Concurrent CBF and BOLD fMRI with dual-echo spiral simultaneous multi-slice acquisitions at 7T

Denizhan Kurban a,*, Dimo Ivanov a, Sriranga Kashyap a, Laurentius Huber a, Gilad Liberman a,b, Benedikt A. Poser a

a Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht 6200MD, the Netherlands
b Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, Massachusetts, United States

A R T I C L E   I N F O

Keywords:
Dual-echo spirals
Arterial spin labeling
Spiral FMRI
Simultaneous multi-slice
Ultra-high field
Concurrent CBF-bold

A B S T R A C T

Measurement of cerebral blood flow (CBF) using the Arterial Spin Labeling (ASL) technique is a desirable fMRI approach due to the higher specificity of CBF to the site of neural activation. However, ASL has inherent limitations, such as a low signal-to-noise ratio (SNR) and low coverage/resolution due to the limited readout window following the labeling. Recently, ASL has been implemented at ultra-high field (UHF) strengths in an attempt to mitigate the SNR challenges. Even though ASL intrinsically allows concurrent acquisition of CBF and BOLD contrasts, a compromise in the echo time (TE) for either of the contrasts is inevitable with single-echo acquisitions. Long durations of the Cartesian EPI readout do not allow for multi-echo acquisitions for resolutions ≤2 mm where both contrasts can be acquired at their optimal TE at UHF. With its higher acquisition efficiency, single-shot spiral imaging provides a promising alternative to EPI, and with a dual-echo, out-in trajectory allows both CBF and BOLD contrasts to be acquired at their respective optimal TE. In this work, we implemented a dual-echo spiral out-in ASL sequence with simultaneous multi-slice (SMS) readout for increased coverage, and validated its application to fMRI with a visuomotor paradigm. Conventional Cartesian EPI acquisitions with matched parameters served as a reference. The dual-echo spiral ASL acquisitions resulted in robust CBF and BOLD activations maps. The absolute and relative CBF changes measured with the dual-echo spiral readout were in agreement with previous reports in the literature as well as the reference Cartesian acquisitions. The BOLD response amplitude was higher compared to the Cartesian acquisitions, attributable to a more optimal TE of the second echo. In conclusion, dual-echo spiral out-in SMS acquisition shows promise for concurrent acquisitions of BOLD and non-BOLD contrasts that require a short TE, with no loss in temporal resolution.

1. Introduction

Arterial spin labeling (ASL) is a non-invasive MRI method that allows quantitative measurements of cerebral blood flow (CBF). ASL involves magnetically labeling arterial blood water as an endogenous tracer (Detre et al., 1992; Williams et al., 1993). The ASL timelseries contain consecutive acquisition of label and non-label (control) images and the difference between the two images is proportional to the amount of blood perfused into tissue. ASL is an attractive method not only for the clinic where it is used for the detection of tissue perfusion alterations due to disease, but also for brain research where it exploits the tight coupling between neural activity and CBF. Changes in perfusion that accompany neural activity have been shown to be better localized to the site of neural activation compared to the blood oxygenation level-dependent (BOLD) signal (Duong et al., 2001; Pfeuffer et al., 2002; Zappe et al., 2008). Additionally, the possibility of acquiring CBF and BOLD signals simultaneously is desirable for studies investigating brain function and connectivity.

Nevertheless, ASL has several challenges especially in its application to fMRI. The signal-to-noise ratio (SNR) of the perfusion-weighted signal is intrinsically low due to the low microvascular density relative to the tissue volume. The label magnetization decays with T1 during the post-labeling delay (PLD), leaving a limited time for signal acquisition. Achieving large brain coverage for dynamic fMRI acquisitions therefore becomes challenging. Use of ultra-high magnetic fields (UHF) can partially mitigate these drawbacks. Increases in SNR and T1 relaxation time at UHF lead to higher perfusion SNR, which translates to larger brain coverage or ASL acquisitions at higher resolutions. These benefits of UHF have been shown in numerous studies for both ASL (Gardener et al., 2009; Ivanov et al., 2017a, 2017b) and BOLD (Donahue et al., 2011; van der Zwaag et al., 2009). However, due to the shorter T2* transverse relaxation times (25–33 ms) at UHF (Peters et al., 2007), simultaneous acquisitions of ASL and BOLD using dual/multi-echo protocols remain

https://doi.org/10.1016/j.neuroimage.2021.118820.
Received 9 August 2021; Received in revised form 9 December 2021; Accepted 13 December 2021
Available online 14 December 2021.
1053-8119/© 2021 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)
challenging. Additionally, the BOLD contamination of the perfusion signal leads to alterations in the temporal dynamics of the CBF response (Lu et al., 2006). In single-echo ASL acquisitions the different optimal echo times for CBF and BOLD contrast require an inevitable trade-off between CBF and BOLD sensitivity. Concurrent CBF and BOLD acquisition with dual-echo ASL protocols can provide more suitable echo times for acquiring each contrast. Most functional studies employing dual-echo acquisitions for concurrent CBF and BOLD are performed at 3T with conventional 2D EPI readout. At UHF and commonly desired spatial resolutions ($\leq 2 \times 2 \text{ mm}^2$ in-plane), however, simultaneous dual-echo acquisition becomes impractical with established EPI techniques as the readout duration precludes using optimal echo times for both CBF and BOLD. A promising alternative is presented by spiral sampling due to its time-efficient $k$-space sampling under the given gradient constraints. Spirals also allow the $k$-space center to be acquired at a very short effective TE (spiral-out) for perfusion acquisition with high SNR and reduced sensitivity to off-resonance effects. Combined into a dual-echo out-in spiral the parameters can furthermore be tuned to acquire the second (spiral-in) echo at an optimal TE for BOLD-weighted fMRI.

Spiral ASL has been shown in various implementations at 3T (Chang et al., 2017; Nielsen and Hernandez-Garcia, 2013; Vidorreta et al., 2013) but demonstrations at 7T are still lacking. The goal of this work was to implement a single-shot dual-echo out-in spiral sequence with simultaneous multi-slice (SMS) capability, in order to achieve concurrent acquisition of CBF and BOLD fMRI with optimal echo times at 7T. Application of the sequence is demonstrated on healthy volunteers using a visuo-motor stimulation paradigm.

2. Methods

2.1. Participants

Five healthy volunteers were scanned on a Siemens Magnetom 7T whole-body scanner (Siemens Healthineers, Erlangen, Germany), equipped with a 32-channel head coil (Nova Medical, Wilmington, MA, USA) and an SC72 gradient system with 70 mT/m peak amplitude and 200 T/m/s slew rate. All volunteers provided written informed consent following the protocols of the local ethics committee. Each volunteer underwent at least one fMRI run performing a visuo-motor task acquired using the spiral readout and Cartesian readout separately. If time allowed, few volunteers completed a second set of visuo-motor task experiments.

2.2. Sequence

The single-shot dual-echo spiral CBF-BOLD sequence was created in-house based on an SMS-EPI implementation (Ivanov et al., 2017b) of an ASL sequence with FAIR QUIPSS II (Wong et al., 1998). The labeling scheme uses an optimized 10 ms tr-FOCI inversion pulse (Hurley et al., 2010), which achieves high inversion efficiency at 7T, despite B1 inhomogeneities and SAR constraints. A variable density spiral trajectory was designed based on methods described in Kim et al. (2003). For smooth transition a spiral-out readout of 12.5 ms was attached to a slightly rotated spiral-in of the same duration, resulting in a total of 25 ms (Fig. 1). Gradient amplitude and slew rate were 29 mT/m and 132 T/m/s, respectively.

2.3. Data acquisition

fMRI measurements: Each volunteer underwent at least one baseline and one task-based ASL acquisitions with spiral and Cartesian EPI readouts separately. One volunteer completed two task-based runs within the same session with both types of acquisitions. The parameters of the dual-echo spiral are as follows: $\text{FoV} = 200 \times 200 \text{ mm}^2$, 24 slices with 2.0 mm isotropic voxel size, 50% slice gap, SMS-factor of 2, $\text{TE}_1/\text{TE}_2 = 2.5/27.5 \text{ ms}$, $\text{TR}_1/\text{TR}_2/\text{TR} = 700/1800/2220 \text{ ms}$, flip angle $= 65^\circ$, undersampling factor=1.6, CAIPII period of 200 μs. Cartesian EPI parameters were as follows: $\text{FoV} = 200 \times 200 \text{ mm}^2$, 24 slices with 2.0 mm isotropic voxel size, 50% slice gap, SMS-factor of 2, $\text{TE} = 11 \text{ ms}$, $\text{TI}_1/\text{TI}_2/\text{TR} = 700/1800/2220 \text{ ms}$, flip angle $= 65^\circ$, GRAPPA factor = 2, CAIPI FoV shift = 2. Note that Cartesian EPI readout allows acquisition of only one echo at this resolution due to long readout duration (19.08 ms ADC on time, 28 ms acquisition duration per slice for one echo), even with partial Fourier of 6/8.

Stimulus: During the task runs participants were presented with a full-screen flickering (approx. 8 Hz) black and white radial checkerboard stimulus for 10 TRs interleaved with 12 TRs rest periods. They were asked to also perform a thumb-to-digits tapping with both hands while the flickering checkerboard stimulus was on. During the rest periods, the participants were asked to fixate on the white fixation cross. Each functional run lasted 293 TRs (~10 min 48 s). The baseline CBF acquisitions involved passive fixation on a white cross presented on an isoluminant gray background. Each baseline run lasted for 4 min 24 s, collecting 60 pairs of label-control images.

Anatomical measurements: High resolution $T_1$-weighted anatomical images were obtained with the MP2RAGE sequence (Marques et al., 2010) at 0.9 mm isotropic resolution ($\text{TE}/\text{TI}_1/\text{TI}_2/\text{TR} = 2.47/900/2750/5000 \text{ ms}$ and $a_1/a_2 = 5^\circ/3^\circ$).

Fieldmap: Multi-echo gradient echo (ME-GRE) scans at matched slice positions, resolution and coverage as the ASL scans were obtained with the following parameters: $\text{TE}_n = 1.5/3.18/5.40/7.50/9.60 \text{ ms}$, flip angle $= 17^\circ$, $\text{TR} = 494 \text{ ms}$. Fieldmaps were extracted for use in $\text{B}_0$ field inhomogeneity correction of the spiral acquisitions, and for the distortion correction for the Cartesian EPI ASL acquisitions.

Calibration scan for CBF: For quantification of CBF, blood equilibrium magnetization ($\text{M}_0$) scans were acquired with each readout scheme separately, with TR increased to 20 s and ASL preparation pulses switched off.

---

**Fig. 1.** Trajectory used in the dual-echo spiral acquisition with simultaneous multi-slice readout. (A) $k_x$-$k_y$-plane view of one spiral echo, showing the relatively denser sampling at the center. (B) Dual-echo out-in spiral gradient waveform, with the CAIPIRINA $k_x$-blips shown in black (see zoomed inset).
2.4. Reconstruction

Data preparation and reconstruction was performed offline in MATLAB and Tensorflow, respectively, using an SMS implementation of the Minimal Linear Networks (MLN) approach developed by Liberman and Poser (2019). The network was trained with session-specific B0 maps separately for the out and in spiral trajectory. The network parameters such as training time, learning rate, number of compressed channels and number of k-space neighbors were selected after optimization of these parameters on pilot data. The network was trained for 2 h per slice using a GPU. Whole volume reconstruction therefore took 24 h (12 slices, MB=2) on a single GPU. Reconstruction of the first and second echo spiral images was performed separately on two GPUs. The Cartesian EPI data were reconstructed on the scanner as per Siemens standard Image Calculation Environment (ICE) reconstruction.

2.5. Data analysis

2.5.1. Anatomical data

Anatomical data were preprocessed in SPM12 (Ashburner, 2012) following the steps described in Kasyap et al. (2020). The second inversion image of the MP2RAGE sequence was automatically segmented using SPM, and was used to create a mask for non-brain tissue. The bias-corrected, T1w-MP2RAGE brain image was provided to Freesurfer (v6.0) (Fischl, 2012) as input for further segmentation. The mean spiral and Cartesian M0 images were coregistered to the T1w-MP2RAGE image using boundary-based registration (Greve and Fischl, 2009) as implemented in FSL-FLIRT (Jenkinson et al., 2012).

2.5.2. Functional data

Preprocessing: Spiral images from baseline and task acquisitions were motion-corrected and registered to their corresponding mean M0 image using SPM12. The fieldmap toolbox in SPM12 was used to calculate a voxel-displacement map from the ME-GRE B0 fieldmaps. Cartesian EPI images were distortion- and motion-corrected using the realign and unwarped function. Note that the baseline Cartesian EPI acquisitions were not distortion-corrected for the calculation of tSNR maps.

Baseline functional acquisitions: tSNR maps and CBF quantification: The first four volumes of baseline acquisitions were excluded from the analysis to eliminate transition effects. From the resting-state acquisitions, perfusion-weighted (PW) time-courses were computed as the simple subtraction of control and label time points (54 PW images). Voxel-wise perfusion and image temporal SNR (tSNR) maps were calculated as the mean of the timeseries divided by their standard deviation, from PW and control point timeseries, respectively. Due to the varying readout durations between spiral and Cartesian acquisitions, voxel-wise tSNR maps were scaled by the square root of the ADC-on t duration of the readout to correct for differences in acquisition time.

Voxel-wise absolute CBF values were calculated using the BASIL toolbox in FSL (Chapell et al., 2009) with the following parameters: ROs = 30 ms, R0 = 28 ms (single slice acquisition times to calculate of inversion time for each slice), T1_tissue = 1800 ms, T1_blood = 2100 ms (Rane and Gore, 2013), labeling efficiency = 0.95, no spatial regularization was employed.

Task-based functional acquisitions: Functional activation and region-of-interest (ROI) analysis: For the spiral images, the PW timeseries were obtained by surround-subtraction of the label and control images of the first echo and the BOLD-weighted timeseries were obtained by surround-averaging of the second echo images. Cartesian EPI PW and BOLD timeseries were obtained by surround-subtraction and -averaging of the single-echo Cartesian acquisitions. Task-based fMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.0, part of FSL (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). A voxel-wise false discovery rate (FDR) correction was applied to the resulting z-statistics maps (q = 0.05).

All ROI analyses were performed in the respective functional space of the spiral and Cartesian acquisitions. The subject-specific quantitative CBF maps from the baseline acquisitions were thresholded at 20 ml/100 g/ min and surviving voxels were assigned as gray matter. Anatomically defined visual and motor ROIs obtained from Freesurfer were transformed into respective functional space of the spiral and Cartesian acquisitions using the inverse transformation matrix obtained from the coregistration of the M0 images to the T1-weighted anatomical image. The overlapping voxels between the anatomically-defined ROI maps obtained in Freesurfer and the gray matter mask were used to further extract the mean activation timeseries from each ROI. In order to obtain the CBF timeseries in physiological units, the surround-subtracted PW timeseries were divided by the M0 image and adjusted for the slice-specific difference in inversion times (TIs). The mean time course signal was then obtained from the hundred most significant voxels within each ROI. This time course was then rescaled into physiological units using the equation for QUlPS II PSL acquisitions in Allop et al. (2015). For this, the same parameters were used as the BASIL analysis mentioned above. Event-related average timeseries were calculated across all runs from all participants. The absolute CBF change was calculated by subtracting the pre-stimulus baseline of each run from the event-related average timeseries. Mean BOLD timeseries per ROI were obtained from the surround-averaged time courses. The BOLD percent signal change was calculated relative to the respective pre-stimulus baseline of each run.

3. Results

Reconstructed spiral images from the first echo, second echo and proton density (M0) scans are shown in Fig. 2 from an example subject. First echo images have a flat, proton-density-weighted contrast as expected from the short echo time. Second echo images show the typical T2* (BOLD) contrast. The short echo time of spirals translates into higher image and perfusion tSNR than observed in the Cartesian EPI data (Fig. 3). Note that the Cartesian tSNR maps were calculated before the distortion correction, however distortion correction did not lead to any measurable change in the tSNR maps. Example slices from voxel-wise quantitative CBF maps are shown in Fig. 3. The CBF maps obtained from the first echo of the spiral acquisitions resulted in similar CBF maps as Cartesian EPI with GM and WM values within the expected physiological range.

Spiral acquisitions resulted in robust perfusion and BOLD activation maps that were comparable to activation maps obtained with Cartesian acquisitions (Fig. 4) (see S. Fig. 1 for single-subject activation results). Absolute and relative changes in CBF during the visuo-motor task were similar across subjects and across acquisitions. The BOLD signal amplitude was higher in spirals due to the optimal echo time provided by the second echo acquisition compared to the Cartesian acquisitions (Fig. 5).

4. Discussion

In this work, we developed an ASL sequence with single-shot dual-echo spiral out-in readout and simultaneous multi-slice capability for concurrent CBF and BOLD acquisitions at 7T. We determined the feasibility of this sequence with in vivo measurements of resting-state and visuo-motor task signals and compared the performance of the spiral ASL approach to reference acquisitions performed with conventional Cartesian EPI readout. Note that in this paper we aimed to show single subject results and only performed a qualitative comparison between the two readouts. Dual-echo single-band spirals have previously been utilized at 3T for simultaneous mapping of CBF and BOLD (Perthen et al., 2008) in task-based functional mapping and resting-state connectivity studies. The present study is, to the best of our knowledge, the first demonstration of this kind at 7T and in combination with simultaneous multi-slice.

We obtained robust quantitative CBF maps from the first echo of the spirals that resulted in physiologically plausible values, similar to the
Fig. 2. Mean raw functional and proton density (M0) images from the spiral (left panel) and Cartesian (right panel) scans are displayed in three orthogonal planes from one subject. The slice position is identical across all the scans.

Fig. 3. Top panel: voxel-wise tSNR maps from the same subject as in Fig. 1. Note that maps are normalized by the ADC on-time (spiral = 12.5 ms, Cartesian = 19.08 ms) of each readout for comparison. Cartesian ADC on-time was calculated as follows: [(Matrix size / GRAPPA) x Partial Fourier] * ADC duration. Bottom panel: Quantitative CBF maps of spiral (left) and Cartesian (right) acquisitions from another subject in units of ml /100 g / min.
CBF maps obtained with the Cartesian acquisition. Task-based spiral acquisitions resulted in robust perfusion and BOLD activation maps from the first and second echo, respectively. Overall, the perfusion activation maps and CBF time courses obtained with spiral acquisitions showed similar results as the Cartesian acquisitions. Absolute CBF changes during the visuomotor task were similar across subjects and across acquisition schemes. These results are in line with previous studies that investigated absolute CBF changes during a visual or motor task (Devi et al., 2020; Uludag et al., 2004; Whittaker et al., 2016). The effect of a more suitable TE for BOLD acquisitions is visible in the magnitude of the BOLD response both in the visual and motor cortex (Fig. 5). The activation maps showed similar BOLD sensitivity between spiral and Cartesian acquisitions, despite the difference between the echo times (S. Fig. 1). However, the magnitude of the BOLD response was higher for spirals at the longer TE.

Even though the Cartesian EPI readout was optimized for ASL acquisition, the minimum TE achieved was 11 ms compared to the 2.5 ms for the spiral-out acquisitions. The latter allowed perfusion mapping with slightly higher tSNR compared to the Cartesian EPI acquisitions. However, the difference in the perfusion tSNR is not as dramatic as one could expect from the echo time difference between spiral and Cartesian acquisitions. For the resolution requirements of the protocol used, the acquisition duration of one slice was 30 ms for the dual-echo spiral readout compared to the 28 ms of the Cartesian EPI readout. This 2 ms difference builds up over the slices, leading to a 22 ms difference in the inversion time for slices 12 and 24 (SMS-factor = 2). This difference in inversion times could also contribute both to the only marginal difference observed in perfusion tSNR between spiral and Cartesian EPI acquisitions and lack of increased perfusion sensitivity in spiral images due to the short echo time. In order to demonstrate the benefit of short TE in spiral-out acquisitions, we acquired ASL data using only the first echo readout. The perfusion tSNR maps shown in supp. Fig. 3 shows that single-echo spiral images have a higher perfusion tSNR compared to the Cartesian images.

Additionally, the benefit of the spirals over Cartesian acquisitions in short TE applications become more obvious for higher resolution studies. For the resolution employed in this study, at the TE of 11 ms Cartesian ASL acquisitions perform reasonably well. However at higher resolutions, performance difference between spiral and Cartesian acquisitions become enhanced. We showed elsewhere that single echo spiral-out readout employed for high resolution (1.25 mm x 1.25 mm x 1.2 mm) ASL fMRI resulted in better perfusion tSNR and stronger activation maps compared to Cartesian acquisitions at TE of 19 ms for the same resolution (See S. Fig. 4) (Kurban et al., 2020a, 2020b).

Chen et al. (2019) recently introduced the center-out EPI (COEPI) acquisition technique where the echo train starts at the center of the k-space to achieve shorter TEs with Cartesian EPI readout. They demonstrated the benefit of applying COEPI readout to diffusion imaging at
Fig. 5. Time courses were obtained from the 100 most significant voxels within the visual and motor ROIs. The plots show the signal change during the task period averaged across all task blocks and participants. The error bars represent the standard error of the mean (SEM) across participants. The green bar starting at 0 s indicates the start and duration of the task block. Note that the scaling of the plots are different between the visual and motor ROIs.

3T with a TE of 4 ms. Similarly, the COEPI method can be an attractive sampling technique for ASL acquisitions not only because of the short TE, but also due to easier reconstruction compared to the spiral acquisitions. However, the application of COEPI in ASL acquisitions at 7T may be challenging due to several reasons. The large jumps between $k_z$ lines makes the trajectory slower and inefficient. Additionally, field inhomogeneities result in blurring in the PE direction, similar to spirals, and off-resonance correction methods are necessary to mitigate these artifacts.

Both spiral and Cartesian acquisitions suffer from artifacts and these artifacts show themselves in different ways in the spiral and Cartesian images. One source of artifacts is the inhomogeneities in the main magnetic field which cause blurring in the images depending on the direction of the magnetic field gradients. In Cartesian images, B0 inhomogeneity artifacts appear as blurring and geometrical distortions along the PE direction (1D) due to the low bandwidth. Spirals on the other hand, exhibit blurring in 2D and ring-shaped artifacts. These artifacts are especially visible in the inferior frontal regions near the nasal cavity (Block and Frahm, 2005). The inferior slices of horizontal acquisitions from the frontal cortex clearly demonstrate the differences in the artifacts observed in spiral and Cartesian images (S. Fig. 2). The spiral images show blurring in all directions and ring-shaped artifacts whereas Cartesian images show clear distortions along the PE direction, especially visible in the most inferior slices. Due to the blurring in all directions in the spiral images, it may appear that the spiral point-spread function (PSF) is larger than the Cartesian PSF. We calculated the theoretical PSF based on an assumed T2* of 25 ms and the readout duration of each acquisition. In S. Fig. 5 we show that the spiral FWHM is only slightly larger than the Cartesian FWHM for the readout direction whereas the Cartesian FWHM in the phase encoding direction is the largest. Based on this, we do not expect the SNR gains in the spiral acquisitions to be related to the difference in PSF.

The presented out-in spirals can readily be employed for other non-BOLD applications that use a magnetization preparation module and require a short echo time. Examples include, but are not limited to, vascular space occupancy (VASO) (Huber et al., 2014; Lu et al., 2003), arterial blood contrast (ABC) (Schulz et al., 2020). Importantly, the dual-echo protocol resulted in a volume TR of 2.2 s for a moderate-resolution large-coverage imaging, matching the conventional fMRI specs (2.5 mm isotropic resolution, TR of 2 s per volume) (Glover, 2012). The lack of temporal resolution loss with the addition of the second echo renders the proposed method a promising approach for fMRI studies. Additionally, multi-echo analysis strategies can be used with the dual-echo spiral images to not only further increase the BOLD contrast-to-noise ratio by means of TE-weighted summing across echoes, but also to detect and remove TE-independent noise components (Kundu et al., 2017a, 2017b). This could be particularly attractive in the case that more than two echoes are acquired.

With their higher acquisition efficiency in k-space and short echo times, spiral trajectories show promise for simultaneous acquisition of BOLD and non-BOLD contrasts. However, spirals are not commonly used in practice because of the challenges such as time-consuming offline reconstruction as well as B0 inhomogeneities and gradient delays causing errors and blurring in the images. In this work, the spiral images were reconstructed using the nominal trajectory. The measured trajectory likely results in improved image quality and higher specificity due to reduced blurring as shown before (Graedel et al., 2020a, 2020b, 2020c; Kasper et al., 2020; Engel et al., 2020). Similarly, a comparable quality can be achieved by using a trajectory correction based on a gradient impulse response function model (Graedel et al., 2020a, 2020b, 2020c; Vannesjo et al., 2016a, 2016b). Even though these methods require additional scans or hardware, such alternatives can be especially beneficial for the second echo images. In this work, we chose to use the MLN reconstruction approach for the spirals, while standard vendor-provided reconstruction was used for the EPI. Other more commonly used spiral reconstructions are available that we have not explored here. In particular, iterative CG-SENSE reconstruction (Pruessmann et al., 2001) as used in the works of Engel et al. (2020) and Kasper et al. (2020) for spiral fMRI applications at 7T will be worthwhile to explore to determine if superior spiral reconstruction quality and tSNRs could be achieved, approaching the theoretically expected SNR advantage of short-TE spirals. Nevertheless, the ability to simultaneously acquire CBF and BOLD contrasts at no cost in sensitivity and temporal resolution can be regarded as an essential step forward.
5. Conclusion

Dual-echo spiral with an out-in trajectory is a well-suited and promising approach for simultaneous acquisitions of CBF and BOLD signals at 7T. The dual-echo readout can be readily implemented after other magnetization preparation modules for concurrent measurements of various non-BOLD contrasts along with BOLD. For moderate resolutions such as employed in this study, the dual-echo spiral sequence with SMS acquisition allows large brain coverage with no temporal loss compared to single-echo Cartesian EPI acquisitions.

Credit authorship contribution statement

Denizhan Kurban: Conceptualization, Formal analysis, Software, Writing – original draft, Writing – review & editing. Dimo Ivanov: Supervision, Writing – review & editing. Sriranga Kashyap: Software, Formal analysis, Writing – review & editing. Laurentius Huber: Software, Formal analysis, Writing – review & editing. Gilad Liberman: Conceptualization, Methodology. Benedikt A. Poser: Supervision, Conceptualization, Methodology, Writing – review & editing, Funding acquisition.

Data and code availability statement

Upon request one sample data set can be shared in nifti format. The code used are either already publicly available or will be made available upon publication.

Acknowledgments

Deni Kurban and Benedikt Poser are funded by the NWOVIDI grant 16.Vidi.178.052. Benedikt Poser is partially funded by the National Institute for Health grant (R01MH-111444) (PI David Feinberg).

Laurentius Huber is funded by the NWO VENI project 016.Veni.198.032.

The data presented here were collected with the kind support of Scannexus and its members.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.118820.

References

Alipan, D.C., Dette, J.A., Golay, X., Günther, M., Hendrikse, J., Hernandez-Garcia, L., Lu, H., Macintosh, B.J., Parkes, L.M., Smith, M., Van Osch, M.J.P., Wang, D.J.J., Wong, E.C., Zaharchuk, G., 2015. Recommended implementation of arterial spin labeled Perfusion MRI for clinical applications: a consensus of the IISMRM perfusion study group and the European consortium for ASL in dementia.Magn. Reson. Med. 73 (1), 102–116.doi:10.1002/mrm.25197.

Ashburner, J., 2012. SPM: a history. In: NeuroImage. Academic Press. pp. 791–800. doi:10.1016/b978-0-12-396810-7.00025-2. 

Chang, Y.V., Vidolceta, M., Wang, Z., Dette, J.A., 2017. 3D-accelerated, stack-of-spirals acquisitions and reconstruction of arterial spin labeling MRI. Magn. Reson. Med. 78 (4), 1405–1419. doi:10.1002/mrm.25649.

Dette, J.A., Leigh, J.S., Williams, D.S., Koresky, A.P., 1992. Perfusion imaging. Magn. Reson. Med. 23 (1), 27–45. doi:10.1002/mrm.1910230106.

Devi, R., Toraff, M., Schlimm, T., Jörn, M., Möller, H.R., 2020. On the relation between positive and negative functional changes of cerebral blood flow and T2* in the human visual cortex. Proc. Int. Soc. Magn. Reson. Med. Med.

Donabue, M.J., Hoogduin, H., Van Zijl, P.C.M., Jezzard, P., Luijten, P.R., Hendrikse, J., 2011. Blood oxygenation level-dependent (BOLD) total and extravascular signal changes and ΔR2* in human visual cortex at 1.5, 3.0 and 7.0 T. NMR Biomed. 24 (1), 25–34. doi:10.1002/nbm.1552.

Duong, T.Q., Kim, D.S., Uggurib, K., Kim, S.G., 2001. Localized cerebral blood flow response at submillimeter columnar resolution. Proc. Natl. Acad. Sci. U.S.A. 98 (19), 10904–10909. doi:10.1073/pnas.191109898.

Engel, M., Kasper, L., Wibl, B., Dietrich, B., Vionnet, L., Hennel, F., Reber, J., & Pruessmann, K.P. (2020). T-Hex: tilted hexagonal grids for rapid 3D imaging. Magnetic Resonance in Medicine, 78(6), 28660. 10.1002/mrm.28600.

Fischl, B., 2012. FreeSurfer. In: NeuroImage. Academic Press, pp. 774–781. doi:10.1016/j.neuroimage.2012.01.021 Vol. 62, Issue 2.
Graedel, N.N., Kasper, L., Engel, M., Nussbaum, J., Wilen, B.J., Pruessmann, K.P., & Vannesjo, S.J. (2020). Feasibility of spiral fMRI based on an LTI gradient model. BioRxiv, 805580. 10.1101/805580.

Kundu, D., Voon, V., Balchandani, P., Lombardo, M.V., Poser, B.A., Bandettini, P.A., 2017b. Multi-echo fMRI: a review of applications in fMRI denoising and analysis of BOLD signals. Neuroimage 154, 59–80. doi:10.1016/j.neuroimage.2017.03.033.

Kurban, D., Huber, L., Liberman, G., Kashyap, S., Ivanov, D., Poser, B.A., 2020b. High-resolution perfusion and blood-volume fMRI at 7T with simultaneous multi-slice spiralout acquisitions. In: Proceedings of the 37th Annual Scientific Meeting. ESMRMB Online.

Vannesjo, S.J., Graedel, N.N., Kasper, L., Gross, S., Busch, J., Haeberlin, M., Barmet, C., Pruessmann, K.P., 2016b. Image reconstruction using a gradient impulse response model for trajectory prediction. Magn. Reson. Med. doi:10.1002/mrm.25841.

Vidorreta, M., Wang, Z., Rodriguez, I., Pastor, M.A., Detre, J.A., Fernández-Seara, M.A., 2013. Comparison of 2D and 3D single-shot ASL perfusion fMRI sequences. Neuroimage doi:10.1016/j.neuroimage.2012.10.087.

Whittaker, J.R., Driver, I.D., Bright, M.G., Murphy, K., 2016. The absolute CBF response to activation is preserved during elevated perfusion: implications for neurovascular coupling measures. Neuroimage 125, 198–207. doi:10.1016/j.neuroimage.2015.10.023.

Williams, D.S., Grandis, D.J., Zhang, W., Koretsky, A.P., 1993. Magnetic resonance imaging of perfusion in the isolated rat heart using spin inversion of arterial water. Magn. Reson. Med. 30 (3), 361–365. doi:10.1002/mrm.1910300314.

Wong, E.C., Buxton, R.B., Frank, L.R., 1998. Quantitative imaging of perfusion using a single subtraction (QUIPSS and QUIPSS II). Magn. Reson. Med. 39 (5), 702–708. doi:10.1002/mrm.1910390506.

Zappe, A.C., Pfeuffer, J., Merkle, H., Logothetis, N.K., Goese, I.B.M., 2008. The effect of labeling parameters on perfusion-based fMRI in nonhuman primates. J. Cereb. Blood Flow Metab. 28 (3), 640–652. doi:10.1038/jcbfm.9600564.

Further reading

Woolrich, M.W., Ripley, B.D., Brady, M., Smith, S.M., 2001. Temporal autocorrelation in univariate linear modeling of fMRI data. Neuroimage 14 (6), 1370–1386. doi:10.1006/nimg.2001.0931.