Original Article

Correlation of Target Volumes on Magnetic Resonance Imaging and Prostate-Specific Membrane Antigen Brain Scans in the Treatment Planning of Glioblastomas

Vutkuri Lavanya, Irukulla Monica Malik, Kavitha Nallapareddy[1], Madhur Srivastava[1], Deepthi Valiyaveettil, Syed Fayaz Ahmed

Departments of Radiation Oncology and [1]Nuclear Medicine, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract

Background: Imaging of gliomas/glioblastomas has always been challenging. Many magnetic resonance imaging (MRI) techniques are available for imaging glioblastomas. MRI cannot always differentiate tumor from nonspecific changes and postoperative changes in brain tissue. Among the new positron emission tomography–computed tomography (PET-CT) tracers, gallium-68 prostate-specific membrane antigen (Ga-68 PSMA-11 PET-CT) appears to be the most promising one. The absence of uptake by normal brain parenchyma leads to high tumor-to-background ratio leading to better visualization of the tumor. **Objective:** The aim of this study was to assess the correlation of target volumes on MRI and PSMA brain scans in the treatment planning of glioblastomas. **Materials and Methods:** Twenty-four patients in the age group of 5–75 years with histologically proven glioblastoma were included in the study following maximum safe resection. Simulation for treatment planning was done with Ga-68 PSMA PET-CT brain with IV iodine-based contrast. The pre- and postoperative MRI images were fused with PSMA simulation images. Gross tumor volumes (GTVs) contoured on T1-contrast MRI and on PSMA scans were compared. **Results:** GTV contoured on MRI and PSMA brain scans showed complete overlap in 17 patients. In seven patients, the target volumes drawn on Ga-68 PSMA brain scans were slightly smaller than the target volumes drawn on MRI brain scans. This difference in volumes could be due to postoperative changes which showed enhancement on the MRI scan. **Conclusion:** Ga-68 PSMA PET-CT shows good correlation with MRI brain in the evaluation and RT planning in glioblastomas. Tumor necrosis and postoperative changes did not show PSMA uptake. Precise target delineation on PSMA PET-CT can potentially result in smaller and more accurate GTVs, which in turn would result in less RT-induced side effects.

Keywords: *Gallium-68 prostate-specific membrane antigen, glioblastoma, gross tumor volumes, positron emission tomography/magnetic resonance imaging correlation*

Introduction

Glioma is a type of tumor that starts in the glial cells of the brain and spine. Gliomas comprise about 30% of all brain tumors and 80% of all malignant brain tumors.[1] Standard treatment for glioblastoma consists of maximal safe resection followed by concurrent chemoradiation with temozolomide followed by six cycles of adjuvant temozolomide.

Many magnetic resonance imaging (MRI) techniques are available for imaging gliomas, for example, diffusion-weighted imaging, perfusion MRI, Magnetic Resonance Spectroscopy (MRS), and diffusion tensor imaging, but they have some associated problems. MRI cannot always differentiate tumor from nonspecific changes in brain tissue. It cannot reliably differentiate tumor from postoperative changes. Many traditional and new positron emission tomography (PET) tracers have also come into existence. Fluorodeoxyglucose (FDG) PET has limitations in the evaluation of gliomas because of high background uptake by normal brain tissue. It may miss tumors with low glucose metabolism.

Among the new tracers, gallium-68 prostate-specific membrane antigen (Ga-68 PSMA-11 PET-CT) appears to be the most promising one. The absence of uptake by normal brain parenchyma leads to high tumor-to-background ratio leading to better visualization of the tumor. Better visualization of the tumor leads to accurate delineation of the target volume for

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Address for correspondence:
Dr. Irukulla Monica Malik, Department of Radiation Oncology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad - 500 082, Telangana, India.
E-mail: dr_monica11@yahoo.com

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radiation therapy leading to better sparing of normal tissues which in turn leads to decrease in the treatment-related sequelae. Till date, only limited studies have been done to assess the usefulness of PSMA PET scan in imaging gliomas. The aim of the present study is to assess the correlation of target volumes on MRI and PSMA brain scans in the treatment planning of glioblastomas.

Materials and Methods

Twenty-four patients in the age group of 5–75 years with histologically proven glioblastoma were included in the study following maximal safe excision. For the purpose of immobilization during simulation and treatment, a customized thermoplastic brain mask was used for every patient. Simulation for treatment planning was done with Ga-68 PSMA PET-CT brain with IV iodine-based contrast. The pre- and postoperative MRI images were fused with PSMA simulation images using rigid registration algorithms on Eclipse™ treatment planning system version 15.1 (Varian Medical Systems, Palo Alto). Contouring of target volumes was done as follows:

- All the contrast-enhancing areas on T1 contrast MRI sequence were included in gross tumor volume (GTV) MRI
- All the Ga-68 PSMA-avid regions on PSMA brain scan are included in GTV PSMA.

The data were analyzed on Microsoft Excel 2019 and SPSS v20 (IBM Statistical Package for Social Sciences, Chicago, IL, USA).

Results

Patient characteristics

All the 24 patients were histologically proven cases of glioblastoma following maximal safe resection. Patient characteristics are summarized in Table 1.

Target volumes

The mean volume of GTV contoured on MRI was 30.10 cm^3, and the mean volume of GTV contoured on PSMA scan was 25.28 cm^3. In our study, we observed that GTV contoured on MRI and PSMA brain scans showed good overlap in 17 patients [Figure 1]. In seven patients, the target volumes drawn on Ga-68 PSMA brain scans are slightly smaller than the target volumes drawn on MRI brain scans. We noticed that this difference in volumes is mainly because of the absence of PSMA uptake in areas of postoperative changes which showed enhancement on the MRI scan.

Survival

The overall median survival [Figure 2] from the date of surgery in our study was 15 months.

Table 1: Details of patients, location of glioblastoma, and immunohistochemistry

Patient characteristics	Number of patients
Female	9
Male	15
Age of the patients (years)	
≤50	14
>50	10
Location of the tumor	
Frontal	9
Temporal	12
Parietal	3
IHC	
IDH-1 wild	17
IDH-1 mutant	3
IDH status unknown	4
ATRX	
ATRX loss	3
ATRX retained	12
ATRX status unknown	9
P53	
Positive	10
Negative	6
Unknown	8
Ki-67 (%)	
≤30	6
>30	9
Unknown	9

IHC: Immunohistochemistry, IDH: Isocitrate dehydrogenase, ATRX: Alpha-thalassemia X-linked mental retardation, Ki-67: Ki-67

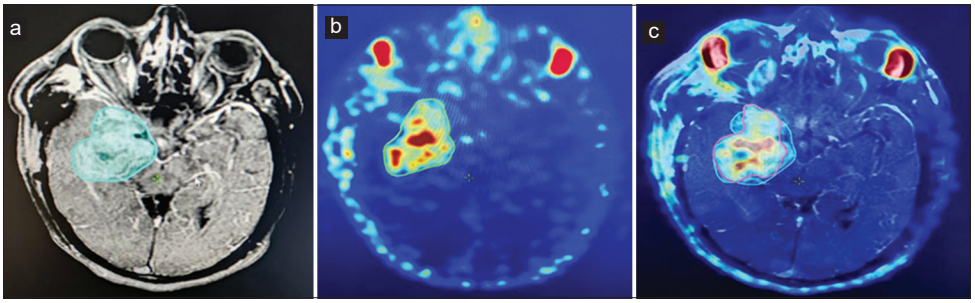

Figure 1: (a) Gross target volume contoured on T1C magnetic resonance imaging brain, (b) Gross target volume on prostate-specific membrane antigen positron emission tomography–computed tomography scan, (c) Overlap image of gross target volume magnetic resonance imaging and gross target volume prostate-specific membrane antigen positron emission tomography–computed tomography Scan showing good correlation

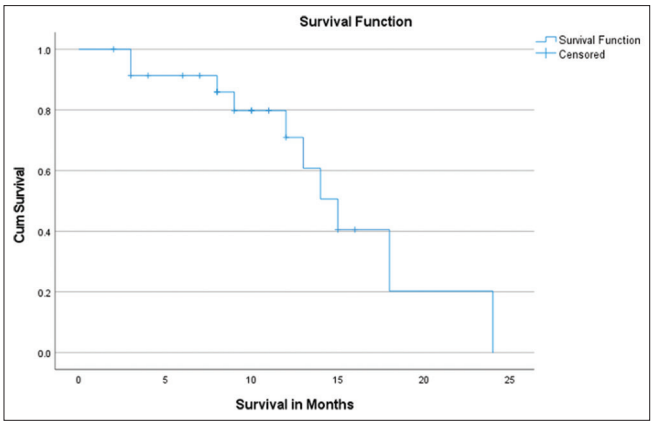

Figure 2: Kaplan–Meier overall survival curve

Imaging of gliomas/glioblastomas has always been challenging. MRI cannot always differentiate tumor from nonspecific changes and postoperative changes in brain tissue. Many traditional and new PET tracers have also come into existence. FDG PET has limitations in the evaluation of gliomas because of high background uptake by normal brain tissue. It may miss tumors with low glucose metabolism.

Among the newer tracers, Ga-68 PSMA is the most promising one. The PSMA is a type II transmembrane protein physiologically expressed by prostate tissue and significantly overexpressed by most of the prostate cancer cells. However, PSMA is not solely expressed by prostate tissue. PSMA overexpression also occurs in pathophysiological processes other than prostate cancer, especially in the neovasculature of many solid tumors (for example, colon, gastric, lung, breast, adrenal, bladder, and renal cell carcinoma). This has important potential implications for PSMA-targeted imaging and possibly also therapies. Tumor specimen analysis and immunohistochemical studies have suggested the presence of PSMA expression of gliomas.[2]

Sasikumar *et al*.[3] conducted a pilot study on ten patients with brain space-occupying lesions (SOLs). Five patients were treated cases of glioblastoma with suspected recurrence. The remaining five cases were imaged to know the nature of the SOL in the brain (primary or metastasis). In the five suspected cases of recurrent glioblastoma, PSMA scan showed good correlation with F^{18}-FDG PET/CT scan. The recurrent lesion was better visualized on PSMA scan owing to its significantly high target-to-background ratio. Among the other five cases, glioma and atypical meningioma showed higher SUV max in the lesion with PSMA than with F^{18}-FDG and converse in lymphoma cases. They concluded that Ga-PSMA-11 PET/CT brain imaging is a potentially useful investigation in the evaluation of gliomas.

Sasikumar *et al*.[4] also performed another study to know the usefulness of PSMA scan in evaluating recurrent glioblastoma cases. PSMA scan was done in ten patients of suspected recurrence on MRI scan. Nine out of these ten cases showed uptake on PSMA scan, and subsequent histopathology confirmed it as recurrent glioblastoma. In the scan-negative case, follow-up MRI at 9-month interval did not show any evidence of lesion.

Bertagna *et al*.[2] have done a literature review of the PubMed/MEDLINE, Scopus, Embase, and Cochrane library database to find relevant published articles about the diagnostic performance of radiolabeled PSMA-binding agents in PET/CT or PET/MRI imaging of patients with suspected gliomas or glioblastomas. They found that seven case reports or case series and three studies enrolling more than ten patients showed that gliomas and glioblastomas are PSMA-avid tumors. There is enough evidence to suggest that glioblastomas show PSMA avidity. Due to high tumor-to-background ratio, contouring of GTV on Ga-68 PSMA scans is easy and precise.

Currently, there are no studies which correlated postoperative MRI and PSMA brain scans in the management of glioblastoma. In our study, we observed that MRI and PSMA brain scans showed good correlation, but the target volumes drawn on Ga-68 PSMA brain scans are slightly smaller than the target volumes drawn on MRI brain scans in some patients which could be due to the absence of PSMA uptake by the central necrotic areas and some postoperative changes which however show enhancement on T1C MRI. Precise contouring of tumor on PSMA brain scan leads to smaller target volumes which in turn results in fewer Radiotherapy (RT)-induced side effects.

Conclusion

Ga-68 PSMA PET-CT shows good correlation with MRI brain in the evaluation and RT planning in glioblastomas. The target volumes drawn on Ga-68 PSMA brain scans are slightly smaller than the target volumes drawn on MRI brain scans in some patients. Tumor necrosis and postoperative changes did not show PSMA uptake. Precise target delineation on PSMA PET-CT results in smaller GTVs which in turn result in less RT-induced side effects. A larger study with histopathological correlation is needed to confirm these results.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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