Expanding the Range of Extracted Dynamic FET Features as Candidate Glioblastoma Response Biomarkers

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ABSTRACT

Purpose: To assess the feasibility of using radiomics features from dynamic FET imaging parameterizations as potential biomarkers of glioblastoma (GBM) treatment response under test–retest conditions.

Methods: Dynamic 18F FET-PET data from 8 test–retest glioblastoma patients (16 datasets) were processed using a standardized pipeline to generate voxel-wise Logan parametric maps. Tumour ROIs were applied per-scan, with optional voxel-level R^2 gating to exclude poorly modelled voxels. Conventional radiomics features were extracted from parametric maps using a fixed, IBSI-aligned preprocessing configuration (3D resampling, fixed bin widths, and defined image types). Feature repeatability was assessed using ICC(1,1) and complementary agreement metrics. Sensitivity analyses evaluated stability under multiple gray-level discretization settings and across common filter families. Volume coupling and proportional bias were screened to identify features driven primarily by ROI size or systematic effects.

Results: A consistent subset of parametric-map features demonstrated high test–retest repeatability. Filter sensitivity analysis showed many stable features persisted across Original/Gaussian/transform families, while wavelet-derived features were substantially less repeatable overall.

Conclusions: Dynamic PET parametric-map radiomics can yield a robust core of repeatable features, but stability depends on discretization, filter choice, and ROI variability.

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INTRODUCTION

- Glioblastoma (GBM) is always lethal, and innovative approaches are required to improve therapies.
- Amino acid-based imaging using 18F-fluoroethyl-L-tyrosine (FET) PET has shown promise for identifying, staging and guiding disease treatment.
- FET PET dynamics could provide a useful layer of features for prognostic models and for identifying progression [1].
- This study utilized a retrospective cohort of GBM patient images to determine the robustness of dynamic FET PET features under test-retest conditions.

METHODS AND MATERIALS

- Data for 24 GBM patients formed an evaluation set, with 8 patients having test-retest FET PET scans taken with up to 7 days between scans.
- Repeatability of static features had already been established in this cohort by Barry et al [2].
- A pipeline was developed (see Figure 1) to extract parametric maps of the distribution-volume, VT, using a Logan (reversible) uptake model [3].
- Tumor and arterial volumes were provided by single observers. Multi-observer uncertainties have previously been quantified [2,4].
- PyRadiomics used for feature extraction.
- Maps resampled to isotropic 2 mm and intensity-normalized, and default bin width of 0.04 mL/mL.
- Repeatability metrics included mean/difference, Bland-Altman, coefficient of variation (wSC) and repeatability coefficient. Presented results include intraclass correlation coefficient (ICC) for one-way random effects and a single rater [ICC(1,1)].
- The impact of image filter was assessed across unfiltered, Laplacian-of-Gaussian (LOG) / Gaussian, intensity transforms, and wavelet transforms.
- The impact of intensity bin-width discretization was investigated by examining results across bin widths of 0.0, 0.04, 0.06 and 0.08 mL/mL.
- Feature/tumor-volume coupling was assessed via Spearman correlation.

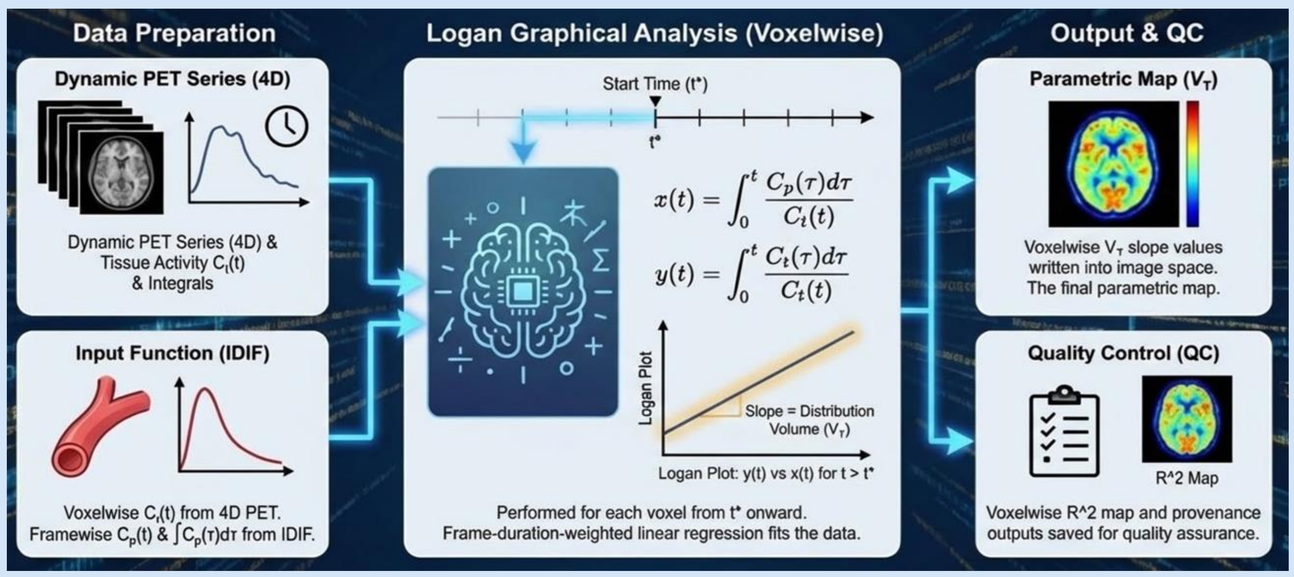

Figure 1. Pipeline for dynamic modelling. The result is a voxel-level map of dynamic parameter V_T, and an uncertainty map. Conventional radiomics features were extracted from the dynamic maps.

- Repeatability was assessed via the number of "keepers" amongst features for specific filter/bin width settings. A keeper was defined as a feature satisfying ICC(1,1)≥ 0.85, without extreme ROI-volume coupling, and without proportional bias after Benjamini–Hochberg adjustment.

Category	Number of features	Number with ICC ≥ 0.85	Stable fraction	Median ICC	Mean ICC	Median wSC
All features	106	67	63.2%	0.937	0.782	18.3%

Table 1. Baseline assessment of repeatability for radiomics features extracted from unfiltered Logan parametric maps for default bin width of 0.04 mL/mL.

RESULTS

- At the baseline level, without filtering and bin width of 0.04 mL/mL, feature extraction yielded 67 of 106 baseline features above the ICC (see Figure 2 and summary in Table 1), classified as "**baseline stable**".
- After assessing correlation with tumor volume, the number of stable features dropped to 56. After proportional bias screening, 51 features remained classified as "keepers" or 63.2%, classified as "**baseline keepers**".
- Application of filters increased the number of keepers and the proportion of all features except for in the case of wavelet filters (see Figure 2).
- Decreasing the bin width in gray-level discretization reduced the number of keepers. Increasing the number of keepers led to 54 at width 0.06 mL/mL and 55 at 0.08 mL/mL (see Figure 3). 44 features remained keepers across all tested bin widths and were classified as the "**consensus bank**" of stable features, being the ideal candidates for downstream modelling applications.
- The final consensus set (see Figure 4) of 44 canonical features comprises:
  - A 39-feature intensity-derived core in the following families;
    - NGTDM (Neighbourhood gray-tone difference matrix)
    - GLSZM (Gray-level size-zone matrix)
    - GLRLM (Gray-level run-length matrix)
    - GLDM (Gray-level dependence matrix)
    - GLCM (Gray-level co-occurrence matrix)
  - 5 shape/geometry-derived features

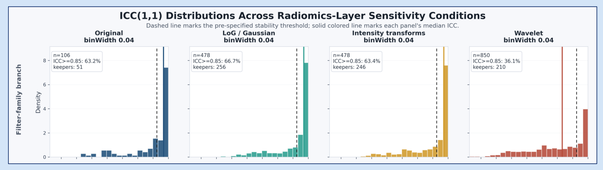

Figure 2. ICC(1,1) distributions across image filtering conditions, indicating both the number and proportion of extractable and stable features, as well as those identified as "keepers".

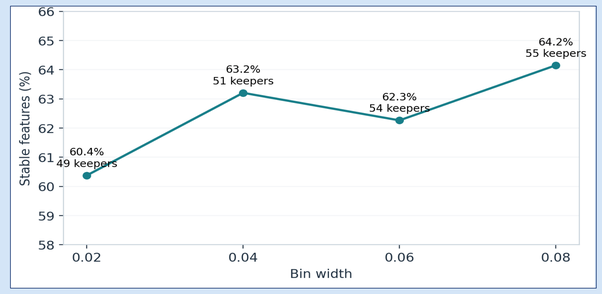

Figure 3. Stable fraction across the four tested bin widths for the Original Logan-derived surrogate V_T feature set, with the underlying Logan-derived surrogate VT map and ROI held fixed across all four conditions. The annotated keeper counts show that similar headline fractions can still conceal meaningful changes in the exact feature set that survives screening.

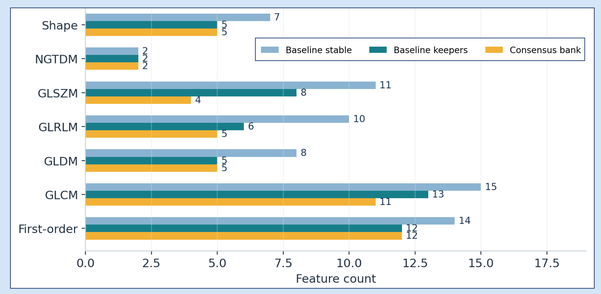

Figure 4. Feature-family breadth after screening, comparing the baseline ICC-stable set, the stricter baseline keeper set, and the final consensus set. The figure shows that conservative robustness screening reduces the feature pool without collapsing it to a single descriptor class.

CONCLUSIONS

Radiomics extracted from parametric maps of dynamic FET PET images yield features that remain stable under test-retest conditions. Consideration across discretization bin widths and image filtering yielded a consensus of 44 features that should be considered candidates for future diagnostic and prognostic modelling in GBM.

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