

Cerebral Perfusion MR Imaging Using FAIR-HASTE in Chronic Carotid Occlusive Disease: Comparison with Dynamic Susceptibility Contrast-perfusion MR Imaging

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To determine the efficacy of flow-sensitive alternating inversion recovery using half-Fourier single-shot turbo spin-echo (FAIR-HASTE) in detecting cerebral hypoperfusion in chronic carotid occlusive disease, we subjected 12 patients with various degrees of cervical internal carotid artery stenoses and/or occlusion (Stenosis group) and 24 volunteers (Normal group) to FAIR-HASTE. In addition, 10 out of 12 patients in the Stenosis group underwent dynamic susceptibility contrast-perfusion magnetic resonance imaging (DSC-pMRI) before and after revascularization in the dominantly affected side. The absolute asymmetry indexes (AIs) of both cerebral hemispheres in the Normal and Stenosis groups were compared in FAIR-HASTE. In addition, the AIs were compared with those in the Stenosis group before and after revascularization in both FAIR-HASTE and regional cerebral blood flow (rCBF), calculated with DSC-pMRI. A statistically significant difference was recognized between the AIs in the Normal and Stenosis groups ($AI = 2.25 \pm 1.92$, 8.09 ± 4.60 , respectively; $p < 0.0001$). Furthermore, in the Stenosis group the AIs on both FAIR-HASTE (8.88 ± 4.93 , 2.22 ± 1.79 , respectively; $p = 0.0003$) and rCBF (7.13 ± 3.57 , 1.25 ± 1.33 , respectively; $p = 0.0003$) significantly decreased after revascularization. In the Stenosis group, before revascularization, signal intensity on both FAIR-HASTE and rCBF had a tendency to be lower in the dominantly affected side. FAIR-HASTE imaging was useful in the detection and evaluation of cerebral hypoperfusion in chronic occlusive carotid disease.

Key words: brain, perfusion, MRI, FAIR, HASTE

Cerebral perfusion has thus far been evaluated by traditional and established nuclear medicine techniques such as single photon emission computed tomography (SPECT) [1-4]. Recently, however,

with rapid developments in clinical magnetic resonance (MR) hardware and software, MR perfusion imaging has been gaining wide use in place of nuclear medicine techniques.

Two major approaches in MR imaging have been developed for use in the evaluation of cerebral perfusion; one is the exogenous tracer method using a paramagnetic contrast agent, and the other is the

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endogenous tracer method using magnetically-labeled water molecules within the arterial blood as a contrast agent. The former method is a technique based on classical tracer kinetics and first-pass imaging [5]. After a bolus administration of an exogenous freely diffusible tracer such as gadolinium contrast agent, the tracer in the tissue is monitored during its first tissue passage by means of the induced susceptibility effect. The methodology has already been fairly conclusively established, and it is beginning to be widely used clinically for dynamic susceptibility contrast (DSC)-perfusion MRI in quite a few institutions, especially in the medical care of acute ischemic stroke and the evaluation of tumor vascularity [6]. The latter method is generally known as arterial spin labeling (ASL), using magnetically labeled water molecules within arterial blood as a freely diffusible endogenous tracer.

ASL is a method of assessing cerebral perfusion by detecting changes of the magnetic states during arterial spin, which occur when labeled water molecules within the blood influence the water molecules within the tissue, and various techniques have been developed for using this method [7-9]. For clinical application, further improvements are necessary, but in ASL repetitive examination becomes possible without using any contrast agent. For this reason, we tend to think that it will come to occupy an important position in the evaluation of cerebral perfusion in the future.

Flow-sensitive alternating inversion recovery (FAIR) imaging is one of the techniques of ASL that does not use any contrast agent [10-12]. Originally FAIR imaging used echo-planar imaging (EPI) for signal data acquisition (FAIR-EPI). Susceptibility artifacts in the areas, such as the posterior cranial fossa, the mesial temporal lobes, the cerebral surface and the spinal cord, however, can easily cause severe spatial distortion, thus often making it very difficult to evaluate cerebral perfusion.

Recently, FAIR imaging using half-Fourier single-shot turbo spin-echo (HASTE) for signal data acquisition (FAIR-HASTE) has been developed, and this procedure is reported to be useful for obtaining cerebral perfusion images with little susceptibility artifact as well as for evaluating cerebral perfusion in patients with temporal epilepsy [13-15]. To our knowledge, however, there are still only a few

reports on FAIR-HASTE imaging. For this reason, we examined the clinical utility of FAIR-HASTE imaging in this study and furthermore compared it with DSC-perfusion MRI.

The purpose of this study was to determine the efficacy of FAIR-HASTE in detecting cerebral hypoperfusion in chronic carotid occlusive disease.

Subjects and Methods

Volunteers and patients. Twelve patients (10 men, 2 women; age range, 60-78 years; mean age, 69 years; the 'Stenosis group' below) with various degrees of cervical internal carotid artery stenoses and/or occlusion (assessed with CT angiography in 11 patients, with MR angiography in 1) and 24 volunteers (14 men, 10 women; age range, 24-53 years; mean age, 33 years; the 'Normal group' below) were enrolled in this study. All patients in the Stenosis group had experienced transient ischemic attacks (TIAs) in the dominantly affected side and dizziness, but routine MR imaging showed no definite infarctions. Immediately after MR imaging, they underwent revascularization, such as carotid endarterectomy (CEA) or carotid artery stenting (CAS) or superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis. Table 1 shows the clinical data for patients in the Stenosis group. No normal volunteers had any symptoms or history of neurological disease or abnormal findings on routine MRI.

MR studies were performed after obtaining full consent from the patients. The protocol followed the university hospital ethical committee's guidelines.

Imaging protocol. All MR studies were acquired by a 1.5-T super-conducting MR system (MAGNETOM VISION, SIEMENS, Erlangen, Germany) with a head coil. All patients in the Stenosis group underwent the same MR studies before and after revascularization. All of the second scans were performed within 4-8 days after patients' surgeries.

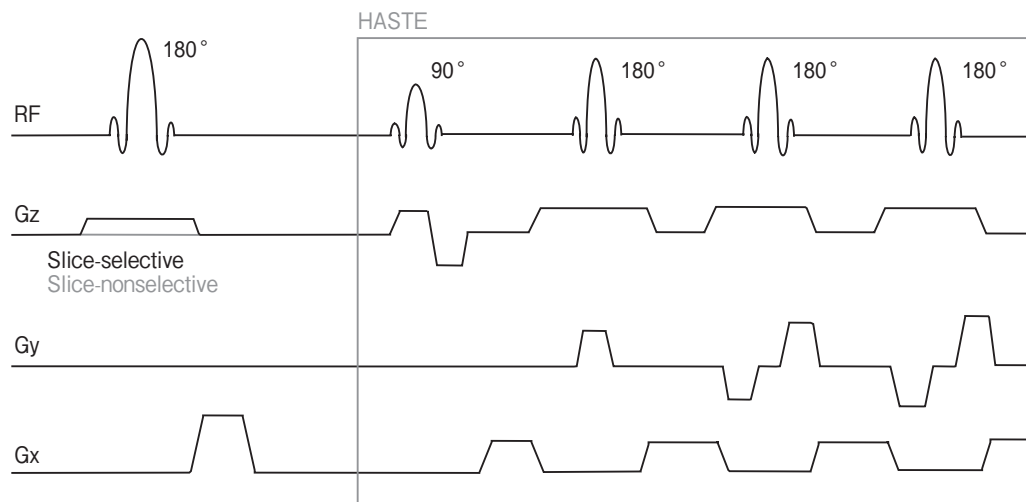
Routine MR imaging. All patients underwent routine MR imaging for cerebral ischemic disease. The examination included the following sequences and parameters: spin-echo (SE)-T1WI (TR/TE = 665/14 msec), fast spin-echo (FSE)-T2WI (TR/TE = 3,800/99 msec), fluid-attenuated inver-

Table 1 Patient (stenosis group) profiles, examinations, and diagnoses

Patient NO.	Sex	Age (y)	Diagnosis*	Operation
1	M	76	Right ICA occlusion and left ICA stenosis (40%) at CTA	Left CAS
2	M	66	Left ICA severe stenosis (90%) at CTA	Left CAS
3	M	60	Right ICA stenosis (60%) and left ICA occlusion at CTA	Left STA-MCA anastomosis
4	F	65	Right ICA stenosis (50%) and left ICA severe stenosis (80%) at CTA	Left CAS
5	M	73	Right ICA severe stenosis (80%) and left ICA stenosis (40%) at CTA	Right CEA
6	F	62	Right ICA occlusion at MRA	Right STA-MCA anastomosis
7	M	78	Right ICA stenosis (50%) and left ICA severe stenosis (90%) at CTA	Left CEA
8	M	72	Right ICA severe stenosis (99%) and left ICA stenosis (40%) at CTA	Right CEA
9	M	69	Right ICA stenosis (50%) at CTA	Right CEA
10	M	69	Right ICA stenosis (50%) at CTA	Right CEA
11	M	71	Right ICA severe stenosis (80%) and left ICA stenosis (40%) at CTA	Right CEA
12	M	67	Right ICA occlusion and left ICA stenosis (40%) at CTA	Left CAS

*CTA, computed tomography angiography; ICA, indicates internal carotid artery; MRA, magnetic resonance angiography.

†DSC-perfusion MRI indicates dynamic susceptibility contrast-perfusion MRI.

**Fig. 1** Pulse sequence diagram of FAIR-HASTE in this study.

sion recovery (FLAIR) (TR/TE/TI = 7,000/105/2,240 msec), and diffusion-weighted imaging (DWI) (TR/TE = 4,000/100, b-factor = 1,000 sec/mm²), where TR indicates repetition time; TE, echo time; TI, inversion time. Section thickness was 6 mm in all sequences.

FAIR-HASTE imaging. After routine MR imaging, single-section FAIR-HASTE imaging was performed. FAIR-HASTE was acquired with the following parameters: inversion recovery (IR)-HASTE, TI, 1,200 msec; TR, 2,000 msec; TE,

17.2 msec; flip angle, 90 deg.; FOV, 220 mm²; matrix, 128 × 128; section thickness, 8 mm; no. meas., 20; scan time, 120 sec. A FAIR-HASTE pulse sequence diagram is shown in Fig. 1. Slice-selective and slice-nonselective images were acquired as 2 separate scans. In each of the 2 scans, 20 images were obtained within a total scan time of 60 sec. An image in the axial plane was positioned at the mid level of the basal ganglia. Slice-selective inversion slab thickness in the axial plane was 20 mm, which adequately contained the imaging section. FAIR signals

were obtained by subtracting the slice-nonspecific images from slice-selective images for each corresponding time point on the scanner's main console. All 20 subtracted images were averaged. As a result, a single FAIR-HASTE perfusion image was obtained. In reference to T2WI, 2 region of interest (ROIs) were created separately over both sides of the cerebral hemisphere, and signal intensity in each ROI was calculated on the main console (Fig. 2). ROIs were carefully created to avoid peripheral vessels and other hyperintense structures. ROIs were created twice, and the mean was adopted. Such ROIs were then applied to all patients' FAIR-HASTE images to calculate the asymmetry index (AI), which was defined as $100 \times \frac{\{SI^*(\text{left}) - SI(\text{right})\}}{\{SI(\text{left}) + SI(\text{right})\}} > [14]$, where SI indicates the mean signal intensity. The AI is a signed value, ranging from -100 to 100 , with negative values indicating left-sided hypoperfusion and positive values indicating right-sided hypoperfusion.

An unpaired *t*-test was used to compare the AIs of the Normal group to those of the Stenosis group, and then a paired *t*-test was used to compare AIs both before and after revascularization in the Stenosis group.

Dynamic susceptibility contrast (DSC)-perfusion MR imaging. After FAIR-HASTE imaging, all patients in the Stenosis group underwent dynamic susceptibility contrast-perfusion MR imaging (DSC-pMRI) using a contrast agent. DSC-pMRI were acquired with the following parameters: single shot gradient-echo EPI; TR, 2,000 msec; TE, 60.7 msec; FA, 90 deg.; FOV, 220 mm²; matrix, 128 × 128; section thickness, 5 mm; no. acq., 25–30; no. slices, 9–11; scan time, 30 sec; injection of contrast agent, 3 ml/sec. After transferring all DSC-pMRI images to a Dr.View/LINUX R2.0 workstation (Asahi Kasei Information System Co., Ltd., Tokyo, Japan), regional cerebral blood flow (rCBF) maps were made by the first-pass method. The rCBF map images covered the whole brain. Of these, one image identical with the FAIR-HASTE image was selected. On the selected rCBF map image, ROIs were created in both of the hemispheres in the same manner as on the FAIR-HASTE image (Fig. 3). Then rCBF was calculated in each ROI to calculate the AI of the rCBF. A paired *t*-test was used to compare the AIs both before and after revasculariza-

tion. Two patients with unilateral occlusion were excluded from this statistical analysis, because they underwent revascularization on the contra-lateral side.

Results

The absolute AIs of FAIR-HASTE were 2.25 ± 1.92 (mean \pm SD) for the Normal group ($n = 24$) and 8.09 ± 4.60 for the Stenosis group ($n = 12$), with a statistically significant difference (unpaired *t*-test, $p < 0.0001$) between them. In cases with large absolute AI values, the FAIR-HASTE signals had identical lateralities corresponding with each AI.

Likewise, the absolute AIs of FAIR-HASTE were 8.88 ± 4.93 for the Stenosis group ($n = 10$) before revascularization and 2.22 ± 1.79 after, showing a statistically significant difference (paired *t*-test, $p = 0.0003$).

The absolute AIs of rCBF were 7.13 ± 3.57 before revascularization and 1.25 ± 1.33 after, showing a statistically significant decrease (paired *t*-test, $p = 0.0003$).

Discussion

FAIR is one technique of ASL that does not use a contrast agent; it was proposed by Kwong *et al.* and Kim *et al.* [10, 11]. To obtain quantitative perfusion information, 2 inversion recovery measurements are performed: one with a slice-selective inversion and one with a slice-nonspecific inversion. In slice-selective inversion, unlabeled (relaxed) blood spins flow into the image slice section and exchange at the capillary level with labeled tissue water from extra-vascular space. In slice-nonspecific inversion, in the same way, labeled (relaxing) spins flow into the image slice section and exchange with the labeled tissue water. A subtraction of these 2 measurements yields a flow-weighted image, because it mainly contains a signal of arterial spins that flow into the slice of interest during the inversion time. It is considered that the obtained FAIR signal pretty closely reflects CBF.

FAIR, free of a contrast agent, is noninvasive and enables repetitive examination. In addition, sections of any orientation can be obtained. This is

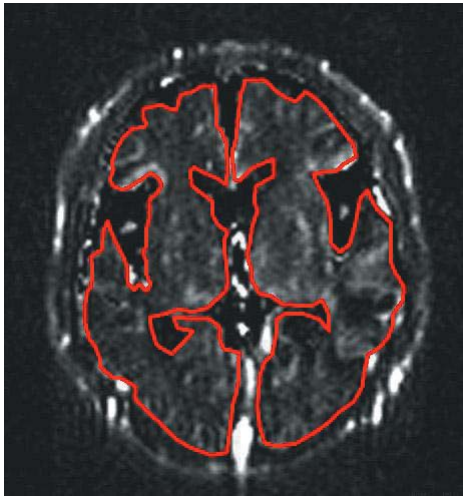


Fig. 2 ROIs created separately over both sides of the cerebral hemisphere on FAIR-HASTE.

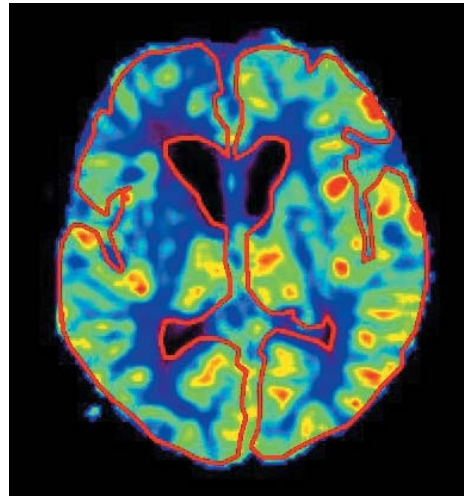


Fig. 3 ROIs created separately over both sides of the cerebral hemisphere on a rCBF map.

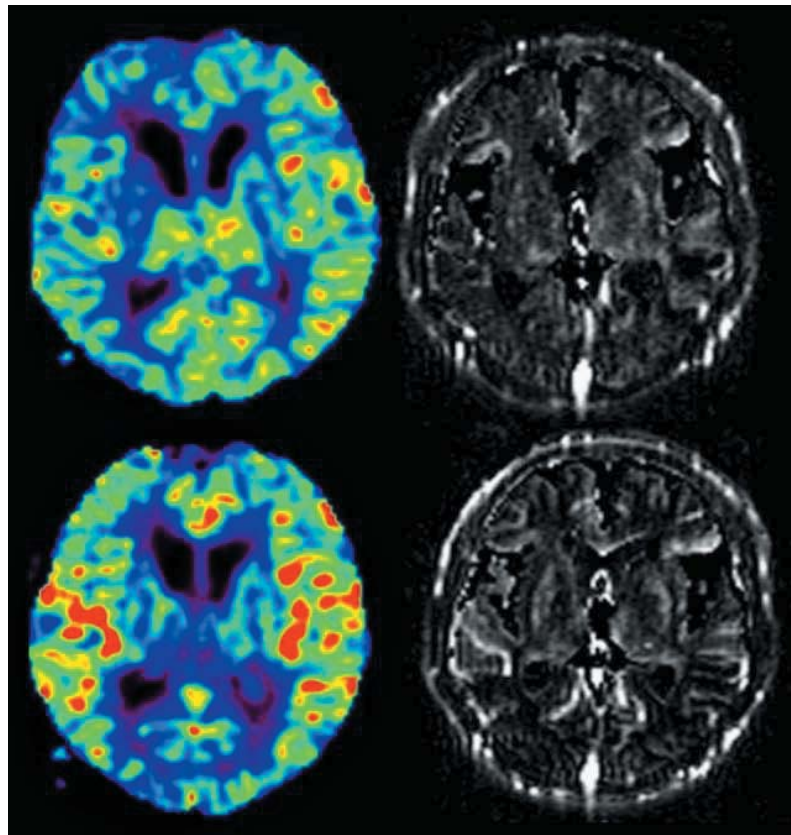


Fig. 4 Comparison of FAIR-HASTE and rCBF map images before and after carotid endarterectomy (CEA) in No. 8 patient with right ICA severe stenosis (99%) and left ICA stenosis (40%). Upper row, left to right: rCBF map and FAIR-HASTE image before CEA. Lower row, left to right: rCBF map and FAIR-HASTE image after CEA in the same patient. Hypo-perfusion in the right hemisphere was improved after CEA.

because the tagging band observed in the signal targeting with alternating radiofrequency (STAR) method is not depicted [7]. On the other hand, because FAIR is a subtracted image, it is very sensitive to any motion in the patients. It is also usually noisy, because the MR signal changes between slice-selective and slice-nonselective images are very small. To improve the signal to noise ratio (SNR), averaging of dozens of images is required, so the scanning takes longer.

In recent years, there have been many reports on the utility of the FAIR method for cerebral perfusion. Arbab *et al.* reported that the left-to-right (L/R) ratio of I-123-IMP SPECT showed significant correlation with those of DSC-pMRI and FAIR-EPI [16]. Furthermore, they reported that FAIR-EPI detected hypoperfused segments with significant correlation to I-123-IMP SPECT, and they concluded that FAIR-EPI imaging, like nuclear medicine study, was complementary to routine MR imaging in the assessment of cerebral perfusion [17]. Hunsche *et al.* reported that both FAIR-EPI and rCBF calculated with DSC-pMRI depict similar relations of perfusion in ischemic stroke patients and healthy subjects [18]. Since that report, multi-slice FAIR has been developed with added improvements to the original FAIR method [19, 20].

Recently, FAIR imaging using HASTE instead of EPI for signal data acquisition has been developed, and it can obtain perfusion images without a susceptibility artifact as well as be useful in evaluating perfusions near the lung, the posterior cranial fossa, and the mesial temporal lobes [14, 21]. There are as yet, however, to our knowledge, few reports of FAIR-HASTE imaging of cerebral perfusion. In FAIR-HASTE, blurring of artifacts can happen according to the phase encoding direction, and switching of phase and frequency encoding direction may be required. In this study, however, there was no area that required switching encoding direction. A calculation method for rCBF using FAIR-HASTE has not yet been completely established, however, so we defined the AI to detect perfusion laterality of both cerebral hemispheres. Because peripheral vessels are depicted as high-signal structures in FAIR images, scrupulous care was taken not to include them or other hyperintense structures in the ROIs.

In this study, a statistically significant difference

was recognized between the absolute AIs of FAIR-HASTE in the Normal group and those in the Stenosis group. Many cases with clinically significant hypoperfusion were included in the Stenosis group, so perfusion lateralities could be detected without acetazolamide stress. Because detection of mild hypoperfusion is notoriously difficult with routine MRI, the usefulness of noninvasive FAIR-HASTE here, free of contrast agent, was carefully evaluated.

A statistically significant decrease was recognized between the absolute AIs of FAIR-HASTE and rCBF before and after revascularization in the Stenosis group. We were persuaded that cerebral perfusion improvement by revascularization was able to be detected in those cases having clinically significant, but mild hypoperfusion in the Stenosis group. Fig. 4 shows the FAIR-HASTE image and rCBF map of a patient with right internal carotid artery (ICA) severe stenosis (99%) and left ICA stenosis (40%). Hypoperfusion in the right hemisphere, which was the dominantly affected vascular side before surgery, was improved and the AI value was decreased after the operation.

Because this study was only a preliminary investigation, no evaluations of FAIR-HASTE in coronal or sagittal sections or in areas of high susceptibility effect were performed. The efficacy of FAIR-HASTE at these points does need further examination, however.

There are 2 limitations to this study. First, optimization of TI, which is one of the important parameters in FAIR-HASTE, was not realized. In our study, the TI value was set to 1200 msec, which is generally used in the FAIR method. Arbab *et al.* reported that TI of 1400 msec detected hypoperfused segments better than that of 1200 msec in FAIR [17]. Yoneda *et al.* reported that a longer TI (= 1,600 msec) in the FAIR method might be more useful than a shorter TI (= 800 msec) for evaluating chronic occlusive disease in the clinical setting [22]. However, in both reports, we think that any difference in the results was slight and that such a small difference of TI had no large influence on this present study. Second, we were not able to grasp the correct cerebral circulation dynamics in the Stenosis group. In chronic occlusive disease, it is thought that dynamic cerebral circulation change is dependent on the degree of complicated collateral development. In

such disease, however, cerebral perfusion decrease often occurs in the dominantly affected hemisphere. In fact, in cases with large absolute AI values, the FAIR-HASTE signals had identical lateralities corresponding with each AI.

A ROI was created in each cerebral hemisphere over both anterior and posterior circulation. Individuals differ in their anterior and posterior circulation; also it has been postulated that a small quantity of collaterals might reach through from the posterior to the anterior circulation. For these reasons we decided not to limit the ROI to the anterior circulation alone. As a result, we chose to evaluate the averaged cerebral perfusion of both circulations.

Although there were individual cases without significant hypoperfusion in the dominantly affected side in the Stenosis group, statistically significant differences were indeed recognized, and the sensitivity of FAIR-HASTE in detecting hypoperfusion areas looks very promising.

Conclusion. FAIR-HASTE was useful in the detection of cerebral hypoperfusion in chronic occlusive carotid disease. This technique is noninvasive and free of the need for a contrast agent, and repetitive examination is possible.

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