

# Contrast-Enhanced Magnetic Resonance Angiography for Evaluation of the Steno-occlusive Disease of the Supraaortic Arteries: Comparison with Computed Tomography Angiography and Digital Subtraction Angiography

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**Purpose :** To intra-individually compare diagnostic accuracy of high-resolution contrast-enhanced magnetic resonance angiography (CE-MRA) with computed tomography angiography (CTA) and digital subtraction angiography (DSA) for the assessment of supraaortic steno-occlusive disease.

**Materials and Methods :** Twenty-eight patients (20 men, 8 women, 53–79 years of age) underwent supraaortic CE-MRA, CTA and DSA. CE-MRA was performed on two 1.5T MR scanners (voxel dimension:  $0.66 \times 0.66 \times 1.1$  or  $1.2 \text{ mm}^3$ ), and CTA on 64-slice CT scanners (voxel dimension:  $0.42 \times 0.42 \times 0.63 \text{ mm}^3$ ). All the three examinations were completed within 40 days (median 19 days; range 1–40 days). Retrospective evaluation and measurement of diameter of 6 extracranial and 9 intracranial arterial segments was done by 2 experienced radiologists.

**Results :** A total of 420 arterial segments were examined by CE-MRA, CTA and DSA. On DSA, 34 stenocclusive lesions were noted at extracranial ( $n=19$ ) and intracranial ( $n=15$ ) vessels. For extracranial stenosis greater than 70%, sensitivity, specificity, positive predictive value (PPV) and negative predictive values (NPV) were 94.7%, 98.7%, 90.0% and 99.3% on CE-MRA, and 94.7%, 99.3%, 94.7% and 99.3% on CTA. For intracranial stenosis greater than 50%, sensitivity, specificity, PPV and NPV were 93.3%, 98.3%, 77.8% and 99.6% on CE-MRA, and 86.7%, 97.9%, 72.2% and 99.1% on CTA, with DSA as the standard of reference.

**Conclusion :** Supraaortic CE-MRA is as reliable as CTA in depicting the arterial stenosis, and is effective in screening of significant stenosis of both extracranial and intracranial arterial stenosis.

**Index words :** Diagnostic accuracy  
Sensitivity and specificity  
Contrast enhanced MR angiography

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## **Introduction**

In patients with clinical suspicion of extracranial and intracranial steno-occlusive lesions, accurate assessment of arteries is important for screening and optimal therapeutic decisions. Although digital subtraction angiography (DSA) is the reference standard for evaluation of the craniocervical vasculature, it has a small risk of transient ischemic attack and permanent neurologic deficit thus making it less ideal as a screening tool and for the longitudinal follow-up of patients with cerebrovascular disease (1-3).

Recent advances in three-dimensional contrast-enhanced magnetic resonance angiography (CE-MRA) are rapidly changing the diagnostic approach to the intracranial as well as extracranial vascular disease, such that DSA is increasingly being reserved for interventional method of vascular lesions including aneurysm (4, 5) as well as steno-occlusive disease (6-13). However, the role of wide field-of-view (FOV) CE-MRA for the screening of steno-occlusive disease of the entire supra-aortic arteries still remains unclear. The purpose of this study was to compare diagnostic accuracy of CE-MRA and CTA for the assessment of steno-occlusive disease of the supra-aortic arteries including extracranial and intracranial arteries with DSA as standard of reference.

## **Materials and Methods**

### **Patients**

Twenty-eight consecutive patients (20 men, 8 women, 53-79 years of age) were identified from the radiology data base who underwent supraaortic CE-MRA, CTA and DSA. Clinical indications for the CE MRA included transient ischemic attack or stroke (n=25) and known extracranial or intracranial atherosclerotic disease (n=3). All the three examinations were completed within 40 days (median 19 days; range 1-40 days).

### **Imaging Methods**

High-resolution (HR) CE-MRA was acquired with 1.5T MR scanners (Signa Twinspeed, GE healthcare, Milwaukee and Intera Achieva, Philips Medical Systems, Netherlands) equipped with a commercially

available phased-array coil. A standard automated bolus injection (Spectris, Medrad) of 0.1 mmol/kg body weight of gadobutrol (Gadovist, Schering, Germany) was used at a flow rate of 1.5 cc/sec, followed by 20 cc of saline flush at the same flow rate. The three-dimensional (3D) MRA sequence with elliptical centric k-space ordering or randomly segmented k-space ordering was started manually as soon as the contrast agent was seen in the common carotid arteries on the two-dimensional (2D) real-time fluoroscopy. Acquisition parameters were as follows: 3D gradient echo-sequence with TR/TE/flip angle (FA), 4.8-5.5 ms / 1.3-1.7 ms / 30-40°, slab thickness, 165-180 mm; and acquisition time, 1min 20 sec-35 sec. An image matrix of 448×448-512×512 on a 300-337 field of view yielded a measured voxel volume of 0.48-0.52 mm<sup>3</sup> (0.66×0.66×1.1 or 1.2 mm<sup>3</sup>) after interpolation.

CTA were performed on a 64-slice CT scanners (Lightspeed VCT, GE Healthcare and Somatome Sensation 64, Siemens Medical Systems), using Ultravist (iopromide, Bayer Schering Pharma, 300 mgI/mL) as the IV contrast material. Contrast material was injected at a rate of 4 cc/sec and was immediately followed by a 50 cc saline bolus flush at the same rate. Patients were placed in the supine position. Helical data were acquired with a 0.625 mm collimation, 40 mm of detector coverage and a table speed of 39.37 mm/s starting at the third thoracic vertebra and proceeding to the cranial vertex. A FOV of 250 mm, slice collimation of 0.625 mm matrix size of 512×512, and reconstruction interval of 0.625 mm, allowed a measured voxel volume of 0.11 mm<sup>3</sup> (0.42×0.42×0.63 mm<sup>3</sup>).

DSA was performed on a single plane Allura Xper system (Philips Medical systems, Netherlands). A 5-French catheter was navigated into both common carotid arteries, and vertebral arteries. If the origin of vertebral artery was narrow or tortuous, ipsilateral subclavian artery was navigated. The Carotid bifurcation and the intracranial arteries were displayed separately in at least 2 projections each by injections of 4-5 cc of contrast material (iodixanol, Visipaque 320 mgI/mL, GE Healthcare, Cork, Ireland).

### **Analysis**

Two readers blinded to all subjects' clinical information independently reviewed all of the MIP

reconstruction images of CE-MRA, and subsequently MIP and VR reconstruction images of the CTA followed by DSA images for presence of stenosis and degree of stenosis. The readers independently identified and characterized the degree of stenosis for each of 15 prespecified extracranial arteries (common carotid artery (CCA), proximal external carotid artery (ECA) and internal carotid arteries (ICA)) and intracranial arteries (A1 segment of anterior cerebral arteries (ACA), M1 segment of middle cerebral arteries (MCA), P1 and P2 segments of posterior cerebral arteries (PCA), basilar artery (BA) and V4 segment of vertebral arteries(VA)). As a consequence, 420 arteries were available for direct comparison with DSA and were included for statistical analysis (56 CCA, 56 ECA, 56 ICA, 56 ACA, 56 MCA, 56 PCA, 28 BA, 56 VA). Degree of intracranial stenosis was calculated using the published method for the Warfarin-Aspirin Symptomatic Intracranial Disease Study: percent stenosis =  $[(1-(D_{stenosis}/D_{normal}))] \times 100$  (14).  $D_{stenosis}$  is the diameter of the diseased segment at its most severe site.  $D_{normal}$  is the diameter of the proximal normal artery. For the measurement at the carotid bifurcation lesion,  $D_{normal}$  was measured at the distal normal artery, analogous to the method used in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (15). All disagreements

of greater than 10% were reviewed by a third reader who decided between the 2 measurements made.

Interobserver agreement was calculated for cutoff points of 50% for intracranial stenosis and 70% for extracranial stenosis between observers of CE-MRA, CTA and DSA, respectively. Sensitivity, specificity, positive and negative predictive values were calculated for CE-MRA and CTA using DSA as the gold standard with 50% cutoff point for intracranial and 70% cutoff point for extracranial stenosis.

**Results**

A total of 420 arterial segments including 168 extracranial and 252 intracranial arterial segments were evaluated by CE-MRA, CTA and DSA. Vascular disease was detected by DSA in the 58 of 420 (13.8%) arteries with the following localizations: 29 cervical ICA, 14 MCA, 6 VA, 5 BA, 2 ECA, 1 ACA, and 1 PCA, and. Occlusion was diagnosed based on the DSA images in 3 of 420 (0.7%), stenosis  $\geq 70\%$  in 22 of 420 (5.2%), stenosis  $\geq 50\%$  and  $< 70\%$  14 of 420 (3.3%), and stenosis  $< 50\%$  in 19 of 420 (4.5%) (Table 1).

Vascular disease was diagnosed in 58 of 420 (13.8%) by CE-MRA, and 52 of 420 (12.4%) by CTA. CE-MRA revealed occlusion in 3 of 420 (0.7%), stenosis  $\geq 70\%$  in 29 of 420 (6.9%), stenosis  $\geq 50\%$  and  $< 70\%$  11 of 420

**Table 1.** Distribution of Diseased Vessel Segments Seen on Digital Subtraction Angiography

	No. of Diseased Segments (n = 58)			Occlusion
	< 50%	50%–70%	> 70%	
Extracranial				
Internal carotid	7	3	17	2
External carotid		2		
Intracranial				
Anterior cerebral	1			
Middle cerebral	8	3	2	1
Posterior cerebral		1		
Vertebral	1	4	1	
Basilar	2	1	2	

**Table 2.** Extracranial Stenosis (>70%) at CTA, CE-MRA versus DSA

DSA stenosis	CE MRA		CTA		Number(n)
	Yes	No	Yes	No	
Yes	18	1	18	1	n = 19
No	2	147	1	148	n = 149
Total	20	148	19	149	n = 168

**Contrast-Enhanced Magnetic Resonance Angiography for Evaluation of the Steno-occlusive Disease of the Supraaortic Arteries**

(2.6%), and stenosis <50% in 15 of 420 (3.6%). CTA revealed occlusion in 3 of 420 (0.7%), stenosis  $\geq$ 70% in 24 of 420 (5.7%), stenosis  $\geq$ 50% and <70% 19 of 420 (4.5%), and stenosis <50% in 6 of 420 (1.4%). Kappa values for interobserver agreement for stenosis grading were 0.739 for DSA, 0.807 for CE-MRA, and 0.749 for CTA.

With the cutoff point of 50% stenosis for intracranial and 70% stenosis for extracranial arteries, overall steno-occlusive lesion was detected by DSA in 34 of 420 (8.1%), with the following localizations: 3 BA, 19 ICA, 6 MCA, 1 PCA, 5 VA. With the same cut-off point, 32 of 34 (94.1%) significant stenosis were correctly diagnosed with CE-MRA.

Among the 19 extracranial stenoses greater than 70% detected on DSA, 18 lesions were correctly classified on both CE-MRA and CTA (Fig. 1) (Table 2), with one false negative result. There were two false positive results on CE-MRA (Fig. 2) and one on CTA. For extracranial

**Table 3.** Comparative Analysis of CTA and CE-MRA versus DSA for Extracranial Stenosis (>70%)

Performance measure	Extracranial stenosis >70%	
	CE-MRA	CTA
Sensitivity	94.7%	94.7%
Specificity	98.7%	99.3%
Positive predictive value	90.0%	99.3%
Negative predictive value	99.3%	94.7%



**Fig. 1.** The proximal cervical ICA in 78-year-old woman with history of stroke was rated by the observers to have segmental stenosis (arrow) of the right internal carotid artery more than 70% on volume-rendered reconstruction image of 3D rotational DSA (a), CTA (b) and CE-MRA (c).

stenosis greater than 70%, sensitivity, specificity, positive and negative predictive values were 94.7%, 98.7%, 90.0% and 99.3% on CE-MRA, and 94.7%, 99.3%, 94.7% and 99.3% on CTA (Table 3).

For intracranial stenosis greater than 50%, 15 lesions were seen on DSA. 14 lesions were correctly classified

on CE-MRA (Fig. 3) with one false negative result, and 13 lesions were identified on CTA with two false negative results (Table 4). There were four false positive results on CE-MRA, and five on CTA. For intracranial stenosis greater than 50%, sensitivity, specificity, negative predictive and positive predictive

**Table 4.** Intracranial Stenosis (>50%) at CTA, CE-MRA versus DSA

DSA stenosis	CE MRA		CTA		Number(n)
	Yes	No	Yes	No	
Yes	14	1	13	2	n = 15
No	4	233	5	232	n = 237
Total	18	234	18	234	n = 252



**Fig. 2.** Images in 73-year-old man show segmental stenosis (arrow) of the left internal carotid artery. Compared to DSA (a) and CT angiography (b), stenosis was overestimated on contrast-enhanced MR angiography (c).

value was 93.3%, 98.3%, 77.8% and 99.6% on CE-MRA, and 86.7%, 97.9%, 72.2% and 99.1% on CTA (Table 5).

**Discussion**

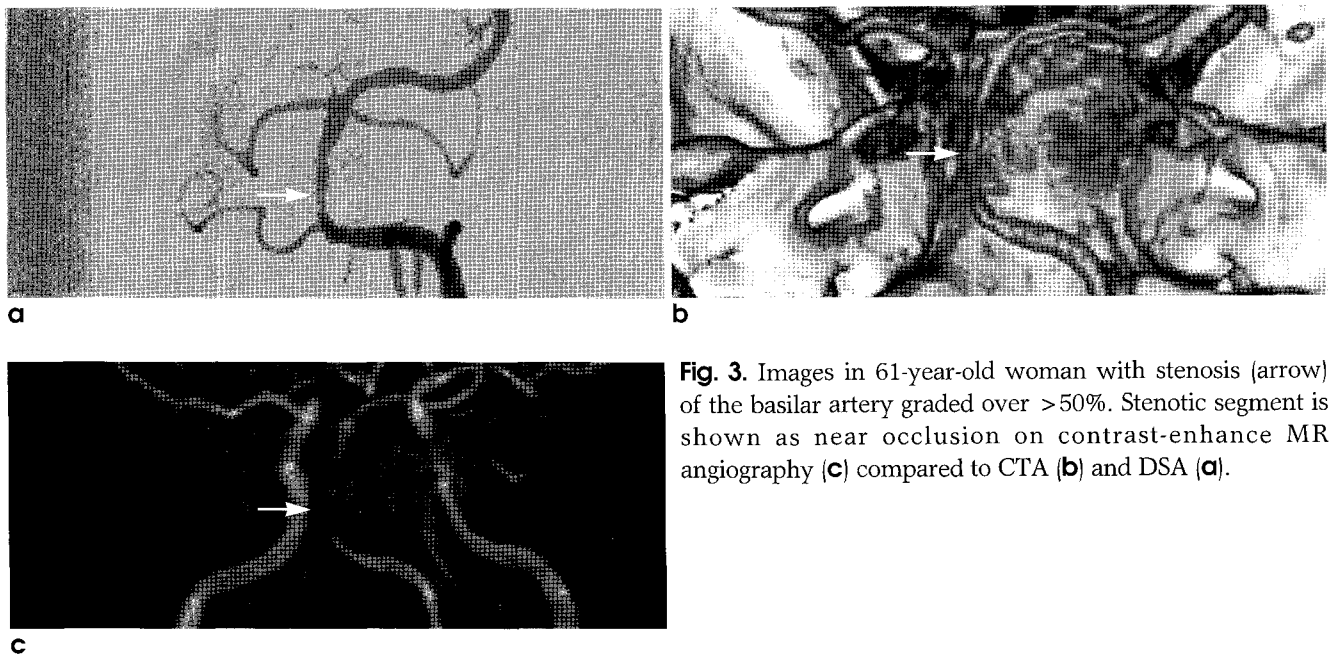
In this consecutive series of patients who had CE-MRA and CTA, and also had conventional angiography, we found that CE-MRA had a high sensitivity and negative predictive value for both extracranial (94.7% and 99.3% for 70% stenosis) and intracranial (93.3% and 99.6% for 50% stenosis) arterial lesions. We use the described CE-MRA protocols for evaluation of the entire supra-aortic arteries from the aortic arch to the intracranial arteries. The ability to provide relatively high spatial resolution with wide field-of-view including entire supra-aortic and intracranial arteries makes the CE-MRA good option as a screening tool in the initial evaluation of patient with suspected extracranial and intracranial stenosis. In a

clinical setting, one must assess which of the available imaging tools is sufficiently accurate to distinguish patients with severe and critical stenosis from those with mild or no stenosis. From the evidence obtained from the randomized trials including NASCET and ECST for cervical internal carotid artery and WASID for intracranial stenosis (15-18), it is crucial to identify an efficient and noninvasive accurate neuroimaging method for triaging patients with significant extracranial (70%) and intracranial stenosis (50%) for emerging therapies to prevent ischemic stroke. Thus cut-off values of stenosis in our study were set to 70% for extracranial and 50% for intracranial disease. High sensitivity in depicting the stenosis involving the extracranial and intracranial arteries in our series means that the test is unlikely to miss important arterial stenosis. The high negative predictive value can also assure the clinician that a negative result is highly predictive of minimal arterial stenosis. Furthermore, additional T2 weighted image of the brain obtained with CE-MRA gives more accurate screening of the remote or recent ischemic insult of the brain without radiation, compared to the CTA.

Our results showed that CE MRA has tendency to overestimate the grade of stenosis with relatively low positive predictive value (90.0% for extracranial and 70.5% for intracranial stenosis) compared to DSA as a standard of reference, especially for the intracranial arteries. Overestimation of arterial luminal narrowing

**Table 5.** Comparative Analysis of CTA and CE-MRA versus DSA for Intracranial Stenosis (>50%)

Performance measure	Intracranial	
	CE-MRA	CTA
Sensitivity	93.3%	86.7%
Specificity	98.3%	97.9%
Positive predictive value	77.8%	72.2%
Negative predictive value	99.6%	99.1%



**Fig. 3.** Images in 61-year-old woman with stenosis (arrow) of the basilar artery graded over >50%. Stenotic segment is shown as near occlusion on contrast-enhance MR angiography (c) compared to CTA (b) and DSA (a).

on CE-MRA can result from the dephasing artifacts along the margin of the lumen and the section thickness causing partial volume averaging effect (19–21). The primary limitation of most CE-MRA applications is their relatively lower spatial resolution. The competing requirements for adequate distance coverage, and acquisition speed, have generally forced a relatively compromised spatial resolution to CTA. This is particularly important in evaluation of small vasculature such as intracranial vessels, in which submillimeter voxels are required for accurate detection and depiction of pathology (13, 22).

For the evaluation of cervical ICA stenosis over 70%, a prior study of 177 patients found that CE-MRA more accurately delineated neurovascular anatomy than does unenhanced 2D TOF MRA, although the administration of gadolinium did not offer a significant advantage in distinguishing surgically treatable cervical ICA stenosis, with CTA as standard of reference (23). The size of voxel ( $1.25 \times 1.25 \times 1.6$  mm) in their study, however, was relatively larger than that used in our study ( $0.66 \times 0.66 \times 1.1$  or 12 mm). The introduction of special k-space filling methods including elliptical centric (24, 25) and randomly segmented (26) k-space ordering in the middle of k-space has improved spatial resolution of CE-MRA, and made it a viable alternative for the evaluation of the smaller vessels including intracranial circulation (4, 9, 11, 13, 27). Further improvements in spatial resolution with parallel imaging and introduction of higher magnetic field units hold the promise of further enhanced performance of CE-MRA (13, 27, 28). In addition, use of contrast agent with higher concentration and higher relaxivity in our study may have the potential to further enhance the spatial resolution (29). Further improvements in coil array geometry and sensitivity profile, and the introduction of higher magnetic field units (7.0 T) with higher SNR boost, hold the promise of further enhanced performance of CE-MRA in terms of speed and spatial resolution, which may lead to improved depiction of intracranial arteries.

Our study has several limitations. Time limit for obtaining all three studies in our retrospective analysis was 40 days. It is possible that a patient's vessel may have changed during that time period. Furthermore, a systematic bias could have been introduced, because CE-MRA was done first in most case for screening of

the atherosclerotic disease and ischemic brain lesion, followed by CTA and DSA. In our study, comparison between the three modalities was retrospective, and inclusion criteria for the study were not prospectively established. During the consecutive evaluation of three examinations, recall bias of the two readers with respect to three examinations could not have been eliminated. The use of consensus readings in this study further introduces a possible reader bias. Because morphology of the stenotic lesion including calcified plaque was not directly compared, the possibility of misevaluation due to dense calcification could not be evaluated in our study. Evaluation of diagnostic accuracy with the data grouped according to arterial segment with confidence interval could not be made at our study. Finally, we used two different MR scanners and protocols with different TR, TE, flip angle, matrix and FOV, and with different k-space filling algorithms for CE-MRA, and also CTA was performed by two different CT machines. To make the bias as little as possible in terms of spatial resolution in our study, the CE-MRA and CTA were obtained with the size of the voxel to similar in each other on both CE-MRA and CTA.

In conclusion, CE-MRA was about as reliable as CTA with DSA as gold standard in depicting the critical stenosis with cutoff of 70% for extracranial arteries and 50% for intracranial artery. High sensitivity and negative predictive value in detection of stenosis make the CE-MRA sufficiently accurate to screen critical stenosis of supraaortic arteries.

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## Contrast-Enhanced Magnetic Resonance Angiography for Evaluation of the Steno-occlusive Disease of the Supraaortic Arteries

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## 조영증강 자기공명 혈관조영술을 이용한 대동맥궁 위 혈관의 협착 및 폐쇄 질환 평가: 전산화 단층 혈관조영술 및 디지털 감산혈관조영술과의 비교

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**목적:** 대동맥궁 상부의 두개강내외 동맥의 협착을 평가함에 있어 3차원 조영증강 자기공명영상 혈관조영술 (contrast-enhanced magnetic resonance angiography, CE-MRA), 전산화 단층 혈관 조영술(computed tomographic angiography, CTA), 그리고 디지털 감산 혈관조영술(digital subtraction angiography)의 진단 정확도를 비교하고자 하였다.

**대상 및 방법:** 총 대동맥궁 상부의 두개강내외 동맥에 대해 CE-MRA (화소크기: 0.66×0.66×1.1 혹은 1.2 mm<sup>3</sup>), CTA (화소크기: 0.42×0.42×0.63 mm<sup>3</sup>), 그리고 DSA를 모두 시행한 28명의 환자(남자20명, 여자 8명, 나이: 53-79세)를 대상으로 하였다. 세 영상검사는 40일 이내에 모두 시행되었다 (중앙값 19일, 1-40일). 두명의 경험 있는 영상의학 전문의가 영상에 대한 평가 및 미리 설정된 15개 구간의 동맥 직경의 측정을 후향적으로 시행하였다.

**결과:** 총 420 구간의 동맥에 대한 평가가 CE-MRA, CTA 및 DSA에서 가능하였다. DSA에서 34부위의 협착 혹은 폐색 병변이 관찰되었으며, 이중 19예는 두개강외에 15예는 두개강내에 위치하였다. DSA를 기준으로 평가하였을 때, 두개강외 혈관에서 70%이상의 혈관협착을 진단하는데 있어 CE-MRA는 민감도 94.7%, 특이도 98.7%, 양성 예측도(PPV) 90.0%, 음성예측도(NPV) 99.3% 였고, CTA는 각각 94.7%, 99.3%, 94.7%, 99.3% 였다. 두개강내 혈관의 50% 이상 혈관 협착을 진단하는데에는 CE-MRA의 민감도가 93.3%, 특이도 98.3%, 양성예측도 (PPV) 77.8%, 음성예측도(NPV) 99.6% 였고, CTA에서는 각각 86.7%, 97.9%, 72.2%, 99.1% 였다.

**결론:** 대동맥궁 상부의 두개강외와 두개강내의 동맥 협착을 진단함에 있어 CE-MRA 는 CTA와 비슷한 정도의 신뢰성을 보이며, 두개강내외의 의미있는 동맥 협착에 대한 선별검사로 효과적이다.

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