# Do DTI Indices Correlate with Neurological Status of Neonates with Congenital Heart Disease Before and After Cardiopulmonary Bypass Surgery?

**R. Liamlahi[1], W. Knirsch[1], B. Latal[2], M. von Rhein[3], I. Scheer[4], H. Dave[5], A. Schmitz[6], V. Bernet[7], C. Kellenberger[4], and M. I. Makki[4]**
[1]Cardiology, University Children Hospital, Zurich, Switzerland, [2]Child Development, University Children Hospital, Zurich, Switzerland, [3]Child Development Center, University Children Hospital, Zurich, Switzerland, [4]Diagnostic Imaging, University Children Hospital, Zurich, Switzerland, [5]Congenital Cardiovascular Surgery, University Children Hospital, Zurich, [6]Anesthesia, University Children Hospital, Zurich, Switzerland, [7]Pediatric Intensive Care, University Children Hospital, Zurich, Switzerland

**Introduction:** As more and more neonates with severe congenital heart disease (CHD) survive, the focus has shifted from mortality to morbidity. It is well known that these vulnerable patients are at increased risk for impaired neurodevelopmental outcome [1-3]. Recent cerebral MRI studies show white matter (WM) injury in up to 50% of all children undergoing cardiopulmonary bypass (CBP) surgery during the neonatal period [4-6]. Diffusion tensor MRI (DTI) quantitatively assess the microstructural development of WM, including fiber bundle integrity, white matter myelination, and presumptive connectivity of axons. It is still unclear whether the delayed maturation of the WM detected by DTI correlates with the neurological status of neonates with CHD. The aim of this study was to test the hypothesis that delayed maturation of the WM of the corticospinal tracts (CST) correlates with the degree of neurologic abnormalities in neonates with CHD undergoing CPB during their first weeks of life.

**Materials and Methods:** Nine neonates (mean gestational age 39.2 ± 1.1 weeks, mean birth weight = 3230 ± 381g) with severe CHD (8 patients with d-type transposition of the great arteries, 1 patient with hypoplastic left heart syndrome) undergoing CPB in the neonatal period were recruited for this prospective longitudinal cohort study and were examined with conventional MRI and DTI in natural sleep before and after first CPB surgery. MRI was performed on a 3T scanner with 8-channel head coil. DTI parameters are: FOV=22 $cm^2$, slice thickness = 2.5 mm, optimal TE and TR, 35 diffusion directions with diffusion sensitivity b = 700 [$s/mm^2$] and 1 T2W volume, matrix = 128x128, reconstructed on 256x256, covering the whole brain. Maps of parallel $\lambda_1$ (major eigenvalue) and perpendicular $\lambda_{23}$ (average of middle $\lambda_2$ and minor $\lambda_3$ eigenvalues) diffusion were measured and the apparent diffusion coefficient (ADC) and the fractional anisotropy (FA) were calculated. To asses inter- and intra-rater reliability two independent observers drew regions of interest (figure 1) and one observer repeated it twice. In addition an experienced neurodevelopmental pediatrician performed a neurodevelopmental examination before and after first CPB surgery. A neuromotor score (NMS) was created to express the severity of neurologic abnormality and involved the assessment of posture, general movements, cranial nerves, muscle tone, reflexes and adaptation [7]. Each category was scored from 0-3 (total score range 0 to 18). The scores of posture, general movements and muscle tone were extracted and combined in one value (range 0 to 9). This was correlated with FA, ADC and $\lambda_{23}$ of bilaterally selected WM structures: posterior limb of internal capsule (PLIC), cerebral peduncle (CP) and inferior part of the corticospinal tracts (CS).

**Results:** Partial correlation controlled for age was carried out separately for pre surgery NMS and pre surgery DTI indices and post surgery NMS with post surgery DTI indices. For the pre surgery data we found no correlation between NMS and DTI parameters. Following surgery NMS correlated positively with ADC ($p=0.04$) and negatively with FA ($p<0.001$) on the left CP. We observed also a negative correlation between NMS and FA ($p=0.02$) of the right CP (figure 2). No correlation was detected between NMS and PLIC or between NMS and CS. After Bonferroni correction for multiple comparisons (2 sides, 3 structures, 3 indices) $p=0.002$ was considered to be significant and there was still a significant negative correlation between NMS and FA of the left CP.

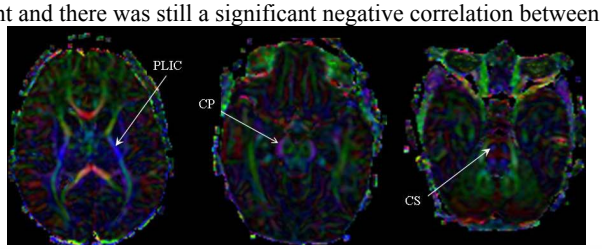
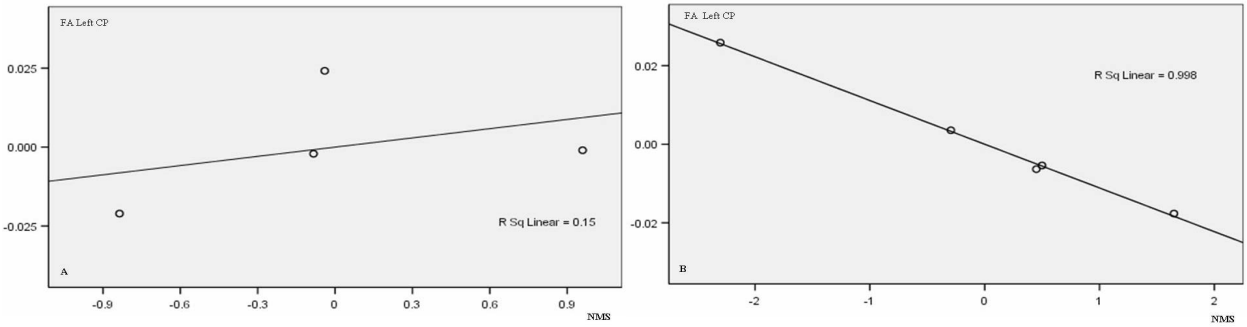



**Figure 1 (left):** FA color encoded map showing the three selected structures PLIC, CP and CS

**Figure 2 (bottom): G**raphs of the partial correlation (controlled for age) showing the association between left FA on the cerebral peduncle and neuromotor score before surgery (A, p = NS) and after surgery (B, $p < 0.001$).




**Conclusion:** Our results indicate that the intactness of the fiber bundles of the CP is affected following CPB surgery and related to abnormal neurological findings in neonates with congenital heart disease. Also our results demonstrate an asymmetry in the CP, which might be a sign of future neuromotor impairments. Association between decreased FA in the CP and unfavourable outcome has been reported in patients with traumatic brain injury suggesting progressive structural degradation [8]. DTI parameters are an objective quantitative marker that may help to predict neurodevelopmental impairments of newborns with CHD undergoing CPB in early stage.

**References**: [1] Ballweg, JA. *Pediatr Cardiol*, (2007); [2] Majnemer A, *J Pediatr*, (2006); [3] Licht DJ, *J Thorac Cardiovasc Surg*, (2009); [4] Mahle, WT *Circulation* (2002); [5] Miller, SP. *N Engl J Med*, (2007); [6] Watanabe K, *J Thorac Cardiovasc Surg*, (2009); [7] Kuenzle, C, et. al. *Neuropediatrics* (1994); Sidaros A, *Brain* (2008).