

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Woodward LJ, Anderson PJ, Austin NC, et al. Neonatal MRI to predict neurodevelopmental outcomes in preterm infants. *N Engl J Med* 2006;355:685-94.

## Scoring White and Gray Matter Abnormalities on Cerebral Magnetic Resonance Imaging in the Preterm Infant at Term

The following protocol was followed in order to obtain good quality images with minimal motion artifact to facilitate accurate qualitative scoring, without using sedation.

1. The infants were fed approximately 45 minutes before the imaging and then wrapped and swaddled in a vacuum air extraction device to support the infant and reduce motion artifact (Figure 1).
2. Because the T2 and T1 relaxation time constants are longer in newborn infants than older children, optimum contrast in T2-weighted images was obtained at longer echo times (TE) on the order of 160 ms and T1-weighted images were optimized with inversion times (TI) on the order of 1100 ms. It is worthy of note that the T1 relaxation time constant varies with magnetic field strength, being greater at higher field strengths, such as 3 T.

Figure 1: Infant wrapped in vacuum extracted bean bag for MRI



The scoring system for the composite white matter and gray matter scores described in this study consisted of eight assessments each using a 3-point scale. The development and use of this system has been described in previous work from our group (1,2).

**White matter abnormality** was graded using five areas of assessment within the white matter with a score of 1 (normal), 2 (mild abnormality) and 3 (moderate-severe abnormality) for each area of assessment. The five areas of white matter abnormality that were scored included:

1. ***The nature and extent of white matter signal abnormality*** - This was scored based on the T1- and T2-weighted signal abnormalities in the white matter best observed in the axial imaging.

Grade 1: normal T1- and T2-weighted signal throughout the white matter.

Grade 2: focal regions of high T1-or T2-weighted signal (2 or fewer regions per hemisphere).

Grade 3: multiple regions of high T1- or T2-weighted signal (more than 2 regions per hemisphere).

2. ***Periventricular white matter volume loss*** – This was also scored based on the combined T1- and T2-weighted imaging analyzing the ratio of periventricular white matter to ventricular volume in both the axial and sagittal imaging.

Grade 1: normal periventricular white matter volume usually associated with small ventricles

Grade 2: mild reduction in white matter volume with mild to moderate increased ventricular size.

Grade 3: marked reduction in white matter volume often occurring with marked increase in the size of the ventricle and/or extra-axial space.

3. ***Cystic abnormalities*** – This was easily assessed on any imaging view or modality but occurred rarely (only 5 percent or less of MR images).

Grade 1: normal, with no cystic abnormality.

Grade 2: less than 2mm single focal cyst.

Grade 3: multiple cysts or a single larger (2mm or greater) single focal cyst which is rare.

4. *Ventricular dilatation* – This was also scored based on the combined T1- and T2-weighted imaging in both the axial and sagittal imaging.

Grade 1: normal with no evidence of ventricular dilatation.

Grade 2: moderate enlargement resulting in mild rounding of the frontal horns, minimal enlargement of the temporal horns and moderate enlargement of the occipital horns.

Grade 3: more global enlargement of a moderate to severe nature including significant enlargement of the frontal, temporal and occipital horns.

5. *Thinning of the corpus callosum* – This was scored based on the sagittal and coronal T1-weighted MR imaging.

Grade 1: normal, with thick corpus callosum visible in all views.

Grade 2 :focal thinning in the corpus callosum often visible in the mid region of the body of the corpus on sagittal images.

Grade 3 :global thinning across the entire corpus callosum.

These 5 assessments of the cerebral white matter were then combined to give an overall white matter abnormality score which was categorized as:

- a) no abnormality - Total score 5 to 6
- b) mild abnormality – Total score 7 to 9
- c) moderate abnormality – Total score 10 to 12
- d) severe abnormality – Total score 13 to 15.

**Gray matter abnormality** was graded using three scales assessing:

1) ***Presence of gray matter cortical signal abnormality*** . This was very rarely detected (in approximately 1% of infants) and thus did not contribute significantly to the overall scoring but was scored on high signal intensity in the cortex on axial T1 and/or loss of cortical ribbon signal on axial T2-weighted MR imaging.

2) ***Quality of gyral maturation*** – Cortical gyration maturation was rated by standard gyral model (3,4) using representative MRI images and cerebral models of gyral development at 34 weeks, 36 weeks, 38 weeks and 40-42 weeks on axial T1- and T2-weighted MR imaging. The gyral pattern assessment in these maturational assignments included at 34-36 weeks the presence of marginal sulcus, paracentral gyrus with secondary sulci present in the frontal lobes, superior and middle temporal, rolandic and occipital regions. By 36-38 weeks the gyral pattern should include additional secondary gyri in the transverse and inferior temporal and cingulated gyri. At 40 weeks' gestation there would be tertiary inferior temporal and inferior occipital gyri and sulci

Grade 1: normal for 40 weeks.

Grade 2: 2 to 4 weeks delay in gyral development (i.e. consistent with 36 to 40 weeks).

Grade 3: more than 4 weeks delay in gyral development.

3) ***Size of the subarachnoid space*** - This was scored based on the sagittal T1 and coronal T1- or T2-weighted MR images for the size of the subarachnoid space in relation to the cerebral mantle.

Grade 1: small subarachnoid space which was barely visible.

Grade 2: mildly enlarged CSF space with visible enlargement of the space between the major sulci and the interhemispheric space in addition to the extracerebral space.

Grade 3: more substantially enlarged global subarachnoid space with visible cerebrospinal fluid between many gyri as well as interhemispheric and extracerebral.

The total gray matter score was then calculated and categorized as

(a) normal - score 3 to 5

(b) abnormal score 6 to 9.

Further details about the clinical and research application of this scoring system can be obtained from Terrie Inder ([inder\\_t@kids.wustl.edu](mailto:inder_t@kids.wustl.edu)).

## References

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2. Woodward L, Mogridge N, Wells S, Inder T. Can neurobehavioural examination predict the presence of cerebral injury in the very low birth weight infant? *Journal of Developmental and Behavioral Pediatrics* 2004;25:326-34.
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4. Martin E, Kikinis R, Zuerrer M, Boesch C, Briner J, Kewitz G, et al. Developmental stages of human brain: an MR study. *J Comput Assist Tomograph* 1988;12(6):917-22.

Supplementary Appendix

Neurodevelopmental Outcomes of Very Preterm Children Born in Christchurch and Melbourne.

Outcome	Christchurch (N = 81)	Melbourne (N = 86)	Total Sample (N=167)	Test of Between Centre Differences p
Mean (SD) MDI cognitive score	85.83 (14.22)	85.27 (20.04)	85.54 (17.36)	.56
% Severe (>2SD) cognitive delay	13.6	19.3	16.5	.33
Mean (SD) PDI psychomotor score	90.46 (15.01)	87.20 (17.46)	88.81 (16.33)	.20
% Severe (>2SD) motor delay	4.9	15.7	10.4	.02
% Cerebral Palsy	12.3	8.1	10.2	.37
% Hearing defect	2.5	8.1	5.4	.11
% Visual defect	8.6	5.8	7.2	.48
% Any neurosensory impairment	9.9	12.8	11.4	.55
% Any neurodevelopmental disability	27.2	29.1	28.1	.78
Mean (SD) total number of disabilities	.43 (.84)	.65 (1.03)	.54 (.94)	.14