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Introduction
Ischemic perinatal stroke (IPS) occurs in 1/5000 live births each year in the United States. Objective, rapid and accurate quantification of ischemic lesion volumes in neonates would have wide clinical application. In particular, effective evaluation and monitoring of ischemic lesions volumes would aid physicians in making treatment decisions. To our knowledge there are no accurate automated methods to quantify neonatal ischemic lesions using ADC maps.

Ischemic brain tissue has a signature hypointensity on ADC maps that indicates a net reduction in water diffusion relative to normal unaffected tissue. The ischemic lesions induced by embolic arterial stroke are prominent within the first 72 hrs of injury and can be defined by identifying and segmenting the hypointense region. Assessment of these ischemic lesions soon after injury would help clinicians make timely, informed treatment decisions. Manual volumetric injury quantification is not used clinically because it is a labor intensive process. Observer (inter-/intra-) variability can also be problematic; however it remains the gold standard. We used a multi-disciplinary approach to develop two semi-automated methods of ischemic injury segmentation, ADC thresholding and hierarchical region splitting, and compared them with manual segmentation results. We believe that this multi-disciplinary approach will provide a fundamental basis for the development of novel and clinically relevant automated segmentation software for rapid and unbiased ischemic injury discrimination.

Methods
A group of five neonates with IPS and two controls underwent routine 1.5T MRI acquisition within 3.75 ± 1.5 days of presumed injury (birth). Each patient’s ADC map was segmented with each method. Manual Delineation: The hypointense regions were manually outlined and segmented from normal appearing brain matter (NABM) on each slice by one observer. ADC Threshold Definition: A normal ADC value was measured in a small region of interest (ROI) in NABM contralateral to the lesion and the threshold ADC value was calculated by taking a percentage of the normal ADC. Using this threshold, all tissue ADC below the threshold was defined as lesion and all tissue above the threshold as NABM. Hierarchical Region Splitting: A hierarchical region splitting algorithm was tested to segment the ADC maps using objectively selected thresholds based on maximizing the mean between two groups within the histogram of the image (Fig. 2). Subsequently, the image was split into sub-images and the connected components were found through multiple iterations. Volumes (healthy or ischemic) were computed by multiplying the number of pixels in each segment by the voxel volume. A one-way repeated measures ANOVA was used to compare the lesion volumes between the methods.

Results
Manual delineation accurately defined the ischemic injury. The ADC threshold also defined the ischemic tissue, but in most cases it appeared to report a smaller volume. Overall, the hierarchical region splitting method reported a smaller lesion volume compared to the other two methods ($p < 0.05$).

Conclusions
Compared to manual segmentation, the ADC threshold definition and hierarchical region splitting methods can accurately segment ischemic lesions from NABM on ADC maps in neonatal IPS patients. Large and discrete ischemic lesions are easily segmented manually while, automated methods are required to accurately define bilateral or diffusions, as in neonatal hypoxic-ischemic encephalopathy. Hierarchical region splitting is objective and because it is not dependent on the presence of NABM it can be used to differentiate a wide range of lesion patterns. Together these automated techniques can help improve methods for automated image segmentation routines in clinical settings where efficiency and accuracy are crucial for therapeutic intervention.