Estimates of relative contrast recirculation obtained from perfusion MRI: a potential tool for guiding treatment decision in acute ischemic stroke

S-P. Wu[1], L. Vidarsson[1], J. Winter[1], D. Mikulis[2], and A. Kassner[1]

[1]Medical Imaging, The Hospital for Sick Children and the University of Toronto, Toronto, Ontario, Canada, [2]Medical Imaging, The Toronto Western Hospital, Toronto, Ontario, Canada

Introduction:

Recombinant tissue plasminogen activator (rt-PA) is an effective therapy for acute ischemic stroke (AIS), but increased risk of hemorrhagic transformation (HT) limits the general use [1]. Advances in physiological MR imaging have the potential to objectively guide rt-PA treatment and, thereby, substantially reducing the risk of HT. One example is permeability MRI, which is currently an add-on sequence to our acute stroke protocol, and was previously demonstrated to be effective for the assessment of blood-brain-barrier (BBB) disruptions, as well as prediction of HT [2]. However, one major limitation of this technique is the long scan time (~5 min), which is problematic for critically ill AIS patients. On the other hand, T_2*-weighted perfusion MRI is part of the routine stroke imaging protocol and can be acquired in less than 2 minutes. From this sequence, it is possible to extract a parameter called relative recirculation (rR), which was previously applied to the assessment of tumor microcirculation [3]. The purpose of this study was to determine the relative efficacy of rR, compared with permeability (KPS), for prediction of HT in AIS patients.

Materials and Methods:

Thirty two AIS patients (aged 38-80 years) were examined < 4 hours of symptom onset. MRI was performed on a 1.5T MR system (GE Healthcare, Milvaukee, USA) equipped with Echo-Speed gradients and an 8 channel head coil. Dynamic contrast-enhanced imaging, including permeability and perfusion MRI, was performed as part of our acute stroke protocol. Permeability (KPS) was obtained from a 3D GRE scan with the following parameters: TR 5.9sec, TE 1.5ms, FOV 240mm, matrix size 256 × 192, flip angle 20º and slice thickness 5mm. The total acquisition time for 31 volumes was 4.8 minutes. rR was obtained from a T2*-weighted single shot EPI scan with the following parameters: TR 1725ms, TE 31.5ms, FOV 240mm, matrix size 96 × 64,flip angle 90º and slice thickness 5mm. The total acquisition time for 25-40 dynamic scans was 1.5 minutes. Gd-DTPA (0.1mmol/kg) was injected (Omniscan, GE healthcare, USA) as a bolus for both scans after a series of baseline acquisitions. Data were analyzed offline using custom designed software (MR analyst vs. 2.1) developed in Matlab. Permeability (KPS) and rR were calculated as previously described by Roberts et al [4] and Kassner et al. [3], respectively. Two regions-of-interest (ROI) were defined on the DWI images, one outlined the core region of the diffusion abnormality and the second one, of similar size, was placed in the contralateral hemisphere. These ROIs were then copied to the permeability and perfusion maps. Mean values for both parameters were recorded for all patients who were grouped based on whether they received rt-PA, and whether they experienced HT (figure 1). A paired t-test compared mean KPS and rR values between lesions and contralateral areas. The relationship between KPS and rR was investigated for all patients, and both hemispheres, using linear regression. Finally, receiver operating characteristic (ROC) curves were computed to determine the HT predictive power for either rR or KPS.

Results:

Thirteen out of 32 patients proceeded to HT; 6 of these received rt-PA. The occurrence rate of HT for patients receiving rt-PA and those without was 43% and 37%, respectively. Mean rR values for all groups are illustrated in figure 2. The overall rR values were significantly higher in lesion (0.19 ± 0.08) compared with contralateral (0.10 ±0.03) areas ($P < 0.01$). For the lesion areas alone, rR values were significantly higher in patients with HT (0.25 ± 0.06, average of group 1 and 3) compared with patients without HT (0.14 ± 0.05, average of group 2 and 4, $P < 0.01$). ROC analysis indicated that a rR threshold of 0.18 provides a sensitivity of 83% and a specificity of 71%. Moreover, the rR values were higher in patients receiving rt-PA therapy (0.23 ± 0.07) compared with patients not receiving rt-PA (0.15 ± 0.06, $P < 0.01$). Mean KPS values for all groups are illustrated in figure 3. The KPS values overall were significantly higher in lesion (0.78 ± 0.55) compared with contralateral (0.35 ± 0.27) areas ($P < 0.01$). In the lesions, KPS values were significantly higher in patients with HT (1.21 ± 0.62, average of group 1 and 3) than those without HT (0.48 ± 0.25, average of group 2 and 4, $P < 0.01$). ROC analysis indicated that a KPS threshold of 0.67 provides a sensitivity of 92% and a specificity of 78%. Moreover, the KPS values were higher in patients receiving rt-PA (1.06 ± 0.59) compared with patients not receiving rt-PA (0.59 ± 0.47, $P < 0.01$). A significant linear regression was observed between rR and KPS ($r = 0.85$, $P<0.001$).

Discussions:

The results of this study demonstrate that both KPS and rR are able to predict HT in AIS patients with similar sensitivity and specificity (as assessed using ROC curves). These KPS results are supported by a previously published study [2]. Furthermore, a significant correlation between rR and KPS was observed. These results suggest that rR and KPS are similarly effective predictors of HT. However, since rR can be obtained faster and is easily computed from routinely-performed T2*-weighted perfusion MRI, it has the potential to serve as a surogate for KPS and aid with treatment decisions immediately following admission.

References:

1. The NINDS Group. Stroke 1997;
2. Kassner A. et al. AJNR 2005;
3. Kassner A et al. JMRI 2000;
4. Roberts HC et al. AJNR 2000.

	rt-PA	HT
Group 1 (N = 11)	-	-
Group 2 (N = 7)	-	✓
Group 3 (N = 8)	✓	-
Group 4 (N = 6)	✓	✓

Figure 1. Patient groups, based on rt-PA treatment and subsequent HT

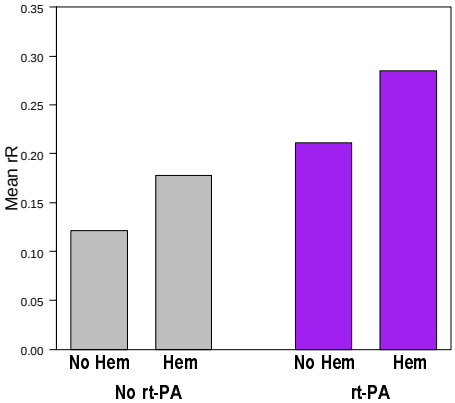

Figure 2. Mean rR for the four groups, demonstrating increased rR in patients who later on hemorrhaged.

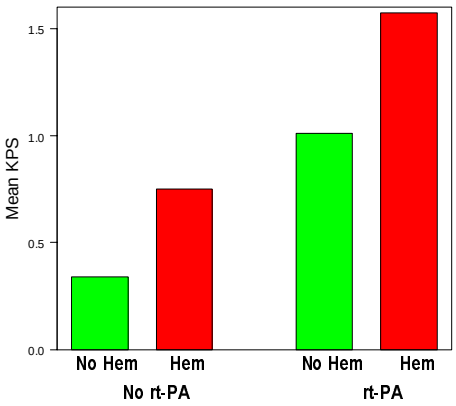

Figure 3. Mean KPS for the four groups, demonstrating increased KPS in patients who later on hemorrhaged.