An Assessment of the Usefulness of Time of Flight in Magnetic Resonance Angiography Covering the Aortic Arch

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Abstract - Carotid angiography covering the aortic arch includes contrast-enhanced magnetic resonance angiography (CEA), which is applied to a large region and usually employs contrast media. However, the use of contrast media can be dangerous in infants, pregnant women, and patients with chronic renal failure (CRF). Follow-up patients informed of a lesion may also want to avoid constant exposure to contrast media. We aimed to apply time-of-flight (TOF) angiography to a large region and compare its usefulness with that of CEA. Ten patients (mean age, 58 years; range, 45～75 years) who visited our hospital for magnetic resonance angiography (MRA) participated in this study. A 3.0 Tesla Achieva magnetic resonance imaging (MRI) system (Philips, Netherland) and the SENSE NeuroVascular 16-channel coil were employed for both methods. Both methods were applied simultaneously to the same patient. Three TOF stacks were connected to cover the aortic arch through the circle of Willis, and CEA was applied in the same manner. For the quantitative assessment, the acquired images were used to set the regions of interest (ROIs) in the common carotid artery (CCA) bifurcation, internal carotid artery, external carotid artery, middle cerebral artery, and vertebral artery, and to obtain the signal-to-noise ratio (SNR) and the contrast-to-noise ratio (CNR) for the soft tissues. Three radiologists and one radiological resident performed the qualitative assessment on a 5-point scale - 1 point, "very bad"; 2 points, "bad"; 3 points, "average"; 4 points, "good"; and 5 points, "very good" - with regard to 4 items: (1) sharpness, (2) distortion, (3) vein contamination, and (4) expression of peripheral vessels. For the quantitative assessment, we estimated the mean SNR and CNR in each of the 5 ROIs. In general, the mean SNR was higher in TOF angiography (166.1, 205.2, 154.39, 172.23, and 161.95) than in CEA (92.05, 95.43, 84.76, 73.69, and 88.3). Both methods had a similar mean CNR: 67.62, 106.71, 55.9, 73.74, and 63.46 for TOF angiography, and 67.82, 71.19, 60.52, 49.45, and 64.07 for CEA. In all ROIs, the mean SNR was statistically significant ($p<0.05$), whereas the mean CNR was insignificant ($p>0.05$). The mean values of TOF angiography and CEA for each item in the qualitative assessment were 4.2 and 4.28, respectively for item 1; 2.93 and 4.55, respectively, for

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item 2; 4.6 and 3.13, respectively, for item 3; and 2.88 and 4.65, respectively, for item 4. Therefore, TOF angiography had a higher mean for item 3, and CEA had a higher mean for items 2 and 4; there was no significant difference between the two methods for item 1. The results for item 1 were statistically insignificant ($p > 0.05$), whereas the results for items 2∼4 were statistically significant ($p < 0.05$). Both methods have advantages and disadvantages and they complement each other. However, CEA is usually applied to a large region covering the aortic arch. Time-of-flight angiography may be useful for people such as infants, pregnant women, CRF patients, and follow-up patients for whom the use of contrast media can be dangerous or unnecessary, depending on the circumstance.

Key words : CEA, CRF, TOF, MRA, MRI

INTRODUCTION

In the field of radiology, the current methods of obtaining angiographic images include digital subtraction angiography, which employs radiography and contrast media; computed tomography angiography (CTA); and magnetic resonance angiography (MRA) (Hashemi and Bradley 2010). Magnetic resonance angiography is useful in several ways: it provides noninvasive angiography without exposure to radiation; it shows vascular distributions on various image sections through image reconstruction after a single image acquisition; and it offers vascular imaging without contrast media. When using a magnetic resonance (MR) contrast agent in this method, it is safe to use a smaller amount of the agent with very few side effects, compared to using iodine X-ray contrast media (Pennell *et al*. 1996; Nichols *et al*. 2011). There are 3 types of MRA procedures. The first procedure is time-of-flight (TOF) angiography, which employs flow-related signal enhancement in which a spin in a certain position is selected by a single radiofrequency (RF). It is read after a certain interval, and any shift in the spin position during this interval reveals the TOF and makes blood flow visible with high signal intensity because of the RF pulses. The second procedure is phase-contrast (PC) angiography in which the spin uses phase shifts caused by the gradient magnetic field to produce 2 images by applying different gradients with positive and negative polarity to the blood flow. The resultant vascular images with positive and negative phase shifts are subtracted from each other. The signals from the blood flow are amplified and those from static tissues are reduced. The third procedure is contrast-enhanced MR angiography (CEA) in which a paramagnetic contrast agent (e.g., gadopentetate dimeglumine) is intravenously injected to shorten T1 remarkably in blood and use the effects of contrast enhancement (Nichols *et al*. 2011). Time-of-flight angiography and PC angiography use no contrast agent, whereas CEA uses a gadolinium-based MR contrast media (Laub 1995). As mentioned previously, MR contrast media indeed causes very few side effects, but they should be cautiously administered to chronic renal failure (CRF) patients or patients at high risk of nephrogenic systemic fibrosis (NSF). Using contrast media weakens renal functions, which then increases the likelihood of NSF in CRF patients. In Korea, NFS has never been observed, but it has reportedly been closely correlated with exposure to MR contrast media (Bakker *et al*. 1999). Two hundred fifteen cases of NSF have been reported around the world, mostly among CRF patients exposed to MRI contrast media (Michaely *et al*. 2006). Chronic renal failure refers to a condition in which the glomerular functions of the kidneys are permanently and irrecoverably weakened, and CRF patients are more likely to develop NSF and are faced with various pathological situations (Hong *et al*. 2010). They suffer an imbalance in diverse hormones and electrolytes and problems with urine formation and water discharge. The kidneys can usually maintain an effective glomerular filtration rate (GFR), despite the loss of 70% to 80% of renal function; however, if the condition persists, the GFR decreases gradually. This condition is caused by vascular stenosis in the passage to the kidneys (Jun *et al*. 2005). This is because the methods of local angiography involving no contrast agents have been developed, although there are some methods of using contrast media to obtain images from a large region in a short period. In brain MRA, TOF angiography is usually used to examine the circle of Willis and CEA is applied to a large region covering the aortic arch. In this study, we aimed to apply TOF angiography to a large region covering the aortic arch and determine its effectiveness in comparison to CEA.

Fig. 1. Magnetic resonance angiography devices.

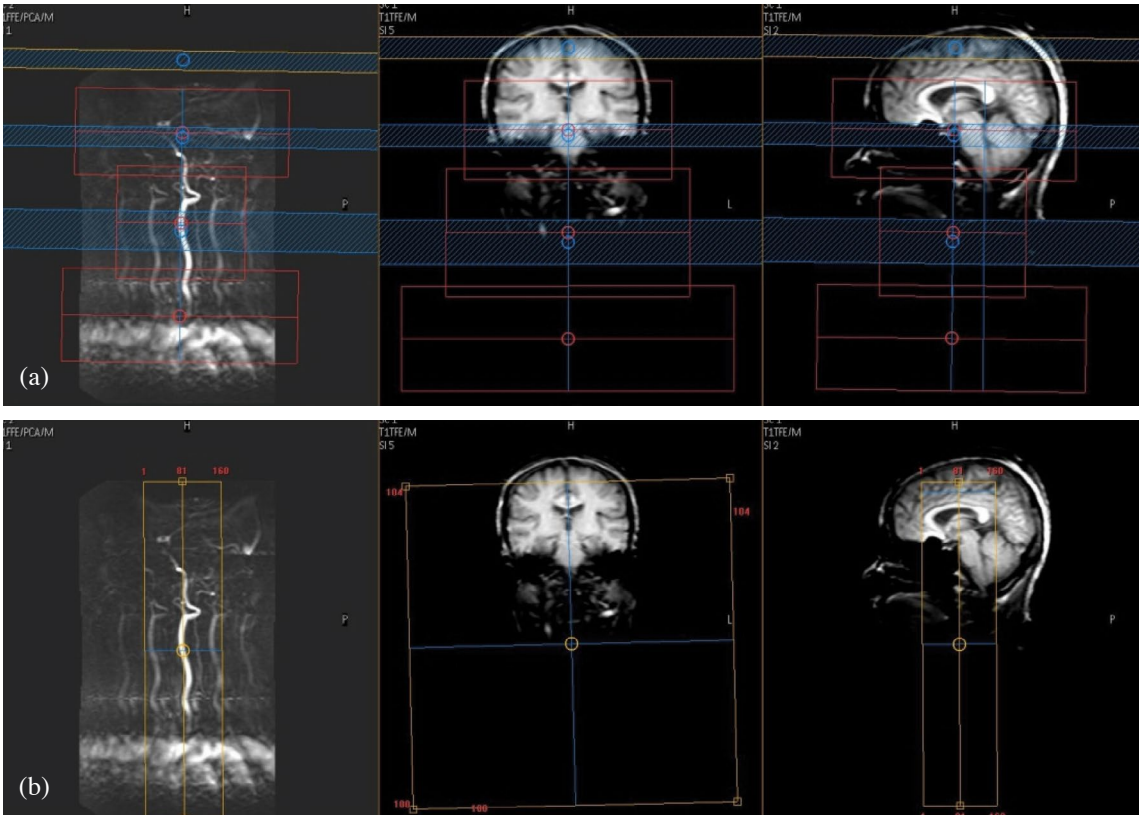

Fig. 2. (a) Time-of-flight plan. (b) Contrast-enhanced magnetic resonance angiography plan.

MATERIALS AND METHODS

Ten patients (mean age, 58 years; age range, 45∼75 years) who visited Kyung Hee University Hospital for MRA were involved in this study. We employed the 3.0 Tesla Achieva MRI system (Philips, Netherland) and the SENSE Neuro-Vascular 16 Channel coil for signal reception (Fig. 1).

Both methods were simultaneously applied to the same patient. Three-dimensional imaging was employed in both methods. Three TOF stacks were connected to cover the aortic arch through the circle of Willis. Imaging was obtained in the upper axial direction. Contrast-enhanced MR angiography covered the same region (Fig. 2). For CEA, we used an autoinjector to inject the contrast agent at the speed of 2.0 mL/s and we imaged in the coronal direction. The resultant TOF upper axial images and CEA coronal images were re-

Table 1. Scan Parameters

		TR/TE	FOV	NEX	F/A	Chunk	Scan time	Etc.
TOF angiography	1 STACK	19/8.1	220×188	1	18	5	2:54	
	2 STACK	18/8.1	220×132	2	18	6	3:27	
	3 STACK	18/8.1	300×243	1	16	5	3:38	No tone pulse used
CEA		5.3/2.0	350×350	1	30	1	1:02	

CEA: contrast-enhanced magnetic resonance angiography, FOV: field of view, TOF: time-of–flight

Table 2. Quantitative assessment and Qualitative assessment was evaluated based on the following four criteria

Evaluated no.	Quantitative assessment	Qualitative assessment
1	CCA	Sharpness
2	ICA	Distortion
3	ECA	Vein contamination
4	MCA	Expression of peripheral vessel
5	VA	

CCA: common carotid artery, ICA: internal carotid artery, ECA: external carotid artery, MCA: middle cerebral artery, VA: vertebral artery

constructed by maximal intensity projection within the devices. Table 1 presents the parameters of the two methods.

For imaging analysis, we used the TOF images and the CEA images to obtain the CNR for soft tissues and the SNR. To do this, we used the software in the MRI system (Eqs. 1, 2).

$$SNR_{ROI} = \frac{SI_{ROI}}{SD_{noise}} \quad (1)$$

$$CNR_{ROI} = \frac{(SI_{ROI} - SI_{Soft\ tissue})}{SD_{noise}} \quad (2)$$

where SI_{ROI} is the intensity against ROI, SD_{noise} the standard deviation of background noises, and the $SI_{Soft\ tissue}$ the intensity against soft tissues.

The quantitative assessment was performed at the regions of interest (ROIs) - the bifurcation of the common carotid artery (CCA), the internal carotid artery (ICA), the external carotid artery (ECA), the middle carotid artery (MCA), and the vertebral artery (VA) - to estimate the signal-to-noise ratio (SNR) and the contrast-to-noise ratio (CNR) for the soft tissues. Three radiologists who had worked in this field for 3 years or more and 1 radiological resident performed the qualitative assessment on a 5-point scale - 1 point, "very bad"; 2 points, "bad"; 3 points, "average"; 4 points, "good"; and 5 points, "very good" - with regard to 4 items: (1) sharpness, (2) distortion, (3) vein contamination, and (4) expression of peripheral vessels. For statistical analysis, a paired t test using the Excel program was employed (Table 2) (Fig. 3).

The image assessment items were evaluated based on the following four criteria:

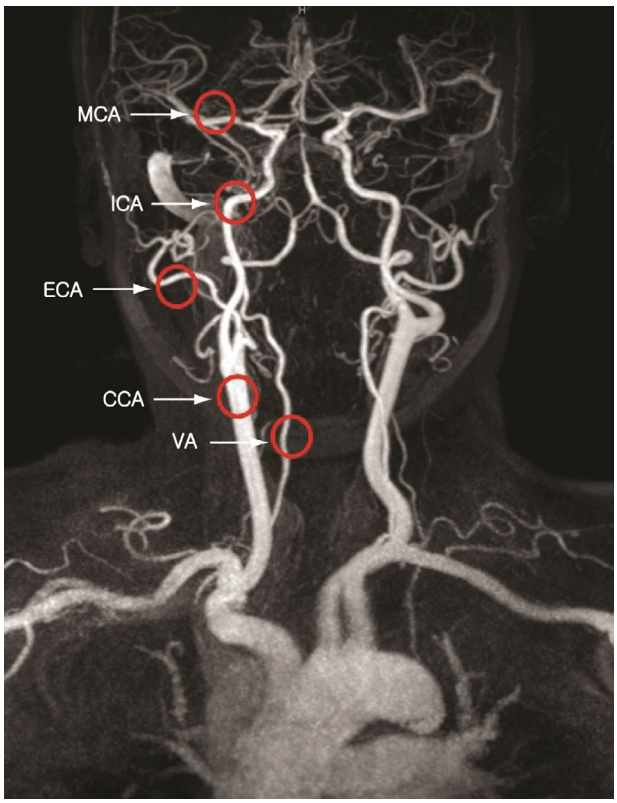

Fig. 3. The regions of interest setting (MCA: middle carotid artery, ICA: internal carotid artery, ECA: external carotid artery, CCA: common carotid artery, VA: vertebral artery).

1. Sharpness of vessels,
2. Distortion of image,
3. Vein contamination, and
4. Expression of peripheral vessels.

RESULTS

For the quantitative assessment, we estimated the mean SNR and CNR in each of the 5 ROIs: CCA, ICA, ECA, MCA, and VA. In general, the mean SNR was higher in TOF angiography (166.1, 205.2, 154.39, 172.23, and 161.95, respectively) than in CEA (92.05, 95.43, 84.76, 73.69, and 88.3, respectively). Both methods had a similar mean CNR: 67.62, 106.71, 55.9, 73.74, and 63.46, respectively, for TOF angiography, and 67.82, 71.19, 60.52, 49.45, and 64.07, respectively, for CEA. For all ROIs, the mean SNR was statistically significant ($p<0.05$), but the mean CNR was insignificant ($p>0.05$) (Tables 3~5). Based on the 4 testers' qualitative assessment of TOF angiography and CEA for the 4 items, the means obtained by TOF angiography and CEA were 4.2 and 4.28, respectively, for item 1; 2.93 and 4.55, respectively, for item 2; 4.6 and 3.13, respectively, for item 3; and 2.88 and 4.65, respectively, for item 4. Therefore, TOF angiography had a higher mean for item 3, and CEA had a higher mean for items 2 and 4; there was no significant difference for item 1. The results for item 1 were statistically insignificant ($p>0.05$), whereas the results for items 2~4 were statistically significant ($p<0.05$) (Tables 2, 5) (Figs. 4~10).

Table 3. Comparison between the Two Methods in the Signal-to-Noise Ratio and the Statistical Significance

	CCA	ICA	ECA	MCA	VA
TOF angiography	166.1	205.2	154.39	172.23	161.95
CEA	92.05	95.43	84.76	73.69	88.3
p	0.027	0.0103	0.018	0.009	0.012

CCA: common carotid artery, ICA: internal carotid artery, ECA: external carotid artery, MCA: middle cerebral artery, VA: vertebral artery, TOF: time-of-flight, CEA: contrast-enhanced magnetic resonance angiography

Table 4. Comparison between the Two Methods in the Contrast-to-noise Ratio and the Statistical Significance

	CCA	ICA	ECA	MCA	VA
TOF angiography	67.62	106.71	55.9	73.74	63.46
CEA	67.82	71.19	60.52	49.45	64.07
p	0.988	0.096	0.646	0.158	0.948

CCA: common carotid artery, ICA: internal carotid artery, ECA: external carotid artery, MCA: middle cerebral artery, VA: vertebral artery, TOF: time-of-flight, CEA: contrast-enhanced magnetic resonance angiography

Table 5. Comparison between the Two Methods in the Results of Qualitative Assessment and the Statistical Significance

	1	2	3	4
TOF angiography	4.20	2.93	4.60	2.88
CEA	4.28	4.55	3.13	4.65
p	0.783	0.041	0.048	0.039

TOF: time-of-flight, CEA: contrast-enhanced magnetic resonance angiography

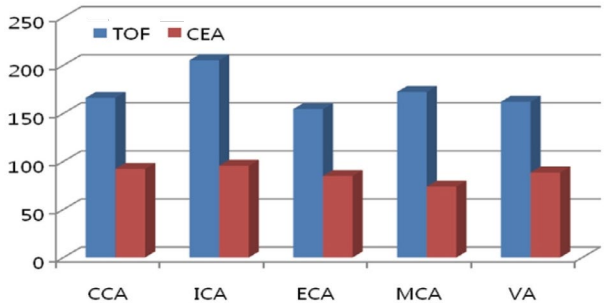

Fig. 4. Comparison between the two methods in the signal-to-noise ratio (CCA: common carotid artery, ICA: internal carotid artery, ECA: external carotid artery, MCA: middle cerebral artery, VA: vertebral artery, TOF: time-of-flight angiography, CEA: contrast-enhanced magnetic resonance angiography).

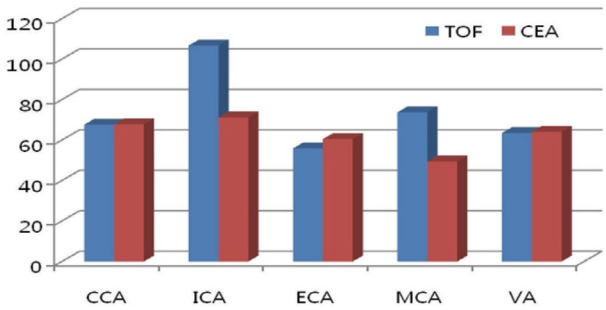

Fig. 5. Comparison between the two methods in the contrast-to-noise ratio (CCA: common carotid artery, ICA: internal carotid artery, ECA: external carotid artery, MCA: middle cerebral artery, VA: vertebral artery, TOF: time-of-flight angiography, CEA: contrast-enhanced magnetic resonance angiography).

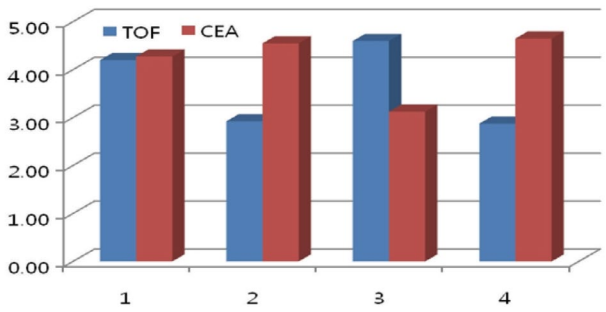

Fig. 6. Comparison between the two methods in the qualitative assessment results (TOF: time-of-flight angiography, CEA: contrast-enhanced magnetic resonance angiography).

DISCUSSION

Time-of-flight angiography with high resolution is good at expressing arteries and has a favorable SNR (Anzalone *et*

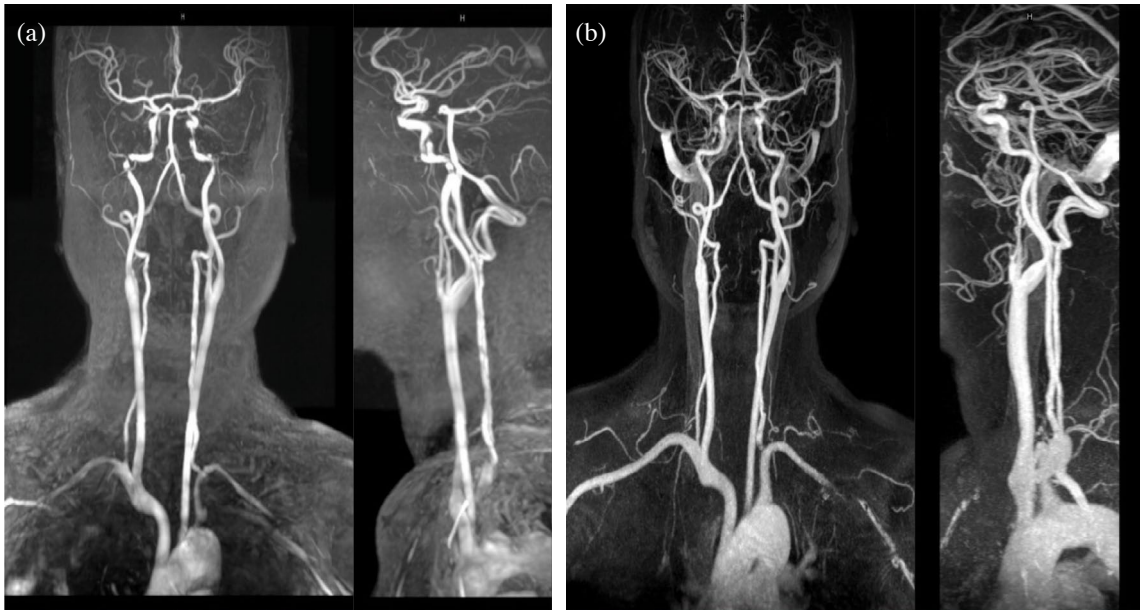

Fig. 7. (a) Time-of-flight angiography. (b) Contrast-enhanced magnetic resonance angiography.

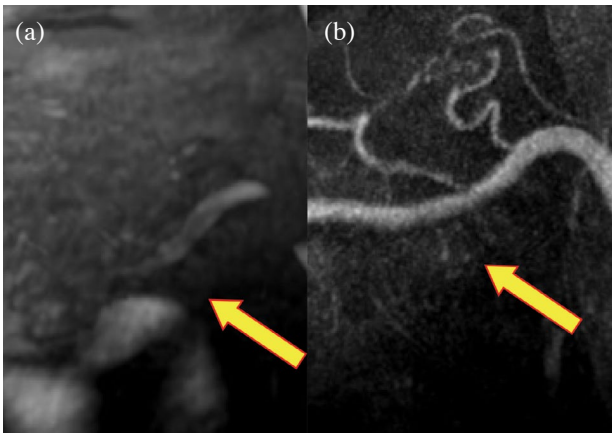

Fig. 8. Signal distortion. The subclavian artery generates greater signal loss (arrows) with (a) time-of-flight angiography than with (b) contrast-enhanced magnetic resonance angiography.

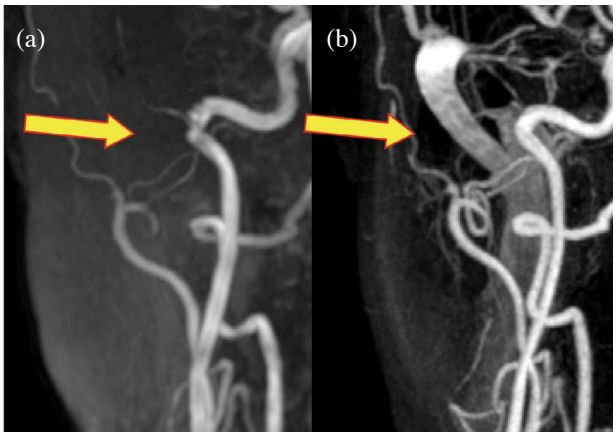

Fig. 9. Vein contamination (arrows) is less serious with (a) time-of-flight angiography than with (b) contrast-enhanced magnetic resonance angiography.

al. 2006; Sadikin *et al*. 2007). Another notable advantage of this method is that it requires no contrast agent. However, its flow-related enhancement characteristic makes it sensitive to blood flow. It is sensitive to a strong blood flow, but it generates substantial signal loss from the turbulent flow in patients with a weak blood flow, vascular stenosis, aneurysm, and so on (Anzalone *et al*. 2006; Sadikin *et al*. 2007). Another disadvantage of TOF angiography is that it requires substantial time to perform. To overcome these disadvantages, several TOF MRA sequences have been developed such as tilted optimized nonsaturating excitation (TONE), magnetization transfer suppression (MTS), and multiple overlapping thin slap acquisition (MOTSA) (Choi *et al*. 2011). Tilted optimized nonsaturating excitation applies a small flip angle in the introduction part and uses a large flip angle in the distal part of the slab to enhance the signal in the distal part. It can maintain a contrast between blood vessels and brain tissues, even in the distal part where spin saturation normally leads to signal loss. Magnetization transfer suppression controls the signal intensity in brain tissues, saturates the immovable spin, and makes the movable one within the blood flow change magnetization. This reduces the signals in the brain tissues and maintains the minimum saturation of the mov-

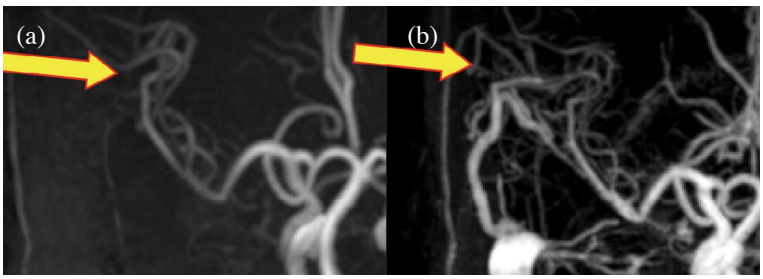

Fig. 10. (a) Time-of-flight angiography expresses peripheral vessels (arrows) less well than (b) contrast-enhanced magnetic resonance angiography.

able spin within the blood flow. This improves the contrast between blood vessels and brain tissues. Multiple overlapping thin slap acquisition uses a thin slab to reduce blood flow saturation and applies a large flip angle to produce high-resolution imaging. Such diverse developments in the TOF MRA sequence have greatly improved the quality of imaging by improving resolution, increasing the blood flow signal intensity, and improving the contrast (Parker *et al*. 1998; Choi *et al*. 2011). By contrast, CEA provides a poor resolution, a low SNR, and vein contamination. However, it shortens T1 in blood when using contrast media and requires less time, and its great vascular resistance leads to good expression of peripheral vessels with weak blood flow. It also generates less signal loss caused by turbulent flow in patients with vascular stenosis, aneurysm, etc. (Parker *et al*. 1998). Because each of the 2 methods has advantages and disadvantages, they complement each other clinically.

This study has some limitations. First, too few patients were involved in this study. Statistical analysis actually requires more study participants. Second, a comparison using 1.5 T devices is also needed to obtain quantitative data. Third, the methods were only applied to patients without specific lesions in their blood vessels. Choi *et al*.(Choi *et al*. 2011). showed that the 2 methods equally led to a diagnosis of the specific condition of cerebral arteriosclerosis, whereas we generally assessed the two methods.

CONCLUSION

Because TOF angiography and CEA are highly complementary to each other, both methods are now employed clinically to complement each other. However, the use of contrast media can be dangerous to some people such as infants, pregnant women, and CRF patients. Follow-up patients informed of a lesion may also want to avoid constant exposure to contrast media. Time-of-flight angiography can also be useful to patients for whom contrast media is unnecessary or dangerous.

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