Clinical Evaluation of Peripheral Vascular Disease using a Hybrid Approach: Unenhanced Quiescent Interval Single Shot and Low-dose TWIST MR Angiography

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Introduction: Peripheral arterial disease (PAD) is associated with increased mortality and morbidity with increased incidence of cerebrovascular and cardiovascular events and mortality rates as high as 30%, 50% and 70% at 5, 10 and 15 years respectively. The incidence of impaired renal function in these patients ranges between 27% and 36%[1].The association between nephrogenic systemic fibrosis and GBCA's has resulted in an FDA issued Public Health Advisory requesting the addition of a boxed warning stating that exposure to GBCA's increases the risk for NSF in patients who have acute or chronic severe renal insufficiency (GFR <30 mL/min/1.73 m^2).

The purpose of this study was to test the hypothesis that a hybrid technique employing a new unenhanced MRA technique, *quiescent interval single shot* (QISS), in combination with low-dose time-resolved (TWIST) MRA of the calf provides comparable diagnostic accuracy to the standard hybrid approach using low-dose TWIST of the calf and high-dose stepping table CE-MRA.

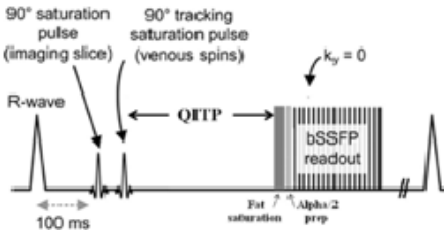


Fig. 1 Pulse sequence diagram for QISS MRA

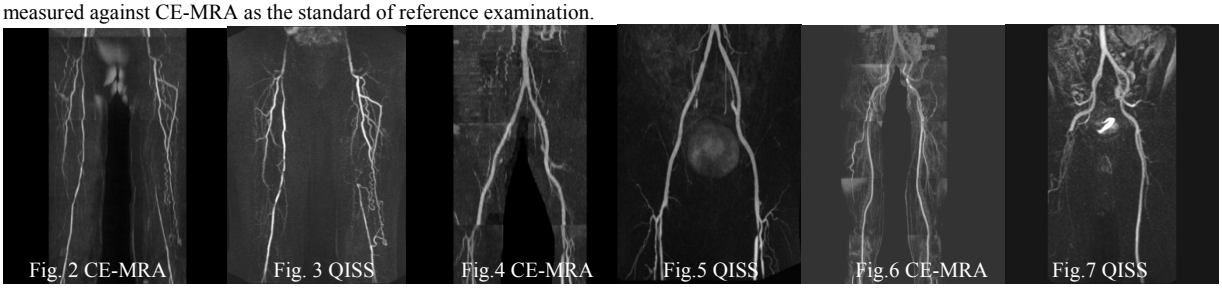
Materials and Methods: 20 prospective patients referred for peripheral MRA with clinical symptoms of PAD underwent 8 station non-enhanced QISS evaluation of the lower extremities prior to contrast-enhanced TWIST MRA of the calf; TWIST was followed by standard stepping table bolus chase technique. TWIST MRA of the calf station was performed with an average of 6.0 cc of GBCA (Gd-BOPTA (Multihance, Bracco Diagnostics) or Gd-DTPA (Magnevist, Bayer Schering Pharma). Stepping table acquisition involved a dual infusion protocol initially at 1.5 cc/sec followed by 0.6 cc/sec. Patients with eGFR <30ml/min/1.73 m^2 were excluded from contrast administration and study inclusion. Imaging was performed on a 1.5 T scanner (Avanto, Siemens Healthcare, Erlangen, Germany). The QISS MRA sequence (**Fig.1**) employs a modified ECG-triggered, fat suppressed, 2D balanced steady-state free precession (bSSFP) and a quiescent inflow time period (QITP) of 228 ms for maximum inflow enhancement. Typical sequence parameters are supplied in **Table 1** below.

Parameters	QISS	TWIST Calf	CE Abdomen	Thigh	Calf
Acquisition time (s)	60 (per station)	30	20	18	29
Spatial resolution (mm3)	3.0mm*	0.7x0.9x1.3	1.5x0.7x1.5	1.5x0.7x1.4	1.4x0.7x0.9
FOV (mm)	400	360	500	500	360
TR (ms)	3.0	2.28	3.0	2.49	2.64
TE (ms)	1.4	0.85	1.1	0.9	0.9
Flip angle	90	25	20	20	20
Matrix	400	512	512	512	512
Slices/slab	60	60	72	60	70
Bandwith (Hz/Px)	676	360	810	540	320

Table 1. Sequence parameters.
*effective slice thickness of 2.4 mm (0.6 mm slice overlap)

Image Analysis: QISS, TWIST and CE-MRA datasets were qualitatively assessed using a 4 point Likert scale (1=not diagnostic 2=suboptimal 3=diagnostic 4=excellent). Blinded to patient identity and history, two radiologists independently evaluated original MRA source partition data and maximum intensity projections for each of the three MRA techniques. Where a significant discrepancy in individual interpretations arose, a third independent reading to achieve consensus was performed. Images were reviewed on a Leonardo workstation (Siemens Healthcare, Erlangen, Germany)

Statistical Analysis: For both QISS and table stepping CE-MRA, the arterial tree was subdivided into 29 arterial segments with the presence or absence of disease at each anatomic segment graded and recorded. For the TWIST MRA analysis of 14 arterial segments in the calf was performed. The presence and degree of the most severe stenosis in each segment was graded as 1=normal or not significant (<50%) stenosis, 2=>50% stenosis or occluded. In all a total of 320 segments were analyzed. Statistical analysis was performed with standardized software (SPSS, version 17.0, SPSS Inc., Chicago, IL). Concordance of the degree of stenosis scores between QISS and CE-MRA and combined QISS and TWIST calf MRA was assessed using Cohen κ analysis. A *P* value less than 0.5 were assumed to indicate statistical significance. Sensitivity, specificity, positive predictive value and negative predictive values for QISS MRA in combination with TWIST MRA of the calf were measured against CE-MRA as the standard of reference examination.



Patients underwent contrast administration in accordance with Departmental Guidelines
GFR 31-59 ml/min/1.73 m^2 0.1mmol/kg Gd-BOPTA (Multihance, Bracco Diagnostics)
GFR >59 ml/min/1.73 m^2 0.2 mmol/kg Gd-DTPA (Magnevist, Bayer Schering Pharma) with 10 patients receiving Magnevist and 10 patients receiving Multihance

Results: The average dose of gadolinium based contrast agent administered was 0.16 mmol/kg reflecting the proportion of patients with reduced GFR. Likert scores for the unenhanced QISS MRA technique were comparable with CE-MRA for pelvic, thigh and proximal calf stations. Sensitivity (94.19%) and specificity (80.0%) for the QISS technique were high in the pelvis and thighs (sensitivity 94.19%, specificity 80.0%) when compared to stepping table CE-MRA as the reference standard. Combining the unenhanced QISS lower extremity technique with low-dose TWIST MRA of the calf station resulted in an overall sensitivity of 97.4%, specificity of 98.3%, a negative predictive value of 98.7% and a positive predictive value of 96.7% using CE-MRA as the reference standard. Cohen kappa analysis for inter-rater indicates almost perfect agreement (κ= 0.86) between the hybrid approach of unenhanced QISS and TWIST and standard hybrid CE-MRA.

Conclusion: Unenhanced QISS MRA demonstrated equivalent diagnostic performance to high-dose stepping table CE-MRA. For optimal evaluation of PAD, we propose a hybrid strategy using QISS MRA followed by low-dose TWIST MRA of the calf. This hybrid strategy permits a dramatic reduction in contrast agent dosage with no loss of diagnostic accuracy.