Quiescent-Interval Single-Shot Magnetic Resonance Angiography

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Introduction

More than 200 million people worldwide are afflicted by peripheral arterial disease (PAD) [1, 2]. Over the last decade, the incidence of PAD has risen by approximately 13% in high-income countries and 29% in low-income countries [3]. Patients with PAD have a high 10-year risk of death of 40%, 3-fold higher risk of all cause death and 6-fold higher risk of cardiovascular-related death than patients without PAD [4]. Accurate diagnosis is thus critical for disease management and for improving patient outcomes.

The availability of accurate non-invasive imaging tests has decreased the need for preoperative digital subtraction angiography (DSA) in the evaluation of PAD. The ankle brachial index (ABI) is an excellent screening test for hemodynamically significant PAD and can be performed in conjunction with Doppler waveform analysis and segmental pressure measurement in an effort to increase accuracy [5]. However, its sensitivity is low in elderly patients and those with diabetes [6]. Moreover, additional imaging is often needed to help plan for interventional procedures. Computed tomographic angiography (CTA) offers high spatial resolution and short scan times without the risks associated with DSA [7]. For ≥50% stenosis, the reported sensitivity of peripheral CTA is on the order of 89%-100%, with specificity reported at 92%-100% [8]. However, the clinical utility of peripheral CTA is diminished by the presence of vessel wall calcifications, which are associated with diabetes, heart dis-

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**QISS* pulse sequence diagram (1A, top) and schematic of vasculature (1B, bottom) showing the effect of pulse-timings on signal manipulation to maximize arterial conspicuity. In-plane saturation and tracking venous saturation RF pulses are applied TD ~ 100 ms after the R-wave; these pulses suppress background and venous signal. Following a preset quiescent interval (QI) of 228 ms, during which unsaturated arterial blood flows into the imaging slice, a fat suppression RF pulse is applied, followed by single-shot TrueFISP readout. This process is repeated in subsequent heart-beats to acquire other slices, usually in foot-to-head direction. In the basic configuration used for survey examinations, one 3 mm-thick slice is acquired per RR interval with 1 x 1 mm in-plane spatial resolution.
ease, and advanced age [9]. CT angiography has the disadvantage of exposing patients to ionizing radiation and there is also the associated risk of contrast-induced nephropathy (CIN), which is of particular concern because nearly 40% of patients with PAD have significant renal dysfunction [10]. Contrast-enhanced magnetic resonance angiography (CEMRA) has also been shown to be highly accurate for the detection of stenoses ≥50% within the lower extremity arterial tree [11]. Unfortunately, the administration of gadolinium-based contrast agents in patients with severely impaired renal function is contraindicated due to the risk of nephrogenic systemic fibrosis (NSF) [12].

Non-enhanced MRA Techniques

Non-enhanced MRA (NEMRA, i.e. MRA without contrast agents) avoids the potential risks of NSF and CIN, as well as ionizing radiation. Two-dimensional time-of-flight NEMRA methods have been available for decades [13, 14]. However, lengthy acquisition times (typically approaching an hour or more) and image artifacts have limited their routine use in favor of contrast-enhanced techniques. Newer subtractive approaches for NEMRA of the peripheral arteries have been proposed which allow efficient depiction of arteries over large fields-of-view and suppress venous signal. These include ECG-gated subtractive 3D turbo spin echo (TSE) imaging such as fresh blood imaging (FBI) [15] and NATIVE SPACE (NATIVE = Non-contrast angiography of the arteries and veins; SPACE = Sampling perfection with application optimized contrast by using different flip angle evolution) [16], as well as variants predicated on 3D balanced steady-state free precession (bSSFP) imaging such as flow-sensitive dephasing [17]. Of these, subtractive TSE MRA techniques have the most clinical validation and are commercially available. However, subtractive TSE MRA is not robust due to its sensitivity to patient motion, pulse wave timing, and abnormal flow patterns [16].

The Quiescent-Interval Single-Shot* (QISS) NEMRA technique was developed as a safer, simple ‘push button’ non-enhanced alternative to CTA and CEMRA (Fig. 1) [18]. Moreover, QISS MRA eliminates the need for point-of-service blood draws to determine eGFR and yields significant cost savings ($180 per study at our institution) compared with CEMRA by eliminating the MR contrast agent and injector kit. QISS offers several advantages over previously described NEMRA techniques (Fig. 2) [19]. It is highly robust with minimal sensitivity to patient motion and cardiac arrhythmias. It has the particular advantage of enabling a simple and efficient workflow, thereby eliminating the need for special technologist expertise.

*QISS is pending 510(k) clearance and is not commercially available in the US.

(2A) 91-year-old smoker with bilaterally occluded superficial femoral arteries (SFA). QISS MRA (left) and CEMRA (right) appear comparable. (2B) CEMRA, QISS, and subtractive TSE MRA (Native SPACE) in a patient with PAD. Multiple ≥50% stenoses in the right anterior and posterior tibial arteries and occlusion of the left posterior tibial artery are identified on CEMRA and QISS MRA. Subtractive TSE MRA shows extensive artifactual signal dropout in the abdomen, upper pelvis and right calf. (Signal dropout in the mid-right SFA is due to a stent.) Adapted with permission from ref. 19
Clinical Validation

QISS MRA has been evaluated at field strengths ranging from 1.5 Tesla to 7 Tesla*, with the reported accuracy at 1.5 Tesla and 3 Tesla generally approaching or matching that of CEMRA.[20-26] The technique has also been specifically evaluated in a diabetic patient population in whom CTA may be problematic due to the frequent presence of vascular calcifications and poor renal function.[27] Using CEMRA as the reference standard, QISS showed excellent diagnostic performance with sensitivity of 89.8%, specificity of 96.4%, positive predictive value of 92.4%, and negative predictive value of 95.0%. An example illustrating the advantage of QISS MRA over CTA for the evaluation of diabetic PAD patients is given in Figure 3.

* MAGNETOM 7T is ongoing research. All data shown are acquired using a non-commercial system under institutional review board permission. MAGNETOM 7T is still under development and not commercially available yet. Its future availability cannot be ensured.

QISS as scout and backup for CEMRA

Currently, many sites use a multi-station, multi-planar scout acquisition to plan the volume placements for stepping table CEMRA. This procedure can be cumbersome since the full extent of the arteries is not visible on the scout images. For such situations, QISS acquisition can potentially serve as a scout image for CEMRA; although it will take longer than the regular scout, it offers more complete and detailed visualization of arterial tree for CEMRA, providing diagnostic information in case of a technical failure with CEMRA. For instance, the patient might move between the time that the pre-contrast mask images and post-contrast images are acquired, resulting in mis-registration artifact on the subtracted CEMRA images. Being a non-subtractive single shot technique with very short scan time (<1/3 second per slice), QISS is resistant to motion artifacts. Moreover, the timing for the CEMRA may be inaccurate, resulting in poor arterial opacification or venous overlap (e.g. due to asymmetric atherosclerotic disease causing slower flow on one side, or due to human error). In all these situations, QISS can be a fallback option to salvage patient exam despite non-diagnostic CEMRA (Fig. 4).

QISS at 3 Tesla

Until QISS, no NEMRA technique had proven effective at 3 Tesla, which is widely considered the optimal field strength for CEMRA. Imaging at 3 Tesla will be necessary to unlock the full clinical potential of NEMRA and to compete with the excellent spatial resolution provided by CTA. In order to take advantage of the large signal-to-noise ratio (SNR) boost at 3 Tesla, one must overcome challenges relating to high specific absorption rate (SAR) and worsened B1 field homogeneity (Table 1).

Shortening the bSSFP shot length, which proportionately reduces RF power deposition, can ameliorate the impact of increased SAR at 3 Tesla. At 1.5 Tesla, we found that GRAPPA acceleration factors in excess of two degraded QISS image quality. Higher GRAPPA acceleration factors (3 to 4) can be used to reduce the shot length at 3 Tesla. With the SNR boost from the higher field strength, one can further reduce the shot length by increasing the sampling bandwidth (~962 Hz/pixel at 3 Tesla vs. 658 Hz/pixel at 1.5 Tesla). The higher sampling bandwidth has the further advantage of reducing bowel-related magnetic susceptibility artifacts in the pelvic region.

We have found that the combination of a GRAPPA factor of 3 and sampling bandwidth of 962 Hz/pixel are sufficient to permit a 90° flip angle to be maintained from the level of the feet through the mid-thigh level. However, this imaging strategy by itself is insufficient for the pelvic and abdominal regions, where SAR limitations are more pronounced due to larger body dimensions. Degradation of image quality from using a flip angle <90° is maximal in the pelvic region because of the additional impact of B1 field inhomogeneity. Unfortunately, a flip angle less than 90° in the pelvis often

Adapted with permission from ref. 20

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**Figure 3**

88-year-old male with claudication and type-2 diabetes. (3A) CTA; (3B) QISS MRA. The CTA was non-diagnostic due to the presence of extensive vascular calcifications. However, QISS MRA was completely unaffected by the vascular calcifications and demonstrated the patency of proximal vessels and occlusions of calf vessels. In this case, note that QISS MRA image quality was adequate despite the fact that the patient had atrial fibrillation. Adapted with permission from ref. 20.
results in unilateral loss of arterial conspicuity with QISS MRA. One straightforward solution is to trigger to every other R-wave, which halves the time-averaged power deposition at the expense of doubling scan time. Since SAR limitations only come into play from the upper thigh region through the abdomen, triggering to every other R-wave is only used for the top three stations. Total scan time for a whole-leg study is increased by ~2-3 minutes (e.g. total scan time ~10 minutes**) which is still reasonable.

A final B1 field-related issue is that the pre-scan image filters typically used to correct for RF coil-dependent signal intensity variations do not adequately normalize signal variations caused by B1 field inhomogeneity at 3 Tesla. This signal variation will tend to obscure the arterial signal on a full-thickness MIP, even when the vessel is apparent on a thin MIP. The effectiveness of the pre-scan filter in the pelvis is impeded by noise amplification in the central portions of the body resulting from the use of a high GRAPPA acceleration factor. This limitation is largely avoided by using the ‘broad’ pre-scan filtering option. Figure 5 illustrates the image quality improvements that can be obtained when several pulse sequence optimizations are combined (e.g. high GRAPPA acceleration factor, high sampling bandwidth, FOCI venous suppression, triggering to every other R-wave for upper stations, and optimized image filtering).

** Developing clinical applications **
Although most clinical efforts using QISS MRA have been directed towards the lower-extremity peripheral arteries, there are several other areas where the technique appears promising. For instance, QISS MRA can be used to evaluate the arteries of the upper extremities and the veins of the lower extremities (Fig. 6). For imaging of the lower extremity veins, we typically place the traveling saturation pulse above the slice and turn off the in-plane saturation pulse (e.g. by setting the RF voltage to zero). Other potential applications include imaging of visceral arteries and veins, pulmonary vessels, and the extracranial carotid arteries. However, additional technical development and clinical validation will be needed for other vascular territories.

** Table 1: Summary of challenges and solutions for 3T QISS **

<table>
<thead>
<tr>
<th>Challenges at 3T</th>
<th>Solutions</th>
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<tr>
<td>Increased SAR</td>
<td>• Shortened shot length using high GRAPPA acceleration factor (3-4) and high sampling bandwidth</td>
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<tr>
<td></td>
<td>• Triggering to every other R-wave</td>
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<td></td>
<td>• QISS with FLASH readout</td>
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<td>B0 inhomogeneity</td>
<td>• Arterial spin labeled (ASL) QISS</td>
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<td>B1 inhomogeneity</td>
<td>• B1-robust saturation RF pulses</td>
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<td>• FOCI inversion RF pulses</td>
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<td>• B1-dependent image filtering</td>
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<td>• High permittivity pad</td>
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** Cases where QISS MRA helped to salvage a non-diagnostic CEMRA. **
(4A) Patient with an abdominal aortic aneurysm. Slow flow in the aneurysm delayed the contrast enhancement of the pelvic arteries, resulting in a non-diagnostic CEMRA exam. However, the pelvic arteries are well shown on the QISS scout study.
(4B) Patient with aorto-iliac and bilateral superficial femoral artery occlusive disease. Left leg motion caused misregistration artifact in part of the CEMRA (arrow), whereas the QISS scout images are diagnostic. *Adapted with permission from ref. 20*
Potential Pitfalls
Although QISS MRA has proven to be a robust imaging technique, there are potential limitations that should be kept in mind in order to avoid artifacts:

1. Cardiac rhythm: The default acquisition window for QISS is approximately 700 ms. In patients with medium or slow heart rates, one slice is acquired per RR interval. With rapid heart rates where the RR interval is less than 700 ms, one slice will be acquired every 2 RR intervals. It is possible to trigger to every RR interval, despite the fast heart rate, by reducing the acquisition window. This can be accomplished by slightly decreasing both the TD (in the special card, default value of 100 ms) and TI (in the contrast card, default value of 350 ms). However, if these values are reduced excessively then loss of flow signal may occur from inadequate inflow or data acquisition during the systolic phase of the cardiac cycle.

   In general, QISS is fairly insensitive to arrhythmias. However, with highly irregular heart rhythms (or with poor triggering due to an inadequate ECG signal), image quality may suffer. Work is currently under way to develop versions of QISS that do not require the use of ECG gating.

2. Fat suppression: QISS relies upon uniform fat suppression for optimal vessel depiction. In some areas where fat suppression is imperfect (e.g. groin area), a simple expedient is to edit out the affected region in the maximum intensity projection. However, in certain regions (e.g. the feet) it can be quite difficult to adequately shim so that fat suppression and hence QISS image quality may be suboptimal. For the pedal vessels, we have found that image quality is further improved by placing a small cushion between the top of each foot and the Peripheral Angio 36 coil, since having the coil touching the foot tends to impair the quality of the shim.

Developing potential future clinical applications for QISS MRA.

(6A) Healthy subject. QISS MRA (acquired with 1.2 mm thick slices) depicts the forearm arteries comparably to TWIST CEMRA.

(6B) Comparison of QISS arteriography (inferior saturation) with QISS venography (superior saturation).
3. Susceptibility artifact: The TrueFISP readout along with fat suppression makes QISS more sensitive to magnetic susceptibility artifacts (e.g., from joint prostheses or bowel gas) than CEMRA (which uses a 3D acquisition with short TE). Using a high readout bandwidth without fat suppression minimizes such artifacts.

4. Flow direction: The use of venous saturation impairs the ability of QISS to depict reversed arterial flow, particularly when the flow reversal extends over a long vessel segment. In cases where flow reversal is suspected, one may acquire an additional QISS data set using arterial saturation instead of venous saturation. These images will show reversed arterial flow (but will also show veins).

5. Spatial resolution: For most peripheral arterial segments, the default slice thickness of 3 mm with no slice overlap is sufficient to show stenotic disease. Thinner slices (e.g., 1.2 mm with 20% slice overlap) are helpful for avoiding partial volume averaging in horizontally oriented vessel segments (e.g., proximal anterior tibial artery) and for imaging small caliber vessels (e.g., in the foot).

Future Developments

1. Alternative k-Space Trajectories: The current implementation of QISS uses a Cartesian k-space trajectory. However, it is also possible to acquire QISS using a radial k-space trajectory [30]. There are potential advantages and disadvantages to a radial trajectory. One advantage for radial is that the number of views, and hence scan duration within each cardiac cycle, can be reduced almost arbitrarily with minimal impact on spatial resolution. This approach may be beneficial for imaging of patients with fast heart rates. However, the signal-to-noise ratio (SNR) is also reduced and radial streak artifacts may become objectionable if the number of views is excessively decreased. By using a golden view angle increment with a radial k-space trajectory, it becomes feasible to sample data throughout the cardiac cycle. One can then generate a cine series of time-resolved QISS images showing the progression of the arterial pulse wave within the arterial tree [31].

2. Alternative Sampling Strategies: Although the TrueFISP readout maximizes acquisition speed and SNR, using other pulse sequences for the readout can prove beneficial in certain circumstances. For instance, the use of a fast low angle shot (FLASH) readout in conjunction with a reduced flip angle excitation avoids SAR limitations at 3 Tesla. The use of an ultra-short TE readout might prove beneficial to reduce susceptibility artifacts around joint prostheses.

3. Alternative Gating Strategies: Currently, QISS images of the pelvis and abdomen are acquired using breath holding. In order to further enhance, patient comfort, it should be feasible to implement non-breathhold acquisitions by respiratory gating with a belt device, with a navigator technique applied to the anterior abdominal wall, or by self-gating [32].

4. 3D QISS: Very thin slices (e.g., 0.3 mm) can be obtained by using a thin-slab 3D implementation of the QISS technique. Although still early in development, the technique has the potential to exceed the spatial resolution available with CEMRA and nearly match that of CTA.

Conclusions

QISS MRA provides a robust, rapid, and easy-to-use technique for imaging of the peripheral arteries at both 1.5 and 3 Tesla. There is generally no need to tailor any of the imaging parameters for individual patients. Additionally it can serve as a backup for CEMRA, or function as a stand-alone technique. Despite similarities in the appearances of the projection angiograms, QISS and CEMRA are predicated on fundamentally different principles and care must be taken to avoid pitfalls specific to each technique. Future developments promise shorter scan times, reduced artifacts, and new clinical applications.

References


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