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Large coverage Black-Bright blood Interleaved imaging sequence (LaBBI) for 3D dynamic contrast-enhanced MRI of vessel wall

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Abstract

Purpose—To propose a Large coverage Black-Bright blood Interleaved imaging sequence (LaBBI) for 3D dynamic contrast-enhanced MRI (DCE-MRI) of vessel wall.

Methods—LaBBI consists of a 3D black-blood stack-of-star golden angle radial acquisition with high spatial resolution for vessel wall imaging and a 2D bright-blood Cartesian acquisition with high temporal resolution for Arterial Input Function (AIF) estimation. The two acquisitions were performed in an interleaved fashion within a single scan. Simulations, phantom experiments and in vivo tests were performed to investigate the feasibility and performance of the proposed LaBBI.

Results—In simulation test, the estimated K^{trans} and v_p by LaBBI were more accurate than conventional bright-blood DCE-MRI with lower root mean square error (RMSE) in all the tested conditions. In phantom test, no signal interference was found on the 2D scan in LaBBI. Pharmacokinetic analysis of the three patients data acquired by LaBBI showed that the K^{trans} was higher in fibrous tissue ($0.0717 \pm 0.0279 \text{ min}^{-1}$), while lower in necrotic core ($0.0206 \pm 0.0040 \text{ min}^{-1}$) and intraplaque hemorrhage ($0.0078 \pm 0.0007 \text{ min}^{-1}$), compared with normal vessel wall ($0.0273 \pm 0.0052 \text{ min}^{-1}$).

Conclusion—The proposed LaBBI sequence, with high spatial and temporal resolution, and large coverage blood suppression, was promising to probe the perfusion properties of vessel wall lesions.

Keywords

vessel wall; inflammation; dynamic contrast-enhanced MRI; black-bright blood interleaved imaging

INTRODUCTION

Vessel wall inflammation plays an important role in the development of vascular diseases such as atherosclerosis and aneurysms (1,2). In several studies, vessel wall inflammation has been shown to be associated with clinical vascular events (3,4). Thus, it is important to image vessel wall inflammation in vivo. Dynamic contrast-enhanced MRI (DCE-MRI) is a useful tool to analyze inflammation in carotid atherosclerosis noninvasively (5–10) by using pharmacokinetic modeling.

However, using DCE-MRI to evaluate inflammation in vessel wall is technically challenging, especially in early lesions. There are two competing requirements in DCE data acquisition (11): high temporal resolution bright-blood imaging for arterial input function (AIF) acquisition, and high spatial resolution black-blood imaging for vessel wall depiction. Currently, most studies have made compromises by acquiring only bright-blood images (6,7,10,12,13) for advanced plaques. The bright-blood technique can estimate the AIF directly, but the temporal resolution (~15s) is compromised by the high spatial resolution required for vessel wall imaging and is usually insufficient to extract AIF accurately. More importantly, thin vessel walls with early lesions cannot be quantified reliably due to signal contamination from the luminal signal. Black-blood DCE techniques have also been proposed for vessel wall imaging (9,14) that allow accurate thin vessel wall imaging by suppressing blood signal. However, AIF cannot be extracted directly from the black-blood images and may introduce bias in the pharmacokinetic analysis using the reference region method or population AIF (9,14).

Recently, several techniques enabling interleaved black-bright blood imaging have been introduced (15–17), which can acquire bright-blood images for AIF and black-blood images for vessel wall in a single scan. However, these techniques are based on a double inversion-recovery (DIR) (18) or quadruple inversion-recovery (QIR) (19) prepulse for black-blood imaging. Thus, they are limited to 2D vessel wall imaging and with limited longitudinal coverage. Mendes J. et al, proposed an interleaved 2D–3D bright-blood imaging sequence to perform 3D vessel wall DCE-MRI (20). However, the vessel wall imaging in this sequence may still suffer from luminal signal contamination, since no black-blood prepulse was used.

In this study, we propose a Large coverage Black-Bright blood Interleaved imaging sequence (LaBBI) for vessel wall DCE-MRI. In this sequence, the 3D large coverage high spatial resolution black-blood vessel wall images and 2D high temporal resolution bright-blood images can be acquired in an interleaved fashion within a single scan. In LaBBI, the spatial and temporal resolution of the two acquisitions can be adjusted flexibly to satisfy the requirements of pharmacokinetic analysis on different targets. Simulation, phantom studies and in vivo experiments were performed to test the feasibility of the proposed LaBBI method.

METHODS

Sequence Design

LaBBI is composed of a 2D high temporal resolution bright-blood imaging module and a 3D high spatial resolution black-blood imaging module (Fig. 1a). For the 3D black-blood imaging module, the stack-of-star (SoS) golden radial acquisition (21) was used, which performed Cartesian sampling in the slice (kz) direction with low-high acquisition order and radial sampling in the kx-ky plane. As shown in Fig. 1a, each 3D shot consisted of the iMSDE (improved Motion Sensitized Driven Equilibrium) black-blood prepulse (22) for large coverage 3D blood signal suppression, SPIR (Spectral Presaturation with Inversion Recovery) fat suppression and data acquisition, where the radial spokes with the same angle through all slices were acquired. The 3D imaging slab was centered at the target vessel wall lesion (Fig. 1c). For bright-blood imaging, 2D fast field echo (FFE) Cartesian data acquisition was used, and the 2D imaging slice was positioned perpendicular to a large vessel adjacent to the vessel wall lesion (Fig. 1c). In the 2D acquisition, a spatial saturation band was placed upstream of the 2D imaging slice (Fig. 1c) and performed in each TR (Fig. 1a). The saturation band was used to induce the saturation recovery of blood signal and then eliminate the interference from the non-selective black-blood prepulse. The proposed sequence supports instantaneous switching (23) between bright- and black-blood imaging modules. In our design, one bright-blood imaging dynamic is interleaved with one 3D imaging block containing the user-defined number of 3D shots of black-blood imaging (Fig. 1a, b).

Image Reconstruction—For the SoS golden angle radial data, the gradient delays in radial sampling was firstly compensated using the method in (24). The radial data was then reconstructed into time series by grouping several blocks of 3D imaging into temporal frames using an established reconstruction method (21), which utilizes parallel imaging and compressed sensing together to reduce undersampling artifacts. The reconstruction equation is as follows:

$$\hat{m} = \arg \min \{ \|FSm - d\|_2^2 + \lambda \|TV_t m\|_1 \} \quad [1]$$

where m is the image series to be reconstructed, d is the acquired multi-coil data, S are the coil sensitivity maps, F is the non-uniform fast Fourier transform (NUFFT) operator, TV_t is the temporal total-variation operator, and λ is the regularization factor. The coil sensitivities were obtained by NUFFT of all radial lines, and λ were selected empirically (21).

Imaging Parameters—All imaging experiments in this study were performed on a 3.0T Philips MR scanner (Achieva TX, Best, the Netherlands). The imaging parameters of LaBBI are shown in Table 1. For the 3D vessel wall imaging module, 15 transverse slices were acquired with a large coverage of 30mm. So the turbo field echo (TFE) factor of the 3D shot was 15, which means that only 15 spokes (duration of about 180ms) were acquired following each iMSDE and SPIR prepulses, so the black-blood contrast and fat suppression can be maintained. Each 3D imaging block was set to contain 3 dummy shots and 10

acquisition shots with the dummy shots to restore the steady-state of the 3D acquisition. The signal evolutions of the 3D imaging during contrast passage with and without dummy shots are demonstrated in Supporting Figure S1. In LaBBI, one 2D dynamic was interleaved with one 3D block, resulting in a temporal resolution of AIF, $T_{aif}=4.7s$. Two 3D blocks with 20 radial spokes per slice were used to reconstruct one frame of the 3D black-blood dynamic image series, resulting in a temporal resolution of vessel wall, $T_{vw}=9.4s$. The distance between the two imaging modules was about 20mm.

Simulation Test

Simulations were performed to investigate the accuracy of pharmacokinetic parameters estimated by LaBBI. The traditional bright-blood DCE imaging sequence (6) was also simulated as a comparison.

Both LaBBI and the traditional bright-blood DCE-MRI used the same 2D Cartesian acquisition for AIF, so the AIF C_p was simulated directly using a biexponential equation (25). The contrast agent concentration in the blood was calculated by:

$$C_b = C_p \cdot (1 - Hct) \quad [2]$$

with an assumed hematocrit (Hct) value of 0.4 (25). The changing T_1 values of blood after contrast injection can be calculated by:

$$1/T_1 = r_1 \cdot C[Gd] + 1/T_{10} \quad [3]$$

where $r_1=4.5L/mmol/s$ (26), $C[Gd]$ is the concentration of contrast agent, T_{10} is the pre-contrast T_1 value. In this study, T_{10} was assumed to be 1650ms for blood (27). Then, signal curve of blood (Sig_b) can be calculated using the saturation recovery (SR) equation (Eq. [4])

$$Sig_b = M_{0b}(1 - \exp(-t_d/T_1))\sin(\alpha) \quad [4]$$

where M_{0b} is the proton density of blood, t_d is saturation delay time and α is the flip angle. Subsequently, the blood signal curves of the traditional bright-blood DCE (6) and the proposed LaBBI were generated by undersampling the Sig_b according to the corresponding temporal resolutions of the two methods. The zero-mean Gaussian noise with standard deviation (SD) = the mean signal of all frames / signal-to-noise ratio (SNR) was then added to the signal curve. The SNR of simulated blood signal was set to be twice that of the vessel wall SNR, which was in agreement with the following in vivo SNR measurements.

For vessel wall imaging, three types of simulations were carried out to simulate the vessel wall dynamic images under different conditions: 9 spheres with 9 evenly distributed K^{trans} values ranging from 0.02 to $0.2min^{-1}$ and fixed $v_p=0.05$, SNR=30; 9 spheres with 9 evenly distributed v_p values ranging from 0.01 to 0.1 and fixed $K^{trans}=0.1min^{-1}$, SNR = 30; 1

sphere with fixed $K^{\text{trans}}=0.1\text{min}^{-1}$, $v_p=0.05$, and simulated with 10 equally spaced SNR levels ranging from 20 to 40.

With known C_p and given K^{trans} , v_p values, the uptake curves of the vessel wall ($C_w(t)$) can be generated using the Patlak model (28):

$$C_w(t)=K^{\text{trans}}\int_0^t C_p(\tau)d\tau+v_p C_p(t) \quad [5]$$

And the changing T_1 values of vessel wall during dynamic imaging can be calculated by Eq. [3] with assumed T_{10} of 1150ms (17).

The simulated spheres were analytic in the Fourier domain (29), which can be calculated by the corresponding acquisition trajectory and image signal. For traditional bright-blood DCE, Cartesian trajectory was simulated with a temporal resolution of 15s (6). The signal curve of the vessel wall ($\text{Sig}_{VW_traditional}$) can be generated based on the spoiled gradient echo (SPGR) equation:

$$\text{Sig}_{VW_traditional}=\frac{M_{0VW}(1-E_{1,traditional})\sin(\theta)}{1-E_1\cos(\theta)} \quad [6]$$

where M_{0VW} is the proton density of vessel wall, $E_{1,traditional}=\exp(-TR_{traditional}/T_1)$, $TR_{traditional}$ is the repetition time, θ is the flip angle. For the 3D vessel wall imaging module in LaBBI, the SoS golden angle radial trajectory was simulated using parameters in Table 1, and the signal of each spoke was generated using Bloch simulation with the iMSDE prepulse represented by a T_2 relaxation term $E_2=\exp(-T_2^{\text{prep}}/T_2)$, where $T_2^{\text{prep}}=11.3\text{ms}$ is duration of iMSDE. The changing T_2 values during dynamic imaging were estimated by:

$$1/T_2=r_2 \cdot C[\text{Gd}]+1/T_{20} \quad [7]$$

where $r_2=5.09\text{L}/\text{mmol}/\text{s}$ (26), and T_{20} was assumed to be 54ms for vessel wall (30). For each simulation, the zero-mean Gaussian noise was added to the simulated k-space. Then dynamic image frames were reconstructed from the simulated k-space data by Fourier Transform for the Cartesian data and the reconstruction method described above for the SoS golden angle radial data.

For pharmacokinetic analysis of the simulations, AIF was obtained by converting the generated signal curve to concentration curve using Eq. [2–4]. For the traditional bright-blood DCE-MRI, pharmacokinetic analysis was performed based on Eq. [3, 5, 6]. For LaBBI, the steady-state signal equation is (the derivation of the steady-state equation is detailed in the Supporting file):

$$M_{ss} = \frac{M_0(1 - E_1)E_2 \sin \beta}{1 - E_1 \cos \beta} \cdot \frac{1 - (E_1 \cos \beta)^K}{1 - E_2(E_1 \cos \beta)^K} \quad [8]$$

where K is the total number of acquired slices. Combining Eq. [3, 5, 7, 8], K^{trans} and v_p can be estimated using the Levenberg-Marquardt curve fit. Then, the K^{trans} and v_p maps were generated for both methods.

Each simulation was repeated 100 times with independent zero-mean Gaussian noise added. The mean value of each simulated sphere was calculated at every simulation. The estimation accuracy of the pharmacokinetic parameters was evaluated by the normalized root mean

square error (RMSE): $\text{RMSE} = \sqrt{\sum_{i=1}^N (P_{e,i} - P_t)^2 / (NP_t^2)}$, where P_e and P_t are the estimated mean values and simulated true values, N is the number of repeated simulations. The average and SD of the 100 repeats were also reported for the three simulation types.

Phantom Study

In this study, phantom scans were performed to test whether there was interference on the 2D bright-blood imaging from the iMSDE prepulse in the black-blood imaging module. A series of tubes with varied concentrations of Gadolinium contrast agent were used to simulate the T_1 (300ms–1600ms) prior and after contrast injection. The phantom was set upright, and the two scan slabs in LaBBI were both performed coronally with a distance of about 20mm. For the 2D imaging module, to induce the saturation recovery of signal, a slice selective SR prepulse at the imaging location was used to simulate the saturation band. All other imaging parameters were the same as the in vivo experiments shown in Table 1. The 3D imaging and 2D imaging modules were first performed in an interleaved fashion (LaBBI scan), and then performed separately with the same imaging settings. The agreement of the 2D images acquired by the interleaved and separate scan was investigated by comparing the acquired signal intensities of different tubes using Pearson correlation.

In vivo Experiments

This study was approved by the institutional review board, and written informed consent was obtained from all participating subjects. Three patients (3 males, age of 70, 72 and 47 years for case 1, case 2 and case 3) with carotid artery atherosclerosis were scanned with a custom designed 36-channel neurovascular coil (31). A 3D iMSDE prepared turbo field echo (TFE) black-blood sequence, 3D MERGE (32) was firstly performed to identify the lesion location with $\text{FOV} = 250 \times 160 \times 40 \text{ mm}^3$, voxel size = $0.8 \times 0.8 \times 0.8 \text{ mm}^3$ and 50 coronal slices. The simultaneous noncontrast angiography and intraplaque hemorrhage (IPH) imaging sequence, SNAP (33), with the same FOV and voxel size to 3D MERGE was also performed. Then, the LaBBI sequence was used to acquire DCE-MRI images with 3D imaging centered at the location with the largest lesion size. Coincident with the third dynamic of the bright-blood imaging, a bolus of 0.1mmol/kg Gd-DTPA (Magnevist; Bayer Schering Pharma, Berlin, Germany) was intravenously injected at a rate of 1.5mL/s, followed by a 20mL saline flush at the same rate. The imaging parameters of LaBBI are shown in Table 1. For two patients

with obvious plaque, the post-contrast images were also acquired by a T1-weighted (T1W) inversion recovery (IR) prepared TFE sequence, with an inversion delay time=500ms, and voxel size=0.8×0.8×0.8mm³.

In vivo Image Analysis—On the 2D bright-blood images of LaBBI, a small region of interest (ROI) was placed around the center of carotid artery lumen, and then a clustering algorithm was used to select voxels with strong enhancement to calculate the signal curve of blood to reduce the influence of inflow artifacts (7). By assuming the $T_{10} = 1650\text{ms}$ (27) and $Hct=0.4$ (25) for blood, the AIF can be acquired by Eq. [2–4].

The 3D SoS golden angle radial data was reconstructed into a dynamic series using Eq. [1] with 20 spokes for each slice per frame. The 3D MERGE and SNAP images were reformatted to 2mm axial slices according to the imaging geometry of LaBBI for analysis. Then, for case 1 and case 2, 7 slices centered at bifurcation were selected from each carotid artery. For case 3, the imaging was targeted at intracranial internal carotid artery with location much higher than the bifurcation, so 5 slices covering artery were selected for each carotid artery.

The ability of the black-blood image of LaBBI to depict vessel wall was evaluated by comparing with 3D MERGE. The frame of LaBBI vessel wall images that visually best depicted vessel wall was selected by one reviewer. Then another experienced reviewer blinded to the image types drew the contours of lumen, outer wall and muscle on the selected slices of LaBBI vessel wall and 3D MERGE using a custom-designed image analysis software (34). The vessel wall area (WA) and maximum wall thickness (MWT) were compared between LaBBI and 3D MERGE using Wilcoxon signed rank test and intra-class correlation coefficient (ICC).

For pharmacokinetic analysis, the regions of necrotic core (NC), calcification and IPH were also identified for slices with plaque, with NC and calcification defined on post-contrast phase of LaBBI vessel wall images with post-contrast T1W and SNAP images as reference (35,36) and IPH defined on SNAP images (33). After registration of the LaBBI vessel wall series (37), the contours of lumen, outer wall, NC and calcification defined on one frame of LaBBI vessel wall images with best vessel wall contrast were propagated to other frames. The reformatted SNAP images were registered to the LaBBI vessel wall images, and then the IPH contours were mapped to LaBBI. The remaining region in the plaque were assumed to be fibrous tissue (FT) (37). Then the signals of LaBBI vessel wall images in the defined contour were averaged to generate the uptake curves. Then as done in the simulation, based on Eq. [3, 5, 7, 8] and assumed T_{10} , T_{20} , the mean K^{trans} and v_p can be estimated for the ROI in each slice. No IPH was observed in the analyzed NC, and pre-contrast T_1 of NC, FT and normal vessel wall, muscle was assumed to be 1150ms (17). For IPH, T_{10} was set to be 500ms (33,38). The pre-contrast T_2 values of normal vessel wall, muscle, FT, NC, and IPH reported in (30) were used in the analysis, as shown in Table 2. The calcification was excluded from analysis due to the lack of pre-contrast T_1 and T_2 .

The SNRs of blood and normal vessel wall were also estimated for the in vivo data. Signal was determined by the mean signal of all the dynamics in the corresponding ROI, while

noise was defined as the standard deviation of the mean signal in a peripheral air region in the same frames.

RESULTS

Simulation and phantom studies

In simulation of different K^{trans} from 0.02 to 0.2 min^{-1} , fixed $v_p=0.05$ and fixed $K^{\text{trans}}=0.1 \text{ min}^{-1}$, different v_p from 0.01 to 0.1, the average K^{trans} and v_p maps of the 100 repeated simulations with vessel wall SNR=30, derived from LaBBI are shown in Fig. 2a, d and Fig. 3a, d. LaBBI tended to underestimate the K^{trans} and v_p values a little, while the bright-blood DCE overestimated the parameters. But the mean K^{trans} and v_p values estimated by LaBBI were consistently closer to the true values with much smaller RMSE than the bright-blood DCE (Fig. 2b, c, e, f and Fig. 3b, c, e, f). For the fixed K^{trans} , the v_p values had little influence on its estimation accuracy in LaBBI, while the estimation error of K^{trans} tended to be lower at larger v_p values in bright-blood DCE (Fig. 2e, f). For the fixed v_p , its estimation accuracy was higher at smaller K^{trans} values in both LaBBI and bright-blood DCE (Fig. 3b, c).

Simulation results of different SNR levels, with $K^{\text{trans}}=0.1 \text{ min}^{-1}$, $v_p=0.05$, are shown in Figure 4. An example of the average K^{trans} and v_p maps of the 100 repeated simulations of LaBBI at SNR=30 of vessel wall are shown in Fig. 4a, d. Higher SNR increased estimation accuracy in both LaBBI and bright-blood DCE methods. However, LaBBI was consistently better than traditional bright-blood DCE in K^{trans} and v_p estimations for all the tested SNR levels (Fig. 4b, c, e, f), with smaller bias and much lower RMSEs (5%–8% vs. 6%–13% for K^{trans} ; 5%–8% vs. 19%–23% for v_p).

For the phantom study, signal intensity acquired by the 2D SR imaging module in the interleaved acquisition, imitating the LaBBI 2D AIF imaging module, agreed well with that of a separate acquisition (Fig. 5, $R=0.99$), suggesting that the 3D black-blood prepulse had little influence on the saturation recovery signal.

In vivo experiments

All 3 subjects were successfully imaged. For comparison of LaBBI vessel wall images with 3D MERGE images, totally 38 slices from the 6 carotid arteries were measured. The WA and MWT measured by LaBBI were (mean $\pm$ SD) $38.66\pm22.23\text{mm}^2$ and $2.240\pm1.513\text{mm}$, and by 3D MERGE were $39.52\pm19.24 \text{ mm}^2$ and $2.245\pm1.269\text{mm}$. No significant difference was found between LaBBI and 3D MERGE (WA: $P=0.27$; MWT: $P=0.25$). And the ICCs indicate good agreements (WA: 0.952, 95% CI, 0.911–0.975; MWT: 0.944, 95% CI, 0.894–0.970), suggesting the LaBBI sequence itself can be used to depict vessel wall.

Among the 38 slices, plaque (focal wall thickness $> 2\text{mm}$) was detected in 21 slices in 4 carotid arteries, among which, one plaque had NC (case 1), and one plaque had IPH (case 2). For case 1, four high spatial resolution dynamic images of a representative slice with carotid plaque and an example slice of the normal vessel wall acquired using the 3D black-blood imaging module in LaBBI are demonstrated (Fig. 6a, b). Blood suppression was sufficient prior and post contrast in both the diseased and healthy locations. For comparison,

the reformatted iMSDE and post-contrast T1W images are also shown in Fig. 6a, b. The locations with and without plaque can be clearly confirmed and a necrotic core (NC) was identified in the diseased slice. High temporal resolution bright-blood dynamic images acquired by the 2D imaging module of LaBBI during contrast agent injection, are also demonstrated (Fig. 6c). For case 2, dynamic black-blood images of the 2 slices with IPH and bright-blood images acquired by LaBBI throughout the contrast injection process are shown in Figure 7. The IPH regions were identified on the SNAP images (Fig. 7a). And for the LaBBI vessel wall images, good blood suppression can be seen for all frames. The LaBBI images of case 3 are shown in Supporting Figure S2.

For pharmacokinetic analysis, one example of the extracted AIF from the bright-blood images in LaBBI is shown in Figure 8. And the average K^{trans} and v_p of the measured slices for normal vessel wall, FT, NC, IPH and muscle were summarized in Table 2. Similar K^{trans} and v_p values were observed for the normal vessel wall and the muscle tissue. Compared to the normal vessel wall, NC and IPH had lower K^{trans} and v_p , while FT showed higher values. The measured SNR of blood in the bright-blood images of the 3 cases was 63.4 ± 3.8 , and the SNR of normal vessel wall was 33.5 ± 3.1 .

DISCUSSION

In this study, a large coverage black-bright blood interleaved imaging sequence, LaBBI, was proposed for vessel wall DCE-MRI. The proposed sequence could acquire both high temporal resolution bright-blood images and 3D large coverage high spatial resolution black-blood vessel wall images simultaneously. Simulations, phantom studies, and in vivo experiments were performed to demonstrate the feasibility and advantages of LaBBI.

The LaBBI sequence was designed to solve the technical problems in vessel wall DCE-MRI. For vessel wall, the imaging target is small, especially in early lesions, and a submillimeter in-plane spatial resolution, such as $0.6 \times 0.6 \text{ mm}^2$ is usually needed (9,10,14,17). The vessel wall lesion may have a large distribution along the diseased artery. Sufficient imaging coverage is important to cover the whole plaque. Vessel wall signal may also be contaminated by luminal blood signal, especially following bolus arrival, making imaging of early lesions or the region near lumen in advanced plaques difficult. Therefore, blood signal should be suppressed in vessel wall DCE imaging (9,14,17). While for AIF acquisition, the blood should not be suppressed, and the high temporal resolution is required for accurate pharmacokinetic analysis of DCE data (11). However, high spatial resolution or large coverage is not needed since AIF can be acquired from one slice of large vessels. In LaBBI scan, a 2D high temporal resolution bright-blood acquisition was interleaved with a 3D large coverage high spatial resolution black-blood acquisition, meeting the different technical requirements of vessel wall imaging and AIF acquisition in vessel wall DCE-MRI.

In the 3D imaging module of LaBBI, a black-blood prepulse, iMSDE (22) was used. Compared with DIR (18) or QIR (19) prepulse, iMSDE has the advantage of large coverage blood suppression, which enables large coverage 3D black-blood imaging in LaBBI. The iMSDE prepulse will introduce T_2 weighting into the vessel wall images. Unlike the traditional DCE analysis method, the T_2 effect should be considered in the conversion from

image signal to contrast concentration, as was done in the simulation and in vivo experiments.

In addition, the 3D imaging module for LaBBI used the SoS golden-angle radial trajectory for acquisition. Utilizing a parallel imaging and compressed sensing combination reconstruction method (21), both high in-plane spatial resolution ($0.6 \times 0.6 \text{ mm}^2$) and large coverage (30m) of the vessel wall imaging were achieved with a temporal resolution of 4.7s for AIF and 9.4s for the vessel wall. However, compared with traditional Cartesian acquisitions (6) the reconstructed images from the SoS golden-angle radial data may have undersampling artifacts, which may introduce bias into the pharmacokinetic modeling. To address these concerns, simulation experiments considering the interleaved acquisition, T_2 effects of iMSDE, SoS golden-angle radial sampling, and reconstruction were carried out. The results showed that the proposed LaBBI sequence had a consistently lower RMSE of estimated kinetic parameters than the conventional bright-blood DCE protocol (6) under all tested conditions. Notably, the simulation experiments did not consider vessel wall signal contamination from lumen in bright-blood DCE, which could further introduce bias into its pharmacokinetic modeling. Therefore, LaBBI, with the ability to acquire high temporal resolution AIF and large coverage high spatial resolution black-blood vessel wall images, has unique advantages for vessel wall DCE-MRI.

A common issue in interleaved black-bright imaging techniques is the difficulty in eliminating the interference of black-blood imaging on the AIF acquisition (15–17,20). In the proposed LaBBI sequence, the non-selective black-blood imaging pulses, iMSDE, will influence the blood signal, and disturb the AIF acquisition. Therefore, a spatial saturation band was used and placed upstream of the 2D imaging slice, eliminating possible interference by inducing saturation recovery of the blood signal. In the phantom test, good agreement of the signal intensities of the 2D SR images acquired by the separate and interleaved scans proved that the interference from iMSDE was successfully eliminated.

In this study, the feasibility of LaBBI was demonstrated on three subjects with carotid atherosclerosis. LaBBI has been shown to successfully evaluate normal thin vessel walls, slightly thickened vessel walls and vessel walls with advanced plaque containing necrotic cores and IPH, with sufficient blood suppression in both pre- and post-contrast images. And the LaBBI vessel wall images can be used to depict vessel wall with good agreement of plaque burden measurements with 3D MERGE. For pharmacokinetic analysis, the normal vessel wall had similar K^{trans} and v_p values to muscle, which agreed with the published work (39). The fibrous tissue which usually had active inflammation or enriched neovasculature (6) showed higher K^{trans} and v_p values, while the necrotic core and IPH, where little contrast agent uptake occurred, had low K^{trans} and v_p values, which echoed the findings of previous studies (37).

Notably, the proposed interleaved acquisition scheme of LaBBI is also flexible for different applications and adjustable for practical imaging demands. For example, to further improve the temporal resolution of AIF, the interleaved scheme can be adjusted by reducing the number of 3D shots between the 2D imaging dynamics, or the spatial resolution of 2D imaging can be decreased when imaging large vessels. To further enlarge the acquisition

coverage of LaBBI for intracranial or femoral artery imaging, the 3D imaging orientation can be changed to a coronal or sagittal orientation with proper adjustment to avoid placing the 2D imaging slice and the spatial saturation band on the targeted vessel wall lesion. Furthermore, the 3D imaging module for LaBBI can also be adjusted to acquire 3D isotropic images for curved arteries, such as the intracranial arteries.

There are several limitations in this study. First, the in vivo experiments lacked histological validation due to the unavailability of histological specimens. However, LaBBI is theoretically similar to the previously histologically validated DCE methods (6,7). And the simulation studies demonstrated that LaBBI should have more accurate quantifications than the conventional method benefiting from the higher temporal resolution. Therefore, LaBBI should be able to quantify neovasculature and inflammation of the vessel wall in a similar way to the previously validated work. Second, the assumed pre-contrast T_1 , T_2 values were used in the pharmacokinetic analysis of LaBBI. In spite of the possible bias introduced by the assumed pre-contrast T_1 and T_2 values, the pharmacokinetic analysis results of the in vivo data had similar findings to previously published work (17,37,39) in regards to normal vessel wall, fibrous tissue, necrotic core and IPH, suggesting the feasibility of LaBBI to characterize perfusion properties of vessel wall lesion. However, in the future study, it's necessary to add pre-contrast T_1 , T_2 quantification (30,40,41) in vessel wall DCE-MRI. Furthermore, the proposed sequence should be further investigated in future studies with larger study population.

CONCLUSIONS

The proposed LaBBI sequence for DCE-MRI of vessel wall has the ability to acquire 2D high temporal resolution bright-blood images and 3D large coverage high spatial resolution black-blood vessel wall images simultaneously. The results of simulation, phantom, and in vivo experiments suggest that LaBBI is accurate in pharmacokinetic modeling and feasible for in vivo vessel wall imaging. Therefore, the LaBBI sequence may be a better tool for the characterization of vessel wall perfusion.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIG. 1.

The design scheme of LaBBI. **a:** Sequence schematic of LaBBI: 2D FFE Cartesian acquisition for AIF with a spatial saturation band performed in each TR; 3D stack-of-star golden angle radial for vessel wall imaging with iMSDE prepulse for blood suppression and fat saturation after iMSDE pulse. **b:** The interleaved scheme of LaBBI with one 2D bright-blood dynamic interleaved with a designated number of 3D shots. **c:** The locations of the spatial saturation band, 2D imaging slice and 3D imaging slab.

FIG. 2.

Results of the simulations in K^{trans} estimation with LaBBI compared with conventional bright-blood DCE method. For K^{trans} ranging from 0.02 to 0.2 min^{-1} , fixed $v_p = 0.05$ and vessel wall SNR=30: **a** shows the average K^{trans} map of 100 repeated simulations of LaBBI; **b, c** shows the mean and SD, RMSE of K^{trans} . For v_p ranging from 0.01–0.1, fixed $K^{\text{trans}} = 0.1 \text{ min}^{-1}$ and vessel wall SNR=30: **d** shows the average K^{trans} map of 100 repeated simulations of LaBBI; **e, f** shows the mean and SD, RMSE of K^{trans} .

FIG. 3.

Results of simulations in v_p estimation with LaBBI compared with a conventional bright-blood DCE method. For K^{trans} ranging from 0.02–0.2 min^{-1} , fixed $v_p = 0.05$ and vessel wall SNR=30: **a** shows the average v_p map of the 100 repeated simulations of LaBBI; **b, c** shows the mean and SD, RMSE of v_p . For v_p ranging from 0.01–0.1, fixed $K^{trans} = 0.1 \text{ min}^{-1}$ and vessel wall SNR=30: **d** shows the average v_p map of 100 repeated simulations of LaBBI; **e, f** shows the mean and SD, RMSE of v_p .

FIG. 4. Simulation results of $K^{\text{trans}} = 0.1\text{min}^{-1}$ and $v_p = 0.05$ with vessel wall SNR ranging from 20–40 by LaBBI and conventional bright-blood DCE. **a, d** shows an example of the average K^{trans} and v_p map of 100 repeated simulations of LaBBI at SNR=30; **b, c, e, f** shows the mean and SD, RMSE of K^{trans} and v_p estimated at different SNR levels. The SNR of AIF was set to be twice that of the vessel wall.

FIG. 5.

Comparison of the interleaved scan in LaBBI and the separate scan using 2D SR. **a:** The signal intensity of tubes with different contrast concentrations acquired by separate 2D SR and interleaved 2D SR scans. **b:** The two signal intensity curves in **a** were in good agreement ($R=0.99$).

FIG. 6.

Dynamic images before, during, and after bolus arrival of case 1 with atherosclerotic plaque acquired by LaBBI, as well as the corresponding iMSDE and post-contrast T1W images. **a:** A typical slice for normal vessel wall in the common carotid artery. **b:** One representative slice of the atherosclerotic plaque. The dynamic LaBBI vessel wall images in **a**, **b** are shown in the same intensity scale. The blue contours outline the outer wall; the red contours outline the lumen; the yellow contours outline the necrotic core. **c:** The dynamic bright-blood images acquired by LaBBI shown in the same intensity scale. One black-blood image frame was interleaved with two bright-blood image frames. The white arrowheads indicate the artery to extract AIF.

FIG. 7. Dynamic images before, during, and after bolus arrival of case 2 with intraplaque hemorrhage acquired by LaBBI. **a:** The slices of IPH with red contours outlining the lumen, blue contours outlining the outer wall and orange contours outlining IPH on SNAP images. The dynamic vessel wall images of LaBBI in **a** are shown in the same level/window. **b:** The dynamic bright-blood images of LaBBI, shown in the same intensity scale. The white arrowheads indicate the artery to extract AIF. One black-blood image frame was interleaved with two bright-blood image frames in LaBBI.

FIG. 8.
The example AIF extracted from the 2D bright-blood images of LaBBI with temporal resolution of 4.7s.

Table 1

Imaging parameters of LaBBI

Parameters	3D black-blood	2D bright-blood
TR/TE	12/5.6	19/4.2
Flip angle	15°	25°
FOV (transverse)	160×160 mm ²	150×150 mm ²
Spatial resolution	0.6×0.6 mm ²	1×1.5 mm ²
Slice thickness	2mm	2mm
Slices	15	1
TFE factor	15	NA ^a
Readout	536	NA
Spokes	429	NA
Dynamics	NA	43
Interleaved mode	1 block ^b	1 dynamic
Temporal resolution	9.4s ^c	4.7s
Total duration	3.4min	
Interval distance ^d	20mm	

^aNA: not applicable.^bOne 3D imaging block contained 3 dummy shots and 10 acquisition shots.^cTemporal resolution of the reconstructed 3D images using 20 spokes in each slice per frame.^dInterval distance: the distance between the 2D and 3D imaging module.

Table 2

Pharmacokinetic analysis results of the 3 patients imaged by LaBBI

	Normal VW	Muscle	FT	NC	IPH
Pre-contrast T_1 , T_2 (ms) ^a	1150, 54	1150, 39	1150, 56	1150, 37	500, 107
Number of slices ^b	17	38	21	4	2
K^{trans} (min ⁻¹) ^c	0.0273±0.0052	0.0206±0.0064	0.0717±0.0279	0.0206±0.0040	0.0078±0.0007
v_p	0.0152±0.0042	0.0107±0.0033	0.1253±0.0248	0.0021±0.0002	0.0043±0.0008

^aThe pre-contrast T_1 , T_2 values used in the pharmacokinetic analysis of LaBBI data

^bThe number of slices to calculate the slice averaged K^{trans} and v_p values

^c mean±SD