Prediction of hemorrhagic transformation in acute ischemic stroke: a comparison of DSC surrogate measures of permeability

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INTRODUCTION:

The clinical use of tissue plasminogen activators (e.g. rt-PA) in acute ischemic stroke (AIS) is limited to patients who present < 4.5h of symptom onset [1]. Beyond this benchmark, rt-PA is known to increase the risk of blood-brain-barrier (BBB) disruption and bleeding into the surrounding tissue or 'hemorrhagic transformation' (HT). What is needed for successful treatment guidance is a method for identifying patients at increased risk of HT. Advances in permeability estimation with dynamic contrast-enhanced (DCE) MRI can delineate areas of BBB disruption and thereby identify patients at increased risk of HT [2]. An alternative to DCE and permeability estimation is a model-free approach to measure the relative recirculation of contrast (*rR*), which we can extract from dynamic susceptibility contrast (DSC) data-sets [3]. It has been previously shown that this measure can achieve sensitivity and specificity similar to DCE-MRI for the prediction of HT [4]. However, a number of other DSC-based surrogate measures of BBB permeability have been proposed in the literature, including *Peak Height*, *% Recovery* [5], and the *Slope* of the ΔR_2^* v. time curve between 50 and 60 seconds post-injection [6]. The purpose of this study was to evaluate the performance of these DSC-based parameters in discriminating between patients who will proceed to HT and those who will not.

MATERIALS AND METHODS:

Eighteen patients (aged 27-89 years) with a working diagnosis of AIS were examined <6h of symptom onset. MRI was performed on a 1.5T MR system (GE Healthcare, Milwaukee, USA) equipped with Echo-Speed gradients and an 8-channel head coil. A DSC protocol with a T2*-weighted single-shot EPI acquisition was performed with the following parameters: TR 1725ms, TE 31.5ms, FOV 240mm, Matrix 96 X 64, Flip Angle 90º, slice thickness 5mm. The total acquisition time for 50 dynamics was 86 s. Gadodiamide was injected as a bolus (0.1mmol/kg Omniscan, GE healthcare, USA) immediately following initiation of the T2*W sequence. HT was determined by follow-up CT and/or MRI 24-72 h after initial imaging. Data were analyzed on an independent workstation, using in-house software (MR analyst v. 4.0) developed in MATLAB. Two regions of interests (ROI) were defined on the DWI images, one placed within the core region of the DWI abnormality (infarct) and the second within the homologous location in the contralateral hemisphere. DWI ROIs were then compared to the equivalent DSC image-set. In addition to *rR* [3], the DSC parameters investigated included *Peak Height* and *% Recovery* [5], as well as the *Slope* of the ΔR_2^* v. time curve between 50 and 60 seconds post-injection [6] (FIG. 1). Mean values for each parameter were recorded and patients were grouped based on HT-status at follow-up. For each DSC parameter, differences between infarct and contralateral ROIs were assessed for significance using Wilcoxon matched pairs tests. Mann-Whitney *U* tests were used to assess differences between HT and no-HT patients for each parameter. Finally, the relationship between *rR* and each of *Peak Height*, *% Recovery*, and *Slope* was investigated using linear regression.

RESULTS:

Eight out of 18 patients proceeded to HT. Mean values for each of the four parameters investigated are listed in TABLE 1. While the mean *rR* for infarct ROIs was significantly greater than for contralateral ROIs, the converse was true for *% Recovery* ($P<0.001$ for each comparison). Similarly, the mean *rR* for HT infarct ROIs was significantly greater than for non-HT ROIs, while the mean *% Recovery* in HT patients was significantly lower than for those without hemorrhagic complications. Logistic regression revealed a negative correlation between *% Recovery* and *rR* (r=-0.875, $P<0.001$). No significant differences were detected with respect to *Peak Height* or *Slope*, either between infarct and contralateral ROIs or between HT and non-HT patients. Neither *Peak Height* nor *Slope* was found to be significantly correlated with *rR*.

DISCUSSION:

Of the four DSC-based parameters investigated in this study, only *rR* and *% Recovery* were capable of discriminating between HT and non-HT infarcts. Unlike Bang and colleagues, we were unable to distinguish between HT and non-HT patients using the 50-60 s *Slope* parameter [6]. While the *rR* results are supported by a previously published study [4], this is the first time (to our knowledge) that the *% Recovery* metric has been evaluated in an AIS population. The significant negative correlation observed between *rR* and *% Recovery* was expected, given that each metric is approximately the complement of the other. The results of this study suggest that both *rR* and *% Recovery* have the potential to predict HT in AIS patients. Given that these parameters can be readily computed from a standard 90 second perfusion scan, DSC imaging has the potential to serve as a surrogate for DCE-MRI and may provide rapid guidance for treatment decision-making.

TABLE 1:

Parameter	Contra.	Infarct	HT	no HT	Pearson's *r* (v. *rR*)
rR	0.08 ± 0.01	0.18 ± 0.02*	0.22 ± 0.06	0.14 ± 0.06**	---
Peak Height	9.17 ± 3.50	8.15 ± 3.37	7.95 ± 2.20	7.41 ± 3.24	-0.362
% Recovery	91 ± 3	79 ± 9*	76 ± 6	82 ± 11†	-0.875§
Slope	-0.02 ± 0.05	-0.02 ± 0.06	-0.02 ± 0.07	-0.02 ± 0.06	-0.180

All values represent mean ± SD; * $P < 0.001$ v. Contra., ** $P < 0.001$ v. HT, † $P < 0.05$ v. HT, § $P < 0.001$ for Pearson's *r*.

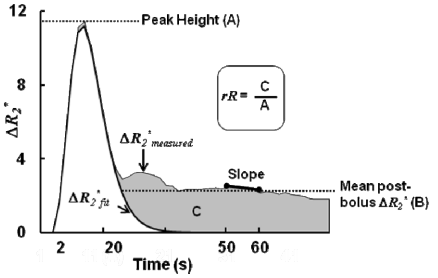

FIG. 1: A ΔR_2^* v. time curve ($\Delta R_2^*_{measured}$), as well as its gamma-variate fit ($\Delta R_2^*_{fit}$). Four DSC parameters were calculated: *rR* (C/A), *Peak Height* (A), *% Recovery* = [100 x (A-B)/A], and *Slope* = slope of $\Delta R_2^*_{measured}$ (t) between 50 and 60 s post-injection.

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