurtosis imaging (DKI).

30.	DSC	Dynamic susceptibility-weighted contrast-enhanced imaging (DSC)
31.	rCBV	relative cerebral blood volume (rCBV).
32.	CNS	Central Nervous System
33.	CECT	Contrast Enhanced CT
34.	CEMRI	Contrast-Enhanced MRI
35.	ROC	Receiver operator characteristics
36.	SUV	Standardised Uptake Value
37.	WM	White Matter
38.	LEHR	Low Energy High Resolution
39.	T/N	Tumor to Normal
40.	ROI	Region of interest
41.	KeV	Kilo electron volt
42.	T/S	Tumor to Scalp
43.	T/N	Tumor to nasopharynx
44.	VOI	Volume of interest
45.	Max	Maximum
46.	Avg	Average
47.	kBq	Kilo Becquerel
48.	SD	Standard Deviation
49.	HPE	Histopathological Examination
50.	T/C	Tumor-to-Cortex
51.	T/GM	Tumor to Grey matter
52.	GN	Glucose Normalised
53.	MTV	Metabolic Tumor Volume
54.	ICSOL	Intracranial Space Occupying Lesions
55.	MRSI	Magnetic Resonance Spectroscopic Imaging

SUMMARY

INTRODUCTION:

In children and adolescents, brain tumors are the leading cause of death and morbidity. The cornerstone of patient care is surgical removal. CT and MRI scans assist surgeons in removing tumors while preserving the normal neurological structures. Functional imaging of brain tumors provides important information about the tumor metabolism, physiology, and functional features. The Tc-99m GHA, SPECT brain tracer used to image brain tumors and it is economical, easy to use, and has better efficacy among different SPECT tracers. F-18-FDG PET is also used in the assessment of brain tumors for various applications.

However, MRI is the gold standard for diagnosing and monitoring primary & secondary brain tumors. It frequently fails to differentiate between tumor-free and viable neoplastic tissues. There is little research comparing the Tc99m GHA SPECT, F-18-FDG PET, and MRI in diagnosis of brain tumors. So, we proposed to compare the imaging of primary brain tumors using Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI in our study.

AIMS & OBJECTIVES:

The aim of our study was to evaluate the role of Tc99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI in the management of primary brain tumors with the primary objective to compare the diagnostic accuracies of these three imaging modalities in a preoperative setting, considering HPE as the reference standard. The secondary objectives were to find an association between histopathological grading and quantitative parameters obtained from Tc-99m GHA SPECT-CT and F-18-FDG PET-CT.

METHODOLOGY:

The current study was a prospective study of patients who visited the Department of Neurosurgery between February 2021 and October 2022. Patients of both sex and all ages who were clinically and/or radiologically suspected of having primary brain tumors were invited to participate in the study. They were only enrolled after obtaining

informed consent. They underwent MRI, Tc-99m GHA SPECT-CT, and F-18-FDG PET-CT within 4 weeks' duration. These scans were performed pre-operatively and their findings were compared with histopathological diagnosis and also correlated with WHO histological types and grading. The image analysis of Tc-99m GHA SPECT-CT and F-18-FDG PET-CT was done both qualitatively and quantitatively. MRI images were analyzed qualitatively.

RESULTS AND DISCUSSION:

MRI showed a sensitivity of 100%, a specificity of 66.7%, a positive predictive value of 97.4%, and a negative predictive value of 100%; Tc99m GHA SPECT-CT showed a sensitivity of 97.3%, a specificity of 100%, positive predictive value of 100%, and a negative predictive value of 33.3% & F-18-FDG PET CT showed a sensitivity of 97.3%, a specificity of 100%, positive predictive value of 100%, and a negative predictive value of 75% in the diagnosis of primary brain tumors. There is no statistically significant difference in the preoperative diagnosis of MRI, F-18-FDG PET-CT, and Tc-99m GHA SPECT-CT in clinically and/or radiologically suspected brain tumors.

Quantitative parameters obtained from Tc-99m GHA SPECT-CT were correlated with WHO grades of brain tumors and a weak negative correlation was obtained for a few parameters. Numerous low-grade tumors (22/31) and variability in GHA uptake may be potential contributing factors for weak correlation. The FDG quantitative parameters based on SUVmax, SUVmean, SUVpeak, and relative quantitative parameters based on SUV showed a moderate positive correlation with WHO histopathological grades. The grade of tumors obtained from MRI showed moderate positive correlation with histopathological grading. F-18-FDG PET-CT quantitative parameters can also be used for the Grading of brain tumors. No significant correlation was obtained for both GHA and FDG parameters with tumor histological types.

CONCLUSION:

Tc99m SPECT-CT, F18 FDG PET-CT and MRI play a comparable role in the diagnosis of brain tumors. Furthermore, F-18-FDG PET-CT derived quantitative parameters might be useful in grading of brain tumors.

INTRODUCTION

Brain and central nervous system (CNS) cancers are a diverse group of malignant cancers that originate in the brain and its surrounding structures (1). Brain tumors form an important cause of mortality and morbidity in children & young adults. The incidence rates of brain and central nervous system (CNS) disorders have been found to be on the rise globally (1,2).

Brain tumors are classified into two types mainly, primary and metastatic. Primary brain tumors are further classified into glial and non-glial tumors. Glial cells are supporting cells and they are divided into astrocytes, ependymal cells, and oligodendrocytes. Glial tumors or gliomas are the most common type of primary brain tumors in prevalence and account for 50 percent of primary brain tumors (2). Gliomas include astrocytomas, oligodendrogliomas, ependymomas, and some rare histological types. Glioblastoma, a grade IV astrocytoma, is the most common and most aggressive type of glioma. Glioblastoma makes up 15% of all primary brain tumors and also accounts for 45% of malignant primary brain tumors, with an incidence of 3.2 per 100,000(3). The non-glial tumors include meningiomas, medulloblastomas, pituitary gland tumors, etc.

Surgical removal is the mainstay of patient management. CT and MRIs help the surgeon in removing the tumor and also avoid the removal of normal neurological structures. MRI has been the gold standard for diagnosing brain tumors.

In brain tumors, SPECT imaging provides important information about the metabolism, physiology, and functional features of the tumor (4).

Functional imaging with SPECT tracers like Thallium-201, Tc-99m GHA, Tc99m-Tetrofosmin and Tc99m-Sestamibi has been found to delineate brain tumors by different uptake mechanisms (5). Because of easy availability, less cost, and more efficacy, the GHA brain tracer can be used for imaging of brain tumors.

Glucoheptonate (GHA) depends on various factors like interstitial fluid, vascular permeability, and cellular uptake. More interstitial fluid in brain tumors than normal brain tissue allows tumor visualization using GHA. Tc-99m GHA follows active transport like glucose analog. Overexpression of GLUT-1 transporters is seen in most

cancers leading to increased GHA uptake in tumor cells. Thus, Tc-99m GHA accumulates more in the viable parts of tumors than in necrotic portions.

There is an increase in the uptake of Tc-99m GHA by the tumor gradually with time but it gets rapidly cleared from inflammatory lesions. It is also reported that Tc-99m GHA SPECT is better when compared to contrast CT and also equally useful as MRI (6,7).

PET imaging is an impressive technique for the evaluation of brain functions and also aids in the non-invasive assessment of cerebral blood flow, metabolism, and receptor binding (8).

PET radioisotopes like C11 methyl-methionine (MET), F18 Dihydroxy phenylalanine (DOPA), and F18 Fluoro ethyl tyrosine (FET) are frequently used for imaging brain tumors. Among them, F-18-FDG is the most commonly used PET radiotracer. It is a glucose analog, which is transported and phosphorylated like glucose. The brain utilizes energy primarily by an aerobic breakdown of glucose (4).

FDG PET detects metabolically active areas of the tumor, aids in achieving complete tumor resection by the surgeon, and detection of tumor recurrence. F-18-FDG PET may have independent prognostic value in brain tumors (9,10). F-18-FDG PET has been effectively used for brain tumor imaging in a wide range of indications, including diagnosis, prognosis, and assessment of treatment response (11).

Magnetic resonance imaging (MRI) is the most commonly used modality for the evaluation of brain tumors because of its superior soft tissue contrast, better anatomical demarcation, and ability to provide functional details. It also gives information about associated findings like hemorrhage, surrounding edema, and mass effects. The contrast material in T1 weighted (T1c) helps to enhance tumor boundaries from surrounding normal tissues. The T2 weighted axial viewing with FLAIR is used for the visualization of non-enhanced tumors (11).

The standard of care for diagnosis & follow-up of primary and secondary brain tumors is multiparametric magnetic resonance imaging (mpMRI). However, MRI cannot frequently discriminate between areas free of tumors and viable neoplastic tissues. In order to get around some of the drawbacks of mpMRI, the radiolabeled molecules can be employed in the following ways: to outline the area of the tumor, to highlight non-

enhancing tumors, to monitor treatment response, and to forecast the patient's outcome (12).

Glucoheptonate (GHA):

The Tc-99m GHA first developed in the 1970s, has been successfully applied to the imaging of brain tumors. The other mechanisms including BBB disruption that were later proposed resulted in more utilization of GHA (13).

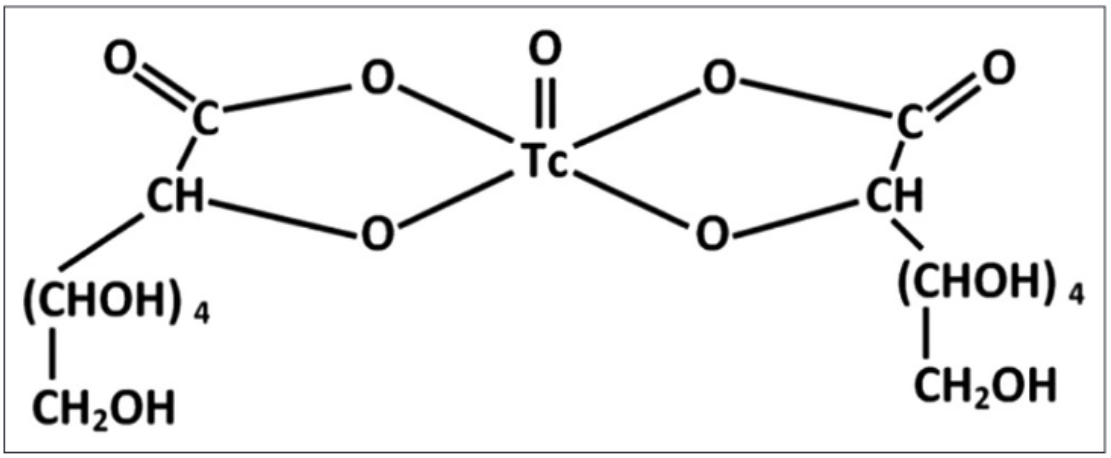


Figure 1: *Technetium-99m glucoheptonate molecular structure (5).*

Two GHA molecules are coupled to the metal (technetium) through carboxylate and alpha hydroxyl groups in the 1:2 Tc (V) complex 99mTechnetium glucoheptonate (13).

Mechanism of GHA:

i) Capillary permeability:

The main absorption mechanism in tumors is disruption of the blood-brain barrier and resulting increased permeability (13). Tc-99m GHA, as a BBB agent, provides a high lesion-to-background ratio with high-quality images for lesion visualization.

ii) Interstitial fluid:

Biochemical and electron-microscope studies have revealed that nearly all brain tumors contain significantly more interstitial fluid than a normal brain. The Tc-99m GHA complex demonstrated the fast filling of the extracellular fluid compartment and subsequent release.

iii) Intracellular uptake:

As a glucose analog, Tc-99m GHA is likely absorbed as an energy source by the tumor tissue and may reflect the metabolic activity of the lesion. While it quickly disappears from inflammatory lesions, Tc-99m GHA is slowly absorbed by viable tumors over time.

iv) Vascularity:

Although vascularity and capillary permeability are undoubtedly among the first and most important factors, the slow accumulation of Tc-99m GHA in the brain tumors is most likely the result of an active transport mechanism given the low blood level of the substance after an hour, which rules out any passive uptake mechanism (13,14).

Dosimetry:

For adults and adolescents, 20–25 mCi (740-925 MBq) of Tc-99m GHA is typically advised. The total effective dosage received after an injection of Tc-99m GHA is 0.0090 mSv/ MBq (0.033 rem/ mCi), according to ICRP. Radiation exposure to the bladder wall is highest which receives 0.21 rad/mCi (0.056 mGy/ MBq) (14).

Imaging:

Although there isn't a set post-injection waiting interval for brain tumor imaging, a 1-hour uptake period is sufficient to get high-quality images. Numerous studies are carried out even after a 30-minute waiting period since the tracer leaves the bloodstream quickly (15).

Interpretation:

Typically, abnormal Tc-99m GHA uptake in brain parenchyma is interpreted as a malignancy. Except for minimal background activity, typical Tc-99m GHA brain scans reveal no aberrant radiotracer uptake inside the brain parenchyma. However, when evaluating the images, physiological uptake in the nasal mucosa and the venous sinuses are taken into account.

Accurate cross-sectional imaging in computed tomography (CT), leads to the visualization of anatomical details without adjacent structures influencing each other. Because CT can distinguish between densities, also air, fat, soft tissue calcification, and

bony involvement are easily discernible. Both reader confidence and specificity are enhanced by the use of hybrid SPECT-CT (16,17).

Application:

It is highly advised for detecting both recurrent and residual tumors following surgery or radiation treatment. It can be utilized as a less expensive option because it has comparable, and occasionally even better, diagnostic performance than other SPECT and PET tracers. The expression of p-glycoprotein does not seem to affect Tc-99m GHA unlike tetrofosmin (18).

For recurrent gliomas, Tc-99m GHA SPECT-CT is suggested as a low-cost substitute for F18-FDOPA PET-CT. Because of its high degree of selectivity for neoplastic brain tissues, GHA can be used to differentiate between neoplastic and non-neoplastic intracranial lesions (16).

Disadvantages:

The background activity in the posterior fossa limits the use of Tc-99m GHA for imaging malignancies in that region (14). Due to the minimal BBB rupture and low metabolic activity of grade I gliomas, GHA revealed very poor sensitivity in these tumors (19). When compared to PET imaging, the main limitation of SPECT imaging is a lower resolution and a lack of precise anatomic details. However, the recent development of integrated hybrid SPECT-CT has improved tumor localization and diagnostic accuracy (15).

F18- FDG:

PET imaging provides insights into the biology of brain tumors and can be used for differential diagnosis, non-invasive grading, delineating the extent of tumor involvement, planning surgery and radiotherapy, and post-treatment monitoring & prognostics. One of the primary advantages of PET radiotracers is not affected by disruption of the BBB. Among the PET radiotracers, F-18-FDG is the most widely available and widely used in clinical nuclear medicine (20,21).

Mechanism:

Glucose transporters (GLUT), primarily GLUT1 and GLUT3, carry F-18-FDG across the intact BBB, and F-18-FDG accumulation in brain tumors is not dependent on BBB (Blood-brain barrier) rupture. Even when oxygen is present, glucose serves as a significant energy source for cancer cells in the brain (aerobic glycolysis; Warburg effect). Tumors, especially aggressive tumors, have elevated levels of GLUT1 and GLUT3. Both the expression of GLUT and the rate of cell proliferation is correlated with the glucose metabolic rate. Both neoplastic and inflammatory lesions have increased expression of glucose uptake transporters (GLUT-1 and GLUT-3), with tumors having higher levels of GLUT-1 expression (21).

When F-18-FDG enters the cells, it is phosphorylated into F-18-FDG-6-phosphate by the hexokinase or glucokinase enzymes. Because, it undergoes minimal subsequent metabolism and its dephosphorylation rate is slow, F-18-FDG-6-phosphate is primarily trapped in cells. Dephosphorylation is especially low or non-existent in tumors (22). Environmental factors, such as hypoxia or hyperglycemia associated with diabetes, can affect F-18-FDG transit along the BBB and in brain tumors (23).

Applications:

PET-CT detectors and reconstruction algorithms have improved significantly in recent years, resulting in higher image resolution and lesion detection with less image noise.

i) Diagnosis:

F-18-FDG PET-CT scanning is a valuable tool for the characterization of suspicious MRI lesions and for identifying the recurrence/persistence of high-grade gliomas (24). Pietrzak et al suggested that including brain imaging in the routine study protocol should be considered because the F-18-FDG PET-CT study may aid in the detection of malignant brain lesions (25).

ii) Tumor grading:

F-18-FDG uptake in WHO grade 3 and grade 4 gliomas are more likely to be higher, or similar to grey matter, whereas F-18-FDG uptake in WHO grade 2 gliomas are more likely to be comparable to white matter (25).

iii) Prognosis:

Furthermore, F-18-FDG uptake is a stand-alone prognostic predictor in WHO grade 4 gliomas and primary central nervous system lymphomas at diagnosis and the beginning of treatment (23). According to some studies, F-18-FDG is the most powerful predictor of progression-free survival and overall survival when compared to other variables like histologic grade (15).

iv) Post-treatment evaluation:

Another major advantage of F-18-FDG PET over structural imaging is the ability to distinguish radiation necrosis from recurrent disease. In contrast to metastatic disease, this feature is more reliable in gliomas (15).

V) Biopsy planning:

F-18-FDG PET is used in stereotactic biopsy planning by improving the delineation of higher-grade foci within a heterogeneous tumor. This improves brain biopsy diagnostic yield (15).

Various Societies recommend the application of F-18-FDG PET-CT in brain tumors (23).

S. No.	Source of Recommendations	Applications
1.	EANM	Non-invasive tumor grading
2.	SNMMI	Benign & malignant brain tumor detection
3.	IAEA	Primary & metastatic brain tumor detection

Table 1: *F-18-FDG PET-CT in brain tumors -International societies' recommendations.*

Limitations:

The main disadvantage of F-18-FDG is the absorption in brain cells, which makes it difficult to distinguish tumors precisely (25). Several techniques have been used to measure the glucose metabolic rate of brain lesions using F-18-FDG PET-CT scans,

but none of them have been proven to be effective (24). F-18-FDG PET is ineffective in differentiating inflammation from high-grade gliomas (26).

MRI:

MRI is highly sensitive to pathologic changes in normal parenchyma and has been used extensively in the evaluation of intracranial tumors. MRI can accurately determine lesion location, extent, mass effect, atrophy, and subacute or chronic haemorrhage, as well as distinguish between a vascular structure and adjacent parenchyma (27).

Because of its excellent soft-tissue contrast, high spatial resolution, and widespread availability, MRI is the diagnostic method of choice for patients with primary and secondary (metastatic) brain tumors (28). MRI is also useful for preoperative grading and treatment. However, conventional MRI (cMRI) provides insufficient accuracy for glioma grading. In addition to morphologic imaging, advanced MR imaging techniques such as diffusion imaging, perfusion imaging, spectroscopy imaging, and others can provide additional functional information on tumor tissue.

The organization of the tissue, including cell density and necrosis, can be detected using a variety of diffusion-weighted imaging (DWI) signal models. The non-Gaussian water diffusion (restricted and hindered diffusion) behavior in cerebral tissues can be described using diffusion kurtosis imaging (DKI).

Dynamic susceptibility-weighted contrast-enhanced imaging (DSC), which can reveal information on endothelial cell proliferation and neovascularization, is the most widely used perfusion MRI technique in clinical settings. The size and density of healthy vessels supplying neoplasms can also be determined using DSC. As an illustration, consider a non-enhancing glioma with increased relative cerebral blood volume (rCBV).

Combining different technologies greatly enhanced the diagnostic performance for brain tumor grading, especially glioma grading, using a variety of current MR techniques (29).

Limitations:

Nevertheless, MRI specificity for neoplastic tissue is low, making it difficult to distinguish between cancer and non-neoplastic lesions, delineate tumor extent,

particularly non-enhancing tumor portions, and distinguish treatment-related changes from tumor relapse (28).

Grading of brain tumors

The brain & spinal cord tumors were graded from I to IV based on several entities, CNS tumor grading has been distinct from the grading of other, non-CNS neoplasms for many years. WHO CNS tumors classification 2021 has brought CNS tumor grading closer to non-CNS neoplasms. CNS tumors are graded within types based on both histological & molecular parameters. Because grading within types correlated with expected clinical and biological behavior; for example, WHO grade I tumors were curable if surgically removed, whereas WHO grade IV tumors were highly malignant, leading to death in relatively short periods in the absence of effective therapy.

Historically, only histology characteristics have been used to grade CNS tumors, but now certain molecular markers can offer useful prognostic data. Due to this, molecular parameters have been included as grading biomarkers and as a means of determining the prognosis of various tumor forms in the newly developed WHO classification system 2021(30). In some situations, a molecular parameter frequently takes priority over histological findings when assigning a grade (31).

As discussed above different imaging modalities are used to diagnose primary brain tumors with each modality having its own shortcomings. These imaging modalities may complement each other in the diagnosis. Comparative studies are available for Tc-99m GHA SPECT with MRI (4) and F-18-FDG PET-CT with MRSI (32). However, there is no study available in the literature on the head-to-head comparison of imaging with Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI in the diagnosis of primary brain tumors. So, we propose to compare Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI in the imaging of primary brain tumors.

REVIEW OF LITERATURE

The study by **Syed Shafiq Alam et al.** concluded that Tc-99m GHA SPECT can differentiate high-grade gliomas from low-grade gliomas as well as metastasis. Based on the histopathological diagnosis, Tc-99m GHA SPECT showed a sensitivity of 90.48%, a specificity of 60.0%, a positive predictive value of 90.48%, and a negative predictive value of 60%. It also suggested that GHA has high sensitivity and specificity in localizing intracranial space-occupying lesions. In patients who are contraindicated for CECT/CEMR or have long waiting lists for such tests, Tc-99m GHA can be used (5).

Santra et al. reported that the sensitivity, specificity, and accuracy of Tc-99m GHA SPECT were 86.5%, 96.5%, and 89.4%, respectively, but for MRI were 94.6%, 24.1%, and 70.5%, respectively in the diagnosis of recurrent brain tumors (14).

However, a study conducted by **Jaiswal S et al**. showed that for neoplastic lesions, the sensitivity, specificity, and accuracy of glucoheptonate were 97.6%, 100%, and 98.1% respectively. Glucoheptonate has more specificity for detecting neoplastic tissues of the brain and may be used as a tracer for SPECT study to differentiate neoplastic intracranial lesions from non-neoplastic ones (16).

Sukanta Barai, et al. in their study found that Tc-99m glucoheptonate (GHA) accumulation does not appear to be affected by p-glycoprotein expression in recurrent tumors. The tumors that did not take up Tc-99m tetrofosmin showed more Tc-99m glucoheptonate concentration in comparison (18).

In a study conducted by **S Barai, GP Bandopadhayaya, et al**. based on the clinical behavior of the patients on follow-up, concluded that 99mTechnetium-glucoheptonate brain SPECT is a sensitive and reliable diagnostic modality to differentiate recurrent tumor and post-radiation gliosis (13).

Waxman et al. also showed that Glucoheptonate was better than pertechnetate as a brain scanning agent. Mittal et al. suggest that Tc-99m GHA SPECT imaging is a good indicator of brain tumor activity and may prove to be a better modality for grading glial tumors of the brain (33).

Kumar et al. conducted a study on clinically/radiologically suspected brain tumor patients and showed that Tc-99m GHA SPECT has a sensitivity of 90%, specificity of 53.55%, and accuracy of 73%(34).

Sodee et al showed that Tc-99m GHA Single-photon emission computed tomography (SPECT) is equally useful compared to magnetic resonance imaging (MRI) and better than computed tomography (CT) with contrast. They also found that viable tissue showed more Glucoheptonate uptake than necrotic tissues (6).

Ray S et al. showed that nuclear imaging was useful in 42% of study cases where CT or MRI was not able to differentiate between neoplastic and non-neoplastic conditions. It also concluded that in conditions where MR spectroscopy is not available or inconclusive, quantifications of neoplastic lesions can be done using nuclear imaging (35).

Luke et al in their study showed that tumor subtypes and grades had a substantial impact on the diagnostic accuracy of MRI in pediatric patients. Ependymomas, sellar, pituitary, pineal, and cranial and/or paraspinal nerve tumors had the highest sensitivities (80.65–100%). Astrocytic gliomas, oligodendrogliomas, choroid plexus tumors, neuronal, mixed neuronal-glial, embryonal, and histiocytic tumors all had slightly lower sensitivity (range 63.33-79.59%). Meningiomas, mesenchymal non-meningothelial, melanocytic, and germ cell tumors all had low sensitivity (range: 0–56.25%). The lobar areas, pineal/tectal plate area, and supratentorial ventricles where the most inaccurate tumor type predictions were made, whereas in the posterior fossa the most correct predictions were obtained (36).

Kosaka et al described that FDG PET may be useful in the differentiation of common enhancing malignant brain tumors, especially to differentiate lymphoma versus high-grade glioma and metastatic tumors. In case of suspicion in diagnosing using MRI alone, FDG PET can give essential information for distinguishing between lymphoma and other enhancing brain tumors (11).

Purandare et al found that F-18-FDG PET may differentiate between the common malignant brain space-occupying lesion by their variable F-18-FDG uptake and is also a valuable tool in narrowing the differential diagnosis particularly when MRI findings are equivocal (37).

Zhao et al analyzed 24 F-18-FDG-PET studies with an accumulated population of 857 patients for differentiating brain tumors, including suspected brain tumors and suspected recurrent brain tumors. In their meta-analysis, they showed that F-18-FDG-PET has a moderately good pooled sensitivity of 71% and a specificity of 77% for differentiating brain tumors (38).

Kim YI et al in their study showed that F-18-FDG PET-CT delayed scan can provide essential details about the proliferation status of the brain tumor and also aid in the detection of most of the lesions (39).

Chen et al. concluded that F18-FDOPA PET was more accurate than F-18-FDG PET for imaging low-grade and evaluating recurrent brain tumors (40).

Pietrzak et al (2021) used the Receiver Operating Characteristics (ROC) analysis in their work to determine the SUVmax cut-off value to distinguish between benign and primary brain lesions in this database. They found the malignant pathology to be 6.1 with the method's sensitivity and specificity being 96% and 83%, respectively, when we examined the SUVmax value levels between groups of the benign and primary brain lesions (23).

They also concluded that it is more difficult to evaluate clinically silent brain lesions when brain imaging is not included in the F-18-FDG PET-CT procedure, which makes it more difficult to guide the proper treatment. When there are only brain malignant lesions present in a patient, it seems to be very crucial. By identifying primary and metastatic brain tumors that are clinically silent, the brain and torso F-18-FDG PET-CT study can yield useful information supporting treatment therapy (23).

Cistaro et al (2021) described that in pediatric neuro-oncology, F-18-FDG PET imaging appeared to be helpful in a variety of clinical contexts, particularly for grading, detecting malignant transformation, and identifying the most suitable bioptic site of tumor aggressiveness. In addition, F-18-FDG PET may be viewed as helpful to MRI for patient prognostic classification, recurrence evaluation, and treatment response evaluation (41).

Binneboese et al (2021) explained that a semi-quantitative assessment of FDG uptake on PET may be a useful metric for predicting survival in patients with primary brain tumors during treatment. When a cut-point ratio of SUVmax/ WM of 1.90 is used, they

showed that FDG-PET has an association with survival in patients who have had treatment for a primary brain tumor. with primary brain tumors (42).

Zhang et al. demonstrated that the use of DSC, DKI, and Multi-b DWI in combination was helpful for preoperative non-invasive glioma grading. The parameters from Multi-b DWI had the best diagnostic accuracy when evaluating each modality separately, and integrating several MR characteristics further improved the diagnostic performance for glioma grading (29).

Sean et al. suggested that F-18-FDG-PET and MR spectroscopic imaging detect similar but not always identical regions of tumor activity, and there is little agreement in the degree of tumor metabolic activity between the two techniques (32).

AIMS AND OBJECTIVES

AIM:

To evaluate the role of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging in the management of primary brain tumors.

OBJECTIVES:

a) Primary objective:

To compare the diagnostic accuracy of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging in a preoperative setting considering HPE as the reference standard.

b) Secondary objective:

1. To find an association between histopathological grading and quantitative parameters obtained from Tc-99m GHA SPECT-CT and F-18-FDG PET-CT.
2. To compare Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging in the evaluation of suspected recurrent brain tumor lesions.

MATERIALS AND METHODS

a) Study design and setting:

This was a prospective study among the patients who attended the Department of neurosurgery with clinically and/ or radiologically suspected primary brain tumors. The study was conducted in the department of Nuclear medicine, AIIMS Jodhpur.

b) Inclusion criteria:

All the patients who attended the Department of Neurosurgery, with clinically and/ or radiologically suspected primary brain tumors.

c) Exclusion criteria

a. Patients who were not willing to participate in the study.
b. Pregnant and lactating women.
c. Patients who underwent prior brain surgery.
d. Patients who received prior cranial irradiation.

d) Sample size calculation:

Using the previous literature for calculation, we estimated a sample size of 40.

Calculation steps:

$$\mathbf{Z^2_{(1-\alpha/2)}\, p(1-p)/d^2 = 40}$$

Where,

a. **p**- taking sensitivity of 90%,
b. $\mathbf{Z_{(1-\alpha/2)}}$-standard normal deviation =1.96 at a 5% level of significance,
c. **±d**- assuming 10% as precision.

A total of 47 participants were included in the study.

e) Study Methodology:

The present study was a prospective study among the patients who attended the Department of Neurosurgery.

Patients of both sex and all age groups who were clinically and radiologically (MRI) suspected with primary brain tumors were approached for participating in the study. Family members of the patient were primed about the study procedure, the possible benefits, and any adverse outcomes, through a patient information sheet (in English/Hindi). They had been enrolled only after we took valid informed consent.

The family members /guardians explained about the same and also informed that no loss of benefit from routine care be experienced if they refuse to take part in the study.

After the patients have given consent to participate, they underwent MRI, Tc-99m GHA SPECT-CT, and F-18-FDG PET-CT within 4 weeks. These scans were performed pre-operatively and later the findings from the three scans were compared with histopathological findings of the surgical specimen based on WHO grading.

The CECT was obtained only during the PET-CT, the same was co-registered to SPECT, to minimize radiation exposure.

The primary outcomes were sensitivity, specificity, positive predictive value, and negative predictive value of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI.

f) Imaging procedures and analysis:

1. MRI:

MRI is acquired in various modalities – conventional (T1/T2/Diffusion/ Susceptibility Weighted imaging), Diffusion Tensor imaging, MR Perfusion (ASL+T2*), MR Spectroscopy, and Contrast-enhanced MRI. For non-cooperative high-grade tumor patients, Conventional and Contrast-enhanced MRIs were done.

MRI scans of all patients were assessed by an experienced Radiologist for the diagnosis of tumors based on available modalities. Based on the findings, diagnosed as either positive or negative for tumors. Other findings like glial or non-glial, extra or intra-axial, and grades either low or high were also noted.

Tumor Positive: Well-demarcated, hypo-intense or isointense relative to the brain on T1-weighted images and hyper-intense on T2-weighted images.

Tumor Negative: No significant lesions on T1 & T2 weighted images.

Other sequences were assessed for the Grading of the tumors.

2. Tc-99m GHA SPECT-CT:

a) Image acquisition

Radioisotope:	Tc-99m
Radiopharmaceutical:	Tc-99m GHA
Dose:	370-740MBq (Children-10mCi; Adults-20 mCi)
Route of administration:	Intravenous
Energy Setting:	140 keV (±10%)
Collimator used:	Low energy high resolution (LEHR)
Matrix size:	128 × 128
Method:	Step and shoot mode
Zoom factor:	1.5
Reconstruction method:	Iterative Reconstruction
Attenuation correction:	CT attenuation map

Sedation will be done for non-cooperative patients if required.

The head is immobilized in a carbon fiber composite immobilizer to prevent motion artefact.

b) Image analysis:

Reconstructed images were displayed and analyzed using axial, coronal, and sagittal views.

A single region of interest (ROI) was placed over the tumor by the consensus of two experienced nuclear medicine physicians. The quantitative ratios of the Tumor to Normal (T/N) were obtained by comparing the tumor area to a symmetrically positioned or contralateral region of interest (ROI). This scintigraphy grading based on the T/N ratio was correlated with the final histopathology grading. In addition, other parameters like Tumor to Scalp (T/S) ratio, Tumor to Nasopharynx (T/NP) ratio, total counts, mean counts, and maximum count values were obtained and correlated.

i) Tc-99m GHA SPECT:

Tumor Positive: Focal abnormal increased radiotracer along the brain parenchyma.

Tumor Negative: No abnormal radiotracer uptake.

ii) Tc-99m GHA SPECT-CT:

Computed Tomography

- Positive: Lesions showing effacement of adjacent sulcal spaces (mass effect), with or without contrast enhancement were interpreted as positive for tumor.
- Negative: Normal CECT or benign lesions with Hounsfield unit values were close to cerebrospinal fluid with no evidence of any mass effect.

Hybrid SPECT-CT images were obtained after co-registering CT with GHA SPECT,

Tumor Positive: Either Tc-99m GHA SPECT or CT positive for Tumor.

Tumor Negative: Both Tc-99m GHA SPECT or CT negative for tumor.

3. F-18-FDG PET-CT:

a) Image acquisition

Radiopharmaceutical	F18-2-Fluoro-2-deoxyglucose.
Route of administration:	Intravenous
Dose	0.10- 0.14 mCi/kg (3.7- 5.18 MBq/kg)
Reconstruction method:	Iterative Reconstruction
Time of acquisition	45-60 min post administration

FDG PET-CT imaging was performed using a PET-CT camera (Discovery MIDR, GE Healthcare).

b) Image analysis:

Reconstructed images were converted to semi-quantitative parameters of standard uptake value (SUV), using the equation mentioned below. A single volume of interest (VOIs) was placed over the tumor by the consensus of two experienced nuclear medicine physicians. In the case of multiple tumors, the largest tumor was selected for analysis.

VOIs over the contralateral Grey matter, contralateral white matter, contralateral cerebellum, contralateral medial temporal lobe, and pons also were placed. Maximum SUV (SUVmax), Average SUV (SUVmean), and Peak SUV (SUVpeak) of tumors were obtained from each regions.

SUV = Activity at a pixel (kBq/cm3) / injection dose (MBq) / weight [kg]

i) F-18-FDG PET:

Pietrzak et al reported that SUVmax valve values greater than 2.5 indicate an abnormality; they also revealed that the minimal SUV value found in their database within the brain was 3.3 (23,25).

Positive: Abnormal radiotracer uptake in the brain parenchyma (either increased or heterogenous), with SUVmax value more than 2.5.

Negative: No significant FDG abnormality or Abnormality with SUV max less than or equal to 2.5.

ii) F18 FDG PET-CT:

Computed Tomography

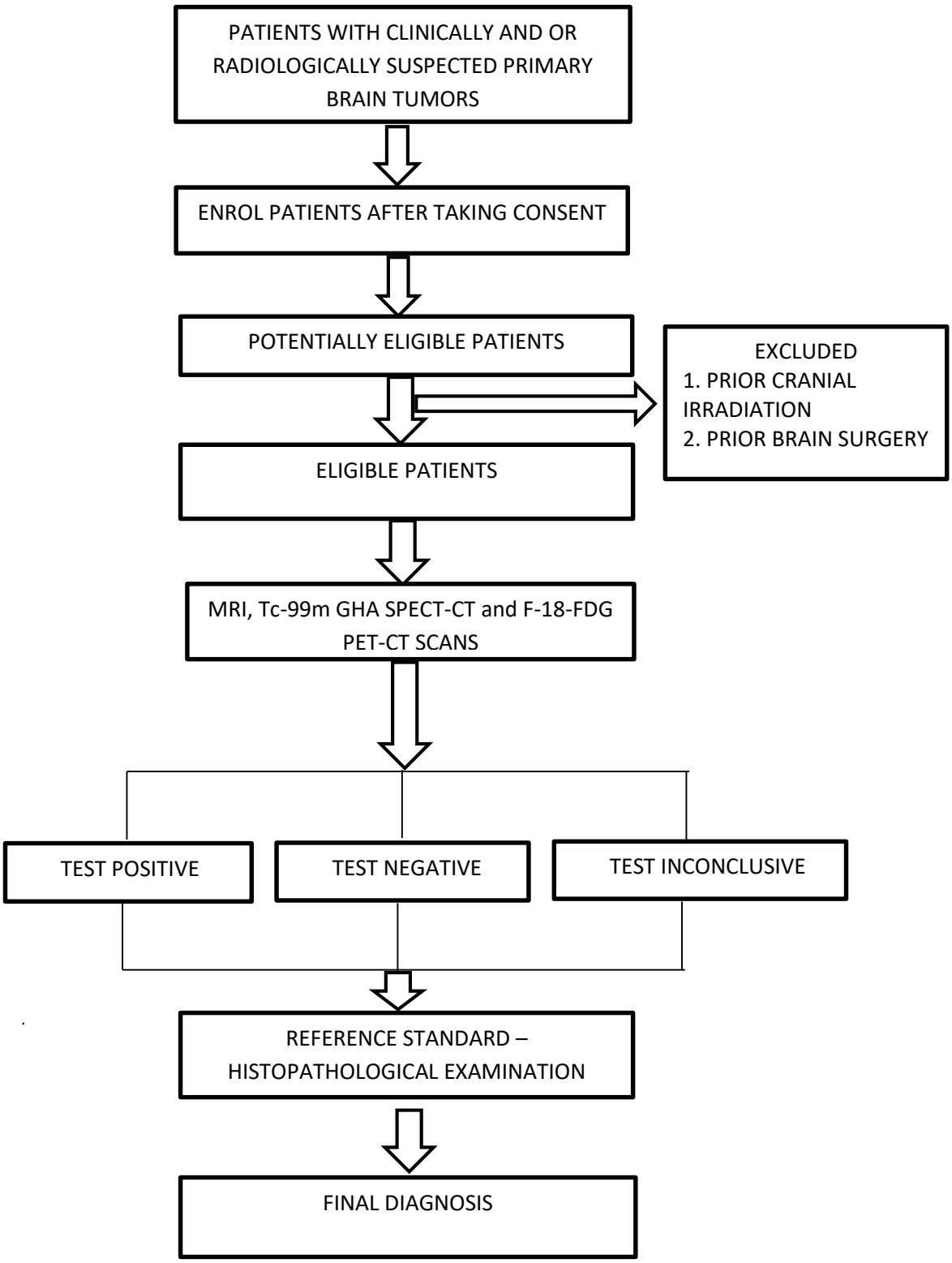
Positive: Lesions showing effacement of adjacent sulcal spaces (mass effect), with or without contrast enhancement were interpreted as positive for tumor.

Negative: Normal CECT or benign lesions with Hounsfield unit values were close to cerebrospinal fluid with no evidence of any mass effect.

Hybrid PET-CT images

Positive: Either F-18-FDG PET or CT positive for Tumor.

Negative: Both F-18-FDG PET or CT negative for tumor.



(Reference: STARD guidelines)

Figure 2: *Flow chart for Research methodology*

g) Statistical analysis

Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging were compared considering histopathological findings as the gold standard.

The sensitivity, specificity, positive predictive value, and negative predictive value of the Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging were calculated by using HPE as the reference standard for each scan and compared by using the test of proportion.

The Data were obtained by quantitative analysis of Tc-99m GHA SPECT-CT and F-18-FDG PET-CT images. The data were presented by different graphs.

For categorical data, non-parametric tests were used, comparison was done using the Mc Nemar test for two data sets or the Cochrane Q test for more than two data sets.

The correlation of quantitative parameters with histopathological grades was done by Spearman correlation method.

A p-value of <0.05 was considered as statistically significant.

The analysis was done by using SPSS software.

h) Ethical consideration

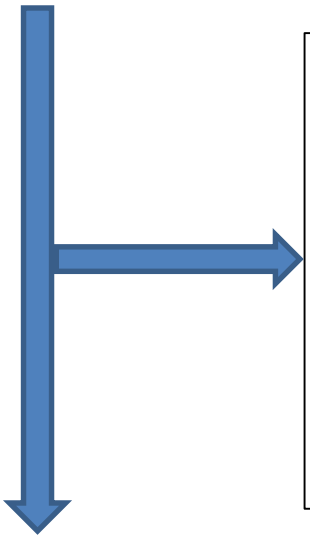
The study was approved by the IEC, AIIMS Jodhpur. Subsequently, patients were recruited with informed consent.

i) Study duration

March 2021 and December 2022.

RESULTS

A total of 47 clinically and /or radiologically suspected brain tumor patients were initially included in this study.



Exclusions:

- Three patients did not undergo PET-CT,
- 1 patient didn't undergo GHA SPECT
- One patient MRI not done within time interval mentioned above.
- One patient didn't undergo surgery.
- One patient had plasma cell neoplasm.

Totally 40 patients were included for analysis.

All 40 patients underwent Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance imaging preoperatively. In our research, we did not find patients with recurrence, so recurrence evaluation for them with the above imaging modalities was not done.

No.	**Characteristics**		
1.	Age	Mean ± SD	39.07 ± 15.53yrs
2.	Sex	Males Females	30 (72.5%) 10 (27.5%)
3.	Site of lesions (40 patients)	• Suprasellar region	3
		• Right frontal region	8
		• Left frontal region	5
		• Right parietal region	1
		• Left parietal region	5
		• Right temporal region	1
		• Left temporal region	3
		• Pontine Region	2
		• Cerebellopontine angle	8
		• Cerebellum	3
		• Cisterna magna region	1

4.	Histopathological results (40 patients)	• Glioma	15
		• Meningioma	9
		• Schwannoma	7
		• Mixed glioneuronal tumor	1
		• Pituitary adenoma	1
		• Medulloblastoma	1
		• Craniopharyngioma	1
		• Ewing sarcoma	1
		• Lymphoma	1
		• Hyperplasia	1
		• Epidermoid cyst	2
5.	Histopathological WHO grades (36 patients)	• Grade I	19
		• Grade II	8
		• Grade III	3
		• Grade IV	6
6.	WHO Classification group, 2021 (37 patients)	• Gliomas, glioneuronal tumors, and neuronal tumors	16
		• Embryonal tumors	1
		• Cranial & Paraspinal nerve tumors	7
		• Meningioma	9
		• Mesenchymal, non-meningothelial tumors involving the CNS	1
		• Haematolymphoid tumors involving the CNS	1
		• Tumors of sellar region	2

Table 2: *Demographic characteristics*

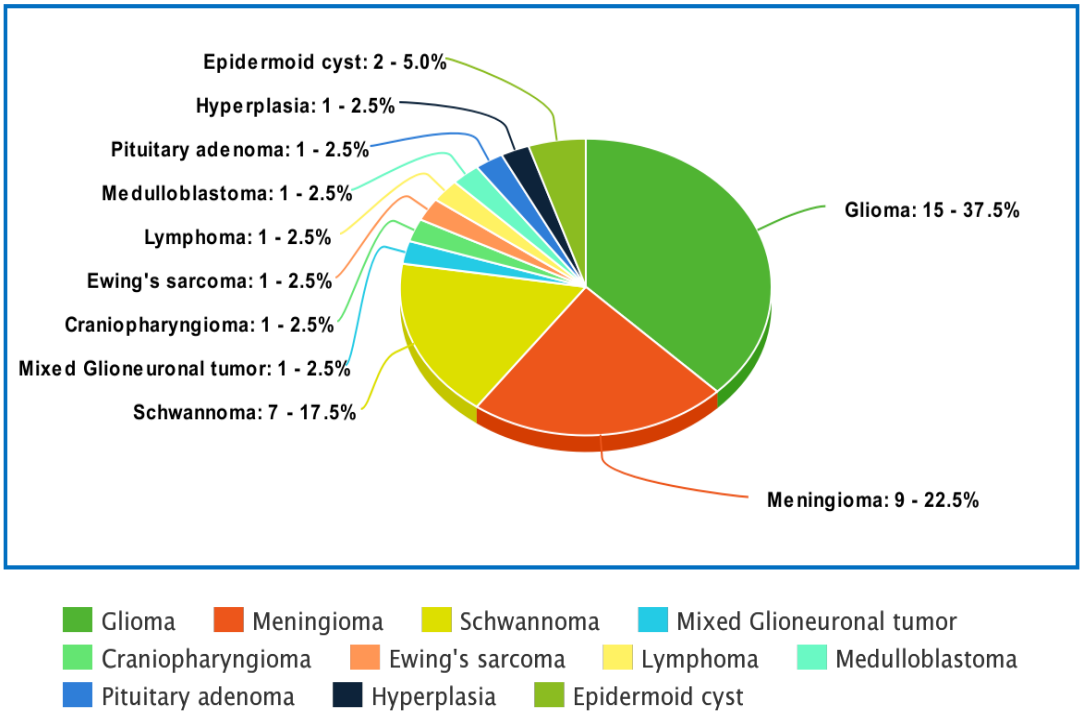


Figure 3: *Histopathological results of study participants (40 patients).*

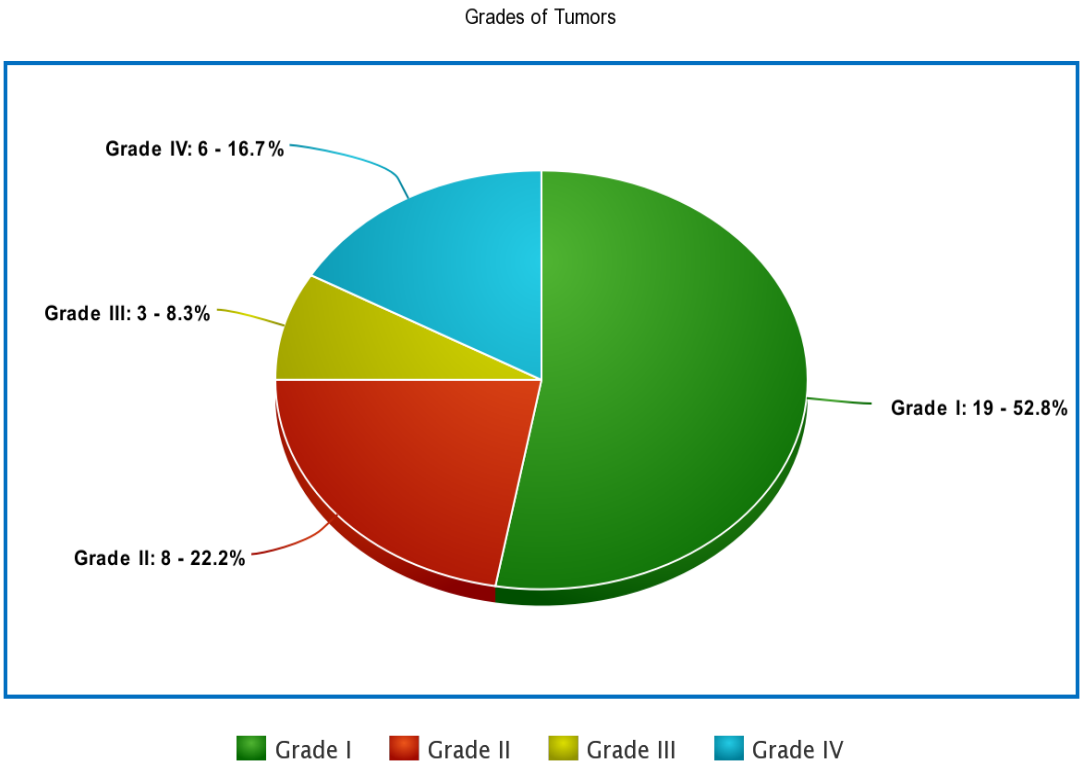


Figure 4: *Distribution of grades of brain tumors (36 patients)*

S. No.	Parameters	Mean (range)	Std. Deviation
1	Tc-99m GHA Dose (MBq)	711.51 (373.7 – 791.8)	98.79
2	F-18-FDG Dose (MBq)	301.55 (114.7 – 647.5)	91.40
3	Blood glucose (mg/dl)	107.40 (80.00 – 198.00)	22.88
4	Weight (Kg)	58.90 (22.88 – 80.00)	14.49
5	Blood urea (mg/dl)	21.72 (7.97 – 11.00)	7.97
6	Creatinine mg/dl	0.87 (0.23 – 0.47)	0.23

Table 3: *Dose & other characteristics (40 patients)*

Image analysis:

1. Diagnosis
2. Quantitative image analysis of Tc-99m GHA SPECT-CT
    a) Correlation of quantitative parameters & various parameter ratios of Tc-99m GHA SPECT-CT with histopathology of Brain tumors
    b) Correlation of quantitative parameters and Various parameter ratios on Tc-99m GHA SPECT-CT with histopathology of Glial brain tumors
3. Quantitative image analysis of F-18-FDG PET-CT
    a) Fixed VOI-based parameters & Ratios
    b) Whole tumor parameters
    c) Correlation of quantitative parameters & various parameter ratios of F18- FDG PET-CT with histopathology of Brain tumors
    d) Correlation of quantitative parameters and various parameter ratios on F18- FDG PET-CT with histopathology of Glial brain tumors
4. MRI analysis

1. Diagnosis:

All 40 patients were analysed for the presence of primary brain tumors in each imaging modalities and diagnostic accuracies were obtained for each imaging modalities taking HPE as standard.

	Tumor on HPE diagnosis		Total
	Positive	Negative	
MRI Positive	37	1	38
MRI Negative	0	2	2
Total	37	3	40

Table 4: *Comparison of MRI diagnosis with HPE diagnosis.* (True positive=37, True negative=2, False positive=1, False negative=0). On MRI scans, we found 38/40 patients as positive and 2/40 as negative.

	Tumor on HPE diagnosis		**Total**
	Positive	**Negative**	
GHA SPECT positive	31	0	31
GHA SPECT Negative	6	3	9
Total	37	3	40

Table 5: *Comparison of Tc-99m GHA SPECT diagnosis with HPE diagnosis.* (True positive=31, True negative=3, False positive=0, False negative=6). On Tc-99m GHA SPECT scans, we found 31/40 patients as positive and 9/ 40 as negative.

	Tumor on HPE diagnosis		**Total**
	Positive	**Negative**	
GHA SPECT-CT positive	36	0	36
GHA SPECT-CT Negative	1	3	4
Total	37	3	40

Table 6: *Comparison Tc-99m GHA SPECT-CT diagnosis with HPE diagnosis.* (True positive=36, True negative=3, False positive=0, False negative=1). On Tc-99m GHA SPECT-CT scans, we found 36/40 patients as positive and 4/ 40 as negative.

	Tumor on HPE diagnosis		**Total**
	Positive	**Negative**	
FDG PET positive	30	0	30
FDG PET Negative	7	3	10
Total	37	3	40

Table 7: *Comparison F-18-FDG PET diagnosis with HPE diagnosis.* (True positive=30, True negative=3, False positive=0, False negative=7). On F-18-FDG PET scans, we found 30/40 patients as positive and 10/ 40 as negative.

	Tumor on HPE diagnosis		**Total**
	Positive	**Negative**	
F-18-FDG PET-CT positive	36	0	36
F-18-FDG PET-CT Negative	1	3	4
Total	37	3	40

Table 8: *Comparison of F-18-FDG PET-CT with HPE diagnosis.* (True positive=36, True negative=3, False positive=0, False negative=1). On F-18-FDG PET-CT scans, we found 36/40 patients as positive and 4/ 40 as negative.

	Tumor on HPE diagnosis		**Total**
	Positive	**Negative**	
CT Positive	35	0	35
CT Negative	2	3	5
Total	37	3	40

Table 9: *Comparison of CT diagnosis with HPE diagnosis.* (True positive=35, True negative=3, False positive=0, False negative=2). On CT scans, we found 30/40 patients as positive and 4/40 patients as negative.

S. No	Scans	Tumor Positive	Tumor Negative
1.	MRI	38	2
2.	Tc-99m GHA SPECT	31	9
3.	Tc-99m GHA SPECT-CT	36	4
4.	F-18-FDG PET	30	10
5.	F-18-FDG PET-CT	36	4
6.	CT	35	5
7.	HPE	37	3

Table 10: *Diagnosis of all modalities for tumors*. No inconclusive results were found for all the imaging and HPE results.

S.No	Scans	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
1.	MRI	100	66.7	97.4	100
2.	Tc-99m GHA SPECT	83.8	100	100	33.3
3.	Tc-99m GHA SPECT-CT	97.3	100	100	75
4.	F-18-FDG PET	81.1	100	100	30
5.	F-18-FDG PET-CT	97.3	100	100	75
6.	CT	94.6	100	100	60

Table 11: *Diagnostic accuracies.* The sensitivity, specificity, positive predictive value, and negative predictive value of the Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging calculated by using HPE as the reference standard.

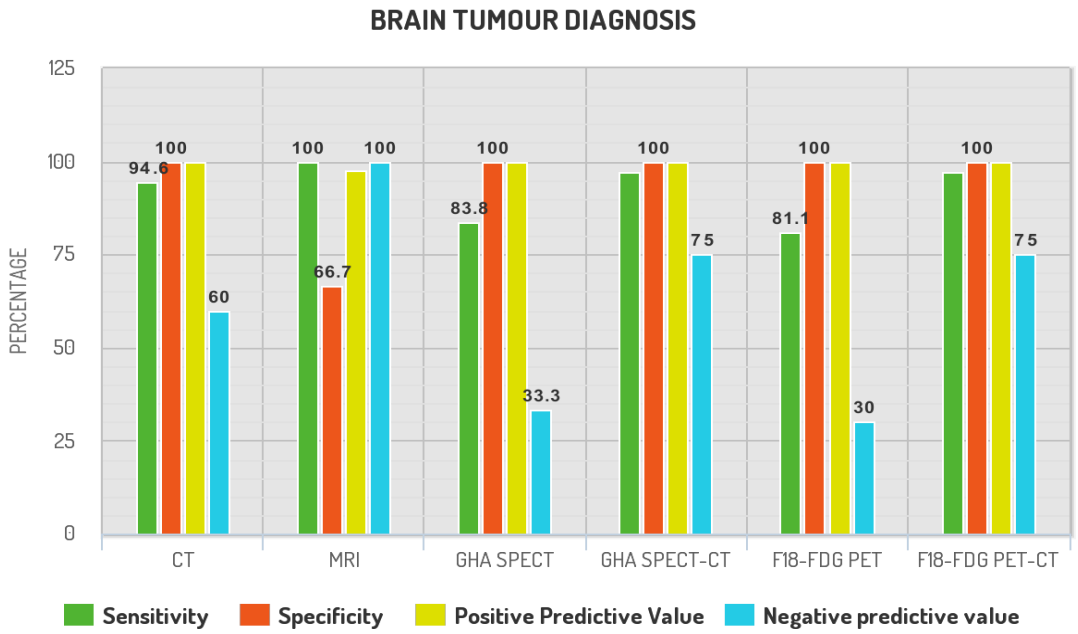


Figure 5: *Diagnostic accuracies of all imaging modalities*

According to the Cochrane Q test, there is a significant difference in the diagnostic accuracies of imaging modalities in overall ($p<0.01$).

S. No	Pairwise comparison using Mc Nemar test		p-value
1.	**MRI**	**Tc-99m GHA SPECT**	**0.016**
2.	**MRI**	**F-18-FDG PET**	**0.008**
3.	MRI	Tc-99m GHA SPECT-CT	0.500
4.	MRI	F-18-FDG PET-CT	0.500
5.	**F-18-FDG PET**	**Tc-99m GHA SPECT**	**0.031**
6.	**F-18-FDG PET**	**Tc-99m GHA SPECT-CT**	**0.031**
7.	**F-18-FDG PET**	**F-18-FDG PET-CT**	**0.031**
8.	Tc-99m GHA SPECT	Tc-99m GHA SPECT-CT	0.063
9.	Tc-99m GHA SPECT	F-18-FDG PET-CT	0.063
10.	F-18-FDG PET-CT	Tc-99m GHA SPECT-CT	1.000

Table 12: *Statistical analysis for the difference in diagnostic accuracies pairwise*

Imaging modalities were compared for the difference in the diagnostic accuracies using the Mc Nemar test pairwise. It showed a significant difference among MRI vs. Tc-99m GHA SPECT, MRI vs. F-18-FDG PET, FDG PET vs. Tc-99m GHA SPECT-CT, and FDG PET vs. FDG PET-CT ($P < 0.05$).

No significant difference was observed between FDG PET-CT, Tc-99m SPECT-CT, and MRI in the diagnosis of brain tumors when compared pairwise.

2. Quantitative image analysis of Tc-99m GHA SPECT-CT:

Various quantitative parameters based on counts in the region of interest (ROI) with fixed pixel areas on the tumor, contralateral region, nasopharynx, pons, and scalp were obtained for 30/36 patients who showed radiotracer avid lesions in SPECT-CT. Minimum, maximum, average, and total counts from the ROI mentioned for the above regions were obtained.

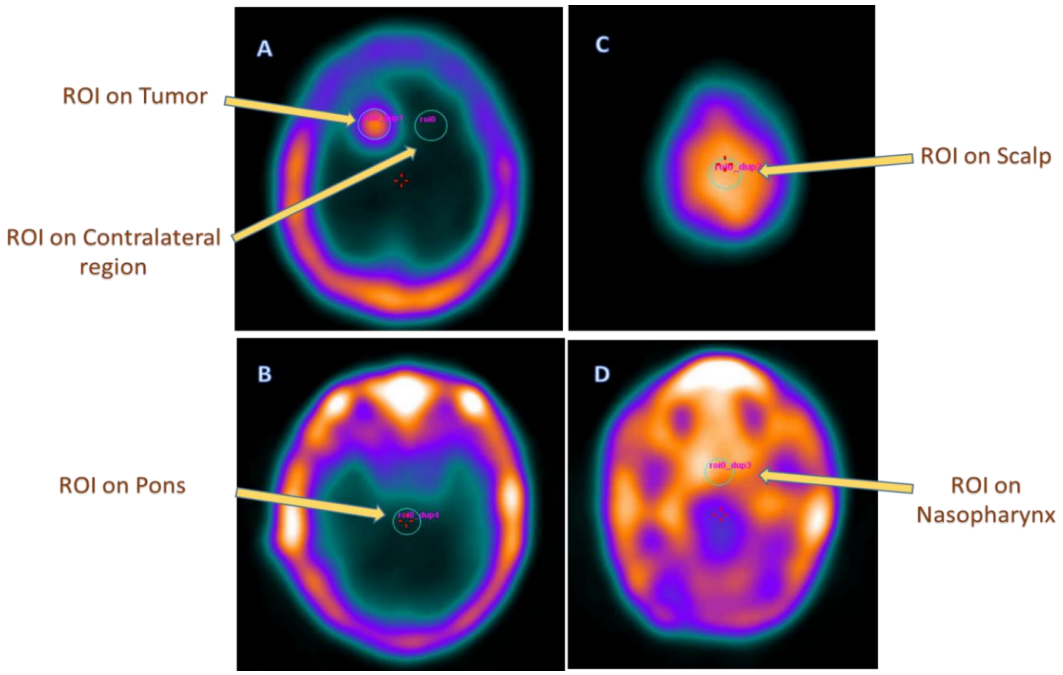


Figure 6: *60 years old female came with complaints of loss of memory and an increase in the frequency of micturition for 15 days, suspected of a brain tumor.* Tc-99m GHA SPECT-CT showed a radiotracer avid lesion in the right frontal lobe. HPE diagnosis: Glioblastoma. Analysis of axial images of Tc-99m GHA SPECT: A) Fixed circular ROI on tumor and contralateral region, B) ROI on pons C) ROI on scalp D) ROI on Nasopharynx.

Shapiro-Wilk statistics: Most parameters followed a non-Gaussian distribution, like Tumor average, Tumor maximum, Tumor total, Contralateral average, Contralateral maximum, Contralateral total, Nasopharynx total, Pons average, Pons maximum, and Pons total. A few parameters like the Nasopharynx average, Nasopharynx maximum, Scalp average, Scalp maximum, and Scalp total followed Gaussian distribution.

Mean ± SD (Standard deviation) was calculated for parameters following Gaussian distribution.

S. No	Tc-99m GHA SPECT-CT Parameters	Median (counts) with interquartile range	Mean± SD (counts)
1	Tumor average	95.50 (49.17 – 155.03)	-
2	Tumor maximum	120.00 (68.0 – 185.0)	-
3	Tumor total	6261.00 (3067.75 – 10628.00)	-
4	Contralateral average	18.40 (9.42 – 35.78)	-
5	Contralateral maximum	30.50 (12.75 – 59.75)	-
6	Contralateral total	1574.50 (554.0 – 2502.75)	-
7	Nasopharynx average	155.79 (107.92 – 194.95)	151.39 ±70.44
8	Nasopharynx maximum	181.50 (129.0 – 230.50)	184.73 ± 84.78
9	Nasopharynx total	9961.50 (5930.75 – 13840.25)	-
10	Pons average	20.28 (14.22- 30.43)	-
11	Pons maximum	37.50 (20.00 – 51.50)	-
12	Pons total	1433.50 (832.5 – 2437.25)	-
13	Scalp average	140.64 (119.41 – 170.59)	142.99 ± 40.21
14	Scalp maximum	159.00 (130.0 – 190.0)	162.30 ± 48.89
15	Scalp total	11366.50 (6679.25 – 14389.5)	10865.57 ± 5382.20

Table 13: *Median & Mean values of quantitative parameters from the Tc-99m GHA SPECT-CT*

S. No	Tc-99m GHA SPECT-CT Parameter Ratios	Median (counts) with interquartile range	Mean (counts) ± SD
1	Tumor total/ contralateral total	4.96 (3.31- 7.53)	5.46 ± 2.98
2	Tumor total/ nasopharynx total	0.63 (0.48 – 0.93)	-
3	Tumor total/ pons total	4.32 (2.49 – 6.48)	-
4	Tumor total/ scalp total	0.59 (0.47 – 0.94)	-
5	Tumor avg/ contralateral avg	5.41 (3.31- 7.53)	5.54 ± 2.96
6	Tumor avg/ nasopharynx avg	0.63 (0.48 – 0.93)	-
7	Tumor avg/ pons avg	4.32 (2.49 – 6.48)	-
8	Tumor avg/ scalp avg	0.59 (0.45 – 0.94)	-
9	Tumor max/ contralateral max	4.25 (2.60 – 7.09)	4.89 ± 2.96
10	Tumor max/ nasopharynx max	0.67 (0.51- 1.01)	-
11	Tumor max/ pons max	3.47 (2.10 – 5.17)	3.73 ± 2.07
12	Tumor max/ scalp max	0.70 (0.54 – 1.01)	-

Table 14: *Median & Mean values of various ratios of quantitative parameters from the Tc-99m GHA SPECT-CT*. Ratios of Tumor counts to other regions for all the above-mentioned parameters are calculated.

2. (a) Correlation of quantitative parameters & various parameter ratios of Tc-99m GHA SPECT-CT with Histopathology of brain tumors:

All above parameters and various ratios of Tc-99m GHA SPECT-CT were assessed for correlation with tumors, 1. WHO grades, 2. Subgroups: Low (Grade I or II) & high (Grade III or IV) grades and 3. Tumor types using the Spearman Correlation method and for each correlation coefficient values are calculated.

S. No.	Tc-99m GHA SPECT-CT Parameters and parameter ratios	WHO grades (I-IV)	
		Correlation Coefficient	p-value
1.	Tumor average	-0.276	0.140
2.	Tumor maximum	-0.326	0.078
3.	Tumor total	-0.336	0.069
4.	Contralateral average	-0.323	0.082
5.	**Contralateral maximum**	**-.368***	**0.046**
6.	Contralateral total	-0.334	0.072
7.	Nasopharynx average	-0.166	0.380
8.	Nasopharynx maximum	-0.212	0.260
9.	Nasopharynx total	-0.244	0.193
10.	Pons average	-0.340	0.066
11.	**Pons maximum**	**-.392***	**0.032**
12.	**Pons total**	**-.386***	**0.035**
13.	Scalp average	-0.358	0.052
14.	**Scalp maximum**	**-.382***	**0.037**
15.	**Scalp total**	**-.374***	**0.042**
16.	Tumor total/ Contralateral total	0.160	0.400
17.	Tumor total/ Nasopharynx total	-0.340	0.066
18.	Tumor total/ Pons total	-0.051	0.788
19.	Tumor total/ Scalp total	-0.308	0.098
20.	Tumor average/ Contralateral average	0.145	0.444
21.	Tumor average/Nasopharynx average	-0.340	0.066
22.	Tumor average/ Pons average	-0.051	0.788
23.	**Tumor average/ Scalp average**	**-.374***	**0.042**
24.	Tumor maximum/ Contralateral maximum	0.260	0.166
25.	Tumor maximum/ Nasopharynx maximum	-0.326	0.079
26.	Tumor maximum/ Pons maximum	-0.079	0.678
27.	Tumor maximum/ Scalp maximum	-0.332	0.073

Table 15: *Correlation coefficients of different quantitative parameters and various ratios on Tc-99m GHA SPECT-CT* ***for WHO grades (I-IV)***. Parameters like Contralateral maximum, Pons maximum, Scalp maximum, pons total and scalp total counts and Ratio of Tumor average/scalp average showed a statistically significant negative weak correlation ($P < 0.05$) for different grades of tumors.

S.No.	Tc-99m GHA SPECT-CT Parameters and parameter ratios	Subgroups low vs high grades	
		Correlation Coefficient	P value
1	Tumor average	-0.172	0.363
2	Tumor maximum	-0.219	0.246
3	Tumor total	-0.223	0.237
4	Contralateral average	-0.214	0.255
5	Contralateral maximum	-0.261	0.164
6	Contralateral total	-0.206	0.275
7	Nasopharynx average	-0.181	0.339
8	Nasopharynx maximum	-0.214	0.255
9	Nasopharynx total	-0.155	0.412
10	Pons average	-0.298	0.109
11	Pons maximum	-0.311	0.094
12	Pons total	-0.298	0.109
13	**Scalp average**	**-.374***	**0.042**
14	**Scalp maximum**	**-.370***	**0.044**
15	Scalp total	-0.307	0.099
16	Tumor total/ contralateral total	0.206	0.275
17	Tumor total/ Nasopharynx total	-0.240	0.202
18	Tumor total/ Pons total	0.013	0.947
19	Tumor total/ scalp total	-0.206	0.275
20	Tumor average/ contralateral average	0.197	0.296
21	Tumor average/ nasopharynx average	-0.240	0.202
22	Tumor average/ pons average	0.013	0.947
23	Tumor average/ scalp average	-0.307	0.099
24	Tumor maximum/ contralateral maximum	0.290	0.120
25	Tumor maximum/ Nasopharynx maximum	-0.231	0.219
26	Tumor maximum/ pons maximum	-0.021	0.912
27	Tumor maximum/ scalp maximum	-0.223	0.237

Table 16: *Correlation coefficients of different quantitative parameters and their ratios on Tc-99m GHA SPECT-CT* ***for Subgroups Low vs high grades***. Parameters like Scalp average & maximum showed a statistically significant negative weak correlation (P <0.05) for subgroups: High vs low grades.

S. No	Tc-99m GHA SPECT-CT Parameters and parameter ratios	Tumor Types	
		Correlation Coefficient	P value
1	Tumor average	-0.183	0.333
2	Tumor maximum	-0.189	0.317
3	Tumor total	-0.179	0.344
4	Contralateral average	0.033	0.864
5	Contralateral maximum	0.010	0.957
6	Contralateral total	-0.007	0.971
7	Nasopharynx average	-0.163	0.388
8	Nasopharynx maximum	-0.208	0.271
9	Nasopharynx total	-0.218	0.248
10	Pons average	-0.100	0.600
11	Pons maximum	-0.188	0.320
12	Pons total	-0.155	0.413
13	Scalp average	-0.178	0.347
14	Scalp maximum	-0.195	0.303
15	Scalp total	-0.171	0.368
16	Tumor total/ contralateral total	-0.182	0.335
17	Tumor total/ Nasopharynx total	-0.031	0.871
18	Tumor total/ pons total	-0.038	0.843
19	Tumor total/scalp total	-0.060	0.752
20	Tumor average/ contralateral average	-0.220	0.244
21	Tumor average/ nasopharynx average	-0.031	0.871
22	Tumor average/ pons average	-0.038	0.843
23	Tumor average/ scalp average	-0.171	0.368
24	Tumor maximum/ contralateral maximum	-0.115	0.544
25	Tumor maximum/ Nasopharynx maximum	-0.015	0.937
26	Tumor maximum/ pons maximum	0.034	0.860
27	Tumor maximum/scalp maximum	-0.109	0.566

Table 17: *Correlation coefficients of different quantitative parameters and various ratios on Tc-99m GHA SPECT-CT (**for Tumor types**).* No significant correlation was found for both individual parameters and different ratios with tumor types.

2 (b) Correlation of quantitative parameters and various ratios on Tc-99m GHA SPECT-CT with histopathological grades of Glial brain tumors:

The parameters obtained from the analysis of Tc-99m GHA SPECT-CT were analyzed for **Glial tumors** (15/60) separately with WHO Grades (I-IV) and high vs low grades groups of tumors by Spearman correlation.

There was no statistically significant correlation was observed between the Tc-99m GHA SPECT-CT parameters and WHO grades & subgroups grades of glial tumors.

3. Quantitative image analysis of F-18-FDG PET-CT:

3 (a). Fixed VOI-based parameters & Ratios:

Fixed VOIs were placed over the tumor (29/40 patients) where uptake values were visually maximum and also for other regions like VOIs over the contralateral Greymatter, contralateral white matter, contralateral cerebellum, contralateral medial temporal lobe, and pons placed. Maximum SUV (SUVmax), Average SUV (SUVmean), and Peak SUV (SUVpeak) of tumors were obtained.

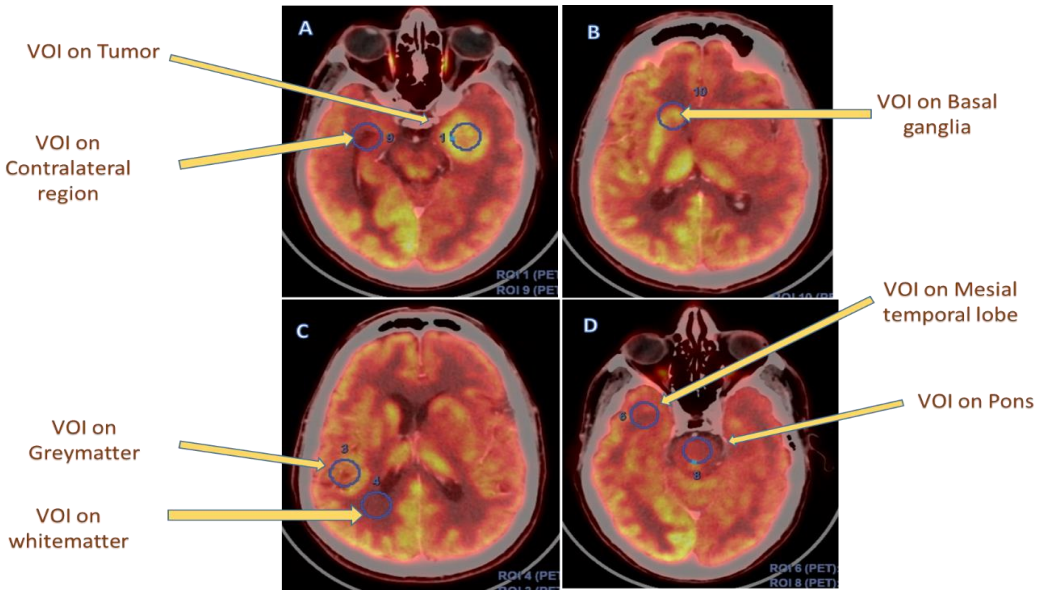


Figure 7: *50 years old male came with complaints of right-sided weakness for 1-2 months, suspected of a brain tumor*. F-18-FDG PET-CT showed FDG avid lesion in the left temporal lobe. HPE diagnosis: Glioblastoma. Analysis of axial images of F-18-FDG PET-CT: Fixed circular A) VOI on tumor and contralateral region, B) VOI on basal ganglia C) VOI on white-matter and Grey-matter D) VOI on the mesial temporal lobe and pons

Shapiro-Wilk statistics: Most parameters followed a non-Gaussian distribution namely, Tumor average (gm/dl), Tumor peak (gm/dl), Contralateral maximum (gm/dl), Contralateral average (gm/dl), Contralateral peak (gm/dl), White matter maximum (gm/dl), White matter average (gm/dl), White matter peak (gm/dl), Greymatter maximum (gm/dl), Greymatter average (gm/dl), Cerebellum average (gm/dl), Cerebellum peak (gm/dl), Mesial temporal maximum (gm/dl) and Tumor maximum(gm/dl).

A few parameters, Greymatter peak (gm/dl), Basal ganglia maximum (gm/dl), Basal ganglia average (gm/dl), Basalganglia peak (gm/dl), Cerebellum maximum (gm/dl), Mesial temporal average (gm/dl), Mesial temporal peak (gm/dl), Pons maximum (gm/dl), Pons average (gm/dl), Pons peak (gm/dl) followed Gaussian distribution.

Mean ± SD (Standard deviation) was calculated for parameters following Gaussian distribution.

Similarly, for Ratios also median with interquartile range and mean ± SD were tabulated (table 19).

S. No.	F-18-FDG PET-CT Parameters	Median with interquartile range	Mean ± SD
1	Tumor maximum(gm/dl)	5.40 (3.82-7.90)	-
2	Tumor average (gm/dl)	3.76 (2.85 -5.89)	-
3	Tumor peak (gm/dl)	3.96 (3.04 – 6.05)	-
4	Contralateral maximum (gm/dl)	7.33 (5.36 – 9.22)	-
5	Contralateral average (gm/dl)	4.18 (3.14 – 5.69)	-
6	Contralateral peak (gm/dl)	4.17 (3.24 – 5.75)	-
7	Whitematter maximum (gm/dl)	2.94 (2.60 – 3.92)	-
8	Whitematter average (gm/dl)	2.07 (1.69 – 2.47)	-
9	Whitematter peak (gm/dl)	1.99 (1.54 – 2.48)	-
10	Greymatter maximum (gm/dl)	8.55 (6.49 – 11.77)	-
11	Greymatter average (gm/dl)	6.45 (4.9 – 8.27)	-
12	Greymatter peak (gm/dl)	6.57 (5.12 – 8.59)	7.04 ± 2.22
13	Basal ganglia maximum (gm/dl)	9.01 (6.27 – 11.88)	9.46 ± 3.88
14	Basalganglia average (gm/dl)	6.20 (4.7 – 7.96)	6.25 ± 2.2
15	Basalganglia peak (gm/dl)	6.74 (5.11- 8.76)	7.00 ± 2.53
16	Cerebellum maximum (gm/dl)	6.82 (5.91- 9.27)	7.59 ± 2.33
17	Cerebellum average (gm/dl)	5.24 (4.38-6.5)	-
18	Cerebellum peak (gm/dl)	5.42 (4.34 – 6.79)	-
19	Mesial temporal maximum (gm/dl)	6.62 (5.39 – 9.30)	-
20	Mesial temporal average (gm/dl)	4.60 (3.67- 6.08)	4.76 ± 1.59
21	Mesial temporal peak (gm/dl)	4.65 (3.55 -6.39)	4.84 ± 1.76
22	Pons maximum (gm/dl)	5.10 (4.25- 7.0)	5.67 ± 2.0
23	Pons average (gm/dl)	3.89 (3.36 – 4.86)	4.09 ± 1.33
24	Pons peak (gm/dl)	4.01 (3.36 – 5.16)	4.26 ± 1.46

Table 18: *Median & Mean values of quantitative parameters from the F-18-FDG PET-CT*

S. No.	F-18-FDG PET-CT Parameter Ratios	Median with interquartile range
1	Tumor max/contralateral max	0.79 (0.55 – 1.45)
2	Tumor mean/contralateral mean	0.94 (0.67 – 1.39)
3	Tumor peak/contralateral peak	0.92 (0.67 – 1.59)
4	Tumor max/whitematter max	1.64 (1.15 – 3.31)
5	Tumor mean/whitematter mean	1.74 (1.24 – 2.86)
6	Tumor peak/whitematter peak	1.79 (1.33 – 3.61)
7	Tumor max/greymatter max	0.55 (0.39 – 0.96)
8	Tumor mean/greymatter mean	0.56 (0.38 – 0.93)
9	Tumor peak/greymatter peak	0.57 (0.38)
10	Tumor max/basal ganglia max	0.57 (0.39 – 1.08)
11	Tumor mean/ basal ganglia mean	0.60 (0.41 – 0.99)
12	Tumor peak/ basal ganglia peak	0.51 (0.38 – 1.01)
13	Tumor max/cerebellum max	0.72 (0.50 – 1.33)
14	Tumormean/ cerebellum mean	0.67 (0.45 – 1.08)
15	Tumorpeak/ cerebellum peak	0.64 (0.46 – 1.18)
16	Tumormax/mesial temporal max	0.73 (0.55 – 1.32)
17	Tumormean/ mesial temporal mean	0.76 (0.60 – 1.42)
18	Tumorpeak/ mesial temporal peak	0.82 (0.62 – 1.5)
19	Tumormax/pons max	0.93 (0.73 – 1.73)
20	Tumormean/ pons mean	0.87 (0.68 - 1.67)
21	Tumorpeak/ pons peak	0.89 (0.68 – 1.83)

Table 19: *Median values of various ratios of quantitative parameter ratios from the F-18-FDG PET-CT*

3 (b). Whole tumor parameters:

Quantitative parameters were obtained from the **whole tumor** (29/40 patients) by the manual segmentation method on CT slices (43). Tumor segmentation was performed manually due to high background counts, which rendered automatic segmentation unlikely.

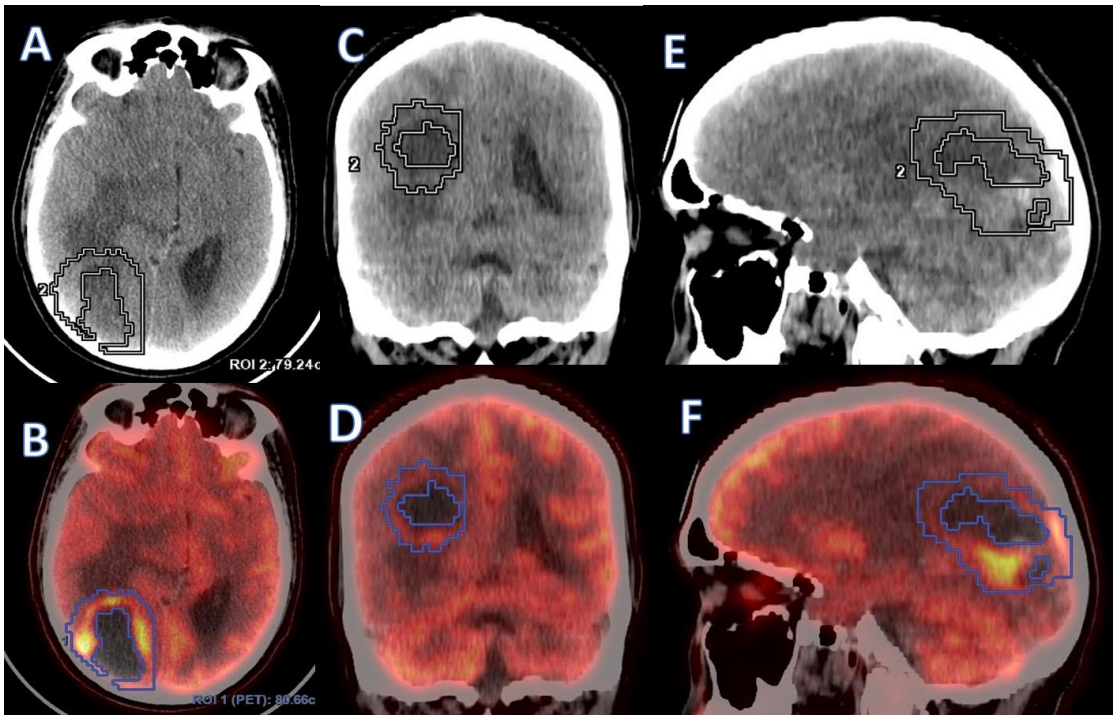


Figure 8: *42 years old came with complaints of headache for 1 month with decreased peripheral vision, suspected of brain tumor.* F18- FDG PET-CT showed peripherally FDG avid centrally necrotic lesion in the right posterior parieto-occiptial region. Image analysis was done by manual segmentation method for the whole Tumor volume. HPE diagnosis: Glioblastoma. Analysis of images of Tc-99m GHA SPECT: A- Axial, C – Coronal & E- Sagittal CT images. B- Axial, D- Coronal, and F- Sagittal F18- FDG PET- CT images.

S. No.	F-18-FDG PET-CT Parameters	Median with interquartile range
1	Volume	35.16 (21.31 – 56.50)
2	SUVmaximum	6.83 (5.2 – 10.37)
3	SUVmean	3.67 (2.80 – 4.88)
4	SUVpeak	4.28 (3.29 – 6.64)
5	Total lesional glycolysis (TLG)	106.45 (58.06 – 216.84)
6	GNmax	6.84 (5.08 – 9.85)
7	GN mean	3.45 (2.66 – 4.85)
8	GNTLG	107.60 (62.55 – 243.9)
9	CT max	717.00 (352.0 – 1280.5)
10	CT avg	51.10 (38.65 – 60.55)
11	CT volume	36.91 (22.01 – 55.93)

Table 20: *Median values of quantitative parameters for the whole tumor from the F-18-FDG PET-CT*

3 (c) Correlation of quantitative parameters & various parameter ratios of F18-FDG PET-CT:

These individual parameters and various ratios were correlated with brain tumor 1. WHO Grades (I-IV), 2. Subgroups as Low (Grade I or II) & high (Grade III or IV) grades, and 3. Tumor Types using the Spearman Correlation method and for each correlation coefficient values are calculated.

S. No.	Parameters	WHO Tumor grades	
		Correlation Coefficient	p-value
a)	*Fixed VOI-based parameters & parameter ratios:*		
1	**Tumor maximum(gm/dl)**	.479**	0.003
2	**Tumor average (gm/dl)**	.417*	0.011
3	**Tumor peak (gm/dl)**	.431**	0.009
4	Contralateral maximum (gm/dl)	0.103	0.557
5	Contralateral average (gm/dl)	0.224	0.195
6	Contralateral peak (gm/dl)	0.259	0.132
7	Whitematter maximum (gm/dl)	-0.309	0.067
8	Whitematter average (gm/dl)	-0.081	0.637
9	Whitematter peak (gm/dl)	-0.114	0.510
10	Greymatter maximum (gm/dl)	-0.258	0.129
11	Greymatter average (gm/dl)	-0.254	0.135
12	Greymatter peak (gm/dl)	-0.278	0.101
13	Basal ganglia maximum (gm/dl)	-0.073	0.673
14	Basalganglia average (gm/dl)	-0.118	0.494
15	Basalganglia peak (gm/dl)	-0.151	0.379
16	Cerebellum maximum (gm/dl)	-0.177	0.303
17	Cerebellum average (gm/dl)	-0.174	0.310
18	Cerebellum peak (gm/dl)	-0.210	0.220
19	Mesial temporal maximum (gm/dl)	-0.198	0.248
20	Mesial temporal average (gm/dl)	-0.286	0.090
21	Mesial temporal peak (gm/dl)	-0.276	0.103
22	Pons maximum (gm/dl)	-0.092	0.592
23	Pons average (gm/dl)	-0.130	0.448
24	Pons peak (gm/dl)	-0.149	0.386
25	**Tumor max/contralateral max**	.501**	0.002
26	**Tumor mean/contralateral mean**	.437**	0.009
27	**Tumor peak/ contralateral peak**	.401*	0.017
28	**Tumor max/ whitematter max**	.595**	0.000

29	**Tumor mean/ whitematter mean**	.474**	0.003
30	**Tumor peak/ whitematter peak**	.524**	0.001
31	**Tumor max/ greymatter max**	.569**	0.000
32	**Tumor mean/ greymatter mean**	.499**	0.002
33	**Tumor peak/ greymatter peak**	.552**	0.000
34	**Tumor max/ basal ganglia max**	.452**	0.006
35	**Tumor mean/ basalganglia mean**	.375*	0.024
36	**Tumor peak/ basal ganglia peak**	.467**	0.004
37	**Tumor max/ cerebellum max**	.552**	0.000
38	**Tumor mean/ cerebellum mean**	.471**	0.004
39	**Tumor peak/ cerebellum peak**	.521**	0.001
40	**Tumor max/ mesial temporal max**	.601**	0.000
41	**Tumor mean/ mesial temporal mean**	.587**	0.000
42	**Tumor peak/ mesial temporal peak**	.612**	0.000
43	**Tumor max/pons max**	.537**	0.001
44	**Tumor mean/ pons mean**	.461**	0.005
45	**Tumor peak/ pons peak**	.526**	0.001
	ii) Whole tumor parameters:		
46	Volume of Tumor	0.011	0.951
47	SUVmaximum of the whole tumor	0.313	0.063
48	**SUVmean of the whole tumor**	.386*	0.020
49	Total lesional glycolysis(TLG)	0.265	0.119
50	GN SUVmaximum of the whole tumor	0.323	0.055
51	**GN SUVmean of the whole tumor**	.387*	0.020
52	GN TLG	0.299	0.076
53	**SUVpeak of the whole tumor**	.506**	0.002
54	CT maximum	-0.207	0.227
55	CT average	-0.188	0.272
56	CTvolume of Tumor	0.014	0.937

Table 21: *Correlation coefficients of different quantitative parameters (VOI based & the Whole tumor based) on F-18-FDG PET-CT* ***for WHO grades I-IV****.*

Fixed VOI parameters like Tumor maximum, Tumor average, Tumor peak & all ratios showed statistically moderate positive correlation, and Whole tumor VOI parameters like SUVmean, SUVpeak, and GN SUVmean showed a statistically significant weak positive correlation for WHO Grades of Brain tumors.

S. No.	Parameters	Low vs high-grade	
		Correlation Coefficient	**p-value**
a)	*Fixed VOI-based parameters & parameter ratios:*		
1	**Tumor maximum(gm/dl)**	.454**	0.005
2	**Tumor average (gm/dl)**	.392*	0.018
3	**Tumor peak (gm/dl)**	.398*	0.016
4	Contralateral maximum (gm/dl)	-0.040	0.818
5	Contralateral average (gm/dl)	0.115	0.512
6	Contralateral peak (gm/dl)	0.135	0.440
7	Whitematter maximum (gm/dl)	-0.256	0.131
8	Whitematter average (gm/dl)	-0.256	0.131
9	Whitematter peak (gm/dl)	-0.185	0.279
10	**Greymatter maximum (gm/dl)**	-.349*	0.037
11	**Greymatter average (gm/dl)**	-.438**	0.007
12	**Greymatter peak (gm/dl)**	-.343*	0.041
13	Basal ganglia maximum (gm/dl)	-0.318	0.059
14	**Basalganglia average (gm/dl)**	-.377*	0.024
15	**Basalganglia peak (gm/dl)**	-.398*	0.016
16	**Cerebellum maximum (gm/dl)**	-.349*	0.037
17	**Cerebellum average (gm/dl)**	-.374*	0.025
18	**Cerebellum peak (gm/dl)**	-.392*	0.018
19	**Mesial temporal maximum (gm/dl)**	-.367*	0.027
20	**Mesial temporal average (gm/dl)**	-.423*	0.010
21	**Mesial temporal peak (gm/dl)**	-.432**	0.008
22	Pons maximum (gm/dl)	-0.293	0.082
23	**Pons average (gm/dl)**	-.349*	0.037
24	**Pons peak (gm/dl)**	-.355*	0.034
25	**Tumor max/contralateral max**	.573**	0.000
26	**Tumor mean/ contralateral mean**	.499**	0.002
27	**Tumor peak/ contralateral peak**	.451**	0.006
28	**Tumor max/ whitematter max**	.584**	0.000
29	**Tumor mean/ whitematter mean**	.547**	0.001
30	**Tumor peak/ whitematter peak**	.522**	0.001
31	**Tumor max/ greymatter max**	.596**	0.000

32	**Tumor mean/ greymatter mean**	.614**	0.000
33	**Tumor peak/ greymatter peak**	.565**	0.000
34	**Tumor max/basal ganglia max**	.540**	0.001
35	**Tumor mean/ basalganglia mean**	.503**	0.002
36	**Tumor peak/ basal ganglia peak**	.534**	0.001
37	**Tumor max/cerebellum max**	.584**	0.000
38	**Tumor mean/ cerebellum mean**	.559**	0.000
39	**Tumor peak/ cerebellum peak**	.565**	0.000
40	**Tumor max/ mesial temporal max**	.633**	0.000
41	**Tumor mean/ mesial temporal mean**	.664**	0.000
42	**Tumor peak/ mesial temporal peak**	.676**	0.000
43	**Tumor max/ pons max**	.608**	0.000
44	**Tumor mean/ pons mean**	.565**	0.000
45	**Tumor peak/ pons peak**	.577**	0.000
	ii) Whole tumor parameters:		
46	Volume of Tumor	-0.324	0.054
47	SUVmaximum of the whole tumor	0.253	0.136
48	**SUVmean of the whole tumor**	.423*	0.010
49	Total lesional glycolysis(TLG)	0.034	0.844
50	GN SUVmaximum	0.275	0.105
51	**GN SUVmean**	.452**	0.005
52	GN TLG	0.065	0.707
53	**SUVpeak of the whole tumor**	.429**	0.009
54	CT maximum	-0.256	0.131
55	CT average	0.127	0.462
56	CT volume of whole Tumor	-0.312	0.064

Table 22: *Correlation coefficients of different quantitative parameters (VOI based & the Whole tumor based) and various parameter ratios on F-18-FDG PET-CT with (**for subgroups high vs low grades**).* Fixed VOI parameters like Tumor maximum, Tumor average, Tumor peak & all ratios and whole VOI parameters like SUVmean, GN SUVmean & SUVpeak showed statistically significant moderate positive correlation with subgroups: Low vs high grades. Parameters from other regions showed weak negative correlation.

No.	Parameters	Tumor types	
		Correlation Coefficient	**p-value**
	i) Fixed VOI- based parameters and Ratios:		
1	Tumor maximum(gm/dl)	-0.093	0.592
2	Tumor average (gm/dl)	-0.187	0.275
3	Tumor peak (gm/dl)	-0.174	0.309
4	Contralateral maximum (gm/dl)	0.078	0.657
5	Contralateral average (gm/dl)	0.057	0.744
6	Contralateral peak (gm/dl)	0.016	0.925
7	Whitematter maximum (gm/dl)	-0.192	0.261
8	Whitematter average (gm/dl)	0.027	0.876
9	Whitematter peak (gm/dl)	0.045	0.794
10	Greymatter maximum (gm/dl)	0.030	0.861
11	Greymatter average (gm/dl)	0.034	0.843
12	Greymatter peak (gm/dl)	0.026	0.879
13	Basal ganglia maximum (gm/dl)	0.058	0.735
14	Basalganglia average (gm/dl)	0.034	0.843
15	Basalganglia peak (gm/dl)	0.124	0.471
16	Cerebellum maximum (gm/dl)	0.098	0.571
17	Cerebellum average (gm/dl)	0.075	0.662
18	Cerebellum peak (gm/dl)	0.085	0.623
19	Mesial temporal maximum (gm/dl)	0.077	0.655
20	Mesial temporal average (gm/dl)	0.010	0.955
21	Mesial temporal peak (gm/dl)	-0.023	0.894
22	Pons maximum (gm/dl)	-0.135	0.433
23	Pons average (gm/dl)	-0.156	0.364
24	Pons peak (gm/dl)	-0.132	0.444
25	Tumor mean/contralateral mean	-0.212	0.222
26	Tumor peak/contralateral peak	-0.194	0.263
27	Tumor max/whitematter max	0.027	0.874
28	Tumor mean/whitematter mean	-0.132	0.444
29	Tumor peak/whitematter peak	-0.108	0.529
30	Tumor max/greymatter max	-0.111	0.520
31	Tumor mean/greymatter mean	-0.225	0.186
32	Tumor peak/greymatter peak	-0.211	0.218

33	Tumor max/basal ganglia max	-0.097	0.575
34	Tumor mean/ basalganglia mean	-0.232	0.174
35	Tumor peak/ basal ganglia peak	-0.263	0.121
36	Tumor max/cerebellum max	-0.163	0.343
37	Tumor mean/ cerebellum mean	-0.229	0.179
38	Tumor peak/ cerebellum peak	-0.199	0.245
39	Tumor max/mesial temporal max	-0.108	0.530
40	Tumor mean/mesial temporal mean	-0.146	0.394
41	Tumor peak/mesial temporal peak	-0.121	0.483
42	Tumor max/pons max	0.048	0.780
43	Tumor mean/ pons mean	-0.037	0.832
44	Tumor peak/ pons peak	-0.019	0.914
	ii) Whole tumor parameters:		
45	Volume of Tumor	-0.241	0.157
46	SUVmaximum of the whole tumor	-0.171	0.318
47	SUVmean of the whole tumor	-0.213	0.212
48	Total lesional glycolysis(TLG)	-0.309	0.067
49	GN maximum	-0.135	0.433
50	GN mean	-0.206	0.227
51	GN TLG	-0.270	0.111
52	SUVpeak of the whole tumor	-0.101	0.557
53	CT maximum	0.051	0.766
54	CT average	-.403	0.015
55	CT Volume of whole Tumor	-0.249	0.143
56	Volume of Tumor	-0.241	0.157

Table 23: *Correlation coefficients of different quantitative parameters and various parameter ratios on F-18-FDG PET-CT with* ***Tumor types***. No significant correlation was found for parameters with types of tumors.

3 (d) Correlation of F18- FDG PET-CT parameters & various parameter ratios with histopathological grades of Glial brain tumors (Annexure VII):

The FDG parameters were also analyzed for Glial tumors (15/16 patients) separately with Grades (I-IV) and high vs low grades groups of tumors by Spearman correlation method.

Most of the quantitative parameters showed a moderate to strong correlation with WHO Grades (I-IV). Among them ratios like Tumor SUVmax/mesial temporal SUVmax ($r= 0.790$, $p< 0.05$) followed by tumor SUVpeak/ pons SUVpeak ($r= 0.787$, $p<0.05$) showed a strong correlation. Many parameters showed better correlation and among them the ratios of tumor SUVmax/mesial temporal SUVmax, tumor SUVmean / mesial temporal SUVmean, and tumor SUVpeak / mesial temporal SUVpeak ($r= 0.812$, $p<0.05$) showed a statistically significant strong correlation with subgroups: high vs low grades.

4. MRI analysis:

Patients positive for tumors in MRI imaging (36/40 patients) were further categorized into low or high-grade tumors by following characteristic findings on image by radiologist with the experience of more than 8 years:

a) Features of Low-Grade tumors:

- Well demarcated lesions with lesions without perilesional edema
- Absence of contrast enhancement
- MR spectroscopy: Choline to creatinine less than 2.5
- MR perfusion: rCBV less than 2.5 times the normal tissue.

a) Features of High-Grade tumors:

- Ill-defined lesion margins with perilesional edema
- Presence of contrast enhancement
- MR spectroscopy: Choline to creatinine more than 2.5.
- MR perfusion: rCBV more than 2.5 times the normal tissue.

.

MRI Diagnosis (36)		**HPE Diagnosis (36)**	
Low-Grade	High-Grade	Low-Grade	High-Grade
24	12	27	9
Correlation coefficient r = 0.68 (p < 0.01)			

Table 24: *Correlation of MRI Grades with HPE Grades.* The grade of tumors obtained from MRI were correlated for histopathological grades by Spearman Correlation method. The correlation coefficient was found to be r= 0.68 (P < 0.01), thus showing a moderate correlation.

DISCUSSION

Cancer ranks as a major cause of death and a significant barrier to improving life expectancy. According to estimates from the World Health Organization (WHO) in 2019, cancer is the first or second major cause of death before the age of 70 in 112 of 183 nations. According to Global Cancer Statistics 2020, 308,102 new cases of brain and CNS cancers were diagnosed in 2020, with 251,329 cancer-related deaths (1,44).

Both primary tumors and metastases are classified as intracranial neoplasms (45). The majority of primary central nervous system (CNS) tumors, or 25% of them, are gliomas, which account for 80% of malignant CNS tumors.

Histological findings supported by ancillary tissue-based tests have long been used to classify CNS tumors. In 2016, the WHO introduced the classification system based on molecular markers in a small set of brain tumors. The recent WHO CNS tumors classification 2021 refers to numerous molecular changes that are critical for the most accurate classification of CNS neoplasms due to the development of molecular biomarkers (31). Hence, it classifies the tumors into four grades using both histologic and molecular information (46).

Many space-occupying lesions are identified in neuroimaging studies, but not all mass-like intracranial lesions are true neoplasms. Many non-neoplastic disease conditions, including infectious, inflammatory, and autoimmune etiologies, can mimic CNS neoplasia. As a result, radiologists and clinicians are faced with a diagnostic quandary. CT and MR are the primary methods for detecting and evaluating such lesions (47). Despite the fact that multiparametric MRI is currently the imaging gold standard for primary and metastatic brain tumors, functional imaging provides the unique and complementary capacity to assess and define the metabolic patterns within the tumor and normal tissues (49). Thus PET and SPECT may help differentiate benign lesions from tumors (48) as well as grading of these tumors (5,47).

Functional imaging of the brain in past with many radiotracers like I-131 labelled human serum albumin, Hg-203 labelled chlormerodrin, Tc-99m pertechnetate, and Tc-99m DTPA had been tried. But each of the tracers had its shortcomings. The intracranial mass lesions were studied using Tc-99m pertechnetate, Thallium-202, Tc-99m-Sestamibi, and Tc-99m GHA.

Kim et al. have demonstrated that brain SPECT with Tc-99m GHA is a very sensitive method for identifying brain tumors. They concluded that Tc-99m GHA could be useful in defining the tumor types prior to surgery, suggesting that it may be utilized as a screening test for brain tumors (5,48).

In patients with a suspicion of recurrent glioma, Karunanithi et al. evaluated the diagnostic accuracies of Tc-99m GHA SPECT-CT and F18 fluorodopa (F18-FDOPA) PET-CT. Tc-99m GHA SPECT-CT had a sensitivity, specificity, and accuracy of 86.4%, 62.5%, and 80%, whereas F-18 FDOPA PET-CT had 100%, 87.5%, and 96%, respectively. They concluded that F18-FDOPA PET-CT could be replaced by Tc-99m GHA SPECT-CT as a less expensive imaging option for recurrent glioma (49).

Alam et al suggested that metastases as well as high-grade and low-grade gliomas can be distinguished using Tc-99m GHA SPECT. It also implied that it could be utilized in patients who cannot undergo CECT/CEMR due to contraindications or if there are lengthy waiting lists for such tests. It further implied that Tc-99m GHA SPECT has high sensitivity and specificity in localizing ICSOLs. In addition, it provides a major contribution to the monitoring of patients who have received radiotherapy after surgery as a complementary investigation to distinguish recurring tumors from post-radiotherapy gliosis (5).

Compared to MRI, Positron Emission Tomography (PET) offers insights into the biology of brain tumors and had many applications. They help in planning surgery and radiotherapy, with differential diagnosis, non-invasive grading, determining the extent of tumor involvement, post-treatment monitoring, and prognosis.

One of the key benefits of PET radiotracers over traditional MRI is that, unlike contrast-enhanced MRI sequences, these radiotracers are typically independent of disruption of the blood-brain barrier (BBB), in addition to image-specific pathophysiological processes. The most extensively used and accessible PET radiotracers are F18-2-fluoro-2-deoxy-D-glucose (F-18-FDG) in clinical nuclear medicine (20,21).

Dongwoo et al in their prospective study discovered that glucose loading reduced F-18-FDG uptake in the normal cortex more than in tumors, particularly high-grade gliomas. As a result, the Tumor to normal cortex uptake ratio increased after glucose loading, increasing the value of F-18-FDG PET-CT for grading cerebral gliomas (50).

With the above understanding, we conducted the present study. The mean age of the research participants was 39.07 ± 15.53 years, which is in line with the most common age range (45.64 ± 15.51) mentioned by Amna et al. The incidence of brain tumors was found to be more in males (72.5%) as mentioned in the literature.

In our study, we found that supratentorial brain tumors accounted for 27/40 patients, especially more in the frontal lobes. It correlates with the most common occurrence of supratentorial lesions. Gliomas accounted for 16/40 patients in our research which corresponds to the majority of glial tumor incidence in brain tumors (51,52).

1. Comparison of the diagnostic accuracies of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and Magnetic Resonance Imaging.

a) Tc-99m GHA SPECT:

Our results showed that, Sensitivity of 83.8 %, Specificity of 100%, Positive predictive value of 100%, and Negative predictive value of 33.3 % for Tc-99m GHA SPECT. Alam et al showed the Sensitivity of 90.48%, Specificity of 60.0%, Positive predictive value of 90.48%, and Negative predictive value of 60% for Tc-99m GHA SPECT in brain tumors (5). Kumar et al. also showed that Tc-99m GHA SPECT has a sensitivity of 90%, specificity of 53.55%, and accuracy of 73% (34).

The Tc-99m GHA SPECT comparatively showed less sensitivity and more specificity than previous studies. Due to variable GHA uptake in low-grade tumors and the inclusion of more patients in our study who tested positive for low-grade tumors (27/36) on HPE.

b) F18 FDG PET:

The current study demonstrated that the F-18-FDG PET has a sensitivity and specificity of 81.1% and 100%, respectively. Zhao et al in their meta-analysis found that diagnostic performance of F-18-FDG PET with a sensitivity of 74% and specificity of 74%, the sensitivity was almost in agreement with the findings of our investigation (38)**.** Nevertheless, our study had a high specificity of 100% because there were less number of tumor-negative individuals (3/37) in the cohort.

c) MRI:

We showed that MRI had a sensitivity of 100% and a specificity of 66.7% in the diagnosis of preoperative primary brain tumors.

Dixon et al. assessed the diagnostic performance of MRI in 550 children with brain tumors using sagittal T1- and axial T2-weighted imaging, coronal fluid attenuated inversion recovery, diffusion weighted imaging/apparent diffusion coefficient of the brain, and post-contrast T1-weighted imaging of the brain and entire spine. They found that sensitivity greatly varied by tumor type, from 0–100%, whilst specificity was generally high ranging from 93.6–100%. They discovered that specificity ranged from 93.6 to 100%, whereas sensitivity varied widely by tumor type, ranging from 0 to 100%. The results of the current study are also in concordance i.e., the sensitivity of 100% (36).

D) Tc-99m GHA SPECT-CT, F-18-FDG PET-CT, and MRI.

According to our knowledge, this is the first study comparing the MRI, F-18-FDG PET-CT, and Tc-99m GHA SPECT-CT in this specific cohort.

In our analysis, MRI showed a sensitivity of 100%, a specificity of 66.7%, a positive predictive value of 97.4%, and a negative predictive value of 100%; Tc-99m GHA SPECT-CT showed a sensitivity of 97.3%, a specificity of 100%, positive predictive value of 100%, and a negative predictive value of 33.3% & F-18-FDG PET CT showed a sensitivity of 97.3%, a specificity of 100%, positive predictive value of 100%, and a negative predictive value of 75% in the diagnosis of primary brain tumors.

There is no statistically significant difference in the preoperative diagnosis of imaging modalities in MRI, F-18-FDG PET-CT, and Tc-99m GHA SPECT-CT. Thus, there was not much difference in diagnosis of these three imaging modalities.

2. Association between histopathological grading and quantitative parameters obtained from Tc-99m GHA SPECT-CT and F-18-FDG PET-CT.

a) Quantitative parameters of Tc-99m GHA SPECT-CT:

Most of the quantitative parameters including their ratios showed a negative and weak correlation. However, few parameters like Contralateral maximum, Pons maximum,

Pons total, Scalp maximum, Scalp total counts, and the ratio of Tumor average/scalp average showed statistically significant negative and weak correlation for different grades of tumors. No statistically significant correlation was found for High vs low-grade groups and tumor types.

Alam et al. discovered that patients with high-grade primary glial tumors had significantly greater T/N (tumor to normal) and T max/N ratios than patients with low-grade tumors and metastases (5). In the present study, the mean values for T/N (Tumor to normal) and T max/N ratios for high-grade tumors were 6.43 (CI 95%: 3.55–9.30) and 6.28 (CI 95%: 3.29–9.26), respectively, and for low-grade tumors, they were 5.04 (CI 95%: 3.86–6.22) and 4.3 (CI 95%: 3.23–5.36), respectively. No statistically significant difference between low-grade and high-grade tumors was found in our GHA indices. This could be due to a large number of low-grade tumors (22/31) and variability in GHA uptake in GHA-positive tumors. We did not find any correlation between the quantitative Tc-99m GHA SPECT-CT parameters and high or low-grade gliomas.

b) Quantitative parameters of F-18-FDG PET-CT:

i) Primary brain tumors:

Correlation with the Grading of tumors (Grade I-IV): Fixed VOI parameters like Tumor maximum, Tumor average, Tumor peak & all the ratios showed moderate positive correlation and Whole tumor VOI parameters like SUVmean, SUVpeak, GN SUVmean showed a weak positive correlation for WHO Grades of Brain tumors ($p<0.05$). The highest correlation is seen with the ratio **Tumor peak/Mesial temporal peak (r = 0.612)**.

Correlation with the Low vs high-grade tumors: Fixed VOI parameters like Tumor maximum, Tumor average, Tumor peak & all the ratios, and whole VOI parameters like SUVmean, GN SUVmean & SUVpeak showed a moderate positive correlation with subgroups Low vs high grades (p value <0.05). The highest correlation is seen with the ratio of **Tumor peak/ Mesial temporal peak (r= 0.676).**

ii) Glial tumors:

In the group of **glial tumors,** many quantitative parameters showed moderate to a strong positive correlation. Among the various parameters, ratios like **Tumor SUVmax/**

Mesial temporal SUVmax (r= 0.790, p< 0.05) and **tumor SUVpeak to pons SUVpeak** (r= 0.787, p<0.05) showed a strong correlation with WHO grades (I-IV). Ratios like **Tumor SUVmax to mesial temporal SUVmax, tumor SUVmean to mesial temporal SUVmean, and tumor SUVpeak to mesial temporal SUVpeak** showed a significant and strong positive correlation with low vs high grades, (r= 0.812, p<0.05).

Dominique et al proposed that the FDG uptake ratio cut-off level can be used to distinguish high-grade from low-grade tumors. They found that the best cut-off level for tumor-to-white matter (T/WM) ratios and tumor-to-cortex (T/C) ratios were 1.5 & 0.6 in gliomas. The sensitivity and specificity were 94% and 77%, respectively, when a T/WM ratio greater than 1.5 was considered indicative of a high-grade tumor. The T/C ratio yielded similar results. PET cut-off levels of 1.5 for the T/WM FDG uptake ratio and 0.6 for the T/C ratio are useful for distinguishing low-grade from high-grade gliomas (53).

In the present study, the obtained T/WM ratio with a median value of 1.64 (Interquartile range: 1.15 to 3.31, r= 0.584 for low vs high grades) and T/C ratio with a median value of 0.79 (interquartile range: 0.55 to 1.45, r= 0.573 for low vs high grades) was in concordance with cut off values as mentioned by Dominique et al.

Comparison between the quantitative parameters of Tc-99m GHA SPECT-CT and F-18-FDG PET-CT for correlation with grading of brain tumors, we found that F-18-FDG PET-CT parameters showed better correlation than Tc-99m GHA SPECT-CT parameters. So, we propose that semi-quantitative FDG parameters would be more appropriate for the Grading of brain tumors. FDG parameters would also help in prognostication of patients.

CONCLUSION

Tc-99m GHA SPECT-CT, F18 FDG PET-CT and MRI play a comparable role in the diagnosis of brain tumors.

F-18-FDG PET-CT can be used as a marker of proliferation, thereby helping in the grading of brain tumors.

This study concludes that the quantitative parameters can expand the utility of F-18-FDG PET-CT beyond localization & metabolic assessment as well as in preoperative grading of brain tumors.

LIMITATIONS

Most of the patients referred for functional imaging had already MRI positive diagnosis. Hence there is a possibility of selection bias.

Although the sample size calculated at the beginning of the study was met still the larger patient number would have been desirable for better correlation with WHO grades.

Considering the standard of care for clinically suspected brain tumors, patients with definite MRI findings of non-tumoral lesions were not referred for functional imaging. This may lead to a lack of accurate demonstration of the specificity of different modalities.

COLOUR PLATE 1

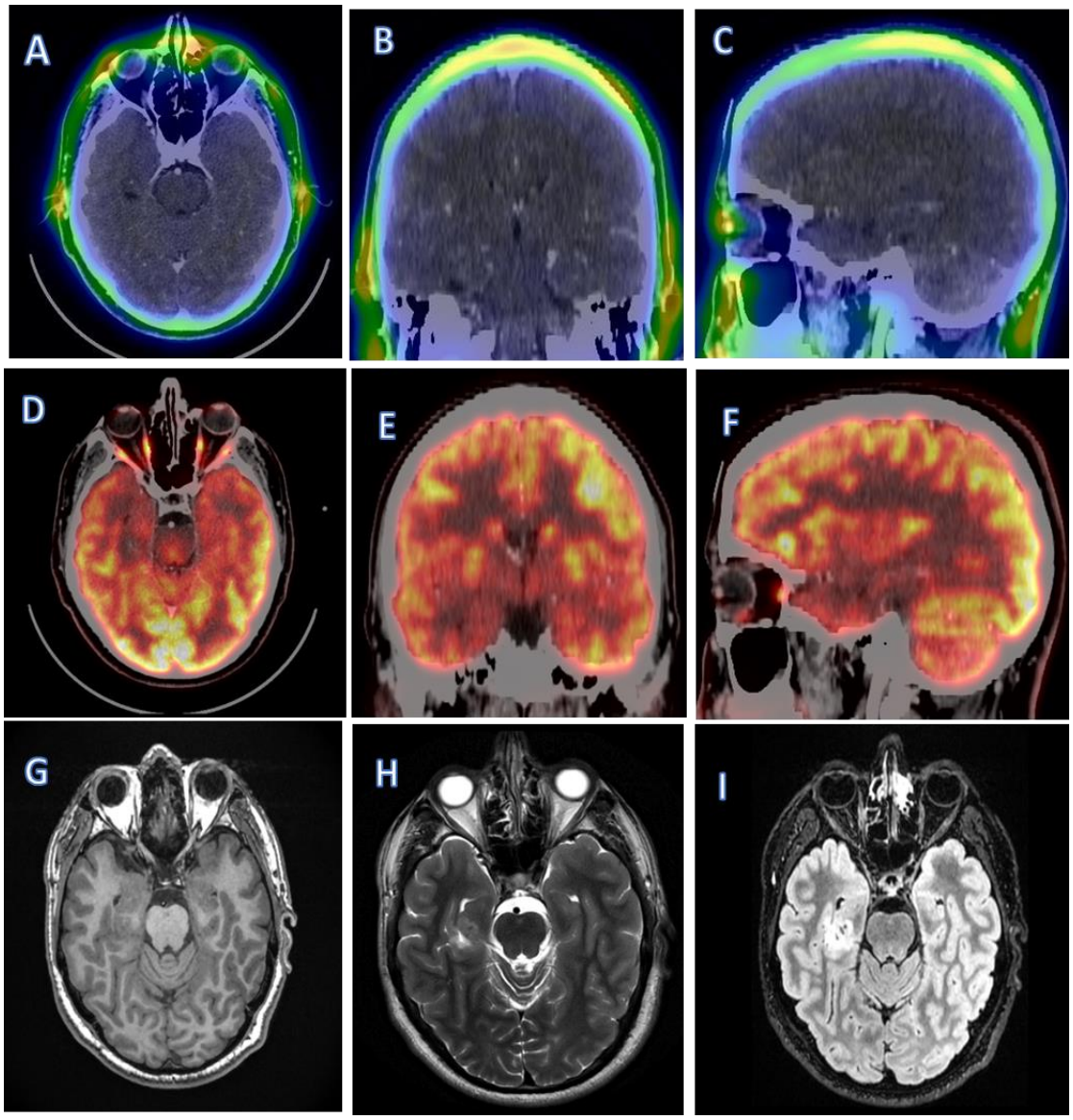


Figure 9: Case of oligodendroglial Hamartoma

32 years old male came with complaints of frequent seizures, and not responding to drugs, and, for him, all three scans were done after taking informed consent. Underwent surgical removal of the lesion, HPE diagnosis came out to be oligodendroglial CT. *hamartoma.*

A- Axial, B-coronal & C – Sagittal images of Tc-99m GHA SPECT-
These images demonstrate no abnormal uptake in Brain parenchyma.
D- Axial, E - coronal & F – Sagittal images of F-18-FDG PET-CT. FDG also showed no significant FDG avid lesion.
G- T1 Axial, H-T2 axial & C- T2- FLAIR images show a lesion in the right mesial temporal lobe.

COLOUR PLATE 2

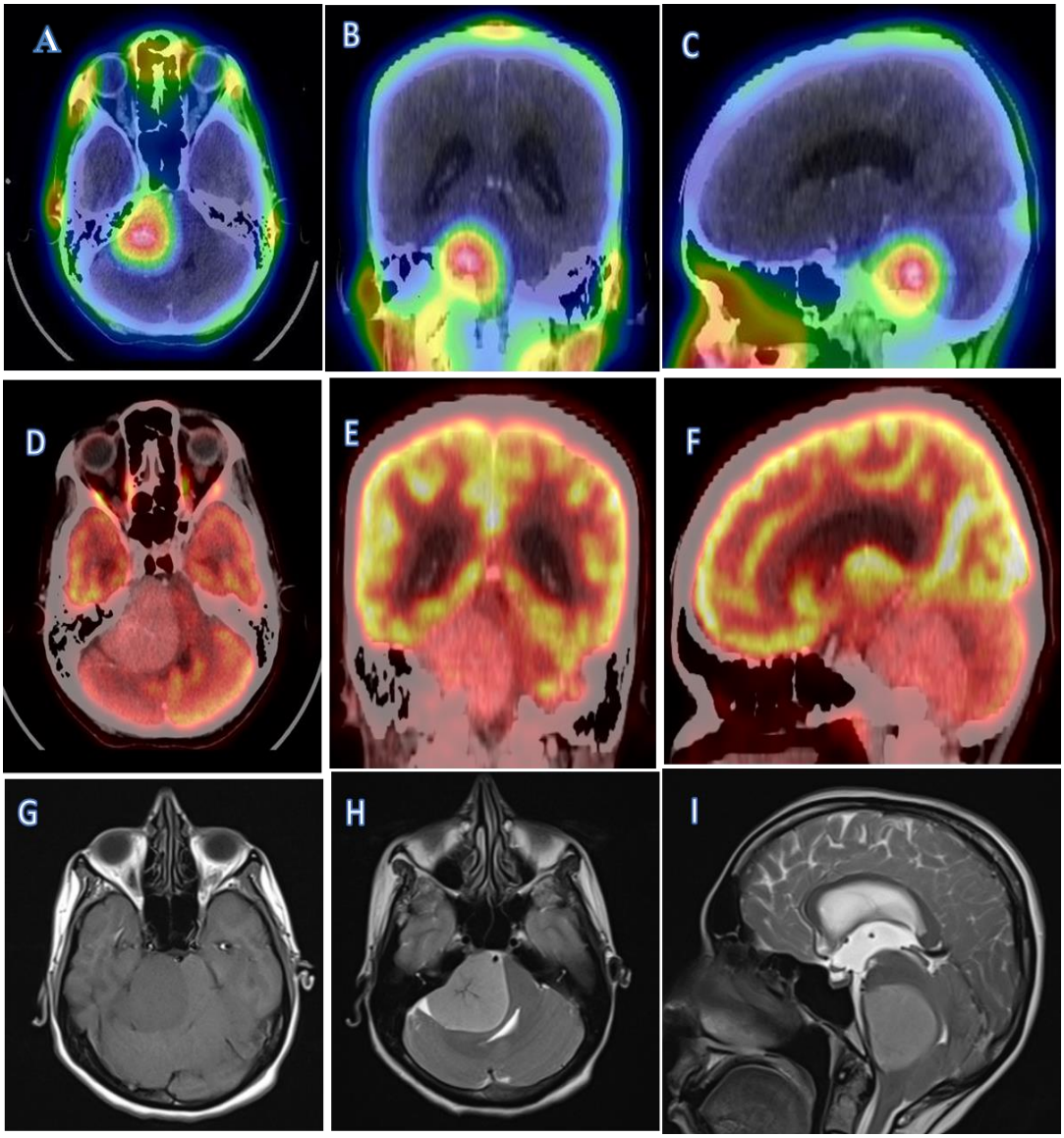


Figure 10: Case of meningioma

38 years old female came with complaints of right-sided hearing loss with involuntary facial movements for 2yrs and for her, all three scans were done after taking informed consent. Underwent surgical removal of the lesion, HPE diagnosis came out to be a meningioma.

A- Axial, B-coronal & C – Sagittal images of Tc-99m GHA SPECT- CT. These images demonstrate abnormal uptake and lesion in the right cerebellopontine angle region.
D- Axial, E - coronal & F – Sagittal images of F-18-FDG PET-CT. FDG also showed heterogeneously FDG avid lesion in the right cerebellopontine angle region
G- T1 Axial, H-T2 axial & C- T2- Sagittal images of MRI show lesion in the right cerebellopontine region.

REFERENCES

1. Fan Y, Zhang X, Gao C, Jiang S, Wu H, Liu Z, et al. Burden and trends of brain and central nervous system cancer from 1990 to 2019 at the global, regional, and country levels. Arch Public Health. 2022 Sep 17;80(1):209.

2. McNeill KA. Epidemiology of Brain Tumors. Neurol Clin. 2016 Nov 1;34(4):981–98.

3. McFaline-Figueroa JR, Lee EQ. Brain Tumors. Am J Med. 2018 Aug;131(8):874–82.

4. Zhang J, Traylor KS, Mountz JM. PET and SPECT Imaging of Brain Tumors. Semin Ultrasound CT MR. 2020 Dec;41(6):530–40.

5. Alam S, Junaid S, Ahmed S. Evaluation of Technetium-99m glucoheptonate single photon emission computed tomography for brain tumor grading. Asian J Neurosurg. 2016 Jun;11(02):118–28.

6. Lele RD. Tc-99m glucoheptonate is poor man's fluorodeoxyglucose. Indian J Nucl Med IJNM Off J Soc Nucl Med India. 2011 Oct;26(4):165–70.

7. Santra A, Kumar R, Sharma P, Bal C, Julka PK, Malhotra A. Detection of recurrence in glioma: a comparative prospective study between Tc-99m GHA SPECT and F-18 FDG PET/CT. Clin Nucl Med. 2011 Aug;36(8):650–5.

8. Das K, Mittal BR, Vasistha RK, Singh P, Mathuriya SN. Role of 18 F-fluorodeoxyglucose Positron Emission Tomography scan in differentiating enhancing brain tumors. Indian J Nucl Med. 2011 Oct 1;26(4):171.

9. Stanescu L, Ishak GE, Khanna PC, Biyyam DR, Shaw DW, Parisi MT. FDG PET of the brain in pediatric patients: imaging spectrum with MR imaging correlation. Radiogr Rev Publ Radiol Soc N Am Inc. 2013 Oct;33(5):1279–303.

10. Basu S, Alavi A. Molecular imaging (PET) of brain tumors. Neuroimaging Clin N Am. 2009 Nov;19(4):625–46.

11. Kosaka N, Tsuchida T, Uematsu H, Kimura H, Okazawa H, Itoh H. 18F-FDG PET of Common Enhancing Malignant Brain Tumors. Am J Roentgenol. 2008 Jun;190(6):W365–9.

12. Zhang-Yin JT, Girard A, Bertaux M. What Does PET Imaging Bring to Neuro-Oncology in 2022? A Review. Cancers. 2022 Feb 10;14(4):879.

13. Barai S, Bandopadhayaya GP, Julka PK, Naik KK, Haloi AK, Kumar R, et al. Role of Tc-glucoheptonic acid brain single photon emission computed tomography in differentiation of recurrent brain tumour and post-radiation gliosis. Australas Radiol. 2004 Sep;48(3):296–301.

14. Santra A, Kumar R, Sharma P. Use of 99m-technetium-glucoheptonate as a tracer for brain tumor imaging: An overview of its strengths and pitfalls. Indian J Nucl Med. 2015 Jan 1;30(1):1.

15. Sadaghiani MS, Sheikhbahaei S, Rowe SP, Pomper MG, Solnes LB. Cellular and Molecular Imaging with SPECT and PET in Brain Tumors. Radiol Clin North Am. 2021 May;59(3):363–75.

16. Jaiswal S, Barai S, Rajkumar, Gambhir S, Ora M, Mahapatra AK. Evaluation of intracranial space-occupying lesion with Tc99m-glucoheptonate brain single photon emission computed tomography in treatment-naïve patients. J Postgrad Med. 2009 Sep;55(3):180–4.

17. Haque MZ, Karim ME, Al-Azad S, Uz-Jahan M. Role of computed tomography in the evaluation of pediatric brain tumor. Bangladesh Med Res Counc Bull. 1970 Jan 1;36(3):89–92.

18. Barai S, Bandopadhayaya GP, Julka PK, Malhotra A, Bal CS, Dhanpathi H. Imaging using Tc99m-tetrofosmin for the detection of the recurrence of brain tumour: a comparative study with Tc99m-glucoheptonate. J Postgrad Med. 2004 Jun;50(2):89–93.

19. Santra A, Sharma P, Kumar R, Bal C, Kumar A, Julka PK, et al. Comparison of glucoheptonate single photon emission computed tomography and contrast-enhanced MRI in detection of recurrent glioma. Nucl Med Commun. 2011 Mar;32(3):206–11.

20. Verger A, Kas A, Darcourt J, Guedj E. PET Imaging in Neuro-Oncology: An Update and Overview of a Rapidly Growing Area. Cancers. 2022 Jan;14(5):1103.

21. Hasnain N, Mustafa RM, Bakhshi SK, Shamim MS. Efficacy of Positron Emission Tomography in distinguishing brain tumours from inflammation. JPMA J Pak Med Assoc. 2020 Dec;70(12(A)):2291–3.

22. Sarikaya I, Sarikaya A, Sharma P. Assessing the Effect of Various Blood Glucose Levels on 18F-FDG Activity in the Brain, Liver, and Blood Pool. J Nucl Med Technol. 2019 Dec;47(4):313–8.

23. Pietrzak A, Marszałek A, Kunikowska J, Piotrowski T, Medak A, Pietrasz K, et al. Detection of clinically silent brain lesions in [18F]FDG PET/CT study in oncological patients: analysis of over 10,000 studies. Sci Rep. 2021 Sep 14;11(1):18293.

24. Withofs N, Kumar R, Alavi A, Hustinx R. Facts and Fictions About [18F]FDG versus Other Tracers in Managing Patients with Brain Tumors: It Is Time to Rectify the Ongoing Misconceptions. PET Clin. 2022 Jul;17(3):327–42.

25. Pietrzak A, Marszałek A, Piotrowski T, Pietrasz K, Medak A, Wojtowicz J, et al. The utility of 18F-FDG PET/CT in brain tumours diagnosis. Rep Pract Oncol Radiother J Gt Cancer Cent Poznan Pol Soc Radiat Oncol. 2022;27(2):235–40.

26. Darcourt J, Booij J, Tatsch K, Varrone A, Vander Borght T, Kapucu OL, et al. EANM procedure guidelines for brain neurotransmission SPECT using (123)I-labelled dopamine transporter ligands, version 2. Eur J Nucl Med Mol Imaging. 2010 Feb;37(2):443–50.

27. Role of MRI in Primary Brain Tumor Evaluation in: Journal of the National Comprehensive Cancer Network Volume 12 Issue 11 (2014) [Internet]. [cited 2022 Nov 4]. Available from: https://jnccn.org/view/journals /jnccn/12/11/article-p1561.xml

28. Galldiks N, Lohmann P, Albert NL, Tonn JC, Langen KJ. Current status of PET imaging in neuro-oncology. Neuro-Oncol Adv. 2019 Dec;1(1):vdz010.

29. Zhang L, Yang LQ, Wen L, Lv SQ, Hu JH, Li QR, et al. Noninvasively Evaluating the Grading of Glioma by Multiparametric Magnetic Resonance Imaging. Acad Radiol. 2021 May;28(5):e137–46.

30. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro-Oncol. 2021 Aug 2;23(8):1231–51.

31. Organisation mondiale de la santé, Centre international de recherche sur le cancer, editors. Central nervous system tumours. 5th ed. Lyon: International agency for research on cancer; 2021. (World health organization classification of tumours).

32. Hipp SJ, Steffen-Smith EA, Patronas N, Herscovitch P, Solomon JM, Bent RS, et al. Molecular imaging of pediatric brain tumors: comparison of tumor metabolism using 18F-FDG-PET and MRSI. J Neurooncol. 2012 Sep;109(3):521–7.

33. Mittal BR, Bhattacharya A, Singh B. 99mTc GHA Brain SPECT in the evaluation of brain tumors. J Clin Oncol. 2005 Jun;23(16_suppl):1549–1549.

34. Kumar RA, Khandelwal N, Sodhi KS, Pathak A, Mittal BR, Radotra BD, et al. Comparison between contrast-enhanced magnetic resonance imaging and technetium 99m glucohepatonic acid single photon emission computed tomography with histopathologic correlation in gliomas. J Comput Assist Tomogr. 2006 Oct;30(5):723–33.

35. Ray S, Kundu B, Kundu S, Roy S, Sharma S. Distinguishing neoplastic and non-neoplastic ring enhancing lesions of the brain detected in CT and/or MRI with the help of correlative nuclear imaging. :5.

36. Dixon L, Jandu GK, Sidpra J, Mankad K. Diagnostic accuracy of qualitative MRI in 550 paediatric brain tumours: evaluating current practice in the computational era. Quant Imaging Med Surg. 2022 Jan;12(1):131–43.

37. Purandare NC, Puranik A, Shah S, Agrawal A, Gupta T, Moiyadi A, et al. Common malignant brain tumors: can 18F-FDG PET/CT aid in differentiation? Nucl Med Commun. 2017 Dec;38(12):1109–16.

38. Zhao C, Zhang Y, Wang J. A Meta-Analysis on the Diagnostic Performance of 18F-FDG and 11C-Methionine PET for Differentiating Brain Tumors. Am J Neuroradiol. 2014 Jun 1;35(6):1058–65.

39. Kim Y il, Cho KG, Jang SJ. Comparison of dual-time point 18F-FDG PET/CT tumor-to-background ratio, intraoperative 5-aminolevulinic acid fluorescence scale, and Ki-67 index in high-grade glioma. Medicine (Baltimore). 2019 Feb;98(8):e14397.

40. Chen W, Silverman DHS, Delaloye S, Czernin J, Kamdar N, Pope W, et al. 18F-FDOPA PET imaging of brain tumors: comparison study with 18F-FDG PET and evaluation of diagnostic accuracy. J Nucl Med Off Publ Soc Nucl Med. 2006 Jun;47(6):904–11.

41. Cistaro A, Albano D, Alongi P, Laudicella R, Pizzuto DA, Formica G, et al. The Role of PET in Supratentorial and Infratentorial Pediatric Brain Tumors. Curr Oncol Tor Ont. 2021 Jul 5;28(4):2481–95.

42. Binneboese A, Covington MF, Horn KP, Archibald ZG, Boucher KM, Morton KA, et al. Correlation between FDG-PET uptake and survival in patients with primary brain tumors. Am J Nucl Med Mol Imaging. 2021;11(3):196–206.

43. Mercieca S, Belderbos J, van Loon J, Gilhuijs K, Julyan P, van Herk M. Comparison of SUVmax and SUVpeak based segmentation to determine primary lung tumour volume on FDG PET-CT correlated with pathology data. Radiother Oncol. 2018 Nov;129(2):227–33.

44. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.

45. Borja AJ, Hancin EC, Raynor WY, Ayubcha C, Detchou DK, Werner TJ, et al. A Critical Review of PET Tracers Used for Brain Tumor Imaging. PET Clin. 2021 Apr;16(2):219–31.

46. Borja AJ, Saini J, Raynor WY, Ayubcha C, Werner TJ, Alavi A, et al. Role of Molecular Imaging with PET/MR Imaging in the Diagnosis and Management of Brain Tumors. PET Clin. 2022 Jul;17(3):431–51.

47. Dunet V, Pomoni A, Hottinger A, Nicod-Lalonde M, Prior JO. Performance of 18F-FET versus 18F-FDG-PET for the diagnosis and grading of brain tumors: systematic review and meta-analysis. Neuro-Oncol. 2016 Mar;18(3):426–34.

48. Kim JH, Lee SH, Lim SM, Hong SW. Evaluation of Brain SPECT Using Tc-99m-Glucoheptonate and Tc-99m-HMPAO in Brain Tumors. J Korean Neurosurg Soc. 18(5):706–15.

49. Karunanithi S, Bandopadhyaya GP, Sharma P, Kumar A, Singla S, Malhotra A, et al. Prospective Comparison of 99mTc-GH SPECT/CT and 18F-FDOPA PET/CT for Detection of Recurrent Glioma: A Pilot Study. Clin Nucl Med. 2014 Feb;39(2):e121–8.

50. Kim D, Ko HY, Lee S, Lee YH, Ryu S, Kim SY, et al. Glucose Loading Enhances the Value of 18F-FDG PET/CT for the Characterization and Delineation of Cerebral Gliomas. Cancers. 2020 Jul 20;12(7):E1977.

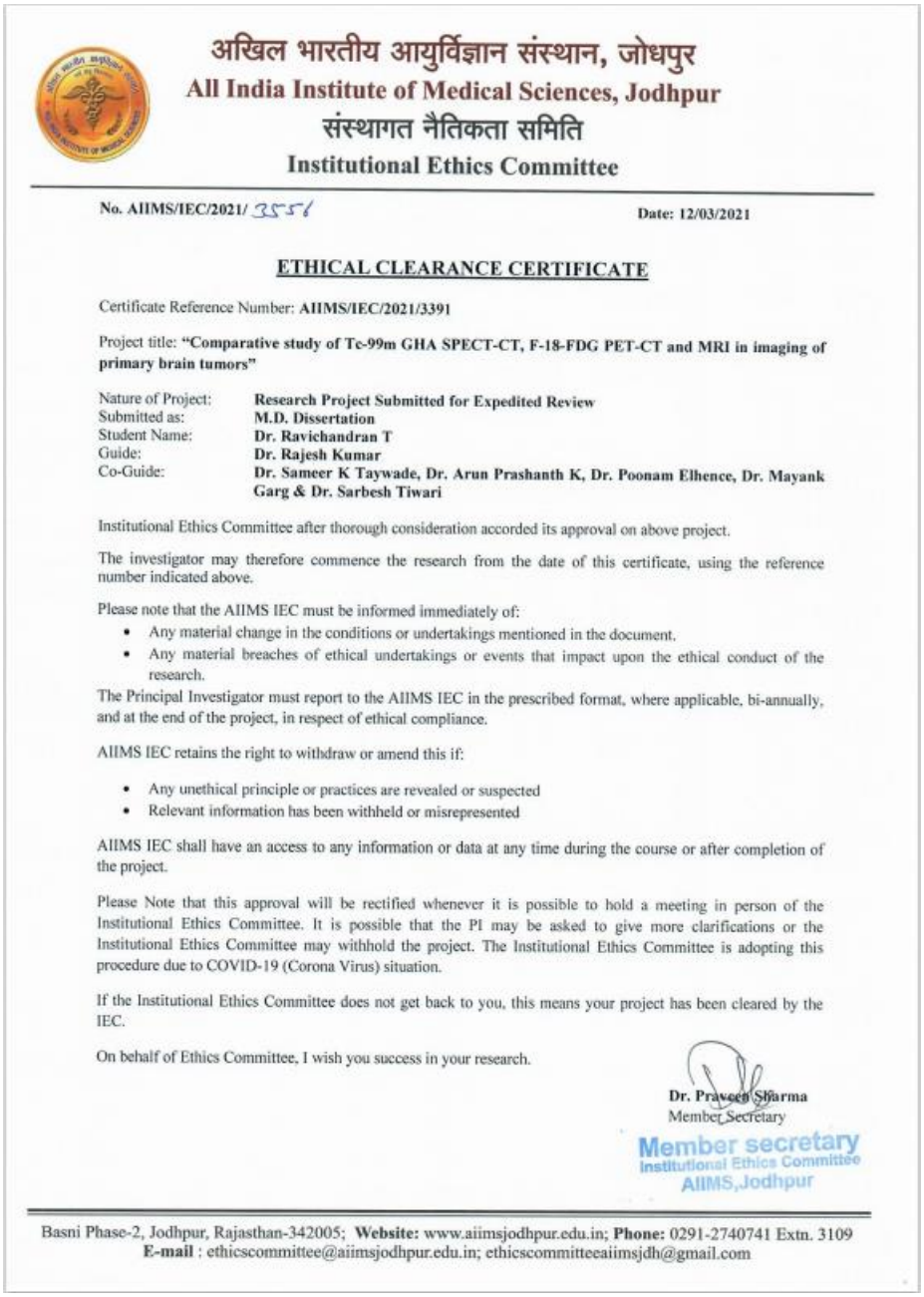
51. Almutrafi A, Bashawry Y, AlShakweer W, Al-Harbi M, Altwairgi A, Al-Dandan S. The Epidemiology of Primary Central Nervous System Tumors at the National Neurologic Institute in Saudi Arabia: A Ten-Year Single-Institution Study. J Cancer Epidemiol. 2020 Feb 15;2020:e1429615.

52. McKinney PA. Brain tumours: incidence, survival, and aetiology. J Neurol Neurosurg Psychiatry. 2004 Jun;75 Suppl 2:ii12-17.

53. Delbeke D, Meyerowitz C, Lapidus RL, Maciunas RJ, Jennings MT, Moots PL, et al. Optimal cutoff levels of F-18 fluorodeoxyglucose uptake in the differentiation of low-grade from high-grade brain tumors with PET. Radiology. 1995 Apr;195(1):47–52.

ANNEXURE - I

Institutional Ethical Clearance certificate



अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/ 3551 Date: 12/03/2021

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3391**

Project title: **"Comparative study of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and MRI in imaging of primary brain tumors"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**M.D. Dissertation**
Student Name:	**Dr. Ravichandran T**
Guide:	**Dr. Rajesh Kumar**
Co-Guide:	**Dr. Sameer K Taywade, Dr. Arun Prashanth K, Dr. Poonam Elhence, Dr. Mayank Garg & Dr. Sarbesh Tiwari**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS, Jodhpur

Basni Phase-2, Jodhpur, Rajasthan-342005; **Website:** www.aiimsjodhpur.edu.in; **Phone:** 0291-2740741 Extn. 3109
E-mail : ethicscommittee@aiimsjodhpur.edu.in; ethicscommitteeaiimsjdh@gmail.com

ANNEXURE-II

CLINICAL SHEET

Name: Age/Sex:

H/o prior brain surgery	
H/o prior cranial irradiation	
H/o contrast allergy	
Blood urea	
Serum creatinine	
Blood glucose	

UHID: Ref. by:

Height/weight	
LMP	

Clinical Details:
Chief complaints:

Past history:

Family history:

Investigations:

Biochemical:

Imaging

	Tc99m GHA SPECT-CT	F-18-FDG PET-CT
Date:		
RP injected:		
Injected by:		
Time of injection:		
Dose Injected:		
Pre syringe:		
Post syringe:		
Acquisition Time:		
Acquired by:		

ANNEXURE - III

INFORMED CONSENT FORM

Title of Thesis/Dissertation : Comparative study of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and MRI in imaging of primary brain tumors.

Name of PG Student : Ravichandran T Tel. No: 8825739423

Patient/Volunteer Identification No. : _____ I,_____
S/o or D/O_____ R/o_____

give my full, free, voluntary consent to be a part of the study "**Comparative study of Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and MRI in imaging of primary brain tumors",** the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary and am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by a responsible individual from _____ (Company Name) or from regulatory authorities. I give permission for these individuals to have access to my records.

Date: _____ _____

Place: _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date: _____ _____

Place: _____ Signature of PG Student

1. Witness 1

_____
Signature
Name: _____
Address: _____
_____

2. Witness 2

_____
Signature
Name: _____
Address: _____
_____

ANNEXURE-IV

अखिल भारतीय आयुर्विज्ञान संस्थान जोधपुर, राजस्थान

सूचित सहमति प्रपत्र

थीसिस / शोध प्रबंध का शीर्षक: प्राथमिक ब्रेन ट्यूमर की इमेजिंग में Tc-99m GHA SPECT-CT, F-18-FDG PET-CT और MRI का तुलनात्मक अध्ययन

पीजी छात्र का नाम: Dr. RAVICHANDRAN T Tel. No. 8825739423

रोगी / स्वयंसेवक पहचान संख्या: _____

मैं, _____ पिता का नाम_____

पता_____

मेरी पूर्ण, मुक्त, स्वैच्छिक सहमति " प्राथमिक ब्रेन ट्यूमर की इमेजिंग में **Tc-99m GHA SPECT-CT, F-18-FDG PET-CT** और **MRI** का तुलनात्मक अध्ययन" अध्ययन का एक हिस्सा बनने के लिए देता हूँ, जिसकी प्रक्रिया और प्रकृति मुझे अपनी भाषा में मेरी पूर्ण संतुष्टि के लिए समझाया है। मैं पुष्टि करता हूं कि मुझे सवाल पूछने का अवसर मिला है।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और बिना किसी कारण के किसी भी समय अध्ययन से बाहर निकलने के मेरे अधिकार से अवगत हूं।

मैं समझता हूं कि मेरे और मेरे किसी भी मेडिकल रिकॉर्ड के बारे में एकत्रित जानकारी को _____ (कंपनी का नाम) या नियामक अधिकारियों के जिम्मेदार व्यक्ति द्वारा देखा जा सकता है। मैं इन व्यक्तियों को अपने रिकॉर्ड तक पहुंचने की अनुमति देता हूं।

दिनांक:_____ _____

जगह: _____ हस्ताक्षर / बाएं अंगूठे का निशान

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है।

दिनांक:_____ _____

स्थान: _____ पीजी छात्र के हस्ताक्षर

1. साक्षी 1

_____

हस्ताक्षर

नाम:_____

पता:_____

_____

2. गवाह 2

_____

हस्ताक्षर

नाम_____

पता_____

_____

ANNEXURE - V

PATIENT INFORMATION SHEET

Name of the patient: **Patient ID:**

1. **Aim of the study:** To compare Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and Magnetic Resonance Imaging in management of primary brain tumors.
2. **Study setting:** Department of Nuclear Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan.
3. **Study procedure:** The participants will have to undergo Tc-99m GHA SPECT-CT, F-18-FDG PET-CT and MRI scans pre-operatively. These scans will be repeated if they suspected of recurrence.
4. **Likely benefit:** The study will add more value in the diagnosis of brain tumors. It will also help in grading of brain tumors preoperatively. This will help in prognostication and better risk assessment.
5. **Confidentiality:** All the data collected from each study participant will be kept highly confidential.
6. **Risk:** Enrolment in the above study poses no substantial risk to any of the study participant and if the participant wants to withdraw himself/ herself, he/ she can do so voluntarily at any point of time during the study.

For further information or questions, the following personnel can be contacted:

Dr. Ravichandran T, Junior Resident, Department of Nuclear Medicine, All India Institute of Medical Sciences, Jodhpur.

Mobile Number: 8825739423, Email: ravit1594@gmail.com

ANNEXURE- VI

रोगी सूचना पत्र

रोगी का नाम: रोगी आईडी:

1. अध्ययन का उद्देश्य: प्राथमिक मस्तिष्क ट्यूमर के प्रबंधन में Tc-99m GHA SPECT-CT, F-18-FDG PET-CT और MRI की तुलना करना।

2. अध्ययन सेटिंग: परमाणु चिकित्सा विभाग, अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर, राजस्थान।

3. अध्ययन प्रक्रिया: प्रतिभागियों को Tc-99m GHA SPECT-CT, F-18-FDG PET-CT और MRI स्कैन पूर्व-संचालन से गुजरना होगा। यदि उन्हें पुनरावृत्ति की आशंका है तो ये स्कैन दोहराए जाएंगे।

4. संभावित लाभ: अध्ययन ब्रेन ट्यूमर के निदान में अधिक मूल्य जोड़ देगा। यह प्रीऑपरेटिव रूप से ब्रेन ट्यूमर की ग्रेडिंग में भी मदद करेगा। यह पूर्वानुमान और बेहतर जोखिम मूल्यांकन में मदद करेगा।

5. गोपनीयता: प्रत्येक अध्ययन प्रतिभागी से एकत्र किए गए सभी डेटा को अत्यधिक गोपनीय रखा जाएगा।

6. जोखिम: उपरोक्त अध्ययन में नामांकन से अध्ययन के किसी भी प्रतिभागी को कोई भारी जोखिम नहीं होता है और यदि प्रतिभागी स्वयं को स्वयं वापस लेना चाहता है, तो वह अध्ययन के दौरान किसी भी समय स्वेच्छा से ऐसा कर सकता है।

अधिक जानकारी या प्रश्नों के लिए, निम्नलिखित कर्मियों से संपर्क किया जा सकता है:

डॉ। रविचंद्रन, जूनियर रेजिडेंट, परमाणु चिकित्सा विभाग, अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर।

मोबाइल नंबर: 8825739423, ईमेल: ravit1594@gmail.com

ANNEXURE VII

No.	Parameters	Tumor grades		Subgroups low vs. high grades		No.	Parameters	Tumor grades		Subgroups Low vs high grades	
		Correlation Coefficient	P value	Correlation Coefficient	p value			Correlation Coefficient	p value	Correlation Coefficient	p value
1	Tumor maximum	0.479	0.060	0.420	0.105	29	Cerebellum mean	-0.444	0.085	-.532*	0.034
2	Tumor mean	0.444	0.085	0.392	0.133	30	Cerebellum peak	-0.444	0.085	-.532*	0.034
3	Tumor peak	0.470	0.066	0.420	0.105	31	Tumor max to cerebellum max	.746**	0.001	.728**	0.001
4	Contralateral maximum	-0.022	0.935	-0.112	0.680	32	Tumor mean to cerebellum mean	.705**	0.002	.728**	0.001
5	Contralateral average	0.200	0.458	0.112	0.680	33	Tumor peak to cerebellum peak	.762**	0.001	.728**	0.001
6	Contralateral peak	0.235	0.381	0.112	0.680	34	Mesial temporal max	-0.368	0.161	-0.448	0.082
7	Tumor max to contralateral max	.590*	0.016	.588*	0.017	35	Mesial temporal avg	-0.441	0.087	-0.476	0.062
8	Tumor mean to contralateral mean	.616*	0.011	.616*	0.011	36	Mesial temporal peak	-0.451	0.080	-.504*	0.046
9	Tumor peak vs contralateral peak	0.425	0.101	0.420	0.105	37	Tumor max to mesial temporal max	.790**	0.000	.812**	0.000
10	Whitematter max	-0.146	0.590	-0.056	0.837	38	Tumor mean to mesial temporal mean	.778**	0.000	.812**	0.000
11	Whitematter avg	-0.369	0.160	-0.449	0.081	39	Tumor peak to mesial temporal peak	.778**	0.000	.812**	0.000

12	Whitematter peak	-0.152	0.573	-0.182	0.500	40	Pons max	-0.403	0.122	-0.476	0.062
13	Tumor max to whitematter max	.574*	0.020	.532*	0.034	41	Pons avg	-0.421	0.105	-.504*	0.046
14	Tumor mean to whitematter mean	.698**	0.003	.700**	0.003	42	Pons peak	-0.413	0.112	-0.476	0.062
15	Tumor peak to whitematter peak	.581*	0.018	.532*	0.034	43	Tumor max to pons max	.739**	0.001	.728**	0.001
16	Greymatter max	-0.457	0.075	-0.420	0.105	44	Tumor mean to pons mean	.752**	0.001	.756**	0.001
17	Greymatter avg	-.581*	0.018	-.616*	0.011	45	Tumor peak to pons peak	.787**	0.000	.756**	0.001
18	Greymatter peak	-0.390	0.135	-0.336	0.203	46	Volume of tumor	-0.289	0.278	-.532*	0.034
19	Tumor max to Greymatter max	.632**	0.009	.616*	0.011	47	SUVmax	0.447	0.082	0.392	0.133
20	Tumor mean to Greymatter mean	.730**	0.001	.784**	0.000	48	SUVmean	.536*	0.032	.504*	0.046
21	Tumor peak to Greymatter peak	.622*	0.010	.616*	0.011	49	TLG	0.108	0.691	-0.168	0.534
22	Basal ganglia max	-0.460	0.073	-.588*	0.017	50	GN max	0.447	0.082	0.392	0.133
23	Basal ganglia avg	-.552*	0.027	-.700**	0.003	51	GN mean	.635**	0.008	.644**	0.007
24	Basal ganglia peak	-0.486	0.057	-.644**	0.007	52	GN TLG	0.114	0.674	-0.140	0.605
25	Tumor max to basal ganglia max	.746**	0.001	.756**	0.001	53	SUVpeak	0.470	0.066	0.392	0.133
26	Tumor mean to	.695**	0.003	.700**	0.003	54	CT max	-0.095	0.726	-0.224	0.404

	basal ganglia mean										
27	Tumor peak to basal ganglia peak	.711**	0.002	.700**	0.003	55	CT avg	.657**	0.006	.700**	0.003
28	Cerebellum maximum	-0.409	0.115	-0.476	0.062	56	CT volume	-0.238	0.375	-0.476	0.062

Table 25: *Correlation coefficients of quantitative parameters and various parameters ratios on F-18-FDG PET-CT for histopathological grades in Glial tumors.*

Correlation significant at level ** ($p < 0.01$) and Correlation significant at level * ($p < 0.05$).