

The standard deviation (Asd, normalized relative anisotropy at 0 – 1 scale) detects neurodegenerative white matter lesions better than the fractional anisotropy (FA)

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Introduction: A consensus has not been reached on the use of the two commonly used diffusion anisotropy indices (DAI) derived from diffusion tensor imaging (DTI)^{1,2}, fractional anisotropy (FA) and relative anisotropy (RA). Some reports suggested that FA has better anisotropy signal to noise ratio (AISNR)³, contrast to noise ratio (CNR)⁴, and better gray matter (GM) to white matter (WM) contrast⁵ than RA. This claim was supported by a theoretical analysis⁶. However, the selection of an appropriate DAI may be dependent on both tissue properties and the experimental conditions⁷. In the present study, FA and Asd (the standard deviation or normalized RA at 0 – 1 scale) of *in vivo* mouse spinal cord were evaluated. Though the two parameters performed similarly, Asd was slightly better at detecting white matter injury.

Materials and Methods: Seven 10-wk-old naïve female C57BL/6 mice were employed to evaluate the baseline FA and Asd *in vivo*. Experimental allergic encephalomyelitis (EAE, a model of multiple sclerosis, n = 8), twitcher (a model of globoid cell leukodystrophy, n = 5), and G93A-SOD1 (a model of amyotrophic lateral sclerosis, n = 7) mice were employed with age-matched littermates to examine FA and Asd sensitivity to spinal cord white matter lesions. All mice underwent *in vivo* DTI examination on a 4.7 T scanner with a respiratory-gated, spin-echo, diffusion-weighted sequence as previously reported⁸.

Results and Discussion: All data for estimating FA and Asd maps had comparable signal-to-noise ratio (SNR) at ~ 40. The FA and Asd maps from naïve mouse spinal cord are shown in Fig.1. Both FA and Asd show highly visible GM/WM contrast (Fig.1a). Consistent with previous reports^{3,4}, FA exhibited a higher CNR and AISNR than Asd (Fig. 1b), with a greater difference seen in AISNR. In general, higher anisotropy values were seen in FA than Asd. FA had narrower histogram in WM than Asd, whereas a narrower GM histogram was seen in Asd than in FA (Fig. 1c and d). Since the CNR and AISNR are mainly driven by the standard deviation of the measurement, the narrow histogram of WM FA may result in the higher AISNR for FA. This suggests that CNR and AISNR may not be ideal measures of the sensitivity of DAI. Thus, the sensitivity of FA and Asd was tested using animal models of neurodegenerative white matter disease. The difference between each lesion FA (or Asd) and the control FA (or Asd) was compared. Without exception, Asd showed a greater difference between the control and lesion than that seen in FA. The paired t-test confirmed that Asd exhibited a bigger difference between the control and lesion WM.

Conclusion: Overall, both FA and Asd demonstrated high contrast between GM and WM with minor differences in histogram distribution. FA showed better CNR and AISNR than Asd. However, Asd detected white matter lesions with better contrast than FA.

References

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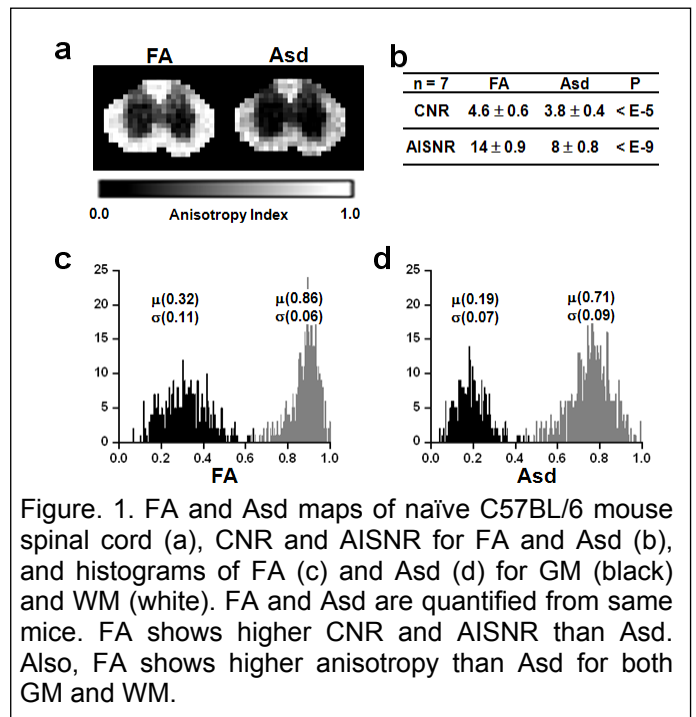


Figure 1. FA and Asd maps of naïve C57BL/6 mouse spinal cord (a), CNR and AISNR for FA and Asd (b), and histograms of FA (c) and Asd (d) for GM (black) and WM (white). FA and Asd are quantified from same mice. FA shows higher CNR and AISNR than Asd. Also, FA shows higher anisotropy than Asd for both GM and WM.

Table 1. The difference of each lesion DAI from mean DAI of control group.

	EAE	SOD1	Twitcher
FA	0.15 ± 0.04	0.054 ± 0.016	0.064 ± 0.021
Asd	0.20 ± 0.04	0.073 ± 0.018	0.091 ± 0.018
P (FA vs Asd)	2.0E-07	2.0E-05	4.0E-04