論 文 要 旨

Histological Grade of Meningioma: Prediction by Intravoxel Incoherent Motion Histogram Parameters

（ Intravoxel incoherent motion ヒストグラムパラメータによる髄膜腫の組織学的グレードの予測 ）

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Introduction and Objectives:

Meningioma is one of the most common intracranial tumors. Although majority are benign (WHO grade I), approximately 10–30% are high-grade meningiomas (WHO grade II/III). Compared to grade I low-grade meningiomas (LGMs), high-grade meningiomas (HGMs) are associated with higher post-surgical recurrence rates and lower 5-year overall survival rates. Histopathological grade, proliferative activity, and extent of resection are considered important factors for recurrence. Thus, preoperative grading would be helpful for determining appropriate therapy. Diffusion-weighted imaging has been used extensively for histologic differentiation of meningiomas, however, conflicting results have been reported. Since the calculated apparent diffusion coefficient (ADC) values reflect both perfusion and true molecular diffusion, it can be overestimated, especially in hypervascular tumors.

Intravoxel incoherent motion (IVIM) imaging is a noninvasive MRI technique that allows separate estimation of diffusion and perfusion parameters reflecting tumor cellularity and vascularity, respectively. It can potentially be more precise method in characterization and discrimination of tumor grades in comparison with conventional ADC. Previous studies have shown that whole tumor histogram analysis might be more reproducible and better than region-of-interest (ROI)-based analysis in reflecting the intratumoral heterogeneity for tumor differentiation. Therefore, the purpose of our study was to evaluate the usefulness of whole-tumor IVIM histogram parameters to distinguish LGMs and HGMs, and predict the proliferation potential of meningiomas.

Materials and Methodology:

Fifty-nine patients with pathologically confirmed meningiomas (45 LGMs and 14 HGMs) underwent MRI examination using a 3.0-T MRI scanner. IVIM imaging was performed using a diffusion-weighted echo-planar imaging sequence with 13 b values ranging from 0 to 1000 s/mm^2. Maps of IVIM parameters (perfusion fraction, f; true diffusion coefficient, D; and pseudo diffusion coefficient, D*) as well as ADC were generated. For each tumor, ROIs were manually drawn by two independent observers to encompass the whole tumor excluding necrotic and cystic areas as much as possible. Histogram analysis was performed using parametric values from all voxels in the ROI and the parameters including mean, standard deviation (SD), variance, kurtosis, skewness, coefficient of variation (CV), entropy and percentiles (5th, 10th, 25th, 50th, 75th, 90th, and 95th) were derived. The Mann-Whitney *U* test was used to compare the histogram results of ADC and IVIM parameters between LGMs and HGMs. Area under the receiver operating characteristic curve (AUC) values were generated to

evaluate how well each parameter could differentiate LGMs from HGMs. In addition, Spearman's rank correlation coefficient was used to evaluate correlations between histogram parameters and Ki-67 expression.

Results:

Compared to LGMs, HGMs showed significantly higher SD, variance, and CV of ADC ($p < 0.006–0.028$; AUC, 0.693–0.748) and D ($p < 0.004–0.032$; AUC, 0.670–0.752), and significantly higher CV of f ($p < 0.005–0.024$; AUC = 0.737). However, means and percentiles of ADC and IVIM parameters did not differ significantly between LGMs and HGMs ($p > 0.05$). There were no significant differences in any histogram parameter of D* to differentiate the tumor grades ($p = 0.084$-0.950).

Significant positive correlations were identified between Ki-67 and histogram parameters, particularly the heterogeneity parameters of ADC (SD [$\rho = 0.312–0.327$, $p = 0.011–0.016$], variance [$\rho = 0.301–0.372$, $p = 0.004–0.021$], kurtosis [$\rho = 0.270–0.304$, $p = 0.019–0.038$], and skewness [$\rho = 0.299–0.362$, $p = 0.005–0.021$], CV [$\rho = 0.277–0.310$, $p = 0.017–0.034$]) and D (SD [$\rho = 0.308–0.316$, $p = 0.015–0.018$], variance [$\rho = 0.293–0.296$, $p = 0.023–0.024$], kurtosis [$\rho = 0.301–0.322$, $p = 0.013–0.021$], CV [$\rho = 0.293–0.299$, $p = 0.021–0.024$]), whereas no significant correlation with Ki-67 was shown for mean or percentiles of ADC and IVIM parameters. The histogram-derived parameters of D* showed no significant correlations with Ki-67.

Conclusion and Analysis:

In the present study, HGMs had significantly higher SD, variance, and CV of D and ADC, and can be regarded as reflecting the heterogeneity in the microstructure of the tumor, whereas mean and percentiles of ADC and D were not significant to differentiate between LGMs and HGMs. This might be partly due to inclusion of chordoid meningiomas as increased ADC values in chordoid subtype has been reported. Also, the inclusion of foci of micronecrosis found in HGMs may have contributed to higher water diffusion increasing ADC.

In our study, CV of f was significantly higher in HGMs than in LGMs, which presumably represents a more heterogeneous vascular architecture of HGM. Mean and percentile parameters of f failed to show significant differences between LGM and HGM as majority of LGMs are hyper-vascular.

There were significant positive correlations of histogram-based parameters, particularly the heterogeneity parameters of ADC (SD, variance, kurtosis, and skewness), D (kurtosis), and f (kurtosis and skewness), with the Ki-67 labeling index, whereas no significant correlations were observed with mean and percentile values, illustrating the effect of intratumoral heterogeneity in evaluating the proliferative activity in meningiomas.

In conclusion, heterogeneity histogram parameters of ADC, D, and f can be helpful in differentiating histopathological grades and predicting the proliferation potential of meningiomas.

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