Mathematical Modeling of Cell Density in Diffusion Weighted Imaging (DWI) - Clinical Application in Crossed Cerebellar Diaschisis

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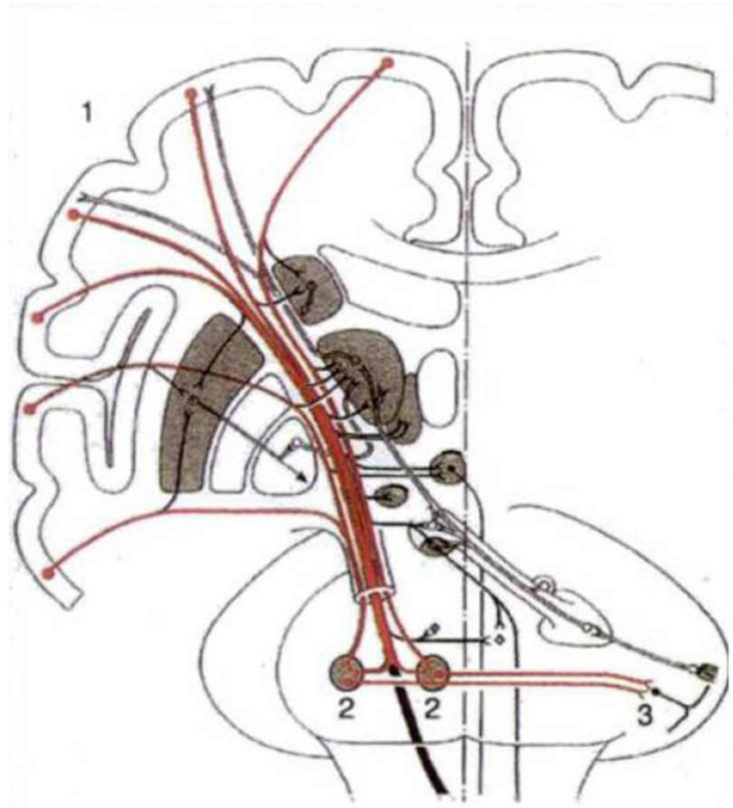
Outline

Introduction

- Crossed cerebellar diaschisis (CCD) refers to transneuronal degeneration in the cerebellum as a result of contralateral cortical pathology and disruption of the corticopontocerebellar pathway.

- Stroke patients with CCD have been found to have a worse prognosis in multiple studies (e.g., Sobesky et al., 2005).

- Our aim in this study is to propose a modeling approach for accurate detection of CCD on routine MRI scans with DWI.



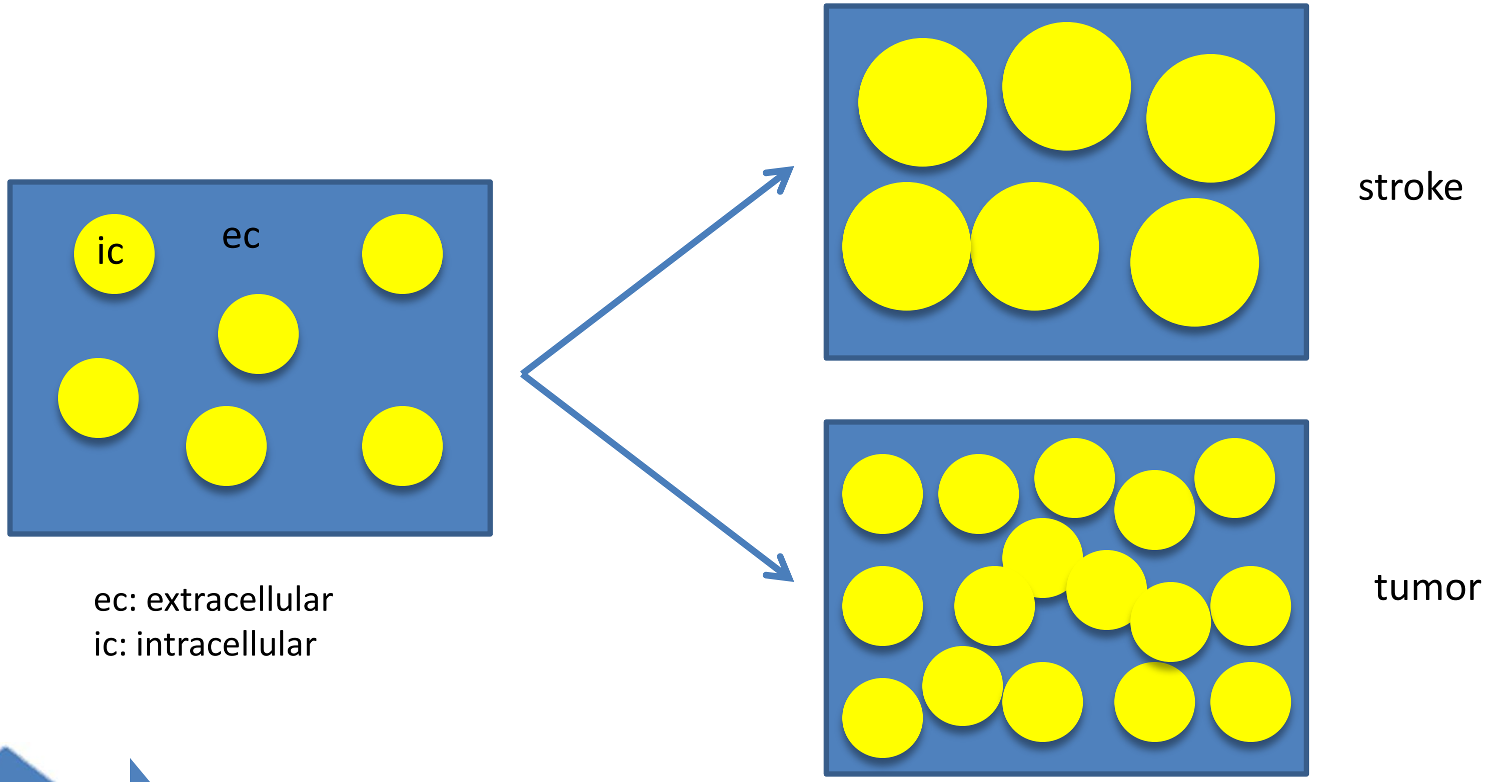
Rabin et al., 1998.

Purpose

- Diffusion weighted imaging (DWI) has become increasingly popular in clinical neuroimaging for evaluation of stroke, tumors, infection and neurodegeneration.
- Apparent Diffusion Coefficient (ADC) maps are typically generated from *b* values based on a presumed, mono-exponential relationship.
- We aim to apply a bi-exponential model, where the DWI signal is presumed to be explained by intracellular and extracellular compartments.

Purpose

In acute stroke and malignancy, one would expect a higher intracellular to extracellular ratio secondary to cytotoxic edema and increased cellularity, respectively.



ec: extracellular
ic: intracellular

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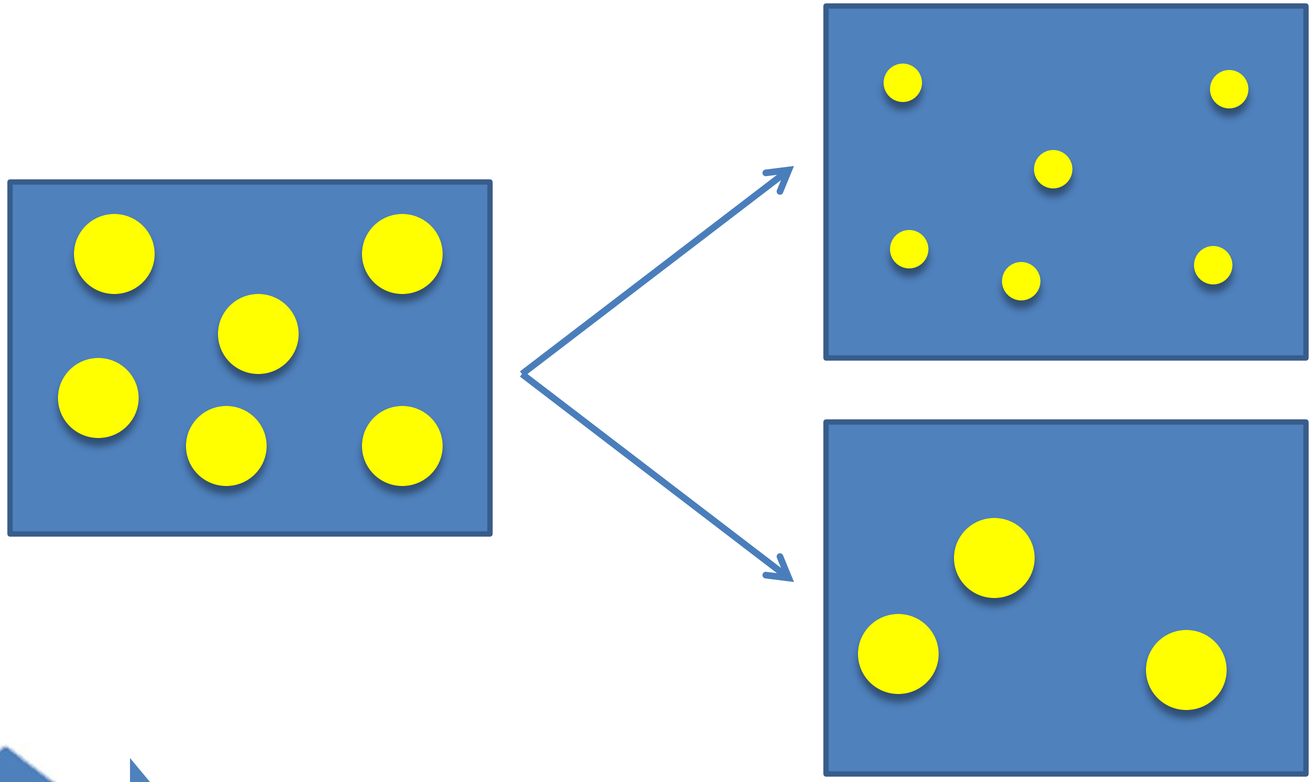
Purpose

Conversely, in the case of CCD, we hypothesize that there will be a higher extracellular contribution to the DWI signal in the abnormal cerebellar hemisphere, secondary to neuronal atrophy and/or decreased number of neurons secondary to cell death.



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Purpose

- Our main hypothesis is that we find a higher extracellular contribution (or alternatively, lower intracellular contribution) to the DWI signal in the cerebellar hemisphere contralateral to cortical pathology, i.e., affected by CCD.

- Bi-exponential models have been previously proposed in experimental DWI studies with multiple *b* values to provide better fits for the DWI signal (e.g., Mulkern et al., 1999; Maier et al., 2001).

- Here, we aim to numerically solve for a biexponential model using three, typically clinically accessible *b* values (i.e., 0, 500, and 1000).

Methods

- We study DWI images of six patients with cortical encephalomalacia, predominantly secondary to old infarction in the middle cerebral artery territory.

- Semi-automatic segmentation of the cerebellum is performed on Matlab (MathWorks, Natick, MA).

Methods

We numerically solve a bi-exponential model at a voxel-by-voxel basis to obtain intracellular and extracellular contributions for each cerebellar hemisphere. Histograms of *f*, the intracellular component coefficient, are then obtained for each cerebellar hemisphere.

signal

intracellular fraction

intracellular diffusion coefficient

extracellular fraction

extracellular diffusion coefficient

$$\frac{S_j}{S_0} = f * e^{-b_j D_i} + (1 - f) * e^{-b_j D_e}$$

Set of two equations with b_j: {500, 1000}

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Methods

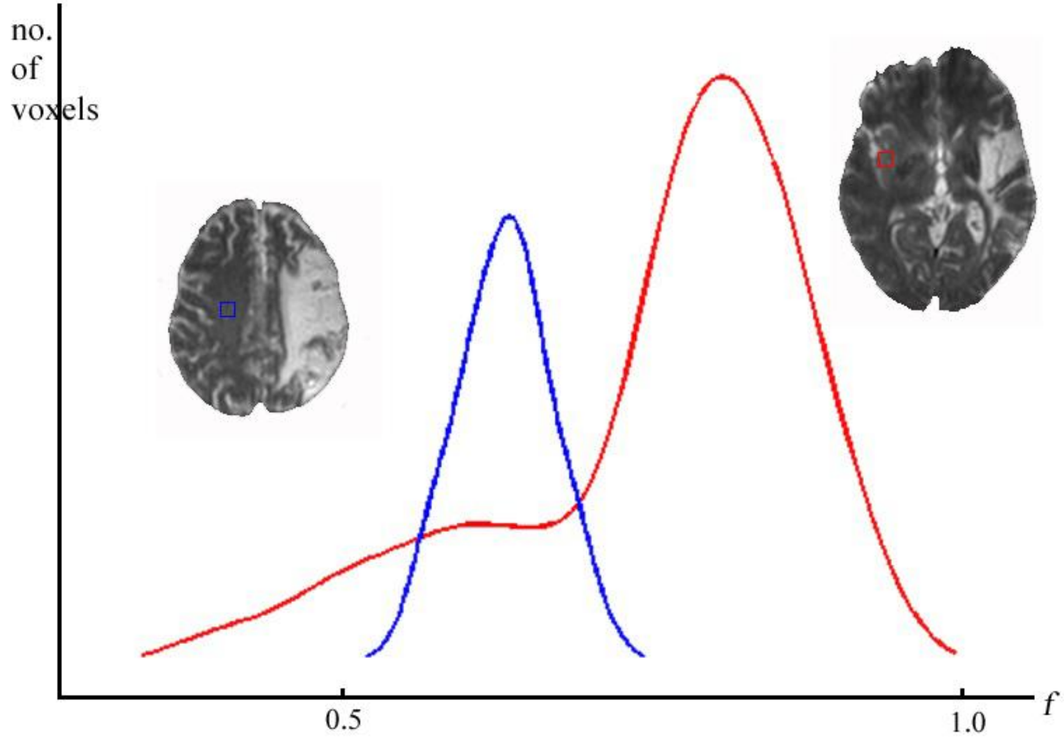
- We additionally select regions of interest in normal-appearing basal ganglia (presumed to be rich in gray matter) and in normal-appearing centrum semiovale (presumed to be rich in white matter).
- Similarly to our analysis of the cerebellum, we solve a voxelwise, bi-exponential model to compare the intracellular and extracellular coefficients between each region of interest and acquire *f* histograms.
- As proof of principle, we expect that the basal ganglia region of interest demonstrates higher *f* (intracellular coefficient) than the centrum semiovale region.

Methods

- After obtaining histograms for intracellular coefficients, *f*, in each cerebellar hemisphere, we compare the distributions via a Mann-Whitney U test and obtain *p* values.
- Our null hypothesis is that two regions being compared result in the same distribution of intracellular coefficients.

Results

As expected, the basal ganglia region of interest (shown here in red) has a significantly higher *f*, i.e., contribution of the intracellular compartment, when compared to the centrum semiovale (shown here in blue; $p \ll 0.001$).



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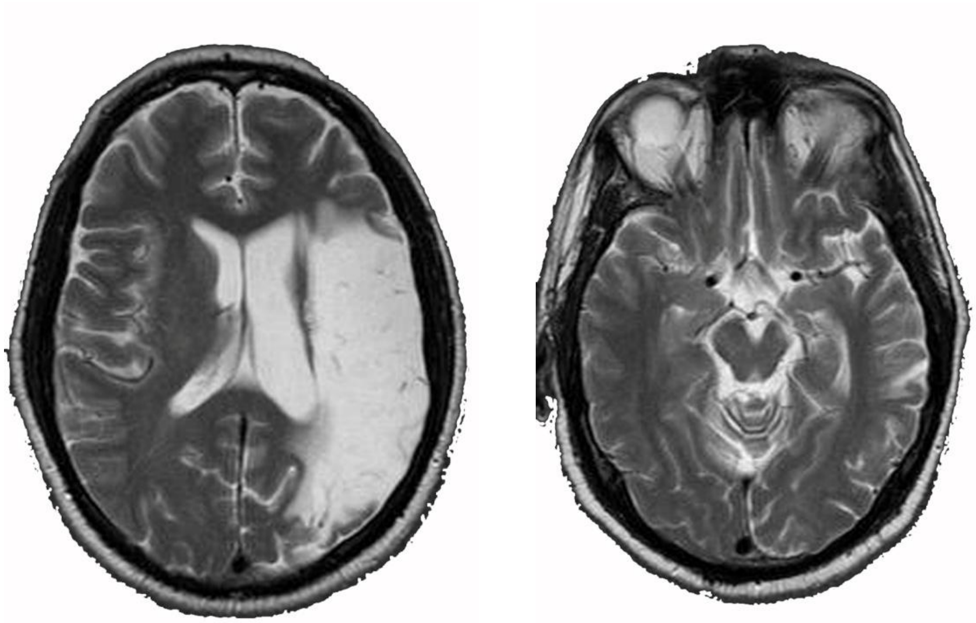
Results

- Axial T2 weighted MRI images are shown for one of our six cases, demonstrating a large, old left MCA territory infarct and Wallerian degeneration of the ipsilateral cerebral peduncle.
- Histograms of the intracellular coefficients for each cerebellar hemisphere are shown in the next slide.



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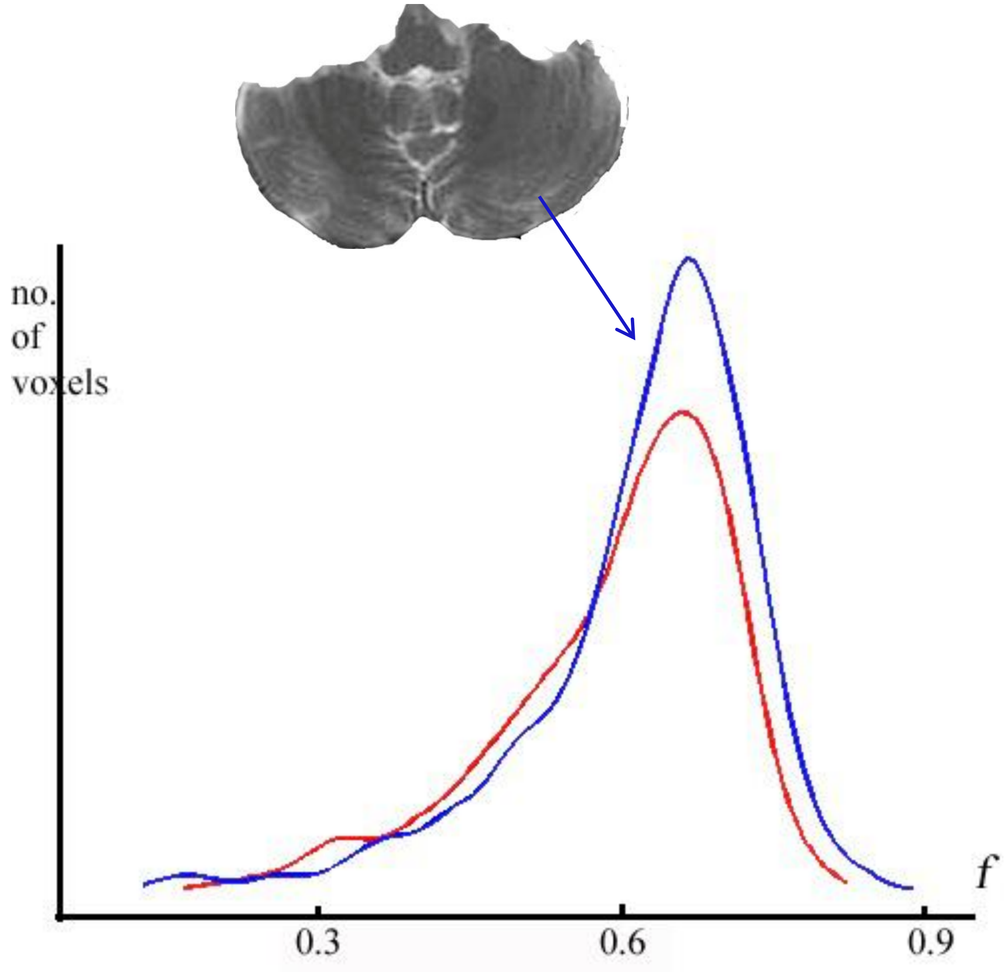
Results

We find a significantly lower intracellular contribution to the DWI signal in the contralateral, right cerebellar hemisphere (red), compared to the left (blue; $p < 0.01$).



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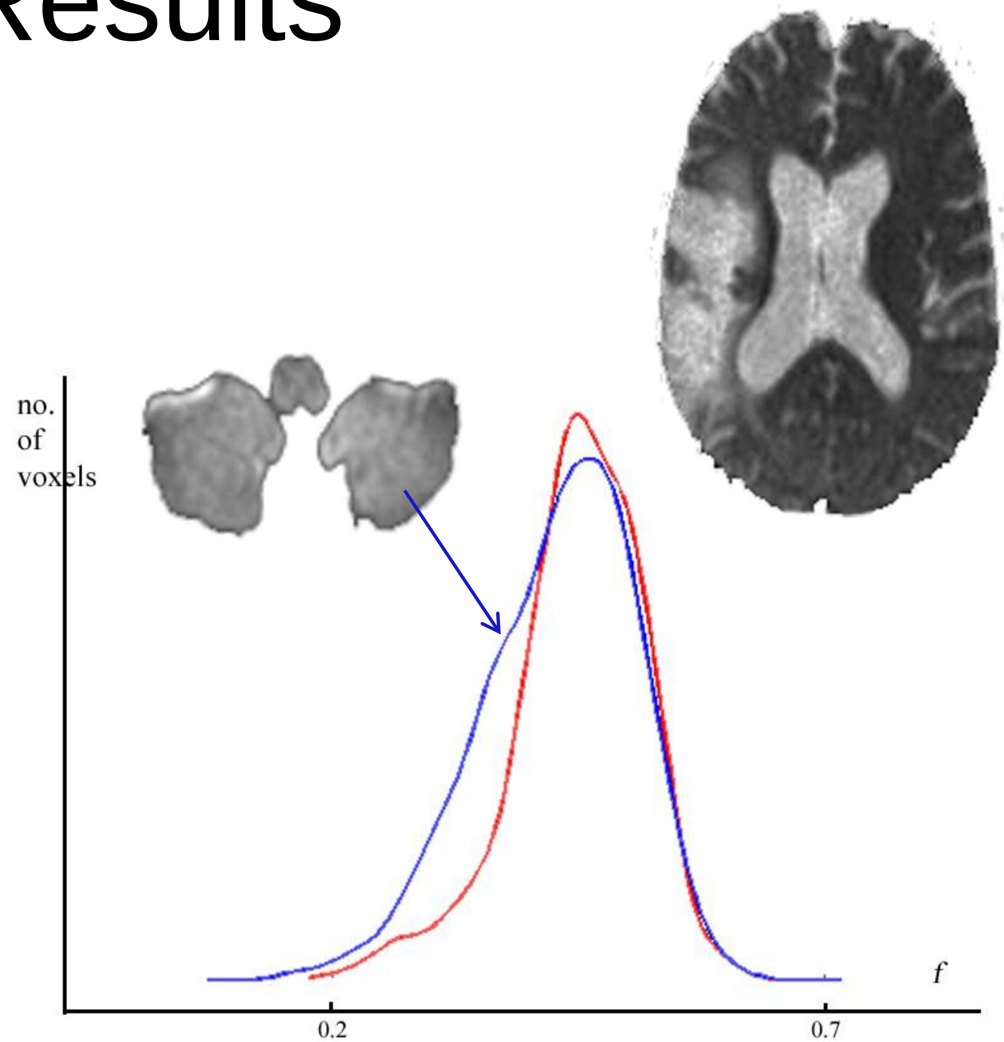
Results

- Another case is shown with right-sided cortical encephalomalacia.

- There is significantly lower intracellular contribution in the contralateral, left cerebellar hemisphere (blue), compared to the right (red; $p < 0.01$).



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Results

- All six cases similarly showed significantly lower intracellular coefficients in the cerebellar hemisphere contralateral to the side of cortical pathology.

- This corroborates our hypothesis in that CCD leads to a lower intracellular to extracellular compartment ratio, presumably as a result of decreased neuronal density.

Discussion

- We apply a bi-exponential model composed of intracellular and extracellular compartments to aid in detection of crossed cerebellar diaschisis on DWI.

- We numerically solve for the contribution of each compartment to the DWI signal. Our method only utilizes three, typically clinically available *b* values.

- Our approach may thus offer promise for detection of sub-threshold signal differences in a variety of clinical scenarios.

Discussion

- CCD has traditionally been diagnosed on PET as asymmetric hypometabolism.
- Asymmetric atrophy on MRI is often subtle and difficult to detect.
- New studies have provided promising results with arterial spin-labeling MRI for detection of CCD (e.g., Kang et al., 2015; Strother et al., 2016).
- We provide a promising, quantitative approach to detection of DWI signal alterations in CCD with the advantage of applicability to clinical cases.

References

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