Advances in Spiral fMRI: A High-resolution Study with Single-shot Acquisition

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Highlights

- This work reports the first fMRI study at 7T with spiral readout gradient waveforms.
- We achieve spiral fMRI with sub-millimeter resolution (0.8 mm, in-plane FOV 230 mm), acquired in a single shot.
- Spiral images exhibit intrinsic geometric congruency to anatomical scans, and spatially highly specific activation patterns.
- Image reconstruction rests on a signal model expanded by measured trajectories and static field maps, inverted by cg-SENSE.
- We assess generalizability of the approach for spiral in/out readouts, providing two images per shot (1.5 mm resolution).

Abstract

Spiral fMRI has been put forward as a viable alternative to rectilinear echo-planar imaging, in particular due to its enhanced average k-space speed and thus high acquisition efficiency. This renders spirals attractive for contemporary fMRI applications that require high spatiotemporal resolution, such as laminar or columnar fMRI. However, in practice, spiral fMRI is typically hampered by its reduced robustness and ensuing blurring artifacts, which arise from imperfections in both static and dynamic magnetic fields.

Recently, these limitations have been overcome by the concerted application of an expanded signal model that accounts for such field imperfections, and its inversion by iterative image reconstruction. In the challenging ultra-high field environment of 7 Tesla, where field inhomogeneity effects are aggravated, both multi-shot and single-shot 2D spiral imaging at sub-millimeter resolution was demonstrated with high depiction quality and anatomical congruency.

In this work, we further these advances towards a time series application of spiral readouts, namely, single-shot spiral BOLD fMRI at 0.8 mm in-plane resolution. We demonstrate that spiral fMRI at 7 T is not only feasible, but delivers both competitive image quality and BOLD sensitivity, with a spatial specificity of the activation maps that is not compromised by artifactual blurring. Furthermore, we show the versatility of the approach with a combined in/out spiral readout at a more typical resolution (1.5 mm), where the high acquisition efficiency allows to acquire two images per shot for improved sensitivity by echo combination.

1 Introduction

Functional MRI (fMRI) is presently the most prominent technique to study human brain
function non-invasively, owing to its favorable spatiotemporal resolution regime with
appealing functional sensitivity. Within this regime, specific research questions require
different trade-offs between spatial and temporal resolution. On the one hand, ultra-high
spatial resolution fMRI at sub-millimeter voxel size successfully targets smaller
organizational structures of the brain, such as cortical laminae (Fracasso et al., 2016; Huber
et al., 2017a; Kashyap et al., 2018; Kok et al., 2016; Lawrence et al., 2018; Martino et al., 2015;
Muckli et al., 2015; Siero et al., 2011) and columns (Cheng et al., 2001; Feinberg et al., 2018;
Yacoub et al., 2008), or subcortical nuclei, but requires compromises on coverage (FOV) or
temporal bandwidth, i.e., volume repetition time (TR). On the other hand, fast sequences
with TRs on the order of 0.5 seconds and below are important for advanced analysis
approaches, e.g., to adequately sample physiological fluctuations (Lewis et al., 2016; Smith
et al., 2013; Uğurbil et al., 2013), at the expense of lowering spatial resolution (2–4 mm).

One means to simultaneously advance the spatial and temporal resolution boundaries of
fMRI is to maximize acquisition efficiency, i.e., sampled k-space area (or volume) per unit
time. Therefore, fMRI nowadays almost exclusively relies on rectilinear echo-planar
imaging (EPI, (Cohen and Schmitt, 2012; Mansfield, 1977; Schmitt et al., 2012)), where
acquisition efficiency is favorable due to optimal acceleration and high terminal velocity
along the straight k-space lines traversed.

To expand spatiotemporal resolution beyond the capabilities of EPI alone, the main
strategy has been parallel imaging acceleration (Griswold et al., 2002; Pruessmann et al.,
1999), in combination with simultaneous multi-slice or 3D excitation (Breuer et al., 2006;
Larkman et al., 2001; Poser et al., 2010; Setsompop et al., 2012). In terms of k-space coverage
per unit time, the benefit of parallel imaging lies in expanding the cross section of what is
effectively a tube of k-space covered along the readout trajectory (Pruessmann, 2006).

By focusing efforts on maximizing acquisition efficiency in this way, another key
determinant of the speed of coverage was less emphasized, which is the average velocity
along the trajectory, i.e., the average instantaneous gradient strength. On this count, EPI is
wasteful because it includes many sharp turns that must be traversed at low speed because
of limited gradient slew rate.

It has long been recognized, also in the context of fMRI (Barth et al., 1999; Glover, 2012;
Noll et al., 1995), that substantially higher average k-space speed and thus acquisition
efficiency is achieved with spiral trajectories, which avoid sharp turns by distributing
curvature more evenly (Ahn et al., 1986; Likes, 1981; Meyer et al., 1992). Typically, single-
shot variants winding out of k-space center, e.g., on an Archimedean spiral, are prevalent
(Glover, 1999; Meyer et al., 1992), but different acquisition schemes, such as spiral-in
(Börnert et al., 2000) or combined in/out readouts (Glover and Law, 2001; Glover and
Thomason, 2004) have been proposed. High resolution fMRI studies have occasionally
employed spirals as well (Jung et al., 2013; Singh et al., 2018), albeit reducing acquisition
efficiency in favor of robustness by acquiring k-space in multiple shots with shorter spiral
readouts.

However, routine use of spiral fMRI has not been established, due to the following three
challenges (Block and Frahm, 2005; Börnert et al., 1999): First, spirals are sensitive to
imperfect magnetic field dynamics (eddy currents and other gradient imperfections, as well
as subject-induced field changes, e.g., via breathing) which lead to blurring and image
distortions. Secondly, non-uniformity of the static B_0 field, caused by varying susceptibility
of the imaged tissues, likewise causes blurring. Finally, in combination with parallel
imaging, spirals pose a somewhat greater reconstruction challenge than Cartesian
trajectories (Pruessmann et al., 2001).

Recently, these obstacles have been overcome (Engel et al., 2018b; Kasper et al., 2018; Wilm
et al., 2017) by (1) employing an expanded signal model that accounts for the actual static
and dynamic fields as well as coil sensitivity encoding (Wilm et al., 2011), and (2) the

inversion of this model by an accompanying iterative image reconstruction (Barmet et al.,
2005; Man et al., 1997; Pruessmann et al., 2001; Sutton et al., 2003). This approach enabled
the use of very long spiral readouts (on the order of 50 ms at 7 Tesla), while maintaining
competitive image quality and anatomical fidelity. In particular, such enhanced spiral
acquisition efficiency was demonstrated by accomplishing T_2^*-weighted images with an in-
plane resolution of 0.8 mm in a single shot. Ultimately, these findings hold promise that
spiral fMRI can now indeed profit from the theoretical advantages of enhanced acquisition
efficiency to expand the spatiotemporal boundaries of fMRI.

Based on these advances in expanded signal modeling and inversion, in this work, we
explore the feasibility and utility of sub-millimeter single-shot spiral fMRI. Specifically, we
first assess image quality and temporal stability of fMRI time series obtained with the
expanded signal model and algebraic reconstruction. We further evaluate the resulting
functional sensitivity, using an established visual quarter-field stimulation to elicit
reference activation patterns and demonstrate spatial specificity and geometric consistency
of the resulting activation at the level of the nominal resolution (0.8 mm). Finally, we
explore the versatility of the approach with a combined in/out spiral readout at a more
typical resolution (1.5 mm). Here, two images per shot can be acquired, translating the high
acquisition efficiency of the spiral into enhanced functional sensitivity by echo
combination (Glover and Law, 2001; Glover and Thomason, 2004; Law and Glover, 2009).

2 Methods

2.1 Setup

All data was acquired on a Philips Achieva 7 Tesla MR System (Philips Healthcare, Best, The Netherlands), with a quadrature transmit coil and 32-channel head receive array (Nova Medical, Wilmington, MA).

Concurrent magnetic field monitoring was performed using 16 fluorine-based NMR field probes, which were integrated into the head setup via a laser-sintered nylon frame positioned between transmit and receive coil (Engel et al., 2018b, Fig. 1). Probe data were recorded and preprocessed (filtering, demodulation) on a dedicated acquisition system (Dietrich et al., 2016a). The final extraction of probe phase evolution and projection onto a spherical harmonic basis set (Barmet et al., 2008) was performed on a PC, yielding readout time courses of global phase k_0 and k-space coefficients k_x, k_y, k_z with 1 MHz bandwidth.

For the fMRI experiments, visual stimulus presentation utilized VisuaStim LCD goggles (Resonance Technology Inc., Northridge, CA, USA). A vendor-specific respiratory bellows and finger pulse plethysmograph recorded subject physiology, i.e., respiratory and cardiac cycle.

2.2 fMRI Paradigm and Subjects

Seven healthy subjects (4 female, mean age 25.7 +/- 4.1 y) took part in this study, after written informed consent and with approval of the local ethics committee. One subject was excluded from further analysis due to reduced signal in multiple channels of the head receive array. Thus, six subjects were analyzed for this study.

The paradigm, a modified version of the one used in (Kasper et al., 2014), comprised two blocks of 15 s duration that presented flickering checkerboard wedges in complementary pairs of the visual quarter-fields. In one block, *u*pper *l*eft and *l*ower *r*ight visual field were

stimulated simultaneously (condition ULLR), while the other block presented the wedges
in the *u*pper *r*ight and *l*ower *l*eft quarter-fields (condition URLL). These stimulation blocks
were interleaved with equally long fixation periods. To keep subjects engaged, they had to
respond to slight contrast changes in the central fixation cross via button presses of the
right hand. A single run of the paradigm took 5 min (5 repetitions of the ULLR-Fixation-
URLL-Fixation sequence).

2.3 Spiral Trajectories and Sequence Timing

Spiral fMRI was based on a slice-selective multi-slice 2D gradient echo sequence (Fig. 1)
with custom-designed spiral readout gradient waveforms. For every third slice, concurrent
field recordings were performed on the dedicated acquisition system (Dietrich et al.,
2016a), with NMR field probes being excited a few milliseconds prior to readout gradient
onset (Fig. 1, bottom row, (Engel et al., 2018b)).

For the spiral trajectories, we selected two variants that had previously provided high-
quality images in individual frames (Engel et al., 2018b, Fig. 2): a high-resolution case
winding out of k-space center on an Archimedean spiral (spiral-out, Fig. 1, black gradient
waveform), and a combined dual-image readout first spiraling into k-space center,
immediately followed by a point-symmetric outward spiral (spiral in/out (Glover and Law,
2001)), Fig. 1, blue gradient waveform).

The spiral-out gradient waveform was designed to deliver the highest spatial resolution
possible under several constraints. First, targeting maximum acquisition efficiency in 2D
commands a single-shot 2D readout, because the sequence overhead, i.e., time spent
without sampling k-space, accrues for each new excitation. Second, the parallel imaging
capability of our receiver array at 7 T allowed for an in-plane acceleration factor of R=4
(determining the spacing of the spiral revolutions, i.e., FOV). We based this choice on
previous experience with spirals of such undersampling using this setup (Engel et al.,
2018b; Kasper et al., 2018), which were free of aliasing artifacts or disproportional noise

amplification. Third, the requirement of concurrent field recordings for the whole spiral

readout limited its maximum duration to below 60 ms. This is the approximate lifetime of

the NMR field probe signal, after which complete dephasing occurs in a subset of probes

for this specific setup, governed by their T_2^* decay time of 24 ms (Engel et al., 2018b).

Finally, the gradient system specifications constrain the maximum possible resolution (or

k-space excursion) of an Archimedean spiral with prescribed FOV and duration. Here, we

used the optimal control algorithm by (Lustig et al., 2008) to design time-optimal spiral

gradient waveforms of 31 mT/m maximum available gradient amplitude, and a 160

mT/m/ms slew rate limit, chosen for reduced peripheral nerve stimulation.

Overall, these requirements led to a spiral-out trajectory with a nominal in-plane resolution

of 0.8 mm (for a FOV of 230 mm), at a total readout acquisition time (TAQ) of 57 ms.

BOLD-weighting was accomplished by shifting the readout start, i.e., TE, to 20 ms.

For the spiral in/out, we followed the same design principles, targeting a minimum dead

time after excitation, and a symmetric readout centered on a TE of 25 ms, slightly shorter

than reported T_2^* values in cortex at 7 T (Peters et al., 2007). This resulted in a gradient

waveform lasting 39 ms, with a nominal resolution of 1.5 mm for each half-shot of the

trajectory.

All other parameters of both spiral sequences were shared, in order to facilitate comparison

of their functional sensitivity. In particular, slice thickness (0.9 mm) and gap (0.1 mm) were

selected for near-isotropic sub-mm resolution for the spiral-out case, while still covering

most of visual cortex. For each slice, the imaging part of the sequence (Fig. 1) was preceded

by a fat suppression module utilizing Spectral Presaturation with Inversion Recovery (SPIR,

(Kaldoudi et al., 1993)).

The sequence duration totaled 90 ms per slice for the spiral-out sequence (TE 20 ms + TAQ

60 ms + SPIR 10 ms), which was maintained for the spiral in/out, even though a shorter

imaging module would have been possible. To arrive at a typical volume repetition time for

fMRI, we chose to acquire 36 slices (TR 3.3 s). Each functional run comprised 100 volume

repetitions, amounting to a scan duration of 5.5 min.

2.4 Image Reconstruction

199   Image reconstruction rested on an expanded model of the coil signal s_γ (Wilm et al., 2011),

200   that – besides transverse magnetization m – incorporates coil sensitivity c_γ, as well as phase

201   accrual by both magnetostatic B₀ field inhomogeneity (offresonance frequency $\Delta\omega_0$)

202   (Barmet et al., 2005) and magnetic field dynamics k_l expanded in different spatial basis

203   functions b_l (Barmet et al., 2008):

$$s_\gamma(t) = \int_V c_\gamma(\boldsymbol{r}) \cdot m(\boldsymbol{r}) \cdot e^{i\sum_l k_l(t)b_l(\boldsymbol{r})} \cdot e^{i\Delta\omega_0(\boldsymbol{r})t} \cdot dV \tag{1}$$

with coil index γ, sampling time t, imaging volume V, and location vector $\boldsymbol{r} = [x\ y\ z]^T$.

For 2D spiral imaging without strong higher order eddy currents (e.g., as induced by

diffusion encoding gradients), this model can be computationally reduced (Engel et al.,

2018b) to facilitate iterative inversion. To this end, we (1) considered only field dynamics

contributing to global phase k_0 and spatially linear phase, i.e., k-space $\boldsymbol{k} = [k_x\ k_y\ k_z]$, as

provided by the concurrent field recordings, and (2) restricted the integration to the excited

2D imaging plane by shifting the coordinate origin to the slice center $\boldsymbol{r_0}$, effectively

factoring slice-orthogonal field dynamics out of the integral:

$$s_\gamma(t)$$
$$= \int_V c_\gamma(\boldsymbol{r}) \cdot m(\boldsymbol{r}) \cdot e^{i(k_0(t)+\boldsymbol{k}(t)\cdot\boldsymbol{r})} \cdot e^{i\Delta\omega_0(\boldsymbol{r})t} \cdot dV$$
$$= e^{i(k_0(t)+\boldsymbol{k}(t)\cdot\boldsymbol{r_0})} \int_V c_\gamma(\boldsymbol{r}) \cdot m(\boldsymbol{r}) \cdot e^{i\boldsymbol{k}(t)\cdot(\boldsymbol{r}-\boldsymbol{r_0})} \cdot e^{i\Delta\omega_0(\boldsymbol{r})t} \cdot dV \tag{2}$$

212   For the demodulated coil signal $\widetilde{s_\gamma}(t) = s_\gamma(t) \cdot \exp(-i(k_0(t) + \boldsymbol{k}(t) \cdot \boldsymbol{r_0}))$, the discretized

213   version of eq. (2) – respecting finite spatial resolution and dwell time of the acquisition

214   system – reads as a system of linear equations

$$\tilde{s}_{(\gamma,\tau)} = \sum_\rho E_{(\gamma,\tau),\rho} m_\rho \tag{3}$$

215   with sampling time index τ, voxel index ρ, $\tilde{s}_{(\gamma,\tau)} = \tilde{s}_\gamma(t_\tau)$, encoding matrix element

216     $E_{(\gamma,\tau),\rho} = c_\gamma(\boldsymbol{r}_\rho) \cdot e^{i\boldsymbol{k}(t_\tau)\cdot(\boldsymbol{r}_\rho - \boldsymbol{r_0})} \cdot e^{i\Delta\omega_0(\boldsymbol{r}_\rho)t_\tau}$, and $m_\rho = m(\boldsymbol{r}_\rho)$.

217   The matrix-vector form of eq. (3) is a general linear model,

$$\tilde{\boldsymbol{s}} = E \, \boldsymbol{m} \tag{4}$$

and can be efficiently solved iteratively by a conjugate gradient (CG) algorithm

(Pruessmann et al., 2001; Shewchuk, 1994). As mentioned above, the restriction to first

order field dynamics enables acceleration of the ensuing matrix-vector multiplications by

(reverse) gridding and fast Fourier transform (FFT) (Beatty et al., 2005; Jackson et al., 1991).

Offresonance effects can also be approximated by FFT using multi-frequency interpolation

(Man et al., 1997).

This image reconstruction algorithm was applied equivalently to the spiral-out and spiral

in/out data. Note, however, that for the latter both field recordings and coil data were split

into their in- and out-part and reconstructed separately, yielding two images per shot.

Taken together, the in-house Matlab (The Mathworks, Natick, MA, R2018a)

implementation of this algorithm led to reconstruction times of about 10 min per slice on

a single CPU core. In order to reconstruct the 3600 2D images per fMRI run, reconstruction

was parallelized over slices on the university's CPU cluster. Depending on cluster load,

reconstructions typically finished over night for the high-resolution spiral out, and within

2 h for the spiral in/out data.

The auxiliary input data for the expanded signal model, i.e., spatial maps for static B_0 field

inhomogeneity $\Delta\omega$ and coil sensitivity c_γ, were derived from a separate fully sampled multi-

echo (ME) Cartesian gradient echo reference scan of 1 mm in-plane resolution, $TE_1 = 4ms$,

$\Delta TE = 1ms$ (Kasper et al., 2018), with slice geometry equivalent to the spiral sequences.

Image reconstruction proceeded as described above for this scan, albeit omitting the

sensitivity and static B_0 map terms. The latter was justified by the high bandwidth of the

Cartesian spin-warp scans (1 kHz).

Sensitivity maps were then computed from the first-echo image, normalizing single coil

images by the root sum of squares over all channels, while the B_0 map was calculated by

regressing the pixel-wise phase evolution over echo images. Both maps were smoothed and

slightly extrapolated via a variational approach (Keeling and Bammer, 2004).

2.5 Data Analysis

2.5.1 Image Quality Assessment

246   The suitability of the raw imaging data for high-resolution fMRI was assessed in terms of

247   both sensitivity and spatial specificity. For sensitivity, we evaluated the temporal statistics

248   of the images, i.e., signal-to-fluctuation noise ratio (SFNR), standard deviation (SD) and

249   coefficient of variation (CoV) maps (Welvaert and Rosseel, 2013), defined as

$$SFNR(\boldsymbol{r}_\rho) = \frac{\overline{m(r_\rho)}}{SD(m(r_\rho))},$$

$$CoV = \frac{1}{SFNR},$$

(5)

where the bar denotes averaging over volumes of a run.

For spatial specificity, we visually compared the spiral images to the ME reference scan,
which exhibits a high geometric veracity due to its spin-warp nature, i.e., high bandwidth.
We overlaid the contour edges (intensity isolines) of the mean (over echoes) of the ME
images onto the mean spiral images $\overline{m(r_\rho)}$ to inspect the congruency of anatomical
boundaries between the scans.

To reduce the impact of subject motion on both assessments, the volumes of the fMRI time
series were first realigned to each other. Then, the mean ME scan was co-registered to the
resulting mean realigned fMRI scan, Importantly, both operations were limited to six-
parameter rigid-body registration, such that nonlinear geometric distortions between
sequences were not corrected through this preprocessing step. Furthermore, to facilitate
visual comparison and contour edge creation, mean ME and spiral images were bias-field
corrected using unified segmentation (Ashburner and Friston, 2005).

All computations were performed in Matlab R2018b, using the Unified NeuroImaging
Quality Control Toolbox (UniQC, (Bollmann et al., 2018)), and SPM12 (Wellcome Centre
for Human Neuroimaging, London, UK, http://www.fil.ion.ucl.ac.uk/spm/).

2.5.2　BOLD fMRI Analysis

The main goal of this analysis was to establish the functional sensitivity of the spiral fMRI
sequences at the single-subject level under standard paradigm and preprocessing choices.
On a qualitative level, we also assessed the spatial specificity of functional activation.

Equivalent preprocessing steps were applied to all spiral fMRI runs using SPM12. After slice-
timing correction, we employed the pipeline described in the previous section
(realignment, co-registration, bias-field correction via unified segmentation). Finally, the
functional images were slightly smoothed with a Gaussian kernel of 0.8mm FWHM, i.e.,
the voxel size of the high-resolution scan.

The general linear model (GLM) contained regressors of the two stimulation blocks (ULLR
and URLL) convolved with the hemodynamic response function (HRF), as well as nuisance
regressors for motion (6 rigid-body parameters) and physiological noise (18 RETROICOR
(Glover et al., 2000) regressors, as specified in (Harvey et al., 2008)), extracted by the
PhysIO Toolbox (Kasper et al., 2017).

To characterize functional sensitivity, we evaluated the differential t-contrasts +/- (ULLR-
URLL) and report results both with and without multiple comparison correction.   For
visualization, Figures 5-7 show activations without correction, at a threshold of p<0.001
(t>3.22). This helps to demonstrate the spatial specificity of activations. By contrast, Table
1 reports activations under whole-brain family-wise error (FWE) correction at the cluster
level (p<0.05), with a cluster defining threshold (p<0.001) that corresponds to the threshold
used for visualization.

Spatial specificity of the activation was qualitatively assessed by overlaying the thresholded
t-contrast maps for both contrasts onto the anatomically veridical mean ME image. We
checked whether activation patterns were restricted to gray matter regions of visual cortex,
as well as whether the spatial separation and symmetry of activations were linked to
distinct quarter-field stimulation patterns, as expected by the retinotopic organization of
visual cortex (Engel et al., 1997; Wandell et al., 2007; Warnking et al., 2002). On top, we also
evaluated the individual contrasts for the ULLR and URLL stimulation blocks to assess the
spatial overlap of their activation patterns as an alternative measure of functional
specificity (since the differential contrasts cannot overlap by design).

This overall analysis procedure was performed for the spiral-out as well as the individual
spiral-in and spiral-out image time series reconstructed from the spiral in/out data. As
spiral in/out sequences are predominantly selected for their potential gain in functional
sensitivity when combining spiral-in and spiral-out images (Glover and Law, 2001), we
additionally repeated the BOLD fMRI analysis for such a surrogate dataset ("in/out
combined"). We chose a signal-weighted combination per voxel (Glover and Thomason,

2004), which is considered the most practical approach for echo combination (Glover,
2012):

$$m_{combined} = w \cdot m_1 + (1 - w) \cdot m_2,$$

$$w = \frac{\overline{m_1}}{\overline{m_1} + \overline{m_2}},$$

(6)

305 with m_1 and m_2 being the in-part and out-part voxel time series, respectively.

2.6 Code and Data Availability

Image reconstruction was performed by an in-house custom Matlab implementation of the
cg-SENSE algorithm (Pruessmann et al., 2001). A demonstration of that algorithm is
publicly available on GitHub (https://github.com/mrtm-zurich/rrsg-arbitrary-sense), with
a static compute capsule for reproducible online re-execution on CodeOcean (Patzig et al.,
2019), which were created in the context of the ISMRM reproducible research study group
challenge (Stikov et al., 2019), albeit without the multi-frequency interpolation employed
here.

Image and fMRI analyses were performed using SPM12 (https://www.fil.ion.ucl.ac.uk/spm
distributed under GPLv2) and the UniQC Toolbox. UniQC is developed in-house, and a
beta-version can be downloaded from the Centre for Advanced Imaging software repository
on GitHub (https://github.com/CAIsr/uniQC); a publicly available stable release will be
made available in 2020 as part of the TAPAS Software Suite
(http://translationalneuromodeling.org/tapas), under a GPLv3 license.

All custom analysis and data visualization scripts will be available on
http://github.com/mrikasper/paper-advances-in-spiral-fmri. This includes both a one-
click analysis (`main.m`) to rerun all image statistics and fMRI analyses, as well as the
automatic re-creation of all figure components found in this manuscript
(`main_create_figures.m`), utilizing the UniQC Toolbox. More details on installation and

execution of the code can be found in the `README.md` file in the main folder of the
repository.

One dataset from this study (`SPIFI_0007`) will be made publicly available on ETH Research
Collection, upon acceptance of this paper, according to the FAIR (Findable, Accessible,
Interoperable, and Re-usable) data principles (Wilkinson et al., 2016). This includes both
the reconstructed images in NIFTI format with BIDS metadata, to validate the analysis
scripts, as well as raw coil and trajectory data in ISMRMRD format. For the other datasets,
we did not obtain explicit subject consent to share all raw data in the public domain.
However, we do provide the mean spiral fMRI images with corresponding activation t-maps
for all subjects on NeuroVault ((Gorgolewski et al., 2015),
https://neurovault.org/collections/6086/).

3 Results

3.1 Spiral Image Quality, Congruency and Stability

In the following, we mainly present images from two subjects (S7: Figs. 2,3, S2: Figs. 4,5,7). However, as illustrated by Fig. 6, results were comparable for all six analyzed datasets. In addition to Fig. 6, this can be inspected in the supplementary material (Fig. S1) or on NeuroVault ((Gorgolewski et al., 2015), https://neurovault.org/collections/6086/).

The mean images (one run of subject S7, after realignment) of the high-resolution spiral-out sequence exhibit good image quality, rich in T_2^* contrast and anatomical detail (Fig. 2A). In the center of the brain, no blurring is apparent, and anatomical boundaries can be clearly delineated, e.g, the optic radiation, down to the single-voxel extent. Moderate residual imaging artifacts (local ringing, blurring) are visible in the orbitofrontal areas, at some brain/skull boundaries, and in the vicinity of larger muscles and fat deposits, e.g., the temporal muscles. For more inferior slices, signal dropouts can be identified at typical sites of through-plane dephasing, e.g., above the ear canals. Individual frames of the time series exhibit similar features (Fig. 2B), though somewhat noisier, as expected because of the reduced SNR.

Interestingly, the mean of the corresponding raw phase images also contains high anatomical detail and few phase wraps (Fig. 2C), which are again located at the interface between brain and skull or close to air cavities. Note that the unwrapped appearance of the phase image is a feature of the B_0-map based correction (Kasper et al., 2018) and does not require any postprocessing.

Mapping the temporal statistics of the spiral image time series (Fig. 3, Table 1) proves its sufficient stability for functional imaging in all slices. The SFNR images (Fig. 3A) are rather homogeneous, with mean values of 15.3 +/- 1.1 in cortical gray matter, averaged over subjects (Table 1). A slight reduction for central brain regions is visible due to the diminished net

sensitivity of the receiver array. Notably, no structured noise amplification through bad

conditioning of the undersampled reconstruction problem (g-factor penalty) is discernible

in this area.

The SD images (Fig. 3B) corroborate this impression, showing peak values in ventricles

(CSF) and highly vascularized areas (insula, ACC). These noise clusters presumably stem

from fluctuations through cardiac pulsation and are not specific to spiral acquisitions.

However, for the raised SD values in voxels close to the cortex borders, it is unclear whether

also CSF fluctuations, the BOLD effect itself, or rather time-varying blurring due to

unaccounted magnetic field fluctuations contribute. This is scrutinized in the GLM analysis

below. Additionally, for the CoV images (Fig. 3C), the internal capsule appears

prominently, presumably due to its reduced average signal level.

In terms of spatial specificity, overlaying contour edges of the anatomical reference (mean

ME spin-warp image, subject S2) (Fig. 4A,E) onto the mean spiral-out image suggests a

geometrically very faithful depiction of the anatomical interfaces (Fig. 4B,F). Boundaries

of the ventricles and cortex to white matter are congruent in general, also for the visual

areas considered in later analyses, and are not blurry. Some regions of the spiral-out images

suffer from ringing (yellow arrow) or signal dropout (white arrow), most likely due to

through-plane dephasing and incomplete in-plane B_0 correction.

Incorporating the mean images of the spiral in/out sequence into the comparison confirms

the nature of these artifacts (Fig. 4C,D,G,H). The in-part images (Fig. 4C) are void of these

artifacts and match the anatomical reference almost completely in terms of edge contours

(Fig. 4G). Only CSF/skull interfaces are slightly compromised by a more global ringing,

presumably from residual fat or high-intensity signal right after slice excitation. The out-

part of the spiral-in/out (Fig. 4D,H) constitutes a compromise between spiral-in and high-

resolution spiral-out in terms of artifact-level. Its shorter readout of only 20 instead of

60 ms alleviates through-plane dephasing or incomplete B_0 correction through inaccurate

mapping.

3.2 Functional Sensitivity and Specificity

Functional sensitivity of the high-resolution spiral-out images is evident at the single-subject level (subject S2) in a differential contrast of both stimulus conditions (+/- ULLR-URLL). The corresponding t-map, overlaid on the mean functional images, reveals expected activation patterns in visual cortex (Fig. 5A). Hemispheric separation of the complementary quarter-field stimulation blocks is visible (left slice), as well as the contrast inversion from inferior to superior slices (left vs second left slice). Notably, significant activation flips between neighboring voxels occur at the cerebral fissure, suggesting spatial specificity at the voxel level.

This functional specificity is confirmed when overlaying the identical activation maps on the mean ME image as anatomical reference (Fig. 5B), again demonstrating the good alignment of functional and structural data seen in the previous subsection (Fig. 4). Clustered activation is almost exclusively constrained to gray matter with no extension into adjacent tissue or skull. Note that no multiple comparison correction was performed for visualization, in order to be more sensitive to such effects, at the expense of occasional false-positive voxels throughout other brain areas.

Gray-matter containment and retinotopic organization of the activation can be further corroborated in the zoomed-in sections of visual cortex for transverse, coronal and sagittal orientation (Fig. 5C). Additionally, we evaluated the ULLR and URLL blocks individually (Fig. 5D), because differential contrasts, by design, do not allow for spatial overlap between significant activation of both conditions. In the individual contrasts, the identified portion of activated visual cortex appears larger, but is still very well restricted to cortical gray matter. Few overlaps exist, and, again, contrast switches between adjacent voxels, pointing to spatial specificity at the prescribed sub-mm resolution.

These findings are reproducible over subjects (Fig. 6). Importantly, similar image quality and geometric congruency are accomplished in all subjects. To verify, we show both the mean spiral and the anatomical ME reference image of the corresponding transverse slice

as underlays for the differential activation patterns. Some subjects exhibit more frontal

blurring artifacts and dropouts (S5, S6, S7) due to different geometry of the air cavities.

Still, the retinotopic organization of visual cortex is recovered in all subjects, as visualized

in the zoomed coronal and sagittal views. Existing differences of the specific activation

patterns are within the expected range of variability in subject anatomy and task

engagement. Quantitatively, peak t-values reach 15.1 on average for the differential

contrasts, with a standard deviation of 2.6, i.e. 17 %, over subjects (Table 1). Activation

clusters comprise 10371 +/- 2480 voxels (after FWE-multiple comparison correction at the

cluster level, p<0.05), i.e., 6467 +/- 1547 mm^3.

3.3 Spiral In/Out Analysis and Echo Combination

We continue to present data from the same subject (S2) as in the high-resolution case, to

facilitate comparison. All findings are generalizable over subjects, as detailed in the

supplementary material (Fig. S2).

Overall, the differential t-contrast maps for the spiral in/out data resemble the activation

patterns of the high-resolution spiral-out case. This holds for all three derived in/out time

series, i.e., the separate reconstructions of the in-part and the out-part, as well as their

combination in the image domain via signal-weighted averaging ("in/out combined").

In terms of functional sensitivity, the in/out sequence provides higher peak t-values and

cluster extents in the differential t-contrasts compared to the high-resolution spiral-out, as

expected due to the larger voxel size and consequential higher SFNR (Table 1). For example,

the in-part itself provides a 61 % SFNR increase in gray matter (averaged over subjects), 17%

increased maximum peak t-value, and 56 % increase in significantly activated gray matter

volume (Table 1, rightmost column).

Comparing the out- to the in-part of the spirals, SFNR is slightly decreased in the out-part

(8 %), while the situation is reversed for the t-maps, with 2 % increase in peak t-value and

14 % increase in cluster extent, compared to the spiral-in. This suggests that higher T_2*-

sensitivity of the spiral-out causes both effects, by both amplifying signal dropouts and
BOLD signal.

The signal-weighted echo combination (eq. (5), (Glover and Thomason, 2004)) provides the
highest functional sensitivity of the three in/out time-series, having a 25 % increased SFNR
compared to the in-part, and 37 % increase compared to the out-part. This translates into
an average increase in peak t-value of 2 % and significant cluster extent of 21 %, compared
to the out-part alone. This is in line with previous findings for high-resolution multi-shot
spiral data (Singh et al., 2018) at 3 T, which also reported contrast-to-noise ratio (CNR)
increases for signal-weighted spiral in/out combinations on the order of 25 %. However, it
falls somewhat short of the 54 % increase in CNR reported originally for low-resolution
single-shot spiral in/out combination (Glover and Thomason, 2004, p. 866).

In terms of spatial specificity, all activation patterns exhibit a good congruency to the
anatomical reference, as evident from a close-up overlaid onto the mean ME image (Fig.
7D). In general, this visualization confirms the overall impression that the echo
combination increases CNR throughout visual cortex, rather than just in regions of higher
dephasing. One remarkable feature of the in-part time series is visible in Fig. 7A: there
seem to be more false positive clusters than in all other spiral variants (Fig. 7A), in
particular close to the temporal muscle, presumably due to the ringing mentioned in the
first results section above.

4 Discussion

4.1 Summary

In this work, we demonstrated that recent advances in high-resolution, single-shot spiral imaging (Engel et al., 2018b) can be deployed to fMRI. The typical drawbacks of spiral fMRI, which have so far limited its routine use, were overcome by an expanded signal model, accurate measurement of its components, and corresponding iterative image reconstruction (Barmet et al., 2005; Pruessmann et al., 2001; Wilm et al., 2011).

Specifically, time series of competitive image quality and stability were obtained that exhibited high geometric congruency to anatomical scans without the need for post-hoc distortion correction. Notably, also the corresponding phase images exhibit high raw data quality (without any postprocessing, e.g., phase unwrapping), and suggest the suitability of spiral acquisition for novel phase- or complex-value based fMRI analysis workflows (Balla et al., 2014; Bianciardi et al., 2014; Calhoun et al., 2002; Menon, 2002).

The functional sensitivity of spiral readouts was confirmed by observing typical activation patterns in response to an established visual quarter-field stimulation. Furthermore, the discriminability of different stimulus conditions in neighboring voxels of 0.8 mm nominal resolution, and the localization of significant activation sites almost exclusively in gray matter points towards a sub-millimeter spatial specificity of spiral fMRI that is not compromised by artifactual blurring.

Finally, we demonstrated the versatility of this approach to spiral fMRI with a combined in/out readout at a more typical resolution (1.5 mm). Here, the high acquisition efficiency of the spiral allowed to measure two images per shot. Both spiral-in and spiral-out part showed sufficient functional sensitivity, and their signal-weighted echo combination (Glover and Thomason, 2004) yielded considerably increased SFNR and CNR of about 20%. The somewhat smaller effect of combination compared to previous work in low-resolution

single-shot spiral in/out might be explained by the expanded signal model employed here,

which improves image quality for the spiral-out part typically degraded by blurring. Also

the higher spatial resolution may contribute to the difference, since a recent multi-shot

spiral study at 3T reported similar increases of 25% for combined in/out spirals in early

visual cortex (Singh et al., 2018). More sophisticated combination of echo images (Glover

and Thomason, 2004), or of k-space data during reconstruction (Jung et al., 2013) could

result in further SNR increases, but is subject to future work.

In summary, the presented advances render spiral fMRI a competitive sampling scheme

that delivers on the long-time postulate of high acquisition efficiency without

compromising image quality. Thus, the spatiotemporal application domain of fMRI on a

standard gradient system was enhanced by acquiring a 230x230x36 mm FOV brain image

at 0.8 mm nominal resolution (i.e., a matrix size of 288x288x36) while maintaining a typical

TR of 3.3 s.

To our knowledge, this is also the first spiral fMRI study at ultra-high field, exhibiting the

highest in-plane resolution for spiral fMRI that has been reported to date. In combination

with the reported geometric accuracy, this makes the presented spiral-out sequence an

attractive candidate for high-resolution applications of fMRI, studying the functional sub-

organization of cortex, e.g., in laminae or columns (Cheng et al., 2001; Feinberg et al., 2018;

Fracasso et al., 2016; Huber et al., 2017a; Kok et al., 2016; Lawrence et al., 2018; Martino et

al., 2015; Muckli et al., 2015; Siero et al., 2011; Uğurbil et al., 2013; Yacoub et al., 2008).

4.2   Signal Model Contributions to Acquisition Efficiency

The maximized acquisition efficiency required for the high-resolution single-shot spirals

presented here was the result of the favorable interplay of all three components of the

expanded signal model, and each aspect contributed to this yield:

First, the spiral readout trajectory offers a higher average speed covering k-space than other

single-shot sequences, notably EPI. For our gradient system, this acceleration amounted to

19 % shortened readout time for the same high resolution. An alternative means to
accelerate the readout is to increase maximum k-space speed, i.e., gradient strength. This
complementary approach to boost the spatiotemporal resolution regime of fMRI requires
dedicated hardware (Van Essen et al., 2012), e.g., head-insert gradients (Foo et al., 2018;
Weiger et al., 2018) and could be readily combined with spiral readouts.

Secondly, properly characterizing static field inhomogeneity $\Delta\omega_0$ allowed to prolong the
spiral readout to nearly 60 ms (at 7 T) without incurring detrimental blurring. This directly
increases acquisition efficiency by enlarging the fraction of shot duration spent on
sampling. Prolonging the readout farther will degrade the conditioning of the
reconstruction problem and amplify noise as well as systematic modeling errors. At the
acquisition stage, this could be alleviated by establishing higher field homogeneity through
slice-wise active shimming (Fillmer et al., 2016; Morrell and Spielman, 1997; Sengupta et al.,
2011; Vannesjo et al., 2017) dedicated regional shim coils (Juchem et al., 2015).

Thirdly, using the coil sensitivity profiles for spatial encoding, i.e., parallel imaging,
increases the radius of the k-space tube covered along the trajectory. Thus, for spirals, it
reduces the number of turns needed to sample k-space of a prescribed resolution. Here,
the amenability of spiral sampling to the parallel imaging reconstruction problem helped
to achieve a high in-plane reduction factor of 4 without prohibitive g-factor-related noise
amplification. Because spiral aliasing is distributed in 2D, the inversion problem becomes
more intertwined in space and information about a voxel is distributed more evenly. This
can be seen from the PSF of the undersampled trajectories: while EPI shows singular
aliasing peaks, spirals exhibit rings in the PSF.

In summary, the individual aspects of the expanded signal model, as well as their
combination, i.e., spiral sampling with long single-shot readouts and parallel imaging
acceleration, achieve an optimal sampling throughput of information content for fMRI of
high spatiotemporal resolution.

4.3 Signal Model Limitations and Alternatives

All components of the expanded signal model are essential to accomplish both high acquisition efficiency and competitive image quality in high-resolution spiral fMRI. As a consequence, the success of the approach is also sensitive to the functionality of each of them:

Of these three components, accounting for static B_0 inhomogeneity is most critical for the robustness of the image reconstruction. The implications of improper B_0 correction for spiral imaging have previously been discussed (Engel et al., 2018b; Kasper et al., 2018; Wilm et al., 2017) and follow from two distinct causes: limitations of the formulation of B_0 effects in the model specification itself, and failure to properly measure B_0. In practice, the challenge to acquire a veridical B_0 map is most relevant. Signal dropouts, chemical shift specimen or very strong intra-voxel gradients of B_0 render the retrieval of a single true offresonance value per voxel impossible, but also highlight the role of proper map processing (smoothing, extrapolation).

Time series applications of spirals aggravate the static B_0 challenge due to their longer overall scan duration. The increased likelihood and magnitude of subject movement during extended time periods evokes stronger disagreement between a previously acquired B_0 map and current B_0 distribution. In this study, for compliant subjects, there was no indication of incomplete B_0 correction in the center of the imaged brain slices. However, at cortex boundaries close to the skull or air cavities, localized blurring, distortion and ringing artifacts could be observed, most prominently in orbitofrontal regions and in the temporal lobe, above the ear canals, as well as in more inferior slices, particularly in the brainstem. Since we focused on visual areas in the occipital cortex for the functional analysis, it might well be that such regions also exhibit less sensitive and spatially specific activation patterns.

To increase the agreement between B_0 map and spiral acquisition geometry, regular updates of the maps via repeated ME scans or calibration parts in the spiral readout for B_0 map co-estimation (Fessler, 2010; Hernando et al., 2008) could be included. Alternatively,

prospective motion correction updating the spiral slice geometry addresses this issue

(Haeberlin et al., 2015, 2014; Maclaren et al., 2013; Speck et al., 2006; Zaitsev et al., 2017)

alongside general motion confounds in fMRI (Power et al., 2015), but unlike re-mapping

cannot account for the orientation dependence of B_o.

Beyond such systematic errors in determining the B_o map, the signal model itself is limited

in its description of static offresonance effects, because it does not account for intra-voxel

dephasing. Even though this is a possible extension, it would not resolve the fundamental

problem of bad conditioning of the model inversion in the presence of steep spatial B_o

variations.

The second crucial ingredient to artifact-free spiral image reconstruction is the accurate

knowledge of the field dynamics (Barmet et al., 2008; Engel et al., 2018b; Kasper et al., 2018;

Wilm et al., 2011, 2017). Here, we relied on concurrent magnetic field monitoring using

NMR field probes to characterize spiral encoding up to linear spatial order, i.e., global field

and k-space, which appeared sufficient given the spiral image quality.

For time series applications such as fMRI, one advantage of concurrent monitoring is its

ability to also capture dynamic irreproducible effects, such as subject-related field changes

induced by breathing or limb motion, as well as system instabilities, e.g., due to heating

through the heavy gradient-duty cycle customary for fMRI. In this respect, we did not

observe any conspicuous problems in the time series statistics, for example, SFNR drops,

nor any indication of time-dependent blurring, which would be the spiral equivalent to

apparent motion in phase encoding direction observed in EPI (Bollmann et al., 2017; Power

et al., 2019). Consequently, the chosen bandwidth of the trajectory measurement of about

4 Hz (i.e., only monitoring every third slice) was sufficient to capture possibly relevant

detrimental dynamic field effects. 2D single-shot sequences are amenable to this approach,

because they reach steady-state eddy current dynamics, since all gradient waveforms repeat

periodically for each slice, and only RF frequencies of the slice-excitation pulse change. For

monitoring every slice or non-periodic gradient waveforms, continuous monitoring

approaches offer a comprehensive solution (Dietrich et al., 2016b), but require short-lived

^{19}F NMR field probes for concurrent operation (Looser et al., 2018).

While concurrent field monitoring is a convenient and generic approach to characterize

the encoding fields, it involves additional hardware that may be technically challenging

and increases the complexity of the measurement setup. Because fMRI already employs

peripheral devices for experimental stimulation and physiological recordings, this might at

times be prohibitive. Alternatively, reproducible field effects, such as the spiral trajectory

and its induced eddy currents, could be measured by calibration approaches in a separate

scan session (Bhavsar et al., 2014; Duyn et al., 1998; Robison et al., 2019, 2010). For more

flexibility, the gradient response to arbitrary input trajectories can be modelled from such

data under linear-time invariant system assumptions (Addy et al., 2012; Campbell-

Washburn et al., 2016; Vannesjo et al., 2014, 2013). The required field measurements for

these calibrations may either rely on a dedicated NMR-probe based field camera (Barmet

et al., 2008; De Zanche et al., 2008; Vannesjo et al., 2014, 2013) or on off-the-shelf NMR

phantoms (Addy et al., 2012; Duyn et al., 1998), with certain trade-offs to measurement

precision and acquisition duration (Graedel et al., 2017). To account for the

aforementioned dynamic field effects as well, the spiral sequence could be augmented by

higher-order field navigators (Splitthoff and Zaitsev, 2009) or a temperature-dependent

gradient response model (Dietrich et al., 2016c; Nussbaum et al., 2019; Stich et al., 2019).

Finally, using coil sensitivity profiles for spatial encoding, i.e., parallel imaging, is also more

intricate in terms of image reconstruction, and less explored for spiral imaging than EPI

(Heidemann et al., 2006; Lustig and Pauly, 2010; Pruessmann et al., 2001; Weiger et al., 2002;

Wright et al., 2014). Here, for our 32-channel receive array at 7 T, we saw that an in-plane

acceleration of R=4 did not incur any spatially structured residual aliasing or excessive

noise amplification, i.e., g-factor penalty (Pruessmann et al., 1999) in the SD maps. This is

in line with previous observations for spiral diffusion and single-shot imaging (Engel et al.,

2018b; Wilm et al., 2017). Going to higher undersampling factors will introduce

exponential noise amplification, arising from fundamental electrodynamic limits to
accelerated array encoding (Wiesinger et al., 2004).

Importantly, the absence of aliasing artifacts in this time series application also points to
the robustness of the reconstruction to motion-induced mismatch of measured and actual
coil sensitivities. Unlike B_0 maps, coil sensitivities are largely independent of head position
(apart from changes in coil load) and intrinsically much smoother, thus more forgiving to
slight displacements throughout the scan duration. If larger motion occurs, joint
estimation of sensitivity map and spiral image is possible, as mentioned for the B_0 map
(Fessler, 2010; Sheng et al., 2007). Denser sampling of the spiral k-space center could easily
retrieve the required auto-calibration data.

In this context, the accomplished robustness of parallel imaging acceleration for the spirals
can also be viewed as an important synergy effect of the expanded signal model. Typically,
the geometries of coil sensitivity maps and spiral scans disagree, since the latter is
compromised by static B_0 inhomogeneity or trajectory errors (Engel et al., 2018b, fig. 6).
This leads to aliasing artifacts, which are rectified by expanding the signal model to include
B_0 maps and actual field dynamics.

4.4 Spiral vs EPI

The demonstrated quality of spirals for high-resolution fMRI raises the question about their
performance in comparison to the established EPI trajectories. However, a fair general
quantitative comparison of both sequences remains intricate: For example, T_2^* weighting
and its impact on the point spread function (PSF) differ between the approaches (Engel et
al., 2018b; Singh et al., 2018). Also, fair matching of sequence parameters depends on the
specific context and could lead to different preferences for equalizing TE, readout length,
resolution or parallel imaging acceleration factor. For example, consider a comparison at
equal spatial resolution: For defining resolution, maximum k-space values or equal area of
covered k-space could be justifiable choices, depending on whether directional or average

values are considered. Independent of that choice, due to the higher speed of spiral
readouts, a comparison at fixed resolution would imply either increased readout duration
or undersampling factor for the EPI, both of which could be disputed.

Thus, a general comparison of both trajectory types is difficult, and should be geared to
specific application cases (Lee et al., 2019), which is beyond the scope of this paper. Instead,
we list the specific advantages of both sequence types in light of the advances for spiral
imaging presented here that alleviate some of its typically perceived downsides (Block and
Frahm, 2005).

First, spiral acquisitions are faster than EPIs, because of their higher average speed
traversing k-space. For our system, an EPI comparable to the 0.8 mm spiral-out trajectory,
i.e., covering a square with the same area as the spiral k-space disc (equivalent to an EPI
with $0.9 \, \text{mm} \approx \sqrt{4/\pi} \cdot 0.8 \, \text{mm}$ in-plane resolution), and equivalent undersampling (R=4)
would have a 22 % increased readout duration of 70 ms. Furthermore, the efficiency loss of
the EPI mainly accrues at turns between traverses, i.e., in outskirts of k-space. According
to the matched-filter theorem, this is only SNR-optimal, if the desired target PSF is the FFT
of that sampling scheme, i.e., an edge-enhancing filter (Kasper et al., 2014). For ringing
filters or Gaussian smoothing typically employed in fMRI, an approximately Gaussian
acquisition density, as intrinsically provided by spiral sampling (Kasper et al., 2015) can
deliver substantial SNR increases, depending on the target FWHM for smoothing (Kasper
et al., 2014). On a similar note, the isotropic PSF of the spirals might be preferable in brain
regions where cortical folding dominates directional organization. Anecdotally, we also
observed that subjects tolerated spiral fMRI sequences better than EPIs. This might be due
to reduced peripheral nerve stimulation and more broadband acoustic noise which was
perceived as less disturbing than the distinct ringing sound at the EPI readout frequency.

EPI, on the other hand, has a lot of advantages due to its sampling on a regular Cartesian
grid. This intrinsically offers a rectangular FOV, and direct application of FFT for faster
image reconstruction. Also, the symmetry of the trajectory can be used for an alternative

means to image acceleration via partial Fourier undersampling (Feinberg et al., 1986),

which works more robustly in practice than for spiral acquisitions. Finally, trajectory

imperfections can also be intrinsically addressed by this symmetry: EPI phase correction,

i.e., acquiring a few extra k-space lines without phase encoding, characterizes both global

field drifts and Nyquist ghosting arising from eddy current discrepancies of odd and even

echoes (Schmitt et al., 2012). This in particular provides a robust and simple alternative to

sequence-specific trajectory calibration or field monitoring for EPI.

4.5 Generalizability of Signal Model and Reconstruction

This work focused on two-dimensional, slice-selective spiral imaging. Simultaneous multi-

slice (SMS) or 3D excitation schemes offer a complementary means of acceleration, by

extending sensitivity encoding to the third encoding (slice) dimension, as, e.g., in stack-of-

spiral trajectories (Deng et al., 2016; Engel et al., 2019, 2018a; Zahneisen et al., 2014), which

also provides SNR benefits (Poser et al., 2010). The expanded signal model and image

reconstruction framework employed here, apart from the 2D-specific simplifications, are

equally applicable to this scenario (Engel et al., 2018b; Pruessmann et al., 2001; Zahneisen

et al., 2015).

While our approach to signal modeling and inversion fundamentally solves the (spiral)

image reconstruction problem, computation efforts are still considerable and would

increase further for 3D and SMS encoding. Note, however, that we did not optimize our

code for speed, with most routines written in Matlab and only gridding and MFI packaged

as compiled C-functions. Since the numerous matrix-vector multiplications (eq. 5) burden

the CG algorithm most, an implementation on graphical processing units (GPUs), which

have become available as a mainstream technology, could significantly accelerate

reconstruction. Without such modifications, the CPU-based implementation could be run

through cloud services as affordable alternative to a local cluster. On a more conceptual

level, the repetitive nature and possible redundancy of time series imaging between

volumes might open up new pathways to accelerated sampling or reconstruction in the
temporal domain (Chiew et al., 2015; Tsao et al., 2003).

4.6 Translation to other fMRI applications

We implemented the spiral sequences at ultra-high field (7T), which has shown particular
utility for high-resolution functional MRI due to its superlinear increase in BOLD CNR
(Uludağ and Blinder, 2018). From an image reconstruction perspective, this might be
considered a challenging scenario because both static and dynamic field perturbations are
exacerbated at ultra-high field and deteriorate conditioning of the expanded signal model.
Thus, the adoption of the presented advances in spiral fMRI to lower field strengths not
only seems straightforward and worthwhile, but might also offer benefits. For example,
spiral readouts could be prolonged in light of the more benign field perturbations,
mitigating the lower CNR.

Furthermore, the successful deployment of the in/out spirals here suggests the feasibility
of other dual-echo variants, such as out-out or in-in acquisition schemes. In particular,
recent correction methods for physiologically or motion-induced noise that rest on multi-
echo acquisition (Kundu et al., 2012; Power et al., 2018) could profit considerably from
spiral-out readouts: compared to EPI, the shorter minimum TE provides first-echo images
with reduced T_2*- weighting and should enhance disentanglement of BOLD- and non-
BOLD related signal fluctuations.

Beyond BOLD, the adaptation of single-shot spiral acquisition for other time series
readouts seems promising. In particular fMRI modalities with different contrast
preparation (Huber et al., 2017b), such as blood-flow sensitive ASL (Detre et al., 2012,
1992), and blood-volume sensitive VASO (Huber et al., 2018; Lu et al., 2013, 2003) benefit
from the shorter TEs offered by spiral-out readouts. These sequences do not rely on T_2*
decay for functional sensitivity, and thus minimizing TE leads to considerable CNR gains
(Cavusoglu et al., 2017; Chang et al., 2017).

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Conflicts of Interest

Klaas Pruessmann holds a research agreement with and receives research support from Philips Healthcare. He is a co-founder and shareholder of Gyrotools LLC. Christoph Barmet and Bertram Wilm are shareholders and part-time employees of Skope Magnetic Resonance Technologies AG.

738 Figures

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Utilized 2D single-shot spiral acquisitions (R=4 undersampling): High-resolution single-
shot spiral-out (nominal resolution 0.8 mm, black) and spiral in/out trajectory (1.5 mm
resolution, blue). Depicted are the gradient waveforms (G_x, G_y, G_z) as well as RF excitation
(Tx) and ADC sampling interval   s (AQ) for both the ^{1}H head coil and the ^{19}F field probes
used to monitor the trajectories and other concurrent encoding fields. Field probe
excitation and acquisition start a few milliseconds before the spiral readout gradient
waveforms.

Figure 2

Overview of image quality for high-resolution (0.8 mm) single-shot spiral-out acquisition.

(A) 8 oblique-transverse slices (of 36) depicting the time-series magnitude mean of one

functional run (subject S7, 100 volumes). (B) Single-volume magnitude images for slices

corresponding to lower row of (A). (C) Mean phase image over one run, without any post-

processing, for slices corresponding to lower row of (A).

 Figure 3

Characterization of image time series fluctuations over 1 spiral-out run (95 volumes,
discarding first five). (A) Signal-to-Noise Fluctuation Ratio (SFNR) image for same slices as
in Fig 2. Rather homogeneous, exhibiting sufficient SFNR levels. (B) Standard deviation
(SD) image over time. Regions of high fluctuation mainly include pulsatile areas close to
ventricles or major blood vessels, and cortex/CSF interfaces. (C) Coefficient of Variation
(CoV) image. Inverse of (A), highlighting regions of high fluctuations relative to their
respective mean. Vascularized/CSF regions appear prominently, as well as the internal
capsule, due to its reduced average signal level.

Figure 4

Image quality and geometric accuracy of spiral images, reconstructed with the expanded signal model. (A) Anatomical Reference: Mean multi-echo (ME) spin-warp image (1 mm resolution) (B) High-resolution (0.8 mm) spiral-out; (C) In-part of spiral in/out (1.5 mm); (D) Out-part of spiral in/out (1.5 mm). (E-H) Overlay of isoline contour edges from (A) onto (A)-(D).

Depicted are the mean images of a single run (subject S2, top row, B-D). The mean ME image (A), used to compute SENSE- and B0-map for the expanded signal model, provides the anatomical reference via its contours (E, red lines). These are overlaid onto the different spiral variants (bottom row, F-H). Arrows indicate residual geometric incongruence by through-plane dephasing (white) or incomplete B_0 mapping and correction (yellow) in the

spiral-out, which are reduced in the out-part and absent in the in-part of the spiral-in/out

sequence.

Figure 5

Visual Activation Maps of high-resolution (0.8 mm) spiral-out fMRI for a single subject
(S2). Representative stimuli of both conditions (ULLR and URLL) are displayed at the top.
(A) Overlay of differential t-contrast maps (p<0.001 uncorrected) on transverse slices of
mean spiral image (hot colormap: URLL-ULLR, cool colormap: ULLR-URLL). (B) Same
contrast maps as in (A), overlaid on mean ME image as anatomical reference. (C) Zoomed-
in sections of differential t-contrast maps in different orientations: transverse (top), coronal
(middle) and sagittal (bottom, left (L) and right (R) hemisphere). (D) t-contrast maps for
individual conditions (blue: ULLR, yellow: URLL), showing more widespread activation
and high spatial specificity, i.e., little spatial overlap (green).

Figure 6

Mean spiral images and activation maps over subjects (S2-S7) for high-resolution spiral-
out fMRI. For each subject, the following 4 sections are displayed, with the mean ME image
as anatomical underlay: transverse, coronal and sagittal slice (for left (L) and right (R)
hemisphere), each chosen for the maximum number of activated voxels (over both
differential statistical t-contrasts, p<0.001 uncorrected). To assess raw spiral data quality,
the corresponding mean functional image is displayed side-by-side to the anatomical
transverse slice as an alternative underlay.

Figure 7

Visual Activation Maps of spiral in/out (1.5mm) fMRI run for a single subject (S2, as in Fig.

5). (A-C) Displayed are the differential t-contrast maps (p<0.001 uncorrected) on transverse

slices of the respective mean spiral images (hot colormap: URLL-ULLR, cool colormap:

ULLR-URLL), based on: (A) Spiral Images reconstructed from in-part of the trajectory. (B)

Spiral images reconstructed from the out-part of the trajectory. (C) Signal-weighted

combination [Glover2004, eq. 6] of images in (A) and (B). (D) Zoomed view of activation

maps in leftmost slice of (A)-(C), overlaid on anatomical reference image (mean ME).

Tables

Table 1

Quantification of temporal stability and functional sensitivity of all spiral fMRI sequences. For the signal-to-fluctuation-noise ratio (SFNR, eq. (5)), the table contains mean +/- SD in a gray matter ROI over the whole imaging volume. For the t-contrast SPMs, peak t-value and number of significant voxels over both differential contrasts (+/- ULLR-URLL) are reported (p<0.05 FWE-corrected for multiple comparisons at the cluster level with a cluster-forming threshold of 0.001). The last column shows relative increases to the previous sequence, i.e., the one reported in the sub-table directly above. Since resolutions differ between spiral-out (0.8 mm) and spiral in/out (1.5 mm), we compare activated volume instead of voxel count.

Measure	Subjects								Increase vs previous spiral
	S2	S3	S4	S5	S6	S7	Mean	SD	
high-resolution spiral out									
SFNR_mean	14.1	17.2	14.9	15.7	14.7	15.2	15.3	1.1	-
SFNR_SD	5.0	5.4	4.6	5.0	4.7	4.9	4.9	0.3	
SPM_T_max	12.9	15.2	16.2	17.5	11.1	17.6	15.1	2.6	-
SPM_T_nVoxels	10957	6157	11673	12202	8682	12553	10371	2480	
SPM_T_volume (mm³)	6832	3839	7279	7609	5414	7828	6467	1547	-
in-part spiral in/out									
SFNR_mean	22.7	28.6	23.5	26.6	22.9	23.9	24.7	2.4	61%
SFNR_SD	7.3	8.2	7.6	7.8	7.3	8.2	7.7	0.4	
SPM_T_max	16.6	19.5	23.5	15.1	15.3	15.9	17.7	3.3	17%
SPM_T_nVoxels	10097	4863	10221	6470	8157	2816	7104	2953	
SPM_T_volume (mm³)	14363	6918	14540	9204	11604	4006	10106	4200	56%
out-part spiral in/out									
SFNR_mean	20.4	26.4	21.4	24.3	21.0	22.9	22.7	2.3	-8%
SFNR_SD	7.3	8.4	7.4	8.0	7.7	7.9	7.8	0.4	
SPM_T_max	17.8	20.2	18.2	20.1	17.2	14.4	18.0	2.1	2%
SPM_T_nVoxels	8976	6087	10661	7923	11606	3312	8094	3054	
SPM_T_volume (mm³)	12769	8659	15166	11271	16510	4711	11514	4344	14%
combined spiral in/out									
SFNR_mean	28.3	35.9	29.5	33.6	28.7	30.3	31.1	3.0	37%
SFNR_SD	9.4	10.9	10.0	10.4	9.9	10.7	10.2	0.5	
SPM_T_max	18.4	19.7	20.3	17.8	15.8	18.3	18.4	1.6	2%
SPM_T_nVoxels	11971	6575	13254	9331	11665	6082	9813	2985	
SPM_T_volume (mm³)	17029	9353	18854	13274	16594	8652	13959	4247	21%

Supplementary Material

Figure S1

Figure collection of high-resolution (0.8 mm) spiral fMRI data. For every subject, 8 figures are shown, each depicting all 36 slices of the acquisition (top left = most inferior slice, bottom left = most superior slice). All underlay images are based on the functional time series after realignment, and the overlaid t-map was computed from the preprocessed data which included smoothing as well (FWHM 0.8 mm). Order of the figures (1) First volume of spiral fMRI time series; (2) Time-series magnitude mean of spiral fMRI run; (3) Bias-field corrected version of (2); (4) Signal-to-Noise Fluctuation Ratio (SFNR) image of spiral fMRI run (display range 0-30); (5) Standard deviation (SD) image over time of the same run (display range 0-0.05); (6) Coefficient of Variation (CoV) image of the same run, inverse of (4) (display range 0-0.2); (7) Magnitude-mean spiral fMRI image, overlaid with edges of anatomical reference (mean multi-echo spin warp); (8) Overlay of differential t-contrast maps (p<0.001 uncorrected) on transverse slices of mean spiral image (hot colormap: URLL-ULLR, cool colormap: ULLR-URLL, display range t=3.2-8).

Figure S2

Figure collection of spiral in/out fMRI data (1.5 mm resolution). For every subject, 24=3x8 figures are shown, i.e., 8 per set of spiral-in, spiral-out, and combined in/out images. Each figure depicts all 36 slices of the acquisition (top left = most inferior slice, bottom left = most superior slice). All underlay images are based on the functional time series after realignment, and the overlaid t-map was computed from the preprocessed data which included smoothing as well (FWHM 0.8 mm). Order of the figures: (1) First volume of spiral fMRI time series; (2) Time-series magnitude mean of spiral fMRI run; (3) Bias-field corrected version of (2); (4) Signal-to-Noise Fluctuation Ratio (SFNR) image of spiral fMRI run (display range 0-30); (5) Standard deviation (SD) image over time of the same run (display range 0-0.05); (6) Coefficient of Variation (CoV) image of the same run, inverse of

(4) (display range 0-0.2); (7) Magnitude-mean spiral fMRI image, overlaid with edges of

anatomical reference (mean multi-echo spin warp); (8) Overlay of differential t-contrast

maps (p<0.001 uncorrected) on transverse slices of mean spiral image (hot colormap:

URLL-ULLR, cool colormap: ULLR-URLL, display range t=3.2-8).

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