# Evaluation of Therapy Impact Using Diffusion/Perfusion MR Imaging

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## ABSTRACT

The combination of radiation and chemotherapy, although effective for long term survival of patients with primitive neuroectodermal tumors of the CNS including medulloblastoma, induce normal tissue effects that result in neurocognitive, endocrine and neurologic deficits. The aim of this study is to assess the usefulness of perfusion and diffusion MR imaging in assessing white matter (WM) damage after craniospinal irradiation and chemotherapy. Perfusion MR imaging provides hemodynamic information while diffusion imaging provides a measure of WM myelin integrity. The test case consisted of perfusion and diffusion data sets before and after radiation therapy. The methodology for perfusion data analysis was to fit a gamma-variate function to the time-series voxel-by-voxel signal intensity to obtain cerebral blood volume (CBV) and the mean transit time (MTT). The resulting CBV and MTT maps provided quantifiable estimates of regional blood volume and flow. Diffusion Tensor Imaging (DTI) data was processed using SPM99 to yield fractional anisotropy (FA) and apparent diffusion coefficient (ADC) maps. A Kohonen Self Organizing Map was used to segment conventional MR brain imaging into normal appearing WM (NAWM) and gray matter (GM). Changes in the histogram peak locations of WM in the frontal/temporal lobes (R1) and parietal/occipital lobes (R2) are reported for pre-therapy and post-therapy. ADC decreased by 8% in R1 and 11% in R2. FA increased by 55% in R1 but decreased by 10% in R2. Relative CBV decreased by 10% in R1 and by 23% in R2. MTT decreased by 33% in R1 and R2 each. Perfusion and diffusion MR imaging, therefore, promise to be useful tools for evaluation and improved understanding of therapy impact on normal brain parenchyma.

## THEORY

Diffusion-weighted MR imaging measures the microscopic random translational motion of water molecules.

**ADC** is a scalar index, invariant to the changes in the frame of reference, which reflects the diffusion characteristics and hence the integrity and organization of the tissue. The ADC measures the average diffusion distance in a region which reflects the extracellular / intracellular volume ratio and is extremely sensitive to acute ischemia. It is calculated as:

$$ADC = Tr\begin{pmatrix} Dxx & Dxy & Dxz \\ Dyx & Dyy & Dyz \\ Dzx & Dzy & Dzz \end{pmatrix} = Dxx + Dyy + Dzz$$

where D is the diffusion tensor.

**FA** is a direction invariant diffusion anisotropy index and reflects the degree of alignment of cellular structures within fiber tracts, as well as their structural integrity. It is calculated as follows:

$$FA = \frac{\sqrt{3\left[(\lambda_1 - \langle\lambda\rangle)^2 + (\lambda_2 - \langle\lambda\rangle)^2 + (\lambda_3 - \langle\lambda\rangle)^2\right]}}{\sqrt{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$

where λ1, λ2 and λ3 are the eigenvalues of the diagonalized diffusion tensor, D.

Perfusion-weighted MR imaging is a functional imaging technique that evaluates the hemodynamic parameters. A voxel-by-voxel concentration-time curve is obtained from a series of $T_2^*$ images acquired following an intravenous bolus injection of paramagnetic contrast agent. The concentration-time curve is then fit by a Γ-variate function defined as:

$$Cr(t) = At^B e^{\frac{-t}{C}}$$

where t is the time and A, B and C are the unknown parameters defining the Γ-variate function.

**CBV** is the cerebral blood volume and is defined as the area under the concentration-time curve given by:

$$CBV = A \cdot C^{B+1} \cdot \Gamma(B+1)$$

**MTT** indicates blood flow and is defined as the first moment of the concentration-time curve given by:

$$MTT = C \cdot (B+1)$$

## METHOD

Three sets of diffusion and perfusion weighted MR images were acquired for a pineoblastoma patient before, 1-month, and 4-months each after craniospinal irradiation and chemotherapy. The diffusion images were processed using Diffusion Toolbox installed in SPM99 to generate FA and ADC maps. The perfusion images were analyzed voxel-by-voxel using the Levenberg-Marquardt method for the non-linear Γ-variate fit yielding CBV and MTT maps. These maps were generated for all three exams and registered to the RF corrected T2 weighted image of the first exam. 3D registration was performed using a normalized mutual information based Powell optimization technique.

A Kohonen Self Organizing Map (SOM) was used to segment conventional brain images into normal appearing white matter and gray matter. The segmented white matter was divided into two regions: frontal and temporal lobes (R1) and parietal and occipital lobes (R2). The ADC, FA, CBV and MTT values for the two regions were extracted from the registered maps and studied.

## RESULTS

Fig. 1 illustrates the ADC, FA, CBV and MTT maps registered to the T2 image along with the SOM classified segmentation map.

Changes in the histogram peak locations of white matter in the frontal/temporal lobes (R1) and parietal/occipital lobes (R2) were studied over the three exams. ADC decreased by 8% in R1 and 11% in R2. FA increased by 55% in R1 but decreased by 10% in R2. Relative CBV decreased by 10% in R1 and by 23% in R2. MTT decreased by 33% in R1 and R2 each. Fig. 2 shows the plots of peak histogram locations for ADC, FA, rCBV and MTT over the three exams.

## CONCLUSION

Perfusion and diffusion MR imaging promise to be useful tools for evaluation and improved understanding of therapy impact on normal brain parenchyma.

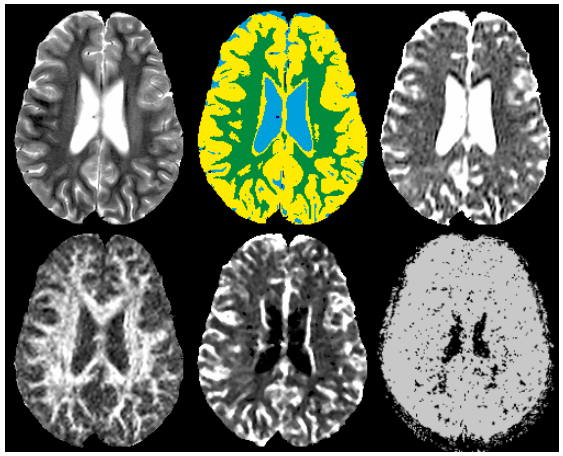

Fig. 1. Registered T2, Segmentation, ADC, FA, CBV and MTT images.

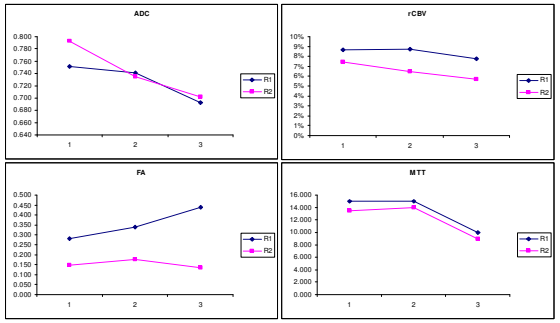


Fig. 2. Plot of peak histogram locations for ADC, FA, rCBV and MTT maps.

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