

Validation of a Cardiovascular MRI Protocol for Combined Assessment of Contrast-Enhanced Whole Body Angiography and Cardiac Function within a Single Examination

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Introduction, Target Audience and Purpose: Cardiac MRI (CMR) has recently developed into the imaging standard for evaluating ventricular function and myocardial viability [1-2]. However a more comprehensive assessment to include MRA of the human vascular tree would be desirable. Recent hardware advances in RF coil connectivity have resulted in the emergence of the WB-MRA technique [3-4] which can provide this 'missing link'. In this work (which will be of interest to cardiovascular MRI Physicists and Radiologists) the primary purpose was to test a combined WB-MRA and CMR protocol on a cohort of human volunteers. More specifically, the aim was to employ multiple observers to undertake quantitative and qualitative evaluation of the CMR and WB-MRA data in order to establish the analysis repeatability that would be representative of a larger scale population-based study.

Methods: Following ethical approval, n=48 asymptomatic volunteers (17 men, 31 women, mean 54 (range 41-71) yrs) were recruited. Imaging was performed using a 3T Magnetom Trio scanner (Siemens, Germany) with head, neck, body matrix (x2), spine and peripheral angio RF coils. The protocol was divided into five phases:

(i) *Localisers.* Three-plane localiser images were acquired for WB-MRA via the use of four 500mm field-of-view (FOV) gradient echo fast low-angle shot (FLASH) sequences from head to foot. Positioning was such that the 'overlap' between each FOV was at least 75mm but adjustable according to the height of the patient. Cardiac-gated TurboFLASH localiser images of the heart were also acquired in the two-chamber (2ch), four-chamber (4ch) and short axis (SA) orientations.

(ii) *CINE MRI of Left Ventricular (LV) Function.* A stack of short axis images of the left ventricle were acquired from the atrio-ventricular ring to the apex using a 2D ECG-gated breath-hold segmented CINE TrueFISP sequence with retrospective gating (25 phases). The key imaging sequence parameters can be seen in the table.

(iii) *WB-MRA of Head (Station 1) and Lower Legs (Station 4).* Pre-contrast WB-MRA 'mask' data were initially acquired at stations 1 and 4 using a 3D TurboFLASH sequence. Subsequently a 10ml dose of Gadoteric Acid (Dotarem, Guerbet, France) was delivered via the antecubital fossa using a Spectris Solaris power injector (MedRad, Pittsburgh, USA) at 1.5ml/sec, followed by a 20ml saline flush. The timing of contrast delivery was controlled by a 'Care Bolus' acquisition (sagittal aortic arch), and post-contrast data were acquired for stations 1 and 4 at the appropriate time. The scanner table movement velocity between the each station was 50cm/sec.

(iv) *Myocardial Late-Gadolinium Contrast Enhancement.* At an average of 11 mins (range 9-16 mins) post-contrast, an ECG gated segmented 2D phase sensitive inversion recovery (PSIR) sequence was applied in the LV short-axis plane in order to characterise 'delayed enhancement' within the myocardium. A short axis stack of images were acquired using an optimised myocardial inversion time for each volunteer. The mean inversion time (TI) used was 376 ms (range 300-450 ms).

(v) *WB-MRA of Abdomen (Station 2) and Upper Legs (Station 3).* Pre- and post-contrast WB-MRA data were acquired for stations 2 and 3, using 3D TurboFLASH as before. In order to generate the post-contrast images a second contrast agent dose (of 15ml) was infused at 1.5ml/sec with 20ml saline flush, and timing was controlled by a 'Care Bolus' acquisition (coronal abdominal aorta). The average time between the first and second contrast injections was 19 mins (range 15-34 mins).

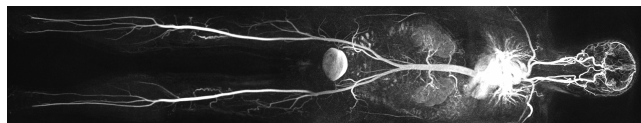
Image Analysis: CMR images were analysed using commercial software ('Argus' VB 15, Siemens). Contours were placed around endo- and epicardial LV borders at end-diastole and end-systole that contained 50% or more full-thickness myocardium by consensus, and quantitative measurements of ejection fraction (EF) and left ventricular mass (LVM) were derived. CMR delayed enhancement and WB-MRA analysis was performed using a radiology workstation (Kodak Carestream PACS Client Suite V10.1, Rochester, USA) on the post-contrast turboFLASH (source) images – with multi-planar reconstructions (MPR) and maximum intensity projection (MIP) images to aid further interpretation. The WB-MRA analysis was performed on 31 arterial segments per dataset, at locations ranging from the internal and common carotid arteries to the trifurcation vessels of the lower limb. Stenosis grading was recorded for each vessel segment as follows: grade 0 = healthy, grade 1 = 1-50% stenosis, grade 2 = 51-70% stenosis, grade 3 = 71-99% stenosis, and grade 4 = vessel occlusion. From this a simple total atheroma score was calculated for each patient as a sum of all stenosis grades recorded. All datasets (n=48) were analysed by four Medical Physics Observers (MPO) for CMR, and four Radiologist Observers (RO) for WB-MRA in order to derive inter-observer variation. Subsets of the data were also analysed by an MPO or RO on two occasions – resulting in four independent assessments of intra-observer variation for CMR and WB-MRA. Repeat analyses were separated by one month in order to eliminate learning effects.

Results: All of the CMR and WB-MRA datasets were acquired successfully. For CMR, the mean value (over n=48 volunteers) for EF was 67.3 +/- 4.8% and 100.3 +/- 22.8g for LVM. Test-retest intra-observer coefficients of repeatability (CoR) ranged from 2.1% to 4.7% for EF and 9.0g to 12.0g for LVM (depending on the observer). Inter-observer CoR's (across all observers) were 8.1% for EF and 19.1g for LVM. There were no cases of myocardial delayed enhancement identified. For the WB-MRA data, of 1488 arterial segments evaluated there was evidence of some degree of vessel luminal narrowing or stenosis at 32 (2.2%) sites - involving n=20 of the 48 volunteers. Where disease was detected, n=26 segments were grade 1 (minor stenosis), n=4 were grade 3 (severe stenosis) and n=2 segments were grade 4 (vessel occlusion). However the vast majority of arterial segments were interpreted as clinically normal. Inter-observer repeatability resulted in consistent scoring for 1255 (87.2%) of 1440 vessel sites evaluated. When total atheroma scores were evaluated between each RO using the Kruskal Wallis test, there was no significant difference detected between the medians of each assessment (p= 0.38). Intra-observer repeatability resulted in consistent test-retest scoring for 343 (range 336-348) of 360 vessel sites (depending on the observer). When the intra-observer total atheroma scores were examined using the Wilcoxon signed-rank test, there was no significant difference between the medians of the first and second repeatability assessments for any RO (p>0.34).

Discussion: This study has demonstrated that it is possible to acquire WB-MRA and CMR data within a single MR protocol – with a scan time ('on the table') lasting around 45 minutes. An added advantage of the protocol is that myocardial delayed enhancement can be ascertained from the initial contrast injection. The repeatability of the technique was evaluated by eight observers (4x MPO for the CMR analysis and 4x RO for the WB-MRA analysis), and good consistency was obtained.

Conclusion: A combined MRI protocol is demonstrated that allows characterisation of whole-body vascular structure and cardiac structure, function and myocardial viability within a single 45 minute evaluation. The associated analysis techniques are repeatable and therefore suitable for larger scale population-based MRI studies.

| Assessment | Sequence | Orientation | TR/TE (ms) | FA ^o | Slice (mm) | Resolution | FOV (mm) |
|---------------|---------------|-------------|------------|-----------------|------------|------------|----------|
| LV Function | 2D TrueFISP | Short Axis | 3.4/1.5 | 50 | 6.0 | 173x256 | <360 |
| WB-MRA (St 1) | 3D TurboFLASH | Coronal Obl | 2.7/1.0 | 19 | 1.1 | 313x512 | 500 |
| WB-MRA (St 4) | 3D TurboFLASH | Coronal Obl | 2.6/1.0 | 22 | 1.0 | 277x448 | 500 |
| WB-MRA (St 2) | 3D TurboFLASH | Coronal Obl | 2.6/1.0 | 16 | 1.3 | 264x512 | 500 |
| WB-MRA (St 3) | 3D TurboFLASH | Coronal Obl | 3.5/1.2 | 37 | 1.4 | 242x448 | 500 |



References: [1] Alfakih K. J. Magn Reson. Imaging 2003; 17(3): 323-329. [2] Rajiah P. Radiographics 2013; 33(5): 1383-1412. [3] Hansen T. Eur Radiol 2006; 16(1): 147-153. [4] Lehrke S. J. Cardiovasc. Magn. Reson 2009; 11: 36-45.