

Introduction MRI has been utilized to differentiate brain tumors from normal tissue but is not specific to heterogeneous features known to be within these lesions. Dynamic contrast MRI has been suggested to enhance the specificity in distinguishing these features but partial volume effects confound these analysis. In this work we employed a linear transformation to segment partial volume effects of known tissue from each voxel in order to determine if heterogeneity within tumors could be defined.

The linear transformation was the Eigenimage filter (1,2). The Eigenimage filter produces a composite image from a weighted summation of a sequence of images. The Eigenimage filter has been shown to compensate for partial volume averaging effects providing differentiation of overlapping tissues in MRI. In this application the Eigenimage filter was used to segment tissues with similar temporal dynamic contrast MRI signal changes by removing the partial volume component from overlapping tissue in each voxel in an iterative manner. The gray level in the resulting images is proportional to the partial volume of each temporal signal change characteristic relative to the other tissues removed. For comparison, the analysis included the calculation of conventional dynamic contrast MRI parameters, i.e. MTT, rCBV and rCBF (3,4), as well as calculations of specific patterns derived from the temporal dynamic contrast MRI curves (5).

Methods The Eigenimage filter was applied to dynamic contrast MRI from five glioma patients. The dynamic contrast MRI consisted of an echo-planar (EPI), gradient recalled image sequence (TE/TR = 40/1900 ms). In addition, conventional T2 and T1 weighted images were acquired for comparison. In Figure 1 the T2 fast spin-echo (FSE) and T1 post-Gd spin-echo (SE) image are shown along with one of the EPI.

Steps used in the analysis:

1. The operator initially defines a region of interest (ROI) to define the temporal EPI signal pattern for normal tissues (i.e. white and gray matter defined from contralateral hemisphere – see Figure 1).
2. The Eigenimage filter removes these normal temporal EPI patterns from each voxel and the resulting image displays the component of each voxel that has a temporal EPI pattern that is different from normal tissue. The resulting image is termed an “Orthogonal” image based on its mathematical derivation. The pixel value in the orthogonal image (see Figure 1 - Orthogonal) displays all tissues that have a component of their temporal EPI pattern that is different from normal tissue. Note in the orthogonal image the normal tissue signal is removed from all voxels and normal vasculature (e.g. venous sinus) and the tumor remain.
3. Orthogonal image is used to define ROI from voxel displaying maximum dissimilarity from normal tissue (i.e. “hot” voxel). This ROI is used to define temporal EPI pattern for this region, termed zones (e.g. zone 1).
4. Temporal pattern from zone 1 ROI and normal tissue are used in Eigenimage filter. Pixel values in the resultant image are proportional to the component of any additional patterns that remain within each voxel after normal and zone 1 tissue patterns are removed (Figure 2 – 2nd Orthogonal). In addition, images displaying the fractional component of each voxel parallel to the temporal patterns defined are segmented (Figure 2 – segmentation images).
5. ROI defined for “hot” voxel from 2nd Orthogonal used as additional pattern in Eigenimage filter. Procedure repeated until resultant image (4th Orthogonal) displays only noise and normal vasculature.
6. Perfusion maps (i.e. rCBV, MTT and rCBF) and temporal curve parameters (i.e. depth of bolus, bolus arrival slope, exit slope and post bolus slope) are calculated on a pixel-by-pixel basis (see Figure 5) to be used in the interpretation of the segmented regions.

Results In all studies the Eigenimage filter was able to segment multiple areas within the lesion. The perfusion maps also distinguished the tumor from the surrounding normal tissue but differences within the tumor were not clearly defined (see Figure 5). Tissue histology, perfusion parameters and calculated temporal curve values from specific biopsy locations in each study are given in the Table. In only 3 cases the rCBV, MTT or rCBF values showed significant differences between tumor zones. In all cases the parameters calculated from the temporal curves showed significant differences between zones. In addition to biopsy samples from the tumor several samples from normal tissue adjacent to the tumor were obtained. For the normal tissue (i.e. HF1295 and HF1186) none of the conventional parameters could distinguish between white and gray matter or between the normal tissue and tumor zones. The Eigenimage filter was able to segment white and gray matter from each other and the tumor zones in all cases.

Discussion In this study we report on a method that can separate partial volume effects in dynamic contrast MRI that allows the voxels with similar dynamic contrast MRI temporal characteristics to be defined. The creation of the segmented images takes only seconds, and an entire patient study can be segmented and presented for interpretation within minutes following the acquisition. The calculation of conventional perfusion maps rely on using the correct model for the acquisition and many of the assumptions that are required for these calculations to be accurate are not true for dynamic contrast MRI. Also, the calculation of the perfusion maps only consider the portion of the temporal curve when the bolus passes. As can be seen from the curves in Figure 5 after the passage of the bolus the curve shape from the different regions are distinct. The Eigenimage filter uses the entire curve resulting in the segmentation of normal tissue and different zones within the tumors.

Study	Biopsy Location	MTT	rCBF	rCBV	Depth of Bolus	Bolus Arrival Slope	Bolus Exit Slope	Post Bolus Slope	Histology Results
HF1292	Tumor Zone 1	5.00	0.51*	2.24*	179*	314*	78	0.87*	dense microvasculature and densely proliferating cells
	Tumor Zone 2	8.20	0.05*	0.46*	440*	68*	56	-0.06*	widely dispersed larger vessels and normal cellularity
HF1293	Tumor Zone 1	2.00	0.90*	1.81*	234*	499*	446*	2.85	isolated endothelial cells with slightly increased cell density
	Tumor Zone 2	2.00	2.13*	4.26*	520*	1141*	1041*	3.20	microvasculature proliferation and hyperplasia with dense cellularity
HF1295	Tumor Zone 1	2.00	1.00	2.00	344‡	691‡	779‡	1.80‡	microvasculature, endothelial cell hyperplasia and semi-solid tumor
	Gray matter	2.00	1.35	2.70	330+	665+	193	2.24+	
	White matter	2.00	0.92	1.84	166‡+	344‡+	101‡	0.97‡+	
HF1186	Zone 1	2.60	0.50	1.09	88*	127*	133*	4.50**	no visible staining of vasculature and dense cellularity
	Zone 2	2.40	0.64	1.48	355*	443**	450**	1.88*	normal vasculature and cellularity
	White matter	2.40	0.46	1.20	133‡	175‡	168‡	2.08‡	
HF1185	Zone 1	6.20*	2.53	15.23*	791*	1593*	1226*	3.53	vascularity and endothelial cell proliferation and hyperplasia
	Zone 2	2.60*	3.44	8.71*	542*	1098*	592*	2.89	minimal vasculature and solid tumor characteristics

* = Difference between zones significant, † = Difference between normal tissue and zone significant, + = Difference between normal tissues significant (p<0.05).

References
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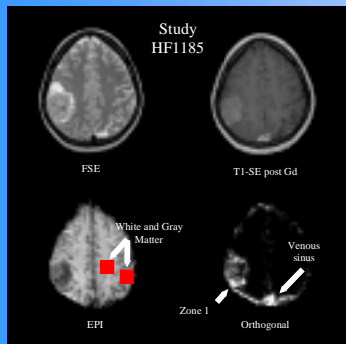


Figure 1

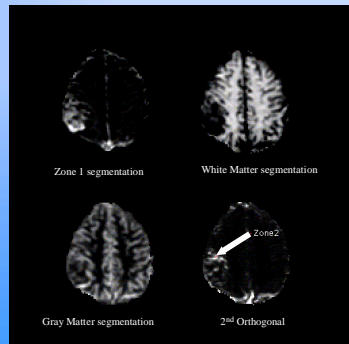


Figure 2

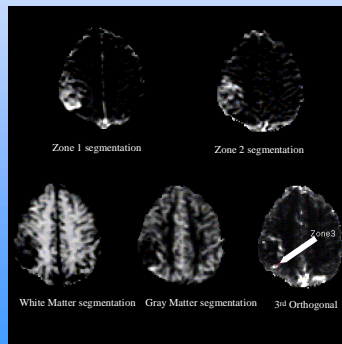


Figure 3

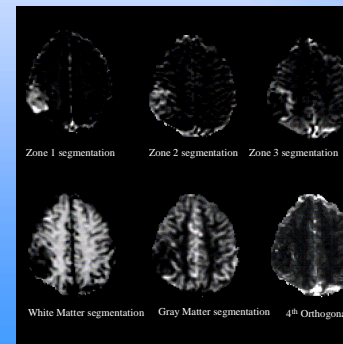


Figure 4

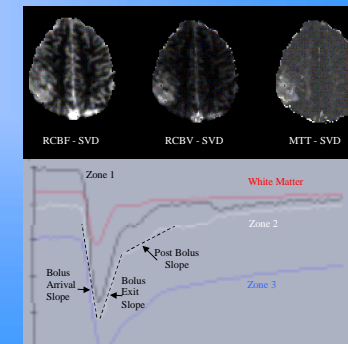


Figure 5