Contrast-Enhanced Carotid Magnetic Resonance Angiography: Comparison of Single-Dose and Double-Dose of Gadolinium Using the Randomly Segmented Central k-Space Ordering Technique

Yu-Chun Lin, RT; Shu-Hang Ng, MD; Jian-Chuan Chen, MS;
Alex Mun-Ching Wong, MD; Yau-Yau Wai, MD

Background: The aim of this study was to evaluate whether the single dose of gadolinium is sufficient for contrast-enhanced magnetic resonance angiography (MRA) of carotid arteries with the use of newly developed randomly segmented central k-space ordering technique called contrast-enhanced timing-robust angiography (CENTRA).

Methods: A total of 44 patients underwent carotid MRA in a 1.5T MR scanner using a fluoroscopically monitored, manually triggered, CENTRA pulse sequence. Patients were randomly assigned into two groups according to the dose of contrast medium (gadolinium chelate) administered: group 1 referred to those who received double doses (0.2 mmol/kg) and group 2 received single doses (0.1 mmol/kg). The contrast-to-noise (CNR) ratios of the seven regions of interest were calculated. The delineation of nine vascular regions and the degree of venous overlay were evaluated by two blinded readers on a five-point scale.

Results: For quantitative evaluation, the CNRs at the brachiocephalic artery were greater in patients in group 1 than that in group 2 ($p = 0.015$), while the differences did not differ between the two groups for the remaining regions of interest ($p > 0.05$). For qualitative evaluation, there were no significant differences between the two groups in delineation of nine vascular regions and venous overlaying ($p > 0.05$).

Conclusion: With the use of the CENTRA technique, carotid MRA may be performed using a single dose of gadolinium and the image quality is comparable to that of the standard double dose protocol.

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Key words: magnetic resonance image (MRI), MR angiography (MRA), carotid artery.

Magnetic resonance angiography (MRA) has emerged as a useful technique for assessing carotid circulation. It is noninvasive and has the advantage of providing images similar to conven-

From the Department of Diagnostic Radiology, Chang Gung Memorial Hospital Taipei; Department of Medical Imaging and Radiological Sciences, Chang Gung University, Taoyuan.
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Address for reprints: Dr. Yau-Yau Wai, Department of Diagnostic Radiology, Chang Gung Memorial Hospital, No. 5, Fushing St., Gueishan Shiang, Taoyuan, Taiwan 333, R.O.C. Tel.: 886-3-3281200 ext. 2575; Fax: 886-3-3971936; E-mail: yauwaiwu@ms4.hinet.net

tional angiography.[1] In contrast to time-of-flight MRA,[2-5] which does not require the administration of contrast medium, contrast-enhanced MRA takes less time perform and its high accuracy in revealing carotid artery stenosis has been well recognized.[1,6-9] In contrast-enhanced MRA, the time of contrast material injection and the timing of image acquisition are crucial to obtain optimal arterial contrast and to avoid overlaying by the internal jugular veins. In order to obtain a high quality MRA, double doses of contrast medium are recommended to keep the intravascular concentration of contrast medium high and constant during the data acquisition.[10,11] However, proper timing of contrast enhancement is still crucial and has limited the success of contrast-enhanced MRA.

A new MR technique of randomly segmented central k-space ordering has been developed. It is also called contrast-enhanced time-robust angiography (CENTRA).[12] This technique samples the central phase-encoding view during the early arterial phase when the pulse sequence is triggered by the arrival of contrast material in the selected area, so it makes contrast-enhanced MRA more robust in timing. This is a modified centric k-space ordering technique which is different from the elliptic centric view ordering.[13] It has been shown that the CENTRA technique with the administration of double doses of contrast medium provides high spatial resolution, wide anatomic coverage and effective venous overlying avoidance in carotid vessels.[12] Theoretically, the more accurate timing of acquisition with such a dedicated k-space filling design may allow the use of a lower dosage of the contrast medium. Gadolinium is an expensive contrast medium for MRI, if the dosage can be reduced, it would help cut the costs of the MRI examination. The aim of this study was to determine the feasibility of the CENTRA technique using a single dose of gadolinium in assessing the extracranial carotid and vertebral artery system.

METHODS

From June through August 2004, 44 consecutive patients (25 men, 19 women; age range, 40-78 years; mean age, 61.3 ± 9.1 years) with suggested cerebrovascular disease were referred for MR angiographic evaluation of the extracranial carotid and vertebral arteries. The patients' average weight was 71.8 ± 9.3 kg (range, 54-86 kg). All patients were initially evaluated using duplex ultrasonography (US) for the carotid circulation. Table 1 shows the basic characteristics and US findings of the patients.

MR imaging was performed using a 1.5T MR scanner (Intera; Philips Medical System, 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, Netherlands) that can cover the regions of the head, neck, and upper chest was used. Before positioning the patient, a 20-gauge intravenous catheter was positioned in the antecubital vein.

Table 1. Basic Characteristics of the Study Population

	Group 1 (N = 22) 0.2 mmol/kg	Group 2 (N = 22) 0.1 mmol/kg	*p* value*
Age (year)	62.8 ± 9.4	59.8 ± 8.7	0.29
Body weight (kg)	72.3 ± 8.9	71.3 ± 9.4	0.74
Heart rate (beat/min)	74.6 ± 6.4	71.9 ± 7.3	0.20
Average total dose of gadolinium (ml)	28.9 ± 3.6	14.3 ± 1.9	
Duplex ultrasonography findings			
Normal	11 (50%)	12 (55%)	
Mild or moderate stenosis†	9 (41%)	7 (31%)	
Severe stenosis or occlusion†	2 (9%)	3 (14%)	

* Two-sample t-test

† Stenosis or occlusions were suspected in one or more than one vessels of supraaortic arteries.

Each patient was randomly assigned into one of the two groups regarding the amount of gadolinium chelate injection (Omniscan; Nycomed, Oslo, Norway): group 1 (n = 22) received double doses of gadolinium of 0.2 mmol/kg and group 2 (n = 22) received single doses of 0.1 mmol/kg. Contrast medium was injected at a rate of 2 ml/sec, followed by flushing with 10 ml of saline solution at the same rate using an MR-compatible power injector (Optistar; Mallinckrodt Inc., Ohio, USA). Contrast-enhanced three-dimensional (3D) MRA was trigged by two-dimensional real-time MR fluoroscopy in the coronal plane.[14] When the MR fluoroscopy revealed the arrival of the bolus of contrast material in the left atrium, the angiographic pulse sequence was started with a delay of 4 seconds. The protocol of the MR fluoroscopy was as the following: a TR/TE/Flip angle = 3.4 ms/1.0 ms/40°, a field of view of 450

mm, a section thickness of 10 mm, and an image acquisition rate of 1 second.

The angiographic MR sequence was performed using a technique of randomly segmented central k-space ordering known as CENTRA. The parameters of CENTRA were as follows: a 3D gradient-echo sequence with 4.6/1.67, a flip angle of 40°, a rectangular field of view of 50%, an image matrix of 416 $\times$ 416 on a 300-mm field of view with 120 partition of 0.7 mm. Total acquisition time was 58 seconds. A single subtracted 3D imaging was calculated by subtracting the unenhanced set from the enhanced set. Maximum intensity projection reconstructions of the subtracted images were generated from single partitions (nine projections at 20° increments within a 180° rotation). All the studies were performed by the single MR imaging technician.

For the quantitative evaluation, the mean signal intensity of the vessel lumen (SIV) in the seven regions of interest, including the brachiocephalic artery, bilateral carotid bifurcations (right and left), bilateral intracranial internal carotid arteries, and bilateral vertebral arteries, and of their surrounding tissue (SIB), were measured (Fig. 1). Image noise (σ) was measured as the standard deviation from the signal intensity of the air surrounding the patient. The contrast-to-noise ratio (CNR) of each region of interest was calculated using the following formula: CNR = (SIV - SIB)/ σ.

For the qualitative assessment, the images were reviewed in a blinded fashion by two investigators who separately reviewed MR images in a randomized order for scoring the delineation of nine vascular regions (brachiocephalic artery, common carotid arteries, internal carotid arteries, external carotid arteries, vertebral arteries, basilar artery, middle cerebral arteries, anterior cerebral arteries and posterior cerebral arteries) and the degree of venous overlay. The rating scale for delineation of the nine vascular regions was as follows: (1) excellent delineation of the arterial lumen and sharp edge; (2) good delineation of the arterial lumen with a mild blurring of the edge; (3) fair delineation of the arterial lumen with noticeable blurring of the edge; (4) poor delineation of the arterial lumen with a major edge blurring; and (5) not assessable. The rating scale for venous overlay was as follows: (1) internal jugular vein not visible; (2) internal jugular vein barely visible; (3) noticeable signal intensity in internal jugular vein; (4) comparable signal intensity in internal jugular vein and internal carotid artery; and (5) greater signal intensity in internal jugular vein than in internal carotid artery.

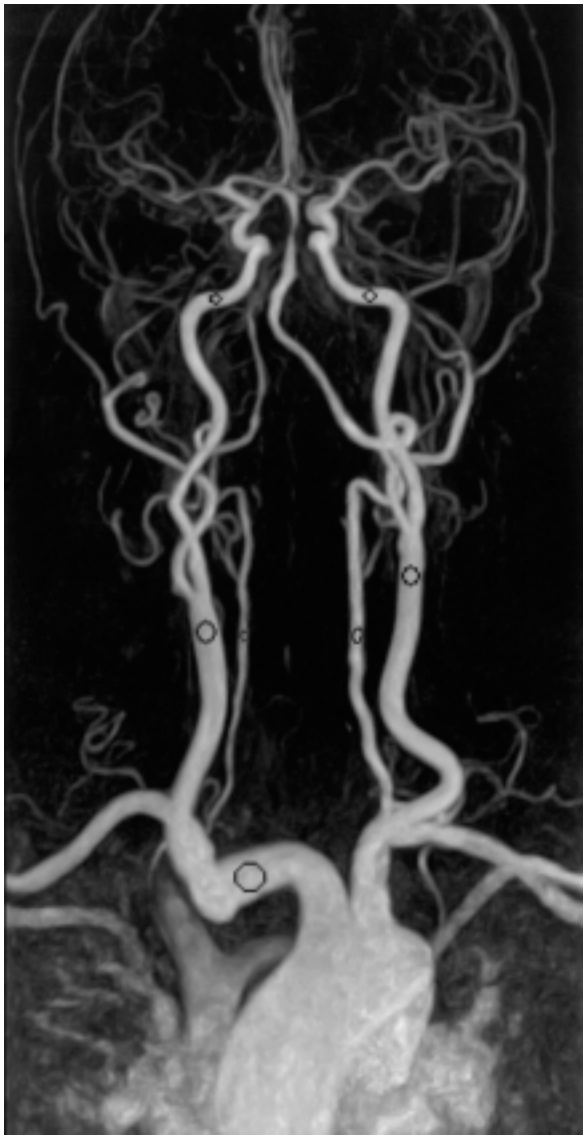

Fig. 1 Maximum intensity projection image of the carotid MR angiography with the CENTRA technique, showing the seven regions of interest (the black blank circle) at the brachiocephalic artery, bilateral carotid artery bifurcations, bilateral intracranial internal carotid arteries, and bilateral vertebral arteries.

Statistical analyses were performed using Excel software (Microsoft, Seattle, Wash, USA) using the

two-tailed Student *t* test. A *p* value less than 0.05 was considered a statistically significant difference. All the values were presented as means ± SDs. The degree of agreement between observers was determined using the κ statistic. Agreement was classified as moderate (κ = 0.40-0.69), good (κ = 0.70-0.89), or excellent (κ = 0.90-1.00).

RESULTS

All of our patients tolerated the procedures well. There were no significant differences in age, body weight and heart rate between the two groups of patients ($p > 0.05$). The procedure lasted approximately 30 minutes for each patient, including all the routine MR imaging and MRA examinations. Quantitative assessment results of the CNRs of the seven regions are shown in Table 2. For the brachiocephalic artery, the CNRs in group 1 were significantly higher than those in group 2 ($p = 0.015$). For bilateral carotid bifurcations, bilateral intracranial internal carotid arteries and bilateral vertebral arteries, there were no statistically significant differences in CNR between these two groups ($p > 0.05$).

The qualitative rating for the delineation of nine vessels and the venous overlapping of the two groups are summarized in Table 3. The brachiocephalic artery, common carotid arteries, internal carotid arteries, external carotid arteries, vertebral arteries were visible on all studies. Parts of the vessels were not visible during the scoring because of severe stenosis or occlusion. The basilar artery was visible in 41 (93%) of 44 patients. The middle cerebral arteries were visible in 80 (91%) of the 88 readings. The anterior cerebral arteries were visible in 76 (86%) of the 88 readings. The posterior cerebral arteries were visible in 82 (93%) of the 88 readings. The internal jugular vein was not seen or was just barely visible in 66 (75%) of the 88 readings. There were no statistically significant differences between these two groups ($p > 0.05$) for such qualitative evaluations. Interobserver agreements for all evaluations were good or excellent, (κ range, 0.84 - 0.95).

Table 2. CNRs of the 7 Regions of Interests with 2 Different Doses of Gadolinium Injected

ROI	CNR		*p*-value
	Group 1 (0.2 mmol/kg)	Group 2 (0.1 mmol/kg)	
Brachiocephalic artery	91.36 ± 6.64	86.82 ± 5.12	0.015
Left CCA	87.68 ± 6.68	89.82 ± 7.88	0.338
Right CCA	87.27 ± 5.51	89.05 ± 7.93	0.394
Left intracranial internal carotid artery	89.36 ± 5.76	87.14 ± 4.81	0.171
Right intracranial internal carotid artery	90.45 ± 8.31	88.50 ± 7.75	0.424
Left vertebral artery	87.68 ± 7.18	84.77 ± 7.45	0.194
Right vertebral artery	87.25 ± 7.89	85.18 ± 8.13	0.392

Abbreviation: CNR: contrast to noise ratio; ROI: region of interest; CCA: common carotid artery.

Table 3. Comparison of Mean Scores of Qualitative Evaluations in 2 Groups

	Score		*p*-value
	Group 1 (0.2 mmol/kg)	Group 2 (0.1 mmol/kg)	
Arteries visualized			
Brachiocephalic (N = 44)	2.2 ± 0.7	2.5 ± 0.8	0.069
Common carotid (N = 88)	1.7 ± 0.7	1.6 ± 0.7	0.534
Internal carotid (N = 88)	1.8 ± 0.6	2.0 ± 0.7	0.318
External carotid (N = 88)	2.0 ± 0.9	2.2 ± 1.0	0.248
Vertebral (N = 88)	2.7 ± 0.9	2.4 ± 0.8	0.123
Basilar (N = 41)	2.5 ± 0.7	2.3 ± 0.8	0.255
Middle cerebral (N = 80)	2.6 ± 0.7	2.8 ± 0.9	0.277
Anterior cerebral (N = 76)	3.2 ± 0.8	3.6 ± 1.1	0.099
Posterior cerebral (N = 82)	3.5 ± 0.9	3.7 ± 1.0	0.242
Venous overlay (N = 44)	2.2 ± 0.9	1.9 ± 0.8	0.090

DISCUSSION

Contrast-enhanced MRA is increasingly been used in imaging of carotid arteries in the past few years.[6-8,15,16] Intravenous injection of contrast material in a bolus manner generates a stronger signal in the patent vessels with better background suppression in a shorter examination time than other injection techniques. However, overlapping of the jugular vein on the carotid bifurcation has been one of the main drawbacks. Recently, the centric k-space ordering technique has remarkably improved the quality of contrast-enhanced MRA of the carotid arteries, resulting in high spatial resolution and sufficient venous suppression.[13,17] In conventional elliptic centric view ordering technique, the samples in the phase-encoding direction are reordered so that the data in the center of k-space is acquired first. It is crucial with this technique that the first views correspond with the bolus peak. Therefore, timing of the

contrast medium bolus peak is critical, however, spatial resolution and coverage are still limited.

In this study, we used the CENTRA technique to solve the main weakness of the conventional elliptic centric view ordering technique. The CENTRA acquires data randomly in the central sector during the full arterial phase, so the first view does not have to correspond with the bolus peak. After data has been acquired in the contrast-determining central disk of the k-space, the acquisition data can extend well beyond the actual arterial passage of the bolus, with preservation of arterial phase image contrast. Since the available acquisition time is longer, there is sufficient time for sampling data for high imaging matrices. In our patients, we used the acquisition time of 58 seconds that yielded matrix sizes of 416 $\times$ 416. This gives higher spatial resolution compared with conventional elliptic ordering technique (176 $\times$ 256 matrix at 20 seconds acquisition time).[17,18]

To our knowledge, few researchers[12,13,19] have addressed the influence of the gadolinium dosage on image quality of carotid MRA with the central k-space ordering techniques. Most of the available clinical studies reported the promising results of carotid MRA with a fixed volume of gadolinium ranging between 20-25 ml.[6,15,20,21] Luccichenti et al.[19] used the elliptically ordered sequence to perform MRA and claimed that optimal image quality would be obtained with gadolinium doses greater than 0.16 mmol/kg of bodyweight in the carotid vessels. The CENTRA technique application was first investigated by Willnek et al.[12] They concluded that the CENTRA was a robust technique for contrast-enhanced 3D MRA and yielded high-quality diagnostic images in patients suggested of having cerebrovascular disease. In their study, double doses (0.2 mmol/kg) of gadolinium injection were used.

Our results showed that the image quality of MR angiography in carotid arteries using the CENTRA technique with a single dose (0.1 mmol/kg) of gadolinium was comparable with that obtained using double doses (0.2 mmol/kg) both quantitatively and qualitatively. The CNR of brachiocephalic artery in the double dose group was higher than that in the single dose group. This may be due to the widened lumen of the brachiocephalic artery, resulting in the reduction in intravascular concentration of gadolinium in the single-dose group during data acquisition. However, this did not affect the delineation of the brachiocephalic artery since there were no significant differences between the two groups in qualitative evaluation of this vessel.

In addition, we used fluoroscopic monitoring of contrast arrival at the carotid arteries to trigger image acquisition so that the arterial phase can be selectively imaged and the venous overlapping can be reduced. The triggering method can provide a comprehensive evaluation of the carotid arteries including all vessel segments from the aortic arch to the circle of Willis.[20,22] However, the success of this technique relies on the experience of the operator. Therefore, in our study, all the scans were performed by a single technician in order to avoid such inter-operator variation. Our results showed no significant differences between the two groups in the evaluation of the venous overlapping. Further studies are required to investigate the reliability of the fluoroscopic triggering technique among different operators.

The accuracy of contrast-enhanced MRA for the evaluation of carotid artery disease has been corroborated by several investigators.[6,19,22] In our study, however, we compared the imaging quality of two groups using different doses of contrast medium but we did not assess their corresponding accuracy in disease evaluation. This was because none of our patients underwent catheter angiography. Further clinical studies are required to assess the diagnostic accuracy of the CENTRA technique with the reduced dosage of contrast medium injection.

In conclusion, the results of this study suggests that with the use of the CENTRA technique, contrast-enhanced MRA of carotid arteries using single dose contrast medium may provide comparable image quality to that using double doses.

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使用中央 k 空間分隔隨機排序技術比較單一劑量和雙倍劑量造影劑在頸部動脈磁振血管造影的表現

林育駿 吳樹鏗 陳建全 黃敏政 衛優遊

背 景： 本研究目的主要在評估使用中央k 空間分隔隨機排序技術在頸部動脈磁振血管造影時，單倍劑量的造影劑是否足夠，進而取代傳統使用的雙倍劑量。

方 法： 我們針對 44 名病患（平均年齡 61.3 ± 9.1 歲），隨機分爲二組，分別使用單一劑量和雙倍劑量來進行頸部動脈磁振血管造影，使用的影像重組方式爲新發展出的中央k空間分隔隨機排序技術。在所有得到的影像我們均取七個特定的部位，測量比較其訊噪比。並且由兩位作者在不知道其影像所使用的劑量之下針對九個區段的動脈呈現的品質以及靜脈回流的程度各別以1 到5 分作評分。

結 果： 針對七個特定的部位中，測得的訊噪比只有在頭臂動脈是雙倍劑量較高，而兩組影像在其餘六個部位的比較上均沒有統計上明顯的差異。而在九段血管的表現以及靜脈回流的程度的比較上，兩組亦沒有統計上的差異 ($p > 0.05$)。

結 論： 使用中央k 空間分隔隨機排序技術應在頸部動脈磁振血管造影時，可將造影劑劑量減少成單倍劑量，而仍然能夠保有和傳統使用雙倍劑量時一樣的影像品質。

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關鍵字： 磁振造影，磁振血管攝影，頸動脈。

長庚紀念醫院　台北院區　放射診斷科系；長庚大學　醫學影像暨放射科學系
受文日期：民國93年10月28日；接受刊載：民國94年5月12日
索取抽印本處：衛優遊醫師，長庚紀念醫院　放射診斷一科。桃園縣333龜山鄉復興街5號。Tel.: (03)3281200轉2575; Fax: (03)3971936; E-mail: yauwaiwu@ms4.hinet.net