Evaluation of surgical outcome of moyamoya disease patients after revascularisation using atlas-based magnetic resonance brain perfusion analysis

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Aims and objectives

Moyamoya disease (MMD) is a cerebral vascular disease. It is characterized by stenosis or occlusion at the terminal portions of the internal carotid artery (ICA) or the proximal areas of anterior cerebral arteries (ACA) or middle cerebral arteries (MCA) [1]. Formation of fine vascular network, which looks like a puff of smoke in angiogram, is a characteristic of MMD. This is why it is named as moyamoya (*puff of smoke* in Japanese) syndrome. Developed MMD reduces the blood circulation in the brain and may cause nervous abnormality, such as movement disorder [2]. Surgical revascularizations are commonly used for reconstructing cerebral blood vessel networks of MMD patients. The direct treatment includes superficial temporal artery branch - middle cerebral artery branch (STA-MCA) anastomosis, and the indirect methods could be encephaloduroarteriosynangiosis (EDAS), encephalomyosynangiosis (EMS), encephaloduroarteriomyosynangiosis (EDMS) and multiple burr hole surgery. The treatments are aimed at improving the cerebral hemodynamic conditions of patients. However, hyperperfusion may occur after the surgery and lead to headache, eye and face pain, vomiting, seizures and neurological deterioration [3]. Thus, it is important to introduce a method to assess the possibility of occurrence of the cerebral hyperperfusion syndrome (CHS).

Pre- and post-operative change in cerebral blood flow (CBF) was shown a useful indicator to recognize CHS [4, 5]. Among various medical imaging techniques, perfusion imaging is commonly used to study blood circulation in the brain. Cerebrovasculature could be observed *in vivo* and the blood flow rate in the whole brain could be determined. Among all other modalities, computed tomography (CT) and magnetic resonance imaging (MRI) are widely used for perfusion [6]. In this study, MRI was chosen since it does not involve ionized radiation [7].

After injection of contrast agent into the patient's body, perfusion weighted images (PWI) could be captured using MRI machines. Concentrations of the contrast in the cerebral region at different time were recorded. The cerebral hemodynamic could be investigated by perfusion parameters, namely, CBF, cerebral blood volume (CBV), mean transit time (MTT) and time to peak (TTP). These four parameters reflect the contrast flow and thus the blood flow conditions could be deduced. In the cerebral region, CBF is determined by the inflow rate of the contrast. CBV is assessed by the volume of contrast passing through. MTT is the average time required for the contrast to flow through the region while the time required for the contrast concentration to reach its peak determines TTP [8]. In this study, the parameters were evaluated based on the central volume principle and singular value decomposition (SVD).
Methods and materials

Overview

PWI and MRA images of the patients before and after the operation were obtained by following the procedures: 1) patient was sent to the MRI machine; 2) a bolus of contrast was injected; 3) MRA and PWI were captured when the contrast was injected in MRI machine. The images were processed for calculating CBF, CBV and MTT of the patient’s brain by deconvolution. The data maps were compared in pair to observe potential changes before and after the surgeries in order to evaluate the vasculature and hemodynamic condition of the patients after revascularization. The working pipeline is shown below:

Fig. 1: A flowchart illustrating the working pipeline of this study

References: Department of imaging and interventional radiology, The Chinese University of Hong Kong, Prince of Wales Hospital - Shatin/HK

Subjects

Fourteen MMD patients have participated in this study. Six in the cohort were found occlusions in their left hemisphere and the others had abnormal vasculature in their right hemisphere. All of them had received surgical treatments including STA-MCA anastomosis and EDMS. In our analysis, the patients were divided into two groups, which are CHS Group, the patients with complication after surgery (number of members = 5), and Non-CHS (NC) Group, the patients without complication after surgery (number of members = 9).
Perfusion Analysis

PWIs were post-processed by a software called Perfusion Mismatch Analyzer (PMA) (Ver.3.4.0.6, ASIST, Japan). The software computes CBF, CBV, MTT and TTP by estimating the contrast concentration using deconvolution by numerical method. The concentration of the contrast at a particular voxel in the brain, $C(t)$ is obtained by the time series PWI. $C(t)$ is related to the tissue flow, $F$, the fraction of contrast remaining in that voxel, or the residue function, $R(t)$, and the arterial blood supply function, $AIF(t)$, by the equation [9]:

(Equation 1): $C(t) = F \int_0^t AIF(u)R(t-u)du$

$C(t)$ was obtained by measurement of contrast concentration from PWI. $AIF(t)$ was evaluated by reference points automatically chosen by the software and assumption on as a constant value was made. The values of $R(t)$ obtained was found by singular value decomposition (SVD) [10] and the four perfusion parameters were calculated. At each voxel, CBF was evaluated by the peak of $R(t)$ and CBV was determined by the area under the curve of $R(t)$. By the central volume principle [11], MTT was calculated as the ratio of CBV to CBF. TTP was the time required for the curve of $R(t)$ to reach its peak.

Statistical Analysis of Perfusion Parameters

Using the MRA data of the 14 patients, a template for the studied cohort was constructed using groupwise registration in ANTs toolbox [12]. With an existing Chinese MRI brain template and the atlas for arterial territories of human brain proposed by Tatu et al. [13], we can construct the atlas for the template in this study using registration-based segmentation techniques. The atlas indicates various arterial regions separated for left and right sides, including terminal and central branches of ACA, MCA and posterior cerebral artery (PCA), anterior choroidal artery, superior cerebellar artery, anterior and posterior inferior cerebellar arteries etc. Since MMD mainly affects the blood supply areas
of ACA, MCA and PCA, the central and terminal areas of ACA & MCA and the terminal areas of PCA were focused on the analysis.

After the brain template space and its atlas were created, all pre- and post-operative PWIs were mapped onto the template space. This process was done by the "coregister function" of SPM8 (Wellcome Department of Imaging Neuroscience, London, United Kingdom). In each brain segment, the statistical values of the four perfusion parameters were computed for further analysis.

With the averaged parameters, paired Student’s t-test was used to compare the pre- and post-operative perfusion parameters in their ACA, MCA and PCA. To minimize the symmetric error of left and right hemispheres, we used the relative perfusion parameter values for comparison, which were calculated by the ratio of parameter value of the surgical side to that on the contralateral side [14]. A significant level of 0.05 was chosen for the test to verify if the changes in the perfusion parameters were statistical significant. Pre- and post-operation comparisons were conducted for all patients and repeated for CHS and non-CHS Groups separately.

![Fig. 3: Screenshots showing the axial, sagittal and coronal views and of the brain template and atlas used in this study](image)

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Images for this section:

**Fig. 1:** A flowchart illustrating the working pipeline of this study

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**Fig. 3:** Screenshots showing the axial, sagittal and coronal views and of the brain template and atlas used in this study
Results

Averaged perfusion parameters in ACA, MCA and PCA were compared. The values of rCBF, rCBV, rMTT and rTTP were determined using PMA and were analyzed using two approaches. Intragroup comparisons were done by comparing the pre- and post-operative readings and inter-group comparisons were conducted by inspecting the differences between CHS and Non-CHS patients. The Student's t-test was used and a significant level of 0.05 was predefined.

It was observed that rCBF at MCA-terminal region significantly raised for all patients (p-value = 0.035, pre- vs post-operative). No significant changes were determined in other regions. For the CHS group (5 patients), rCBF increased significantly (p-value = 0.011) while, no such changes were found in the non-CHS group (p-value = 0.471). The significant greater increment of post-operative rCBF versus the pre-operative rCBF for the CHS group than non-CHS group was founded (p-value = 0.023).

Another major observation is that there were significant drops in rMTT at the MCA-central area for all patients (p-value = 0.012). The decreasing trends also appeared when analyzing the CHS and the non-CHS separately (p-value = 0.107 and p-value = 0.030 respectively).
Conclusion

Among the fourteen patients, five of them were found suffering from cerebral hyperperfusion syndromes after revascularization surgery. Referring to the previous publications of similar studies, it was expected that there would be significant increases in rCBF and rCBV and delays in rMTT [14-17]. Our results agreed with the prediction in rCBF (increase in the MCA region) and rMTT (decreased at the MCA regions). On the contrary, it was inconclusive regarding rCBV and rTTP. The increasing gradients for CHS patients were notability larger than those of the non-CHS patients. Our proposal of using perfusion analysis and atlas-based registration for prediction of CHS was validated. In the future, we plan to expand the size of our research in order to develop a reliable baseline for measurement of rCBF variations. The results would be useful for implementation of MR perfusion for occurrence of CHS prediction after brain surgeries.
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