Objectives:
The aim of this prospective cohort study was to examine the relationship between very early brain structure (structural MRI), white matter integrity (diffusion MRI) and neurological function at 30 weeks post menstrual age (PMA) in infants born very preterm. In this study, we investigate this on a sub cohort of infants with no evidence of brain injury.

Participants:
At 30 weeks PMA 71 infants born <33 weeks were assessed: 44 male, mean gestational age (GA) at birth 28.2 wks (SD=1.7), mean birthweight (BW) 1106g (SD=321.2), mean PMA at MRI scan 32.17wks (SD=1.4). This is a sub cohort of the full study (n=110), with inclusion criteria
- MRI acquired and passed quality control.
- MRI abnormality classification of normal or mild (Kidokoro 2013).
- General Movements classification of normal or poor repertoire.

Methods:
Infants underwent 3T MRI using an MRI compatible incubator without sedation at 30-32 weeks PMA with structural and diffusion MRI imaging. The structural MRI was segmented in gray matter (GM), white matter (WM) and cortical fluid (CSF), and labelled using the Albert Atlas (Gousias 2014). A population specific Fractional Anisotropy (FA) atlas was created and aligned to the John Hopkins Unit (JHU) neonatal Atlas.
Clinical assessment was performed within a week of MRI. It consisted of General Movements Assessment (GMA), Hammersmith Neonatal Neurological Examination (HNNE) and Premie-Neuro (PN). The relationship between regional volumetric (n=8) or diffusion measures (n=18) and clinical assessment were investigated using general linear models with adjustments for GA at birth, sex, BW and PMA at MRI scanning with statistical significance accounting for multiple comparisons set at 0.002.

Results: Structural
Our 30 week structural MR images appear consistent with previous studies (Zacharia 2006). Although motion and the resolution of the scans generally limited the accuracy of the quantification. We found:
- Total intracranial volume (TIV) was significantly associated with PMA-at-birth (p < 0.01), PMA-at-scan (p < 0.001), and GA-at-birth was only weakly associated with cortical volumetry after adjusting for TIV, PMA-at-scan and gender.

Results: DTI
Our 30 week DTI measures were consistent with previous studies acquired on older cohorts (Rose 2014 for 34-38 weeks and Doshi 2011 for 37-53 weeks). In particular:
- Posterior aspects had higher FA as compared with anterior aspects (e.g. See Posterior to Anterior Corona Radiata and internal capsule in Figure 3).
- Centrally located fibres had higher FA compared to peripheral tracts (e.g. See PULIC to RILIC to PTR to SS in Figure 3).
- FA values lower and MD values higher than reported in previous near term data. However, this relates to PMA and the PMA adjusted trend is remarkably similar to Rose et al (Figure 4).

Results: Associations
Response: MRI measures and 30 week Clinical Assessment
In our cohort, no association was found between thalamus or other volumetry and prematurity, or with corpus callosum DTI measures. A box plot showing FA measures in GMA groups is illustrated in Figure 5. No significant association between DTI regional measures and GMA was found.

Weak association (which doesn’t survive multiple comparison correction) was observed between total HNNE and Cerebral Peduncle.

Response: 40 week Clinical Assessment
Regional DT assessment did not find a significant association between 40 week clinical assessments and 30 week MRI measures.

Response: 30 week Clinical Assessment
Although a weak association can be seen in many regions between HNNE and DT measures (Figure 6). No significant associations remain after controlling for GA, PMA-at-scan, BW and gender and correcting for multiple comparisons. We did not find a correlation (0.002 < p < 0.05) associations require further investigation (PCR, internal capsule, CP, PTR, SS and SLF and MD (SCR)).

Conclusions:
In this preliminary study of very early brain development in infants born preterm with no evidence of brain injury:
1) Our Structural and DTI measures were consistent with MRI studies acquired at near term equivalent age.
2) A weak association was observed between bed-side neurological assessment and structural or diffusion MRI at 30 weeks PMA.

Infants can be scanned safely early and advanced imaging with corresponding clinical tools has an important role to play in earlier detection of motor delay and infants at risk of a later diagnosis of Cerebral Palsy.

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Figure 1: Scatter graph of early DTI values (mean PMA-at-scan=32.2 weeks) for (top) Fractional Anisotropy and (bottom) Mean Diffusivity in various tracts.