Imaging with referenceless distortion correction and flexible regions of interest using single-shot biaxial spatiotemporally encoded MRI

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Owing to its intrinsic characteristics, spatiotemporally encoded (SPEN) imaging is less sensitive to adverse effects due to field inhomogeneity in comparison with echo planar imaging, a feature highly desired for functional, diffusion, and real-time MRI. However, the quality of images obtained with SPEN MRI is still degraded by geometric distortions when field inhomogeneity exists. In this study, a single-shot biaxial SPEN (bi-SPEN) pulse sequence is implemented, utilizing a 90° and a 180° chirp pulse incorporated with two orthogonal gradients. A referenceless geometric-distortion correction based on the single-shot bi-SPEN sequence is then proposed. The distorted image acquired with the single-shot bi-SPEN sequence is corrected by iterative super-resolved reconstruction involving the field gradients estimated from a field map, which in turn is obtained from its own super-resolved data after a phase-unwrapping procedure without additional scans. In addition, the distortion correction method is applied to improve the quality of the multiple region-of-interest images obtained with single-shot bi-SPEN sequence.

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Introduction

Accelerating the image acquisition process, or equivalently increasing the achievable resolution with a fixed acquisition time, is of major interest in magnetic resonance imaging (MRI). Ultrafast MRI plays an essential role in experiments demanding high temporal resolution like functional MRI (Biswal et al., 1995; Chen et al., 2013a; Deichmann et al., 2002; Matthews and Jezzard, 2004; Preibisch et al., 2003), free-breath heart imaging (Epstein et al., 1999) and high-dimensionality experiments such as diffusion tensor imaging (Bammer et al., 2002; Bihan et al., 1977; Mansfield, 1977; Preibisch et al., 2003) is one of the most popular protocols due to its good temporal resolution. It is well-known that EPI images often have severe geometric distortion because of the $B_0$ field inhomogeneity and phase error accumulation in single-shot $k$-space acquisition (Chiou et al., 2003; Weiskopf et al., 2005). In the past few years, various field inhomogeneity mapping and data processing techniques have been developed for EPI geometric-distortion correction (Airaksinen et al., 2010; Hutton et al., 2002; Jeopard and Balaban, 1995; Knopp et al., 2009; Nam and Park, 2011; Nguyen et al., 2009; Weiskopf et al., 2005; Zeng and Constable, 2002; Zeng et al., 2004). It has been shown that, only after geometric-distortion correction, EPI-based dynamic or functional data can be accurately co-registered with structural images (usually acquired with other time-consuming MRI pulse sequences) (Andersson et al., 2003; Nam and Park, 2011; Weiskopf et al., 2005). However, there are several limitations in the previously reported field mapping and EPI distortion correction methods. Firstly, $B_0$ field mapping requires extra scans, which may not be ideal for certain clinical studies or MR-guided intervention (Chen and Wyrwicz, 2001; Knopp et al., 2009). Secondly, if the subject's position has been changed after the field mapping scan in the EPI studies, the measured $B_0$ field inhomogeneity information may be invalid for EPI distortion correction (Chen and Wyrwicz, 2001; Chen et al., 2008; Chiou et al., 2003; Hutton et al., 2002; Zaitsev et al., 2004; Zeng and Constable, 2002; Zeng et al., 2004). Thirdly, these geometric-distortion correction methods are generally very dependent on the quality of field map obtained with additional scans. When there are errors in the final field map (especially in the region with strong

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local field inhomogeneity), the quality of the corrected results will be degraded (Chen and Wyrwicz, 2001; Wang et al., 1997; Weiskopf et al., 2005). Fourthly, the distortion correction methods will be invalid when the $B_0$ field inhomogeneity is so serious that folding has occurred in the spin-echo EPI images (Chiou et al., 2003; Holland et al., 2010; Knopp et al., 2009; Nam and Park, 2011; Nguyen et al., 2009; Truong et al., 2010; Weiskopf et al., 2005; Zaitsev et al., 2004; Zeng and Constable, 2002; Zeng et al., 2004), or when the k-space energy peaks are shifted completely outside the sampling window due to a very significant in-plane local field gradient in the gradient-echo EPI (Chen et al., 2006; Truong et al., 2010).

In contrast to EPI's reliance on signals contributed simultaneously from the entire excited body, a single-shot spatiotemporally-encoded (SPEN) MRI method recently proposed by the Frydman group and a single-shot MRI method based on rapid acquisition by sequential excitation and refocusing (RASER) proposed by the Garwood group rely on local signals contributed progressively along the SPEN direction (Airaksinen et al., 2010; Ben-Eliezer et al., 2010a, 2012, 2014; Chamberlain et al., 2007; Goerke et al., 2011; Idyattulin et al., 2006; Shen and Xiang, 2010). These single-shot MRI sequences, termed “Hybrid” SPEN scheme, replace EPI's phase encoding with spatiotemporal encoding while retaining a k-space readout acquisition. As a consequence they possess comparable temporal resolution as EPI. For both k-space encoded methods and SPEN methods, the low-frequency signal arises from the center focus point while the high-resolution information is encoded at the periphery of this focus point. For k-space encoded methods, the center focus point is fixed at the center of k-space data, whereas for SPEN methods, the center focus point shifts in the FOV along the low-bandwidth dimension (Ben-Eliezer et al., 2014; Tal and Frydman, 2010). Compared to EPI method, SPEN method possesses two obvious advantages. Firstly, it can realize reduced field-of-view (FOV) imaging for a single-shot bi-SPEN MRI with suitably tailored decoding gradients to image locally two or more ROIs with high immunity and local spatial information. Secondly, since images acquired from bi-SPEN MRI have low resolution and super-resolved (SR) reconstruction is necessary (Ben-Eliezer et al., 2010a; Cai et al., 2013; Chen et al., 2013a). Hence, SPEN method possesses a higher built-in immunity to the field inhomogeneity, including global $B_0$ field inhomogeneity and local field inhomogeneity. The degree of immunity of SPEN MRI to the $B_0$ field inhomogeneity is mainly determined by the absolute value of the product between the strength ($g_{20}$) and the duration ($T_{90}$) of the gradient pulse during spatiotemporal encoding (Ben-Eliezer et al., 2014; Chen et al., 2013a). The greater the absolute value of this product is, the larger the blip gradients between rows are, and the better the immunity to the $B_0$ field inhomogeneity will be. In addition, if one would like to utilize the capability of spatiotemporal encoding to overcome field inhomogeneities, stronger blips are needed compared to EPI's, but this will result in lower signal intensity. Namely, the high immunity of spatiotemporal encoding to field inhomogeneities is achieved at the expense of signal-to-noise ratio (SNR) in comparison with EPI (Ben-Eliezer et al., 2010b, 2014; Cai et al., 2013; Chen et al., 2013a). Although the SPEN imaging has a better performance than EPI in the aspect of the inherent robustness to field inhomogeneities, the quality of SPEN images will still be degraded by geometric distortions, especially when there exist heavily susceptibility inhomogeneities (Schmidt and Frydman, 2013).

Recently, a single-shot biaxial SPEN (bi-SPEN) sequence, which is operated under a full-refocusing (or self-refocusing) condition, has been proposed by the Frydman group (Schmidt and Frydman, 2013, 2014; Solomon et al., 2013). This bi-SPEN sequence imparts on the spins a two-dimensional (2D) elliptic paraboloid phase at the encoding stage, with only the spins near the stationary phase point contributing appreciably to the sampling data at the decoding stage, and the motion of the stationary phase point is controlled by the decoding gradients (Chamberlain et al., 2007; Dumez and Frydman, 2013; Goerke et al., 2011; Schmidt and Frydman, 2014). In addition, this bi-SPEN sequence, executed in a first-in-last-out manner under a fully-refocusing condition, allows each desired line of signal to evolve in a spin-echo way, which eliminates the phase terms caused by the inhomogeneous field. Therefore, the signals from spins at different positions are acquired at different echo times (TEs), and the final sampled data have 2D spatially-dependent $T_2^*$-weighted character (Ben-Eliezer et al., 2010b; Chamberlain et al., 2007; Goerke et al., 2011). The spatially-dependent $T_2^*$-weighting will result in different SNRs at different positions along the low-bandwidth dimension. The fully-refocusing SPEN sequence demands the encoding time to be equal to the decoding time when 90° chirp pulse is applied along the low-bandwidth dimension, or equal to half of the decoding time when 180° chirp pulse is applied along the low-bandwidth dimension. In addition the decoding time is always long (about tens of milliseconds). The difference of the evolution time for spins in different decoding positions along the low-bandwidth dimension is therefore very large and the largest difference can be about twice of the decoding time. Hence the intensity difference of the signals acquired at different decoding times will also be large, and the SNR difference can be more serious for the bi-SPEN sequence with fully-refocusing mode. To alleviate the spatially-dependent $T_2^*$-weighting effect and obtain the phase terms caused by inhomogeneous field, we implement a first-in-first-out bi-SPEN sequence with non-fully-refocusing mode in this paper. It utilizes a 90° and a 180° chirp pulse incorporated with two orthogonal gradients to spatiotemporally encode two dimensions, and the acquisition mode is similar to that of the Hybrid SPEN sequence (Schmidt and Frydman, 2013, 2014). The durations of the 90° and 180° chirp pulses are much shorter than the echo-train duration. We further apply super-resolved (SR) reconstruction on the bi-SPEN images using a SR algorithm which we have developed based on singular value decomposition (SVD) (Chen et al., 2013a), since images acquired from bi-SPEN MRI have low resolution and super-resolved (SR) reconstruction is necessary (Ben-Eliezer et al., 2010a; Cai et al., 2013; Chen et al., 2013a,b; Shen and Xiang, 2010). Note that the SVD method is just used to improve the robustness of SR reconstruction and is used without random sampling, which is different from the work of Chen and co-workers (Chen et al., 2013a). The SR algorithm not only reconstructs a SR image with spatially-dependent $T_2^*$-weighted character but also results in a phase map that reflects the distribution of $B_0$ field. It has been reported that the field inhomogeneity may be calculated more reliably from $T_2^*$-weighted EPI images corresponding to multiple TEs and the distorted EPI images can be corrected by involving the calculated field inhomogeneity (Deichmann et al., 2002; Posse, 1992). However, the multi-TE MRI field mapping requires multiple shots. Furthermore, the measured field maps may be invalid if the object changes position during dynamic scans. Inspired by the above idea of EPI image correction, we proposed a geometric-distortion correction method based on the single-shot bi-SPEN MRI. The susceptibility field gradients are first directly estimated by surface fitting to the field map of the distorted bi-SPEN image with spatially-dependent $T_2^*$-weighted character. Then the distorted bi-SPEN image is corrected by iterative SR reconstruction involving the susceptibility field gradients without additional scans. Different from the multi-TE MRI field mapping, our method only needs a single shot for field mapping.

In many ultrafast imaging applications, region-of-interest (ROI) imaging method is used to improve the local spatial resolution of images. The band-selective excitation and the stationary-phase character of bi-SPEN approach offer an inherent applicability to ROI imaging. In this work, we use single-shot bi-SPEN MRI with suitably tailored decoding gradients to image locally two or more ROIs with spatial locations far away from each other. The spatial resolution is improved within the same experimental time as what conventional full field of view (FOV) method takes, and the distorted image with two or more separated ROIs can also be corrected based on the self-field map.
Materials and methods

In this section, the principle of single-shot bi-SPEN MRI is briefly discussed (Schmidt and Frydman, 2013, 2014). The geometric-distortion correction method based on the single-shot bi-SPEN method is presented. The correction method is realized by the iterative SR reconstruction involving the susceptibility field gradients, which can be directly estimated by surface fitting to the field map of the distorted bi-SPEN data without additional scan. It is referred to as referenceless distortion correction method in the following. The SNR and ROI imaging (including the correction to the ROI image) based on the bi-SPEN method are also discussed.

Principles of bi-SPEN MRI

In this sub-section, the principles of bi-SPEN MRI. The single-shot bi-SPEN MRI sequence is shown in Fig. 1 (Schmidt and Frydman, 2014). To overcome the inhomogeneity distortions and Nyquist ghosting along the low-bandwidth dimension, a 90° chirp pulse with high full acquisition number (see “Experiments” section for the definition of Nfull) is applied along the y direction (Schmidt and Frydman, 2014; Solomon et al., 2013). The 180° chirp pulse is applied along the x direction. The bi-SPEN sequence imparts a 2D elliptic paraboloid phase to the overall spins in the 2D excited FOV (Schmidt and Frydman, 2014). For the bi-SPEN sequence shown in Fig. 1, the entire time-domain signal acquired during the acquisition period can be approximately calculated by the following integral (Schmidt and Frydman, 2013, 2014):

$$ s(t_{acq}) = \int_{t_{acq}} \rho(x,y) \cdot e^{i\left(-\frac{\gamma G_{90} T_{90} y^2}{2 L_y} + \frac{\gamma G_{90} T_{90} y}{2} - \frac{\gamma G_{180} T_{180} x^2}{8} - \frac{\gamma G_{180} T_{180} x}{2} + \frac{\gamma G_{180} T_{180} L_y}{4} \right)} \left( + \frac{\gamma G_{ef} T_{ef} \cdot y + \gamma G_{ef} T_{ef} \cdot x}{L_y} + \gamma \int_{0}^{T_{acq,slow}} G_{acq,slow} dt \cdot y + \gamma \int_{0}^{T_{acq,fast}} G_{acq,fast} dt \cdot y \right) dt $$

(1)

where $G_{ef}$ is the gradient strength during the duration $T_{ef}$ of 90° chirp pulse, $G_{180}$ is the gradient strength during the duration $T_{180}$ of 180° chirp pulse, $L_y$ and $L_x$ are the excited FOV along the y and x directions respectively, $\gamma$ is the gyromagnetic ratio, and $t_{acq}$ and $t_{ef}$ are certain instants in corresponding decoding times $T_{acq,slow}$ and $T_{acq,fast}$. $T_{acq,slow}$ is the sampling/decoding time along the high-bandwidth dimension (i.e. x direction), and $T_{acq,fast}$ is the sampling/decoding time along the low-bandwidth dimension (i.e. y direction). $G_{acq,fast}$ and $G_{acq,slow}$ are magnitudes of the decoding gradients (acquisition gradients) along the x and y directions respectively. $G_{ef}$ is the magnitude and $T_{ef}$ is the duration of the rephasing gradient of the encoding gradient $G_{ef}$ and $G_{ef}$ is the magnitude and $T_{ef}$ is the duration of the rephasing gradient of the decoding gradient $G_{acq,fast}$ and $G_{acq,slow}$ and $\rho(x,y)$ is the spin density of the scanned object. To ensure that the full FOV along the x and y directions are decoded respectively, $G_{acq,fast}$ and $G_{acq,slow}$ need to be applied over the corresponding decoding time $T_{acq,fast}$ and $T_{acq,slow}$ and fulfill the condition: $2 \cdot |G_{180} T_{180}| = \int_{0}^{T_{acq,fast}} G_{acq,fast} (t) dt$ and $|G_{90} T_{90}| = \int_{0}^{T_{acq,slow}} G_{acq,slow} (t) dt$.

Fig. 1. The bi-SPEN MRI sequence used in this study, where $|G_{ef} T_{ef}| = 2 \cdot |G_{ef} T_{ef}| = 2 |G_{ef} T_{ef}| = \int_{0}^{T_{acq,fast}} G_{ef} (t) dt$ and $2 \cdot |G_{ef} T_{ef}| = \int_{0}^{T_{acq,slow}} G_{ef} (t) dt$. The sampling number in y direction is $N_{fe} = 2 \cdot N_{lines} \cdot \left( \left( \frac{T_{acq,slow}}{T_{sample}} + T_{blip} \right) \right)$, where $T_{sample}$ is the duration of one “blips” gradient along the low-bandwidth dimension (i.e. y direction). Note that the signs of $G_{ef}$ and $G_{ef}$ are the opposite to the signs of $G_{ef}$ and $G_{ef}$, respectively, while the sign of $G_{ef}$ is always opposite to the sign of odd $G_{ef}$ and the same as the sign of even $G_{ef}$.
According to the de-convolution algorithm (Cai et al., 2013), Eq. (1) can be transformed to

\[
I(x', y') \propto \int_{\Omega} \left[ p(x, y) \cdot \phi_x(x, x) \right] \cdot \phi_y(y, y) dy,
\]

where \( \phi_x(x, x) = \exp[iG_{inh}x^2/2] \) and \( \phi_y(y, y) = \exp[-iG_{inh}y^2/2] \). The quadratic phase component has been eliminated from the transformation from \( s(t_{ax}, t_{ay}) \) to \( I(x', y') \) where \( I(x', y') \) is the space-domain signal with a simple phase distribution defined as

\[
I(x', y') = s(x', y') \cdot e^{-i \left( \frac{\frac{G_{inh}x^2}{2} + \frac{G_{inh}y^2}{2} - \frac{G_{inh}x}{2} + \frac{G_{inh}y}{2} - Y}{2} \right)}.
\]

The SR image \( p(x, y) \) can be found by solving Eq. (3) using the method reported previously (Chen et al., 2013a). For bi-SPEN MRI, this SR algorithm can be applied first along one SPEN dimension and subsequently along the other dimension.

Referenceless geometric-distortion correction

The \( B_0 \) field inhomogeneity can be expressed as a combination of field gradients with different orders, which affects the frequency offset of spins in the main field \( B_0 \). Due to the influence of \( B_0 \) inhomogeneous field, the image will have geometric distortion. Low order polynomials were often used to fit the background field inhomogeneity (de Rochefort et al., 2008; Clover and Schneider, 1991; Langham et al., 2009). So here we focus on the influence of 1st and 2nd order \( B_0 \) inhomogeneous fields along the \( xy \) imaging plane. The 1st and 2nd order \( B_0 \) inhomogeneous field gradients can be expressed as follows:

\[
G_{inh} = \left[ g_{0x} \; g_{0y} \; g_{inmx} \; g_{inmy} \; g_{inmx2} \; g_{inmy2} \right]^T.
\]

where \( G_{inh} \) is the vector-value function related to the 1st and 2nd order inhomogeneous field gradients (the procedure to calculate \( G_{inh} \) value is presented in Appendix A); \( g_0 \) is the constant inhomogeneous field gradient; \( g_{inx} \) and \( g_{iny} \) are the 1st order inhomogeneous field gradient along the \( x \) and \( y \) directions respectively; \( g_{inmx} \) and \( g_{inmy} \) are the 2nd order inhomogeneous field gradient along the \( x \) and \( y \) directions respectively; and \( g_{inmx2} \) and \( g_{inmy2} \) are the 2nd order inhomogeneous field gradient across the \( x \) and \( y \) directions.

The quadratic phase profiles, which are imposed on the spins after excited by 90° and 180° chirp pulses in combination with the encoding gradients \( G_{90} \) and \( G_{180} \) under \( B_0 \) inhomogeneous field, can be express as follows:

\[
\begin{align*}
\psi_{inh}^\pi(y) &= -\frac{\gamma G_{90}}{2 \Omega} y^2 + \frac{\gamma G_{180}}{2 \Omega} y^2 - \frac{\gamma G_{90}G_{180}}{8 \Omega} y - \frac{\Omega_2^2 T_{90} T_{180}}{2} y + \frac{\Omega_1 T_{90} + \Omega_2 T_{180}}{2}, \\
\psi_{inh}(x) &= -\frac{\gamma G_{90}}{2 \Omega} x^2 + \frac{\gamma G_{180}}{2 \Omega} x^2 - \frac{2 \Omega_1 T_{90} T_{180}}{\gamma} x - \frac{\Omega_2^2 T_{90} T_{180}}{2} x + \frac{\Omega_1 T_{90} + \Omega_2 T_{180}}{2} x.
\end{align*}
\]

where \( \Omega_1 = \Omega + \gamma g_{inmx} \times x + \gamma g_{inmy} \times y + \gamma g_{inmx2} \times x^2 + \gamma g_{inmy2} \times y^2 \), which is the frequency offset of spins induced by the inhomogeneous field, and \( \Omega_0 = \gamma \cdot g_0 \).

The entire signal acquired under the \( B_0 \) inhomogeneous field can be approximately calculated by using the following integral:

\[
s(t_{ax}, t_{ay}, t_{eff}) = \int_{\Omega_{xy}} \rho(x, y) \cdot e^{\left( \int_{t_{ay}}^{t_{ay}} \psi_{inh}^\pi(y) - \psi_{inh}(x) \right)} \cdot e^{\left( + \gamma G_{90} T_{90} \cdot y + \gamma G_{180} T_{180} \cdot y + \gamma G_{inh} T_{inh} \cdot y \pm \gamma \int_0^{t_{ax}} G_{inh} dt \cdot x + \gamma \int_0^{t_{ay}} G_{inh} dt \cdot y \right)} dx dy.
\]

where \( t_{ax} \) is the evolution time from the center of 180° sinc pulse (i.e. point \( d \)) to the decoding time point \( (t_{ax}, t_{ay}) \). For the bi-SPEN sequence shown in Fig. 1, the effective echo time \( T_{E_{eff}} \) for spins in position \( y \) \((y \in [-1/2, 1/2])\) can be expressed as \( T_{E_{eff}} = \frac{1}{2} T_{eff} \), and the sign of \( T_{E_{eff}} \) is always negative because \( T_{E_{eff}} \) is smaller than \( T_{E_{2}} \) (see Fig. 1) in this study. Because the evolution time for spins in different positions along the low bandwidth dimension is different, \( T_{E_{eff}} \) is different for spins in different positions, depending on the excitation instant. The detailed derivation of Eq. (6) is presented in Appendix B.

According to the principle of SPEN MRI (Schmidt and Frydman, 2014), the stationary phase point in the 2D elliptic paraboloid under the \( B_0 \) inhomogeneous field can be found by calculating the first spatial derivative of the overall phase and the real time decoding trajectory \( (x', y') \) can be
approximately defined as

\[
\begin{align*}
\chi' &= \left( \pm \gamma G0y T_{res} \mp y \right) \int_{0}^{L_{x}} e^{\frac{-\gamma G0x - y G0y (t + T_{eff})}{L_{x}}} \cdot y - 2 \left( \frac{\Omega_0 + y G0y \cdot y}{L_{x}} T_{180} + \frac{y G0y T_{90} \cdot y}{L_{y}} \right) \\
y' &= \left( \gamma G0y T_{res} + \gamma \int_{0}^{L_{x}} e^{\frac{-\gamma G0x + y G0y (t + T_{eff})}{L_{x}}} \cdot y + 2 \frac{y G0y T_{180} \cdot y - (\Omega_0 + y G0y \cdot x) T_{90}}{L_{y}} \right)
\end{align*}
\]

(7)

After “phase smoothing” (i.e., removing the quadratic phase component from the acquired data \(s(t_{ax}, t_{ay}, t_{tt})\)) (Cai et al., 2013; Chen et al., 2013a), we can have

\[l(x', y', t_{tt})_{inh} = s(t_{ax}, t_{ay}, t_{tt})_{inh} \cdot e^{-i \left( \gamma (G00 + 2y G0y) T_{90} \cdot y \cdot y' - \gamma (G180 + 2y G0y) T_{180} \cdot x \cdot x' - 2 \frac{y G0y T_{90} \cdot y}{L_{x}} \cdot x' \cdot y' \right)}
\]

(8)

where \(l(x', y', t_{tt})\) is the space-domain signal. The relation between \((x', y')\) and \((t_{ax}, t_{ay})\) can be concluded from Eq. (7). Detailed derivation is presented in Appendix C. Then Eq. (6) can be transformed to

\[
l(x', y', t_{tt})_{inh} \propto \int_{fov} \rho(x, y) \cdot e^{\frac{\gamma (G00 + 2y G0y) T_{90} \cdot (y - y') \cdot (y - y')}{2L_{y}}} \cdot \frac{\gamma G0y T_{90} \cdot (x - x') \cdot (y - y')}{L_{x}} + 2 \frac{y G0y T_{180} \cdot (x - x') \cdot (y - y')}{L_{y}} + \frac{y G0y T_{90} \cdot (t + T_{eff}) \cdot (x - x') \cdot (y - y')}{2} \cdot \left( \frac{\Omega_0}{2} T_{90} \cdot y + \frac{\Omega_1}{2} \right) dy.
\]

(9)

The SR image \(\rho(x, y)\) can be found by solving Eq. (9) using the method reported previously (Chen et al., 2013a). Meanwhile, the distorted image including the influence of \(G_{inh}\) will be corrected. In practice, the distorted image will be effectively improved after a few iterations. A discrete form of Eq. (9) is

\[
L_{inh} = \Phi_{inh} \rho,
\]

(10)

where \(L_{inh} \in \mathbb{C}^{(M_{ax} \times N_{ax})}\) is an interpolation of \(l(x', y', t_{tt})\), \(\rho \in \mathbb{C}^{(M_{ay} \times N_{ay})}\) is the corrected 2D SR image, and \(\Phi_{inh} \in \mathbb{C}^{(M_{ax} \times N_{ax}) \times (M_{ax} \times N_{ax})}\) denotes the quadratic phase modulation under the \(B_{0}\) inhomogeneous field. \(\rho\) can be achieved by solving Eq. (10). However, the \(\Phi_{inh}\) matrix has a size of \((M_{ax} \times N_{ax}) \times (M_{ax} \times N_{ax})\). For a Cartesian acquisition like the one in Fig. 1, the \(\Phi_{inh}\) matrix has \((M_{ax} \times N_{ax})^2\) elements, so the SR reconstruction will need huge computer memory and CPU time, even for a modest 2D reconstructed matrix with \(128 \times 128\) pixels. To surmount this challenge, some simplification can be performed in Eq. (9). In the SR reconstruction, we find that it is vital to obtain exact decoding trajectory \((x', y')\) and space-domain signal \(l(x', y', t_{tt})\) (i.e., Eq. (8)). For the phase terms in the right side of Eq. (9), the influences from the 2nd order inhomogeneous field gradients can be ignored, such as \(y G0y (t + T_{eff}) \cdot (x - x')^2\), \(y G0y (t + T_{eff}) \cdot (y - y')^2\), and \(y G0y (t + T_{eff}) \cdot (x - x') \cdot (y - y')\), because the values of \(G00, G0y\) and \(G0xy\) are usually much smaller than the values of \(G00\) and \(G180\) (about two orders of magnitude smaller). Eq. (9) is approximately modified to

\[
l(x', y', t_{tt}(x', y'))_{inh} \propto \int_{I_{D_{x}}} \rho(x, y) \cdot \phi_{inh}(x, x') dx \cdot \phi_{inh}(y', y') dy.
\]

(11)

where \(\phi_{inh}(x, x') = e^{i \gamma (G00 + 2y G0y) T_{180} \cdot (x - x')^2 / L_{x}}\), and \(\phi_{inh}(y', y') = e^{i \gamma (G00 + 2y G0y) T_{90} \cdot (y - y')^2 / L_{y}}\). After this simplification, the SR reconstruction under the \(B_{0}\) inhomogeneous field can be applied as in the case of homogeneous field. Eq. (11) can be discretized as follows:

\[
L_{inh} \approx \Phi_{inh} \rho \Phi_{inh}^{'\prime}
\]

(12)

where \(\Phi_{inh} \in \mathbb{C}^{M_{ax} \times M_{ax}}\) and \(\Phi_{inh}^{'} \in \mathbb{C}^{N_{ax} \times N_{ax}}\).

Now, the spin density \(\rho\) can be achieved by solving Eq. (12) with greatly reduced CPU time and computer memory in comparison with the requirement for solving Eq. (10). The process of SR reconstruction and distortion correction via field map is depicted schematically in Fig. 2, using a
numerical model as an example. It should be pointed out that the neglect of these 2nd order \( \Delta B_0 \) terms is not obliged and is only to reduce the time of data processing. Only when the effects of these 2nd order \( \Delta B_0 \) terms are very little and do not spoil the reconstructed quality, these 2nd order \( \Delta B_0 \) terms can be neglected. Otherwise, the final reconstruction must involve all 2nd order \( \Delta B_0 \) terms. Some simulated results are given in Appendix D to show the effect of neglecting 2nd order \( \Delta B_0 \) terms.

As has been reported (Ben-Eliezer et al., 2014; Chen et al., 2013b), the Hybrid SPEN sequence can be used to implement 2D limited FOV acquisition without suffering from aliasing artifacts. According to Eq. (7), the stationary phase point of the paraboloid can be shifted flexibly inside the FOV during the acquisition via suitably tailored gradients \( G_{acq}^{fast}(t) \) and \( G_{acq}^{slow}(t) \), and the 2D ROI imaging information can be sought directly in the spatial domain with no need for Fourier transform along any dimension. Therefore, the bi-SPEN sequence possesses the potential to realize more flexible ROI imaging, i.e., the ROIs distributed dispersedly can be simultaneously imaged in a single-shot bi-SPEN MRI. Compared to the full FOV acquisition, this superiority improves the spatial resolution of images because of more sampling points in each ROI. The intensive sampling will lengthen the imaging time on a ROI, especially when it applies along the low-bandwidth dimension (i.e., \( y \) direction). When there is field inhomogeneity in the ROI, longer imaging time will enlarge the impact of field inhomogeneity and the ROI image may be spoiled by the geometric distortion. According to Eq. (5), the field inhomogeneity in the ROI can be expressed as

\[
\mathbf{G}_{\text{inh}}^{\text{ROI}} = \begin{bmatrix} g_0 & g_{inx} & g_{inyy} & g_{inx2} & g_{inyy2} & g_{myy} \\ \end{bmatrix}^T
\]  

(13)
where $G_{\text{acq}}^{\text{SPEN}}$ is the vector-value function related to the 1st and 2nd order inhomogeneous field gradients in the ROI. The value of $G_{\text{acq}}^{\text{SPEN}}$ can be calculated according to the procedure in Appendix A. The SR ROI image $\rho(x, y)$ can be obtained by solving Eq. (9). Meanwhile, when the SR reconstruction involves $G_{\text{acq}}^{\text{SPEN}}$, the distorted ROI image can be corrected according to Eqs. (7)–(9).

Signal-to-noise ratio

High SNR usually benefits single-shot MRI in clinical application. The SNR of k-space encoded EPI and SPEN MRI can be compared by (Ben-Eliezer et al., 2014; Tal and Frydman, 2010):

$$\frac{SNR^{\text{(SPEN)}}}{SNR^{\text{(EPI)}}} = \sqrt{\frac{\alpha G^{\text{SPEN}}}{\alpha G^{\text{EPI}}}} = \sqrt{\frac{\sqrt{\text{sw}^{\text{EPI}}}}{\sqrt{\text{sw}^{\text{SPEN}}}}} = \sqrt{\alpha}$$

(14)

where $G^{\text{SPEN}}$ and $G^{\text{EPI}}$ are acquisition gradients, and the acquisition frequency bandwidths are $\text{sw}^{\text{EPI}} = \gamma G_{\text{acq}}^{\text{EPI}} \cdot \text{FOV}$ and $\text{sw}^{\text{SPEN}} = \gamma G_{\text{acq}}^{\text{SPEN}} \cdot \text{FOV}$; $\alpha$ is the ratio of full acquisition number between SPEN imaging and EPI. Therefore SPEN imaging will suffer a $\sqrt{\alpha}$ reduction in SNR compared to the EPI. It should be noted that $\alpha \leq 1$, meaning that SPEN MRI can, under equal acquisition conditions, have similar SNR as EPI, especially when $\alpha = 1$. The SNR of bi-SPEN MRI versus the SNR of EPI can be expressed as

$$\frac{SNR^{(\text{bi-SPEN)}}}{SNR^{\text{(EPI)}}} = \sqrt{\frac{\alpha G^{\text{EPI}} \cdot G_{\text{acq}}^{\text{EPI}}}{\alpha G^{\text{SPEN}} \cdot G_{\text{acq}}^{\text{SPEN}}}} = \sqrt{\alpha}$$

(15)

where $G^{\text{SPEN}}$ and $G^{\text{EPI}}$ are the acquisition gradient of EPI along the frequency- and phase-encoded direction respectively. From Eq. (15), we can find that when $\alpha \geq 1$, the bi-SPEN MRI may receive a similar SNR or even higher SNR than EPI under a similar experimental condition. For SPEN MRI, a relatively strong acquisition gradient is used to cope with the field inhomogeneity along the $y$ direction compared to EPI, which in turn will lead to a lower SNR. To redeem the reduction of SNR induced by the strong gradient along the $y$ direction, a relatively weak acquisition gradient compared to the frequency-encoding gradient in EPI and Hybrid SPEN MRI is applied along the $x$ direction in bi-SPEN MRI. Meanwhile the diffusion attenuation of signal and eddy effects will also be reduced because of the weaker oscillating acquisition gradient along the $x$ direction. Both benefit the SNR of bi-SPEN MRI. Note that the weak acquisition gradient along the $x$ direction will reduce the immunity of spatiotemporal encoding to the field inhomogeneity theoretically, and the resulting image will be prone to distortion. However, since the acquisition time along this dimension is very short, e.g. 256 μs, the impact from field inhomogeneity is very weak.

Experiments

Experiments were carried out using the single-shot sequence depicted in Fig. 1. The biaxial spatial encoding was applied along the frequency- and phase-encoding dimensions of EPI. All bi-SPEN MRI experiments utilized Cartesian trajectory to cover the FOV. The decoding gradients $G_{\text{acq}}^{\text{fast}}$ and $G_{\text{acq}}^{\text{slow}}$ were applied over the acquisition time $T_{\text{acq}}^{\text{fast}}$ and $T_{\text{acq}}^{\text{slow}}$ for the full FOV imaging. For the bi-SPEN approach used here, to achieve its immunity to inhomogeneous field along the low-bandwidth dimension (i.e. the $y$ direction), strong encoding and decoding gradients were selected, thereby a high bandwidth ($sw = \gamma G_{\text{acq}}^{\text{slow}} L_y$) was used along the low-bandwidth dimension. According to the Nyquist sampling theorem, to avoid undersampled aliasing, the actual acquisition bandwidth $\text{sw}_{\text{acq}}$ ($\text{sw}_{\text{acq}} = 2m/\text{acq} = 2m N_{\text{pe}} T_{\text{acq}}^{\text{slow}}$, where $\text{acq}$ is the sampling time interval, $N_{\text{pe}}$ is the number of sampling echoes along the low-bandwidth dimension, and $T_{\text{acq}}^{\text{slow}}$ is the acquisition time) should reach $sw$, i.e. $\text{sw}_{\text{acq}} = sw$. According to the principle of SPEN MRI (i.e. $[G_{\text{acq}}^{\text{fast}}] = [G_{\text{acq}}^{\text{slow}} + \text{acq}]$), we should have $N_{\text{pe}} \geq \gamma G_{\text{acq}}^{\text{slow}} L_y/2\pi = \gamma G_{\text{acq}}^{\text{slow}} L_y/2\pi = \Delta O_{\text{Hz}} T_{\text{acq}}^{\text{slow}}$ (where $\Delta O_{\text{Hz}}$ is the bandwidth of chirp pulse, Hz) (Chen et al., 2013b). Here we define the full acquisition number $N_{\text{full}} = \Delta O_{\text{Hz}} T_{\text{acq}}^{\text{slow}}$. Consequently, to avoid undersampled aliasing, at least $N_{\text{pe}} = N_{\text{full}}$ echo signals along the $y$ direction should be acquired. In practice, it is impossible for a single-shot 2D sequence to acquire so many echo signals due to relaxation effects. Therefore, the number of sampling echoes $N_{\text{pe}}$ along the low-bandwidth dimension is usually smaller than the full acquisition number $N_{\text{full}}$ in SPEN MRI. This condition is called undersampling. When $N_{\text{full}} = 256$ and $N_{\text{pe}} = 64$, we call this condition four-fold undersampling. For k-space encoded EPI method, the echo time (TE) refers to the time between the center of 90° pulse and the focus point along the low-bandwidth dimension. For the bi-SPEN method, the echo time $T_{\text{E}}$ refers to the time between the center of 90° chirp pulse and the first spin-echo position (i.e. point $c$ in Fig. 1) for the spins at the center of FOV along the low-bandwidth dimension, and the echo time $T_{\text{E}}$ refer to the time between the first spin-echo position (i.e. point $c$ in Fig. 1) and the second spin-echo position at the decoding period for the spins at the center of FOV along the low-bandwidth dimension. To reduce the total acquisition time, $T_{\text{E}}$ in general is smaller than the echo train time. For each experiment, detailed experimental parameters are given in the caption of relevant figure. For the representation of sampling data matrix size $m \times n$, $m$ is along the horizontal axis and $n$ is along the vertical axis if not specially specified. The vertical axis is phase/spatiotemporally-encoded axis and the horizontal axis is frequency-encoded axis. The final image matrix size is all $256 \times 256$.

The MRI scans were performed on a 7T/160 mm bore Varian MRI system (Agilent Technologies, Santa Clara, CA, USA) using a quadrature-coil probe. Super-resolved reconstruction was achieved with home-made codes running on MatLab software (The MathWorks Inc., Natick, MA, USA). The effectiveness of the proposed imaging scheme and distortion correction was demonstrated by experiments on lemon, water phantom and in vivo rat brain. In vivo imaging was carried out on a seven weeks old Sprague–Dawley rat. The experiment was performed in accordance with the procedures approved by the Animal Experimental Center of our university. Before the experiment, the rat was anesthetized with injection of chloral hydrate solution of 10% in concentration at 0.4 ml/100 g.
by the bi-SPEN MRI, the problems of geometric distortion and “stripes” can both be alleviated, and the veins of lemon and gyri of rat brain can be clearly seen. This is due to the nature of bi-SPEN sequence and the relatively small gradient along the high-bandwidth dimension. Meanwhile, the SNRs of images produced by the bi-SPEN MRI are higher than those produced by the spin-echo EPI and Hybrid SPEN MRI for lemon and in vivo rat brain. The SNR value was measured as $\text{SNR} = 10 \log_{10} \left( \frac{\text{Mean}^2}{\text{Var}} \right)$, where Mean and Var are for the average signal power of the signal region and Var (Noise) refers to the noise intensity variance of background region. Different from EPI, the SNR of SPEN image is also affected by the spatially-dependent $T_2^*$ weighting. Different regions may have different spatially-dependent $T_2^*$ weighting character, and this will affect the SNR calculation. To ensure that the SNR results are reliable and robust, signal regions are chosen from the regions near the center of FOV to reduce the effect of spatially-dependent $T_2^*$ weighting, and the background regions are chosen from the regions near the two edges along the high-bandwidth dimension to avoid the effect of residual reconstruction-related signal. The selected signal regions and background regions are circumscribed with green and red rectangles respectively in Figs. 3A and 4A (results for selection verification are not shown for concision).

**Referenceless distortion correction**

The simulated results under different kinds of inhomogeneous fields are shown in Fig. 5. The numerical model (Fig. 5A) and the reconstructed image (Fig. 5B) under a homogeneous field are shown

![Fig. 3](image-url) Imaging results of lemon at axial plane in a well-shimmed magnetic field. Slice thickness = 1 mm, FOV (horizontal) = FOV (vertical) = 65 mm. (A) Reference multi-shot gradient echo image (resolution = 0.25 × 0.25 mm², sampling data matrix size = 256 × 256, TE = 1 ms, TR = 200 ms, total acquisition time = 51.2 s), (B) Single-shot spin-echo EPI image (resolution = 0.25 × 0.67 mm², sampling data matrix size = 256 × 96, TE = 71.6 ms, echo train time = 66.6 ms, $G_{\text{acq}}^{\text{fast}} = 18.1$ G/cm, $G_{\text{acq}}^{\text{slow}} = 18.1$ G/cm, total acquisition time = 106.2 ms), (C) Single-shot Hybrid SPEN image (resolution = 0.25 × 0.67 mm², sampling data matrix size = 256 × 96, TE = 71.6 ms, echo train time = 66.6 ms, $G_{\text{acq}}^{\text{fast}} = 18.1$ G/cm, $G_{\text{acq}}^{\text{slow}} = 4.52$ G/cm, total acquisition time = 106 ms, SPEN parameters: $\Delta O_{g0} = 96$ kHz, $T_{eo} = 3$ ms, encoding along the vertical direction), (D) Single-shot bi-SPEN image (resolution = 0.30 × 0.50 mm², sampling data matrix size = 216 × 128, TE1 = 71.6 ms, TE2 = 71.6 ms, echo train time = 66.6 ms, $G_{\text{acq}}^{\text{fast}} = 14.5$ G/cm, $G_{\text{acq}}^{\text{fast}} = 4.06$ G/cm, total acquisition time = 176 ms, SPEN parameters: $\Delta O_{g0} = 96$ kHz, $T_{eo} = 3$ ms, encoding along the vertical direction; $\Delta O_{g0} = 20$ kHz, $T_{eo} = 4$ ms, encoding along the horizontal direction).

![Fig. 4](image-url) Imaging results of in vivo rat brain at coronal plane in a well-shimmed magnetic field. Slice thickness = 2 mm, FOV (horizontal) = FOV (vertical) = 45 mm. (A) Reference multi-shot gradient echo image (resolution = 0.35 × 0.35 mm², sampling data matrix size = 256 × 256, TE = 3 ms, TR = 8 ms, total acquisition time = 1.0 s, average = 16), (B) Single-shot spin-echo EPI image (resolution = 0.35 × 0.71 mm², sampling data matrix size = 128 × 64, TE = 35 ms, echo train time = 28 ms, $G_{\text{acq}}^{\text{fast}} = 26.1$ G/cm, $G_{\text{acq}}^{\text{slow}} = 2.61$ G/cm, total acquisition time = 43.1 ms), (C) Single-shot Hybrid SPEN image (resolution = 0.35 × 0.71 mm², sampling data matrix size = 128 × 64, TE = 33.8 ms, echo train time = 28 ms, $G_{\text{acq}}^{\text{fast}} = 26.1$ G/cm, $G_{\text{acq}}^{\text{slow}} = 5.59$ G/cm, total acquisition time = 43.1 ms, SPEN parameters: $\Delta O_{g0} = 64$ kHz, $T_{eo} = 3$ ms, encoding along the vertical direction), (D) Single-shot bi-SPEN image (resolution = 0.50 × 0.63 mm², sampling data matrix size = 90 × 72, TE1 = 7.5 ms, TE2 = 32 ms, echo train time = 27 ms, $G_{\text{acq}}^{\text{fast}} = 17.4$ G/cm, $G_{\text{acq}}^{\text{fast}} = 4.97$ G/cm, total acquisition time = 54.5 ms, SPEN parameters: $\Delta O_{g0} = 64$ kHz, $T_{eo} = 3$ ms, encoding along the vertical direction, $\Delta O_{g0} = 10.7$ kHz, $T_{eo} = 3$ ms, encoding along the horizontal direction).
for comparison. The reconstructed image under a linear inhomogeneous field is skewed along the $x$ dimension (horizontal) and deformed along the $y$ dimension (vertical), as shown in Fig. 5C. The reconstructed image shown in Fig. 5E was obtained in a magnetic field consisting of linear and nonlinear inhomogeneity. Though spatial encoding itself can cope with the inhomogeneous field to some extent, the skew and distortion along the two directions can also be seen in Figs. 5C and E because of the heavy inhomogeneous background field. After the referenceless distortion correction, the geometric distortions of reconstructed images under the linear and nonlinear inhomogeneous fields can be effectively corrected without additional field mapping scan, as shown in Figs. 5D and F.

The results of phantom experiments under a well-shimmed magnetic field and deliberately off-shimmed magnetic fields are shown in Fig. 6. The results acquired by using the bi-SPEN sequence without distortion correction are shown in Figs. 6E–H and the results after effectively geometric-distortion correction are shown in Figs. 6J–L correspondingly. Images from single-shot spin-echo EPI sequence (Figs. 6A–D) and the reference image from multi-shot gradient echo sequence (Fig. 6I) are also shown for comparison. All images in the same row were acquired in the same $B_0$ field condition. To visually display the different field conditions, the $B_0$ field maps obtained from the multi-shot gradient echo sequence are shown with pseudo-color in Figs. 6M–P. The images shown in the first row are acquired in a well-shimmed field. It can be seen from Fig. 6M that there is about 200 Hz field inhomogeneity. The EPI image (Fig. 6A) under this well-shimmed field still has much larger geometric distortion compared with the bi-SPEN image (Fig. 6E), which possesses a good geometric shape. The images shown in the second row are acquired in the field with all currents in the shim coils set to 0. There is more than 900 Hz high-order field inhomogeneity, as shown in Fig. 6N. The images acquired with the EPI (Fig. 6B) and bi-SPEN (Fig. 6F) sequences are both disorderly skewed and deformed, though the distortion of the bi-SPEN image is much smaller than that of the EPI image. The images shown in the third row are obtained with misadjusted $x$- and $y$-shim values and suffered from more than 900 Hz linear field inhomogeneity, as shown in Fig. 6O. The images acquired with the EPI (Fig. 6C) and bi-SPEN (Fig. 6G) sequences are both skewed along the $x$ dimension (horizontal) and deformed along the $y$ dimension (vertical). The images shown in the last row are acquired with misadjusted $x$-, $y$- and $xy$-shim values and suffered from more than 600 Hz nonlinear inhomogeneous field, as shown in Fig. 6P. The EPI image (Fig. 6D) and bi-SPEN image (Fig. 6H) not only show skew along the $x$ dimension (horizontal) and deformation along the $y$ dimension, but also show serious distortion in the $xy$ plane. Meanwhile, it is also noticeable that the EPI images show much more serious distortion than bi-SPEN images, and even some EPI images possess folding artifacts.

After the referenceless distortion correction based on the bi-SPEN approach, the geometric distortions in the linear and nonlinear inhomogeneous fields can be effectively removed without additional field mapping scan, as shown in Figs. 6J–L. It should be pointed out that some artifacts occur in the bi-SPEN images. They are caused by the vast under-sampling along the low-bandwidth dimension (Cai et al., 2013; Chen et al., 2013a). This kind of artifacts can be eliminated by random sampling technique (Chen et al., 2013a). The combination of random sampling technique and bi-SPEN needs further study. On the other hand, the artifacts in the SR reconstruction images of lemon and in vivo rat brain are not as obvious as that of water phantom because the edges of the former are not as sharp as the edges of the water phantom (Cai et al., 2013; Chen et al., 2013a).

The results of in vivo rat brain from bi-SPEN imaging and EPI under different background fields are presented in Fig. 7. From Fig. 7C, obvious geometric distortions can be seen in two selected coronal slices of rat brain. Compared to the images (Fig. 7C) acquired by the bi-SPEN MRI, much more serious geometric distortions exist in the EPI images (Fig. 7D) and folding has occurred. The comparison of corrected bi-SPEN images (Fig. 7A) and the reference images (Fig. 7B) indicates that most geometric distortions in single-shot
bi-SPEN SR images of in vivo rat brain can be removed with the proposed technique.

Fig. 8 demonstrates imaging results of different sequences on axial slices of in vivo rat brain when the rat revives a little from deep anesthesia. In Fig. 8G, a conventional spin-echo image, with no distortion in horizontal and vertical direction, is shown as a reference image. However, there are motion artifacts in Fig. 8G, as indicated by the green arrow. Meanwhile, images produced by single-shot spin-echo EPI sequence (Figs. 8A and B) are also shown for comparison. The results acquired by using the bi-SPEN sequence without distortion correction are shown in Figs. 8C and D and the results after geometric-distortion correction are shown in Figs. 8E and F correspondingly. The images shown in the first row are acquired in a relative homogeneous field and the images shown in the second row are acquired in an inhomogeneous field.

Note that there exists a large amount of distortions in the single-shot EPI images (Figs. 8A and B) in comparison with the single-shot bi-SPEN images (Figs. 8C and D). It can be seen from the regions indicated by the red arrow in Fig. 8D that the single-shot bi-SPEN image is also spoiled by the “stripes” artifacts, which are introduced by the inhomogeneous field. The comparison among the single-shot bi-SPEN images and the reference image indicates that not only the majority of the geometric distortions but also the “stripes” artifacts in the single-shot bi-SPEN images are removed with the proposed correction method.

Flexible ROI imaging

The experimental result of flexible ROI imaging on a water phantom is shown in Fig. 9C. The images produced by multi-shot gradient echo
sequence (Fig. 9A) and single-shot bi-SPEN sequence with full FOV imaging (Fig. 9B) are shown for comparison. The images shown in Fig. 9B and C were acquired using the same scan time and encoding parameters but different decoding gradient "paths" along the x and y directions. The results after effectively geometric-distortion correction to Fig. 9C are shown in Fig. 9D. Compared to the image (Fig. 9B) achieved by the full FOV imaging, images (Figs. 9C and D) achieved by the flexible ROI imaging show higher spatial resolution. According to the principle of bi-SPEN MRI, the imaging trajectory can be varied freely by using specially designed decoding gradient. However, compared to the image shown in Fig. 9B, the image obtained with two isolated ROI imaging (Fig. 9D) is deformed along the y direction. This is because much more imaging trajectories travel inside the target imaging region which is optimized to have high resolution, and the influence of local

**Fig. 7.** Imaging results of in vivo rat brain. Top and bottom images are obtained from different slices under different inhomogeneous fields. (A) SR images after geometric distortion correction to (C). (B) Reference images obtained with 4-shot segmented bi-SPEN sequence in a well-shimmed field. (C) SR images obtained with single-shot bi-SPEN sequence in a poorly-shimmed field. (D) Single-shot spin-echo EPI images acquired in the same field condition as (C). EPI parameters: resolution $= 0.7 \times 0.7$ mm$^2$, sampling data matrix size $= 64 \times 64$, $TE = 32$ ms, echo train time $= 26.9$ ms, $G_{\text{acq fast}} = 13.0$ G/cm, $G_{\text{acq slow}} = 1.45$ G/cm, total acquisition time $= 47.0$ ms. The common parameters for the bi-SPEN experiments: Slice thickness $= 2$ mm, FOV$_x$ (horizontal) $= FOV_y$ (vertical) $= 45$ mm, resolution $= 0.7 \times 0.7$ mm$^2$, sampling data matrix size $= 64 \times 64$, $TE_1 = 3.6$ ms, $TE_2 = 32$ ms, echo train time $= 26.9$ ms, $G_{\text{acq fast}} = 13.0$ G/cm, $G_{\text{acq slow}} = 4.35$ G/cm, total acquisition time $= 50.1$ ms. SPEN parameters: $\Delta O_{90} = 64$ kHz, $\tau_{90} = 3$ ms, encoding along the vertical direction; $\Delta O_{180} = 8$ kHz, $\tau_{180} = 4$ ms, encoding along the horizontal direction.

**Fig. 8.** Imaging results of in vivo rat brain. (A) Single-shot spin-echo EPI image acquired in a relatively homogeneous field (resolution $= 0.85 \times 0.85$ mm$^2$, sampling data matrix size $= 64 \times 64$, $TE = 32.9$ ms, echo train time $= 26.9$ ms, $G_{\text{acq fast}} = 10.7$ G/cm, $G_{\text{acq slow}} = 4.35$ G/cm, total acquisition time $= 47.9$ ms). (B) Single-shot spin-echo EPI image acquired in an inhomogeneous field. (C) SR image obtained with single-shot bi-SPEN sequence acquired in the same field condition as (A). (D) SR image obtained with single-shot bi-SPEN sequence acquired in the same field condition as (B). (E) Geometric-distortion corrected image of (C). (F) Geometric-distortion corrected image of (D). (G) Reference conventional spin-echo image acquired in the same field condition as (A) (resolution $= 0.43 \times 0.43$ mm$^2$, sampling data matrix size $= 128 \times 128$, $TE = 10.5$ ms, TR $= 1$ s, dummy scan $= 16$, total acquisition time $= 144$ s). The common parameters for the bi-SPEN experiments: Slice thickness $= 2$ mm, FOV$_x$ (horizontal) $= FOV_y$ (vertical) $= 55$ mm, resolution $= 0.85 \times 0.85$ mm$^2$, sampling data matrix size $= 64 \times 64$, $TE_1 = 8.3$ ms, $TE_2 = 32.9$ ms, echo train time $= 26.9$ ms, $G_{\text{acq fast}} = 10.7$ G/cm, $G_{\text{acq slow}} = 4.0$ G/cm, total acquisition time $= 55.7$ ms. SPEN parameters: $\Delta O_{90} = 64$ kHz, $\tau_{90} = 3$ ms, encoding along the vertical direction; $\Delta O_{180} = 8$ kHz, $\tau_{180} = 4$ ms, encoding along the horizontal direction.
inhomogeneous field is greater because of longer imaging time for the target imaging region and smaller decoding gradients. After the distortion correction, the geometric distortions in Fig. 9C can be effectively removed without additional field mapping scan, as shown in Fig. 9D.

The experimental results of in vivo rat brain are shown in Fig. 10. Images acquired by the multi-shot gradient echo sequence (Fig. 10A) and single-shot bi-SPEN sequence with full FOV imaging (Fig. 10B) are shown for comparison. Two isolated ROIs are marked by green and red squares in Fig. 10B respectively, and the corresponding results acquired by the flexible ROI imaging are shown in Fig. 10C. It can be seen that the region marked by the red square has higher spatial resolution in Fig. 10C than in Fig. 10B, and the vein is clearly shown in Fig. 10C. It should be pointed out that the advantage of the flexible ROI imaging is not so obvious for in vivo rat brain experiments. This may be because the relaxation attenuation of the rat brain signal is too fast under 7 T magnetic field, the rat brain does not show much texture under ultrafast imaging.

Fig. 9. Experimental results of the flexible ROI imaging on a water phantom. The phantom consists of six tubes filled with water and different plastic objects. Slice thickness = 2 mm, FOV_x (horizontal) = FOV_y (vertical) = 70 mm. (A) Reference multi-shot gradient echo image (resolution = 0.54 × 0.54 mm², sampling data matrix size = 128 × 128, TR = 4 ms, TE = 2.8 ms, total acquisition time = 25.6 s). (B) Single-shot bi-SPEN image (resolution 1.1 × 1.1 mm², sampling data matrix size = 64 × 64, TE_1 = 33.4 ms, TE_2 = 33.4 ms, echo train time = 26.928 ms, G_{acq, fast} = 8.39 G/cm, G_{acq, slow} = 1.12 G/cm, total acquisition time = 81.9 ms. SPEN parameters: ΔO_90 = 64 kHz, T_90 = 4 ms, encoding along the vertical direction; ΔO_180 = 8 kHz, T_180 = 4 ms, encoding along the horizontal direction). (C) Image achieved by flexible ROI imaging. (D) Image after distortion correction to (C).

Fig. 10. Imaging results of in vivo rat brain. Slice thickness = 2 mm, FOV_x (horizontal) = FOV_y (vertical) = 45 mm. (A) Reference multi-shot gradient echo image (resolution = 0.35 × 0.35 mm², TE = 2.8 ms, TR = 8 ms, total acquisition time = 1 s). (B) Single-shot bi-SPEN image. (C) ROI image for the regions indicated in (B). The parameters of the bi-SPEN experiments are the same: resolution 0.70 × 0.70 mm², sampling data matrix size = 64 × 64, TE_1 = 6.3 ms, TE_2 = 32.0 ms, echo train time = 26.9 ms, G_{acq, fast} = 13.1 G/cm, G_{acq, slow} = 4.35 G/cm, total acquisition time = 51.3 ms. Spatial encoding parameters: ΔO_90 = 64 kHz, T_90 = 3 ms, encoding along the vertical direction, ΔO_180 = 8 kHz, T_180 = 4 ms, encoding along the horizontal direction.
imaging and the resolution enhancement is not clear. A better performance may be realized for human brain under clinical MRI scanner.

Discussion

In this article, a referenceless distortion correction method and a flexible ROI method based on bi-SPEN MRI have been proposed. The bi-SPEN sequence itself is robust to the moderate $B_0$ inhomogeneity. However, if the $B_0$ inhomogeneity is severe, the bi-SPEN image will be distorted, and distortion correction is necessary. The proposed correction method is realized by the iterative SR reconstruction. The susceptibility field gradients ($\mathbf{g}_{\text{mag}}$) used in reconstruction is directly estimated by fitting to the field map of the distorted bi-SPEN data without additional scan. Though the fitting accuracy will increase with the increment of the order of polynomials, the complexity and time-consuming will also increase. Therefore, the 1st and 2nd order field inhomogeneities are adopted to represent the main background field inhomogeneity, similar to other previous studies (de Rochefort et al., 2008; Glover and Schneider, 1991; Liu et al., 2011). After the 1st and 2nd order background field inhomogeneities are removed by the referenceless correction, the image quality can be improved a lot. Meanwhile, the effects of the remnant background field and local inhomogeneous field caused by the tissue susceptibility difference can be coped with by the SPEN sequence itself. Consequently, the residual distortions are very weak and do not spoil the corrected images, as can be seen from the results shown in Figs. 6–8.

The present correction method is superior to the conventional field-map-based EPI correction methods in two aspects. Firstly, due to the inherent robustness of spatial encoding to field inhomogeneity in comparison with EPI, the present correction method can perform very well even in a severe inhomogeneous $B_0$ field, while the field-map-based EPI correction methods may not work under such a condition since more severe geometric distortion and folding will occur in the EPI image. Secondly, different from conventional field-map-based EPI correction methods which need exact whole field map to correct distortions, the SPEN-based referenceless correction only needs to fit the 1st and 2nd order inhomogeneity field maps. In such fitting, not all field map data points need to be involved. Therefore, the field map data points with relatively high quality (i.e., with relatively high signal intensity or small phase variation between adjacent points) are selected. This means that inaccurate field map data points can be discarded, and the robustness of the correction can be enhanced. Given this, the proposed method might have a low demand for the field map compared to conventional field-map-based EPI correction methods. For an accurate field map, however, further research needs to be carried out to quantify and correct the residual errors in the corrected field map achieved by the proposed method.

It should be pointed out that a relatively reliable global field map is important for the proposed correction method. When the global field inhomogeneity is so severe that the absolute value of phase difference between two adjacent voxels is bigger than $\pi$, the correction will fail. Assume that the FOV is about 6 cm and the $B_0$ field is 7 T, a reliable field map can be obtained only when the absolute value of phase difference between two adjacent voxels is smaller than $\pi$. In such case the inhomogeneity between two adjacent voxels would be less than 500 Hz for a maximum echo time difference of about 1 ms, and the whole inhomogeneity across the entire sample would be less than 30 kHz if linear inhomogeneity is assumed. This inhomogeneity is larger than most of the real inhomogeneity.

Another point that should be noted is that the local susceptibility inhomogeneity is assumed to be coped solely with by the bi-SPEN sequence itself. From the results shown in Figs. 6–8, we can see that the distortions caused by severe inhomogeneous background fields are effectively corrected by the proposed correction method, and the bi-SPEN images show less local distortions near the air-tissue or air-cavity regions compared to the EPI images. Certainly, if the local susceptibility inhomogeneity (e.g. the region of eyeball shown in Fig. 7) is very severe, the corrected results might not be as effective. It can be seen from Fig. 7A that there still exists local distortion in the region of eyeball, likely because the local susceptibility inhomogeneity in the region of eyeball is too severe to be completely eliminated by the SPEN sequence. However, the result in the region of eyeball is still improved to some extent compared to the pre-corrected results shown in Fig. 7C.

The biaxial spatial encoding possesses a good potential to correct the distorted image due to the local susceptibility inhomogeneity. According to the principle of bi-SPEN MRI, the final acquired data are no longer k-space data, but space-domain data. Therefore, the scanned object can be mathematically divided into many small sub-regions so that the field gradient caused by the susceptibility inhomogeneity in each region may be described by a same quadratic function (like Eq. (A.3)). By applying the proposed correction method to the sub-regions, the local distortion of image could be corrected. However, it might be difficult to combine the corrected sub-regions into a single image, which needs further study. The proposed method also depends on the result of surface fitting which is used to obtain the susceptibility field gradient from the phase map; and the phase map depends on a proper phase unwrapping, and on a suitable masking/weighting of low-trust regions.

Owing to the characteristics of bi-SPEN MRI, flexible ROI can be tailored to improve the image resolution under the same scan time. Several ROIs distributed dispersely can be imaged simultaneously in a single shot. Note that the signals originating from the spins outside the ROIs might affect the signals inside the ROIs. To alleviate the disturbance of the signals outside the ROIs, a bigger FOV (about 1.5 times of the size of ROI) is selected for ROI imaging in this paper. The spatial resolution of every ROI will be improved with the increase of sampling points in unit space. However, the increase of sampling points in unit space requires longer imaging time on the ROI and consequently the ROI image will suffer more influence from the inhomogeneous field. This makes the ROI image further deformed along the y direction (Fig. 9C). After the distortion correction, the geometric distortions in Fig. 9C can be partly removed without additional field mapping scan, as shown in Fig. 9D. The correction to the ROI image proves that the proposed correction method in combination with bi-SPEN method possesses the potential to correct local distortion. Much work is still necessary in this aspect.

The ROI imaging is realized by making use of the spatial selectivity of biaxial spatiotemporal encoding. This spatial selectivity can also be executed during the excitation. During the excitation, the ROI can be bi-SPEN by two modified chirp pulses and the regions of non-interest can be excluded from excitation. The ROI image can thus be protected from the influence of adjacent regions of non-interest with serious local inhomogeneous field, such as the influence from the eyeballs on brain imaging, and the influence from the heart on thoracic vertebra imaging.

Conclusion

In this paper, a referenceless geometric-distortion correction method and a flexible ROI imaging method based on the bi-SPEN sequence are proposed. The geometric distortion stemming from inhomogeneous fields can be effectively corrected by the method. The correction method performs well even under a severe inhomogeneous $B_0$ field condition, in which it would be very difficult for the EPI image to be corrected. The flexible ROI imaging method can image any regions in an FOV in a single shot and improve the spatial resolution of image. The two proposed methods make the single-shot bi-SPEN MRI a potential candidate for ultrafast imaging such as functional MRI, and diffusion MRI.

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Appendix A. $B_0$ inhomogeneous field gradient vector $G_{inh}$

In general, the field gradient $G_{inh}$ is unknown for the first SR reconstruction and is assumed to be zero. After phase processing to the acquired data $s_t(x,y)$, with $G_{inh} = 0$, according to Eq. (6), only quadratic phase component is eliminated and the phase induced by the $B_0$ inhomogeneous field remains in the phase map of SR image (see Fig. 2). The rough $B_0$ inhomogeneous field gradient $G_{inh}$ can then be estimated from the field map of the bi-SPEN image after a successful phase-unwrapping procedure. The influence of $G_{inh}$ is expressed as the phase terms in Eq. (6). For simplicity, the terms in Eq. (6) with little effects are ignored and Eq. (6) can be rewritten as follows:

$$s(t_{ax}, t_{ay}, t_{inh}) = \int_{\Omega} \rho(x,y) \cdot e^{i \left[ \gamma (tt + \Delta t) g_{inh} \cdot x + \gamma (tt + \Delta t) g_{inh} \cdot y + \gamma (tt + \Delta t) g_{inh} \cdot xy + \gamma (tt + \Delta t) g_{inh} \cdot y^2 \right]} \cdot dx \cdot dy.$$  \hspace{1cm} (A.1)

So after SR reconstruction to the distorted bi-SPEN data with overlooking the influence from inhomogeneous field, the final acquired spin density $\rho_{inh}(x,y)$ in inhomogeneous field can be express as follows:

$$\rho_{inh}(x,y,t) = \rho(x,y) \cdot e^{i \left[ \gamma (tt + \Delta t) g_{inh} \cdot x + \gamma (tt + \Delta t) g_{inh} \cdot y + \gamma (tt + \Delta t) g_{inh} \cdot xy + \gamma (tt + \Delta t) g_{inh} \cdot y^2 \right]}.$$  \hspace{1cm} (A.2)

According to Eq. (A.2), the phase of spin density $\rho_{inh}(x,y)$ affected by $G_{inh}$ can be approximately expressed as follows:

$$\phi_{inh}^{SR}(x,y,t) = \Omega_t \cdot \left( tt + \Delta t \right) + \gamma g_{inh} \cdot \left( tt + \Delta t \right) \cdot x + \gamma g_{inh} \cdot \left( tt + \Delta t \right) \cdot y + \gamma g_{inh} \cdot \left( tt + \Delta t \right) \cdot xy + \gamma g_{inh} \cdot \left( tt + \Delta t \right) \cdot y^2.$$  \hspace{1cm} (A.3)

Here $\phi_{inh}^{SR}(x,y,t)$ is the phase map of the SR image from single-shot bi-SPEN MRI in the $B_0$ inhomogeneous field. According to Eq. (A.3), the field gradient $G_{inh}$ can be achieved by surface fitting to the field map achieved from the bi-SPEN MRI data.

The general operation of distortion correction can follow the following steps:

1. Execute the SR reconstruction to the acquired data according to Eq. (A.1); the value of field gradient vector $G_{inh}$ is zero for the first SR construction;
2. Unwrap the phase map achieved from the SR image;
3. Calculate the effective echo time $\Delta t_{eff} = \left( \frac{L_x}{2} \frac{L_y}{2} \right)$ for each pixel and achieve the corresponding $\Delta B_0$;
4. Surface fitting to the field map according to Eq. (A.3) and obtain offset value of field gradient vector $G_{inh-offset}$;
5. Approach a new $G_{inh}$ value following the equation: $G_{inh} = G_{inh} + G_{inh-offset}$;
6. Restart from step 1 (with the new $G_{inh}$ value until successful correction.

Here the condition for successful correction (“correction OK” in Fig. 2) is that the unwrapped phase map of final corrected image has little change between two or more adjacent pixel points. It can also be determined by comparing the angular frequency of corrected image $\Delta \omega = \Delta \phi_{corrected}/\Delta t$ with the angular frequency of distorted image $\Delta \omega_{before} = \Delta \phi_{distorted}/\Delta t$. If $\Delta \omega$ is much smaller than $\Delta \omega_{before}$ or smaller than a threshold value (an empirical value depends on the experiment. In general, $\Delta \omega$ is 5 times smaller than $\Delta \omega_{before}$), the condition for “correction OK” is supposed to be satisfied.

Appendix B. Derivation of signal expression in a $B_0$ inhomogeneous field

In single-shot bi-SPEN imaging, 2D spatiotemporal encoding is achieved by a $\pi/2$-chirp pulse combined with a corresponding encoding gradient $G_{x0}$ along the $y$ direction and a $\pi$-chirp pulse combined with a corresponding encoding gradient $G_{180}$ along the $x$ direction during the excitation period. The quadratic phase profiles, which are imposed on the spins after the $\pi/2$- and $\pi$-chirp pulses in combination with the encoding gradients $G_{x0}$ and $G_{180}$ in $B_0$ inhomogeneous field can be written as follows (Tal and Frydman, 2010):

$$\phi_{inh}^{\pi/2}(y) = -\frac{\gamma G_{x0} T_{90}}{2 L_y} y^2 + \frac{\gamma G_{y0} T_{90}}{8} y - \frac{\pi}{2} - \frac{\Omega_1 T_{90}}{L_y} y + \frac{\Omega_1 T_{90}}{2}.$$ \hspace{1cm} (B.1)

$$\phi_{inh}^{\pi}(x) = -\frac{\gamma G_{180} T_{180}}{L_x} x^2 - \frac{\gamma G_{180} T_{180}}{4} L_x x - \phi_0 - \frac{2 \Omega_1 T_{180}}{L_x} x.$$ \hspace{1cm} (B.2)
Here Eqs. (B.1) and (B.2) overlook the quadratic component of $\Omega_1$ in Eq. (5), and $\Omega_1 = \Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot x^2 + \gamma g_{\text{inv2}} \cdot y^2$. Introducing $\Omega_1$ expression into Eqs. (B.1) and (B.2), we have

\[
\phi_{\text{inh}}(y) = -\frac{\gamma g_{\text{inv}}}{2L_y} y^2 + \frac{\gamma g_{\text{inv}}}{2L_y} y - \frac{\gamma g_{\text{inv}}}{8} \pi - \frac{\pi}{2} - \frac{\left(\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_y} \cdot y
\]

\[
+ \left(\frac{\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2}{2}\right) T_{90},
\]

\[
\phi_{\text{inh}}(x) = -\frac{\gamma g_{\text{inv}}}{L_x} x^2 - \frac{\gamma g_{\text{inv}}}{4} x - \frac{\pi}{2} - \frac{\pi}{2} + \frac{\left(\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_x} \cdot x.
\]

After the moment indicated as dashed line in Fig. 1, the accumulated phase of spins in the 2D excited FOV can be expressed as

\[
\phi_{\text{exclal}}(x,y) = \frac{\gamma g_{\text{inv}}}{L_x} x^2 + \frac{\gamma g_{\text{inv}}}{4} x + \frac{\gamma g_{\text{inv2}} T_{\text{eff}}}{L_x} x + \gamma g_{\text{inv2}} T_{\text{eff}} \cdot x^2
\]

\[
- \frac{\gamma g_{\text{inv}}}{2L_y} y^2 + \frac{\gamma g_{\text{inv}}}{2L_y} y - \frac{\gamma g_{\text{inv}}}{8} \pi - \frac{\pi}{2} + \frac{\left(\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_x} \cdot y
\]

\[
+ \frac{\left(\Omega_0 \cdot y + \gamma g_{\text{inv}} \cdot xy + \gamma g_{\text{inv}} \cdot y^2 + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2 + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_x}
\]

\[
+ \frac{\left(\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{2}
\]

where $T_{\text{eff}} = \frac{I_x}{\pi} y - \frac{I_x}{\pi} x).$ is the effective echo time. After that moment, the phase of spins gets a new term as follows:

\[
\phi_{\text{arq}}(x, y, t, \text{IT}) = \gamma \int_0^{I_{\text{arq}}^{\text{fast}}} g(x_{\text{arq}} \cdot t \cdot x + \gamma g_{\text{arq}} \cdot T_{\text{arq}} \cdot x + \gamma g_{\text{inv}} \cdot t \cdot x + \gamma g_{\text{inv2}} \cdot t \cdot x^2
\]

\[
+ \gamma \int_0^{I_{\text{arq}}^{\text{slow}}} g(x_{\text{arq}} \cdot t \cdot y + \gamma g_{\text{arq}} \cdot T_{\text{arq}} \cdot y + \gamma g_{\text{inv}} \cdot t \cdot y^2
\]

\[
+ \gamma g_{\text{inv}} \cdot t \cdot xy + \Omega_0 \cdot t.
\]

The overall phase in the acquisition period can be expressed as follows:

\[
\phi_{\text{overall}} = -\frac{\gamma g_{\text{inv}}}{2L_y} y^2 + \frac{\gamma g_{\text{inv}}}{2L_y} y - \frac{\gamma g_{\text{inv}}}{8} \pi - \frac{\pi}{2} - \frac{\left(\Omega_0 + \gamma g_{\text{inv}} \cdot x + \gamma g_{\text{inv}} \cdot y + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_y}
\]

\[
+ \frac{\left(\Omega_0 \cdot x + \gamma g_{\text{inv}} \cdot xy + \gamma g_{\text{inv}} \cdot y^2 + \gamma g_{\text{inv2}} \cdot x^2 + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{L_y}
\]

\[
+ \frac{\left(\Omega_0 \cdot y + \gamma g_{\text{inv}} \cdot xy + \gamma g_{\text{inv}} \cdot y^2 + \gamma g_{\text{inv2}} \cdot xy + \gamma g_{\text{inv2}} \cdot y^2\right) T_{90}}{2}
\]

\[
+ \gamma g_{\text{inv}} \cdot \left(t + T_{\text{eff}}\right) \cdot x + \gamma g_{\text{inv}} \cdot \left(t + T_{\text{eff}}\right) \cdot y + \gamma g_{\text{inv}} \cdot \left(t + T_{\text{eff}}\right) \cdot xy
\]

\[
+ \gamma g_{\text{inv2}} \cdot \left(t + T_{\text{eff}}\right) \cdot x^2 + \gamma g_{\text{inv2}} \cdot \left(t + T_{\text{eff}}\right) \cdot y^2 + \Omega_0 \cdot \left(t + T_{\text{eff}}\right).
\]
where \(t_t\) is the evolution time from the center of 180° sinc pulse (i.e. point \(d\)) to the decoding time point \((t_{an}, t_{op})\). The entire signal acquired in the \(B_0\) inhomogeneous field can be approximated following the using the following integral:

\[
s(t_{an}, t_{op}, t)_{inh} = \int_0^{t_{inh}} \rho(x, y) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot x' + \gamma \frac{G_{x0} \cdot T_{90}}{4} \cdot x^2} \, dt_x + \gamma \int_0^{t_{inh}} \rho(x, y) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot y' + \gamma \frac{G_{y0} \cdot T_{90}}{4} \cdot y^2} \, dt_y.
\]

**Appendix C. Phase smoothing to the acquired data**

Given the quadratic \(x\)- and \(y\)-dependence of the excited phases \(\phi_{inh}(x)\) and \(\phi_{inh}(y)\), the spin phase will vary rapidly across the sample, except at the single stationary-phase point where the first spatial derivative of the overall phase vanishes: \(\nabla_{(x,y)}[\phi_{overall}(x, y, t_{an}, t_{op})] = (0, 0)\). According to this stationary-phase approximation (Ben-Eliezer et al., 2010b, 2012; Goerke et al., 2011; Schmidt and Frydman, 2014), only spins close to this time-dependent point \((x, y)\) will have their spins in phase and contribute to the observable signal \(s(t_{an}, t_{op}, t)_{inh}\). Therefore, a bridge linking spatial position \((x, y)\) and decoding time \((t_{an}, t_{op})\) is built by the decoding gradients \(G_{x0, y0} \cdot t_{inh}\). So, according to Eq. (B.8), this relation can be expressed as

\[
\begin{align*}
\rho(x, y) &\approx \rho(x, y, t_{anh}, t_{oph}) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot x' + \gamma \frac{G_{x0} \cdot T_{90}}{4} \cdot x^2} \, dt_x + \gamma \int_0^{t_{inh}} \rho(x, y) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot y' + \gamma \frac{G_{y0} \cdot T_{90}}{4} \cdot y^2} \, dt_y. \\
\end{align*}
\]

Substituting Eq. (C.1) into Eq. (B.8) and rearranging the equation, we have

\[
s(x', y', t(x', y'))_{inh} = \int_0^{t_{inh}} \rho(x, y) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot x' + \gamma \frac{G_{x0} \cdot T_{90}}{4} \cdot x^2} \, dt_x + \gamma \int_0^{t_{inh}} \rho(x, y) \cdot e^{i \gamma \frac{(G_{x0} + 2G_{y0}) \cdot T_{90}}{2} \cdot y' + \gamma \frac{G_{y0} \cdot T_{90}}{4} \cdot y^2} \, dt_y.
\]
Since the third-order terms of spatial position in Eq. (C2) have much less influence on the resulting signal compared to the 1st and 2nd order terms, they can be ignored and Eq. (C2) can be rewritten as

\[
\gamma \left( G_{90} + 2G_{180} \right) \frac{T_{90}}{2L_y} y^2 + \frac{\gamma (G_{90} + 2G_{180}) T_{90} y y'}{L_y} + \frac{\gamma G_{180} + 2G_{180} }{L_x} \frac{T_{180} x^2}{2} - 2 \gamma (G_{180} + 2G_{180}) T_{180} x x' \\
\gamma \frac{\gamma_{inxy} T_{90} x y}{L_y} + \frac{\gamma_{inxy} T_{90} x y'}{L_y} + \frac{\gamma_{inxy} T_{90} y x'}{L_y} + \frac{2 + \gamma_{inxy} T_{180} x y - 2 \gamma_{inxy} T_{180} x y'}{L_y} - \frac{\gamma_{inxy} T_{180} x x'}{L_y} \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) - \frac{\gamma_{inxy} T_{180} L_x}{4} - \frac{\gamma_{inxy} T_{90} L_y}{8} - \frac{\Omega_0 T_{exc}}{2} - \frac{\Omega_0 T_{90}}{2}
\]

Eq. (C3) can be further modified into

\[
\frac{\gamma \left( G_{90} + 2G_{180} \right) \frac{T_{90}}{2L_y} y^2 + \frac{\gamma (G_{90} + 2G_{180}) T_{90} y y'}{L_y} + \frac{\gamma G_{180} + 2G_{180} }{L_x} \frac{T_{180} x^2}{2} - 2 \gamma (G_{180} + 2G_{180}) T_{180} x x'}{dx dy} \\
\frac{\gamma_{inxy} T_{90} x y}{L_y} + \frac{\gamma_{inxy} T_{90} x y'}{L_y} + \frac{\gamma_{inxy} T_{90} y x'}{L_y} + \frac{2 + \gamma_{inxy} T_{180} x y - 2 \gamma_{inxy} T_{180} x y'}{L_y} - \frac{\gamma_{inxy} T_{180} x x'}{L_y} \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) - \frac{\gamma_{inxy} T_{180} L_x}{4} - \frac{\gamma_{inxy} T_{90} L_y}{8} - \frac{\Omega_0 T_{exc}}{2} - \frac{\Omega_0 T_{90}}{2}
\]

In Eq. (C4), the variables of integration are \( x \) and \( y \), so the constant and terms including \( x' \) and \( y' \) can be transferred to the left side. Eq. (C4) can then be expressed as follows:

\[
\frac{\gamma \left( G_{90} + 2G_{180} \right) \frac{T_{90}}{2L_y} y^2 + \frac{\gamma (G_{90} + 2G_{180}) T_{90} y y'}{L_y} + \frac{\gamma G_{180} + 2G_{180} }{L_x} \frac{T_{180} x^2}{2} - 2 \gamma (G_{180} + 2G_{180}) T_{180} x x'}{dx dy} \\
\frac{\gamma_{inxy} T_{90} x y}{L_y} + \frac{\gamma_{inxy} T_{90} x y'}{L_y} + \frac{\gamma_{inxy} T_{90} y x'}{L_y} + \frac{2 + \gamma_{inxy} T_{180} x y - 2 \gamma_{inxy} T_{180} x y'}{L_y} - \frac{\gamma_{inxy} T_{180} x x'}{L_y} \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) \\
\gamma_{inxy} \left( x x' - 2 \gamma_{inxy} T_{180} x x' \right) - \frac{\gamma_{inxy} T_{180} L_x}{4} - \frac{\gamma_{inxy} T_{90} L_y}{8} - \frac{\Omega_0 T_{exc}}{2} - \frac{\Omega_0 T_{90}}{2}
\]

where

\[
l(x', y', tt(x', y'))_{\text{inh}} = s(x', y', tt(x', y'))_{\text{inh}} - e^{-t}
\]

**Appendix D. Justification for neglecting 2nd order \( \Delta B_0 \) terms in reconstruction**

The proposed correction method is realized by the iterative SR reconstruction involving susceptibility field gradients, which can be directly estimated from surface fitting to the field map of the distorted bi-SPEN data without additional scan. When Eqs. (9) or (10), including all 2nd order \( \Delta B_0 \) terms, is used to reconstruct the bi-SPEN data to obtain the SR corrected image \( \rho(x, y) \), the data processing will be very time-consuming, especially when several iterative SR reconstructions are needed. Therefore, for time saving, an approximate reconstruction equation (i.e. Eqs. (11) or (12)) is used. The effects of the 2nd order \( \Delta B_0 \) terms do not vanish completely when the 2nd order \( \Delta B_0 \) terms in Eq. (9) are neglected for final reconstruction. From
Eq. (8), we can see that all 2nd order $\Delta B_0$ terms are involved in the signal $i(x', y', \tau)$. Therefore, even if the 2nd order $\Delta B_0$ terms are neglected in Eq. (9), the effects of 2nd order $\Delta B_0$ terms are included in $i(x', y', \tau)$. Note that this approximation will introduce error into the resulting $B_0$ map. This error can be ignored in most cases, because the values of 2nd order $\Delta B_0$ terms are small. When the values of 2nd order $\Delta B_0$ terms are so big that the error is beyond the trusted scope, all 2nd order $\Delta B_0$ terms should be involved in correction.

In the following, some simulated results are given in Fig. D.1 to show the effects of 2nd order $\Delta B_0$ terms. The original distorted amplitude image (Fig. D.1A) and phase map (Fig. D.1B) are shown for comparison. The corrected amplitude image (Fig. D.1C) and phase map (Fig. D.1D) are obtained by using the correction method based on Eqs. (8) and (9). The corrected amplitude image (Fig. D.1D) and phase map (Fig. D.1H) are obtained by using the correction method based on Eqs. (8) and (11). All 2nd order $\Delta B_0$ terms are removed from Eqs. (8) and (9), the corresponding corrected amplitude image and phase map are shown in Figs. D.1F and J. It can be seen from the amplitude difference image (Fig. D.1E) and phase difference image (Fig. D.1I) that the amplitude image and phase map obtained by correction with 2nd order $\Delta B_0$ terms removed from Eq. (9) are very close to the ones obtained by correction with all 2nd order $\Delta B_0$ terms involved. There are still distortions in the amplitude image and phase map (Figs. D.1F and J) when the 2nd order $\Delta B_0$ terms are completely neglected in the final reconstruction (i.e. the 2nd order $\Delta B_0$ terms are completely removed from Eqs. (8) and (9)). The amplitude difference image (Fig. D.1E) and phase difference map (Fig. D.1I) indicate that the approximation like Eq. (11) is tolerable in some cases (e.g. in the correction of in vivo rat brain image) and the effects of 2nd order $\Delta B_0$ terms could be expressed by Eq. (8). Finally, it should be noted that the neglect of 2nd order $\Delta B_0$ terms is not obliged and is only utilized to reduce the time of data processing. The 2nd order $\Delta B_0$ terms can be neglected only when their effects are very small and do not spoil the quality of reconstructed images.

References


