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Sagittal Fresh Blood Imaging with Interleaved Acquisition of Systolic and Diastolic Data for Improved Robustness to Motion

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Abstract

Purpose—To improve robustness to patient motion of ‘fresh blood imaging’ (FBI) for lower extremity non-contrast MRA.

Methods—In FBI, two sets of 3D fast spin echo images are acquired at different cardiac phases and subtracted to generate bright-blood angiograms. Routinely performed with a single coronal slab and sequential acquisition of systolic and diastolic data, FBI is prone to subtraction errors due to patient motion. In this preliminary feasibility study, FBI was implemented with two sagittal imaging slabs, and the systolic and diastolic acquisitions were interleaved to minimize sensitivity to motion. The proposed technique was evaluated in volunteers and patients.

Results—In ten volunteers, imaged while performing controlled movements, interleaved FBI demonstrated better tolerance to subject motion than sequential FBI. In one patient with peripheral arterial disease, interleaved FBI offered better depiction of collateral flow by reducing sensitivity to inadvertent motion.

Conclusions—FBI with interleaved acquisition of diastolic and systolic data in two sagittal imaging slabs offers improved tolerance to patient motion.

Keywords

angiography; non-contrast MRA; lower extremity MRA; ECG-gated FSE; fresh blood imaging

Introduction

Assessment of peripheral arterial disease (PAD) is routinely performed with gadolinium-enhanced MR angiography (MRA) (1). However, concerns about the cost of gadolinium and the risk of nephrogenic systemic fibrosis in patients with renal insufficiency (2) have prompted interest in MRA techniques that do not require exogenous contrast material (3).

One such technique, known as “Fresh blood imaging” (FBI) (4), exploits differences in arterial and venous flow velocity over the course of the cardiac cycle. In this approach, two sets of images are acquired, one in systole and one in diastole, with a three-dimensional (3D) fast spin echo (FSE) sequence. Arteries appear bright in diastole when flow is slow, but darker in systole due to flow-induced signal dephasing. Bright-blood arterial angiograms are obtained by subtracting systolic from diastolic images.

Clinical evaluation of FBI in PAD patients (5-10) has demonstrated that the technique is susceptible to motion artifacts, with two studies reporting non-diagnostic results in as many as 47% of all cases (7,8). In FBI, systolic and diastolic phase datasets are acquired sequentially, over the course of several minutes. Any motion between the two acquisitions can lead to subtraction errors due to misregistration, obscuring arteries on the difference images. One way to improve tolerance to patient motion is to alternate between systolic and diastolic acquisitions in consecutive heart beats. This strategy would shorten the time interval between collection of systolic data and the corresponding diastolic data from minutes to seconds.

A foreseeable challenge for this approach is the resultant variation in repetition time (TR) between consecutive readouts. Since diastolic and systolic acquisitions require different trigger delays, alternating between them produces a non-uniform TR. Diastolic imaging is frequently performed at end-diastole, with a trigger delay of zero, while systolic data collection is timed to peak arterial flow and thus has a subject-specific trigger delay, usually 200-300 ms after the R-wave. If data are acquired every heartbeat, then, in a sequential approach, TR equals the duration of the cardiac cycle (1RR). In an interleaved approach, however, TR alternates between 1RR-TD and 1RR+TD, where TD is the systolic trigger delay. This leads to unequal T_1 relaxation before the systolic and diastolic acquisitions.

Non-uniform TR could potentially cause suboptimal depiction of small arteries and vessel edges. Since the period of T_1 recovery would be longer prior to the systolic acquisition than the diastolic acquisition, background tissue would have slightly higher signal on the systolic images than the diastolic images. This could be problematic for voxels that contain both background tissue and arterial lumen, such as those at vessel edges or small arterial branches, where partial volume effects are at play. Upon subtraction of systolic from diastolic data, any positive difference in arterial signal due to flow-related dephasing may be canceled out by the negative difference in signal from background tissue within the same voxel. As a consequence, the artery may not be visible on the subtracted images. In addition to partial volume effects, arterial depiction may be further compromised in vessel branches with low systolic velocity. If the flow-related signal attenuation during systole is not sufficient to overcome the signal enhancement associated with greater T_1 recovery, then, once again, vessel conspicuity on the subtracted images may be degraded.

Performing data collection every other heartbeat, or less frequently, can mitigate non-uniform T_1 relaxation by reducing the fractional difference between systolic and diastolic TR. However, decreased acquisition frequency leads to an increase in scan time. The trade-off between T_1 uniformity and scan efficiency can be eliminated with the use of two sagittally-oriented imaging slabs, one for each leg. Imaging in a sagittal plane greatly reduces the size of the phase-encoding dimension, thereby allowing two sagittal slabs to be imaged in the same scan time as one coronal slab. Furthermore, the use of two separate imaging slabs permits alternation between the right and left legs in consecutive heart beats. As a result, if data are collected every heart beat, each extremity will have an effective TR of $2RR \pm TD$, allowing for prolonged T_1 recovery without scan time penalties.

As an added benefit, the use of separate imaging slabs also allows acquisition parameters to be customized for each extremity. This may be valuable when disease leads to flow asymmetry between the legs. For example, a delayed systolic peak, typical of the tardus parvus waveform, may be accommodated by using a longer TD in the affected leg. Similarly, the flow-sensitivity of the sequence may be optimized independently for each leg by the use of different flip angles for the refocusing pulses in each slab (11).

The objectives of this study were to demonstrate the feasibility of FBI with interleaved diastolic/systolic acquisition in two sagittal imaging slabs and to evaluate the robustness to motion of the proposed technique.

Methods

Non-contrast imaging of the distal lower extremities was conducted in 10 healthy volunteers (1 female, 9 male, age range 29 – 65 yrs; mean age 41 yrs), one subject with known PAD (male, age 72), and 3 patients (1 female, 2 male; age range 63 – 66 yrs; mean age 63 yrs), who were referred for contrast-enhanced MRA because of suspected or known PAD. The study was approved by the Institutional Review Board of our medical center, and written informed consent was obtained from all participants. Imaging was performed on a whole-body 1.5T system (Avanto, Siemens Healthcare, Erlangen, Germany) with a maximum gradient strength of 45 mT/m and maximum slew rate of 200 T/m/s. The integrated body coil was used for radio-frequency (RF) excitation, while a 16-element peripheral matrix coil and a spine coil array were employed for signal reception.

Interleaved FBI Sequence

Interleaved FBI was implemented using two 3D imaging slabs, oriented sagittally, with the frequency-encoding direction (k_x) head-foot, the phase-encoding direction (k_y) anterior-posterior, and the partition-encoding direction (k_z) right-left (Fig. 1a). The 3D FSE acquisition was ECG-triggered and a complete k-space partition (i.e. an entire k_x - k_y plane) was acquired per heartbeat. Data acquisition alternated between left and right legs and between systolic and diastolic phases (Fig. 1b) as follows:

1. data collected in the right leg during systole
2. data collected in the left leg during systole
3. data collected in the right leg during diastole
4. data collected in the left leg during diastole

Data obtained from the right leg during the first and third readout periods are subtracted, and, similarly, data obtained from the left leg during readouts 2 and 4 are subtracted. This pattern is repeated until the entire 3D k-space of both imaging slabs is sampled.

Assuming that data are collected every cardiac cycle, $TR_{diastole} = 2 \cdot RR - TD$, while $TR_{systole} = 2 \cdot RR + TD$. To estimate the effect of non-uniform T_1 relaxation in this scenario, the difference in longitudinal magnetization immediately before the systolic and diastolic acquisitions was calculated in background tissue and blood for heart rates (HR) ranging from 50 – 100 beats/min (bpm). Complete loss of magnetization was assumed following the readout and a saturation recovery equation was used to calculate the magnetization of blood and muscle immediately before the subsequent excitation, using $TD = 250$ ms, arterial $T_1 = 1200$ ms (12) and muscle $T_1 = 1008$ ms (13). For low heart rates ($HR < 50$ bpm) the difference in longitudinal magnetization ΔM_z between diastole and systole was found to be negligible ($\Delta M_z < 0.05 \cdot M_0$ in muscle and $\Delta M_z < 0.06 \cdot M_0$ in blood, where M_0 is the equilibrium magnetization). In muscle, ΔM_z reached $0.1 \cdot M_0$ at $HR \sim 78$ bpm, while in blood

it reached the same threshold at HR ~70 bpm. These calculations suggest that data acquisition every RR interval should be adequate in subjects with HR = 80 bpm, while it may be necessary to image every other heart beat in patients with HR > 80 bpm.

Imaging Protocol

Sequential FBI was performed with a matrix size of $384 \times 244 \times 64$ ($N_x \times N_y \times N_z$), FOV = $500 \times 375 \times 96$ mm³ and slice resolution 75%, giving a true voxel size of $1.3 \times 1.5 \times 2.0$ mm³ ($\Delta x \times \Delta y \times \Delta z$). Other parameters included: receiver bandwidth (BW) = 766 Hz/px, echo time (TE) = 19 ms, nonselective excitation and refocusing pulses, echo spacing 3.2 ms, echo train length 214 ms. Data collection was performed every 1 – 2 cardiac cycles, according to heart rate, using 2 shots per partition. Generalized partially parallel acquisition (GRAPPA) was employed with an acceleration factor of 2 and 24 reference lines. Partial Fourier was not used.

Interleaved FBI imaging was performed in two sagittal slabs, each of which had a matrix size of $384 \times 51 \times 64$ ($N_x \times N_y \times N_z$) and FOV = $500 \times 101 \times 96$ mm³, giving a true voxel size of $1.3 \times 2.0 \times 1.5$ mm³ ($\Delta x \times \Delta y \times \Delta z$). Since the phase- and partition-encoding directions were swapped between sequential and interleaved FBI, this ensured that the voxel dimensions were identical along each physical direction, i.e. 1.3 mm head/foot, 1.5 mm left/right and 2.0 mm anterior/posterior. To permit multi-slab acquisition, interleaved FBI employed spatially selective excitation and refocusing pulses, which lengthened the echo spacing to 5.0 ms. Other parameters were matched as closely as possible to the sequential acquisition: BW = 766 Hz/px, TE = 20 ms, and echo train duration = 255 ms, which was achieved using 1 shot per partition without parallel imaging or partial Fourier acceleration. Data were acquired every 1 – 2 cardiac cycles according to heart rate.

For both sequences, TD was fixed at 0 ms for diastole and set to the time of peak flow in the popliteal artery for systole. The latter was determined individually in each subject by cine MRI (2D TrueFISP sequence, axial plane, voxel size 1.6×1.6 mm², slice thickness = 6 mm, FA = 70°). The interleaved FBI sequence offered the possibility to input two systolic TDs, one for each leg. It also allowed the flip angle of the refocusing pulses to be customized for each leg to achieve optimal flow sensitivity. Based on prior *in vivo* experience (11,14), a FA of 120° was chosen for the healthy volunteers. In subjects with known or suspected PAD, flow velocities were measured using phase contrast imaging in an axial plane through the popliteal artery (in-plane voxel size 1.5×1.5 mm², slice thickness 5mm, venc = 90cm/s, FA = 30°) and the results were used to guide the selection of a lower or higher flip angle.

The performance of interleaved FBI was compared with that of sequential FBI using three different paradigms:

I. Healthy volunteer scans with motion challenge—Ten healthy volunteers were imaged with both sequential and interleaved FBI while instructed to hold still. To test for tolerance to motion, the same subjects underwent additional imaging during which they were periodically asked via the intercom to move their feet in a controlled manner. Four data sets with motion challenge were obtained per volunteer. First, subjects were asked to flex and relax their toes vigorously 3-4 times, while being careful not to displace either extremity from its original position. Sequential and interleaved FBI sequences were run, with the motion repeated every 30-40 seconds during image acquisition. Next, the volunteers were instructed to rotate both feet externally 3 times at the ankle joint. The subjects were asked to return both extremities to their original position after the rotation. Again, the motion was repeated every 30-40 seconds during imaging with both techniques. To illustrate the possibility of using separate flip angles for each leg with interleaved FBI, one volunteer

underwent a further interleaved FBI scan in which the flip angle was reduced to 60° in the left leg.

II: Clinical comparison against Gd-MRA in patients—Three patients underwent sequential and interleaved FBI, followed by gadolinium-enhanced dynamic imaging of the calves and multi-station bolus-chase MRA. A total of 0.15 mmol/kg Gd-DTPA were injected, of which 0.04 mmol/kg were used for time-resolved imaging and 0.11 mmol/kg for the bolus-chase. Timing of the injection was based on time-to-peak enhancement of the distal infrarenal aorta and a standard formula (15). Dynamic imaging was performed using Time-resolved angiography With Interleaved Stochastic Trajectories (TWIST) and the following parameters: TR/TE = 3.1/1.0 ms, FA = 25°, nominal voxel size = 1.0 mm x 1.3 mm x 1.3 mm, slice resolution = 93%. The distal station of the bolus-chase acquisition was performed with a 3D T1-weighted Fast Low-Angle Shot (FLASH) sequence, using: TR/TE = 2.94/0.9 ms, FA = 25°, nominal voxel size = 1.0 mm x 1.6 mm x 1.4 mm, slice resolution = 60%.

III: Effect of TR in a subject with known PAD and high heart rate—One subject with known PAD and a high heart rate was imaged with sequential and interleaved FBI, while instructed to hold still. Both sequences were run with data collection every cardiac cycle and then repeated with data acquisition every second heart beat, in order to evaluate the effect of TR on arterial visualization.

Image Quality Assessment

All data were de-identified and randomized for blinded review by two radiologists who independently scored the images. Source, subtracted, and maximum intensity projection (MIP) images of all sequences were available to the readers, but primary interpretation relied on the MIPs. Ten arterial segments were assessed per leg (popliteal, tibioperoneal trunk, proximal and distal anterior tibial artery, proximal and distal peroneal artery, proximal and distal posterior tibial artery, dorsalis pedis, and plantar artery) and diagnostic quality was graded on a 4-point scale (1 = non-diagnostic, 2 = poor, 3 = satisfactory, 4 = excellent).

Statistical Analysis

Image quality scores for all angiograms obtained in healthy volunteers were averaged over the two readers and analyzed using the statistical toolbox in Matlab (Mathworks, Natick, MA). The Wilcoxon matched-pairs signed rank test was used to evaluate differences in arterial depiction between sequential and interleaved FBI for all three motion paradigms: minimal motion, toe flexion, and external foot rotation. In all tests, a P value < 0.05 was considered to be significant. Statistical analysis of patient data was not performed due to the small number of patient cases included in the study.

Results

Imaging at rest

Coronal and sagittal projections of interleaved and sequential FBI angiograms obtained in a healthy volunteer are displayed in Fig. 2. On projection images, apparent vessel thickness differed between the two techniques despite the voxel dimensions in each physical direction being identical. The origin of the difference is probably T2 blurring, since the phase- and partition-encoding directions were swapped between the two acquisitions. On coronal MIPs, vessel blurring was more pronounced with sequential-FBI, while on sagittal views the filtering effect was more apparent on interleaved-FBI images. Figure 3 displays interleaved FBI MRA with different flip angle settings for each leg. Using a lower flip angle for the left

leg resulted in undesirable signal loss at the center of the popliteal artery, but better depiction of branch vessels, consistent with greater flow sensitivity.

In healthy volunteers, the two FBI versions had comparable quality when the subjects were instructed to hold still (Fig. 4a, d). Overall image quality of interleaved FBI and sequential-FBI was excellent and averaged 3.78 ± 0.21 and 3.60 ± 0.51 respectively on a scale of 1 to 4, where 4 is best. Similar results were obtained in the patient cohort, where both interleaved and sequential FBI exhibited image quality comparable to Gd-MRA. Image quality ratings obtained in volunteers and patients are summarized in Table 1. Among the patients, hemodynamically significant disease was found in only one subject. In this case, the disease was bilateral, but flow asymmetry between the legs, in terms of systolic peak timing and flow velocity, was not observed.

Fig. 5 displays angiograms obtained in a 72 year old subject with PAD and heart rate of 90 bpm, who was instructed to hold still. When data were acquired every cardiac cycle (Fig. 5a, b), the right leg was better depicted with interleaved FBI due to inadvertent patient motion, which produced artifacts on sequential FBI. Imperfect visualization of the left leg vasculature in interleaved FBI (Fig 5b) was likely due to non-uniform T_1 relaxation. When TR was doubled by triggering every second heart beat, sequential FBI (Fig. 5c) resulted in non-diagnostic images of the right leg and poor image quality in the left leg due to motion artifacts. However, interleaved FBI (Fig. 5d) exhibited excellent image quality and offered improved depiction of collateral flow compared to the case with shorter TR. It is likely that this improvement stems from two separate mechanisms: first, collecting data every second cardiac cycle mitigates non-uniform T_1 relaxation by reducing the fractional difference in TR between diastole and systole, and, second, it improves overall signal-to-noise ratio by allowing greater T_1 recovery for both diastolic and systolic acquisitions.

Imaging with motion challenge

In healthy volunteers, the image quality of both interleaved and sequential FBI deteriorated when deliberate motion was present; however, interleaved FBI received significantly higher image quality scores. In the case of mild to moderate motion, i.e. toe flexion (Fig. 4b, e), the image quality ratings obtained with interleaved FBI (3.32 ± 0.74) were slightly lower than the motion-free case, but the difference was not statistically significant. The image quality obtained with sequential-FBI, however, dropped significantly (2.22 ± 1.01). When severe motion (foot rotation) was present (Fig. 4c, f), sequential-FBI produced non-diagnostic images in half of the volunteers, with satisfactory or higher image quality observed in only 2 cases. In contrast, interleaved FBI was rated non-diagnostic in one volunteer, and satisfactory or better in 8 out of 10 cases.

Discussion

We have demonstrated that it is feasible to perform FBI with interleaved systolic and diastolic acquisitions in two sagittal imaging slabs. In volunteers and patients imaged at rest, the interleaved FBI sequence produced excellent image quality, comparable to results obtained with sequential FBI and Gd-MRA. Furthermore, our results indicate that the interleaved technique improves tolerance to patient motion. This is due to shortening of the time interval between the acquisition of corresponding systolic and diastolic partitions from 1 – 2 minutes in the sequential case to two cardiac cycles in the interleaved case. Better tolerance to patient motion may improve the overall clinical performance of the FBI technique.

The use of two sagittal imaging slabs was a necessary requirement for the interleaved technique, since a longer average TR is necessary to mitigate the effect of unequal T_1

recovery before the diastolic and systolic acquisitions. By alternating between the right and left legs in consecutive cardiac cycles, it was possible to lengthen the effective TR to $2RR \pm TD$ without scan time penalties. This exploits the fact that imaging in a sagittal plane greatly reduces the size of the phase-encoding dimension.

Parallel imaging was not used for the sagittal scans because the geometry of the receiver coil elements did not permit acceleration in the anterior-posterior direction, which coincided with the phase-encoding axis for interleaved FBI. However, the interleaved acquisition could nevertheless be performed in the same scan time as the sequential acquisition because the sagittal prescription reduced the number of phase-encoding lines per slab by more than a factor of 4 (from 244 to 51). Thus, despite the need for two slabs instead of one, and despite the longer echo spacing required for spatially-selective RF pulses (5.0 ms as opposed to 3.2 ms), interleaved FBI had the same scan time and approximately the same echo train duration as sequential FBI. It should be noted that a multi-slab implementation of 3D FSE with echo spacing shorter than 5.0 ms has been reported using Variable-Rate Selective Excitation (VERSE) pulses (16). Incorporating these pulses into the interleaved FBI sequence could allow for shorter echo train duration and reduced T2-blurring compared to sequential FBI.

In this study interleaved FBI had approximately 2.4 times higher specific absorption rate (SAR) than sequential FBI due to the use of spatially-selective RF pulses. In this study SAR limits were not exceeded with either version of the sequence, but it is necessary to bear in mind that a transition to higher field strengths may be challenging. At higher fields the magnitude of the largest flip angle achievable within SAR safety limits would be reduced compared to 1.5T. Since the flow sensitivity of the FBI sequence increases for smaller refocusing pulse FAs (11,14), inability to play out RF pulses with large (120°) FAs may compromise arterial visibility in vessels with relatively fast diastolic flow. Using interleaved FBI at higher fields without scan time and image quality penalties may require the design of lower SAR refocusing pulses.

Imaging patients with irregular or high heart rates is a challenging aspect of both sequential and interleaved FBI. A rapid heart rate is especially problematic for interleaved FBI because it exacerbates the effect of non-uniform TR between systole and diastole. Our theoretical calculations and in vivo experience with interleaved FBI suggest that triggering every second heart beat is necessary to ensure satisfactory image quality in patients with irregular or high heart rate (> 80 bpm). It should be noted that a restore (tip-up) pulse was not used in this study. However, applying a restore pulse at the end of the echo train to speed up T_1 recovery may additionally improve arterial depiction, particularly in the event of high heart rates.

The use of separate imaging slabs for each extremity permits the use of different flow-sensitizing sequence parameters for each leg. Whether this flexibility improves the robustness of the technique to flow asymmetry requires evaluation in a larger clinical population. Differential flow was not observed in the small patient group imaged in this study, so the potential benefits of parameter customization could not be assessed.

Conclusions

We have presented a modification of the FBI technique for non-contrast MRA that is designed to offer better robustness to patient motion and flow asymmetry. Initial results in volunteers, imaged while performing controlled movements, suggest improved tolerance to subject motion compared to the original technique. The modified technique, however, is not expected to withstand severe or constant motion. It remains to be studied whether the proposed modifications will improve the overall clinical performance FBI.

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Figure 1.

(a) Slab positioning. Interleaved-FBI uses two sagittal 3D imaging slabs, with frequency encoding head-foot, phase encoding anterior-posterior and partition encoding right-left (H = head, F = foot, R = right, L = left, A = anterior, P = posterior, X = frequency-encoding direction, Y = phase-encoding direction, Z = partition-encoding direction).

(b) Sequence diagram. The readout is ECG-triggered and data acquisition alternates between left and right legs in consecutive cardiac cycles. Imaging in a sagittal plane greatly reduces the size of the phase-encoding dimension and permits acquisition of a full k-space partition (an entire k_x - k_y plane) every cardiac cycle, therefore allowing two sagittal slabs to be imaged in the same scan time as one coronal slab. The TR for each extremity in interleaved-FBI is approximately twice that of sequential-FBI for the same scan time.

Figure 2.

Right leg angiograms obtained in a 50 year-old male with heart rate = 60 bpm, instructed to hold still. Note the reduced sharpness and increased apparent caliber of the vessels on the sequential acquisition (a), in the case of coronal projection, and on the interleaved acquisition (d), in the case of sagittal projection. Since the voxel dimensions were identical between the two sequences along each direction in physical space (i.e. 1.3mm H/F, 1.5mm R/L, and 2.0mm A/P), these differences probably reflect T2 blurring along the phase-encoding direction, which was oriented left/right in the case of sequential FBI and anterior/posterior in the case of interleaved FBI.

Figure 3.

Right (a) and left (b) leg angiograms obtained using interleaved FBI in a 29 year-old male with heart rate = 72 bpm, instructed to hold still. The two extremities were imaged during the same acquisition, but with different flip angles. The use of a lower flip angle for the left leg resulted in undesirable signal loss at the center of the popliteal artery (arrow), but better visualization of small branch vessels. The flexibility to use separate flow-sensitizing parameters for each leg may be valuable when pathology is present.

Figure 4. Comparison between interleaved-FBI and sequential-FBI for different motion paradigms in a 33 year old healthy subject. Interleaved-FBI offered improved tolerance to subject motion.

Figure 5.

Interleaved-FBI and sequential-FBI angiograms in a 72 year old volunteer with PAD and heart rate 90 bpm. Sequential FBI exhibited motion artifacts, which were exacerbated when TR was doubled from 1 R-R interval (a) to 2 R-R intervals (c). Interleaved FBI provided satisfactory image quality when data were collected every cardiac cycle (b), and excellent image quality when data were acquired every second cardiac cycle (d). The improvement in image quality from (b) to (d) is likely due to mitigation of non-uniform T_1 recovery with the longer average TR.

Table 1

Image quality ratings (1 = non-diagnostic, 2 = poor, 3 = satisfactory, 4 = excellent) for sequential-FBI and interleaved-FBI in 10 volunteers and 3 patients.

	Sequence	No Motion	Minimal Motion	Foot rotation
Volunteers	Sequential FBI	3.60 ± 0.51	2.22 ± 1.01 *	1.63 ± 0.78 *
	Interleaved FBI	3.78 ± 0.21	3.32 ± 0.74 *	2.72 ± 0.72 *
Patients	Sequential FBI	3.73 ± 0.32		
	Interleaved FBI	3.80 ± 0.26		
	Gd-MRA	3.90 ± 0.19		

*
p < 0.05