**Supplementary Information**

**Article title:** Diffusion- and Perfusion-weighted MRI Radiomics for Survival Prediction in Patients with Lower-grade Gliomas

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**Supplementary Fig. 1** Flow chart of the patient population

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**Supplementary material S1.** MR image acquisition and perfusion MRI preprocessing

**1. MR image acquisition parameters**

A 3.0-T MRI scanner (Achieva or Ingenia, Philips Healthcare) and an 8-channel SENSE head-coil were used for all preoperative MRI scans. The conventional MRI protocol included FLAIR (TR/TE 10,000/125 ms; FOV 240 mm; section thickness, 5 mm; matrix, 256 × 256) and three-dimensional T1C (TR/TE 6.3–8.3/3.1–4 ms; FOV, 240 mm; section thickness, 1 mm; matrix, 224 × 224). T1C images were acquired after administering 0.1 mL/kg gadolinium-based contrast material (Gadovist, Bayer, Toronto, ON, Canada).

Diffusion-weighted image (DWI) was acquired in three orthogonal directions, and the images are combined into a trace image. DWI was obtained using the following parameters: TR/TE, 3000/56 ms; diffusion gradient encoding, b = 0, and 1000 s/mm2; FOV, 250 mm; section thickness/gap, 5mm/2 mm; matrix, 256 × 256; and acquisition time, 46s.

For dynamic contrast-enhanced (DCE) MRI, 60 dynamic phases of DCE T1-weighted images were obtained with the following parameters: TR/TE, 6.3/3.1 ms; FOV, 240 mm; matrix, 192 ×192; section thickness, 3 mm; temporal resolution, 3.5 s; and flip angle, 8°. After the fifth dynamic phase, gadolinium-based contrast (0.1 mL/kg gadobutrol, Gadovist, Bayer) was injected at a rate of 3mL/s. The total acquisition time for DCE MRI was 5 min and 50 s. Following DCE, dynamic susceptibility contrast (DSC) perfusion MRI images were obtained with a gradient-echo, echo-planar sequence during the administration of the standard dose (0.1mL/kg) of gadobutrol. A dynamic bolus was administered as a standard dose of 0.1 mL/kg gadobutrol delivered at a rate of 4 mL/s using an MRI compatible power injector (Sonic shot GX, Nemoto). The bolus of contrast material was followed by a 20-mL bolus of saline, injected at the same rate. The imaging parameters for DSC perfusion MRI were as follows: TR/TE, 1600/30 ms; FOV, 24 cm; section thickness, 5 mm; matrix, 256 × 256; and flip angle, 40°. The total acquisition time was 1 min and 54 s.

**2. Dynamic contrast-enhanced (DCE) and Dynamic susceptibility contrast (DSC) preprocessing**

Commercial software (NordicICE; NordicNeuroLab) was used to process DCE and DSC images. Based on the pharmacokinetic model of Tofts et al. [1], the DCE MRI parameters (map of the volume transfer constant [Ktrans], rate transfer coefficient [Kep], extravascular extracellular volume fraction [Ve], and plasma volume fraction [Vp]) were generated after motion correction calibration. The arterial input function was semiautomatically detected at the level of the horizontal segment of the middle cerebral artery to minimize subjectivity. In this study, the baseline T1 value was fixed at 1400 ms.

The method described by Weisskoff et al. [2] and the adaptation described by Boxerman et al. [3] used to correct T1 and T2 contamination, were applied for cerebral blood volume (CBV) leakage correction. According to these corrective methods, leakage was estimated from the deviation of each voxel from a nonleakage referent tissue response curve. The whole-brain relative CBV (rCBV) and relative cerebral blood flow (rCBF) were then calculated. The normalization of rCBV and that of rCBF maps were automatically performed using the mean blood volume outside the tumor without any observer intervention.

The co-registration between FLAIR images and parametric maps from DCE and DSC was accomplished automatically using affine transformation with normalized mutual information as a cost function [4, 5].

**Supplementary Fig. 2** Radiomics pipeline



**Supplementary material S2.** A total of 14 radiomics features selected in a combined DWI and PWI radiomics model

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| --- | --- |
| Selected features | Coefficients |
| First order: Skewness (ADC) | 0.172 |
| First order: Energy (DSC) | 1.141 x 10-7 |
| GLCM: InverseVariance (ADC) | 1.015 |
| GLCM: Imc1 (DCE) | 1.325 |
| First order: Variance (DSC) | 0.026 |
| GLSZM: Small Area Low Gray Level Emphasis (DSC) | 45.702 |
| First order: Kurtosis (ADC) | 0.015 |
| NGTDM: Busyness (DCE) | 0.003 |
| GLSZM: Size Zone Non Uniformity Normalized (DCE) | 1.147 |
| GLCM: Inverse Variance (DSC) | 1.815 |
| First order: 90 Percentile (DSC) | 0.021 |
| First order: Minimum (DCE) | 0.040 |
| GLCM: Joint Energy (ADC) | 1.122 |
| First order: Interquartile Range (DCE) | 0.877 |

Features are presented in a descending order according to relative standard deviation

DWI = Diffusion-weighted imaging, PWI = Perfusion-weighted imaging, ADC = Apparent diffusion coefficient, DSC = Dynamic susceptibility contrast, DCE = dynamic contrast-enhanced, GLCM = gray level co-occurrence matrix, GLSZM = gray level size zone matrix, NGTDM = neighboring gray tone difference matrix

**Supplementary Fig. 3** Kaplan–Meier curves of low-risk and high-risk groups stratified based on the optimal cut-off value in (**a**) training and (**b**) test sets. The optimal cut-off value of the radiomics risk score stratified patients into two groups with significantly different overall survival in both training and test set





**References**

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