Original Research

Comparison of 0.5M Gadoterate and 1.0M Gadobutrol in Peripheral MRA: A Prospective, Single-Center, Randomized, Crossover, Double-Blind Study

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Purpose: To evaluate the diagnostic efficacy of macrocyclic paramagnetic gadolinium (Gd) chelates gadoterate (0.5 mmol/mL) and gadobutrol (1.0 mmol/mL) for the diagnosis of clinically significant abdominal/lower limb arterial diseases at 3.0T.

Materials and Methods: This study was conducted as a prospective, single-center, randomized, double-blind, intraindividual study comparing single dose (0.1 mmol/kg) gadoterate enhanced-MRA (magnetic resonance angiography) with gadobutrol enhanced-MRA at 3.0T for their diagnostic potential in patients with peripheral artery disease. A total of 20 patients were included in this trial.

Results: Fourteen patients were eligible for the final efficacy analysis. The overall image quality (excellent/more than adequate) was better rated with gadoterate than with gadobutrol (100% vs. 78.6%, 100% vs. 92.9%, 100% vs. 85.7%, 100% vs. 85.7% for readers 1, 2, 3, 4, respectively). Diagnostic confidence was rated high/excellent in 100% (readers 1, 2, and 3) and 92.9% (reader 4) with gadoterate compared to 92.9% (readers 1 and 2) and 85.7% (readers 3 and 4) with gadobutrol. Higher signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) values were obtained for gadobutrol compared to gadoterate (26.1/23.4, $P = 0.01$, and 22.7/20.2, $P = 0.01$). For the secondary criteria, no differences between groups were reported. No adverse events were reported.

Conclusion: Gadobutrol yielded significantly higher SNR/CNR while gadoterate was better rated in terms of overall image quality and diagnostic confidence ($P > 0.05$).

Key Words: MRA; gadoterate; gadobutrol; PAOD
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IN PERIPHERAL ARTERY occlusive disease (PAOD), the anatomic vascular tree needs to be imaged precisely to allow exact planning of revascularization procedures (1). Numerous imaging methods are used clinically to depict arterial diseases. Conventional x-ray angiography is usually performed using a subtraction technique (digital subtraction angiography [DSA] the gold standard method), but DSA is characterized by its invasiveness and expensive character and the associated risks of iodinated contrast agents and ionizing radiation (2,3).

Computed tomography angiography (CTA) is a minimally invasive imaging test, providing a short examination time and high diagnostic accuracy (4).

Magnetic resonance angiography (MRA) is considered a clinically useful tool in the evaluation of vascular disease and it is currently regarded as the most appropriate noninvasive imaging method (5). Today, contrast-enhanced (CE) MRA is widely used for diagnosing PAOD. Systematic reviews have assessed the diagnostic performance of peripheral CE-MRA (6–8), and its advantages are that the examination is noninvasive, has high diagnostic accuracy, is cost-effective, and has a 3D approach to the vessel and pathology (9,10). Moreover, moving-table MRA has gained increasing importance in diagnosis due to its ability to depict both the anatomy and pathology of the arterial tree covering the whole length of the lower extremities with higher robustness and shorter overall image acquisition times compared to conventional stepping table-techniques (11–13).

Due to the association of linear Gd-chelates with nephrogenic systemic fibrosis, macrocyclic Gd-chelates,

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which are considered low risk by the European Medicines Agency (EMA), are now broadly used in clinical practice (14). Therefore, the aim of this study was to compare the image quality of the two most commonly applied macrocyclic extracellular contrast agents gadoterate (0.5 mmol/mL) and gadobutrol (1 mmol/mL) at equimolar doses of gadolinium for peripheral MRA at 3.0T.

MATERIALS AND METHODS

Study Design

This was a prospective, randomized, double-blind, intraindividual, crossover, exploratory phase IV study to compare the macrocyclic contrast agents 1.0M gadobutrol (Gadovist, BayerHealthCare, Berlin, Germany) and 0.5M gadoterate (Dotarem, Guerbet, Roissy, France) in terms of image quality in MRA at 3.0T in patients with PAOD, at an equal dose of 0.1 mmol/kg body weight.

The chart shown in Fig. 1 summarizes the steps and imaging procedures performed within this study. The first MRA (first procedure) occurred within 21 days (including the first day) after completing screening assessments. The second MRA (second procedure) was performed within 30 days but at least 24 hours after completing the first examination.

Approval was obtained from the Institutional Review Board before initiation of the study. The procedures set out in the trial protocol were designed in accordance with the principles of the Good Clinical Practices guidelines of the International Conference on Harmonization. The trial was carried out in keeping with local legal requirements. Informed written consent was obtained from each patient before any study-specific procedure was performed. The study was registered at www.clinicaltrials.gov under accession number NCT00955617. The authors who are not employees of the supporting company had at every time full control of inclusion of any data and full access to all information.

Patients

Patients eligible for the study were aged over 18 years (male or female) with PAOD Fontaine stage II or III. Female patients had to be using effective contraception or be surgically sterilized or postmenopausal. Women of childbearing potential were required to have a documented negative urine pregnancy test at screening. Patients with a contraindication to MRI (eg, pacemaker, aneurysm clip, severe claustrophobia, metallic joint replacement) or patients with severely impaired renal function (estimated glomerular filtration rate <50 mL/min, based on recent [<21 days] serum creatinine) were excluded. Patients who had received an MRA or x-ray contrast media within 48 hours before administration of the investigational products were also excluded. Other exclusion criteria were patients with known severe adverse drug reaction or contraindication to one of the investigational products, patients planned to undergo therapeutic intervention in the vessels of interest between the two MRA procedures, patients who had a major cardiovascular event within 30 days prior to the inclusion, pregnancy or lactation. A power calculation was done beforehand during study preparation.

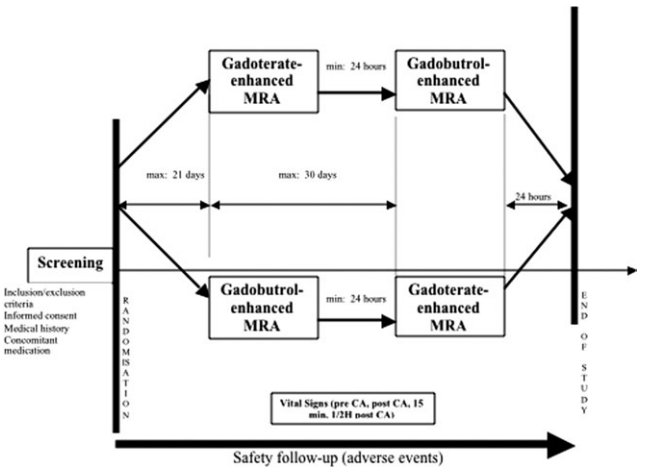

Figure 1. In this diagram the study design, including the chronology of the MRAs, is summarized.

Contrast Agents

Gadoterate was administered at a dose of 0.1 mmol/kg (0.2 mL/kg), injected at a rate of exactly 1 mL/sec. Gadobutrol was administered at a dose of 0.1 mmol/kg (0.1 mL/kg), injected at a rate of exactly 0.5 mL/sec to achieve equimolar amounts of gadolinium and to obtain equal bolus lengths. The study doses were injected in an antecubital vein via an 18G intravenous access using a power injector (MedRad Spectris Solaris, MedRad, Indianola, PA) and followed with a 25–30 mL normal saline flush at the same flow rate.

MR Equipment and Imaging Procedures

The MRA examinations were carried out on a 3.0T MR-scanner (Siemens MAGNETOM TimTrio, 102x32, Erlangen, Germany) using a dedicated 36-element peripheral angiography-coil in combination with one or two 6-element body matrix coils (depending on the patients size) and elements of the inbuilt 32-element spine matrix coil. For MRA examinations, patients were positioned feet-first supine for this exam. For MRA the move-during-scan technology TimCT was used. TimCT allows acquiring the entire field of view in z-direction seamlessly in a single acquisition by employing a continuously moving table throughout the MRA acquisition, as described elsewhere (11,15,16). This approach allowed for fast, time-efficient, and patient-friendly imaging with high robustness.

The imaging protocol included the following steps: localizer (abdomen to feet), vessel scout localizer (abdomen to feet), nonenhanced TimCT MRA acquisition (acquired twice for later noise calculation), transversal test bolus at the level of the renal artery (2.0 mL for gadoterate and 1.0 mL for gadobutrol), contrast-

Table 1
Detailed Sequence Parameters

	Units	TimCT-MRA
Sequence type	—	3D-FLASH
Parallel imaging	—	GRAPPA 2
Acquisition time	[s]	62
Acquired spatial resolution	[mm^3]	1.2 × 1.2 × 1.96
Reconstructed spatial resolution	[mm^3]	1.2 × 1.2 × 1.2
Field of view (FoV)	[mm]	1280 × 337
Repetition time (TR)	[ms]	2.43
Echo time (TE)	[ms]	1.02
Flip angle	[°]	21
Matri×	[mm^2]	384 × 312
Slices/slab	—	88
Bandwidth	[Hz/Px]	1000
Orientation	—	Coronal

enhanced TimCT MRA acquisition. If the calf station was clinically not assessable a separate time-resolved TWIST MRA was ordered by the physician using 0.03 mmol/kg contrast agent, which was not part of this study. The timing of the contrast-enhanced TimCT MRA was calculated by using the test bolus information. The detailed sequence parameters of the TimCT-MRA sequence are presented in Table 1.

Imaging Evaluation Criteria

Primary Criterion

The primary criterion for evaluation was the overall image quality of each MRA examination. All images were displayed in a blinded and randomized manner to four radiologists (two on-site and two off-site radiologists). Each of the four readers independently assessed image quality on an ordinal 5-point scale: excellent (5), more than adequate (4), adequate (3), less than adequate (2), and nondiagnostic (1). The experience of the readers differed between 5 and 13 years of vascular MRI.

Evaluated Segments

One of the secondary criteria was the number of evaluated arterial segments among all the segments. The aorto-iliac, femoral, popliteal, calf, and foot vascular territories from the leg region per patient were assessed by four independent readers. For the purpose of analysis the vascular tree was divided into 21 bilateral segments (except the infrarenal aorta), including: 1, aorta; 2 and 3, common iliac arteries; 4 and 5, external arteries; 6 and 7, femoral arteries; 8 and 9, superficial femoral arteries; 10 and 11, deep femoral arteries; 12 and 13, popliteal arteries; 14 and 15, tibioperoneal trunk; 16 and 17, anterior tibial arteries; 18 and 19, posterior tibial arteries; 20 and 21, peroneal arteries. Vessel segments containing metallic stents were excluded from further analysis because of the associated artifacts known to be seen at contrast-enhanced MRA. The four readers independently evaluated each of the 21 segments of the peripheral arteries in terms of "assessable" or "not assessable." A segment was considered as "assessable" if its image allowed the reader to determine whether this segment is affected by a stenosis, and in case of stenosis, its image allowed the reader to measure the detected stenosis (arterial diameter and stenosis length).

Other Secondary Criteria

Other secondary criteria included the number of significant stenosis depicted by patient (stenosis >50%) and their localization; the collateral circulation visualization (yes/no); the pedal vessel and smaller branches graded for visualization on an ordinal 5-point scale in the foot territory (excellent, more than adequate, adequate, less than adequate, nondiagnostic); the level of diagnostic confidence assessed on a 5-point scale by patient (nil, poor, moderate, high, excellent); the venous overlap that interfered with arterial visualization evaluated on a 4-grade scale by patient (not seen: no venous overlap depicted; partially seen: venous overlap partially depicted but not difficult to distinguish from the artery; seen: venous overlap difficult to distinguish from the artery; and unassessable); objective measures of enhancement (signal to noise ratio (SNR), contrast to noise ratio (CNR)); circular regions of interest (ROI) of ~0.5 cm^2 were placed on 3 points: one on common iliac artery (right or left), one on popliteal artery (right or left), and one on the calf arteries (either anterior or posterior tibial artery, peroneal artery); this ROI for the calf arteries was placed in the leading vessel of each individual patient to determine the signal intensity of the vessel. The noise was measured as follows. The two acquired nonenhanced TimCT MRA datasets were subtracted from each other yielding a noise distribution map as described elsewhere (17). The circular ROIs were then copied from the contrast-enhanced image to be located at the same position. The standard deviation of the signal intensity measured in these ROIs was used for further noise calculation. For the CNR assessment a circular ROI was placed in the iliopsoas muscle, the thigh muscles or the calf muscles for CNR assessment of the pelvic, thigh and calf arteries. SNR and CNR were calculated as follows: $SNR = SI_{artery}/SD_{noise}$; $CNR = (SI_{artery}\text{-}SI_{muscle})/SD_{noise}$.

Safety Assessment

Adverse events were assessed during the patient's study participation, from inclusion to 24 ± 4 hours after last contrast product bolus injection. Additionally, following the contrast product bolus injection, patients were followed over a 30-minute period for clinical safety on site (vital signs and injection-site tolerance).

Statistical Analysis

The present study was conducted as a pilot study without specific hypotheses allowing a sample size calculation. Statistical analyses were conducted using the software SAS v. 9.2 (SAS Institute, Cary, NC).

Exploratory statistical tests were performed comparing the two contrast agents, for each reader and all readers pooled. Generalized estimating equation (GEE) regression models were used to model the image quality or the diagnostic confidence as a function of the two MRA (gadoterate and gadobutrol MRI) and the injection order and the subject considered as a cluster of correlated measures (MRA and readers). The same models were used for testing the following probabilities: Prob(MR Confidence = Excellent); Prob(MR Assessable segment = Yes); Prob(MR Presence of stenosis = Yes); Prob(MR Significant stenosis (>50%) = Yes). *P*-values come from the Wald chi-square statistics for correlated binary data using the SAS proc Genmod (GEE) with an exchangeable correlation matrix. Statistical significance was assumed with $P < 0.05$. Descriptive statistics were also performed on other parameters. For image quality, the percentage of interreader agreements was assessed using a kappa test.

RESULTS

Patients and Examination Conditions

A total of 20 patients (15 male, 5 female) were enrolled in this study. Their mean age was 61.5 years (45–77) and mean body mass index was 27.0 kg/m^2 (19.0–37.1). A total of 14 patients who had both MRAs performed completed the study and there were six withdrawals. The main reasons for withdrawal were withdrawal of consent (3), patient lost to follow-up (1), technical incident (1), other reason (conventional angiography after the first MRA-procedure) (1). Therefore, the efficacy analysis was carried out on 14 patients by the four readers. As expected due to the different product concentration, the volume administered was higher with gadoterate (18.3 ± 4.1 mL, range: 10.0–24.8) as compared to gadobutrol (9.5 ± 2.0 mL, range: 7.0–13.5).

Primary Criterion: Image Quality

As shown in Table 2, the overall image quality obtained was better rated with gadoterate than with gadobutrol ($P > 0.05$). All of the readers assessed all of the images using gadoterate as "more than adequate" or "excellent" (100%). All of the readers assessed between 78% and 86% of the images as "more than adequate" or "excellent" using gadobutrol. Regarding excellent image quality by reader, no statistically significant difference was observed between groups. All of the readers assessed between 7% and 22% of the images rated as "inadequate" for gadobutrol and 0% for gadoterate. The main reasons were technical limitations of the MRAs with gadobutrol as imperfect bolus timing and overlying artifacts. When pooling all readers, the overall image quality ("more than adequate" and "excellent") remained rated better with gadoterate than with gadobutrol (100% vs. 85.7%). The Wald χ^2 test analysis on excellent image quality showed no statistically significant difference between contrast agents. Interreader agreement results were between 42% and 93% for gadoterate and between 57% and 86% for gadobutrol. Representative image examples with "more than adequate," respectively "excellent" image quality and diagnostic confidence, are given in the Figs. 2–4.

Secondary Criteria

Diagnostic Confidence

As shown in Table 2, the diagnostic confidence obtained was better rated with gadoterate than with gadobutrol. Diagnostic confidence was "high" or "excellent" in 100% (readers 1, 2, and 3) and 92.9% (reader 4) of patients diagnosed using gadoterate-enhanced MRA compared with 92.9% (readers 1 and 2) and 85.7% (readers 3 and 4) using gadobutrol-enhanced MRA. All of the readers assessed between 7% and 15% of the images rated as "moderate" using gadobutrol, and from 0%–7.1% for gadoterate. When pooling all readers, the excellent diagnostic confidence remained rated better with gadoterate than with gadobutrol without any statistically significant difference (53.6% vs. 48.2%, $P = 0.48$). The Wald χ^2 test analysis on excellent diagnostic confidence showed that no statistically significant difference between contrast agents was observed except for reader 1 ($P = 0.01$).

Visualization of Collateral Circulation

As shown in Table 3, the collateral circulation was visualized in 100% (readers 1 and 3), 85.7% (reader 2), and 78.6% (reader 4) of patients diagnosed using gadoterate-enhanced MRA compared with 100% (readers 1 and 2) and 92.9% (readers 3 and 4) using gadobutrol-enhanced MRA.

Pedal Vessel and Smaller Branches in the Foot Territory Assessment

Assessment of the pedal vessels was rated as "more than adequate" or "excellent" in 100% (reader 3), 92.9% (reader 1), 85.7% (reader 4), and 28.6% (reader 2) of patients diagnosed using gadoterate-enhanced MRA compared with 92.9% (reader 3), 85.8% (reader 4), 62.3% (reader 1), and 42.9% (reader 2) using gadobutrol-enhanced MRA (Table 2). The Wald χ^2 test analysis on excellent assessment showed no statistically significant difference between contrast agents ($P > 0.05$).

Venous Overlap That Interfered With Arterial Visualization Assessment

Venous overlay was "partially seen" or "not seen" in 100% (readers 1, 2, and 4) and 92.8% (reader 3) of patients diagnosed using gadoterate-enhanced MRA compared with 100% (readers 2, 3, and 4) and 85.7% (reader 1) using gadobutrol-enhanced MRA. The results from individual readers are given in Table 3.

*Overall Evaluable Segments (*n = *294) and Depiction of Stenosis*

Rates of evaluable segments were 95.6% (reader 1), 93.9% (reader 2), 96.3% (reader 3), and 97.6% (reader

Table 2
Results of the Imaging Evaluation: Image Quality / Diagnostic Confidence / Assessment of Pedal Vessels

	Image quality*				Diagnostic confidence**				Assessment of pedal vessels***			
Reader	Category	Gadoterate	Gadobutrol	Wald chi 2- test	Category	Gadoterate	Gadobutrol	Wald chi 2- test	Category	Gadoterate	Gadobutrol	Wald chi 2- test
1	Adequate	0	21.4		Moderate	0	7.1		Adequate	7.1	28.6	
	More than adequate	57.1	35.7		High	14.3	42.9		More than adequate	64.3	21.4	
	Excellent	42.9	42.9	0%; $P = 1.00$	Excellent	85.7	50.0	35.7%; $P = 0.01$	Excellent	28.6	42.9	−14.3%; $P = 0.30$
2	Adequate	0	7.1		Moderate	0	7.1		Adequate	64.3	50	
	More than adequate	50	42.9		High	64.3	57.1		More than adequate	28.6	42.9	
	Excellent	50	50	0%; $P = 1.00$	Excellent	35.7	35.7	0%; $P = 1.00$	Excellent	0	0	–
3	Adequate	0	14.3		Moderate	0	14.3		Adequate	0	7.1	
	More than adequate	28.6	21.4		High	57.1	42.9		More than adequate	57.1	64.3	
	Excellent	71.4	64.3	7.1%; $P = 0.65$	Excellent	42.9	42.9	0%; $P = 1.00$	Excellent	42.9	28.6	14.3%; $P = 0.30$
4	Adequate	0	14.3		Moderate	7.1	14.3		Adequate	14.3	14.3	
	More than adequate	21.4	21.4		High	42.9	21.4		More than adequate	50.0	42.9	
	Excellent	78.6	64.3	14.3%; $P = 0.30$	Excellent	50.0	64.3	−14.3%; $P = 0.30$	Excellent	35.7	42.9	−7.1%; $P = 0.65$
Over all readers	More than adequate/ excellent	100	85.7		Excellent	53.6	48.2	5.4%; $P = 0.48$	Excellent	26.8	28.6	−1.8%; $P = 0.80$

Note:
*in % of segments;
**in % of segments;
***assessable segments of the pedal vessel and smaller branches in the foot territory in %.

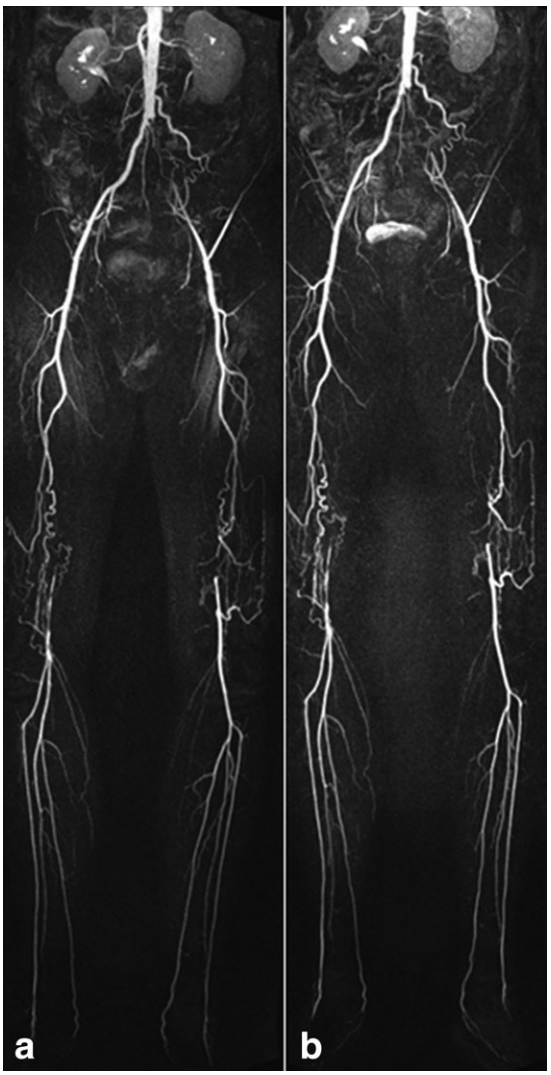

Figure 2. These maximum intensity projection (MIP) images are representative examples of one patient with PAOD affecting the pelvis and the thigh station. Prominent collateral vessels bridging the occluded left common iliac artery as well as from the profound femoral artery to the superficial femoral artery bilaterally are well depicted with both contrast agents: (**a**) gadobutrol vs. (**b**) gadoterate.

4) for patients diagnosed using gadoterate-enhanced MRA compared with 94.2% (reader 1), 94.9% (reader 2), 95.2% (reader 3), and 96.9% (reader 4) for patients using gadobutrol-enhanced MRA. When pooling all readers, the Wald χ^2 test analysis showed that no statistically significant difference ($P = 0.58$) between contrast agents was observed for the number of evaluable segments. Figure 5 shows the overall depiction of stenosis in percent of all assessed segments given for each reader. The results were comparable between gadoterate and gadobutrol for each reader. Significant stenoses (>50%) compared to the overall depicted stenoses were noted in 37.1% with gadoterate vs. 43.9% with gadobutrol for reader 1 ($P = 0.04$), 53.8% vs. 45.0% for reader 2 ($P = 0.53$), 41.9% vs. 46.2% for reader 3 ($P = 0.17$), 54.4% vs. 48.7% for reader 4 ($P = 0.41$). When pooling all readers, no statistical significance between contrast agents was observed (45.8% with gadoterate vs. 46.2% with gadobutrol, $P = 0.81$).

SNR and CNR

The SNR is shown in Fig. 6. The overall SNR detected was high with both contrast agents but slightly higher with gadobutrol. The SNR was 22.7 ± 10.3 with gadoterate and 26.1 ± 10.5 with gadobutrol ($\Delta = -3.4$, $P = 0.01$). The CNR was 20.2 ± 9.7 with gadoterate and 23.4 ± 9.9 with gadobutrol ($\Delta = -3.2$, $P = 0.01$).

Safety Results

There were no reported adverse events and no injection site reactions during this study.

DISCUSSION

Our study was a realistic, pragmatic approach designed to compare the impact of the macrocyclic paramagnetic gadolinium chelates gadobutrol and gadoterate on image quality for the diagnosis of

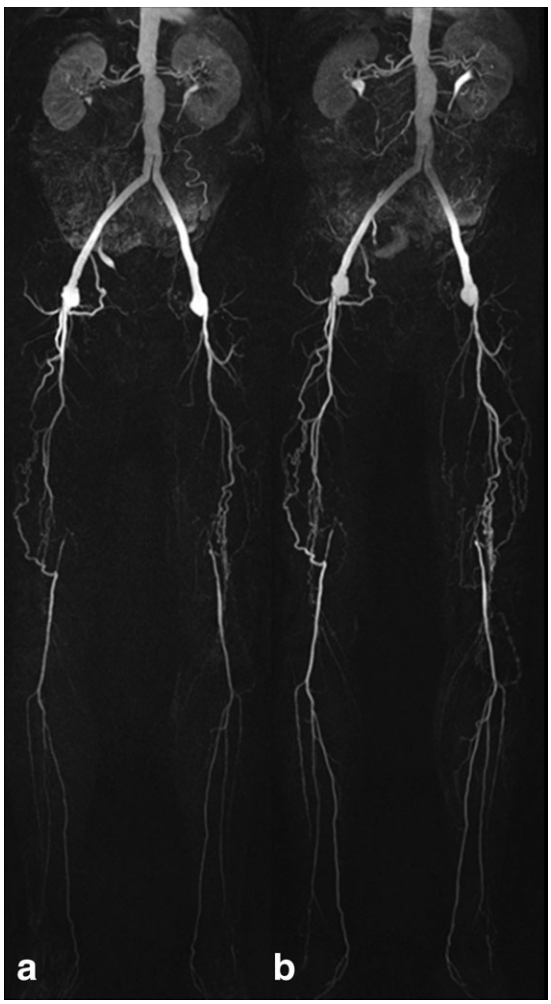

Figure 3. a: MRA with gadoterate. **b:** MRA with gadobutrol. These MIP images show a patient post aorto-bi-iliac graft with a complete bilateral occlusion of the superficial femoral. Despite the extensive PAOD affecting the pelvis and thighs, the run-off in the calves is well preserved.

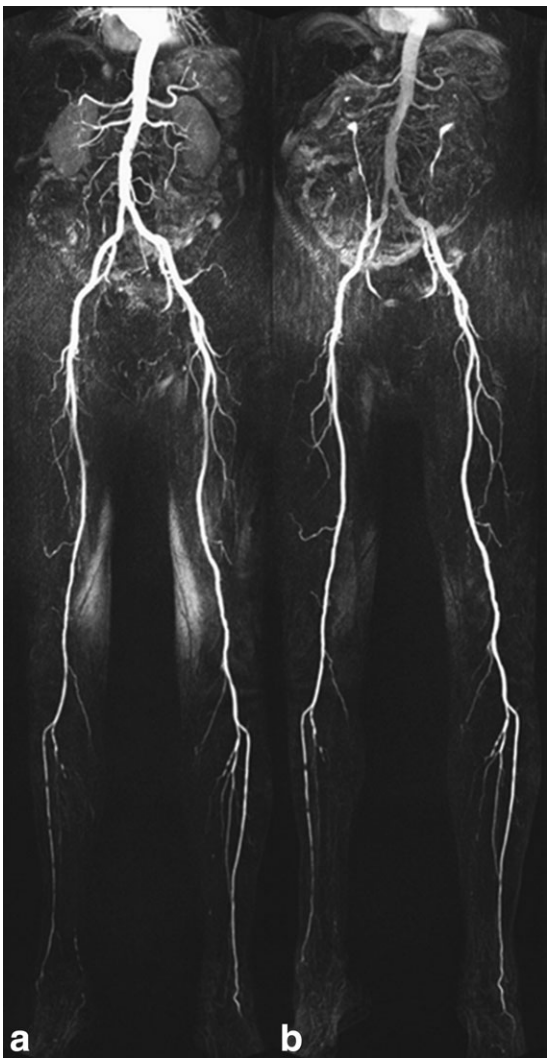

Figure 4. Both MRA (**A** gadobutrol vs. **B** gadoterate) datasets demonstrate PAOD primarily affecting the calf station where the anterior tibial artery represents the leading vessel supplying the foot. On the right side multisegmental high-grade stenoses of the anterior tibial artery can be seen.

clinically significant abdominal/lower limb arterial diseases. Our findings showed no significant advantage in terms of image quality of 1.0M gadobutrol over 0.5M gadoterate for contrast-enhanced MRA in the diagnosis of clinically significant abdominal or lower limb arterial diseases.

Our study demonstrated that the overall image quality was high for both contrast agents; however,

Table 3
Results of the Imaging Evaluation: Collateral Circulation / Venous Overlap

	Collateral circulation*		Venous overlap**	
Reader	Gadoterate	Gadobutrol	Gadoterate	Gadobutrol
1	100%	100%	100%	85.7%
2	85.7%	100%	100%	100%
3	100%	92.9%	92.8%	100%
4	78.6%	92.9%	100%	100%

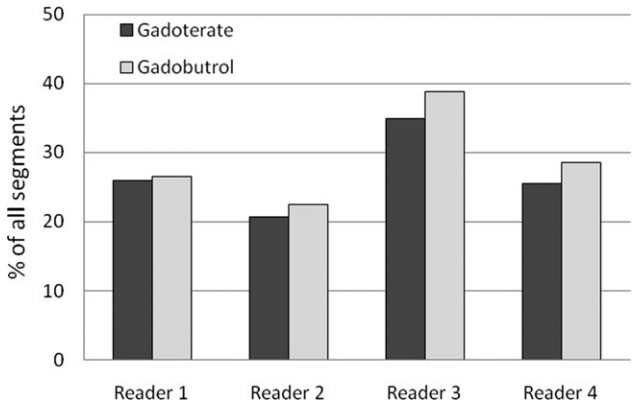

Figure 5. An overall depiction of stenoses, given as percents of the segments, split for all readers and both contrast agents. No significant differences were found.

there was a tendency for better image rating with gadoterate than with gadobutrol. All of the readers rated all images as "more than adequate" or "excellent" (100%) with gadoterate as compared to 78%–86% with gadobutrol. The same tendency was obtained for the diagnostic confidence. Reassessing the 2/14 (14%) MRAs with gadobutrol, which were rated as "adequate" in terms of overall image quality and diagnostic confidence, presented technical limitations such as imperfect bolus timing, despite the same techniques being used in all MRAs. The different levels of experience with vascular MRI might explain the differences of the ratings between the readers. These results contradict in part the results of other authors demonstrating the superiority of 1.0M gadobutrol over conventional 0.5M contrast agents (18–25), while in concordance with those of other studies (12,26). The intensity of the signal detected was high with both contrast agents; however, a significantly higher SNR/CNR was observed with gadobutrol, and although a correspondingly higher image quality and diagnostic confidence might be expected with a higher SNR/CNR, this was not found to be the case in our

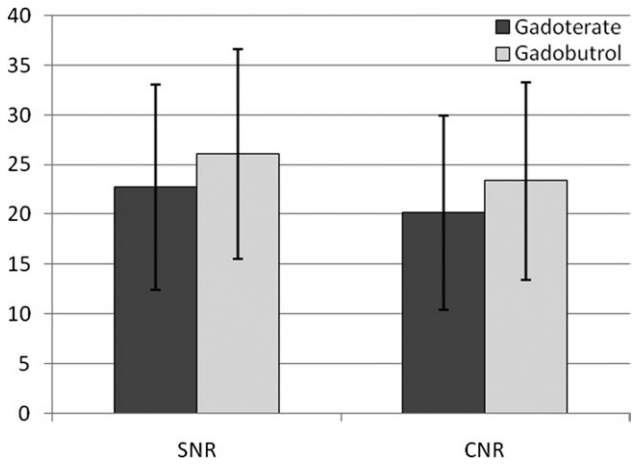

Figure 6. The SNR and CNR, split for the two contrast agents. SNR and CNR were significantly higher for gadobutrol than for gadoterate.

study. Further investigation would be needed to explain this, but this finding is in agreement with that reported by Fink et al (26), who suggested that measurable differences in SNR and CNR are irrelevant for subjectively rated image quality. Other current studies investigating the influence of the 1-molar concentration of gadobutrol on image quality concluded that due to the small amounts of contrast agent administered in MRI, higher concentration does not play such a crucial role as in computed tomography (CT), for example (27). Overall, the available data on contrast-enhanced MRA with 1.0M gadobutrol and 0.5M gadoterate yield equivocal results. Factors that might contribute to this and which were different between all the above-mentioned studies are the contrast agent dose, flow rate of the contrast agent, as well as amount and flow rate of the saline chaser.

Apart from the concentration of the contrast agents, their relaxivity is a key factor determining the SNR/CNR and thus ultimately image quality. Initial MRA studies on gadobutrol found a dramatically higher SNR with gadobutrol compared to conventional 0.5M Gd-chelates (20) at 1.5T. At 3.0T field strength, the differences in contrast media r1 relaxivities decline (28). Therefore, at 3.0T a smaller difference in SNR between gadobutrol and 0.5M contrast agents such as gadoterate can be expected. Due to the better background suppression of nonenhanced tissues at 3.0T, the vessel conspicuity is generally higher at 3.0T than at 1.5T (29). Therefore, doses of less than 0.1 mmol/kg yield diagnostic image quality as shown for gadobutrol (16) and even allow for high clinical accuracy with regard to grading of stenotic lesions in PAOD for both gadobutrol and gadoterate (30). The EMA has issued a new recommendation that recommends minimizing doses of contrast media independent of the stage of renal function (14). This current study underlines that state-of-the art MRA with a single dose of either gadobutrol or gadoterate yields robust and comparable results in patients with PAOD II and III. In particular, the EMA has subclassified MR-contrast media into high-risk, medium-risk, and low-risk agents; among the latter group comprising only macrocyclic agents, gadobutrol and gadoterate are also listed. For these agents a low risk of nephrogenic systemic fibrosis is assumed, which is underlined by various preclinical data from animal studies in which no relevant release of Gd-ions from the macrocylic chelators was found (31).

The moving table technique employed in this study was also scientifically investigated in various publications. Kramer et al (11) found the image quality and detection of stenoses equivalent to a conventional stepping table MRA. In a further study on the technical robustness and total acquisition time of the moving table MRA technique in comparison to a conventional stepping table technique, Koziel et al (13) demonstrated that 30% faster acquisitions with fewer dropouts are feasible with moving table MRA. According the latest AHA guidelines CE-MRA is considered the recommended diagnostic tool for PAOD. Significant advances in MRA imaging techniques such as higher field strengths and time-resolved 3D imaging with view-sharing techniques are not even included in these recommendations and will further strengthen the role of CE-MRA. Completely omitting the use of contrast agent and switching to nonenhanced MRA-techniques whose contrast is based on the different properties of flowing arterial and venous blood is another trend that arose with the advent of nephrogenic systemic fibrosis (32,33). Current studies confirmed that nonenhanced MRA has a high sensitivity and negative predictive value for the detection and grading of relevant arterial stenoses, with a tendency to overestimate the degree of stenosis (34,35). In those two studies the technical success rate of the nonenhanced MRA was low, with up to 40% of nondiagnostic image quality over all vessel segments. Newer 2D nonenhanced MRA techniques seem to be more robust but have acquisition times of more than 12 minutes (36). Therefore, fast and robust CE-MRA continues to be a valuable clinical tool that allows fast, robust, and accurate depiction of the lower extremity vasculature which—as shown in this study—can be achieved with single-dose gadobutrol or gadoterate.

In conclusion, MRA of the lower extremities can be acquired with high quality with a macrocyclic contrast agent, either gadobutrol or gadoterate, with a dose of 0.1mmol/kg at 3.0T. Gadobutrol yielded significantly higher SNR/CNR while gadoterate was better rated in terms of overall image quality and diagnostic confidence.

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