Multicenter Validation of Amide Proton Transfer Weighted Imaging for the Classification of Adult-type Diffuse Gliomas

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INTRODUCTION: In the 2021 Classification of Central Nervous System Tumors by the World Health Organization (WHO), diffuse gliomas were categorized for the first time into adult-type and pediatric-type[1]. Accurate grading and isocitrate dehydrogenase (IDH) mutation analysis are crucial for determining prognosis and guiding treatment decisions in adult-type diffuse gliomas. CEST imaging has shown promise in classifying these tumors according to prior studies[2-4]. However, multicenter validation studies to assess reproducibility have not been reported to date. This work aims to evaluate the reproducibility of CEST APTw imaging for the classification of adult-type diffuse gliomas across three centers, focusing on tumor grading and IDH genotyping.

METHODS: All the patients (n=110) from three centers (**Table 1**) were scanned on 3T Siemens scanners with the same SPACE CEST protocol[5]. Tumor ROIs were delineated on T2W images with a deep learning-based segmentation tool[6]. Subsequently, CEST maps and T2W images were coregistered to T1W images, with the ROIs transformed to T1W images[7,8]. APT-related metric maps including CESTR, CESTR^{nr}, and MTR$_{Rex}$[9] were calculated from the CEST source images, and transformed ROIs were overlaid on metric maps to calculate the mean values. To evaluate the classification ability of APT-derived metrics, two-sample t-tests were performed between IDH mutant and IDH wildtype groups, and between low-grade and high-grade groups. The mean values of the metrics for each group were compared across the three centers using unpaired t-tests to assess reproducibility. $P < 0.05$ was considered significant. The receiver operating characteristic curves (ROC) were plotted and the Delong tests were implemented for further analysis.

	BeijingTiantan Hospital	The 2nd XiangYa Hospital of CSU	The First Affiliated Hospital of ZZU	All
No.of patients	38	42	30	110
Male	20	22	17	59
Female	18	20	13	51
Age(years)	45.95±11.86	51.24±13.14	49.00±13.00	48.80±12.87
IDH_mutant	28	11	10	49
IDH_wildtype	10	31	20	61
Low grade	18	11	8	37
High grade	20	31	22	73

Table 1. Demographics.

RESULTS: There was no significant difference in patient ages and group mean metric values between each pair of the three centers. Among the three centers, each metric in the IDH wildtype group was significantly higher than in the IDH mutant group ($p<0.01$), and each metric in the high-grade group was significantly greater than in the low-grade group ($p<0.01$). The area under the receiver operating curves indicated good classification performance with APT-related metrics (**Table 2**). Notably, the highest AUC of CESTR^{nr} reached 0.930 between IDH mutant and IDH wildtype in Center 3. The AUC values of the ROC curves of the pooled data from the three centers were all above 0.8 (**Figure 1**).

Center	Task	AUC of CESTR(95%CI)	AUC of CESTR^{nr}(95%CI)	AUC of MTR$_{Rex}$(95%CI)
Center 1 (BeijingTiantan Hospital)	IDH genotyping	0.871(0.723-0.958)	0.886(0.741-0.966)	0.854(0.701-0.947)
	Grading	0.800(0.639-0.912)	0.792(0.629-0.906)	0.744(0.577-0.872)
Center 2 (The 2nd XiangYa Hospital of CSU)	IDH genotyping	0.833(0.686-0.930)	0.827(0.676-0.924)	0.777(0.622-0.891)
	Grading	0.827(0.679-0.926)	0.886(0.750-0.963)	0.906(0.776-0.974)
Center 3 (The First Affiliated Hospital of ZZU)	IDH genotyping	0.920(0.761-0.987)	0.930(0.775-0.991)	0.905(0.741-0.981)
	Grading	0.818(0.635-0.934)	0.835(0.655-0.945)	0.824(0.642-0.938)

Table 2. ROC results of all the metrics in three centers.

DISCUSSION AND CONCLUSION: To the best of our knowledge, this is the first multicenter validation study investigating the utility of APTw imaging for classifying adult-type diffuse gliomas. In this work, APTw imaging was proved to be an effective tool to differentiate genotypes and grades of adult-type diffuse gliomas in multicenter data, providing good performance across centers. Future studies may focus on validating the performance of APTw imaging across vendors.

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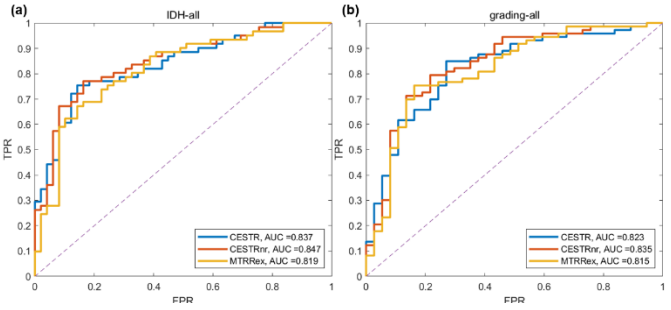

Figure 1. ROC results of pooled data:(a)IDH genotyping, (b)grading.