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Winfried A. Willinek, MD
Jürgen Gieseke, PhD
Rudolf Conrad, MD
Holger Strunk, MD
Romhild Hoogeveen, PhD
Marcus von Falkenhausen, MD
Ewald Keller, MD
Horst Urbach, MD
Christiane K. Kuhl, MD
Hans H. Schild, MD

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Abbreviations:
CENTRA = contrast-enhanced timing-robust angiography
CNR = contrast-to-noise ratio
ICA = internal carotid artery
IJV = internal jugular vein
MIP = maximum intensity projection
ROI = region of interest
SNR = signal-to-noise ratio
3D = three-dimensional

[1] From the Department of Radiology, University of Bonn, Sigmund-Freud-Strasse 25, D-53105 Bonn, Germany (W.A.W., R.C., H.S., M.v.F., E.K., H.U., C.K.K., H.H.S.); and Philips Medical Systems, Best, the Netherlands (J.G., R.H.). Received July 9, 2001; revision requested August 20; final revision received January 11, 2002; accepted February 25. **Address correspondence to** W.A.W. (e-mail: *willinek@uni-bonn.de*).

Author contributions:
Guarantors of integrity of entire study, W.A.W., H.H.S.; study concepts and design, W.A.W., J.G.; literature research, W.A.W., M.v.F.; clinical studies, W.A.W., M.v.F., R.C., H.S., E.K., H.U.; data acquisition and analysis/interpretation, W.A.W., R.C., H.S., E.K., H.U.; statistical analysis, W.A.W.; manuscript preparation, W.A.W.; manuscript definition of intellectual content, W.A.W., J.G., R.H., C.K.K.; manuscript editing, W.A.W., M.v.F., R.C., H.S., E.K., H.U.; manuscript revision/review, W.A.W., J.G., R.H., C.K.K., H.H.S.; manuscript final version approval, all authors.

Randomly Segmented Central k-Space Ordering in High-Spatial-Resolution Contrast-enhanced MR Angiography of the Supraaortic Arteries: Initial Experience[1]

Contrast material–enhanced three-dimensional (3D) magnetic resonance (MR) angiography of the supraaortic arteries with randomly segmented central k-space ordering (ie, contrast-enhanced timing-robust angiography [CENTRA]) was performed in 16 patients. CENTRA enabled reliable depiction of the aortic arch up to the circle of Willis at high spatial resolution (true voxel size, 0.81 × 0.81 × 1.0 mm^3). With CENTRA, the divergent demands of high spatial resolution, wide anatomic coverage, and arterial phase imaging have been reconciled. The random order of central k-space acquisition may minimize artifacts in contrast-enhanced 3D MR angiography caused by unstable contrast material opacification at the initiation of sampling.

Since contrast material–enhanced magnetic resonance (MR) angiography was introduced (1,2) it has gained increasing importance as a first-line diagnostic tool in the preoperative work-up of patients with carotid artery stenosis. Contrast-enhanced MR angiography of the carotid arteries appears to be an adequate replacement for conventional angiography in the evaluation of patients for endarterectomy (3). In contrast-enhanced MR angiography, the timing of contrast material injection and image acquisition is of utmost importance in obtaining optimal arterial contrast while avoiding venous vessel overlay. Because the window of time during the diagnostically suitable arterial phase is small, image acquisition time is restricted, thus limiting the achievable spatial resolution.

A contrast-enhanced MR angiography technique with elliptic centric k-space ordering has been described that samples the central phase-encoding views entirely during the arterial phase when the start of the pulse sequence is triggered by the arrival of contrast material in the area of interest (3–5). It is critical to initiate elliptic centric k-space sampling so that the first views correspond to the peak of arterial contrast opacification to avoid the presence of marked edge-enhancement artifacts with little contrast in the centers of the arteries (3). The technique of fluoroscopically triggered contrast-enhanced MR angiography with elliptic centric k-space ordering has been widely used for imaging the supraaortic vessels.

Even with these highly advanced acquisition techniques, contrast-enhanced MR angiography harbors several limitations, including persistent venous overlay, timing errors, and insufficient spatial resolution; all of these problems result in limited imaging coverage (6). This limited anatomic coverage explains why most published studies have focused on either the intracranial or the proximal supraaortic and neck vessels, although most clinical decisions require assessment of both territories (6).

Our objective was to evaluate a technique for contrast-enhanced MR angio-

graphic data acquisition with random segmentation of the central k-space (ie, contrast-enhanced timing-robust angiography [CENTRA]).

Materials and Methods

A prospective study was performed with 16 consecutive patients (14 men, two women; age range, 44–81 years; mean age, 62 years) suspected of having cerebrovascular disease. The study was approved by our institutional review board, and informed consent was obtained from all patients.

MR imaging was performed with a 1.5-T MR unit (Intera; Philips Medical Systems, Best, the Netherlands) with a maximal achievable gradient amplitude of 30 mT/m, a rise time of 0.2 msec, and a slew rate of 150 T/m/sec. A commercially available phased-array coil (Synergy head and neck coil; Philips Medical Systems) that covered the regions of the upper chest, neck, and head was used.

Contrast-enhanced three-dimensional (3D) MR angiography was performed with power injection (Spectris MR Injection System; Medrad Europe, Maastricht, the Netherlands) of 0.4 mL per kilogram of body weight of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) at a flow rate of 3.0 mL/sec followed by a flush of 30 mL of saline solution. Two-dimensional real-time fluoroscopy in the coronal plane was used to trigger contrast-enhanced 3D MR angiography (5,7), which was performed with a repetition time msec/echo time msec of 3.4/1.0, a flip angle of 40°, a field of view of 450 mm, a section thickness of 10 mm, and an image acquisition rate of 1 second. When fluoroscopy revealed that the bolus of contrast material had reached the left atrium, the actual angiographic pulse sequence was started manually with a delay of 4 seconds. Patients were asked to hold their breath during the initial 15 seconds of data acquisition.

The acquisition parameters for the angiographic pulse (ie, CENTRA) sequence were as follows: a 3D gradient-echo sequence with 4.8/1.48, a flip angle of 40°, a rectangular field of view of 50%, a slab thickness of 60 mm, and an image matrix of 432 × 432 on a 350-mm field of view with 60 thin partitions of 1.0 mm (with a 0.5-mm overlap), yielding an almost isotropic voxel size of 0.81 × 0.81 × 1.0 mm (0.66 mm^3) before zero filling. Total acquisition time for the CENTRA data was 58 seconds.

A technique of randomly segmented k-space ordering is used in CENTRA (8). The technique samples central phase-encoding views during the early arterial phase; this has been shown to provide effective venous suppression (4). In elliptic centric view ordering, the samples in the phase-encoding directions k_y and k_z are reordered so that the center of k-space (ie; 0,0) is acquired first, followed by points in k-space that have an increasingly greater distance from the center (5).

In contrast to elliptic centric view ordering, the starting point in CENTRA is not in the middle of k-space. Instead, a central disk is first delineated, and the samples are acquired in a random order from this central disk (Fig 1). The size of the central disk is determined by the duration of the arterial window. In our study, a 4-second duration was chosen as the minimum for the carotid arterial window. The view order then proceeded outward from the central disk on the basis of the actual k-space radius.

The theoretical background for using a technique of random k-space segmentation is the randomization of data from the middle of k-space. Because image contrast is determined primarily in the center of k-space, it is crucial in standard centric acquisition techniques, in which the middle point of k-space is sampled first, that the first views correspond to the peak of the contrast-over-time curve (3). In CENTRA the central sphere is randomly sampled during the full arterial window, and the first view does not have to correspond to the bolus peak. This allows k-space sampling during both the beginning and the end of the contrast-over-time curve.

Like other techniques of elliptic centric view ordering, CENTRA enables the acquisition of MR angiographic data to extend well beyond the actual passage of the bolus of contrast material through the arteries, so high spatial resolution over a large field of view is achieved. Theory implies and experimentation has shown that acquisition times longer than 40 seconds can provide higher spatial resolution compared with shorter acquisition times, although contrast agent concentration levels decrease with increasing time (5,9).

For data evaluation, maximum intensity projections (MIPs) of the 16 MR angiograms were reviewed by three experienced readers (H.S., W.A.W., R.C.) as hard-copy images in two steps: First, each angiogram was independently assigned a rating by each of the three radiologists, resulting in a total of 48 ratings. The readers were then asked to rate the images for presence or absence of venous overlay, the degree of image-quality degradation by artifacts (eg, blurring, motion artifacts, signal fall-off, typical edge-enhancement artifacts), and overall diagnostic quality.

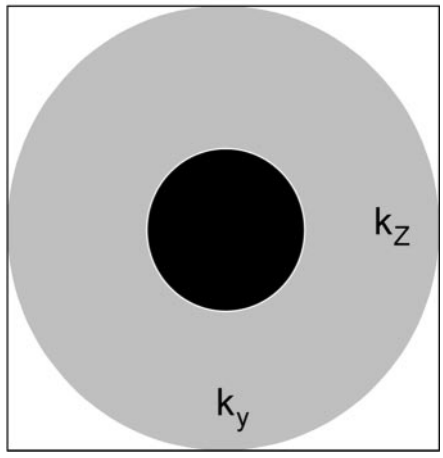


Figure 1. Schematic of k-space sampling in CENTRA. The central region of k-space (represented by the black circle) is randomly segmented. Images in this two-dimensional central disk are acquired during the 4-second-long arterial window. The imaging order then proceeds outward from this central disk into the region illustrated by the larger gray circle. k_y = the y direction of k-space, k_z = the z direction of k-space.

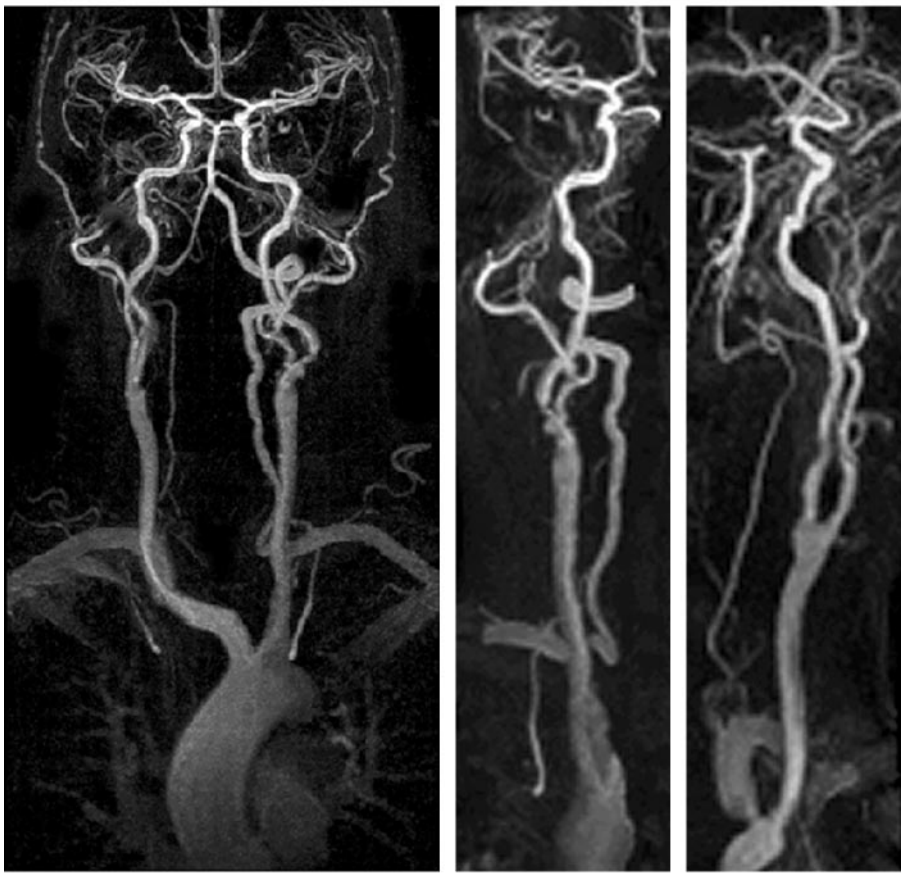
The rating scale for venous overlay was as follows: 1, internal jugular vein (IJV) not visible; 2, IJV barely visible; 3, noticeable signal intensity in IJV; 4, comparable signal intensity in IJV and internal carotid artery (ICA); and 5, greater signal intensity in IJV than in ICA.

Degradation of image quality by artifacts was rated as 1, absent; 2, minimal; 3, moderate; 4, interfering with image interpretation; or 5, causing examination to be nondiagnostic.

The rating scale for overall diagnostic quality of the image was as follows: 1, excellent; 2, more than adequate for diagnosis; 3, adequate for diagnosis; 4, resulting in a questionable diagnosis; and 5, useless for diagnosis.

In a second step, angiograms were reviewed again and arterial delineation of each vascular territory was rated in consensus as excellent, fair, or not useful for diagnosis. Consensus was defined as agreement between at least two of the three readers. There was no case in which none of the readers agreed.

The following 15 vascular territories were assessed, for a total of 240 territories in 16 patients: the common carotid arteries, the external and internal carotid ar-



a. b. c.

Figure 2. MIPs from gadolinium-enhanced high-spatial-resolution 3D gradient-echo MR angiography with CENTRA show clear delineation of the brain-supplying arteries, without venous overlay, in the following three views: **(a)** coronal, **(b)** sagittal from left, and **(c)** sagittal from right.

teries, the vertebral arteries, the basilar artery, the middle cerebral arteries, and the anterior and posterior cerebral arteries.

In a subset of six patients, conventional angiograms obtained with a digital subtraction technique were available for comparison. Conventional angiography and MR angiography were performed within 10 days of each other in all six patients. Both MR angiograms and conventional angiograms were reviewed at different times in a randomized order by two radiologists in consensus; diameters of luminal stenoses were determined on both MR and conventional angiograms according to the North American Symptomatic Carotid Endarterectomy Trial technique (10). The degree of stenosis was classified according to the following scale: 0, stenosis not detected; I, mild (≤29%); II, moderate (30%–69%); III, severe (70%–99%); and IV, occlusion (100%). Results were compared and correlation coefficients and partial correlation coefficients were computed with the Spearman correlation.

For quantitative evaluation, the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were calculated from source images in each patient by using the largest region of interest (ROI) at the carotid bifurcation (ROI size range, 11.22–26.17 mm^2) and middle cerebral artery (ROI size range, 2.80–5.61 mm^2). The SNR was determined as the mean value of signal intensity in the enhanced arterial lumen divided by the SD of the value of signal intensity in the background. The signal intensity of the background was measured outside the body of the patient in a phase-encoding direction at the level of the carotid bifurcation and the middle cerebral artery (ROI size range, 37.85–98.13 mm^2). The CNR was defined as the mean value of the difference between the signal intensity in the arterial lumen and the signal intensity in the surrounding soft tissue, divided by the SD of the signal intensity in the background. The vein-to-artery signal intensity enhancement ratio was calculated by dividing the venous contrast measurement by the arterial contrast measurement.

The Kendall *W* coefficient of concordance was computed to compare the three raters in their assessment of image quality, venous enhancement, and artifacts. Kendall *W* coefficients between 0.5 and 0.8 were considered to indicate good agreement, and coefficients higher than 0.8 were considered to indicate excellent agreement. All statistical analyses were performed with SPSS version 10.0 (SPSS, Chicago, Ill).

Results

The high-spatial-resolution gadolinium-enhanced imaging technique with CENTRA for MR angiography of the supraaortic arteries was successful in 16 of 16 cases, and a diagnostic image was obtained in all patients (Fig 2).

For the total of 240 vascular territories that were evaluated, arterial delineation was excellent in 234 (98%). Delineation of the main cerebral arteries (middle cerebral artery and anterior and posterior cerebral arteries) was excellent in 92 (96%) of 96 such arteries. Because of pulsation artifacts, the delineation of the anterior cerebral artery was impaired in two cases. Delineation of the vertebral arteries was not helpful for diagnosis in one patient because the distal parts of the vertebral arteries were not included in the imaging volume.

Overall diagnostic quality was excellent or more than adequate for diagnosis in 16 (100%) of 16 MR angiograms. Contrast-enhanced 3D MR angiograms obtained with CENTRA were rated as having no or only minimal artifacts in 43 (90%) of 48 readings. The IJV was not seen or was only barely visible in 42 (88%) of 48 readings (Fig 3). Mean SNR ± SD and mean CNR ± SD, respectively, were 28.59 ± 4.92 and 24.98 ± 4.78 in the carotid bifurcation and 39.11 ± 7.47 and 36.31 ± 7.94 in the middle cerebral artery. In all 16 MR angiograms, the SNR and CNR were higher in the middle cerebral artery than in the carotid bifurcation. The mean vein-to-artery signal intensity enhancement ratio ± SD was calculated to be 0.16 ± 0.06. In all cases venous signal intensity was lower than arterial signal intensity.

Interobserver agreement in grading artifacts, venous overlay, and overall image quality was excellent, with coefficients of

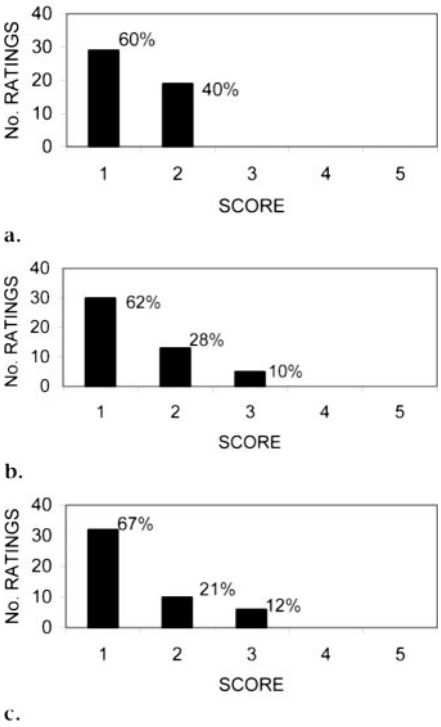


Figure 3. Bar graphs depict **(a)** results for rating overall diagnostic quality of contrast-enhanced 3D MR angiograms, **(b)** results for rating artifacts on contrast-enhanced 3D MR angiograms, and **(c)** results for rating venous overlay on contrast-enhanced 3D MR angiograms. (For descriptions of the scales used to rate these factors, please see the Materials and Methods section.)

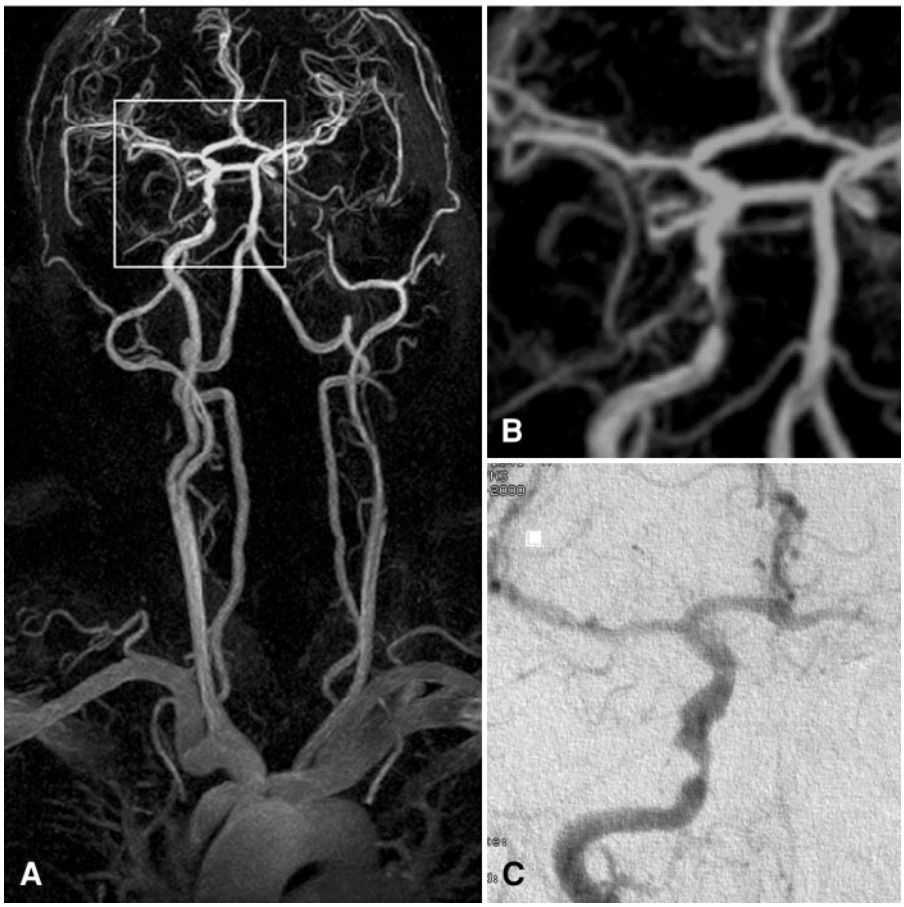


Figure 4. MIPs from gadolinium-enhanced 3D gradient-echo MR angiography with CENTRA in a single patient. *(A)* Coronal view shows occlusion of the left ICA and severe stenosis (grade III) of the right ICA (box). *(B)* Enlarged (×3) MIP of the petrous segment of the right ICA shows a severe stenosis that was confirmed at *(C)* conventional x-ray angiography.

concordance of 0.91, 0.82, and 0.95, respectively.

A strong correlation between the degree of luminal stenosis depicted on MR angiograms and that depicted on conventional angiograms was observed when the two types of images were compared in the subset of six patients in whom both were available (correlation coefficient, 0.941 with $P < .001$; partial correlation coefficient, 0.921 with $P < .001$). Eighteen of 19 cases of disease (ie, stenosis or occlusion) in these six patients were accurately diagnosed with MR angiography. One moderate stenosis in the petrous segment of the left ICA that was depicted at conventional angiography was missed during the review of MR angiograms but could be diagnosed retrospectively. All instances of severe stenosis or occlusion (grade III or IV) that were diagnosed at conventional angiography were correctly identified at contrast-enhanced 3D MR angiography with CENTRA (Fig 4). In addition, overestimation of stenosis at MR angiography did not occur (Fig 5).

Discussion

Contrast-enhanced MR angiography has been shown to be superior to time-of-flight and phase-contrast angiography in depicting carotid artery stenosis (11). In addition, like conventional angiography, contrast-enhanced 3D MR angiography is very sensitive to slow flow (3,12).

Since contrast-enhanced 3D MR angiography has been used for imaging of the supraaortic vessels, it has been shown that for optimal arterial contrast, short acquisition times and accurate sampling of the contrast-determining central k-space lines are crucial for avoiding venous overlay. Especially in carotid artery imaging, venous suppression is crucial if reliable identification of arterial disease is to be achieved (5). Elliptic centric k-space ordering has been described as producing such arterial phase images with high arterial-to-venous contrast ratios, if the arrival of contrast material during the arterial phase is triggered properly (4). Fluoroscopic triggering is widely used to reliably establish the arrival of the contrast material bolus despite varying circulation times. The centric k-space ordering approach and fluoroscopic triggering have remarkably improved the quality of contrast-enhanced 3D MR angiography of the carotid arteries, resulting in high temporal resolution and sufficient venous suppression (4,5). However, timing of the contrast material bolus peak is crucial and spatial resolution and coverage are still limited.

To randomize sampling points in the middle of k-space, where contrast material concentration is not maximal at the time of acquisition, random segmentation of the central disk is used in CENTRA. In this k-space ordering method, the central contrast-determining, phase-encoding views are randomly sampled during the arterial phase. In fact, in the implementation of random segmentation, the middle point in k-space is never acquired first; in this way ringing artifacts

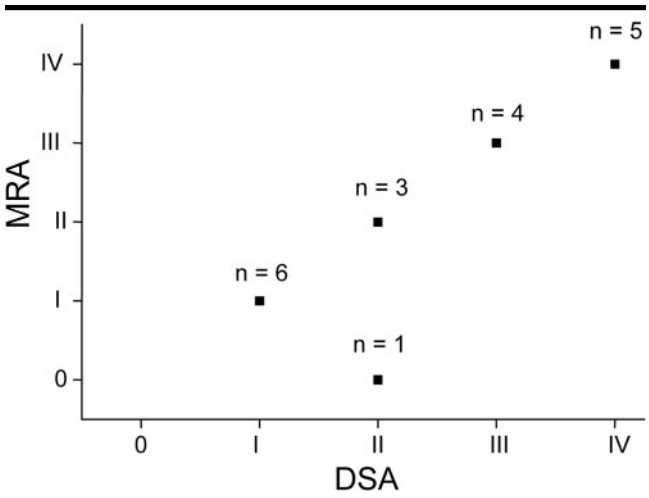


Figure 5. Graph shows correlation between rating of stenosis at gadolinium-enhanced MR angiography *(MRA)* with CENTRA and rating of stenosis at digital subtraction angiography *(DSA)* in six patients with 19 cases of stenosis or occlusion. The correlation coefficient was 0.94 ($P < .001$). The partial correlation coefficient (adjusted for each patient) was 0.92 ($P < .001$). (For description of the scale used to rate stenosis, please see the Materials and Methods section.)

are avoided, even if arterial opacification has not been fully realized (8). The segmentation of the central sphere in k-space enables the start of data acquisition during the up-slope of the contrast-over-time curve. A delay of 4 seconds was set between the mouse click that started the angiographic sequence and the first acquisition of data. We therefore manually initiated the actual pulse sequence when the contrast material bolus reached the left atrium.

After data is acquired in the contrast-determining central disk of k-space, the CENTRA technique allows one to extend the acquisition of MR angiographic data well beyond the actual arterial passage of the bolus, while preserving arterial phase image contrast. Because of the longer time that is made available for data acquisition, there is sufficient time for sampling data for high imaging matrices over a wide field of view. As described by Wilman and colleagues in 1998 (5), acquisition of k-space data for longer than the short arterial window can improve spatial resolution. The reason is that the concentration of contrast material in the arteries will not decrease to zero after the arterial window is closed. Because of recirculation, a relatively high degree of signal intensity will remain in the arteries, even after 40 seconds (5,9). To ensure that the acquisition of k-space data was completed with sufficient signal intensity, a double dose of contrast material was injected. In addition to the technique of randomly segmented central k-space ordering, this might in part have contributed to the high degree of contrast resolution seen in our study.

The aim of our study was to assess whether CENTRA would enable accurate arterial phase angiographic assessment over a large field of view. Thus, one MR angiographic measurement was performed that covered the supraaortic vessels from the aortic arch to the circle of Willis at the very high image matrix of 432×432.

CENTRA resulted in excellent delineation of the brain and depicted arteries from their origins in the aortic arch up to the circle of Willis in 98% of the study patients. In addition, clear delineation of the main cerebral arteries, including the anterior, posterior, and middle cerebral arteries, was observed in 92 (96%) of 96 readings. CENTRA resulted in reliable acquisition of arterial phase MR angiograms, which were of optimal diagnostic quality in all 16 patients. With the random k-space ordering technique, diagnostic image quality was not impaired by artifacts; even the typical edge-enhancement artifact that can occur if contrast-enhanced 3D MR angiography is begun slightly too early was absent in all cases. This may suggest that the random method of central k-space acquisition also randomizes and minimizes any artifact due to unstable concentrations of contrast material.

In studies of contrast-enhanced 3D MR angiography, voxel sizes for carotid artery imaging ranged between 0.90 and 1.80 mm^3 before zero filling (3,5–7,12). The effect of decreased voxel size on image quality has been demonstrated: Decreased voxel size improves the delineation of cervical carotid and vertebral arteries on contrast-enhanced 3D MR angiograms (6). The voxel size used in this study with CENTRA was 0.66 mm^3 ($0.81 \times 0.81 \times 1.0$ mm^3), without zero filling. With 120 sections overlapping by 0.5 mm, the effective voxel size is 0.33 mm^3. To our knowledge, MR angiography of all the brain-supplying arteries, including the circle of Willis, within one single measurement and at this spatial resolution has not been reported.

The high quality of the MR angiograms obtained with CENTRA was additionally confirmed by the high degree of observer agreement in evaluating overall image quality, artifacts, and presence or absence of venous overlay. Despite the short arterial time window in the carotid arteries and different circulation times, the CENTRA technique resulted in a high degree of venous suppression, with barely visible or absent IJV signal observed in 88% of ratings. The results of evaluation of MIPs also demonstrated that this particular k-space sampling technique enables relatively long acquisition times of 58 seconds for high imaging matrix sampling, yet results in image contrast that corresponds to that observed on early arterial phase MR angiograms.

It was not our aim in this study to determine the precise diagnostic accuracy of the CENTRA technique. In the subset of six patients in whom conventional angiograms were obtained for comparison, 18 (95%) of a total of 19 pathologic findings were correctly identified with MR angiography. This correlation is consistent with the results obtained in another study of contrast-enhanced MR angiography of the carotid bifurcation in a larger group of patients prior to endarterectomy (3).

Despite the limited number of study subjects, our initial results clearly indicate that CENTRA works in a clinical setting. CENTRA provides optimal arterial contrast and very high spatial and temporal resolution in contrast-enhanced 3D MR angiography of the brain-supplying arteries, including the circle of Willis. Random k-space segmentation enabled reliable high-spatial-resolution arterial phase MR angiography without artifacts caused by unstable arterial opacification, suggesting that it is a robust technique for contrast-enhanced 3D MR angiography and yields high-quality diagnostic

images in patients suspected of having cerebrovascular disease.

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