# MEASURING THE TIMING INFORMATION OF BLOOD FLOW IN ACUTE STROKE WITH THE "BACKGROUND NOISE" OF BOLD SIGNAL

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**Target audience:** Radiologists, neurologists, scientists and MRI researchers interested in stroke and brain perfusion imaging.

**Introduction**: Low-frequency fluctuation in the range of 0.01–0.1 Hz is commonly observed in BOLD signal and has been widely used for analyzing brain functional activation patterns. These signals are believed to reflect a combination of cerebral blood flow, neuronal activation and systemic hemodynamics, although their origin and regulatory mechanisms are still unclear. Recent studies have found that the averaged whole-brain BOLD signal (global signal) in this frequency band (which usually is regressed out as the background noise) could potentially be a pattern for measuring cerebral vascular regulation1. The results of these studies demonstrate that the "background noise" in different brain areas includes the same temporal patterns, but is affected by different time delays with respect to the global signal. Because of this, extracting a global signal "template" by averaging the time series extracted from the whole brain, will include the same temporal pattern in different phases2. We hypothesized that the temporal pattern might be altered in patients with brain vascular diseases. In this study, an iterative algorithm was used to extract the time-shift-corrected time series pattern of whole-brain BOLD signal. The time-shift map of stroke patients was obtained by calculating the time delay between the template and each voxel and then compared with the TTP map obtained from dynamic susceptibility contrast (DSC) MR.

**Materials and methods:** 5 patients with acute stroke participated in this preliminary study. MRI exam included a general protocol for stroke patients (including DSC) and one resting-state fMRI (rs-fMRI) session. All data were collected on a MAGNETOM Trio 3T MR scanner (Siemens AG, Erlangen, Germany). The parameters are as following: DSC: TR=1500 ms, TE=30 ms, flip angle=90°, 24 slices, slice thickness=5 mm, distance factor=20%, FOV=210 mm×210 mm, matrix= 128×128, measurements=80. Resting-state fMRI: TR=2000 ms, TE=30 ms, flip angle=90°, 33 slices, slice thickness=3.5 mm, distance factor=20%, FOV=210 mm×210 mm, matrix= 70×70, measurements=300. The data of DSC-MR were analyzed using Perfusion Evaluation tools on a syngo.via workstation (Siemens AG, Erlangen, Germany). The fMRI data were pre-processed with standard pipeline for resting-state data analysis (without regressing out the global signal). After pre-processing, the time-shift map was calculated applying the following steps: 1) Averaging the time series of the whole brain to create the first time-series template. 2) For each voxel, the time course was shifted from -8TR to +8TR and correlated with the template at each TR. Each voxel was then labeled as the number of TR that has the highest correlation coefficient value. 3) Realigning the time series of all voxels based on their time-shift value determined by step 2. 4) Averaging the re-aligned time series of the whole brain to create a new global template. 5) Repeating step 2 to 4 until the number of voxel, who had changed their time-shift value between two iterations, is less than 100. The rs-fMRI data were then cut into the first 5min and compute the time-shift map with the same steps. The areas that show abnormal TTP in SMS DSC and long time delay in TSM were used for computing the degree of overlap among all subjects.

**Results:** In order to visually compare the results of DSC-MR with time-shift map (TSM) obtained from rs-fMRI, the time-shift map was overlaid onto the TTP map (Fig.1 and Fig.2). The 0 value of time-delay represents no time shift between the time series of global template and the time-series extracted from the specific voxel, while a large time-delay value represents the blood flow arriving late in this area. The perfusion deficit areas shown in the time-shift map matches with the area showing long TTP obtained from DSC-MR quite accurately. The mean degree of overlap between TTP and TSM of the five subjects is 0.81 (figure 2 second row). If the global template is created by simply averaging the time series of the whole brain (non-iteratively), the degree of overlap drops to 0.48 (figure 2, fourth row). By applying the iteration steps, the TSM calculated from a shorter 5-min rs-fMRI examination also shows and acceptable performance (degree of overlap=0.67, fig 2 third row).

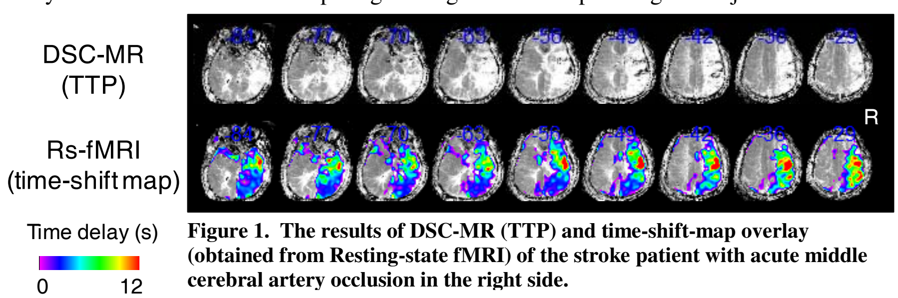


**Figure 1. The results of DSC-MR (TTP) and time-shift-map overlay (obtained from Resting-state fMRI) of the stroke patient with acute middle cerebral artery occlusion in the right side.**

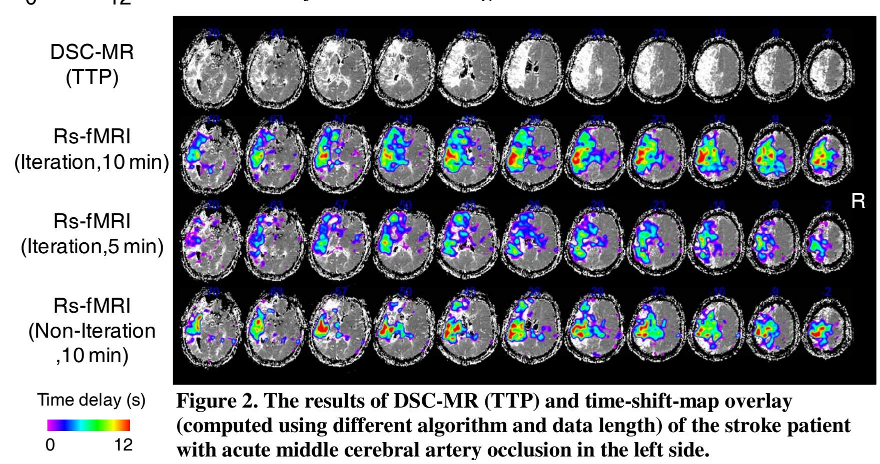


**Figure 2. The results of DSC-MR (TTP) and time-shift-map overlay (computed using different algorithm and data length) of the stroke patient with acute middle cerebral artery occlusion in the left side.**

**Conclusions:** The timing information of blood flow could be estimated with the low-frequency fluctuation component in rs-fMRI data without the use of a contrast injection and with a large degree of overlap with DSC-computed TTP maps. The iterative algorithm for computing the global template of the time series pattern is able to increase the estimation performance significantly while reducing the amount of required rs-fMRI data; shortening the examination time, which is of great importance for potential future clinical applications.

**References:** 1. Tong Y, et al., NeuroImage 2010. 2. Lv Y, et al., Annuals of Neurology 2013.