High-Resolution, Contrast-Enhanced Magnetic Resonance Angiography With Elliptical Centric k-Space Ordering of Supra-aortic Arteries Compared With Selective X-Ray Angiography

Ralf Wutke, MD; Werner Lang, MD; Claudia Fellner, PhD; Rolf Janka, MD; Christian Denzel, MD; Michael Lell, MD; Werner Bautz, MD; Franz A. Fellner, MD

Background and Purpose—The objective of this study was to evaluate the relative value of high-resolution, contrast-enhanced MR angiography (CE MRA) with elliptical centric k-space ordering compared with intra-arterial x-ray angiography for imaging carotid stenosis.

Methods—Thirty patients with suspected stenosis of the carotid arteries were examined with CE MRA (1.5-T scanner) and x-ray angiography (aortic arch survey and selective imaging of both common carotid arteries). For the first time, not only the extracranial carotid bifurcation but all the vessel segments from the aortic arch to the circle of Willis were assessed by independent investigators.

Results—For the internal carotid artery in the region of the extracranial carotid bifurcation, there was a very close correlation between CE MRA and x-ray angiography (sensitivity, 100%; specificity, 92%). The initially suspected overestimation of stenosis on CE MRA in 3 cases was ultimately revealed to be an underestimation on x-ray angiography. CE MRA showed slightly poorer imaging of the basal vessel segments at the level of the aortic arch (because of breathing artifacts) and the intracranial vessel segments (because of small vessel caliber and venous superimposition due to delayed sequence starts).

Conclusions—The MRA technique described here provides reliable results in the diagnosis of carotid stenosis and is thus suitable for replacing the invasive conventional x-ray angiography method in most cases. Further technical developments with regard to spatial resolution are still required for improved visualization of small vessels (terminal carotid branches and intracranial vessels). (Stroke. 2002;33:1522-1529.)

Key Words: carotid stenosis ■ contrast media ■ magnetic resonance angiography ■ magnetic resonance imaging

Arteriosclerotic changes at the extracranial carotid bifurcation are an important factor in the etiology of cerebral infarction. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the Asymptomatic Carotid Atherosclerosis Study (ACAS) have shown that patients with high-grade carotid artery stenosis (70% to 99%) of the internal carotid artery (ICA) can benefit from endarterectomy. In certain cases endarterectomy can also be indicated in symptomatic moderate stenosis. Catheter angiography is an invasive procedure with attendant complications and is associated with mortality and morbidity rates of 0.1% and 1%, respectively (disabling stroke). Thus, there is a demand for a noninvasive diagnostic procedure for the entire carotid system to rule out relevant stenoses at the origins of the major vessels and stenoses in the vessels cranial to the carotid bifurcation that cannot reliably be diagnosed by ultrasound.

MR angiography (MRA) is a suitable noninvasive technique for this purpose. Because of their long acquisition times, MRA sequences without intravenous contrast agents with adequate spatial resolution, such as 3-dimensional time-of-flight (TOF) MRA sequences, only permit reliable evaluation of the extracranial carotid bifurcation. Only contrast-enhanced MRA (CE MRA) enables visualization of the entire supply area. The development of dedicated coil systems has created a further vital platform. Modern CE MRA techniques vary with regard to their spatial resolution capabilities and provide correspondingly different results. The various CE MRA techniques encompass time-resolved or dynamic CE MRA, after prior matching of the arteriovenous time interval with linear k-space ordering, and CE MRA fluoroscopic triggering and elliptical centric k-space ordering. The
latter allows measurement times of ≥30 seconds without venous overlap, thus increasing spatial resolution.

The purpose of this study was to evaluate the relative value of high-resolution, CE MRA (with elliptical centric k-space ordering) compared with intra-arterial x-ray angiography for assessing the degree of carotid stenosis. The entire carotid supply region rather than only the carotid bifurcation was included. To our knowledge, no dedicated comparison between CE MRA and selective x-ray angiography differentiating between the various vessel segments from the aortic arch to the intracranial vessels has been conducted to date.

Subjects and Methods

Patients
Thirty patients with suspected arteriosclerotic changes in the extracranial carotid arteries on ultrasound who were candidates for x-ray angiography for further clarification underwent both CE MRA and x-ray angiography. None of the patients revealed clinical signs of vertebrobasilar ischemia. The patient group consisted of 19 men and 11 women aged between 49 and 78 years (mean age, 67±8 years). All the patients had given their written informed consent. In none of the cases did the interval between the MRA and the x-ray angiography investigations exceed 4 days.

Investigative Techniques

MR Angiography
All the MR investigations were performed with a 1.5-T whole-body system (Magnetom Symphony, Siemens) with a combination of a phased-array head coil and a phased-array neck coil. The maximum gradient field strength was 20 mT/m; the minimum gradient rise time was 400 μs.

The CE MRA was conducted as a 3-dimensional fast low-angle shot (FLASH) sequence with elliptical centric k-space ordering and fluoroscopic triggering (manual sequence start): repetition time = 6.0 ms, echo time = 2.16 ms, flip angle = 30°, rectangular field of view = 188×300 mm, matrix size = 160×512, voxel size = 1.2×0.6×0.8 mm³, slab thickness = 64 mm, 80 partitions, slice thickness after zero filling = 0.8 mm (measured slice thickness = 1.3 mm), coronal slab orientation, scan time = 31 seconds.

Fluoroscopic triggering was performed with a 2-dimensional turbo FLASH sequence at a frequency of 1 image per second; 25 mL Gd-DTPA (Magnevist, Schering) was injected intravenously at a rate of 2 mL/s with an automatic injector (Spectris, Medrad). The CE MRA was performed with the use of the subtraction technique. For this purpose, a 3-dimensional FLASH scan was acquired before and after the contrast agent was administered. The native data set was then subtracted from the contrast-enhanced data set. The subtractions were then processed with maximum-intensity projections. Eleven projections were routinely processed over a range of 180°.

All patients were required to hold their breath during the MRA acquisitions.

X-Ray Angiography
All the investigations were conducted on a conventional x-ray angiography system (Polytron, Siemens). First an aortic arch survey was performed with a 4F pigtail catheter through a transfemoral access to the ascending aorta (25 mL contrast agent: Imeron, Byk Gulden, flow 15 mL/s, automatic injector). Selective catheterization of both common carotid arteries (CCAs) was then performed with a 4F selective catheter. Films were taken of the supra-aortic vessels on both sides in at least 3 planes (per injection 6 mL contrast agent, flow 3 mL/s, Medrad automatic injector).

Image Analysis
The investigations were evaluated with anonymous patient data by different assessors, none of whom had been informed of the results provided by the other diagnostic method. The supra-aortic vessels were divided into the following segments: CCA (proximal): from the aortic arch to 3 cm caudal to the extracranial carotid bifurcation; CCA (distal): from 3 cm caudal to the extracranial carotid bifurcation to the bifurcation; ICA in the region of the extracranial bifurcation: from the bifurcation to a point 3 cm cranial to the bifurcation; external carotid artery (ECA): origin of the ECA from the extracranial carotid bifurcation; ICA distal to the extracranial carotid bifurcation: from 3 cm cranial to the bifurcation to the circle of Willis; middle cerebral artery (MCA): from the origin to the central

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Certain</th>
<th>Uncertain</th>
<th>Not Possible</th>
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<tbody>
<tr>
<td>CCA proximal</td>
<td>41</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>CCA distal</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ICA bifurcation</td>
<td>60</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ICA distal</td>
<td>54</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>MCA</td>
<td>47</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>ACA</td>
<td>47</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

TABLE 1. Evaluability of Supra-aortic Vessels in CE MRA, Classified According to Different Vessel Segments (n=60)

TABLE 2. Stenoses of the ICA in the Region of the Extracranial Carotid Bifurcation in 10% Increments on CE MRA vs Conventional X-Ray Angiography
TABLE 3. Comparison Between CE MRA and X-Ray Angiography for Stenosis Grades of the ICA (in the Region of the Extracranial Carotid Bifurcation) (n=60)

<table>
<thead>
<tr>
<th>Stenosis Grade (%) on X-Ray Angiography</th>
<th>1 (0–49%)</th>
<th>2 (50–69%)</th>
<th>3 (70–99%)</th>
<th>4 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (0–49%)</td>
<td>29</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2 (50–69%)</td>
<td>0</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3 (70–99%)</td>
<td>0</td>
<td>0</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>4 (100%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

branches (M1 segment); and anterior cerebral artery (ACA); from the origin to the anterior communicating artery (A1 segment).

MR Angiography
Two independent assessors (F.A.F., R.J.) evaluated the image quality of the different vessel segments on the following scale: 1 = definitely evaluable, 2 = evaluable with limitations, 3 = not evaluable.

Vessel segments were classified as not evaluable if they were not completely in the field of view or if no assessment was possible because of artifacts or venous superimposition. The degree of stenosis for the ICA at the level of the bifurcation was then determined visually in 10% increments according to the NASCET criteria. These results were then classified as 1 of the following degrees of stenosis: first degree, 0% to 49%; second degree, 50% to 69%; third degree, 70% to 99%; and fourth degree, occlusion. All other segments were evaluated with this scale.

X-Ray Angiography
Two independent assessors (R.W., W.L.) evaluated the degree of stenosis in each vessel segment on the selective x-ray angiography films. The aforementioned stenosis assessment in 10% increments was used, followed by the subsequent classification into degree of stenosis.

Statistical Analysis
For recognizing high-grade stenoses and occlusions in the various vessel segments, the sensitivity, specificity, positive predictive value, and negative predictive value were determined for MRA in relation to x-ray angiography. The vessel segments that were not evaluable were not included in this assessment. Furthermore, the Spearman test with the corresponding level of significance was applied to calculate the interobserver correlation between the 2 MRA assessors.

Results
The MRA investigation was performed on 30 consecutive patients. The complete examination was also possible for 2 patients with mild claustrophobia. Twenty-two patients were able to hold their breath, and 8 patients could not hold their breath.

The evaluability of the various vessel segments is shown in Table 1.

All the vessel segments were sufficiently evaluable in the region of the extracranial carotid bifurcation (distal CCA, proximal ICA, proximal ECA). Differentiation of the vessel segment of the CCA proximal to the aorta was uncertain in 15 and impossible in 4 of 60 vessels. In 6 cases the distal ICA could not be differentiated. In 5 cases ACA and MCA were questionable, and in 8 cases they were definitely not evaluable.

Analysis of the stenosis assessment (ICA in the region of the bifurcation) in 10% increments (Table 2) revealed that higher-grade stenosis was assessed in a few cases with MRA than with conventional x-ray angiography. Identical findings with MRA and x-ray angiography were found in 25 of 60 cases, stenosis was assessed as higher in 34 segments with MRA, and higher-grade stenosis was only assessed in 1 case with x-ray angiography.

The discrepancy between MRA and x-ray angiography diminishes when the stenoses are classified into 4 degrees of stenosis (Table 3). Third-degree (70% to 99%) stenosis and occlusion are significant. In this critical range, there was a close correlation between MRA and x-ray angiography. However, in 3 cases MRA diagnosed high-grade stenosis, although analysis of the conventional intra-arterial x-ray angiography showed only low- to medium-grade stenosis. In these cases ultrasonography also showed high-grade stenosis. All 3 patients had surgery, and the pathological examination of the endarterectomy specimens confirmed high-grade stenosis in all 3 cases.

MRA had a sensitivity and a negative predictive value of 100% for all vessel segments (Table 4). With values ranging between 84% and 100%, the specificity was in part considerably lower. Here it must be noted that only 53 segments were evaluable for the proximal CCA, and only 52 segments each were evaluable for the distal ICA, ACA, and MCA. The interobserver correlation (Table 5) was very high for both the ICA at the level of the extracranial carotid bifurcation and the distal CCA, and the level of significance was similarly very high. For the remaining vessel segments the correlation.

TABLE 4. MRA vs X-Ray Angiography in Identifying 70–99% Stenoses and Occlusions for Different Vessel Segments

<table>
<thead>
<tr>
<th>Segment</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA proximal to aortic arch</td>
<td>100</td>
<td>98</td>
<td>67</td>
<td>100</td>
<td>53</td>
</tr>
<tr>
<td>CCA at level of bifurcation</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>ICA bifurcation</td>
<td>100</td>
<td>92</td>
<td>89</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>ECA bifurcation</td>
<td>100</td>
<td>90</td>
<td>44</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>ICA distal to bifurcation</td>
<td>100</td>
<td>90</td>
<td>25</td>
<td>100</td>
<td>52</td>
</tr>
<tr>
<td>MCA*</td>
<td>98</td>
<td>0</td>
<td>100</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>100</td>
<td>84</td>
<td>11</td>
<td>100</td>
<td>52</td>
</tr>
</tbody>
</table>

PPV indicates positive predictive value; NPV, negative predictive value.

*No case with high-grade stenosis or occlusion.
coefficients were lower, with the lowest being 0.63 (for the ACA).

Discussion
CE MRA of the extracranial vessels supplying the brain is a relatively new method. Intra-arterial x-ray angiography remains the gold standard for imaging diagnostics of carotid stenosis. This is an invasive method with a 1% risk of causing a permanent neurological deficit. Hence, it is desirable to replace x-ray angiography by a noninvasive imaging procedure. MRA in 3-dimensional TOF technique has already provided acceptable levels of sensitivity and specificity for stenoses of the extracranial carotid bifurcation. However, this method is restricted to the extracranial carotid bifurcation region for reasons of acquisition time. Nevertheless, to compete with x-ray angiography, MRA must be capable of imaging the entire vascular tree from the aortic arch to the intracranial vessels (Figure 1). This has been possible since the introduction of dedicated coils for the entire course of the vessels and CE MRA. But CE MRA presents a fundamental problem: to achieve acceptable local definition, a minimum amount of acquisition time is required. However, the available acquisition time is limited by the transcranial blood flow with its rapid intracranial and extracranial venous phases. Venous superimposition can severely limit the evaluation of CE MRA investigations. In the meantime, a number of techniques have been developed within CE MRA to solve this problem. The dynamic or time-resolved variant of CE MRA provides poor spatial resolution, and the results it provides are unacceptable for clinical use. Of the remaining techniques—CE MRA with linear k-space ordering (with prior matching of the arteriovenous time interval) and CE MRA fluoroscopic triggering and elliptical centric k-space ordering (in which the sequence is started under MR fluoroscopy)—elliptical centric CE MRA was used in this study for comparison with selective intra-arterial x-ray angiography. The early results with this method have been most encouraging. In the present study, not only the extracranial carotid bifurcation but also all the remaining vessel segments from the aortic arch to the circle of Willis were evaluated in comparison with x-ray angiography.

The gold standard, x-ray angiography, was performed in an optimized form, ie, after the survey x-ray angiography,

### Table 5. Interobserver Correlation for CE MRA

<table>
<thead>
<tr>
<th>Segment</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA proximal to aortic arch</td>
<td>0.82</td>
<td>0.01</td>
</tr>
<tr>
<td>CCA at bifurcation</td>
<td>0.91</td>
<td>0.01</td>
</tr>
<tr>
<td>ICA at bifurcation</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>ECA at bifurcation</td>
<td>0.88</td>
<td>0.01</td>
</tr>
<tr>
<td>ICA distal to bifurcation</td>
<td>0.79</td>
<td>0.01</td>
</tr>
<tr>
<td>MCA</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>ACA</td>
<td>0.63</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Spearman correlation coefficient.

Figure 1. Image of the entire vascular region from the aortic arch to the intracranial vessels. Patient had a history of endarterectomy on the left side and now exhibits high-grade stenosis of the right ICA (arrows). Occlusion of the ECA is evident on the right side. a, X-ray angiography (aortic arch survey); b, CE MRA.
bilateral selective x-ray angiography of the CCA with selective imaging in at least 3 planes was performed.

In this study not all the vessel segments provided equal image quality. However, in the region of the extracranial carotid bifurcation, reliable differentiation was possible in all cases (Figure 2). Problems arose with imaging the CCA at its origin at the aortic arch. In our opinion, the main reason for this is breathing artifacts (Figure 3); we found these artifacts only in those patients who could not hold their breath. For this reason it seems important to perform the investigation with breath-holding. The reduced image quality of the distal ICA can be explained by the increasing reduction in the caliber of the vessel, the tortuous course of the vessel at the carotid siphon (most probably spin-dephasing effects), and possible venous superimposition in the region of the base of the skull.

In addition to the small vessel caliber, the latter was also the cause of the poorer image quality of the MCA and the ACA in a number of cases. By starting the sequence at the right time, venous superimposition can be reduced considerably or even abolished. The examining staff members have a relatively short learning curve for detecting the contrast agent bolus in the aortic arch. In those cases in which the vessel segments were evaluable, CE MRA achieved a sensitivity of 100% and a specificity of 84% to 100% for relevant stenoses (70% to 99%) and vascular occlusion. There are 2 possible explanations for the low specificity of CE MRA: (1) stenosis

Figure 2. High-grade stenosis of the origin of the right ICA (arrows). CE MRA (a) shows the vessel filled with contrast agent and a short, high-grade stenosis with discrete poststenotic dilatation. The supplemental 3-dimensional TOF MRA shows a linear signal increase in the sense of accelerated intrastenotic flow. In the region of the poststenotic dilatation, a reduced signal indicates turbulent flow (b). Selective x-ray angiography (c) shows the stenosis and hemodynamics analogously to the CE MRA and 3-dimensional TOF MRA. Note evidence of high-grade stenosis in the angioscopic (d) and the electron microscopic investigation (courtesy of Professor Müller, Department of Pathology, Bochum) (e) of the endarterectomy specimen.
overestimation by MRA and (2) stenosis underestimation by x-ray angiography.

The possibility of stenosis overestimation by MRA is explained by the poor spatial resolution compared with x-ray angiography (Figure 4). This is a problem with MRA that has been recognized since the early days of TOF MRA (2-dimensional TOF MRA and 3-dimensional TOF MRA with poor spatial resolution).

Alternatively, Pan and coworkers 19 showed that concentric stenoses are very rare. Most stenoses are asymmetrical and eccentric. Elgersma and coworkers 20 have examined carotid stenoses with MRA, conventional x-ray angiography, and rotational x-ray angiography. They showed that both MRA and rotational x-ray angiography identified more high-grade stenoses than x-ray angiography with its limited number of projections. This gives rise to the possibility of conventional x-ray angiography tending to underestimate high-grade stenoses rather than MRA overestimating stenoses 15 (Figure 5). This puts the low figures for CE MRA specificity into better perspective (Table 4). The low specificity value of 92% for CE MRA with regard to the ICA in the region of the carotid bifurcation applies when x-ray angiography is used as the gold standard. However, preoperative ultrasound and pathological examinations of the endarterectomy specimens in 3 cases showed that CE MRA provided the correct results. Thus, its specificity must be higher because x-ray angiography actually underestimated high-grade stenoses in these cases.

The extent to which CE MRA is capable of reliable differentiation between diffuse subtotal occlusion and complete occlusion remains to be clarified by studies with sufficiently high case numbers in comparison with selective x-ray angiography. In the present study 1 case of pseudo-occlusion of the ICA was correctly identified. In a series of 21 patients, Remonda and coworkers 11 described 3 patients with pseudo-occlusion that was correctly identified with CE MRA. Thus, CE MRA may have the potential to be accurate in detection of this disease. Nevertheless, a number of centers are already performing noninvasive diagnostics alone for carotid stenosis. A number of reports consider CE MRA to be equal to x-ray angiography. 21–23 CE MRA is certainly already suitable as a noninvasive supplement to color-Doppler ultrasonography, 24,25 which does not always provide clear results, even when used by an expert.26

Figure 3. Two patients with high-grade stenosis of the origin of the left ICA. CE MRA without (a) and with (b) breath-holding is shown. Note reduced differentiation of the aortic arch and basal segments of the major supra-aortic vessels without breath-holding.

Figure 4. Comparison of voxel and pixel sizes in CE MRA (a) and x-ray angiography (b).
Because of the good results provided by CE MRA in assessing stenoses in the region of the extracranial carotid bifurcation, this technique is probably already capable of replacing conventional x-ray angiography in most cases. This applies to the high-resolution, CE MRA techniques, ie, CE MRA with elliptical centric k-space ordering and high-resolution, CE MRA with prior matching of the arteriovenous time interval. The so-called time-resolved CE MRA with short acquisition times and reduced spatial resolution provides poorer results in this respect and is thus unacceptable, since better techniques with higher resolution are available.

In our opinion, the following procedure can be recommended today: The basic investigation in all cases should be ultrasound. In cases with positive or unclear findings, additional CE MRA should be performed when adequate investigation techniques are available.

In conclusion, the MRA technique presented here is capable of providing reliable results in the diagnosis of stenoses of the carotid arteries, and it has largely replaced x-ray angiography in everyday clinical routine at a number of centers. X-ray angiography investigations are only necessary in a few selected cases, eg, when MRI is contraindicated. However, when CT angiography is available, the indication for x-ray angiography becomes smaller still.

Acknowledgments
We thank Hans and Gerti Fischer-Stiftung, Essen, Germany, and Klaus Balzer, MD, Muelheim, Germany, for cooperation and partially supporting this work.

References


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Stroke. 2002;33:1522-1529
doi: 10.1161/01.STR.0000016972.70366.D6

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