Appendix 1

Inclusion and exclusion criteria

Inclusion criteria: (I) patients diagnosed with brain tumors confirmed by histopathology; (II) patients who have undergone brain positron emission tomography/magnetic resonance (PET/MR) imaging using standard clinical protocols; (III) PET scans performed with available raw data suitable for image reconstruction; (IV) age between 18 and 80 years.

Exclusion criteria: (I) patients with prior brain surgery, radiotherapy, or chemotherapy within 4 weeks before PET imaging, which may significantly alter PET signal; (II) PET scans with severe motion artifacts or technical issues rendering images unusable; (III) patients with significant comorbid neurological disorders that may affect PET image interpretation; (IV) patients without O-(2-^{18}F-fluoroethyl)-L-tyrosine (^{18}F-FET) avid findings on PET scans; (V) pregnancy or breastfeeding; (VI) incomplete clinical, imaging, or histopathological data.

Detailed information about the participants

There were 35 males and 27 females, with a mean age of 54±14 years (range, 19–79 years). The patients had an average weight of 68.9±14.1 kg (range, 36.0–117.0 kg). The distribution of the 62 cases was as follows: 37 gliomas and 25 metastatic tumors. Glioma diagnoses from before 2021 were classified according to the World Health Organization (WHO) 2016 classification, whereas those from 2021 onward followed the WHO 2021 classification. For the patients with multiple brain metastases, only the single FET-avid lesion with the largest volume was analyzed. All the patients were required to fast for a minimum of 4 hours before undergoing the imaging protocol. They were then intravenously injected with 261.6±65.8 MBq (range, 196.1–410.7 MBq) of ^{18}F-FET. The average injection dose per kilogram was 3.94±1.22 MBq/kg (range, 2.31–7.09 MBq/kg). The lesion volume was 36.13±34.63 mL (range, 1.32–145.79 mL).

Scanning parameters for MRI

Scanning parameters for three-dimensional T1-weighted (3D-T1) MRI were as follows: 3 ms echo time (TE), 7.2 ms repetition time (TR), 1 mm slice thickness, 256 mm × 256 mm FOV, and 256×100 acquisition matrix. Scanning parameters for T2-FLAIR MRI were as follows: 100.4 ms TE, 8,000 ms TR, 5 mm slice thickness, 256 mm × 256 mm FOV, and 256×100 acquisition matrix.

Quantitative feature extraction

Normalized ^{18}F-FET uptake was achieved using the standardized uptake value (SUV), which involves dividing the tissue radioactivity by the injected radioactivity per kilogram of body weight. We placed a spherical volume of interest (VOI) with constant size of 30 mm diameter and 14 mL volume in the contralateral hemisphere to the tumor as normal tissue, including gray and white matter. The tumor VOI was automatically segmented using a three-dimensional (3D) auto-contouring process with a tumor-to-brain ratio (TBR) of 1.6 or higher. This threshold has been reported to most effectively distinguish between vital tumors and healthy brain parenchyma in ^{18}F-FET PET based on a biopsy-controlled study (39,40). Eight common metabolic features of SUVmean, SUVmax, TBRmean, TBRmax, metabolic tumor volume (MTV), total lesion uptake (TLU), SUVmedian, and SUVpeak were automatically calculated for the VOI placed by the open-source software 3D Slicer (version 5.2.1). The MTV was defined as the total volume of voxels within the placed VOI. Radiomics features were also calculated on the ^{18}F-FET PET reconstruction images for each VOI using 3D Slicer. Shape features represent geometric features describing the form of regions or lesions in medical images. First-order features represent statistical features derived directly from voxel intensities within a region of interest. GLDM features describe the dependence between pairs of voxels based on their gray-level intensities. Gray-level run length matrix (GLRLM) features describe the distribution of co-linear voxels with the same gray-level intensity in various directions. GLSZM features describe the distribution of connected regions based on their gray-level intensities. In total, 57 radiomics features (14 shape, 15 first-order, 11 GLDM, 8 GLRLM, 9 GLSZM) were extracted.

SNR

As *Figure S1* indicates, HYPER iterative with time-of-flight (TOF) (HIWT) consistently achieved the highest SNR across all acquisition durations, suggesting superior noise performance. Ordered subset expectation maximization with TOF (OWT) also showed competitive SNR, particularly as acquisition duration increased. In contrast, ordered subset expectation maximization (OSEM) exhibited the lowest

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SNR values throughout the experiment. As acquisition time increased, the SNR and image quality improved. These findings were essential for optimizing PET imaging protocols to achieve an optimal balance between acquisition duration and image quality.

The impact of reconstruction settings on the reproducibility of radiomic features

The impact of reconstruction settings involving the number of iterations, point spread function (PSF) inclusion, and Gaussian post-filtering on the reproducibility of radiomic features was further studied. The parameters investigated included iteration numbers (3, 5, and 7), Gaussian filter full width at half maximum (FWHM) values (2, 4, and 6 mm), and reconstruction methods (OSEM + PSF + TOF, OSEM + PSF, OSEM + TOF, and OSEM). Specifically, each parameter was varied individually while keeping all other settings constant to assess their individual effects on intraclass correlation coefficient (ICC). The default reconstruction settings were: 20 subsets, a matrix size of 256×256, pixel dimensions of 1.2×1.2×1.4 mm, a FOV of 30 cm, an acquisition time of 20 minutes, 5 iterations, a Gaussian filter with an FWHM of 4 mm, and the OSEM + PSF + TOF reconstruction algorithm. The corresponding heat map is presented in *Figure S2*. Across different settings, 49, 46, and 44 radiomic features had ICC values above 0.95 for iteration numbers, PSF inclusion, and Gaussian filter FWHM, respectively. Among them, 2 features of first-order, 8 features of GLRLM, 9 features of GLSZM, 11 features of GLDM, and 14 features of shape were robust against all reconstruction parameter changes.

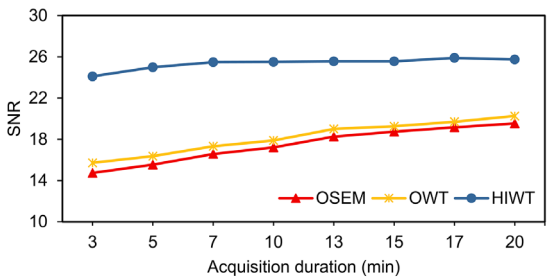

Figure S1 Change in SNR with acquisition duration for the three reconstruction algorithms: OSEM, OWT, and HIWT. HIWT, HYPER iterative with TOF; OSEM, ordered subset expectation maximization; OWT, OSEM with TOF; SNR, signal-to-noise ratio; TOF, time-of-flight.

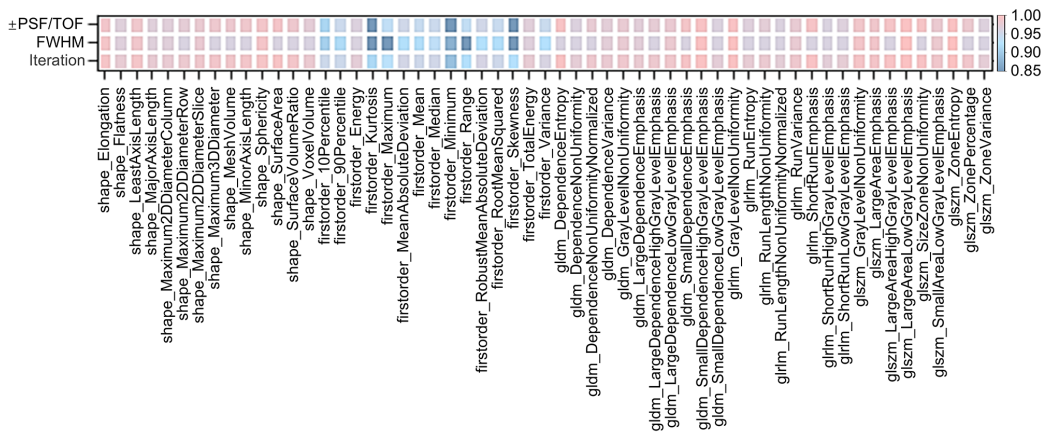

Figure S2 Heat map of ICC of radiomic features against different settings. FWHM, full width at half maximum; GLDM, gray-level dependence matrix; GLRLM, gray-level run length matrix; GLSZM, gray-level size zone matrix; ICC, intraclass correlation coefficient; PSF, point spread function; TOF, time-of-flight.

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