Long term follow-up of patients with coiled intracranial aneurysms

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Chapter

3

Evaluation of occlusion status of coiled intracranial aneurysms with MRI at 3T: is contrast enhancement necessary?

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ABSTRACT

Background and Purpose: Magnetic Resonance Angiography (MRA) is increasingly used as a non-invasive imaging modality for the follow-up of coiled intracranial aneurysms. The need for contrast enhancement is not yet elucidated. We compared 3D time-of-flight (TOF-MRA) and contrast enhanced (CE-MRA) at 3T with catheter-angiography.

Methods: Sixty-seven patients with 72 aneurysms had TOF-MRA, CE-MRA and catheter-angiography 6 months after coiling. Occlusion status on MRA was classified as adequate (complete and neck remnant) or incomplete by two independent observers. For TOF-MRA and CE-MRA, inter-observer agreement, inter-modality agreement and correlation with angiography was assessed by κ-statistics. Test characteristics of TOF-MRA and CE-MRA were calculated and the areas under the receiver operating characteristic curve (AUROC) were compared.

Results: Catheter-angiography revealed incomplete occlusion in 12 (17%) of the 69 aneurysms, 3 aneurysms were excluded due to MR-artifacts. Inter-observer agreement was good for CE-MRA (κ=0.77, 95%CI 0.55-0.98) and very good for TOF-MRA (κ=0.89, 95%CI 0.75-1.00). Correlation of TOF-MRA and CE-MRA with angiography was good. All 5 incompletely occluded aneurysms that were additionally treated were correctly identified with both MRA techniques. AUROC for TOF-MRA and CE-MRA was 0.90 (95%CI: 0.79-1.00) and 0.91 (95%CI: 0.79-1.00). Inter-modality agreement between TOF-MRA and CE-MRA was very good (κ=0.83 95% CI 0.65-1.00) with full agreement in 66(96%) of the 69 aneurysms.

Conclusion: TOF-MRA and CE-MRA at 3T are equivalent in evaluating the occlusion status of intracranial aneurysms after coiling. Since TOF-MRA does not involve contrast administration, this method is preferred over CE-MRA.

INTRODUCTION

Coiling of intracranial aneurysms is an established method to occlude intracranial aneurysms[1]. A shortcoming of coiling is a risk for reopening of the aneurysm, which occurs in about 20% of coiled aneurysms. [2-5] Since patients with reopened aneurysms are at risk for hemorrhage, additional treatment is advocated. Follow-up imaging is therefore highly recommended. The standard follow-up imaging modality after coiling is catheter-angiography, but this diagnostic procedure is invasive, uses ionizing radiation, and exposes the patient to a small risk of serious complications.[6, 7]

Magnetic Resonance Angiography (MRA) has been used as an alternative non-invasive imaging modality to assess occlusion of coiled intracranial aneurysms with promising, but not yet conclusive results.[8-22] MRA can be performed without contrast enhancement with 3D time-of-flight (TOF-MRA) or with contrast enhancement (CE-MRA). Contrast administration has several disadvantages such as patient discomfort, risk of renal damage,[23] risk of allergic reaction and higher cost. From published data, it is unclear which of the 2 MRA techniques, if any, provides the better diagnostic accuracy. No studies are available that directly compare TOF-MRA and CE-MRA at 3T with angiography as reference standard in the detection of reopening of coiled aneurysms.

The purpose of our study was to compare diagnostic performance for 6 months follow-up of coiled intracranial aneurysms of TOF-MRA with CE-MRA at 3T with catheter-angiography as reference.

MATERIALS AND METHODS

Patients
The study was approved by the institutional review board. Written informed consent was obtained from all patients.

Between May 2005 and November 2007, all patients with coiled intracranial aneurysms scheduled for 6 month follow-up angiography were approached to participate in this study. Patients were requested to undergo TOF-MRA and CE-MRA at 3T on the same day as their standard follow-up angiogram. Patients were not considered eligible when they were younger than 18 years, when additional aneurysms were treated with neuro-surgical clips, when they suffered from claustrophobia or when a pacemaker was implanted. Complications of catheter-angiography and CE-MRA were recorded.

Imaging technique: angiography
Follow-up angiography was performed on a single-plane angiographic unit (Integris Allura Neuro; Philips Medical Systems, Best, The Netherlands). Six to eight mL of nonionic contrast material (iodixanol, Visipaque 320 mgI/mL; Amersham Health, Cork, Ireland) was injected into the internal carotid or vertebral artery with a power injector at 4–6 mL/s. Three views were acquired in each patient, including the working projection of the endovascular treatment. Three-dimensional rotational angiography was usually not performed at follow-up.

Imaging techniques: MRA
MR imaging examinations were performed on a 3T system (Intera R10; Philips Medical Systems, Best, the Netherlands) by using the sensitivity encoding (SENSE) 8 channel phased-array head coil. The protocol included transversal T1-weighted spin echo and T2-weighted fast spin echo

sequences, phase contrast survey MRA as preparation for MRA, 3D TOF-MRA with multiple overlapping thin slab acquisition (MOTSA) and CE-MRA sequences.

Imaging parameters for T1-weighted spin echo sequence were TR/TE 500/10 ms, 256x205 matrix (reconstructed to 512x410), FOV 230x184 mm (i.e. 80% rectangular FOV) and 4 mm slice thickness with a 1 mm gap. Parameters for the T2-weighted fast spin echo sequence were TR/TE 3000/80 ms, 400x320 matrix (reconstructed to 512x410), FOV 230x184 mm (i.e. 80% rectangular FOV), 4 mm slice thickness with a 1 mm gap and a TSE factor of 15.

For MRA gradient echo techniques were used. TOF images were acquired in the transverse plane with the following parameters: TR/TE 20/4 ms (shortest), flip angle 20°, 512x328 matrix (reconstructed to 1024x870), FOV 200x170 mm (i.e. 85% rectangular FOV), 1.0 mm thick sections interpolated to 0.5 mm, 220 sections acquired in ten chunks resulting in a coverage area of 110 mm. The measured voxel size of the TOF-MRA image was 0.39 x 0.61 x 1 mm, and the reconstructed voxel size was 0.2 x 0.2 x 0.5 mm. The scan time of MOTSA 3D TOF sequences was reduced by using sensitivity encoding (SENSE). We used a SENSE reduction factor of 1.5 which resulted in an acquisition time of 7 minutes.

The timing for the 3D CE-MRA was calculated from the time to peak of a dynamic 2D (0.9 sec cycle time) gradient echo sequence with a mid sagittal slice of 50 mm thickness following injection of 1 mL of gadopentetate dimeglumine (Magnevist, Bayer Health Care Pharmaceuticals, USA) intravenously. Subsequently 15 mL of gadopentetate dimeglumine was injected with a rate of 2 mL/s for acquisition of 3D CE-MRA. Imaging parameters were as follows: TR/TE 5.3/1.7 ms (shortest), flip angle 30°, FOV 250x200 mm (i.e. 80% rectangular FOV), 368x263 matrix (reconstructed to 512x410), 1.0 mm thick sections interpolated to 0.5 mm. The measured voxel size of 3D CE-MRA image was 0.68 x 0.76 x 1.00 mm, and the reconstructed voxel size was 0.49 x 0.49 x 0.50 mm. SENSE was also used in 3D CE-MRA imaging with a SENSE reduction factor of 2 and resulting scan duration of 36 seconds. Also the CENTRA (randomly sampled central k-space) technique was applied here.

Total scan-duration was 20 minutes. Adverse events during MRA were registered.

Image evaluation

Aneurysm occlusion status on 6 month follow-up angiography was assessed by an experienced interventional neuroradiologist (WJvR) who was blinded to parallel MRA results. The occlusion status of the coiled aneurysms on TOF- and CE-MRA were classified both in a 3 tier scale as complete occlusion, neck remnant and incomplete occlusion, and in a 2 tier scale as adequate occlusion (complete occlusion and neck remnant) and incomplete occlusion. All TOF-MRA and CE-MRA images were evaluated independently and in random order by 2 experienced interventional neuroradiologists (RB and MS) who were unaware of the parallel angiography results. Source images, 3D maximum-intensity projections and 3D volume rendered reconstructions were available on a 3D Vitrea workstation (Vital Images Inc, Minnetonka, Minnesota, USA). Occlusion status of the coiled aneurysms was classified in the same way as for angiography. Discordant results in TOF-MRA images between the observers after completion of the evaluation were jointly reassessed in a second reading session to reach consensus, similar was done for the CE-MRA images.
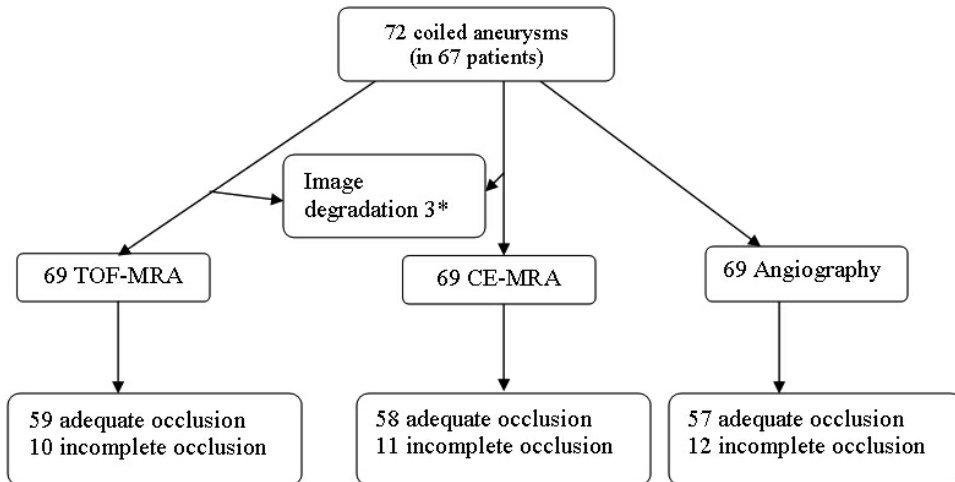
Figure 1
Flow chart of all coiled aneurysms at 6 months follow-up.
* Three aneurysms were excluded due to coil artifacts and venous over projection on
CE-MRA. One of these aneurysms was also excluded due to coil artifacts on TOF-MRA

Data analysis
κ -statistics were used to assess inter-observer agreement for TOF-MRA and CE-MRA, inter-modality agreement between TOF-MRA and CE-MRA and to correlate the consensus data of both MRA techniques with angiography findings. The interpretation of kappa was: <0.20 poor agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 good agreement, and 0.81-1.00 very good agreement. [24]
Test characteristics of TOF-MRA and CE-MRA with corresponding 95% confidence intervals (CI) were calculated for the 2 tier occlusion scale. This was done since only the classification of incomplete occlusion is important in clinical decision making in terms of considering additional treatment. We compared the areas under the receiver operating characteristic curve (AUROC) for TOF-MRA and CE-MRA.

RESULTS

Patients
Sixty-seven patients (46 women, 21 men; mean age 49±12 years) with 72 coiled aneurysms, agreed to participate in the study. Of 72 coiled aneurysms 60 were ruptured. Mean aneurysm size was 7 mm (SD ± 5 mm). Twenty-nine aneurysms were located on the carotid artery, 28 on the anterior cerebral artery, 8 on the middle cerebral artery and 7 in the posterior circulation. On CE-MRA, 3 aneurysms could not be assessed due to coil artifacts and venous overlap and were excluded, leaving 69 aneurysms with CE-MRA. On TOF-MRA one aneurysm could not be assessed due to coil artifacts, this aneurysm showed similar coil artifacts on CE-MRA and was already excluded, leaving 71 aneurysms with TOF-MRA.

As a result, 69 similar aneurysms in 64 patients were used for the analyses of inter-modality agreement and correlation between the imaging techniques (Fig 1). There were no complications, neither from angiography nor from MRA.

Angiography
On 6 months follow-up angiography, 57 coiled aneurysms were adequately occluded and 12 aneurysms were incompletely occluded (Fig 1). Of the 12 incompletely occluded aneurysms, 5 were additionally treated.

Inter-observer agreement for MRA
Inter-observer agreement for TOF-MRA for the 3 tier classification was good (κ=0.74 (95%CI 0.60-0.88) with full agreement in 58 (82%) of the 71 aneurysms that could be evaluated. For the 2 tier classification inter-observer agreement was very good (κ=0.89, 95%CI 0.75-1.00) with full agreement in 69 (97%) of 71 aneurysms.
Inter-observer agreement for CE-MRA for the 3 tier classification was good (κ=0.67, 95%CI 0.51-0.82) with full agreement in 53 (77%) of 69 aneurysms. For the 2 tier classification inter-observer agreement was also good (κ=0.77, 95%CI 0.55-0.98) with full agreement in 65 (94%) of 69 aneurysms.

TOF-MRA compared to angiography
Correlation between TOF-MRA and angiography for the 3 tier classification was moderate (κ=0.57 95%CI 0.40-0.74) with full agreement in 47 (68%) of 69 aneurysms. For the 2 tier classification the correlation between TOF-MRA and angiography was good (κ=0.78 95% CI 0.58-0.99), with full agreement in 65 (94%) of 69 aneurysms (Table 1).
TOF-MRA classified 3 of the 12 incompletely occluded aneurysms wrongly as adequately occluded: a ruptured 4 mm carotid tip aneurysm (Fig 2), a ruptured 4 mm middle cerebral artery aneurysm (Fig 3) and a ruptured 7 mm carotid artery aneurysm (Fig 4). In none of these three aneurysms additional treatment was judged indicated. All 5 incompletely occluded aneurysms that were additionally treated were correctly identified with TOF-MRA as incompletely occluded (Fig 5). One ruptured 6 mm basilar tip aneurysm that was completely occluded on angiography was incorrectly classified by TOF-MRA as incompletely occluded. Sensitivity of TOF-MRA was 75% (95% CI: 43-95%), specificity of TOF-MRA was 98% (95% CI: 91-100%). All test characteristics of TOF-MRA and AUROC are displayed in Table 2.

CE-MRA compared to angiography
Correlation between CE-MRA and angiography for the 3 tier classification was moderate (κ=0.52 95%CI 0.35-0.69) with full agreement in 44 (64%) of 69 aneurysms. For the 2 tier classification correlation between CE-MRA and angiography was good (κ=0.74 95% CI 0.52-0.96) with full agreement in 64 (93%) of 69 aneurysms (Table 3). CE-MRA classified 3 of the 12 incompletely occluded aneurysms wrongly as adequately occluded. These were the same 3 aneurysms that were not correctly classified as incompletely occluded with TOF-MRA (Fig 2-4).
All 5 incompletely occluded aneurysms that were additionally treated were correctly identified with CE-MRA as incompletely occluded (Fig 5).
CE MRA incorrectly classified 2 adequately occluded aneurysms as incompletely occluded: a ruptured 3 mm anterior communicating artery aneurysm and a ruptured 6 mm pericallosal artery

aneurysm. Sensitivity of CE-MRA was 75% (95%CI: 43-95%), specificity of CE-MRA was 97% (95%CI: 88-100%). All test characteristics of CE-MRA and AUROC are displayed in Table 2.

Inter-modality agreement

Inter-modality agreement between TOF-MRA and CE-MRA for the 3 tier classification was good (κ=0.71 95%CI 0.57-0.85) with full agreement in 54 (78%) of the 69 aneurysms (Table 4). Inter-modality agreement between both MR techniques for the 2 tier classification was very good (κ=0.83 95% CI 0.65-1.00) with full agreement in 66 (96%) of the 69 aneurysms (Table 4).
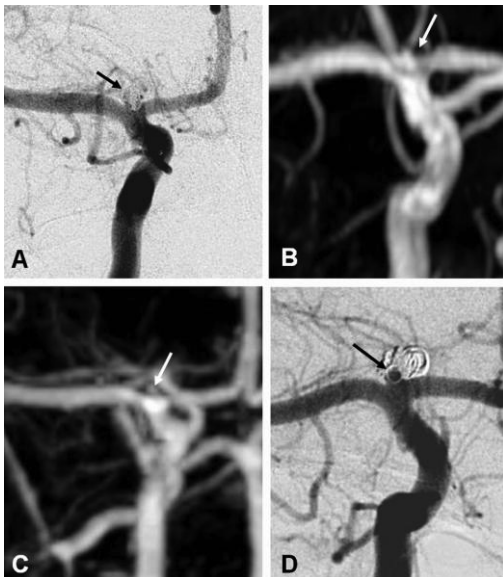

Figure 2

Disagreement between both TOF-MRA and CE-MRA with angiography on the occlusion of a carotid tip aneurysm.

A. angiography immediately after coiling shows adequate occlusion with a small neck remnant.

B. follow-up TOF MRA at 6 months was classified as complete occlusion

C. follow-up CE-MRA at 6 months was classified as a small neck remnant

D. follow-up angiography at 6 months was classified as incomplete occlusion

Since geometry of the reopened aneurysm was unfavorable,

this patient was not retreated but subjected to extended follow-up

Figure 3

Disagreement between both TOF-MRA and CE-MRA with angiography on the occlusion of a middle cerebral artery aneurysm.

A. angiography immediately after coiling shows a small neck remnant

B. follow-up TOF MRA at 6 months was classified a small neck remnant

C. follow-up CE-MRA at 6 months was classified as a small neck remnant

D. follow-up angiography was classifeid as incomplete occlusion

Since geometry of the reopened aneurysm was unfavorable, this patient was not retreated but subjected to extended follow-up.

Figure 4

Disagreement between both TOF-MRA and CE-MRA with angiography on the occlusion of a carotid artery aneurysm.

A. angiography immediately after coiling shows a small neck remnant

B. follow-up TOF MRA at 6 months was classified as a small neck remnant

C. follow-up CE-MRA at 6 months was classified as a small neck remnant

D. follow-up angiography at 6 months was classified as incomplete occlusion.

Since geometry of the reopened aneurysm was unfavorable, this patient was not retreated but subjected to extended follow-up.
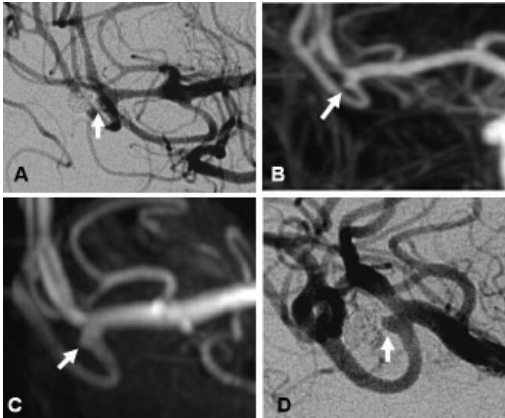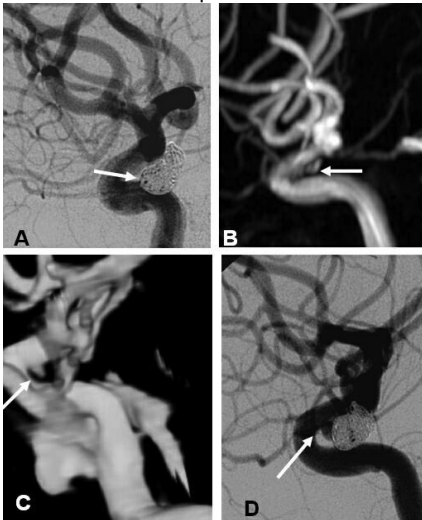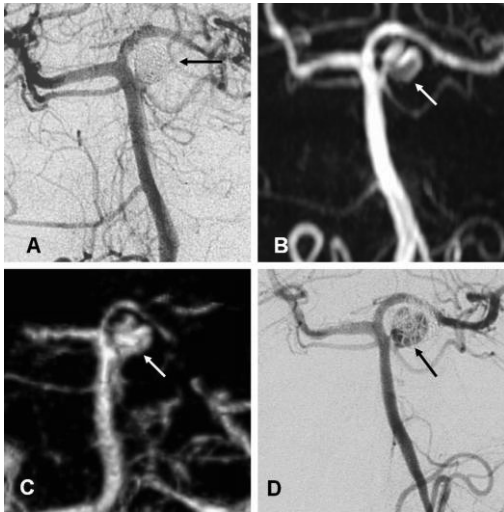
Figure 5
Agreement between TOF-MRA, CE-MRA and angiography on the occlusion of a partially thrombosed superior cerebellar artery aneurysm.
A. angiography immediately after coiling shows complete occlusion
B. follow-up TOF MRA at 6 months was classified as incomplete occlusion
C. follow-up CE-MRA at 6 month was classified as incomplete occlusion
D. follow-up angiography at 6 month was classified as incomplete occlusion
The aneurysm was additionally coiled without complications and complete occlusion was achieved

		Angiography			
			Adequate occlusion		
		Incomplete occlusion	Neck Remnant	Complete occlusion	Total
TOF-MRA					
	Incomplete occlusion	9	0	1	10
Adequate occlusion	Neck remnant	3	14	5	22
	Complete occlusion	0	13	24	37
	Total	12	27	30	69

Table 1
Correlation between TOF MRA and angiography.
Correlation for the 3 tier classification was moderate ($\kappa=0.57$ 95%CI 0.40-0.74) with a full agreement in 47 (68%) of 69 aneurysms. Correlation for the two tier classification, adequate and incomplete occlusion, was good ($\kappa=0.78$ 95% CI 0.58-0.99) with a full agreement in 65 (94%) of 69 aneurysms.

	TOF-MRA	CE-MRA
Sensitivity (95% CI)	75% (43-95%)	75% (43-95%)
Specificity (95% CI)	98% (91-100%)	97% (88-100%)
PPV (95% CI)	90% (56-100%)	82% (48-98%)
NPV (95% CI)	95% (86-99%)	95% (86-99%)
AUROC (95% CI)	0.90 (0.79-1.02)	0.91 (0.79-1.02)

Table 2
Test characteristics of TOF-MRA and CE-MRA compared to angiography.
95% CI= 95% Confidence Interval, PPV= positive predictive value, NPV = negative predictive value, AUROC= area under the receiver operating curve

Angiography

		Incomplete occlusion	Neck Remnant	Complete occlusion	Total
			Adequate occlusion		
CE-MRA	Incomplete occlusion	9	2	0	11
Adequate occlusion	Neck remnant	2	10	5	17
	Complete occlusion	1	15	25	41
	Total	12	27	30	69

Table 3
Correlation between CE-MRA and angiography.
Correlation for the three tier classification was moderate (κ=0.52 95%CI 0.35-0.69) with full agreement in 44 (64%) of 69 aneurysms. Correlation for the two tier classification, adequate and incomplete occlusion, was good (κ=0.74 95% CI: 0.52-0.96) with a full agreement in 64 (93%) of 69 aneurysms.

		TOF-MRA			
			Adequate occlusion		
		Incomplete occlusion	Neck Remnant	Complete occlusion	Total
CE-MRA	Incomplete occlusion	9	2	0	11
Adequate occlusion — Neck remnant	1	12	4	17
Complete occlusion	0	8	33	41
Total	10	22	37	69

Table 4

Inter-modality agreement between TOF MRA and CE-MRA.

Inter-modality agreement for the 3 tier classification was good (κ=0.71 95%CI 0.57-0.85) with full agreement in 54 (78%) of the 69 aneurysms. Inter-modality agreement for the 2 tier classification, adequate and incomplete occlusion, was very good (κ=0.83 95% CI 0.65-1.00) with full agreement 66 (96%) of the 69 aneurysms.

DISCUSSION

For evaluation of aneurysm occlusion status 6 months after coiling, diagnostic performance of TOF-MRA equals that of CE-MRA. Inter-observer agreement of both MRA techniques was good. Also correlation with angiography as reference standard was similar and good for both techniques. The negative predictive values for incomplete occlusion at 6 months follow-up of coiled aneurysms were exactly the same for TOF-MRA and CE-MRA. This implies that contrast enhancement does not have additional value in excluding incomplete occlusion if the TOF-MRA shows an adequate occlusion. The positive predictive value of CE-MRA was somewhat lower than that of TOF-MRA. Thus, in our study group contrast enhancement had no additional value in ruling in incomplete aneurysms either.

Despite favorable test characteristics, 3 of 12 incompletely occluded aneurysms were wrongly classified as adequately occluded. Both TOF-MRA and CE-MRA failed to identify the same 3 incompletely occluded aneurysms. However, in none of these three aneurysms additional treatment was judged indicated and the incorrect classification had thus no clinical consequences. The assessment of the occlusion status was to some extent limited by the use of a classification that allows room for subjective differences. Apparently, it was sometimes difficult to classify a small residual lumen as borderline adequate- or borderline incomplete occlusion.[25] All 5 incompletely occluded aneurysms that were additionally treated were correctly identified with both MRA techniques.

Another 3 adequately occluded aneurysms were wrongly classified as incompletely occluded, 1 with TOF-MRA and 2 with CE-MRA. This implies that classification of incomplete aneurysm occlusion with MRA should be verified with angiography.

Three aneurysms were excluded from assessment due to artifacts on CE-MRA, compared to one aneurysm on TOF-MRA.

We could not find other studies comparing TOF-MRA and CE-MRA at 3T assessed separately in the same patients with angiography as reference. Previous studies have evaluated either TOF-MRA

or CE-MRA for coiled aneurysms.[15-18] Other studies have evaluated TOF-MRA and CE-MRA with catheter-angiography as reference[10, 14, 19, 23] of which some reported better diagnostic performance of CE-MRA.[19] However, all these studies have been performed on 1.5T and evaluation of the two MR techniques independently was not done. One study compared independently TOF-MRA and CE-MRA at 1.5T with catheter-angiography as reference, in which they found no significant difference between TOF-MRA and CE-MRA.[13] A meta-analysis of 16 studies on diagnostic performance of MRA found no difference between TOF-MRA and CE-MRA.[20] However, these findings should be interpreted with some caution because the included studies were of moderate methodological quality and all pooled estimates were subject to heterogeneity. A recent study on 3T but without catheter-angiography as reference showed similar classification of aneurysm occlusion on TOF MRA and CE-MRA, although the visualization of residual flow was considered better on CE-MRA. [10]

Inter-observer and inter-modality agreements were substantially better in the two tier scales in concordance with a study on aneurysm assessment scales. [24] Apparently, in the 3 tier scale it was sometimes difficult to differentiate between a completely occluded aneurysm and a small neck remnant. Although the two tier scales may not identify these subgroups, this has little clinical impact since additional treatment is only considered in incompletely occluded aneurysms.

A limitation of our study is the small sample size of 69 aneurysms, of which 12 (17%) were incompletely occluded, which precludes definitive conclusions on whether or not MRA can replace catheter-angiography in the follow up of coiled aneurysms. However, all patients underwent both TOF-MRA and CE-MRA resulting in 138 MRA datasets for comparison with angiography, which was sufficient to draw conclusions about the additional value of contrast enhancement in MRA.

Although in several previous studies CE-MRA is considered superior to TOF-MRA, this could not be confirmed in this study. Our TOF-MRA technique was optimized by using short TE and the MOTSA technique in stead of a single volume 3D-TOF sequence that is used by others.[10] We used in the MOTSA sequence a slice thickness of 1 mm, which might seem large for modern scanner technology. However, complete coverage within an acceptable time frame with a good signal to noise limits minimum slice thickness. To enhance signal to noise we used the overlapping slab technique. Halving the slice thickness from 1 mm to 0.5 mm, while maintaining the signal to noise, would require a fourfold increase in acquisition time. Since the parameters we used resulted in a relatively long acquisition time of 7 minutes, a substantial longer acquisition time was not considered an option. MOTSA minimizes signal intensity loss due to spin saturation and maintains small voxels and short TE's to minimize intravoxel phase dispersion. Our MOTSA TOF technique resulted in a reconstructed voxel size of 0.2 x 0.2 x 0.5 mm, while for the CE-MRA sequence the reconstructed voxel size was 0.49 x 0.49 x 0.5mm. The problem of image degrading by venous over projection can be decreased by faster imaging with higher SENSE factors, at the expense of decreased signal-to-noise ratio.[10] Large aneurysm remnants may be better visualized by CE-MRA than by TOF-MRA due to saturation effects and signal intensity loss with TOF [10]. Since in our study no large aneurysm remnants were present, this possible advantage of CE-MRA could not be substantiated.[22]

In summary, in this study TOF-MRA and CE-MRA at 3T were equivalent in evaluating the occlusion status of coiled intracranial aneurysms. Since TOF-MRA does not involve contrast administration, this method is preferred over CE-MRA in the majority of patients if MRA is used in stead of catheter-angiography for the follow-up of coiled intracranial aneurysms.

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