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Prospective Comparison of CAPR MRA with CTA for Evaluation of Below the Knee Runoff

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Abstract

Purpose—To prospectively compare the assessment of stenosis and radiologist confidence in the evaluation of below the knee lower extremity runoff vessels between computed tomographic angiography (CTA) and contrast enhanced magnetic resonance angiography (MRA) in a cohort of 19 clinical patients.

Materials and Methods—Our study was HIPAA compliant and IRB-approved. 19 consecutive patients with known or suspected peripheral arterial disease were imaged with both CTA and a recently developed MRA technique performed within 24 hours of each other and prior to any therapeutic intervention. Resulting images were randomized and interpreted in blinded fashion by four board certified radiologists with expertise in CTA and MRA. Vasculature of the lower leg was apportioned into 22 segments, 11 for each leg. For each segment, degree of stenosis and confidence of diagnosis were each determined using a three-point scale. Differences between CTA and MRA were assessed for significance using pooled histograms which were analyzed using the Wilcoxon signed rank test.

Results—For assessment of stenosis, there was no difference in CTA vs. MRA for 20/22 segments. For confidence of diagnosis, assessment of popliteal arteries was superior on CTA compared to MRA ($p < 0.05$). Confidence in assessment of both tibioperoneal trunks and the left proximal anterior tibial artery was not significantly different between CTA and MRA. Confidence in assessment of all other 17 segments was superior with MRA than CTA ($p < 0.02$).

Conclusion—MRA using the method described here is a promising technique for evaluating lower extremity arterial runoff. MRA had an overall superior performance in radiologist confidence when compared to CTA for imaging runoff vessels below the knee.

Introduction

Contrast enhanced magnetic resonance angiography (MRA) and computed tomographic angiography (CTA) are widely used for noninvasive evaluation of lower extremity arterial vasculature (1-4). With current routine MRA methods the image acquisition time used for imaging the runoff vessels generally extends over and beyond the arterial phase of the

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Two of the authors (CRH, SJR) have filed a patent application on MRI coil technology described herein. None of the other authors has a conflict of interest.

contrast bolus, typically several tens of seconds long. There is a tradeoff in how this time can be used, either for forming a single 3D image with very high spatial resolution or in apportioning the time into multiple, time-resolved 3D images which have reduced spatial resolution (5). Also, with time-resolved studies the possibility of a non-diagnostic study secondary to bolus mis-timing to the distal lower extremities is essentially eliminated. Recently several authors such as (6-8) have demonstrated that parallel acquisition techniques such as 2D Sensitivity Encoding (SENSE) (9) and Generalized Autocalibrating Partially Parallel Acquisition (GRAPPA) (10) can be incorporated into time-resolved MRA acquisition of the lower extremities. This approach typically results in excellent image quality and correlation to conventional angiography, although to date these techniques typically obtain lower spatial resolution datasets than CT.

Because CTA and MRA techniques both have potential advantages and disadvantages, the best choice of exam for a specific patient with suspected peripheral vascular disease is not entirely clear. Unfortunately, there is little data prospectively comparing the efficacy and accuracy of CTA with MRA exams performed using state-of-the-art techniques, particularly for assessment of distal runoff vessels which can be important to evaluate when determining therapeutic options in patients with critical limb ischemia.

Recently an MRA technique has been developed – Cartesian Acquisition with Projection-like Reconstruction (CAPR) - in order to generate high spatial and temporal resolution time-resolved MRA images. (11-13) The high acceleration provided by 2D SENSE and partial Fourier acceleration, as allowed by the specialized receiver coils, enables imaging the distal runoff vessels with 1 mm isotropic spatial resolution and a frame time of 4.9 sec, and has been shown to provide high fidelity in imaging an advancing contrast bolus. (14) Initial implementation has demonstrated that this technique can be successfully employed to evaluate lower extremity arterial vasculature (12). In this current work we sought to prospectively compare the degree of stenosis assessed by CAPR and CTA, as well as the confidence of the radiologist when evaluating patients with known or suspected peripheral vascular disease with both CAPR and CTA exams performed at our institution. The end goal was to establish whether the technical developments achieved in CAPR MRA would translate into a clinical tool which compared favorably to our current standard clinical approach in terms of stenosis assessment and radiologist confidence in assessing runoff vessels in the calf.

Materials and Methods

This prospective study was HIPAA compliant and approved by the institutional review board, and all subjects signed informed consent prior to enrollment. From March 2009 to December 2009, subjects with known or suspected peripheral vascular disease who were clinically referred for imaging with CTA were also recruited as subjects for CAPR MRA, and no patients were excluded from recruitment as subjects. Both exams were performed within 24 hours of each other and prior to any therapeutic intervention. The patients all were clinically referred first to CTA and recruited for the MRA without respect to clinical factors. All subjects had a creatinine clearance calculated within seven days of the exam, and in all cases the eGFR was >30 mL/min/1.73m² according to the MDRD formula (15). A total of 47 potential participants met inclusion criteria and were approached for participation, and 19 consented to participation. Mean patient age was 65.8 years (range 47-85), with 7 females and 12 males. Risk factors for vascular disease included current or former heavy smoking in 13/19, hypertension in 10/19, and type 2 diabetes mellitus in 3/19.

The CTA technique was performed according to our current standard clinical practice. It employed a 64-detector row scanner (Definition, Siemens, Erlangen, Germany) with

injection of 145 mL iodinated contrast (Iohexol, Omnipaque 350: GE Healthcare, Waukesha, Wisconsin, USA) 25 mL at 5 ml/sec and 120 ml at 4 ml/sec, followed by 30 ml of saline at 4 ml/sec. The CT examination covered from 4 cm above the iliac crest to the bottom of the feet. Parameters included 0.5 sec rotation time, pitch 0.8, 15 mm/rotation, 120 kVp, 250 mAs. Automated triggering and exposure control were employed. CT spatial resolution was $0.6 \times 0.6 \times 2.0 \text{ mm}^3$. The table speed was 30 mm/sec. A second run was immediately performed after the first run from the knees to the toes in order to minimize the chance of missing the contrast bolus due to inflow disease – this is our standard clinical practice.

CAPR MRA followed a previously described technique: 20 mL gadobenate dimeglumine (Multihance, Bracco Imaging, Princeton, New Jersey, USA) injected at 3 ml/sec followed by 20 ml saline at 3 ml/sec (12). Imaging was performed on a 3T scanner (Signa v. 20.0, GE Healthcare, Waukesha, Wisconsin, USA) using a custom eight-element receive array coil designed in-house (13). At the time, gadobenate was the highest relaxivity agent available on formulary at our institution. The MRA sequence was a 3D gradient recalled echo sequence, TR/TE = 5.85/2.7 msec, flip angle 30° , bandwidth = $\pm 62.5 \text{ KHz}$, field of view 40 (superior/inferior) $\times$ 32 (left/right) $\times$ 13.2 (anterior/posterior) cm^3 , 2D SENSE with acceleration R=8, isotropic spatial resolution of 1 mm^3 during acquisition, frame time 4.9 sec, temporal footprint 17 sec. The temporal footprint is defined as the time over which data are acquired in forming a single image of the volume. The MRA exam covered a single field of view extending from the knees to the ankles. No patients were specifically referred for inclusion in the study for CAPR MRA because of suboptimal CTA.

Four board-certified radiologists, each experienced in CT and MR, reviewed the exams independently and in blinded, randomized fashion, using either a thin client server (TeraRecon, San Mateo, California, USA) or a workstation (Advantage Windows, GE Healthcare, Waukesha, Wisconsin, USA) according to preference (both are used clinically at our institution). Although the CTA was performed prior to the MRA in all subjects, the images were reviewed in blinded and anonymized fashion rather than by the order in which they were acquired. For both CTA and MRA source images were reviewed primarily, with multiplanar reformat capabilities and targeted MIPs used adjunctively. The reviewers assessed the vessels of the calf from the knee joint to the ankle joint, and the vessels in each leg were divided into 11 segments. The popliteal artery and tibioperoneal trunk were each considered single segments, while the anterior tibial, posterior tibial, and peroneal arteries were each divided into three segments (proximal, middle, and distal thirds). The result was 11 segments in each leg for each of the 19 subjects, which were each graded by 4 readers, resulting in a total number of 1672 evaluations on each modality. The CT and MR images were graded both for stenosis and confidence of assessment. The stenoses criteria were graded as 0 (less than 50%), 1 (greater than 50% but not occluded), or 2 (occluded). These criteria were chosen because differentiating between a 50%, 70%, and 90% stenosis can be extremely difficult when imaging vessels as small as 1 mm, and the intent was to distinguish vessels which were occluded or have a potentially hemodynamically significant stenosis from those without significant stenosis. Radiologist confidence was scored as 1 (full diagnostic confidence), 2 (moderate uncertainty), or 3 (cannot be reliably assessed). Also recorded was presence or absence of calcification, and any artifacts such as might be caused by the SENSE acceleration for the MRA results.

Following evaluation, pooled histograms of the scores for each vessel segment were created and analyzed for any difference using the Wilcoxon signed rank test. The difference in the stenosis scores, CTA-MRA, was formed for each reviewer at each vessel segment. Pooled histograms of the difference in stenosis indicate whether there was greater (positive difference), equal (zero difference), or lesser (negative difference) extent of disease assessed

on CTA compared to MRA. Similarly, histograms of the difference in confidence indicate whether the readers were more (positive difference), equal, or less (negative difference) confident in the diagnosis on MRA compared to CTA. In comparing the assessment of stenosis, scores were only used in the histogram analysis if the radiologist had full confidence (confidence score = 1) in his/her interpretation of both the MRA and CTA results for that segment.

Subsequent to interpretation, the time of arrival of peak arterial contrast in the tibioperoneal trunk or first enhancing collateral artery was determined from the time-resolved MRA images by visual inspection of the time series of coronal MIPs and recorded separately for each leg in each patient (Table 1). For the MRA studies the absolute time from initiation of contrast injection to acquisition of each MRA image is known.

Results

All exams were successfully completed, with no adverse events for any subject. There was a significant disease burden in the study population: 80/418 segments (19.1%) were assessed by two or more reviewers to have a stenosis score greater than zero on both CTA and MRA. Overall, 14/19 patients (73.7%) were assessed by two or more reviewers to have a stenosis score greater than 0 in at least one segment.

Histograms of the difference in pooled stenosis scores for each vessel segment were created (Figure 1). Only scores for which the readers had full confidence (confidence score = 1) are included. The overall evaluation includes readings from 1046 of the total 1672 segments. Of these, 890 (85 %) have a difference of zero (i.e. no difference in assessment of stenosis), 55 (6%) have a positive difference or greater disease on CTA than MRA, and 101 (9%) have a negative difference or greater disease on MRA than CTA. In the evaluation of individual segments, for two segments (left proximal anterior tibial and left distal peroneal artery) MRA resulted in statistically higher stenosis scores ($p < 0.05$), but for the other 20/22 there was no significant difference in the degree of stenosis assessed by the two modalities.

Similarly, histograms of the difference in radiologist confidence scores (CTA vs. CAPR MRA) were pooled for the left and right popliteal arteries (Figure 2a). Confidence in assessment of both popliteal arteries was superior on CTA compared to MRA ($p < 0.05$). Assessment of both tibioperoneal trunks and the left proximal anterior tibial artery was not significantly different between CTA and MRA (histograms not shown). The confidence in assessment of all other 17 segments individually was superior with MRA when compared to CTA ($p < 0.02$ for proximal right anterior tibial artery, $p < 0.01$ for all 16 other segments) and in aggregate for the three segments of the three runoff vessels ($p < 0.0001$, Fig. 2b).

On CTA, 182/1672 segments (10.9%) had significant vascular calcification, and of these 141/182 calcified segments (77%) were not confidently assessed on CTA (confidence score = 3). 58/141 (41%) segments not confidently assessed on CTA were distal segments, 41/141 (29%) were middle segments, and 36/141 (26%) were proximal segments of the calf vessels. 5/141 (4%) were tibioperoneal trunks, and 1 popliteal artery was not confidently assessed on CTA. When the calcified segments were assessed with MRA, 133/141 (94%) were assessed with full diagnostic confidence, 3/141 (2%) with moderate uncertainty, and 5/141 (4%) were not confidently assessed.

On MRA, SENSE-acceleration-related artifact did not limit assessment in any segments. 25/1672 segments (1%) were not confidently assessed on CAPR. 14/25 (56%) were popliteal arteries, 5/28 were tibioperoneal trunks, and 6/25 were proximal runoff vessel segments. When assessed with CTA, 21/25 (84%) were assessed with full diagnostic

confidence, 1/25 with moderate uncertainty, and 3/25 were not confidently assessed. Representative images are shown in Figures 3-5.

There was notable variability in overall transit times, with peak opacification occurring as early as 24.5 seconds after injection in four subjects, and as late as 53.9 seconds in four subjects. Between legs in the same individual, the difference in time of contrast arrival between the two legs was greater than 10 seconds in 7/19 patients, as long as 24.5 seconds in one case.

Discussion

Compared to CTA, CAPR MRA had less than one fifth (25 vs. 141 of 1672 total) the number of arterial segments which could not be evaluated. The improved confidence of visualization seen with CAPR was evident in the three runoff vessels (anterior and posterior tibial arteries and the peroneal arteries) but not the popliteal arteries. In particular, the improved visualization with CAPR was more notable in the distal segments of the calf vessels, where issues related to calcification, bolus timing uncertainties on CTA, and diminishing contrast levels are more pronounced because of small vessel diameter and distance traveled from the location of the timing bolus in the low abdominal aorta. Although CTA had a higher overall in plane spatial resolution (and could be increased further if the axial slices were reconstructed more thinly) even very small vessels were more likely to be confidently evaluated with MRA. Conversely, CTA was superior for evaluation of the popliteal arteries – this was primarily related to signal dropoff in the MRA images in the proximal calf because of limited coil size and geometry (e.g. Figure 3). Further development in coil design will likely address this limitation, within the limits of anatomic coverage imposed by field homogeneity.

In two segments (left proximal anterior tibial and left distal peroneal) the degree of stenosis was considered more severe on MRA than CTA. This may be related to characteristics of a few specific subjects given the relatively small number of subject in this study. It is possible that MRA would be more accurate in assessing severity of stenosis in small vessels with calcification. Overall, the correlation of the two modalities was robust, with 20/22 segments showing no significant difference in the degree of stenosis assessed by either modality. For the cases in which a difference was observed, we do not have a separate metric against which to assess “accuracy” of the two modalities. However, overall radiologist confidence was higher with MRA than CTA.

Although we cannot draw generalized conclusions about which test is superior for a specific patient because of the small number of patients studied, the study does have some clinical implications. In most cases, both CTA and MRA were able to evaluate all the vessels in the calf, and over 90% of segments were well evaluated on both modalities –92% for CTA and 99% for MRA. In the cases for which CAPR MRA was superior to CTA, the major advantages were the time-resolved visualization of vessel opacification allowing confident assessment in the setting of inflow disease or rapid shunting from hyperemia, as well as the presence of calcification causing artifacts on CT which were not apparent on MR.

The higher confidence in MRA interpretation was notable in the diabetic patients. There were five subjects in the study who had three or more vessel segments which could not be evaluated by at least two readers. Three of these five were the only three subjects with diabetes mellitus. Although this is a small number of patients, it is consistent with our clinically based decision to encourage referring physicians to consider MRA as the first line test in diabetic patients or those with known significant atherosclerotic calcifications.

A recent report has indicated that CTA can be suboptimal in approximately 20% of exams and nondiagnostic in 2-3% of exams for the distal runoff vessels (16). The broad range in contrast arrival times noted in Table 1 with time-resolved MRA suggests a potential advantage of the time-resolved MRA technique in patients who have known inflow disease, or if the clinical need is to determine a distal target for potential bypass surgery. In these cases, timing of opacification is more likely to be problematic in the symptomatic leg, and distal bypass target vessels may not be well opacified at the time of imaging because of diminished inflow. In our clinical practice, we sometimes perform CAPR exams of the calves and/or feet as first-line tests in such patients, as well as for those who have had a previous nondiagnostic or limited CTA.

A limitation of the CAPR MRA technique in its current implementation is the limited anatomic coverage available, about 35 cm in the craniocaudal dimension. Although longer coverage is possible with multi-station MRA methods, unless multiple contrast injections are used these are generally not time resolved (17,18). While we only evaluated the calf vessels in this comparison due to the limited number of coil elements and receiver channels, the CTA exams obtained extended anatomic coverage from the abdominal aorta through the toes. This is a current limit to more extensive clinical implementation of the CAPR technique. Our laboratory is currently developing multistation MRA imaging with CAPR using multiple such coil arrays and real-time reconstruction to monitor contrast transit and provide interactive table advance with a goal of extending the performance of CAPR MRA to extended anatomic coverage with a single injection (19).

Another current limitation to more widespread implementation of the CAPR MRA technique as described in this work is the desirability for a fully circumferential coil array with eight or more elements. Such multi-element coil arrays for imaging of the lower extremity are not widely available at this time. However, as commercial MRI scanners have evolved to have more than eight receiver channels, multi-element receiver coils for various applications are also becoming more prevalent. Similar to MR, ongoing technical developments in CTA, including dual energy subtraction techniques and time-resolved CTA in shuttle mode may help to overcome some of the traditional limitations of CT technology, although to date visualization of distal vessels remains problematic even with these techniques (16, 20-22). Moreover, both of these methods exacerbate the issue of patient radiation exposure in CTA if the same image quality is to be retained. While these two techniques can address separate issues of calcification and bolus timing on CT, neither addresses both; time-resolved MRA on the other hand does. In any given clinical situation, there are likely to be multiple factors influencing the decision of which modality to select, including the technology available and expertise of the radiologist performing and interpreting the exam.

Our protocol employed a 20 ml bolus of gadobenate dimeglumine for time-resolved MRA; as seen in Table 1 this corresponded on average to 0.012 mmol/kg of contrast for the patients enrolled. While this is standard protocol in our clinical practice for patients without significant renal impairment, it is likely that the dose could be reduced, particularly in patients at higher risk of nephrogenic systemic fibrosis, with preservation of good image quality (23). We have reduced the dose of gadobenate in some clinical patients receiving CAPR MRA and still obtained high quality images.

In addition to the limited anatomic coverage discussed above, which is currently being addressed, this study is also limited by the small number of enrolled subjects and the lack of a true reference standard with which to independently compare CTA and MRA. We did not employ conventional angiography as a reference standard because this has largely been supplanted by noninvasive imaging at our institution, and invasive diagnostic angiography is

no longer a standard procedure for primary diagnostic imaging of lower extremity runoff in patients with claudication or critical limb ischemia. Therefore, expert radiologist confidence was studied as an endpoint, rather than comparison of both modalities against a reference standard. The limited number of included subjects also makes it impossible to make statistical analysis of subgroups (diabetics, for example) which may be particularly better served with one of the two technologies.

In conclusion, MRA using the method described here is a promising technique for evaluating popliteal and tibial arterial runoff. MRA had an overall superior performance in radiologist confidence when compared to CTA, with improvement most notable in the distal runoff vessels and in diabetic patients. MRA can overcome some of the limitations to CTA, and can be a first line technique in certain patients. Further developments in coil technology and implementation of the CAPR sequence may allow more widespread application of this technique in the future.

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Fig. 1. Histogram analysis of pooled status (stenosis) scores - Difference in status scores is presented separately for the right popliteal artery (1a) and the proximal, middle, and distal segments of the runoff vessels (1b).

Fig. 2. Histogram analysis of pooled confidence scores - Results are presented separately for the popliteal segments (2a) and the proximal, middle, and distal segments of the runoff vessels (2b). Higher confidence in CTA is indicated by higher numbers in the leftward (negative)

columns, while higher confidence in CAPR MRA is indicated by higher numbers in the rightward (positive) columns.

Fig. 3. Comparison CTA and CAPR MRA images in a 73 year old male hypertensive diabetic patient with critical ischemia of both lower extremities - (a) CTA MIP with bones removed demonstrates calcification throughout the course of the posterior tibial artery (arrow), precluding evaluation. (b) CAPR MRA demonstrates non-filling of the posterior tibial artery (arrow), confirming occlusion. Small collateral vessels from the left peroneal artery are apparent. Dropoff of coil signal is also notable proximally.

Fig. 4. Comparison images in an 83 year old male with - (a) CTA MIP with bones removed demonstrates a patent bypass graft to the left posterior tibial artery, and a patent left peroneal artery. On the right, there is moderate calcification in the tibioperoneal trunk and an occluded proximal anterior tibial artery. (b-d) Consecutive coronal MIPs from the CAPR MRA image series demonstrating retrograde filling of the left peroneal artery not apparent on CTA (arrows c, d), as well as stenosis in the tibioperoneal trunk which is more easily appreciated in the absence of calcification.

Fig. 5. Magnified images of nondiagnostic CTA and diagnostic CAPR MRA from a 52 year old man – (a) CTA is non-diagnostic because of inaccurate bolus timing resulting in low arterial contrast concentration and high venous concentration. (b) Single temporal frame from time-resolved CAPR MRA demonstrates arterial opacification without venous contamination and opacification of small collateral arterial branches in the calf.

Table 1

Patient information

			Arrival time (sec)	
Gender	Age	mmol/kg	Left leg	Right leg
M	70	0.1	34.3	29.4
M	52	0.09	34.3	34.3
M	61	0.12	39.2	39.2
F	79	0.17	34.3	29.4
M	47	0.12	24.5	24.5
F	69	0.17	24.5	39.2
M	57	0.1	39.2	53.9
M	78	0.1	53.9	29.4
F	74	0.13	29.4	34.3
M	73	0.11	34.3	34.3
F	65	0.12	34.3	49
M	83	0.09	49	53.9
M	59	0.08	53.9	34.3
M	59	0.12	29.4	39.2
F	85	0.15	44.1	24.5
M	53	0.08	24.5	29.4
F	73	0.12	29.4	34.3
F	66	0.1	34.3	39.2
M	51	0.12	34.3	53.9
Min	47	0.08	24.5	24.5
Max	85	0.17	53.9	53.9
Mean	66	0.12	35.8	37.1