[RRA1-1] Normalization of Fractional Anisotropy and Apparent Diffusion Coefficient Values Facilitate Appropriate Comparison of Corpus Callosum Microstructural Changes in the Developing Newborn

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Background:
MRI diffusion tensor imaging (DTI) utilizes the movement of water molecules within brain tissue to probe its structural properties1. Fractional Anisotropy (FA) and Apparent Diffusion Coefficient (ADC) values are common DTI metrics which have previously demonstrated sensitivity to developmental changes, including white matter myelination1. The corpus callosum is a highly active region of white matter development in infants and may be a good anatomical area to track brain development2. Previous work examining these DTI values in infants has examined absolute values, without accounting for time in between scans3. We hypothesize that accounting for this time by adjusting for post conceptual age (PCA) will facilitate a better comparison of microstructural brain development.

Methods:
This prospective study examined 75 patients with various types of congenital heart disease who underwent corrective surgery (either single ventricle palliation (1V) or two ventricle repair (2V)) within the first 30 days of life. These infants had preoperative (Scan 1), 7-day postoperative (Scan 2), and follow up MRIs (Scan 3) at 3-6 months of age. We analyzed the relationship of perioperative injury and surgical palliation on changes in both unadjusted FA and ADC values and FA and ADC values adjusted for PCA between preoperative and postoperative scans as well as between preoperative and follow up scans. FA and ADC values were adjusted by applying a simple linear transformation using the PCA at the time of MRI scan (Figures 1 and 2).

Results:
Both patient groups (1V vs. 2V) and the presence of brain injury (Table 1) had differential effects depending on whether adjusted values or unadjusted values were used. In some cases, the observed effect in the unadjusted values was completely attenuated or the opposite trend was seen. After adjusting for PCA, the actual differences between scans were much smaller when stratified either by brain injury status or surgical palliation.

Conclusions:
Future comparisons of MRI DTI data should consider factoring days between scans to appropriately compare groups of patients. In the absence of a gold standard, a linear transformation may be the best approximation to appropriately adjust for PCA.

References:
1.Mori S et al. Neuron 51:527-539.
2.Wu TC et al. Dev Neurosci 32(5-6):361-73.
3.Miller SP et al. NEJM 357:1928-38.

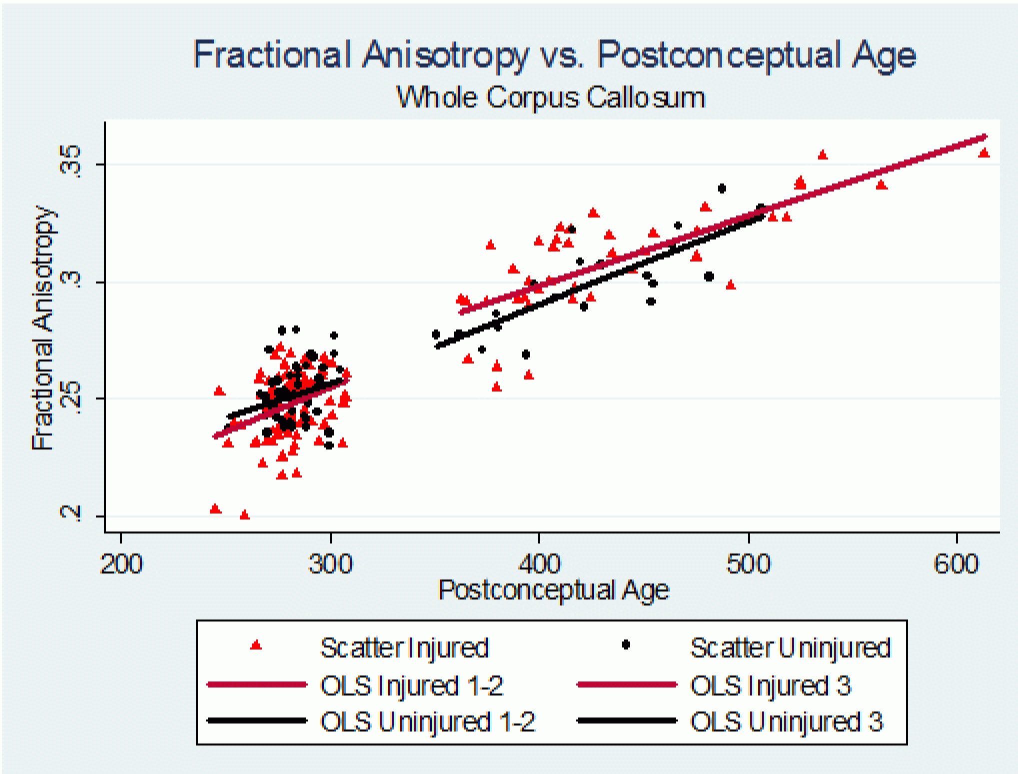

Figure 1. Fractional Anisotropy vs. Postconceptual Age (Days) by Injury Status, Best Fit Lines plotted for Scan 1 and 2 (Preoperative and Postoperative) together and Scan 3 (Follow-up) separately, OLS = Ordinary Least Squares

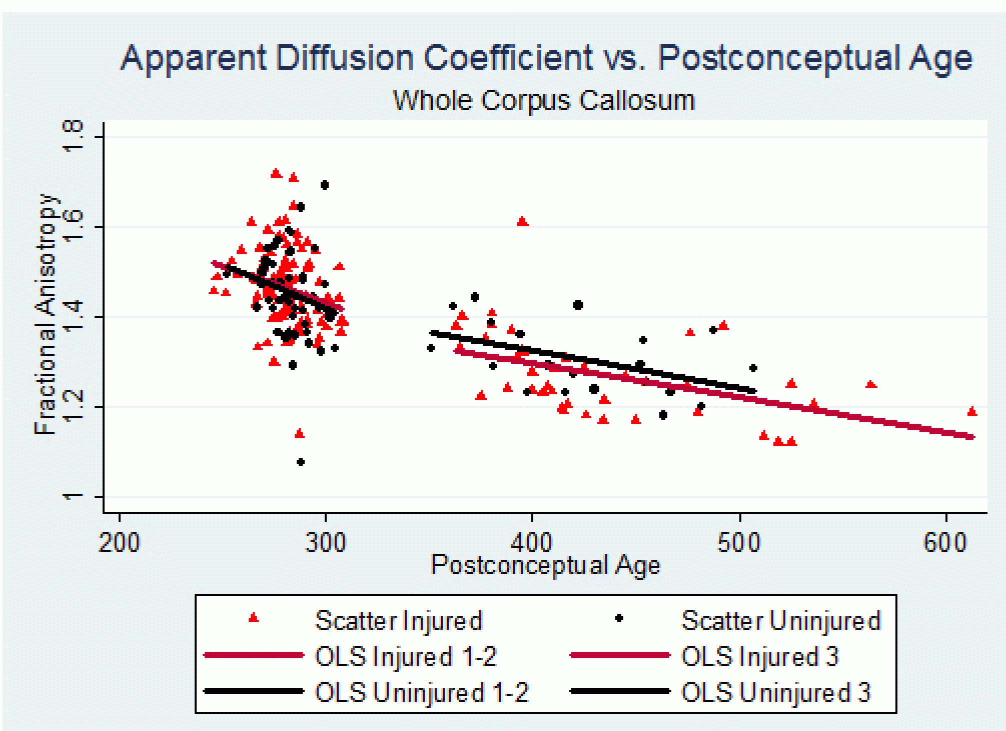

Figure 2. Apparent Diffusion Coefficient vs. Postconceptual Age (Days) by Injury Status, Best Fit Lines plotted for Scan 1 and 2 (Preoperative and Postoperative) together and Scan 3 (Follow-up) separately, OLS = Ordinary Least Squares

	Scan 2/Scan 1 Difference		Scan 3/Scan 1 Difference	
Unadjusted	**FA**	**ADC**	**FA**	**ADC**
No Injury	0.0004	0.0076	0.047	-0.16
Injury	-0.0013	0.0065	0.063	-0.20
Adjusted	**FA**	**ADC**	**FA**	**ADC**
No Injury	-0.000029	-0.00014	-0.00019	-0.0021
Injury	-0.000031	-0.00013	-0.00018	-0.0024
Unadjusted	**FA**	**ADC**	**FA**	**ADC**
Single Ventricle	-0.0009	0.0042	0.051	-0.16
Two Ventricle	-0.0006	0.0100	0.066	-0.22
Adjusted	**FA**	**ADC**	**FA**	**ADC**
Single Ventricle	-0.000035	-0.00017	-0.00018	-0.0022
Two Ventricle	-0.000025	-0.00010	-0.00019	-0.0024

Table 1. Adjusted (raw value/PCA in days) and Unadjusted Differences (raw value) by Injury and Surgical Palliation