

# Diffusion tensor MR imaging in the evaluation of Wallerian degeneration in pediatric strokes: work-in-progress

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## Synopsis:

We use DTI to detect and quantify Wallerian degeneration (WD) in pediatric MCA strokes. Fractional anisotropy (FA) and mean diffusivity (MD) of the infarction, ipsilateral internal capsule (PLIC) and cerebral peduncle (CP) were measured in nine children and compared to the matched contralateral side. WD was characterized by statistically significant differences in FA, but not MD, of the ipsilateral PLIC and CP compared to the normal side. FA was reduced in all children, whilst corresponding hyperintense signals on T2-weighted images were seen in five children. DTI is more sensitive than conventional MRI and can be used to detect and quantify WD.

## Purpose:

Wallerian degeneration (WD), the anterograde degeneration of axons and myelin sheaths after proximal axonal or cell body injury, is known to occur after cerebral infarction (1). In this preliminary study, we aim to evaluate if DTI, using the indices fractional anisotropy (FA) and mean diffusivity (MD), can detect and quantify Wallerian degeneration in pediatric middle cerebral artery (MCA) strokes and to compare the findings with conventional MR imaging. As the prognostic indicators of neuromotor outcome in pediatric strokes are multifactorial and not well defined (2), our future goal is to determine its relationship with neuromotor outcome.

## Materials and Methods:

Patients between one year and 18 years of age with evidence of a unilateral infarction in the MCA territory by CT scan or MRI were recruited. Those with congenital structural anomalies, mitochondrial disease, traumatic hemorrhage, Moya Moya disease were excluded.

MRI was performed using a Signa 1.5 Tesla imager (GE Medical Systems, Milwaukee, WI, USA) with a standard head coil. Axial spin-echo T1-weighted (500/10/23/256 X 224 [TR/TE/FOV/acquisition matrix]), fast spin-echo proton density (2400/10 [TR/TE]) and T2-weighted images (4000/ 100/ 23/ 320 x 224 [TR/TE/FOV/acquisition matrix]) were performed. DTI was performed using single-shot spin-echo echo-planar imaging (10000/ minimum/28/128 x 128[TR/TE/FOV/acquisition matrix]). Diffusion-sensitizing gradient encoding was applied in 25 directions by using a diffusion-weighted factor  $b=1200\text{s/mm}^2$ . Quantitative values of FA and MD were obtained by manually placing regions-of-interest (ROI) within the infarction, and in selected areas along the ipsilateral corticospinal tract, i.e. the posterior limb of the internal capsule at the level of the globus pallidus (PLIC) and cerebral peduncle (CP). Identical ROIs were placed in the matched contralateral regions. Student's t-test was used to detect any statistically significant differences in FA and MD between the infarction hemisphere and the contralateral normal region. The corticospinal tract FA was derived from the mean value of PLIC FA and CP FA. The patients were further divided into two groups, those with corticospinal tract FA ratio (infarct hemisphere/normal hemisphere) of  $< 0.8$  and  $\geq 0.8$ , and compared with brain-stem area asymmetry (cross-sectional area of the CP) and the largest cross-sectional area of the infarction on T2-weighted axial image, using student's t-test.  $P < 0.05$  was considered statistically significant.

The presence of signal intensity changes in the internal capsule and cerebral peduncles on T2-weighted images were recorded.

## Results:

There were nine children aged between 14 months and 17 years of age (mean: 92.5 months) who presented with hemiplegia between birth and 10 years of age (mean: 20 months). The cause of stroke was congenital heart disease ( $n=5$ ), perinatal ( $n=1$ ), severe dehydration ( $n=1$ ) and indeterminate ( $n=2$ ). The infarction was right sided in five children and left sided in four children. Area of infarction ranged between  $212\text{mm}^2$  and  $2997\text{mm}^2$  (mean:  $1075\text{mm}^2$ ).

WD was detected on conventional T2-weighted image by hyperintense signals in the PLIC in four children and CP in one child. The area of CP was smaller on the infarct hemisphere compared to the normal hemisphere in all children, with the reduction in area ranging between 6% and 28% (mean: 15%).

The FA of the infarction, PLIC and CP were reduced, and the MD of the infarction and PLIC were increased on the infarct hemisphere compared to the normal hemisphere in all children, whilst the MD of the CP was increased in six children only. The mean FA ratios of the infarct hemisphere to the normal hemisphere in the infarction, PLIC and CP were 0.45, 0.77 and 0.79 respectively and the differences were statistically significant in all sites ( $p=0.029$ ,  $p=0.014$  and  $0.008$  respectively). The mean MD ratio of the infarction to the contralateral normal side was 2.55 ( $p < 0.001$ ). The differences in MD in the other sites were not statistically significant.

	FA		MD ( $\times 10^{-3}\text{mm}^2\text{s}^{-1}$ )	
	Infarction Side	Normal Side	Infarction Side	Normal Side
Infarction	0.069(0.014)*	0.194(0.147)	2.945(0.577) ***	1.168(0.160)
PLIC	0.367(0.108)*	0.475(0.041)	1.23(0.205)	1.041(0.116)
CP	0.337(0.082) **	0.426(0.055)	1.419(0.124)	1.347(0.099)
Corticospinal Tract	0.352(0.087)**	0.451(0.046)	1.307(0.101)	1.194(0.087)

Table showing the mean FA and MD values of nine children with unilateral MCA stroke. \* $p < 0.05$ , \*\* $p < 0.01$ , \*\*\* $p < 0.001$  (student t-test).

For the groups with corticospinal tract FA ratio of  $< 0.8$  ( $n=4$ ) and  $\geq 0.8$  ( $n=5$ ), the reduction in area of the CP in the infarct hemisphere was 17% and 13% respectively, and the area of infarction was  $1268.5\text{mm}^2$  and  $919.4\text{mm}^2$  respectively. These differences were not statistically significant ( $p=0.378$  and  $p=0.622$ ).

## Conclusion:

We have shown that in pediatric strokes, there is significant loss of anisotropy in Wallerian degeneration and reduction is less severe than in the infarction site. Also, DTI, using the index FA, is more sensitive than conventional MR imaging for the detection of Wallerian degeneration. This is in agreement with findings in adult stroke patients (3). DTI is therefore useful for monitoring the evolution of pediatric strokes and quantifying the severity of Wallerian degeneration. Further studies are required to determine if the measurement of FA in Wallerian degeneration can be used as an indicator of neuromotor outcome.

## References:

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