Multiparametric MRI correlation with tissue outcome in early phase of acute ischemic stroke in rats

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Introduction

Diffusion and perfusion MRI have been used in combination to assess brain status in acute ischemia with a view to separate ischemic core and penumbra [1, 2]. Recently, $T_{1\rho}$ has been shown to be a sensitive MRI marker for tissue outcome shortly after onset of ischemia [3, 4]. From clinical stand point, it is essential to have information about tissue status in hand at the time of incidence to guide selection between available treatment strategies, such as thrombolysis, hypothermia or i.v. albumin infusion, to maximize volume of salvaged tissue. Modern imaging technology makes it possible to acquire several ischemia-sensitive MR scans in ten minutes or so. These data, as processed through multiparametric approaches, are expected to provide clinicians with tissue status and long-term outcome at the time of data collection. Here, we have measured absolute MRI parameters, including diffusion, T_2, $T_{1\rho}$ and perfusion, shortly after middle cerebral artery occlusion (MCAo) in rats to assess value of these parameters to predict long-term tissue outcome determined by quantitative cells count.

Fig.1: Schematic plot of the ROIs. Str = striatum, CStr = contralateral striatum, Ins = insular cortex, Exp = lesion expansion to cortex at 24h.

Methods

Male Wistar rats (N = 13) were anesthetized with 1.5 - 2 % isoflurane in 70/30 N_2O/O_2 for 60 minutes of MCAo [5]. MRI experiments were performed in a horizontal 4.7 T magnet interfaced to a Varian Inova console. MRI scans were acquired at two time points (60 - 90 and 150 - 180 minutes) after MCAo. The axial imaging plane (thickness 1.5 mm) was positioned 5 mm caudally from the olfactory bulb. A volume coil was used as transmitter and a quadrature half-volume coil as receiver (Rapid Biomedical GmbH, Rimpar, Germany). Fast spin-echo readout (64 x 128 pixels, echo spacing 10 ms, FOV 2.56 x 2.56 cm^2) was used for T_1, $T_{1\rho}$ and T_2 MRI (TR = 3 s for T_1, TR = 2.5 s for $T_{1\rho}$ and T_2). D_{av} was quantified using a SE sequence incorporating four bipolar gradients along each axis with four b-values ranging from 0 to 1370 s/mm^2 (TR = 1.5 s, TE = 55 ms). Absolute $T_{1\rho}$ images were acquired using both conventional spin lock (SL) technique (AHP-SL-AHP) and AFP pulses with HS8 modulation function (train of 4 - 32 AFPs, pulse duration 2 ms, no inter pulse delay). Perfusion was measured using arterial spin labeling technique with a continuous RF pulse (CASL, TR = 3 s, TI = 500 ms). Seven ROIs were chosen on ipsi- and contralateral sides including an area showing the lesion expansion between three and 24 hours (Fig. 1) from MCAo.

Quantitative maps of diffusion, relaxation times and CBF were calculated and ROIs in ischemic core (striatum), expansion area (enlargement of lesion from 3h - 24h) and lesion-free cortex as well as in corresponding contralateral areas were determined. Quantitative cell counts were obtained from corresponding areas from Nissl stained histological sections. Correlation between cell counts and MRI parameters were assessed using a linear multiparametric correlation approach. To evaluate goodness of MRI parameter combinations, we first determined the single MRI parameter with best correlation with outcome and then added any parameter one by one to obtain the best combination.

Results

Severe ischemia was evident in all animals in ischemia group, as ipsilateral D_{av} decreased by ~30-45 % in striatum during occlusion. All other MRI variables, including drop of CBF, behaved consistent with ongoing ischemic infarction [4]. After the MCAo some recovery of CBF and D_{av} was detected, but relaxation times remained at ischemic levels or continued to increase.

Multiparametric correlation analysis results between MRI data obtained in acute phase and cell density at 24 hours are shown (Table 1). Maximum correlation was typically achieved by combining three to four MRI parameters, which typically involved one or two of the relaxation parameters and either diffusion or CBF. Interestingly, the best combination of parameters was dependent on brain region as well.

Table 1: Correlation coefficients (r) between MRI parameters obtained 60-90 and 150-180 minutes post-ischemia and cell counts at 24 hours. CCE = combination of all cortical areas (see Fig 1)

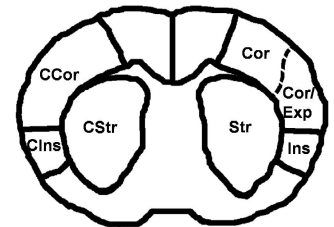|			Number of parameters in correlation analysis					
			1	2	3	4	5	6
60 min post MCAo	**Str&CStr**	$T_{1\rho,CW}$	0.73					
		$T_{1\rho,HS8}$	0.70	0.78				
		T_1	0.70	0.75	0.81			
		Diff	0.39	0.76	0.81	0.84		
		T_2	0.57	0.75	0.79	0.81	0.84	
		CBF	0.50	0.74	0.79	0.81	0.84	0.84
	Ins	T_2	0.47					
		T_1	0.17	0.60				
		$T_{1\rho,HS8}$	0.46	0.50	0.64			
		CBF	0.24	0.47	0.60	0.64		
		$T_{1\rho,CW}$	0.24	0.55	0.60	0.64	0.64	
		Diff	0.26	0.47	0.60	0.64	0.64	0.64
	CCE	T_2	0.60					
		$T_{1\rho,HS8}$	0.58	0.67				
		T_1	0.52	0.66	0.68			
		CBF	0.07	0.61	0.68	0.70		
		Diff	0.38	0.60	0.67	0.68	0.71	
		$T_{1\rho,CW}$	0.57	0.65	0.68	0.68	0.70	0.71
150 min post MCAo	**Str&CStr**	$T_{1\rho,CW}$	0.79					
		CBF	0.69	0.83				
		T_2	0.79	0.80	0.85			
		T_1	0.71	0.80	0.83	0.86		
		$T_{1\rho,HS8}$	0.78	0.82	0.84	0.86	0.86	
		Diff	0.40	0.76	0.79	0.85	0.86	0.87
	Ins	$T_{1\rho,CW}$	0.55					
		Diff	0.25	0.71				
		T_1	0.32	0.60	0.79			
		$T_{1\rho,HS8}$	0.29	0.55	0.78	0.82		
		T_2	0.55	0.58	0.72	0.79	0.82	
		CBF	0.13	0.57	0.73	0.80	0.82	0.82
	CCE	T_2	0.61					
		Diff	0.08	0.75				
		$T_{1\rho,CW}$	0.47	0.62	0.77			
		$T_{1\rho,HS8}$	0.44	0.62	0.77	0.81		
		T_1	0.45	0.62	0.76	0.78	0.83	
		CBF	0.29	0.64	0.75	0.77	0.81	0.85

Conclusions

These results show that multi-parametric MRI provides improved prediction for stroke outcome in the animal models than any of the parameters in isolation. We show that by using three to four MRI contrasts together a 0.64-0.86 correlation with the histological outcome is obtained. The correlation depends both on region and age of lesion. Our data suggest that MRI may predict lesion expansion and fate of tissue at risk of stroke in a clinically useful manner.

References:

[1] Warach, S., et al., JCBFM 1996 Jan;16(1):53-9. [2] Shen Q., et al. JCBFM 2005 Oct;25(10):1336-45. [3] Gröhn, O.H., et al., JCBFM 2000. 20: 1457-66. [4] Jokivarsi, KT., et al., JCBFM 2008 Oct 1;doi:10.1038/jcbfm.2008.113. [5] Longa, E.Z., et al., Stroke, 1989. 20: 84-91.