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Introducing MANTis: Morphological adaptive neonate tissue segmentation. Unified segmentation for neonates

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Target Audience: These methods will be useful to researchers using magnetic resonance imaging of newborns to investigate prematurity and brain development.

Purpose: Deviation from typical development trajectories around birth can lead to long-term cognitive deficits. Magnetic resonance (MR) imaging is a vital tool allowing in-vivo measurement of many aspects of brain structure, such as distribution of brain tissue types (i.e. tissue classification). Tissue classification allows volumes to be generated, and is a precursor of many complementary analysis approaches. Automated methods for tissue classification in MR images of adults are well established. However, challenges specific to neonatal MR images have meant that development of specialised, population-specific methods for tissue classification are required.

This project introduces *MANTiS* (Morphological Adaptive Neonate Tissue Segmentation), which extends the "unified segmentation" approach[1] to tissue classification implemented in SPM software to neonates.

Methods: Brain tissue classification methods require prior information and a mechanism to adapt this information to novel data (i.e. the neonate being classified). The prior information takes a variety of forms, including tissue brightness and spatial distributions. Adaptation may occur via the classification process, registration or a mixture of both. Probabilistic atlases provide a compact and convenient form of prior information that can be the basis for stable and accurate segmentation procedures if the novel data is not too different from the atlas. However providing adaptability while retaining stability is challenging. Data driven procedures are adaptable but difficult to develop and stabilise.

We introduce a 3-phase process utilizing a combination of unified segmentation, template adaptation via morphological segmentation tools and topological filtering to produce a fast, reliable and accurate neonate segmentation method that is able to perform well in the presence of pathologies common to preterm infants. We utilize the Imperial College London 40-week neonate template[2] and segment 8 tissue classes: cortical gray matter, white matter, subcortical gray matter, hippocampus, amygdala, cerebellum, brain stem and cerebral spinal fluid. Subcortical GM classes were combined as "deep gray matter" for validation purposes. The processing steps are:

> **1)** Unified segmentation using neonate template. **2)** Template adaptation and brightness adjustment: **2a)** Refined template using improved CSF segmentation from a morphological watershed from markers[3]. **2b)** White matter brightness correction using morphological reconstruction by dilation. **3)** Second phase of unified segmentation using adapted template

Kappa scores were used to compare MANTiS results to those of the ANTs package (incorporating Atropos segmentation[4]) followed by manual adjustment.

Three groups of participants were examined in this study – preterm infants born prior to 30 weeks postmenstrual age (PMA) (n=12) and scanned at 27 to 32 weeks PMA, preterm infants (n=12) scanned at term-equivalent (37-41 weeks PMA) and healthy, term-born infants (n=12) scanned within the first week of life. Subjects were studied using a Siemens (Erlangen, Germany) 3T Trio scanner using an infant-specific quadrature head coil (Advanced Imaging Research, Cleveland, OH). T2-weighted images were obtained using a turbo spin echo sequence (TR/TE 8600/161ms, voxel size=1×1×1mm^3).

Results:

Table 1. Median kappa overlap scores for MANTiS compared with manually adjusted ANTs Atropos results

	Cortical gray matter	Deep gray matter	White matter	Cerebellum
Preterm (27-32wk scan)	0.69 (IQR=0.665, 0.713)	0.795 (IQR=0.775, 0.813)	0.855 (IQR=0.835, 0.863)	0.755 (IQR=0.735, 0.773)
Preterm (TEA scan)	0.77 (IQR=0.718, 0.790)	0.815 (IQR=0.808, 0.823)	0.840 (IQR=0.808, 0.863)	0.81 (IQR=0.788, 0.833)
Term controls (TEA scan)	0.80 (IQR=0.780, 0.813)	0.805 (IQR=0.800, 0.820)	0.850 (IQR=0.815, 0.853)	0.830 (IQR=0.818, 0.840)

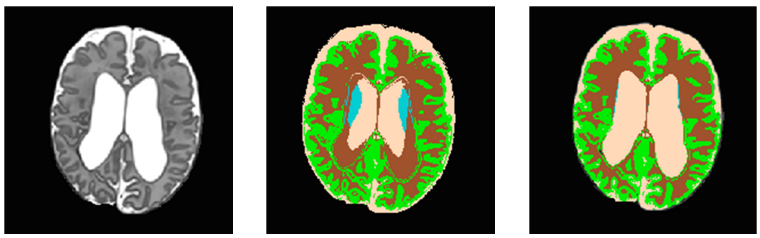

Figure 1. Segmentation stages (left to right). Original image, initial hard segmentation using unified segmentation (note incorrect ventricle size) and final segmentation following morphological adaptation.

Discussion and Conclusion: MANTiS produces segmentations with "substantial" to "almost perfect" kappa scores when compared with manually edited segmentations. It is able to process scans with typical characteristics seen in preterm infants (e.g. enlarged ventricles and white matter pathology) without user intervention. MANTiS is a fast (15min) and useful tool for volumetric analysis of neonate scans.

References: [1] Ashburner J, Friston KJ. Unified Segmentation. *NeuroImage*. 2005;26:839-51. [2] Kuklisova-Murgasova M, et al. A dynamic 4D probabilistic atlas of the developing brain. *NeuroImage*. 2011;54:2750-63. [3] Beucher S, Meyer F. The morphological approach to segmentation: the watershed transformation. *OPTICAL ENGINEERING-NEW YORK-MARCEL DEKKER*. 1992;34:433-. [4] Avants BB, et al. An open source multivariate framework for n-tissue segmentation with evaluation on public data. *Neuroinformatics*. 2011;9:381-400.