

## Acute change of tissue perfusion in acute stroke patients after tPA treatment

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### Introduction

Effective tissue reperfusion can prevent death in vulnerable cells while they are still alive. Without reperfusion, the at-risk tissue will progress into infarction in time. The fate of ischemic tissue highly depends on tissue status (reversible vs. irreversible damaged) as well as reperfusion status within a few hours after stroke onset. In this study, two sequential MR scans were performed within 6.5 hours after stroke and regions of reperfusion and nonreperfusion were identified on a voxel basis. We sought to evaluate whether regions with a severe perfusion deficit is more likely to remain hypoperfused, and whether new hypoperfusion might occur beyond the initial lesion after tPA. Finally, risk of infarction was assessed in these regions.

### Methods

Thirteen tPA treated (1.8±0.5 hours from symptom onset) acute ischemic stroke patients were included with informed consent. All patients were serially scanned with MRI (3T Siemens) at 2.7 ± 0.7 hours (tp1), at 6.4± 0.4 hours (tp2) and at 1 month (tp3) after stroke onset. For both tp1 and tp2, the imaging protocols included FLAIR and dynamic susceptibility contrast (DSC) PWI images. Mean transit time (MTT) maps were computed. FLAIR scan was acquired at tp3 to determine the final lesion. Image registration was performed to align all images from different tps. MTT prolongation was computed as MTT- mean MTT of the the contralateral hemisphere. A voxel with an MTT prolongation ≥ 4 seconds was defined as “hypoperfusion.” A “reperfused” voxel was defined as a voxel which was hypoperfused at tp1 but not at tp2, whereas a ‘nonreperfused’ voxel remained hypoperfused from tp1 to tp2. A voxel without hypoperfusion at tp1 but with hypoperfusion at tp2 was termed “new” hypoperfusion. Isolated regions small than 1 ml were removed from analysis to minimize potential image mis-registration and noise induced variations. Values of MTT prolongation and risk of infarction were examined within the regions of reperfusion, nonreperfusion and new hypoperfusion, respectively. One way ANOVA with the Bonferroni multiple comparison was performed to compare the MTT values and the risk of infarction.

### Results

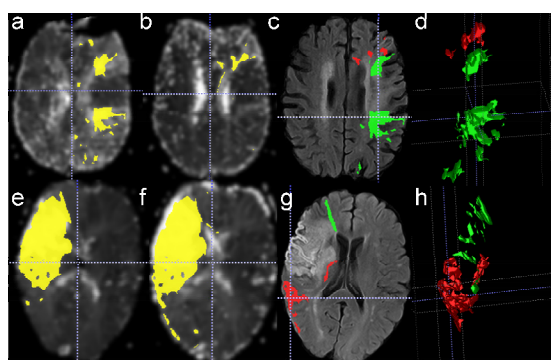


Figure 1. Representative MTT at tp1 (a, e) and tp2 (b, f) from two patients (upper and lower rows). The hypoperfused region at both time points are marked in yellow (a,b,e,f). Reperfused (marked in green) and new hypoperfusion (marked in red) regions are overlaid onto the tp3 FLAIR maps for both patients (c, g). 3D rendered reperfed (marked in green) and new hypoperfused (marked in red) regions are shown in d and h.

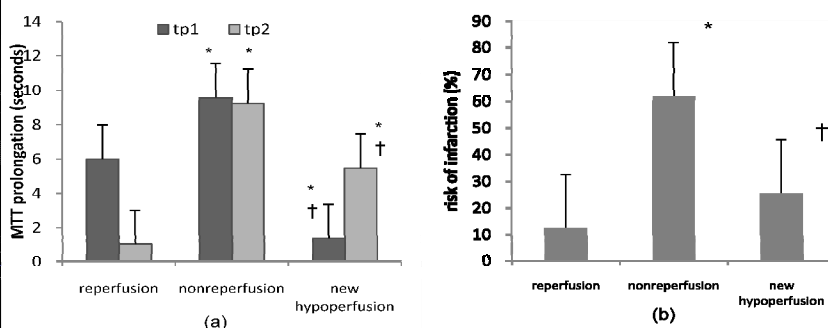


Figure 2. (a) MTT prolongation in reperfed, nonreperfused and newly hypoperfused regions. (b) Risk of infarction of reperfed, nonreperfused and newly hypoperfused regions. \* represents a  $P<0.01$  when compared to the reperfed regions. † represents a  $P<0.01$  when compared to the nonreperfused regions.

region remained hypoperfused at tp2 (yellow regions, Fig 1b). Moreover, a small newly hypoperfused region was observed in this patient (marked in red, Figure 1c and d). In contrast, the second patient showed a relatively small size of reperfed region (marked in green, Figure 1g and h) but a large newly hypoperfused region from tp1 to tp2 (marked in red, Figure 1g and h). The mean and standard deviation of the MTT prolongation were plotted in Figure 2a for the regions of reperfusion, nonreperfusion and new hypoperfusion. The MTT values in the nonreperfused regions were significantly higher than both the reperfed ( $P<0.01$ ) and the newly hypoperfused ( $P<0.01$ ) regions at both tp1 and tp2. The MTT values in the new hypoperfused regions were significantly lower than that in the reperfed region at tp1 ( $P<0.01$ ) and significantly higher at tp2 ( $P<0.01$ ). The mean risk of infarction in the reperfed, nonreperfused and new hypoperfused regions were 12.3±12.7%, 61.6±30.6% and 25.4±29.4%, respectively (Figure 2b). The risk of infarction in the nonreperfused regions was significantly higher than both the reperfed ( $P<0.001$ ) and the new hypoperfused ( $P<0.05$ ) regions, while the risk of infarction in the newly hypoperfused regions showed a trend of increase when compared to the reperfed regions.

### Discussion and Conclusions

Spatial heterogeneity of tissue perfusion status change was detected in acute patients after tPA treatment. Compared to the reperfed region, the nonreperfused region had a significantly greater initial MTT prolongation ( $P<0.01$ ), suggesting that tissue with a more severe initial injury is more likely to remain hypoperfused. Vascular pathophysiological studies have demonstrated that compression of the microvascular lumen by both vascular pathology such as the platelet activation, fibrin deposition and leukocyte activation, together with endothelium swelling might be responsible for the ‘no-reflow’ phenomenon<sup>1-4</sup>. The observed nonreperfusion in the more severe hypoperfused region may indicate that a downstream microvascular occlusion might have occurred in these regions. Another finding of this study is the concurrent development of reperfusion and new hypoperfusion in hyperacute stroke patients. Failure of collateral flow<sup>5</sup>, clot propagation and recurrent embolization might be responsible for this phenomena. New hypoperfusion increased the risk of infarction to 25.4%, which is still significantly lower than that in the nonreperfused region (61.6%). In accordance with a previous finding, the significant difference in MTT prolongation in these two regions at tp2 (5.5 seconds vs. 9.2 seconds  $P<0.01$ ) may explain this difference<sup>6</sup>.

### Reference

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