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Feasibility of Non-contrast-enhanced Magnetic Resonance Angiography for Imaging Upper Extremity Vasculature Prior to Vascular Access Creation

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WHAT THIS PAPER ADDS

- The present study is the first to investigate the potential of non-contrast-enhanced balanced turbo field echo (bTFE) magnetic resonance angiography (MRA) for depiction of upper extremity arteries and veins prior to vascular access creation, thereby enabling the vascular surgeon to obtain detailed information about the upper extremity vascular tree without risking the induction of nephrogenic systemic fibrosis. Non-contrast-enhanced MRA image quality is lower regarding the arterial vascular tree, while venous depiction is superior to contrast-enhanced MRA. Non-contrast-enhanced MRA is a feasible diagnostic modality in patients with end-stage renal disease who need imaging of the upper extremity vasculature prior to dialysis access creation

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ABSTRACT

Objectives: Preoperative mapping of arterial and venous anatomy helps to prevent postoperative complications after vascular access creation. The use of gadolinium in contrast-enhanced (CE) magnetic resonance angiography (MRA) has been linked to nephrogenic systemic fibrosis in patients with end-stage renal disease (ESRD). The purpose of this study was to evaluate non-contrast-enhanced (NCE) MRA for assessment of upper extremity and central vasculature and to compare it with CE-MRA.
Methods: NCE and CE-MRA images were acquired in 10 healthy volunteers and 15 patients with ESRD. In each data set, two observers analysed 11 arterial and 16 venous segments with regard to image quality (0–4), presence of artefacts (0–2) and vessel-to-background ratio.
Results: More arterial segments were depicted using CE-MRA compared to NCE-MRA (99% vs. 96%, $p = 0.001$) with mean image quality of 3.80 vs. 2.68, ($p < 0.001$) and mean vessel-to-background ratio of 6.47 vs. 4.14 ($p < 0.001$). Ninety-one percent of the venous segments were portrayed using NCE-MRA vs. 80% using CE-MRA ($p < 0.001$). Mean image quality and vessel-to-background ratio were 2.41 vs. 2.21 ($p = 0.140$) and 5.13 vs. 3.88 ($p < 0.001$), respectively.
Conclusions: Although arterial image quality and vessel-to-background ratios were lower, NCE-MRA is considered a feasible alternative to CE-MRA in patients with ESRD who need imaging of the upper extremity and central vasculature prior to dialysis access creation.

The global patient population with end-stage renal disease (ESRD) increases rapidly. Presently, the annual growth rate lies at about 8%, resulting in an estimated 7.1 million patients depending on renal replacement therapy by the year 2030.[1,2] A substantial number of these patients will be treated by haemodialysis (HD) for which a functional vascular access (VA) is mandatory.

Guidelines of the National Kidney Foundation and the Vascular Access Society as well as numerous clinical trials have emphasised

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the relevance of vascular assessment using imaging techniques prior to creation of a VA.[3,4] However, despite preoperative ultrasound evaluation, the number of complications (non-maturation, steal syndrome and cardiac failure) remains high.[5] In an effort to decrease these complications and improve long-term patency, the 'patient-specific image-based computational modelling for improvement of short- and long-term outcome of vascular access in patients on haemodialysis therapy' (ARCH) project consortium (7th Framework European collaborative project) investigates alternative preoperative imaging modalities and develops predictive models to aid clinical decision making,[6] similar to those already used in other fields of vascular surgery.[7,8]

Earlier studies of our group have established contrast-enhanced magnetic resonance angiography (CE-MRA) to be of additional value in the preoperative work-up of patients awaiting VA creation. For instance, CE-MRA may identify arterial and venous stenoses not detected by duplex ultrasonography (DUS), that are associated with VA early failure and non-maturation.[9] Furthermore, MRA enables luminal diameter measurements over the entire arterial inflow and venous outflow trajectory, including the central vessels. Therefore, a more comprehensive assessment of upper extremity vasculature can be performed, compared to selective diameter measurements when using DUS. In addition, CE-MRA facilitates extraction of complete upper extremity vascular geometry, which is desirable for patient-specific modelling. However, recently it has become clear that administration of gadolinium-based contrast agents (GBCAs) in patients with ESRD may result in the development of nephrogenic systemic fibrosis (NSF),[10,11] which is a potentially serious complication.[12]

In an effort to preserve the potential diagnostic advantages of preoperative MRA in patients with ESRD, we developed a non-contrast enhanced (NCE) MRA technique for the upper extremity based on a modified balanced turbo field echo (bTFE) sequence introduced by Gjesdal et al.[13] The purpose of this study was to assess the feasibility of this NCE-MRA technique and to compare objective and subjective image quality with CE-MRA, which served as the standard of reference.

Materials and Methods

The current study was performed as part of the ARCH project (ICT-224390). For the complete clinical study protocol, the reader is referred to Bode et al.[6]

Study population

For evaluation of upper extremity vasculature NCE-MRA was compared to CE-MRA in 10 healthy subjects (five female, five male, mean age (±SD): 26.2 (±4.2) years) without any known cardiovascular disease or diabetes mellitus. After having established the initial feasibility of the technique in the healthy subjects, 15 patients with ESRD (seven female, eight male, mean age (±SD): 61.5 (±15.9) years, mean eGRF[14] (±SD): 9.3 (±4.0) ml min^{-1}) awaiting their first VA creation were enrolled.

A random upper extremity was imaged in the healthy subjects while in patients the extremity was chosen in which the preoperative duplex examination was performed. The study was approved by the local medical ethical committee. After explanation of the potential risks and benefits (including NSF), written informed consent was obtained from all individuals and patients prior to enrolment in the study.

MR imaging technique

All MR acquisitions were performed with a clinically available 1.5T MR scanner (Gyroscan Intera, software release 11.3.1, Philips Medical Systems, Best, The Netherlands) using the Synergy Flex-L surface coil for the distal upper extremity and the Synergy Body coil for the proximal upper extremity and chest acquisitions. The subject was put in a semi-oblique supine position with an intravenous (IV) needle in the contralateral dorsum of the hand.

The vasculature in the distal upper extremity was always imaged first, followed by the proximal upper extremity and the chest. In each station, first the NCE-MRA sequence was performed, followed by the CE-MRA acquisition.

NCE-MRA

For NCE-MRA acquisitions, a modified version of the bTFE sequence as described by Gjesdal et al. was used,[13] which produces images with increased signal from fluid, analogous to T2-weighted sequences, along with retaining T1-weighted tissue contrast. Detailed image parameters are listed in Table 1.

CE-MRA

CE-MRA acquisition consisted of dynamic, multiphasic T1-weighted gradient recalled echo sequences of the distal upper extremity (first acquisition), followed by the proximal upper extremity and the chest (second acquisition). A macrocyclic contrast agent (Gadovist, BayerSchering Pharma, Berlin, Germany), for which no unconfounded cases of NSF have been reported in patients with renal failure, was administered via a contralateral intravenous cannula. Contrast medium was diluted using saline in a 1:1 ratio (10 ml Gadovist and 10 ml saline) and administered in two separate injections of 10 ml each for the distal and proximal acquisitions, respectively.

Table 1
Sequence parameters of NCE-MRA and CE-MRA.

	NCE-MRA			CE-MRA	
	Central	Proximal	Distal	Proximal	Distal
Repetition time (ms)	4.5	5.6	5.8	5.4	5.4
Echo time (ms)	2.2	2.8	2.9	1.61	1.55
Flip angle (degrees)	90	90	90	40	40
Number of stacks	1	2	2	1	1
Field of view (mm)	300	175	175	430	325
Rectangular field of view (%)	65	65	55	85	25
Matrix (scan/reconstruction)	244/384	224/512	224/512	432/512	432/512
Number of slices	125	120	120	90	125
Slice thickness (mm)	0.79	0.79	0.79	1.25	0.84
Acquired voxel size (mm)	1.34 × 0.84 × 0.78	0.78 × 0.78 × 0.79	0.78 × 0.78 × 0.79	1.00 × 1.81 × 2.50	0.75 × 1.38 × 1.68
Reconstructed voxel size (mm)	0.78 × 0.78 × 0.78	0.34 × 0.34 × 0.79	0.34 × 0.34 × 0.79	0.84 × 0.84 × 1.25	0.63 × 0.63 × 0.84
Scan duration (min)	4:45	5:48	4:54	1:52	0:45
Number of phases acquired	1	1	1	4	4

As advocated by recent guidelines, patients already dependent on HD therapy were scheduled to undergo a complete 4-h dialysis session directly after the MR acquisition, followed by regular dialysis sessions 2 and 4 days later.[15–17] The relevance of these recommendations is underscored by the study of Prince et al.[18] who identified a decreased risk for the development of NSF in patients in whom a non-macrocyclic GBCA was administered with an estimated glomerular filtration rate (eGFR) lower than 15 ml min^{-1} and who underwent post-procedural HD. All patients were monitored for symptoms related to NSF at regular intervals: in HD patients, a physical examination was performed every week, while predialysis patients were examined every 6 weeks during regular follow-up of their residual renal function.

MR image analysis protocol

The obtained data sets were reviewed by two experienced radiologists (NP and TL with 8 and 15 years of experience in reading cardiovascular MR images, respectively) in a blinded fashion. For both NCE-MRA and CE-MRA, both reviewers evaluated all source images and had the possibility to create maximum intensity projections (MIPs) and multi-planar reformations (MPRs).

The upper extremity vascular tree was divided into 11 arterial and 16 venous segments (Fig. 1), which were assessed for image quality and artefacts as described in Table 2. In addition, vessel-to-background contrast was calculated for the main arteries and veins in the upper extremity by a single observer by measuring signal

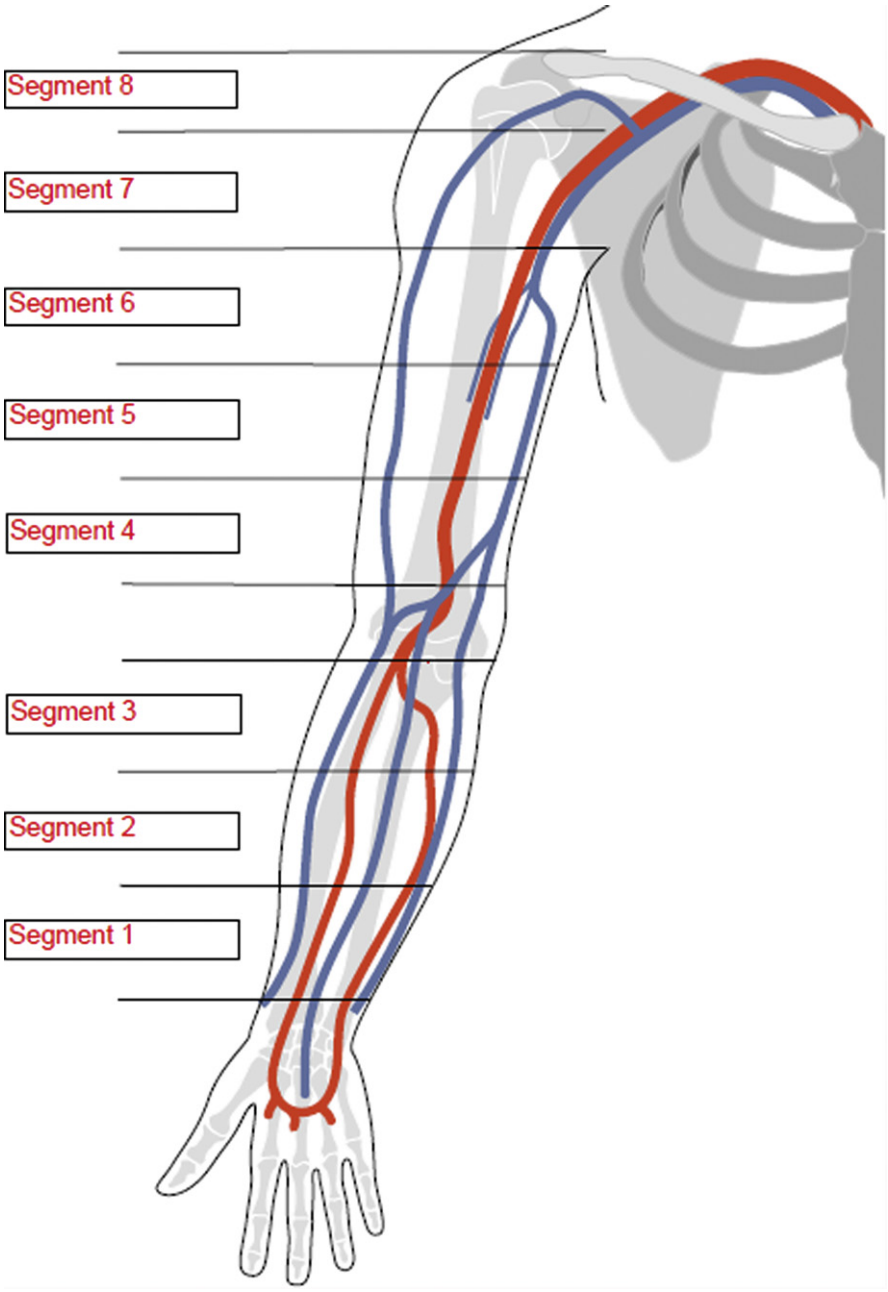

Figure 1. Segmentation of the vascular tree for image analysis: The following segments were evaluated in the distal upper extremity: proximal, middle and distal segments of the radial artery, ulnar artery, cephalic vein and basilic vein. In the proximal upper extremity and chest, the following segments were evaluated: proximal, middle and distal segments of the brachial artery, cephalic vein and basilic vein and proximal and distal segments of the subclavian artery, cephalic vein and subclavian vein.

Table 2
Subjective parameters for image analysis.

Assessment	Score
Image Quality	Score 0: Not assessable; vessels not visible or diagnostic information not obtained Score 1: Poor; vessels visible but suboptimally depicted due to incomplete filling, blurring or other artefacts Score 2: Moderate; vessels visible with low signal intensity but the complete course identifiable despite artefacts Score 3: Good; vessels visible with high signal intensity with minimal artefacts Score 4: Excellent; vessels visible with high signal intensity without artefacts
Artefacts	Score 0: None
Flow artefacts	Score 1: Minor artefacts, not hampering image interpretation
Black-banding artefacts	Score 2: Major artefacts hampering image interpretation
Compression artefacts	

intensity within the lumen of the vessel segment and dividing this value by the standard deviation of signal intensity of muscle adjacent to the lumen.

Subsequently, the presence of stenoses and occlusions was evaluated with both techniques. A five-point ordinal scale was used for grading: 0 for 0–19% stenosis, 1 for 20–49% stenosis, 2 for 50–74% stenosis, 3 for 75–99% stenosis and 4 for occlusion.[19] The degree of stenosis was calculated by dividing the smallest in-plane diameter of the vessel at the site of the stenosis by the diameter of the closest normal-appearing vessel segment. A stenosis grade of 50% or more was considered haemodynamically significant. The potential of NCE-MRA for detection of stenosis was compared to CE-MRA, which was used as the standard of reference.

Statistical analysis

The total number of visible segments as well as the mean artefact score and vessel-to-background values in healthy volunteers and ESRD patients were compared using the non-parametric McNemar and Wilcoxon signed ranks tests for paired samples. Interobserver agreement regarding diagnostic image quality (image quality ≥ 2) was assessed by the Cohen κ test ($\kappa < 0$ indicating no agreement and 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial and 0.81–1 as almost perfect agreement).[20] In all statistical analyses, p values <0.05 were considered to be statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 17.0.0 (SPSS Inc, Chicago, IL, USA) for Windows (Microsoft, Redmond, WA, USA).

Results

All CE-MRA and NCE-MRA examinations were performed successfully. No side effects after administration of GBCA were noted. None of the patients developed any symptoms of NSF (mean follow-up: 586 ± 100 days).

Healthy subjects

Results of objective and subjective image quality are listed in Table 3A. Typical examples of CE-MRA and NCE-MRA acquisitions are shown in Figs. 2 and 3. For the arterial vascular tree, CE-MRA resulted in superior image quality and less artefacts due to flow or magnetic field inhomogeneity, compared to NCE-MRA. In addition, CE-MRA resulted in a better vessel-to-background ratio when compared to NCE-MRA. On the other hand, for the venous system, NCE-MRA resulted in visualisation of more vessel segments, better image quality and higher vessel-to-background ratio compared to CE-MRA. However, NCE-MRA examinations were prone to more flow- and magnetic field inhomogeneity artefacts. In healthy volunteers, there was moderate interobserver agreement regarding the determination of diagnostic image quality in NCE-MRA and CE-MRA sequences. Kappa values were 0.50 and 0.58, for NCE-MRA and CE-MRA, respectively.

Patients

In the ESRD patient population we found superior arterial depiction with CE-MRA compared to NCE-MRA, as well as less artefacts related to flow or magnetic field inhomogeneity. On the other hand, more venous segments were visualised using NCE-MRA. Image quality for veins was comparable with the two sequences (Table 3B). Flow- and black-banding artefacts were not present in the CE-MRA images. There was moderate interobserver agreement regarding the determination of diagnostic image quality in NCE-MRA ($\kappa = 0.51$) and a good interobserver agreement in CE-MRA ($\kappa = 0.64$).

Blinded review of the CE-MRA and NCE-MRA data sets resulted in the identification of six low-grade stenoses (grade 0 and I) in the subclavian artery (2), the radial artery (3) and the ulnar artery (1) using CE-MRA, and three low-grade stenosis in the subclavian artery (1) and the radial artery (2) with NCE-MRA. Two out of three stenoses identified with NCE-MRA corresponded with CE-MRA findings. In one case, irregularities in the subclavian artery as seen with NCE-MRA were not seen with CE-MRA. Conversely, at CE-MRA four non-significant stenoses were visualised which were classified as normal with NCE-MRA. None of these stenoses were depicted in the preoperative DUS examination.

Table 3A
Results in healthy volunteers ($N = 10$).

	Observer	Arterial vascular tree			Venous vascular tree		
		NCE-MRA	CE-MRA	*P*-value	NCE-MRA	CE-MRA	*P*-value
Visible segments with image quality > 0 (%)	1	107/110 (97)	110/110 (100)	NA	150/155 (97)	125/155 (81)	<0.001
	2	108/110 (98)	110/110 (100)	NA	150/155 (97)	131/155 (85)	<0.001
Image Quality (0–4)	1	3.19 (±0.94)	3.99 (±0.10)	<0.001	2.86 (±1.22)	2.44 (±1.60)	0.003
	2	3.38 (±0.82)	3.95 (±0.27)	<0.001	2.90 (±1.13)	2.14 (±1.31)	<0.001
Flow artefacts (0–2)	1	0.49 (±0.80)	0.11 (±0.65)	<0.001	0.49 (±0.72)	0.13 (±0.62)	0.002
	2	0.41 (±0.60)	0.07 (±0.54)	<0.001	0.43 (±0.65)	0.16 (±0.63)	<0.001
Magnetic field inhomogeneities artefacts (0–2)	1	0.10 (±0.39)	0.00 (±0.00)	0.009	0.20 (±0.56)	0.00 (±0.00)	0.004
	2	0.10 (±0.30)	0.00 (±0.00)	0.001	0.31 (±0.59)	0.00 (±0.00)	<0.001
Compression artefacts (0–2)	1	0.01 (±0.10)	0.00 (±0.00)	0.317	0.23 (±0.62)	0.33 (±0.72)	0.380
	2	0.00 (±0.00)	0.00 (±0.00)	1.000	0.28 (±0.68)	0.32 (±0.69)	0.083
Vessel-to-background ratio		4.55 (±1.36)	6.01 (±2.39)	0.001	5.41 (±2.00)	4.53 (±2.82)	0.012

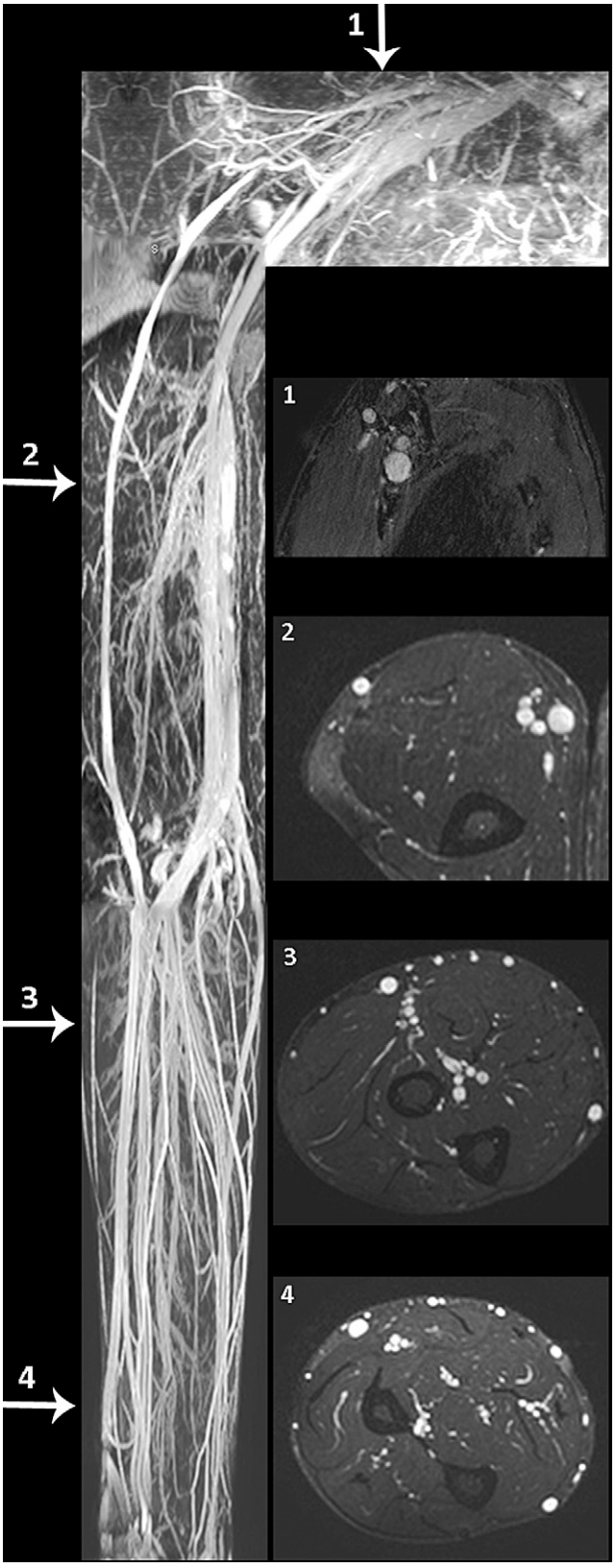

Figure 2. Composite whole volume maximum intensity projection of typical NCE-MRA acquisition with corresponding cross-sectional reformations; 1) central vessels, 2) upper arm, 3–4) lower arm. Despite both arteries and veins being depicted in the NCE-MRA data set, arteries and veins can easily be differentiated in the axial source images because of the high spatial resolution. Note high signal intensity due to presence of synovial fluid.

Discussion

In this study, we found that upper extremity vasculature can be depicted relatively adequately using bTFE NCE-MRA. Nevertheless, with the described image protocol, CE-MRA remains superior in terms of total number of visible arterial segments and overall image quality. However, NCE-MRA was of diagnostic quality (image quality $\geq$ 2) in the vast majority arterial segments (82%). For depiction of venous structures, on the other hand, we found NCE-MRA to be superior to dynamic CE-MRA because of the high intrinsic vessel-to-background contrast, regardless of the presence of contrast material.

In clinical routine, DUS is the method of choice in the preoperative work-up of patients with ESRD. DUS is a highly valuable imaging modality and its use has been associated with significant reductions in postoperative access-related complications.[21,22] Nevertheless, postoperative access failure rates remain unacceptably high,[5] which has sparked the search for alternative techniques of preoperative assessment. Prior work by our group found CE-MRA to yield additional insights in vascular geometry, vascular dimensions and the presence of pathology, particularly on locations where DUS examination lacks diagnostic accuracy (e.g., the central arteries and veins). Moreover, MRA enables time-efficient interrogation of the entire upper extremity vascular tree, instead of just several discrete locations. The present study was motivated because there is a paucity of data on the clinical feasibility and accuracy of novel NCE-MRA techniques for evaluation of upper extremity vasculature.

Unlike the lower extremity, reports on NCE-MRA protocols for depiction of upper extremity vasculature are scarce, particularly in patients awaiting VA creation. Most of these publications deal with either outdated NCE techniques suffering from major artefacts, limited field of views (FOVs) and long acquisition times.[23–25] Although local venous anatomy could be identified, more proximal and central vessels could not be depicted because of limited surface coil coverage and difficulties in patient positioning.

The recently described lower extremity NCE-MRA protocol of Gjesdal and collegues[13] was adapted in such a way that it facilitated depiction of the upper extremity vascular tree. Despite the excellent results in the lower extremities, we found our sequence to be prone to artefacts, as was reflected in lower image quality and higher artefact scores. Most likely, this is induced by the off-centre positioning of the upper extremity inside the bore of the MR, where magnetic field inhomogeneities are more pronounced.[26] Nevertheless, diagnostic images were obtained in the vast majority of subjects.

In the patient population, six low-grade stenoses (grade 0 and I) were detected using CE-MRA compared to three low-grade stenoses with NCE-MRA. In the three remaining cases, the narrowings were not seen with NCE-MRA. Although these stenoses were not haemodynamically significant, they were not found in the preoperative DUS examination, emphasising the potential additional value of obtaining complete vascular geometry for diameter measurements over the complete arterial and venous vascular tree. In this limited sample, both MRA techniques excluded the presence of significant (>50% luminal narrowing) stenoses, thus confirming findings at DUS. The most likely explanation for the minor mismatches is the better spatial resolution of the NCE-MRA data, which is less prone to partial volume effects. Our results reflect those of Gupta et al. who found that bTFE is capable of accurately detecting stenoses.[27]

What is the potential additional value of MRA in clinical practice considering the higher costs and lower availability in the era of widespread DUS usage? With regard to the current results, we hypothesise that routine preoperative assessment using the described NCE-MRA sequence is potentially beneficial in all patients prior to dialysis access creation because vascular

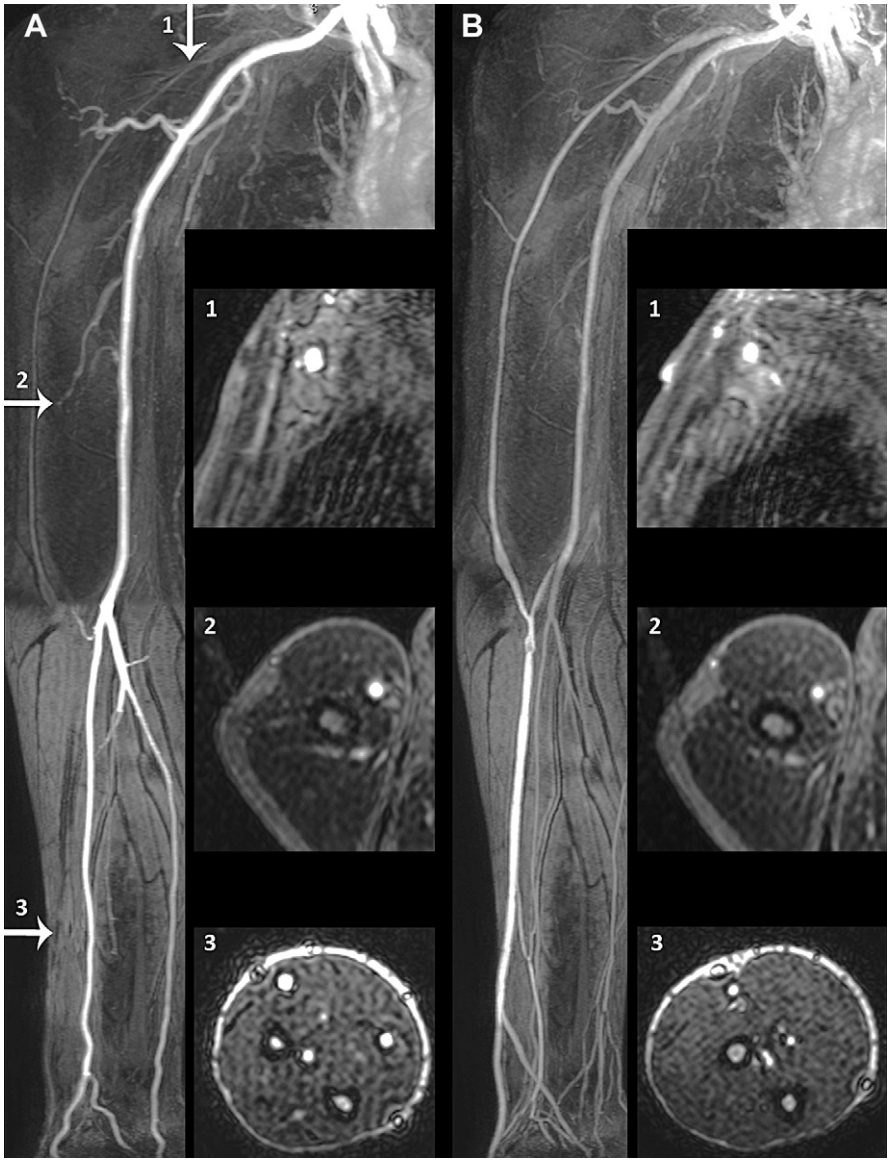

Figure 3. Composite whole volume maximum intensity projection of typical CE-MRA acquisition in arterial phase (A) and venous phase (B) with corresponding cross-sectional reformations.

pathology overlooked with DUS may be identified and anticipated on, and non-invasive extraction of vascular geometry for patient-specific computational modelling becomes feasible. Nonetheless, until its clinical relevancy has been established in a large clinical trial, NCE-MRA should always be performed as a supplementary examination to DUS and, therefore, will result in additional costs in the preoperative work-up. To what extent these additional costs may be compensated by a reduction in the management costs of

Table 3B
Results in ESRD patients ($N = 15$).

	Observer	Arterial vascular tree			Venous vascular tree		
		NCE-MRA	CE-MRA	*P*-value	NCE-MRA	CE-MRA	*P*-value
Visible segments with image quality > 0 (%)	1	157/165 (95)	163/165 (99)	0.109	219/240 (91)	197/240 (82)	<0.001
	2	154/165 (93)	164/165 (99)	0.006	198/240 (83)	180/240 (75)	0.015
Image Quality (0–4)	1	2.25 (±0.97)	3.53 (±0.69)	<0.001	2.19 (±1.16)	2.22 (±1.40)	0.701
	2	2.30 (±1.12)	3.81 (±0.55)	<0.001	2.01 (±1.35)	2.09 (±1.53)	0.358
Flow artefacts (0–2)	1	0.34 (±0.59)	0.00 (±0.00)	<0.001	0.29 (±0.54)	0.07 (±0.34)	<0.001
	2	0.31 (±0.94)	0.00 (±0.00)	<0.001	0.30 (±0.57)	0.04 (±0.24)	<0.001
Magnetic field inhomogeneities artefacts (0–2)	1	0.59 (±0.77)	0.04 (±0.19)	<0.001	0.57 (±0.80)	0.05 (±0.25)	<0.001
	2	0.59 (±0.86)	0.00 (±0.00)	<0.001	0.53 (±0.84)	0.00 (±0.00)	<0.001
Compression artefacts (0–2)	1	0.02 (±0.13)	0.00 (±0.00)	0.083	0.15 (±0.48)	0.17 (±0.54)	0.444
	2	0.01 (±0.16)	0.01 (±0.08)	0.655	0.21 (±0.59)	0.33 (±0.72)	0.001
Vessel-to-background ratio		3.87 (±3.67)	6.77 (±3.56)	<0.001	4.93 (±3.20)	3.42 (±1.47)	<0.001

postoperative complications needs to be elucidated in further studies. For that reason, one might argue to perform NCE-MRA only in patients with a high probability of vascular pathology or post-operative fistula dysfunction (e.g., patients with marginal duplex findings, patients with multiple previous failures or patients with multiple previous CVC's).

This study has limitations. First, we compared high spatial resolution NCE-MRA images with slightly lower resolution CE-MRA images. This discrepancy was unavoidable because both the arterial and venous systems needed to be depicted with a limited dose of non-bloodpool macrocyclic contrast agent. Because of the difference in voxel size between CE-MRA and NCE-MRA, we did not compare vascular diameter measurements between the two techniques. Nonetheless, we believe that NCE-MRA images can be used for accurate appraisal of vascular diameters due to the high spatial resolution, bearing in mind our prior study which found lower spatial resolution CE-MRA diameter assessment to correspond reasonably well with DUS assessment and intra-operative measurements.[28] Second, acquisition of distal, proximal and central stations required repositioning of the patient using multiple surface coils. Future work should be aimed at the 'real world' value of an NCE-acquisition of the complete upper extremity, preferably within a single acquisition using large coverage coils in combination with continuously moving table techniques.[29] Furthermore, there was no comparison with intra-arterial digital subtraction angiography, which is the established reference standard with the highest spatial resolution. Finally, we have not investigated the impact of NCE-MRA on clinical outcome, but this was not the objective of this study.

In conclusion, we have demonstrated that bTFE NCE-MRA is a feasible alternative to CE-MRA for depiction of upper extremity vasculature. NCE-MRA has the potential to also provide valuable complementary information to CE-MRA. Future studies are needed to investigate the value of NCE-MRA prior to VA creation and the potential of patient-specific modelling using patient-specific geometry obtained by NCE-MRA.

Conflict of Interest

None.

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