CAN DIFFUSION TENSOR MR IMAGING IDENTIFY GLIOMA IDH MUTATION STATUS?

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Background

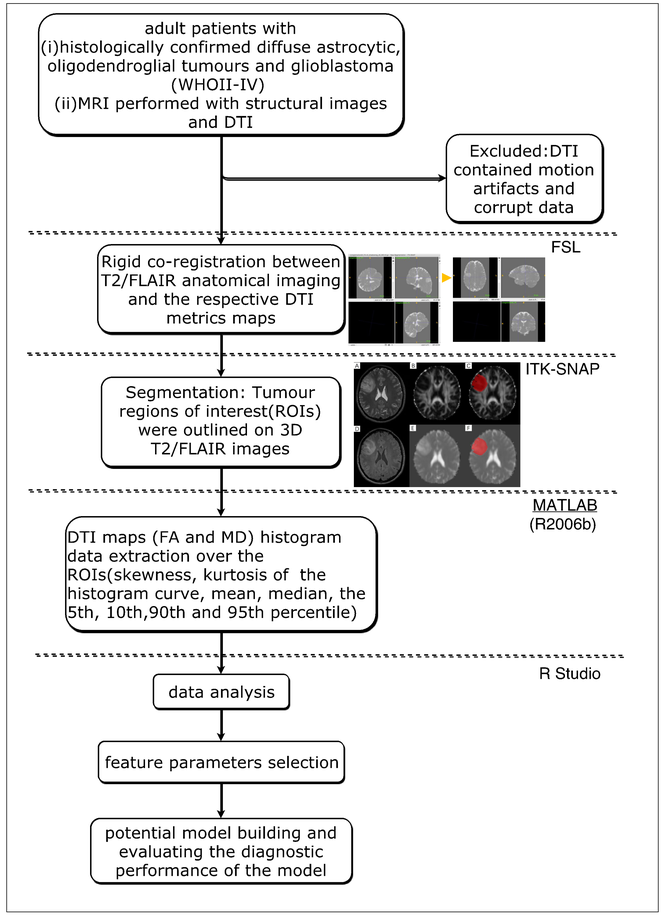
The isocitrate dehydrogenase (IDH) mutation status is a recognized molecular biomarker for glioma stratification. Glioma clinical management benefits from advanced MRI sequences including diffusion tensor imaging (DTI).
For first time, we investigated the diagnostic power of DTI to characterize gliomas with respect to IDH mutation status.

Aims and objectives

- To evaluate whether DTI derived scalar measurements (FA, MD) can act as surrogate biomarkers of IDH mutant and wildtype gliomas
- To assess the diagnostic accuracy of DTI metrics for IDH mutation

Methodology

This retrospective study examines the accuracy of DTI for staging of IDH mutant (98) and wild-type (67) gliomas in a treatment-naïve setting. The tumour was manually segmented in the MRI and two DTI-derived parameters, namely fractional anisotropy (FA) and mean diffusivity (MD) values were calculated and plotted as histograms. Thresholds for the optimal diagnostic performance in terms of IDH mutation were sought in selected histogram parameters of FA and MD maps using parametric and non-parametric tests as well as receiver operating characteristic curve analysis.



Key References:
Hempel, Johann-Martin, Sotirios Bisdas, Jens Schittenhelm, Cornelia Brendle, Benjamin Bender, Henk Wassmann, Marco Skardelly, et al. "In Vivo Molecular Profiling of Human Glioma Using Diffusion Kurtosis Imaging." Journal of Neuro-Oncology 131, no. 1 (January 1, 2017): 93–101. doi:10.1007/s11060-016-2272-0.
Tan, W. L., W. Y. Huang, B. Yin, J. Xiong, J. S. Wu, and D. Y. Geng. "Can Diffusion Tensor Imaging Noninvasively Detect IDH1 Gene Mutations in Astrogliomas? A Retrospective Study of 112 Cases." American Journal of Neuroradiology 35, no. 5 (May 1, 2014): 920–27. doi:10.3174/ajnr.A3803.
Xiong, Ji, Wen-Li Tan, Jia-Wei Pan, Yin Wang, Bo Yin, Jun Zhang, and Dao-Ying Geng. "Detecting Isocitrate Dehydrogenase Gene Mutations in Oligodendroglial Tumors Using Diffusion Tensor Imaging Metrics and Their Correlations with Proliferation and Microvascular Density." Journal of Magnetic Resonance Imaging: JMRI 43, no. 1 (January 2016): 45–54. doi:10.1002/jmri.24958.

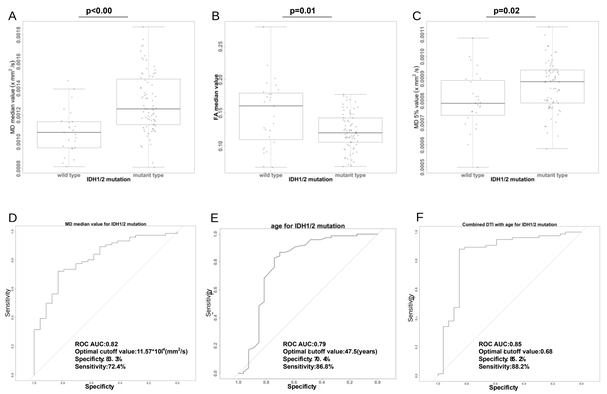
Results

Differences of clinical characteristics between IDH1/2 mutant and wildtype (55 exhibited grade II tumours and 48 exhibited grade III—IV tumours)

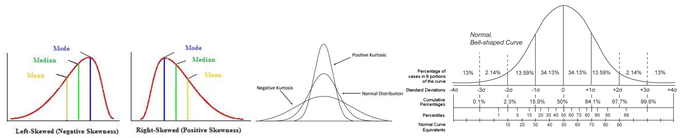
	Total	IDH1/2 mutant	IDH1/2 wild type	P value
	165	98	67	
IDH1		96		
IDH2		2		
Age (mean±SD, years)		38.8±8.6	52.3±14.9	8.968e-05*
Gender				0.4825+
Male		48	30	
Female		50	37	
Diagnosis				0.0785+
LGG		55	35	
HGG		43	32	

*The difference between the two groups was evaluated using the Welch Two Sample t-test
+The difference between the two groups was evaluated using Pearson's Chi-squared test with Yates' continuity correction

Examples of statistically significant parameters between IDH genotypes and the ROC curves:



Differences of histogram parameters derived from DTI maps between IDH mutant and wildtype group



	Mean value		P value
	IDH mutant(76) (MD: mm^2/s)	IDH wild-type(27) (MD: mm^2/s)	
MD skewness✶	-2.00±0.79	0.64± 0.95	<0.00
MD mean	(12.87±1.98) x 10^{-4}	(11.73±2.72) x 10^{-4}	<0.00
MD median	(12.94±2.22) x 10^{-4}	(11.53±3.27) x 10^{-4}	<0.00
MD 5%✶	(8.71±1.32) x 10^{-4}	(8.00±1.29) x 10^{-4}	0.02
MD 10%✶	(9.56±1.35) x 10^{-4}	(8.61±1.35) x 10^{-4}	0.01
MD 90%	(16.04±2.78) x 10^{-4}	(15.25±4.25) x 10^{-4}	0.04
FA mean	0.15±0.03	0.17±0.04	0.03
FA median	0.13±0.03	0.15±0.05	0.01

✶ Data showed normal distribution (Welch two-sample *t*-test)
For parameters without ✶, either one or both groups no sign: either one or both group of data showed no normal distribution, and the difference between the two groups was evaluated using a Wilcoxon rank sum test with continuity correction.

Why different performance in FA and MD in predicting IDH mutational status?

FA is a summary reflection of microstructural integrity, which is sensitive to microstructural changes rather than what type of change. While MD is sensitive to cellularity, oedema, and necrosis, which can reflect the heterogeneities of the tumour.
In our study, a large part of the tumours were involved in the cortex, which may attenuate the power of identifying difference using FA, but MD value is very similar for both GM and WM, therefore tumour's location will not affect the MD value.

Conclusion

- The MD median value was the most significantly different histogram parameter when comparing IDH1/2 mutant and wildtype gliomas.
- Histogram analysis of FA and MD metrics based on entire tumour volume may serve as surrogate biomarkers for distinguishing IDH mutational status in gliomas.
- Hope our findings can provide integrated diagnosis for gliomas in a non invasive way in future clinical practice.