Jan Menke
Jörg Larsen

Contrast-enhanced magnetic resonance angiography in carotid artery disease: does automated image registration improve image quality?

Received: 14 August 2008
Accepted: 6 November 2008
Published online: 10 January 2009
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Electronic supplementary material The online version of this article (doi:10.1007/s00330-008-1257-6) contains supplementary material, which is available to authorized users.

J. Menke (✉)
Department of Diagnostic Radiology,
University Hospital,
Robert Koch Strasse 40,
37075 Goettingen, Germany
e-mail: Menke-J@T-Online.de
Tel.: +49-551-5053614
Fax: +49-551-5053614

J. Larsen
Institute for Roentgendiagnosics,
Braunschweig Teaching Hospitals,
Freiestrasse 9–10,
38118 Braunschweig, Germany

Abstract Contrast-enhanced magnetic resonance angiography (MRA) is a noninvasive imaging alternative to digital subtraction angiography (DSA) for patients with carotid artery disease. In DSA, image quality can be improved by shifting the mask image if the patient has moved during angiography. This study investigated whether such image registration may also help to improve the image quality of carotid MRA. Data from 370 carotid MRA examinations of patients likely to have carotid artery disease were prospectively collected. The standard nonregistered MRAs were compared to automatically linear, affine and warp registered MRA by using three image quality parameters: the vessel detection probability (VDP) in maximum intensity projection (MIP) images, contrast-to-noise ratio (CNR) in MIP images, and contrast-to-noise ratio in three-dimensional image vol-

umes. A body shift of less than 1 mm occurred in 96.2% of cases. Analysis of variance revealed no significant influence of image registration and body shift on image quality ($p>0.05$). In conclusion, standard contrast-enhanced carotid MRA usually requires no image registration to improve image quality and is generally robust against any naturally occurring body shift.

Keywords Carotid artery disease · Carotid stenosis · Magnetic resonance angiography · Automated image registration

Abbreviations CNR-3D: contrast-to-noise ratio (CNR) of three-dimensional (3D) images · CNR-MIP: CNR of angiographic maximum intensity projection (MIP) images · VDP: vessel detection probability

Introduction

Atherosclerotic extracranial carotid stenosis has a high prevalence in the elderly and is a treatable risk factor for ischaemic stroke, causing approximately 20% of cases [1–4]. Duplex ultrasonography is the primary imaging investigation in the assessment of carotid stenosis, whereas catheter-based digital subtraction angiography (DSA) represents the gold standard [5]. For solely diagnostic purposes, DSA is increasingly being replaced by noninvasive imaging alternatives, which include computed tomographic angiography (CTA) and contrast-enhanced magnetic resonance angiography (MRA) [5–7].

Angiographic image quality in DSA can be improved by digitally moving the mask image in cases when a patient has moved slightly during the image acquisition. This so-called image registration intends to eliminate the effect of the patient's body shift, such that the final subtracted DSA images are ideally free of motion artefacts. The quality of carotid subtraction CTA can also be increased by image registration with the intention to eliminate high-density structures such as bones, calcified plaques or implanted stent material from the final angiographic images [8–10]. Furthermore, the angiographic quality of lower leg MRA may be improved by image registration if the patient has moved their legs by 1 mm or more between acquisitions of

the unenhanced and contrast-enhanced sequences [11]. The purpose of this study was to investigate whether such image registration could also improve the image quality in contrast-enhanced carotid MRA.

Materials and methods

Patients

Data from 375 carotid MRA examinations of patients with known or suspected carotid stenosis were prospectively collected over a period of 4 years. Informed patient consent had been obtained before MRA. The local institutional review board waived ethical approval of this study on image quality. MRA with sequences different from that described below were not included. Five MRAs were excluded from further analysis: one with insufficient arterial contrast, two with excessive venous contrast and two with technical artefacts. The remaining 370 MRA examinations had been obtained in 343 patients, including 27 follow-up MRAs. These follow-up MRAs were not excluded to prevent a selection bias, when transferring the study results to a similar MRA collective, i.e. an MRA collective that also includes follow-up MRA. Patient age ranged from 42 to 89 years (median 69) and body weight from 47 to 170 kg (median 79); the patient sample thus comprised a broad range of patient age and body size. The female-to-male gender ratio was 1:2.

Magnetic resonance angiography

The cervical MRAs were performed on clinical 1.5-T magnet systems (Magnetom Symphony and Sonata, Siemens, Erlangen, Germany) with standard head and neck receiver coils. Patients were placed headfirst in the magnet and were instructed to keep still. The need to reduce body motion was facilitated by gentle head fixation. Additionally the patients were advised not to breathe or swallow during image acquisition. The arterial circulation time was measured by using a 2-mL gadopentetate dimeglumine test bolus (Gd-DPTA, Magnevist, Schering, Germany). This bolus was injected into an antecubital vein and flushed with 25 mL physiological saline at a constant rate of 3 mL/s using an MR injector (Spectris Medrad, Indianola, PA, USA). Thereafter, the supra-aortic arteries were imaged from the aortic arch to the circle of Willis by using a three-dimensional (3D) gradient-echo sequence, resulting in 72 consecutive coronal slices (FLASH 3D, TR 3.54 ms, TE 1.39 ms, flip angle 25°, FOV 320×208 pixels, isotropic voxel size 1.1×1.1×1.1 mm, acquisition time 21 s). This 3D sequence was applied with sequential *k*-space ordering and multidimensional 6/8 partial Fourier acquisitions in both the phase- and slice-encoding directions. First, such a 3D sequence was measured unenhanced. Then 0.2 mL/kg

Gd-DPTA was injected intravenously and flushed with 25 mL saline at a rate of 3 mL/s. The subsequent bolus-timed gadolinium-enhanced 3D sequence was started such that central *k*-space acquisition coincided with the estimated arterial time-to-peak. The unenhanced 3D sequence was then subtracted from the gadolinium-enhanced 3D sequence to enhance the vascular contrast and suppress surrounding neck tissues [12]. From these 3D subtraction images, targeted maximum intensity projections (MIPs) were derived to depict the neck arteries [13]. Diagnostic radiological evaluation was based on these maximum intensity projections and on the original MRA images.

Postprocessing with automated image registration

The original DICOM images were converted to three-dimensional ANALYZE image volumes by using the freeware program MRICro (Rorden C, MRICro version 1.40, <http://www.sph.sc.edu/comd/rorden/mricro.html>). The unenhanced image volume was then subtracted from the contrast-enhanced image volume to enhance the arteries and to reduce signals from the surrounding tissue. Angiographic maximum intensity projection (MIP) images were then generated at 12 different view angles in steps of 15° to simulate a rotational projection angiography. The resulting images are standard MRA images without image registration. Additionally automated image registration with linear, affine and warp registration was applied to optimally fit the unenhanced image volume to its contrast-enhanced counterpart [14, 15]. This was done with the freeware automated image registration software package AIR 5.2.5 (Woods RP, AIR 5.2.5, <http://bishopw.loni.ucla.edu/AIR5/>). The registration time for automated image registration refers to calculation on a personal computer with a 2.4-GHz Pentium Quad processor and 1.5-GB working memory. Further postprocessing details are given in the [Electronic supplementary material](#).

Body shift

Body shift between the unenhanced and contrast-enhanced 3D images was estimated without user interaction from the automated linear registration results by averaging the calculated three-dimensional shift of all tissue voxels in the corresponding organ region. This body shift was stratified into five shift classes from 0 mm to ≥ 4 mm in steps of 1 mm.

Quantitative computer-assisted evaluation

The MRA image quality was assessed by computer-assisted evaluation, which results in identical findings when repeated. In each single evaluation the automated

analysis was blinded regarding the patient details and the results of the other evaluations. With reference to Sun and Parker, three image quality parameters were calculated [13]: (a) the vessel detection probability of an MIP image (VDP), (b) the contrast-to-noise ratio of an MIP image (CNR-MIP), and (c) the contrast-to-noise ratio of a 3D subtraction image (CNR-3D). For any MIP image, VDP quantifies the fraction of the vessels that can be detected within their surrounding tissue. The surrounding tissue was defined as the region at a distance of up to 5 mm away from the vessels. For any MIP image, CNR-MIP quantifies the ratio of vessel contrast (mean vessel intensity minus mean surrounding tissue intensity) to background noise (standard deviation of surrounding tissue intensities). For any 3D subtraction image, CNR-3D quantifies a similar ratio. The influence of body shift and registration method on the three image quality parameters was studied by two-factor analysis of variance (ANOVA) for the whole study group [16, 17]. A further subgroup ANOVA was added for cases with 1-mm or greater body shift to exclude any statistical influence from the cases with less than 1-mm body shift.

Statistics

Statistical analyses were performed using Statgraphics Plus for Windows 2.1 (1994, Manugistics, Rockville, Maryland, USA). The two-sided significance level was set to $p < 0.05$.

Results

Registration time

In the included 370 MRAs the average ($\pm$ SD) registration time was 53 ($\pm$ 37) s for linear registration, 124 ($\pm$ 118) s for affine registration and 13 ($\pm$ 4) min for warp registration.

Body shift

For 356 out of 370 cases (96.2%) a body shift of less than 1 mm occurred between acquisition of the unenhanced and

the contrast-enhanced MR sequences. A body shift of at least 1 mm (shift class ≥ 2) was found in 14 cases (3.8%). Only five cases (1.4%) exhibited a body shift of 2 mm or more.

Quantitative computer-assisted evaluation of MRA image quality

In almost all cases, VDP was already nearly 100% without image registration, indicating that the cervical arteries are identified well on nonregistered angiographic MIP images (Table 1). Analysis of the CNR-MIP and CNR-3D parameters showed that the angiographic contrast-to-noise ratio was on average slightly higher with image registration than without (Fig. 1a and b). However, in the ANOVA this small improvement in image quality was not significant ($p > 0.05$; Table 2). ANOVA of the whole study group showed that neither image registration nor body shift had a significant influence on the quality of the carotid MRA images (Table 2). The additional subgroup ANOVA of the 14 cases with a body shift of 1 mm or more also showed a slight trend of image quality to improve with image registration, but this effect was also not significant ($p > 0.05$; Fig. 1c and d). These results indicate firstly that standard carotid MRA needs no image registration to improve image quality. Secondly, standard breath-hold carotid MRA is generally robust against any natural body shift that may occur between acquisition of the unenhanced and the contrast-enhanced MRA sequences.

Illustrative case

Figure 2 shows an illustrative case with a body shift of 2.4 mm (shift class 3). The image quality parameters are given in Table 3. Although this body shift is relatively large, the image quality of the angiographic MIP image is high even without image registration. Automated image registration was then applied, similar to standard pixel-shifting that is routinely used in DSA. However, such image registration resulted in nearly identical images and did not improve image quality much further. These results indicate that nonregistered carotid MRA was robust against

Table 1 Image quality parameters with and without image registration for the whole study group

Registration method	Sample size	VDP (%)		CNR-MIP		CNR-3D	
		Mean	(SD)	Mean	(SD)	Mean	(SD)
None	370	99.9	(0.8)	7.02	(1.57)	13.37	(3.09)
Linear	370	99.9	(0.8)	7.05	(1.58)	13.44	(3.14)
Affine	370	99.9	(0.8)	7.05	(1.58)	13.46	(3.14)
Warp	370	99.9	(0.8)	7.06	(1.58)	13.52	(3.16)

Comparison of image registration methods by ANOVA is summarized in Table 2

VDP vessel detection probability, CNR-MIP contrast-to-noise ratio in MIP images, CNR-3D contrast-to-noise ratio in 3D subtraction image volumes, SD standard deviation

Fig. 1 Comparison of image registration methods: 1 no image registration, 2 linear, 3 affine and 4 warp registration. The ANOVA of all 370 MRAs showed a slight trend of CNR-MIP (**a**) and CNR-3D (**b**) to improve with image registration, but this effect was not significant ($p>0.05$). An additional subgroup ANOVA of the 14 cases with body shift ≥ 1 mm showed a similar trend for CNR-MIP (**c**) and CNR-3D (**d**) that was also not significant ($p>0.05$)

body shift in this case. Additional information is given in the legend of Fig. 2.

Discussion

Carotid artery stenosis is a treatable risk factor for ischaemic stroke [1–4]. Current guidelines recommend endarterectomy or stent-protected percutaneous transluminal angioplasty as treatments for symptomatic severe carotid stenosis with 70–99% reduction in luminal diameter, as defined by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [1]. Symptomatic moderate degree carotid stenoses in the 50–69% range

may equally require treatment [1]. In addition, in selected patients with asymptomatic 60–99% carotid stenosis, endarterectomy may also be considered as a primary preventative measure according to current guidelines [2]. Quantitative assessment of carotid stenosis is thus an essential prerequisite for therapeutic decision-making in individual cases [18]. Such grading requires adequate angiographic image quality.

DSA is the current gold standard in carotid artery imaging since it combines high image contrast with high spatial resolution. However, catheter-based DSA bears the risk of complications due to its invasiveness, specifically the risk of stroke. Noninvasive diagnostic alternatives include duplex ultrasonography, CTA and MRA [5, 19].

Table 2 Comparison of image registration methods by two-factor ANOVA

Image quality parameter	Source of variation	Degrees of freedom	Mean square	<i>F</i> ratio ^a	<i>P</i> value
VDP	Registration method	3	0.01	0.01	0.999
	Body shift class	2	0.65	1.08	0.338
	Residual	1,474	0.60		
CNR-MIP	Registration method	3	0.13	0.05	0.984
	Body shift class	2	2.87	1.15	0.317
	Residual	1,474	2.49		
CNR-3D	Registration method	3	1.48	0.15	0.929
	Body shift class	2	22.82	2.33	0.098
	Residual	1,474	9.81		

ANOVA (analysis of variance) of the three image quality parameters with the two independent factors “image registration method” and “body shift class” revealed no statistically significant results at $p<0.05$, i.e. neither image registration nor body shift had a significant influence on the MRA image quality. A comparison of registration methods is given in Fig. 1 VDP vessel detection probability, CNR-MIP contrast-to-noise ratio in MIP images, CNR-3D contrast-to-noise ratio in 3D subtraction image volumes

^aAll *F* ratios (variance ratios) are based on the residual mean square error

Fig. 2 Illustrative case. A 73-year-old woman was admitted for coronary artery bypass surgery. Duplex ultrasonography in the preoperative workup revealed bilateral carotid stenoses that were further evaluated by using contrast-enhanced MRA with the subtraction technique. Coronal maximum intensity projection (MIP) images are shown without image registration (**a**) and with linear (**b**), affine (**c**) and warp (**d**) registration. The arteries are depicted well, although there was an estimated body shift of 2.4 mm between acquisition of the unenhanced and the subsequent contrast-enhanced MRA sequences. The registered images (**b–d**) looked relatively similar to the nonregistered image (**a**), indicating no need

for image registration in this case. There is greater than 80% stenosis at the origin of the right internal carotid artery (*arrow*), greater than 60% stenosis at the origin of the left internal carotid artery (*arrow*) and an occlusion of the right vertebral artery. The carotid stenoses and the unilateral vertebral occlusion were asymptomatic. In addition to the intended coronary bypass grafting, the more severe right-sided carotid stenosis was treated with endarterectomy and patch angioplasty for stroke prevention. The patient has had no signs or symptoms of cerebral ischaemia on the current follow-up interval of 3 years

Duplex ultrasonography is being used as a screening method, whereas CTA and MRA provide images of the entire cervical arterial tree that may be referred to during surgical or neuroendovascular intervention [7, 19, 20]. For the detection of severe 70–99% carotid artery stenosis according to the NASCET criteria, a recent meta-analysis found contrast-enhanced MRA to be more sensitive and specific than CTA or duplex ultrasonography (respective sensitivities of 94%, 76% and 89% with specificities of 93%, 94% and 84%) [7].

Carotid CTA and MRA are competitive methods with specific advantages and disadvantages [7]. Currently, CTA with multidetector CT can provide higher spatial resolution but with less vascular contrast than MRA. Such carotid CTA is usually performed *without* mask subtraction, i.e. only a primarily contrast-enhanced data set is acquired. Diagnosis is

then based on the resulting three-dimensional image volume. Multiplanar reformation allows a detailed analysis of individual arteries, particularly the quantification of luminal narrowing. However, without mask subtraction it is difficult to generate DSA-like images since bony anatomy and calcified plaque components frequently overlie the cervical arteries in radiographic projections, even after manual image segmentation [8, 9, 21]. Such DSA-like images may, however, still be useful to attending clinicians who are used to interpreting DSA images.

In this context it is noteworthy that CTA can also be used *with* mask subtraction whereby an unenhanced CTA data set is subtracted from a subsequently acquired contrast-enhanced counterpart [8–10, 22]. However, subtraction artefacts due to slight body shifts may occur between scans in such examinations [22]. It has been shown that these artefacts may be eliminated and overall image quality of carotid subtraction CTA improved by image registration [8–10]. Furthermore, considering MRA in peripheral arterial disease, it has been shown that automated image registration may improve angiographic image quality significantly, specifically in the lower leg and in circumstances when a patient has shifted their legs by 1 mm or more between acquisition of the unenhanced and the contrast-enhanced MR sequences. This led to the question whether the image quality of contrast-enhanced carotid

Table 3 Image quality parameters in the illustrative case

Registration method	Image quality parameter		
	VDP	CNR-MIP	CNR-3D
None	100	6.54	11.86
Linear	100	6.68	12.25
Affine	100	6.77	12.43
Warp	100	6.86	12.49

MRA might equally be improved by image registration. However, the present study did not find a similar effect of image registration in carotid MRA within the observed limits of natural body shift. This nonsignificant study result is, nonetheless, a positive finding for conventional carotid MRA since it confirms that carotid MRA is robust against naturally occurring body shifts. This is in contrast to subtraction CTA, where angiographic image quality was found to be decreased by such shifts that may occur between acquisition of the unenhanced and the contrast-enhanced CTA sequences [8, 9].

The study finding may be explained in the context of neck anatomy and corresponding MRA signal intensities: the T1-weighted MRA images are dominated by signals from contrast-enhanced neck arteries as well as from surrounding fatty tissue. In contrast to the arteries in the lower leg, the cervical arteries are surrounded by less fatty

soft tissue or marrow in adjacent bones that might cause subtraction artefacts in the case of body shift. In addition, naturally occurring body shift in the neck appears to be less than in the lower legs. Furthermore, in comparison to DSA and CTA, arterial calcifications and bony anatomy in the neck return little or no MR signal and thus cannot cause subtraction artefacts in carotid MRA [8–10].

In conclusion, standard contrast-enhanced carotid MRA usually requires no image registration to improve image quality and is generally robust against any naturally occurring body shift that may take place between acquisition of the unenhanced and the contrast-enhanced MRA sequences.

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