Evaluation of the hemodynamic effects of surgical revascularization in pediatric moyamoya syndrome using perfusion MRI

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Introduction: Moyamoya syndrome (MMS) is an angiographically defined cerebrovascular disorder with terminal internal carotid artery (ICA) occlusion and basal collateral vessels. Surgical revascularization (SR) is a potential treatment, but the indications for, and efficacy of, this intervention are controversial [1,2]. Despite the problems associated with the analysis of MR perfusion data in this group of patients [3], it has been shown that quantitative regional analysis of summary parameters (with the regions defined by segmenting the tissue based on its time-to-peak (TTP)) can identify hemodynamic abnormalities, and that this may provide clinically relevant information [3]. Perfusion MRI may, therefore, also play an important role in the evaluation of treatment outcome. However, the quantitative regional analysis described previously is not suitable for comparison of scans performed before and after SR, since the segmented regions in the 2 scans would not necessarily correspond with each other. An alternative approach would be to manually define anatomical regions of interest. However, given the variability of arterial territories between individuals, this would be relatively subjective. The use of histograms of MR measures has been proposed as an objective quantitative technique to analyze magnetization transfer ratios, T_1 relaxation, diffusion and vascular permeability [4-7]. In this study we investigate this approach in the evaluation of SR in patients with MMS.

Methods: Seven children with angiographically confirmed MMS were studied before and after SR. They were aged 1.3–10.5 years at presentation (median 6 years) and 1.8–13.3 years (median 9 years) at the time of SR. ICA disease was graded using a modification of the Suzuki classification [8] and was stage 1 in 2 hemispheres, stage 2 in 6 hemispheres and stage 3 in 6 hemispheres. All patients had cerebral infarcts in the ICA territory at the time of surgery. Two patients had extensive infarcts between the two scans and were therefore excluded from further analysis, since differences in the histograms would reflect comparisons of different brain tissue (since the infarcted areas were excluded from the analysis, see below). The five remaining patients had recurrent transient ischaemic attacks (TIAs). Perfusion MRI was acquired on a 1.5T Siemens Vision system using a multi-slice SE-EPI sequence (TE/TR=100/1250ms) after the injection of a bolus of 0.15 mmol/kg of Gd-DTPA using an MR-compatible power injector (Medrad). For the histogram analysis, TTP maps were calculated for each patient. This summary parameter was chosen because it is the only parameter that can be robustly calculated on a pixel-by-pixel basis without the need to fit to a gamma-variate function [3], and the gray-white matter values are similar in normal tissue. In this study TTP was calculated by fitting a second-order polynomial to the 5 points across the peak maximum, and a 3x3-smoothing kernel was used on the raw data before fitting to improve the SNR [3]. To minimize the variability due to differences in arterial input function [9], a region of interest in the cerebellum was used as a reference to calculate TTP differences (rTTP) [3]. The rTTP histograms were calculated for each hemisphere after excluding infarcted pixels. Each histogram was parameterized in terms of its mean, median, variance, skewness and kurtosis. The rTTP histograms (and their corresponding parameters) calculated using the pre-surgical MR data were compared to those obtained in the follow-up post-surgical scan. For the visual assessment of the histograms, the distributions were normalized to the same number of pixels. A marked overall reduction in rTTP was considered to constitute an improvement.

Results: The histogram assessment revealed visually obvious hemodynamic changes after SR: the position and shape of the hemispheric rTTP distributions were different post-surgically in all of the patients studied. This is illustrated in Fig. 1, which shows the histograms for two patients. The histograms show a visually obvious location shift and change in dispersion. Based on the visual assessment of the histograms, hemodynamic status improved in 3/5 patients following SR (e.g. Fig. 1a) and deteriorated in the remaining 2 patients (e.g. Fig. 1b). Of the 3 patients with hemodynamic improvement, 2 had a reduction in the frequency of TIAs, but one continued to have frequent attacks. Of the remaining 2 patients one was clinically stable and the other had a marked reduction of TIAs, despite the hemodynamic deterioration.

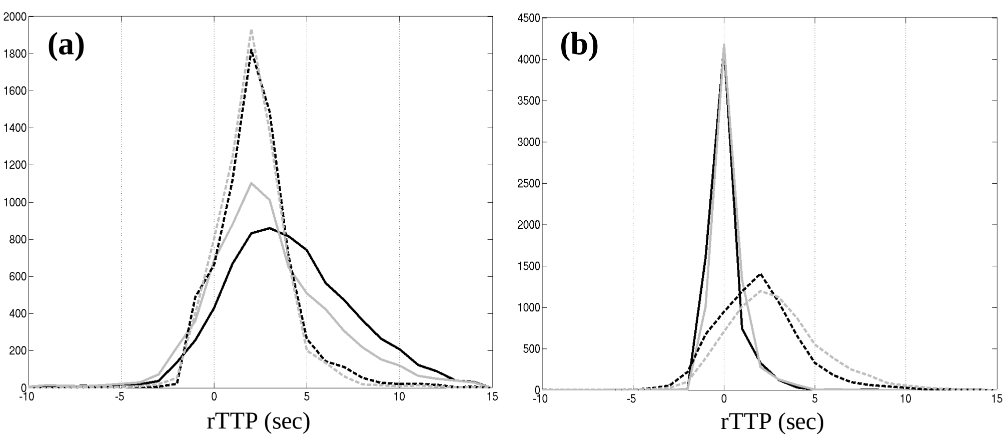

Figure 1: **(a)** rTTP histograms for a 6 year old boy with bilateral MMS, showing an improvement in hemodynamic status following SR, in conjunction with improved clinical status. **(b)** rTTP histograms for a 11.5 year old girl with bilateral MMS, the patient whose hemodynamic status deteriorated following SR despite the marked reduction in the frequency of TIAs. The solid lines show the histograms from the pre-surgical scan, and the dashed lines those from the post-surgical scan. The black (gray) lines correspond to the results from the right (left) hemisphere.

Discussion: An approach to evaluate the hemodynamic changes following SR is proposed. The method is based on the quantitative analysis of the hemispheric rTTP histogram. In the cases studied here, a visual histogram assessment was sufficient, but it is envisaged that, in general, a full histogram parameterization will be required to characterize the hemodynamic changes following SR. Improvement in hemodynamic status was observed in 3/5 patients. Only 2 of these 3 patients showed an improved clinical status. Potential reasons for the discrepancies include the limitations of using summary parameters to obtain hemodynamic information [3,9]; global histogram analysis could be insensitive to more localized changes in some cases; clinically effective SR may not improve resting hemodynamic status but may improve the cerebrovascular reactivity; and the use of data from the cerebellum as a reference [3]. Despite this, these preliminary results suggest that this approach has potential as a tool to evaluate hemodynamic changes following SR, and further work is required to establish the clinical role of such investigations. With increased patient numbers, a quantitative characterization of the distributions (e.g. mean, variance, skewness, kurtosis) could be used in predictive models by adopting a receiver operator characteristics (ROC) approach.

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