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Data Article

A dataset of [^{68}Ga]Ga-Pentixafor PET/CT images of patients with high-grade Glioma

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ABSTRACT

This paper contains single-center prospective information showing illustrative examples of chemokine receptor-4 (CXCR4) targeting in high-grade glial brain tumors in treatment-naïve adult patients using a novel radiolabeled PET tracer: [^{68}Ga]Ga-CXCR4 PET/CT.

High-grade glioma is one of the most resistant malignancies to treatment. Despite major breakthroughs in diagnostic and therapeutic approaches, the overall 5-year survival rate remains in the 5–10% range. CXCR4 is a chemokine with the C-X-C motif that is overexpressed in high-grade gliomas.

The 24 consecutive treatment- naïve enrolled patients underwent PET/CT images using the SIEMENS scanner (Biograph6 TrueV) and received the radiotracer intravenously. After approximately 60 min, the PET/CT acquisition was performed with a dedicated scanner and in 10 min time per bed position. The images were reconstructed and analyzed with the 3D-OSEM algorithm, applying point spread function (PSF) or resolution recovery algorithm (TrueX in Syngo ® software, Siemens Medical Solution), 3 iterations, and 21 subsets using a 3 mm Gaussian post-smoothing filter.

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These data would be potentially beneficial for automatic tumor delineation machine learning after augmented with other data retrieved from different papers as well as for differentiation between an active viable tumor vs. post-surgery/necrosis in indeterminate cases. The theranostics potential (CXCR4-tageted labeled beta emitters) is one of the most novel areas of interest for future studies.

Specifications Table

Subject	Health and medical sciences
Specific subject area	Medical Imaging, Nuclear medicine
Type of data	Clinical images (computed tomography, positron emission tomography), DICOM images, Table
How the data were acquired	Biograph 6 True Point True PET/CT scanner (Siemens Healthcare, Erlangen, Germany) was used for image acquisition, and Syngo® software, SIEMENS Medical Solution was applied for image analysis.
Data format	Raw and analyzed data
Description of data collection	Patients with biopsy-proven (stereotactic or excisional) high-grade brain glioma were enrolled before initiation of therapy for in vivo assessment of CXCR4 expression using [^{68}Ga]Ga-Pentixafor as a novel CXCR4-PET imaging.
Data source location	Ghaem Hospital and Razavi Hospital, Mashhad, Iran
Data accessibility	Data are provided in this article and the Mendeley Data website. Repository name: Roustaei, Hessamoddin; Vosoughi, Habibeh; Aryana, Kamran; Norouzbeigi, Nasim (2023), "[68G*a*]Ga-Pentixafor PET/CT images of glioma patients ", Mendeley Data, V1, doi:10.17632/4xs94489rw.1 Direct URL to data: https://data.mendeley.com/datasets/4xs94489rw

Value of the Data

- The data represent the illustrative PET/CT images with the ability to diagnose high-grade glioma. Also, they explain how to in vivo assess CXCR4 receptor expression in high-grade glial tumors lesions on positron emission tomography (PET).
- These data are meant to be valuable for differentiating viable tumoral tissue from non-tumoral residue which is one of the main shortcomings of the conventional imaging modalities. And it would be useful for following up of the treated patients.
- These data would be helpful for artificial intelligence analysis (e.g., Deep Learning), in multicenter studies, for in vivo assessment of brain tumors and potentially reduce the need for surgical tissue sampling for diagnosis.
- These data would be beneficial for further investigations toward tumor delineation for radiation therapy on patients suffering from brain tumors.
- These data would be useful for further research focusing CXCR4 targeted therapies; theranostic application.

1. Objective

High-grade glioma is one of the most prevalent and fatal primary brain tumors among adults. Yet, there is no definite curative treatment. Invasive tissue sampling is the main method of diagnosis. Although Magnetic Rresonance Imaging (MRI) is the most common modality for brain tumor imaging, molecular imaging like PET/CT is often acquired for the characterization and de-

tection of the metabolically active part of the tumor [1,2]. In the MRI images, the disruption of the blood-brain barrier is detected only; not tumor activity. So, it may result in a false positive output. To overcome the limitations of conventional MRI, multimodal MRI such as Magnetic Resonance Spectroscopy (MRS), Diffusion-Weighted imaging (DWi), and Perfusion-Weighted imaging (PWI) have been acquired. Using PET radiopharmaceuticals based on radiolabeled amino acid (e.g., [^{18}F]F-FOPA and [^{18}F]F-FET) for the imaging of brain tumors was also proposed [3,4].

Surprisingly, CXCR4 has been reported to be overexpressed in viable high-grade glioma e.g., glioblastoma (GBM), without uptake in normal brain tissue [1,5]. The new PET conjugated radiotracer targeting CXCR, [^{68}Ga]Ga-Pentixafor, has been applied for brain tumor imaging, and it could be used as a new potential agent for targeted radionuclide therapy in the future after validation.

The objective of these data is to provide information for the diagnosis, delineation, and potential differentiation of high-grade glioma tumors with a non-invasive, precise, and molecular tracer.

2. Data Description

This study was performed prospectively in one PET/CT institute. The data consists of 24 treatment-naïve patients with glioma (neither radiotherapy nor chemotherapy), and all underwent PET/CT imaging examination after surgery. They were referred to the nuclear medicine department, which was equipped with a PET/CT scanner, for assessment of CXCR4 receptor expression in high-grade glioma. The overall 5-year survival rate remains in the 5–10% range. CXCR4 is a chemokine with the C-X-C motif that is overexpressed in high-grade gliomas [6–8]. For more information, please see our project's recently published research supplements [9,10]. Our data consisted of raw and analyzed data. The raw dataset includes the PET and CT images of the patients as DICOM files in a certain folder related to patient numbers that are available on the Mendeley data website.

The patients' sex ratio (Male/Female) was 1.18 and the range of age was 17 to 72 years (mean: 52.63±14.9 y). The injected activity of [^{68}Ga]Ga-Pentixafor radiopharmaceutical ranged from 105.5 to 193.5 MBq (mean: 151.3 ± 22.8 MBq). It was almost constant among all patients without considering the weight. The location of tumors was variable in the brain and for quantitative analysis standard uptake value of the hottest voxel (SUV_{max}) within the delineated tumor was used. Summary of patients' information were presented in Table 1.

Figs. 1, 2, and 3 demonstrate examples of diagnostic PET and Fusion images of High-grade (III & IV) Glioma tumors in three different patients.

Table 1
Patient characteristics.

Patient No.	Age	Sex	Injected Activity (MBq)	Tumor location	Grade of Glioma	SUV_{max} of tumor
1	63	M	166.5	Rt-Temporal	**IV**	2.56
2	56	M	188.7	Rt-Frontotemporal	**IV**	2.50
3	58	F	105.45	Lt-Frontotemporal	**IV**	3.01
4	31	M	182.78	Rt-Frontotemporal	**IV**	6.62
5	33	M	129.5	Lt-Occipitoparietal	**IV**	3.03
6	68	M	165.39	Rt-Frontoparietal	**IV**	3.67
7	59	F	114.7	Lt-Occipitoparietal	**IV**	4.91
8	56	M	153.92	Rt-Frontoparietal	**IV**	2.80
9	55	F	161.69	Lt-Basal Ganglia	**IV**	5.75
10	65	F	148	Lt-Parietal	**IV**	3.56
11	65	F	118.4	Rt-Frontal	**IV**	5.02
12	62	M	148	Rt-Occipitoparietal	**IV**	1.87
13	64	F	138.01	Rt-Parietal	**IV**	1.84
14	46	M	140.6	Rt-Parietotemporal	**IV**	2.52
15	50	M	119.88	Lt-Frontotemporal	**IV**	2.31
16	63	F	160.95	Rt-Occipital	**IV**	9.96
17	33	F	149.11	Lt-Occipitoparietal	**III**	1.68
18	66	F	160.58	Rt-Parietotemporal	**IV**	4.63
19	17	M	177.97	Rt-Parietal	**IV**	1.30
20	51	M	193.51	Lt-Temporal	**IV**	3.14
21	35	M	155.03	Rt-Frontal	**III**	1.34
22	63	F	148	Lt-Frontal	**III**	0.74
23	31	F	149.85	Rt-Parietotemporal	**III**	2.05
24	72	M	155.4	Lt-Frontotemporal	**IV**	3.12

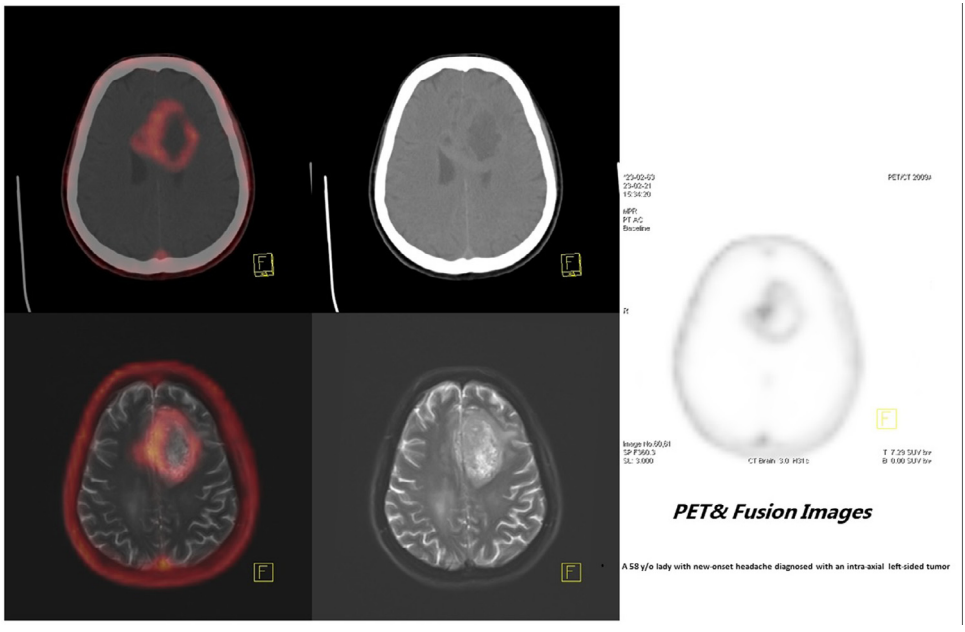

Fig. 1. PET, CT, MRI and fusion of PET and CT/MR images of a 58 y/o woman with new-onset headache diagnosed with the left intra-axial para-falcine mass with extension to the contra-lateral hemisphere which is confirmed with High-grade glioma (WHO IV). Based on WHO classification 2016.

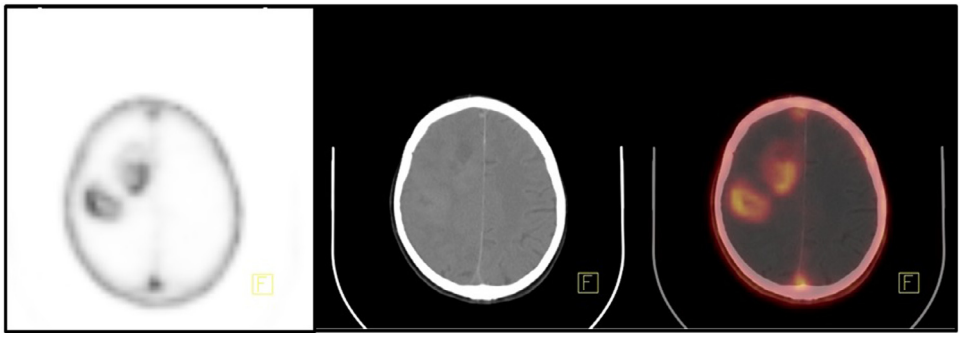

Fig. 2. A 68-year-old man with recent-onset left-sided limb paresthesia and no prior history of known malignancy diagnosed with the right fronto-parietal hypodense masses which after stereotactic Bx confined to High-grade glioma (WHO IV) IDH-1 Wild-type.

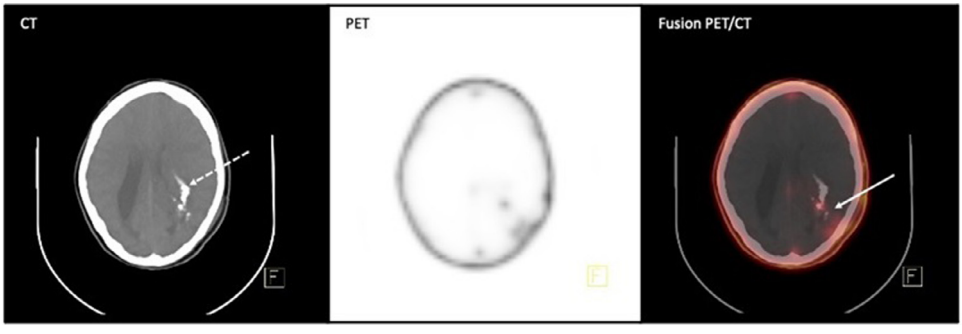

Fig. 3. PET, CT, and Fusion PET/CT images of a Thirty-three-year-old lady with a history of worsening headache from few months ago and new-onset seizure diagnosed with a left occipito-parietal mass spreading to lateral ventricle and basal ganglia (not shown). Excisional biopsy revealed Oligodendroglioma (WHO III). She was referred for in vivo evaluation of CXCR4 expression. Dashed arrow is pointing the calcification. Solid arrow shows minimal residual tumoral tissue.

3. Experimental Design, Materials and Methods

3.1. Patients

Over one year period, treatment-naïve patients with a solid brain tumor, high-grade glioma (grade III and IV), were consecutively enrolled and scanned for determination of tumor after the stereotactic or excisional biopsy. They were referred for imaging by an experienced oncologist based on the approved criteria of our study. The study was in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration. Written Informed consent was obtained. The demographic data and comprehensive medical history were obtained and recorded (Table 2).

Table 2
Inclusion & exclusion criteria.

Inclusion criteria	Exclusion criteria
Histopathologicaly proven High-grade glioma	If proven otherwise
Treatment-naive	If proven otherwise
Patient older than 18 years old	

4. Radiopharmaceutical, PET/CT Acquisition and Image Reconstruction

The following are descriptions of the injected radiopharmaceutical, image acquisition, and reconstruction.

- **Radiopharmaceutical**

The radiolabeling of ^{68}Ga-pentixafor was performed using a fully-automated (Scintomics GmbH) labeling module, which was carried out in accordance with GMP regulations. ^{68}Ga radioisotope was eluted with 0.1 M HCl from a PARS-GalluGEN ^{68}Ge/^{68}Ga generator and used in the radio-labeling process. Radioactivity was transferred to a strong cation exchange (SCX) cartridge. ^{68}Ga was eluted with NaCl (1.7 ml, 5 M) and transferred to a borosilicate vial containing 25 µg pentixafor and HEPES (3 ml, 1.5 M) as a buffer. The reaction mixture was heated to 125 °C for 6 min. After that, the reaction mixture was cooled and passed through a preconditioned C-18 cartridge. Cartridge was washed three times with water and eluted with 2 mL EtOH/H_2O (50/50) solution to obtain the [^{68}Ga]Ga-pentixafor. The pH was adjusted by adding 20 ml phosphate buffer saline (PBS). The final product was sterilized by a 0.22 µ Millex-LG filter (EMD Millipore) before clinical use. [^{68}Ga]Ga-pentixafor used in this study was characterized by [1] high radiochemical purity (> 98%), [2] radionuclide purity (> 99%), [3] endotoxin level (< 175 EU/ml), and [4] pH of 5–8.5.

- **Acquisition Protocol**

Patients were administrated with intravenous injection of [^{68}Ga]Ga-Pentixafor radiotracer, injected activity ranged from 114.7 to 193.5 MBq (mean: 154±21 MBq). Image acquisition was performed using the PET/CT scanner (Biograph 6 TrueV, SIEMENS Healthcare, Erlangen, Germany) with a 6-slice spiral CT component. The PET axial field of view was 21.6 cm and whole skull placed in one bed. Data were collected using the time-based method for 10 min per bed position, 60 min post intravenous injection. Diagnostic CT scans of the brain were acquired before PET scans for lesion localization, attenuation, and scatter corrections (240 mAs, 130 kV, 512×512 matrix size, 3 mm slice thickness, Recon increment of 1.5 mm, 1 s rotation time and pitch of 0.55).

- **Image Reconstruction**

PET image reconstructions were performed using the available PET/CT scanner software. Raw PET data were reconstructed with 3D-OSEM algorithm applying PSF resolution recovery (TrueX in Syngo ® software, SIEMENS Medical Solution), 3 iteration and 21 subsets using 3 mm Gaussian post smoothing filter. Matrix size was 168×168 resulting in 4.07 mm pixel size. Decay correction, attenuation and scatter correction were applied.

5. Image Analysis and Interpretation

Image analysis was performed using Syngo ® software (SIEMENS Medical Solution). 3D 50% isocontour volume of interest was drawn over the lesion(s). Maximum voxel value was recorded and SUV_{max} was calculated. Other VOIs in the same slice (level) were drawn over the contralateral normal brain tissue and brain venous blood pool (as background), for tumor-to-background ratio. PET images reported positive if there was more than background activity corresponding to concomitant CT findings. Firstly, Images were assessed qualitatively (visually) and then semi-quantitative analyses were done and the images were reported by two independent physicians who were trained in nuclear medicine. They were blinded to other imaging modalities of the patient (i.e., MRI, CT).

Ethics Statements

All procedures performed in studies involving human participants complied with the ethical standards of the institutional research committee as well as with the 1964 Helsinki declaration and its later amendments or other comparable ethical standards. Additionally, all patients provided written informed consent.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

[68Ga]Ga-Pentixafor PET/CT images of Glioma patients (Original data) (Mendeley Data).

CRediT Author Statement

Hessamoddin Roustaei: Investigation, Methodology, Writing – original draft; **Nasim Norouzbeigi:** Investigation, Funding acquisition; **Habibeh Vosoughi:** Methodology, Investigation, Writing – original draft; **Kamran Aryana:** Methodology, Supervision, Project administration, Funding acquisition.

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