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***Research article***

**Accurate prediction of glioma grades from radiomics using a multi-filter and multi-objective-based method**

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**Supplementary**

**S1. Robustness analysis of the number of obtained features in each category of the filter features**

In the first step of identifying radiomic biomarkers, for each category of the filter features, we chose the number ten as the number of obtained features. To further show the influence of the number of obtained features on the prediction accuracy, we took the features of wavelet filter and original image in the T1-Gd modality as examples, and reset the number of obtained features to 8, 10, 15, 20, respectively. From Table S1, we can see both the training and test AUC values exhibited slight changes when varying the number of obtained features in the first step, suggesting the robustness of this parameter.

**Table S1.** AUC values of wavelet and original filters across different number of features (8, 10, 15, 20) in the first step.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Filter | Dataset | 8 | 10 | 15 | 20 |
| Wavelet | Training | 0.929 | 0.93 | 0.931 | 0.936 |
| Test BraTS-2013 | 0.915 | 0.93 | 0.925 | 0.925 |
| Original | Training  | 0.94 | 0.952 | 0.963 | 0.966 |
|  | Test BraTS-2013 | 0.88 | 0.88 | 0.885 | 0.865 |

In the second step of identifying radiomic biomarkers, we select the top three features from each of the five filters and then select the final ten features from the fifteen features. The number three here is not fixed and can be changed. To demonstrate this point, we changed this number to 4 and 5. In such cases, we will select the final 10 features from 20 and 25 features, respectively. Table S2 shows that both the training and test AUC exhibited slight changes, suggesting the robustness of the model performance with respect to different number of features from each filter.

**Table S2.** AUC values with respect to different number of features from each filter in the second step.

|  |  |  |  |
| --- | --- | --- | --- |
| Dataset | 3 | 4 | 5 |
| Training | 0.962 | 0.948 | 0.942 |
| Test BraTS-2013 | 0.95 | 0.94 | 0.94 |

**S2. Image Biomarker Standardisation Initiative (IBSI) checklist**

**Table S3.** IBSI check list for radiomics analysis.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Topic | Item | Requirements by IBSI (Not all items may be applicable) | Check to the proposed study | Description of the dataset in the proposed study |
| **Patient** |
| Region of Interest (ROI) | 1 | Describe the region of interest that is being imaged. | ✓ | All pre-operative mMRI volumes were re-oriented to the LPS (left-posterior-superior) coordinate system, and resampled to 1 mm3 voxel resolution. In the ROI, tumors were masked into 3 sub-regions: the enhancing part of the tumor core (ET), the non-enhancing part of the tumor core (NET), and the peritumoral edema (ED) |
| Patient preparation | 2a | Describe specific instructions given to patients prior to image acquisition, e.g., fasting prior to imaging. | NA | MRI images were collected from the TCGA-LGG, TCGA-GBM, lvyGAP and BraTS-2013 collection. We have no information about patient preparation. However, we can know MRI data and segmentation labels providers from reference (https://doi.org/10.7937/K9/TCIA.2016.L4LTD3TK, https://doi.org/10.7937/K9/TCIA.2016.RNYFUYE9,PMID: 33118182, PMID: 31613783, PMID: 25494501). It makes us believe that patients were prepared well following the US law. |
| 2b | Describe administration of drugs to the patientprior to image acquisition, e.g., muscle relaxants. | NA |
| 2c | Describe the use of specific equipment for patient comfort during scanning, e.g., ear plugs. | NA |
| Radioactive tracer PET, SPECT | 3a | Describe which radioactive tracer was administered to the patient, e.g., 18F-FDG. | NA | These data collections contains multimodal MRI images, including: T1-weighted pre-contrast (T1), T1-weighted post-contrast (T1-Gd), T2, and T2-FLAIR. The proposed research used two modalities MRI images, including: T1-weighted pre-contrast (T1), T1-weighted post-contrast (T1-Gd). All patients did not investigate PET/SPECT images. |
| 3b | Describe the administration method | NA |
| 3c | Describe the injected activity of the radioactivetracer at administration | NA |
| 3d | Describe the uptake time prior to image acquisition. | NA |
| 3e | Describe how competing substance levels werecontrolled. | NA |
| Contrast agent | 4a | Describe which contrast agent was administered to the patient. | ✓ | Gadolinium |
| 4b | Describe the administration method. | ✓ | Injection  |
| 4c | Describe the injected quantity of contrast agent. | NA |  |
| 4d | Describe the uptake time prior to image acquisition. | NA |  |
| 4e | Describe how competing substance levels werecontrolled. | NA |  |
| Comorbidities | 5 | Describe if the patients have comorbidities that affect imaging | NA |  |
| **Acquisition** |
| Acquisition protocol | 6 | Describe whether a standard imaging protocolwas used, and where its description may be found. | ✓ | TCGA-LGG and TCGA-GBM collected all available in TCIA scans for subjects whose tissue specimens had passed the quality evaluation ofthe NCI/NIH/TCGA program. lvyGAP is available in TCIA scans. BraTS-2013 is available in International Brain Tumor Segmentation (BraTS) challenge. |
| Scanner type | 7 | Describe the scanner type(s) and vendor(s) used in the study. | ✓ |
| Imaging modality | 8 | Clearly state the imaging modality that was used in the study, e.g., CT, MRI | ✓ | The proposed research used two modalities MRI images, including: T1-weighted pre-contrast (T1), T1-weighted post-contrast (T1-Gd) |
| Static/dynamic scans | 9a | State if the scans were static or dynamic | NA |  |
| 9b | Describe the acquisition time per time frame (for dynamic scans) | NA |  |
| 9c | Describe any temporal modelling techniquethat was used (for dynamic scans) | NA |  |
| Scanner calibration | 10 | Describe how and when the scanner was calibrated | NA |  |
| Patient instructions | 11 | Describe specific instructions given to the patient during acquisition, e.g., breath holding. | NA |  |
| Anatomical motioncorrection | 12 | Describe the method used to minimize the effect of anatomical motion. | NA |  |
| Scan duration | 13 | Describe the duration of the complete scan or the time per bed position. | NA |  |
| Tube voltage CT scan | 14 | Describe the peak kilo voltage output of the X-ray source | NA |  |
| Tube current CT scan | 15 | Describe the tube current in mA. | NA |  |
| Time-of-flight PET | 16 | State if scanner time-of-flight capabilities areused during acquisition. | NA |  |
| Radiofrequency (RF) coil MRI | 17 | Describe what kind RF coil used for acquisition, including vendor. | NA |  |
| Scanning sequence MRI | 18a | Describe which scanning sequence was acquired.  | NA |  |
| 18b | Describe which sequence variant was acquired. | NA |  |
| 18c | Describe which scan options apply to the current sequence, e.g., flow compensation, cardiac gating. | NA |  |
| Repetition time MRI | 19 | Describe the time in ms between subsequent pulse sequences. | NA |  |
| Echo time MRI  | 20 | Describe the echo time in ms. | NA |  |
| Echo train length MRI | 21 | Describe the number of lines in k-space that are acquired per excitation pulse. | NA |  |
| Inversion time MRI | 22 | Describe the time in ms between the middle ofthe inverting RF pulse to the middle of the excitation pulse. | NA |  |
| Flip angle MRI | 23 | Describe the flip angle produced by the RF pulses. | NA |  |
| Acquisition type MRI | 24 | Describe the acquisition type of the MRI scan, e.g., 3D. | ✓ | 2D or 3D MRI scan |
| k-space traversal MRI | 25 | Describe the acquisition trajectory of the k-space. | NA |  |
| Number of averages/ excitations MRI | 26 | Describe the number of times each point in k-space is sampled | NA |  |
| Magnetic field strength MRI | 27 | Describe the nominal strength of the MR magnetic field. | ✓ | 1.5 and 3.0 Tesla |
| **Reconstruction** |
| In-plane resolution | 28 | Describe the distance between pixels, or alternatively the field of view and matrix size. | NA |  |
| Image slice thickness  | 29 | Describe the slice thickness. | NA |  |
| Image slice spacing | 30 | Describe the distance between image slices. | NA |  |
| Convolution kernel CT scan | 31a | Describe the convolution kernel used to reconstruct the image | NA |  |
| 31b | Describe settings pertaining to iterative reconstruction algorithms. | NA |  |
| Exposure CT scan | 31c | Describe the exposure (in mAs) in slices containing the region of interest. | NA |  |
| Reconstructionmethod PET | 32a | Describe which reconstruction method was used, e.g., 3D OSEM. | NA |  |
| 32b | Describe the number of iterations for iterative reconstruction. | NA |  |
| 32c | Describe the number of subsets for iterative reconstruction. | NA |  |
| Point spread function modelling PET | 33 | Describe if and how point-spread functionmodelling was performed | NA |  |
| Image corrections PET | 34a | Describe if and how attenuation correction wasperformed | NA |  |
| 34b | Describe if and how other forms of correctionwere performed, e.g., scatter correction, random correction, dead time correction etc. | NA |  |
| Reconstructionmethod MRI  | 35a | Describe the reconstruction method used to reconstruct the image from the k-space information. | NA |  |
|  | 35b | Describe any artifact suppression methodsused during reconstruction to suppress artifacts due to undersampling of k-space. | NA |  |
| Diffusion-weighted imaging (DWI) MRI | 36 | Describe the b-values used for diffusion weighting | NA | There are none Diffusion Weighted Imaging (DWI) MRI data in the proposed study |
| **Image registration** |
| Registration method  | 37 | Describe the method used to register multimodality imaging. | ✓ | Retrospective research to collect MRI images |
| **Image processing - data conversion** |
| SUV normalization PET | 38 | Describe which standardized uptake value (SUV) normalization method is used. | NA |  |
| ADC computation DWI-MRI  | 39 | Describe how apparent diffusion coefficient (ADC) values were calculated. | NA |  |
| Other data conversions | 40 | Describe any other conversions that are performed to generate e.g., perfusion maps. | NA |  |
| **Image processing - post-acquisition processing** |
| Anti-aliasing  | 41 | Describe the method used to deal with antialiasing when down-sampling during interpolation. | NA |  |
| Noise suppression  | 42 | Describe methods used to suppress image noise. | NA |
| Post-reconstructionsmoothing filter PET  | 43 | Describe the width of the Gaussian filter (FWHM) to spatially smooth intensities | NA |  |
| Skull stripping MRI (brain) | 44 | Describe method used to perform skull stripping | ✓ | The volumes of all the modalities for each patient were then skull-stripped using the Brain Extraction Tool (BET) , Cancer Imaging Phenomics Toolkit (CaPTk) or Insight Toolkit (ITK) |
| Non-uniformity correction MRI  | 45 | Describe the method and settings used to perform non-uniformity correction | NA | The authors did not use any non-parametric, non-uniform intensity normalization algorithm to correct for intensity non-uniformities caused by the inhomogeneity of the scanner’s magnetic field during image acquisition |
| Intensity normalization | 46 | Describe the method and settings used to normalize intensity distributions within a patient or patient cohort. | NA |
| Other post-acquisitionprocessing methods | 47 | Describe any other methods that were used to process the image and are not mentioned separately in this list. | NA |  |
| **Segmentation** |
| Segmentation method | 48a | Describe how regions of interest were segmented, e.g., manually. | ✓ | Computer-aided segmentation was applied. Then, manual revision of the segmentation labels was performed by experienced experts |
|  | 48b | Describe the number of experts, their expertise and consensus strategies for manual delineation. | NA |  |
|  | 48c | Describe methods and settings used for semiautomatic and fully automatic segmentation. | ✓ | A tumor was segmented automatically by into 3 sub-regions: enhancing part of the tumor core (ET), the non-enhancing part of the tumor core (NET), and the peritumoral edema (ED) |
|  | 48d | Describe which image was used to define segmentation in case of multi-modality imaging. | NA |  |
| Conversion to mask  | 49 | Describe the method used to convert polygonal or mesh-based segmentations to a voxel-based mask. | NA |  |
| **Image processing—image interpolation** |
| Interpolation method | 50a | Describe which interpolation algorithm was used to interpolate the image. | NA |  |
| 50b | Describe how the position of the interpolation grid was defined, e.g., align by center. | NA |  |
| 50c | Describe how the dimensions of the interpolation grid were defined, e.g., rounded to nearest integer. | NA |  |
| 50d | Describe how extrapolation beyond the original image was handled. | NA |  |
| Voxel dimensions  | 51 | Describe the size of the interpolated voxels. | NA |  |
| Intensity rounding CT | 52 | Describe how fractional Hounsfield Units are rounded to integer values after interpolation. | NA |  |
| **Image processing—ROI interpolation** |
| Interpolation method | 53 | Describe which interpolation algorithm wasused to interpolate the region of interest mask | NA |  |
| Partially masked voxels | 54 | Describe how partially masked voxels after interpolation are handled. | NA |  |
| **Image processing—re-segmentation** |
| Re-segmentationmethods | 55 | Describe which methods and settings are usedto re-segment the ROI intensity mask. | NA |  |
| **Image processing—discretization** |
| Discretization method | 56a | Describe the method used to discretize image intensities. | NA |  |
| 56b | Describe the number of bins (fixed bin number FBN) or the bin size (fixed bin size FBS) used for discretization. | NA |  |
| 56c | Describe the lowest intensity in the first bin for FBS discretization | NA |  |
| **Image processing—image transformation** |
| Image filter  | 57 | Describe the methods and settings used to filterimages, e.g., Laplacian-of-Gaussian. | ✓ | Wavelet (including eight channels: HHH, HHL, HLH, HLL, LHH, LHL, LLH and LLL), LoG (Laplacian of Gaussian, with kernel size being 2, 3, 4 and 5), Square, Square Root, Logarithm, Exponential, and Gradient. |
| **Image biomarker computation** |
| Biomarker set |  | Describe which set of image biomarkers is computed and refer to their definitions orprovide these. | ✓ |  |
| IBSI compliance  | 59 | State if the software used to extract the set of image biomarkers is able to reproduce the IBSI feature reference values. | NA |  |
| Robustness  | 60 | Describe how robustness of the image biomarkers was assessed, e.g., test-retest analysis. | NA |  |
| Software availability | 61 | Describe which software and version was used to compute image biomarkers. | ✓ |  |
| **Image biomarker computation—texture parameters** |
| Texture matrix aggregation | 62 | Define how texture-matrix based biomarkers were computed from underlying texture matrices. | NA |  |
| Distance weighting | 63 | Define how CM, RLM, NGTDM and NGLDMweight distances, e.g., no weighting. | NA |  |
| CM symmetry | 64 | Define whether symmetric or asymmetric cooccurrence matrices were computed. | NA |  |
| CM distance  | 65 | Define the (Chebyshev) distance at which cooccurrence of intensities is determined, e.g., 1. | NA |  |
| SZM linkage distance | 66 | Define the distance and distance norm for which voxels with the same intensity are considered to belong to the same zone for the purpose of constructing an SZM, e.g., Chebyshev distance of 1. | NA |  |
| DZM linkage distance  | 67 | Define the distance and distance norm for which voxels with the same intensity are considered to belong to the same zone for the purpose of constructing a DZM, e.g., Chebyshev distance of 1. | NA |  |
| DZM zone distance norm | 68 | Define the distance norm for determining the distance of zones to the border of the ROI, e.g., Manhattan distance. | NA |  |
| NGTDM distance | 69 | Define the neighbourhood distance and distance norm for the NGTDM, e.g., Chebyshev distance of 1 | NA |  |
| NGLDM distance  | 70 | Define the neighbourhood distance and distance norm for the NGLDM, e.g., Chebyshev distance of 1. | NA |  |
| NGLDM coarseness | 71 | Define the coarseness parameter for the NGLDM, e.g., 0 | NA |  |
| **Machine learning and radiomics analysis** |
| Diagnostic and prognostic modelling | 72 | See the TRIPOD guidelines for reporting on diagnostic and prognostic modelling | NA |  |
| Comparison with known factors | 73 | Describe where performance of radiomics models is compared with known (clinical) factors. | NA |  |
| Multicollinearity | 74 | Describe where the multicollinearity betweenimage biomarkers in the signature is assessed. | NA |  |
| Model availability  | 75 | Describe where radiomics models with the necessary pre-processing information may be found. | ✓ |  |
| Data availability | 76 | Describe where imaging data and relevant meta-data used in the study may be found. | ✓ |  |

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