

## Classification of Ischemic Pathologies by Quantification of T1Sat: A T1Sat increase of 25% or more signifies disruption of the Blood Brain Barrier

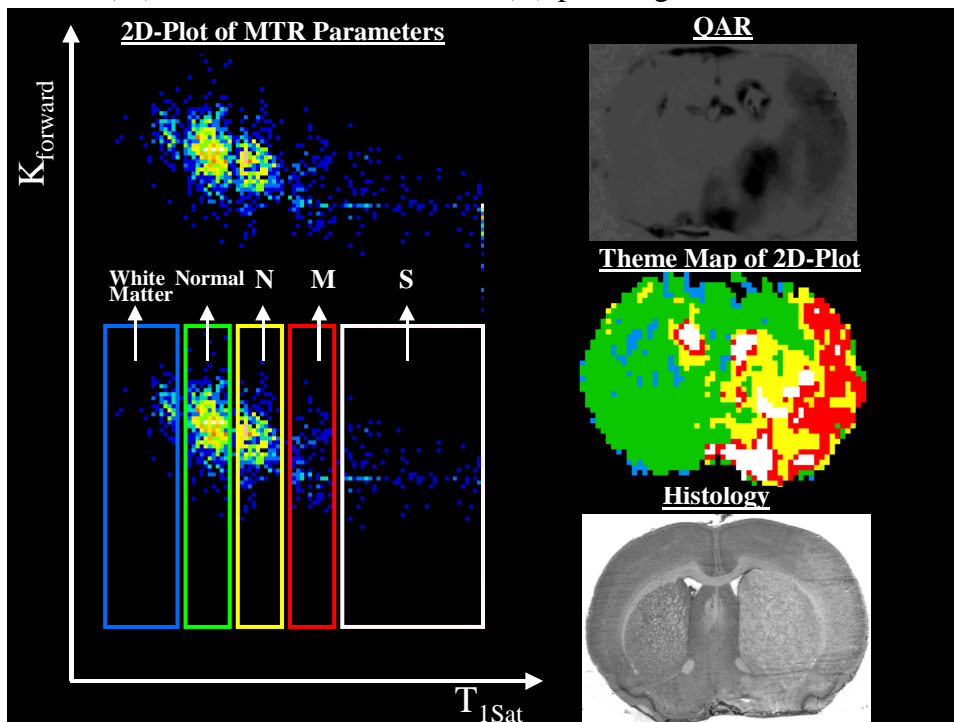
V. Nagesh<sup>1</sup>, R. A. Knight<sup>1,2</sup>, T. N. Nagaraja<sup>3</sup>, J. Xu<sup>3</sup>, K. A. Keenan<sup>3</sup>, P. A. Whitton<sup>1</sup>, J. D. Fenstermacher<sup>3</sup>, J. R. Ewing<sup>1,2</sup>

<sup>1</sup>NMR Research, Neurology, Henry Ford Health Systems, Detroit, MI, United States, <sup>2</sup>Physics, Oakland University, Rochester, MI, United States, <sup>3</sup>Anesthesiology, Henry Ford Health Systems, Detroit, MI, United States

**INTRODUCTION:** Acute management of stroke behooves rapid, accurate imaging techniques that evaluate the dysfunction of the microvascular system within the ischemic tissue. To address this, the contrast inherent in magnetization transfer imaging (MTC) and its associated parameters were investigated as possible indices of blood-brain barrier (BBB) opening.

**METHODS:** Transient focal ischemia was induced in 20 male Wistar rats by intraluminal suture occlusion of the middle cerebral artery; three hours later reperfusion was initiated by withdrawing the filament. Rapid estimates of  $T_1$ ,  $T_{1sat}$ ,  $K_{for}$  (apparent forward rate constant) and MTR (magnetization transfer ratio) maps were obtained from composite images using the Phase Incremented Progressive Saturation (PIPS) method<sup>1</sup>, 4 hours post-ictus in a 20-cm bore 7 Tesla magnet. MTC images were acquired from a single 2mm thick slice (FOV = 32 mm, 128x128 matrix). Imaging time for the sequence was 12 minutes. Cluster scattergrams of  $K_{for}$  vs.  $T_{1sat}$  were generated. Theme maps depicting distribution of distinct tissue types were constructed from the columnar clusters of pixels identified on the 2D scattergram (2DS). After MRI measures, rats were injected with <sup>14</sup>C-Gd-DTPA for quantitative autoradiographic (QAR) confirmation of BBB damage (BBBD). Alternate brain sections from these rats were stained with cresyl violet for histological demarcation of the area of ischemic injury.

**RESULTS:** Distinct, well-separated columns of pixels on 2DS, corresponding to severe BBBD (S), moderate BBBD (M) and non-BBBD ischemic (N) pathologies were noted [See Figure]. There was striking spatial and



quantitative correlation between 2DS, QAR and histology of all 20 animals. There were no significant differences in areas identified by 2DS and the corresponding pathology (paired t-test, S+M vs. QAR:  $p = 0.756$ , S+M+N vs. Histology:  $p = 0.634$ ). Post-hoc measures of  $T_{1sat}$  from S, M, and N regions identified by 2DS and expressed as a ratio of contralateral normal tissue yielded markedly

| Tissue | $T_{1sat}$ Ratio |
|--------|------------------|
| S      | $1.74 \pm 0.15$  |
| M      | $1.46 \pm 0.04$  |
| N      | $1.22 \pm 0.01$  |

different ratios among the regions of injury (see table above).

**Conclusions:** We have described an MT tissue signature model to simplify and facilitate rapid characterization of ischemic tissue. The characteristic quantitative  $T_{1sat}$  changes observed in-vivo can be used to accurately and non-invasively detect the sites and degree of BBB opening and also to identify ischemia-injured tissue with normal barrier function. In summary, MT offers the potential for specific characterization of BBB failure within ischemic tissue.

### References:

1. Ewing JR, Jiang Q, Boska M et al Magn Res Med. 1999; 41, 696-705. This work was supported in part by NINDS grant RO1NS38540.