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# Impact of $B_0$ field imperfections correction on BOLD sensitivity in 3D-SPARKLING fMRI data

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**Purpose:** Static and dynamic  $B_0$  field imperfections are detrimental to functional MRI (fMRI) applications, especially at ultra-high magnetic fields (UHF). In this work, a field camera is used to assess the benefits of retrospectively correcting  $B_0$  field perturbations on Blood Oxygen Level Dependent (BOLD) sensitivity in non-Cartesian 3D-SPARKLING fMRI acquisitions.

**Methods:** fMRI data was acquired at  $1\text{mm}^3$  and for a  $2.4\text{s}$ -TR while concurrently monitoring in real-time field perturbations using a Skope Clip-on field camera in a novel experimental setting involving a shorter TR than the required minimal TR of the field probes. Measurements of the dynamic field deviations were used along with a static  $\Delta B_0$  map to retrospectively correct static and dynamic field imperfections, respectively. In order to evaluate the impact of such a correction on fMRI volumes, a comparative study was conducted on healthy volunteers.

**Results:** Correction of  $B_0$  deviations improved image quality and yielded between 20% and 30% increase in median temporal signal-to-noise ratio (tSNR). Using fMRI data collected during a retinotopic mapping experiment, we demonstrated a significant increase in sensitivity to the BOLD contrast and improved accuracy of the BOLD phase maps: 44% (resp., 159%) more activated voxels were retrieved when using a significance control level based on a p-value of 0.001 without correcting for multiple comparisons (resp., 0.05 with a false discovery rate correction).

**Conclusion:** 3D-SPARKLING fMRI hugely benefits from static and dynamic  $B_0$  imperfections correction. However, the proposed experimental protocol is flexible enough to be deployed on a large spectrum of encoding schemes, including arbitrary non-Cartesian readouts.

**Total number of words and figures/tables :** 5226 words and 9 Figures/Tables

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fMRI,  $B_0$  inhomogeneities, NMR probes, Field monitoring, non-Cartesian, 3D-SPARKLING

## 1 | INTRODUCTION

The race towards higher resolution in fMRI has motivated a significant amount of technological development in both hardware (higher fields and better coil architectures) and software (acquisition, reconstruction, and preprocessing tools)<sup>1</sup>. In this collective endeavor to reach sub-second and/or sub-millimeter resolution, accelerated acquisition schemes play a major role: Cartesian Echo-Planar-Imaging (EPI) schemes such as 2D SMS-EPI<sup>2</sup> and 3D-EPI<sup>3</sup> combined with parallel imaging are today the proven norm in high-resolution fMRI studies due to their efficient use of the gradient capabilities. They are currently challenged by spiral readouts<sup>4</sup> which are today one of the most promising and investigated non-Cartesian sampling patterns for high-resolution fMRI. 3D-SPARKLING<sup>5</sup> is a novel non-Cartesian acquisition method based on compressed sensing (CS) theories. It generates optimization-driven multi-shot sampling patterns that fit a target sampling density in k-space and meet the hardware constraints regarding maximum gradient amplitude and slew rate. This multi-shot readout performs a variable density sampling while maintaining local uniformity in the sampling, and results in arbitrary shots. It produces low-level noise-like artifacts after CS-based MR image reconstruction. Upon comparison with 3D-EPI at 1mm isotropic spatial resolution and 2.4s-TR<sup>6</sup>, 3D-SPARKLING has recently been assessed as a competitive acquisition technique for high spatial resolution task-based fMRI.

Like EPI and spiral readouts, 3D-SPARKLING is sensitive to static and dynamic  $B_0$  perturbations, which can be detrimental for fMRI applications as they degrade the sensitivity to the BOLD contrast and the tSNR<sup>7</sup>. On one hand, moving to UHF ensures a higher tSNR and temporal Contrast-to-Noise Ratio (tCNR) and, therefore, improved sensitivity to the BOLD effect<sup>8</sup>. Additionally, at UHF, the boost in the contribution of capillaries in the BOLD contrast is more pronounced as compared to large veins<sup>9</sup>, which enhances spatial specificity. On the other hand, the influence of  $B_0$  imperfections becomes more prominent at UHF (7T and beyond). If uncorrected, such imperfections can cancel out the gain in sensitivity and specificity expected by moving to higher fields: Correcting off-resonance effects due to  $B_0$  inhomogeneities is therefore one way to secure the advantages of high fields without being subject to their disadvantages.

The static contribution of spatially varying  $B_0$  field offsets arises mainly from the susceptibility differences at tissue-air interfaces and is, to some extent, routinely corrected in MRI in general. In brain MRI, this issue is most prominent near the sinuses, buccal cavity and ear canals. Static  $B_0$  inhomogeneities can cause geometric distortions, blurring, shading as well as strong signal loss. They are usually minimized by means of shimming: Optimizing shimming for brain MRI, especially at high fields (3T and beyond) is an active field

of research<sup>10,11</sup>. However, shimming is never perfect and residual  $B_0$  inhomogeneities must be accounted for using a  $\Delta B_0$  map during image reconstruction<sup>12,13,14</sup>. Preprocessing steps such as the TOPUP approach<sup>15,16</sup> can also be applied in the case of EPI fMRI to further correct geometric  $\Delta B_0$  distortions.

Dynamic perturbations of the  $B_0$  field can stem from the system (instabilities in the gradient system, temperature drifts, eddy currents<sup>17</sup>) or from the volunteer (e.g. breathing and heart rate). They are typically divided into a global zeroth order term, first-order deviations from the nominal trajectories, and some higher-order terms<sup>18,19</sup>. Dynamic field fluctuations are time-varying and constitute a potential confound for fMRI in regions where a significant BOLD effect is sought<sup>20</sup>: They may act as nuisance variables<sup>21</sup> by causing intensity changes that are unrelated to the neuro-vascular coupling and degrade the tSNR. Similar to static field inhomogeneities, dynamic field fluctuations can be compensated prospectively during the acquisition or corrected retrospectively during image reconstruction using time-varying estimates<sup>14</sup>: Navigators are typically implemented into sequences to monitor dynamic field fluctuations<sup>22</sup>. However, navigators require alteration of the pulse sequences and sometimes lengthen the acquisition time. Physiological probes such as breathing belts can also be used to correct physiology-related field fluctuations during acquisition but only give an indirect measure of the induced field perturbations.

A method that uses NMR probes<sup>23,24</sup> to monitor the field fluctuations has been proposed<sup>25</sup>. Unlike navigators, using NMR probes does not require alteration of the pulse sequence and allows for field monitoring in a time-locked fashion instead of having access only to average measurements of the temporal field fluctuations. The system presented in<sup>23,24</sup>, uses transmit and receive probes that contain an NMR active product excited by applying a radio frequency (RF) pulse at its Larmor frequency. It later evolved into a field camera using doped Fluorine (<sup>19</sup>F) NMR probes and was used for field monitoring with anatomical and functional MRI<sup>26,19,27</sup>. Given the difference in Larmor frequency of doped Fluorine and Hydrogen, such probes enable monitoring the field concurrently with the imaging process in the case of proton MR imaging. However, the  $T_2$  relaxation time of the probes is around 45ms at 7T, implying that a relatively long  $TR_{probe}$  is needed to eliminate residual transverse magnetization between the shots and achieve a proper steady-state at the level of the probes. Using only RF spoiling, the field camera requires a constraining minimum  $TR_{probe}$  of roughly 110ms. Such a situation is particularly challenging for 3D fMRI applications as all shots are, ideally, monitored in real-time using  $TR_{probe} = TR_{shot} \leq 50$ ms.

In<sup>27</sup>, the authors managed to use this system to acquire realistic 3D-EPI fMRI data with a short  $TR_{shot}$  and a long

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$TR_{probe}$ : They assumed repeatable readouts between the shots, skipped monitoring some shots and interpolated the missing NMR probe data. A similar strategy was used in<sup>4</sup> where the same system was used to correct up-to-the-first-order dynamic field fluctuations in single-shot high-resolution spiral fMRI data: Field fluctuations were recorded for every third shot using a  $TR_{probe} = 270\text{ms}$  and a  $TR_{shot} = 90\text{ms}$ . Such strategies are impractical for 3D-SPARKLING applications given the pseudo-random nature of the sampling pattern, i.e. the variability across shots and thus the impossibility to interpolate NMR probe data across shots: In<sup>28</sup>, we studied the benefit of correcting  $\Delta B_0$  perturbations on dynamic 3D-SPARKLING acquisitions without extending the study to realistic fMRI data because of the long  $TR_{probe}$  constraint.

In this paper, we alleviate this issue using an external spoiling gradient and adapting the experimental protocol to enable the use of Skope's Clip-on field Camera with  $TR_{probe} = TR_{shot} = 50\text{ms}$  challenging its long  $TR_{probe}$  constraint and evaluate it for  $1\text{mm}^3$  3D-SPARKLING retinotopic mapping and resting-state fMRI acquisitions. We demonstrate the feasibility of our experimental protocol and study the impact of static and dynamic  $B_0$  field imperfections correction during image reconstruction on fMRI data in terms of image quality, tSNR, sensitivity to the BOLD contrast and quality of the retinotopic maps. To the best of our knowledge, it is the first time such a thorough comparison has been performed using the Skope Clip-on field Camera for fMRI data at 7T and non-Fourier reconstruction.

## 2 | THEORY

### 2.1 | Extended signal model

3D-SPARKLING sampling patterns are segmented into  $N_{shot}$  shots of duration  $T_{obs}$ . Each of them samples the center of k-space at the echo time ( $TE$ ). Therefore, during the  $s$ -th shot, the NMR signal  $\mu_\ell^s(t)$  collected by the  $\ell$ -th coil for each  $t \in [TE - \frac{T_{obs}}{2}, TE + \frac{T_{obs}}{2}]$  (in s) can be modeled by the extended signal model as follows:

$$\mu_\ell^s(t) = \underbrace{e^{-ik_0^s(t)}}_{\text{FOV}} \int \bar{x}_\ell(\mathbf{r}) e^{-2i\pi[\Delta B_{0,stat}(\mathbf{r})t + \tilde{\mathbf{k}}^s(t) \cdot \mathbf{r}]} d\mathbf{r} \quad (1)$$

where  $\bar{x}_\ell(\mathbf{r}) = \zeta_\ell(\mathbf{r})x(\mathbf{r})$  is the image  $x$  multiplied by the sensitivity profile of the  $\ell$ -th coil  $\zeta_\ell$  at the spatial position  $\mathbf{r}$ . Note that  $\Delta B_{0,stat}(\mathbf{r})$  (in Hz) denotes the static inhomogeneities of the  $B_0$  field in space whereas  $\Delta B_{0,dyn}^s$  (in Hz) and  $\tilde{\mathbf{k}}^s = \mathbf{k}^s + \delta\mathbf{k}^s$  (in  $\text{m}^{-1}$ ) denote respectively its zeroth order dynamic fluctuation and the measured trajectory deviated from the prescribed one ( $\mathbf{k}^s$ ) due to first order fluctuation  $\delta\mathbf{k}^s$ .  $\Delta B_{0,dyn}^s$  is slowly varying and considered constant during

a shot but a more temporally resolved measure can be written as  $k_0^s(t) \simeq 2\pi t \Delta B_{0,dyn}^s$  (in rad).

In Eq. (1), the term  $\Delta B_{0,stat}(\mathbf{r})t$  depends on the image domain making the integral dependent both on the image and k-space domains which is not compatible with the usual (non-uniform) Fourier transform model.

### 2.2 | Linear approximation of the non-Fourier model

According to Eq. (1), the discretized adjoint operator can be written as follows:

$$\bar{x}_\ell(\mathbf{r}_n) = \sum_t e^{2i\pi t \Delta B_{0,dyn}^s} \mu_\ell^s(t) e^{2i\pi[\Delta B_{0,stat}(\mathbf{r})t + \tilde{\mathbf{k}}^s(t) \cdot \mathbf{r}]} \quad (2)$$

The mixed term  $e^{2i\pi t \Delta B_{0,stat}(\mathbf{r}_m)t} = \sum_{p=1}^P b_{m,p} c_{p,n}$  can be split in a rank- $P$  linear decomposition using a SVD<sup>13,29</sup> to recover a sum of  $P$  (non-uniform) Fourier transform as follows:

$$\bar{x}_\ell(\mathbf{r}_n) = \sum_{p=1}^P c_{p,n} \sum_{t_m=0}^{T_{obs}} b_{m,p} \underbrace{e^{2i\pi t \Delta B_{0,dyn}^s} \mu_\ell^s(t_m)}_{\tilde{\mu}_\ell^s(t_m)} e^{2i\pi \tilde{\mathbf{k}}^s(t_m) \cdot \mathbf{r}_n} \quad (3)$$

Since the term related to  $\Delta B_{0,dyn}^s$  is outside of the integral in Eq. (1), the zeroth order dynamic fluctuations can be corrected by simply demodulating each  $\mu_\ell^s(t)$  with the corresponding  $e^{2i\pi t \Delta B_{0,dyn}^s} \simeq e^{ik_0^s(t)}$  to obtain  $\tilde{\mu}_\ell^s(t)$ . As Eq. (3) holds for all frequencies  $\tilde{\mathbf{k}}^s$  and locations  $\mathbf{r}_n$  across the  $N_{shot}$  readouts, we can summarize the perturbed acquisition in Eq. (4), as a sum of adjoint non-uniform Fourier transforms  $\mathcal{F}_{\tilde{\Omega}}$ , yielding a coil-specific image  $\bar{x}_\ell$  from the measured frequencies locations  $\tilde{\Omega}$  and associated corrected values ( $\tilde{\mu}_\ell$ ):

$$\bar{x}_\ell = \sum_{p=1}^P c_p \odot \mathcal{F}_{\tilde{\Omega}}^*(b_p \odot \tilde{\mu}_\ell) = \tilde{\mathcal{F}}_{P,\tilde{\Omega}}^*(\tilde{\mu}_\ell), \quad (4)$$

where  $\odot$  denotes the element-wise product.

## 3 | METHODS

### 3.1 | Experimental protocol and data acquisition

The study was conducted at 7T MRI (7T Magnetom investigational device, Siemens Healthineers, Erlangen, Germany) on three healthy volunteers (2 males) aged between 20 and 40 years old with normal-to-corrected vision using a 1Tx-32Rx head coil (Nova Medical, Willmington, CO, USA). The experimental protocol was approved by the national ethics committee (Comité de Protection des Personnes) under the protocol identifier CPP 100048 (CPP Sud Méditerranée 4 number 180913, IDRCB:2018-A011761-53). All participants gave their written informed consent.

Task-based fMRI was performed using two consecutive runs (one clockwise and one counter-clockwise) of a classical retinotopic mapping paradigm using the stimulation code available online\*. Retinotopic mapping and resting-state data with normal breathing (NB) was collected from the three participants. Additional data with forced breathing (FB) and while performing a hand-to-chin movement (HC) was collected at resting-state from one volunteer. The functional data was collected with  $T_2^*$ -weighted 3D-SPARKLING acquisitions at a spatial resolution of  $1\text{mm}^3$ , a temporal resolution of 2.4s,  $TR_{shot}/TE=50/20\text{ms}$  and a 3D field-of-view (FOV) of  $(192,192,128)\text{mm}^3$ . A three-echo 3D gradient recalled echo (3D GRE) sequence was used to obtain both a  $\Delta B_0$  ( $\Delta B_{0,stat}$ ) and external sensitivity maps. Table 1 details the parameters of the sequences.

Concurrently and for each acquired fMRI volume, 16 NMR probes from the field Camera, Cranberries edition (Skopec Magnetic Resonance Technologies AG, Zurich, Switzerland) were used to monitor and record the zeroth order field fluctuations over the acquisition window  $k_0 = [k_{0,1}, \dots, k_{0,N_{shot}}] \simeq [2\pi t \Delta B_{0,dyn,1}, \dots, 2\pi t \Delta B_{0,dyn,N_{shot}}]$  and measure the trajectories played by the MR system  $\tilde{k} = [\tilde{k}_1, \dots, \tilde{k}_{N_{shot}}]$  for a  $TR_{probe} = TR_{shot} = 50\text{ms}$ . The residual magnetization resulting from the use of such a short  $TR_{probe}$  was destroyed using the strongest spoiling gradient ( $470\text{mT}^*\text{ms/m}$ ) implementable within a  $50\text{ms}-TR_{shot}$  3D-SPARKLING sequence.

### 3.2 | Image reconstruction and preprocessing

The fMRI volumes were reconstructed independently from each other following the extended recorded signal model in Eq. (1) and by solving the minimization problem in Eq. (S1) in Supporting Information Section S1 using the Proximal Optimized Gradient Method (POGM) algorithm. This method is implemented in the `pysap-mri`<sup>30</sup> plugin<sup>†</sup> of the `pySAP` package<sup>31</sup>.

Motion correction and co-registration of the functional and the  $T_1$ -weighted anatomical data were applied using SPM12<sup>‡</sup>. Except for a very specific step when estimating BOLD phase maps, no spatial smoothing was applied to maintain the native spatial resolution. The segmentation of the cortical surface into a pial, white, inflated, and sulcus meshes was performed using the  $T_1$ -weighted anatomical scan and `FreeSurfer 7`.

### 3.3 | Statistical analysis

Retinotopic mapping data was analyzed for each participant separately, using a two-session first-level general linear model (GLM) and the following block-diagonal design-matrix  $\mathbf{X}$ :

$$\mathbf{X} = \begin{pmatrix} \mathbf{X}_1 & \mathbf{0}_{N_{vol}, Q/2} \\ \mathbf{0}_{N_{vol}, Q/2} & \mathbf{X}_2 \end{pmatrix}$$

where  $N_{vol}$  and  $Q/2$  are respectively, the number of volumes and the number of regressors within a single retinotopic session. The non-zero diagonal blocks  $\mathbf{X}_1$  and  $\mathbf{X}_2$  are respectively associated with the experimental paradigm that is carried out during the clockwise and counter-clockwise sessions. Each block  $\mathbf{X}_s$  is defined as follows:

$$\mathbf{X}_s = \begin{pmatrix} \mathbf{x}_{s,1}^{task} & \mathbf{x}_{s,2}^{task} & \mathbf{x}_{s,1}^{mot} & \dots & \mathbf{x}_{s,6}^{mot} & \mathbf{x}_{s,1}^{pol} & \mathbf{x}_{s,1}^{bas} \end{pmatrix} \in \mathbb{R}^{N_{vol} \times Q/2}, \quad (5)$$

where two paradigm-related parametric, continuous and sinusoidal regressors ( $\mathbf{x}_{s,1}$  and  $\mathbf{x}_{s,2}$ ) serve to capture the BOLD fluctuations elicited by the stimulus presentation. The motion regressors are denoted  $\mathbf{x}_{s,1}^{mot}$  to  $\mathbf{x}_{s,6}^{mot}$  and  $\mathbf{x}_{s,1}^{pol}$  and  $\mathbf{x}_{s,1}^{bas}$  model a polynomial drift and the baseline respectively.

First, a Fisher test over the task-related regressors ( $x_{1,1}^{task}$ ,  $x_{1,2}^{task}$ ,  $x_{2,1}^{task}$  and  $x_{2,2}^{task}$ ) was used to estimate the global effect of interest after thresholding the F-statistic maps over the entire brain for two different strategies:

- (i)  $p < 0.001$  without correcting for multiple comparisons
- (ii)  $p < 0.05$  with false discovery rate (FDR) control<sup>32</sup>.

The thresholded F-statistic maps were further used to create activation masks over the regions where the activations are statistically significant.

Second, a Student t-test was performed over each task-related regressor separately and the corresponding z-scores were used to estimate the BOLD phase maps  $\phi_{Clock}$  and  $\phi_{CClock}$  as the voxel-wise arctangent of the ratio of the corresponding task-regressors ( $x_{1,1}^{task}$  and  $x_{1,2}^{task}$  for the clockwise session and  $x_{2,1}^{task}$  and  $x_{2,2}^{task}$  for the counter-clockwise session).

Then, after compensating for the recorded BOLD response delay ( $d_h = \frac{\phi_{Clock} + \phi_{CClock}}{2}$ ) due to the haemodynamic delay in  $\phi_{Clock}$  and  $\phi_{CClock}$ , we derived the overall retinotopic phase estimate as follows:

$$\phi = \frac{\phi_{Clock} - \phi_{CClock}}{2}. \quad (6)$$

The implementation was done through the `Nilearn`<sup>§</sup> package.

### 3.4 | Evaluation

The mean images computed from the resting-state time series were used to inspect the impact of  $B_0$  perturbations correction

\*[https://github.com/hbp-brain-charting/public\\_protocols](https://github.com/hbp-brain-charting/public_protocols)

†[https://github.com/CEA\\_COSMIC/pysap-mri](https://github.com/CEA_COSMIC/pysap-mri)

‡<https://www.fil.ion.ucl.ac.uk/spm/doc/biblio/>

§<https://nilearn.github.io/stable/index.html>

on image quality qualitatively. In order to gain a deeper insight into the impact of each field term, six distinct reconstruction strategies accounting for different combinations of field terms were used [cf Table S1 in Supporting Information Section S2]:

- (a) **No correction**: None of the field terms were taken into account.
- (b)  $\Delta B_{0,dyn}$ : Only the zeroth order dynamic contribution was accounted for by the correcting the data itself.
- (c)  $\Delta B_{0,dyn}$  &  $\delta k$ : The zeroth and first-order dynamic field fluctuations were corrected.
- (d)  $\Delta B_{0,stat}$ : Only the static inhomogeneities were corrected.
- (e)  $\Delta B_{0,stat}$  &  $\Delta B_{0,dyn}$ : Static inhomogeneities and zeroth order dynamic fluctuations were corrected.
- (f)  $\Delta B_{0,stat}$  &  $\Delta B_{0,dyn}$  &  $\delta k$ : Static and up-to-the-first-order dynamic contributions were included in the signal model for reconstruction.

The resting-state fMRI scans were reconstructed using strategies (a)-(f) and further used to compute the tSNR maps in order to rank the impact of each contribution both visually on the image quality and quantitatively.

In order to gain insight on the differences between the three volunteers and several physiological noise scenarios, the power spectra of the recorded  $\Delta B_{0,dyn}$  measurements were computed over the whole resting-state fMRI acquisition at an individual level and visualized for specific frequency intervals.

To go one step further and investigate the influence of  $B_0$  imperfections correction on the statistical performances when detecting evoked brain activity, the retinotopic mapping fMRI data was used to estimate activation maps by computing z-score maps from the global effects of interest at the subject level. The impact on the sensitivity to the BOLD effect as well as the prevalence of true versus false positives was assessed according to the following qualitative (q) and quantitative (Q) criteria:

- 1) **qActiv1**: The statistically significant z-score maps obtained from the fMRI volumes reconstructed with strategies (a) and (f) and thresholded according to strategies (i)-(ii) as explained in Section 3.3 were compared one another subjectwise.
- 2) **QActiv1**: The Number of activated voxels (defined using thresholding strategies (i)-(ii)) and maximum z-score values were compared at the subject level once the fMRI volumes were reconstructed using strategies (a) and (f).

Finally, the impact on the quality of the BOLD phase maps was evaluated according to the following criterion:

- 3) **qPhase1**: The volumetric BOLD phase map derived from the fMRI scans reconstructed using strategies (a) and (f) were compared subjectwise. Furthermore, the BOLD phase maps corresponding to V#1 were projected onto the cortical surface for both hemispheres and visually assessed.

## 4 | RESULTS

### 4.1 | Achieving steady state signal of the NMR probes

Figure 1 depicts  $S_{raw}(t = 0)$  (the raw signal measured by the field camera before any estimation of field fluctuations) for the first 96 consecutive shots of the multi-repetition 3D-SPARKLING sequence used to acquire in vivo fMRI data without/with the application of an external spoiling gradient through the 3D-SPARKLING sequence and using a  $TR_{shot} = TR_{probe} = 50ms$ . The data plotted in this figure is acquired in vitro (phantom data) and comes from a single probe. It illustrates the temporal evolution of the  $^{18}F$  NMR signal in the absence of participant-induced perturbations: Stimulated echoes due to the very short  $TR_{probe}$  prevent steady-state at the level of the probes in the absence of a spoiling gradient (blue trace) whereas an external  $470mT^*ms/m$  spoiling gradient overcomes this issue (orange trace). Therefore, It becomes possible to use the field monitoring system in this alternative setting to challenge its long  $TR_{probe}$  constraint by simply applying an external spoiling gradient that is strong enough to eradicate the residual transverse magnetization.

However, according to the signal equation at steady state, even at the Ernst angle, using a smaller TR induces a lower NMR signal and, therefore, a degraded SNR at the level of the probes. The following subsections will demonstrate that even with a degraded SNR, the field camera manages to estimate field fluctuations that are accurate enough to yield beneficial correction for fMRI data.

### 4.2 | Enhanced image quality

Figure 2 shows a comparison of the mean images computed from the resting-state fMRI data collected in volunteer #1 (V#1) and reconstructed according to the strategies (a) to (f) mentioned in Section 3.4. It is noteworthy that the image quality associated with strategy (a) is very degraded. Additionally, the figure demonstrates that the overall  $T_2^*$  contrast is significantly enhanced when correction of both static and dynamic fluctuations of the  $B_0$  field is performed: The blue arrows illustrate how the correction of either the dynamic or static contribution alone (strategy (c) or (d)) resulted in partial improvement whereas correcting both terms (strategy (f)) induced a more significant enhancement. Moreover, the

lost signal in strategy (a) is now recovered, and anatomical details are more finely reconstructed as depicted by the orange and green arrows respectively. Again, it is worth noting that strategies (b)-(e) yield limited improvement when compared to strategy (f) suggesting that none of the field terms has a negligible influence on image quality.

Figure 3 (A) displays a subjectwise comparison between the mean images from the resting-state sequence of fMRI scans reconstructed without and with static and up-to-the-first-order dynamic field terms correction: The gain in image quality is systematic across the three volunteers and for three physiological movement scenarios namely NB, FB and HC.

### 4.3 | Increased tSNR

Figure 3 (B) qualitatively depicts the boost in tSNR obtained when correcting static and up-to-the-first-order dynamic field terms: A notable increase is observed across the three volunteers for the normal breathing scenario, notably in the anterior and posterior cortex and, along the edges of the brain suggesting that subtle head movement-induced field fluctuations related to breathing were compensated. V#2, however, yielded slightly superior tSNR maps compared to the two other participants. This is likely due to the fact that they had less energetic breathing fluctuations, as demonstrated in Figure S1 (A) (in Supporting Information Section S3) where the power spectra of the breathing-induced field fluctuations during the NB scenario are shown for each subject. Despite a discernible increase in tSNR in the data collected in V#3 during forced breathing and when performing the hand-to-chin movement, we did not recover levels that are comparable with the normal breathing scenario. This is likely due to the involvement of additional large-amplitude head movements that we are currently unable to correct using our current protocol (cf Figure S2 in Supporting Information, Section S4).

These qualitative findings are quantitatively supported by Table 2 : It reports the relative gain in % of median tSNR computed over the brain mask when correcting the different field terms during image reconstruction. Although the increase is systematic across volunteers and scenarios, the relative gain for V#2 is approximately one-half (resp, one-third) lower than for the two other volunteers when strategies (b) and (c) (resp., strategies (e) and (f)) are used. Otherwise, the relative gain in median tSNR reaches a plateau around 30% at maximum. The limited improvement in the tSNR maps corresponding to the FB and HC scenarios (Figure 3 (B)) highlights the limits of the correction in extreme cases.

### 4.4 | Increased sensitivity to the BOLD contrast

Figure 4 illustrates a subjectwise comparison of the statistically significant activation patterns thresholded using alternatives (i) and (ii) and yielded by the uncorrected (strategy (a)) and fully corrected (strategy (f)) data ( $q_{\text{Activ1}}$ ) on selected axial slices.

First, a larger effect size is associated with  $B_0$  imperfections correction for both statistical thresholding strategies. This is reproducible across the three volunteers but most visible in V#1 where, in addition to an increased statistical significance, the activation pattern seems to better delineate the gray matter in the visual cortex suggesting a finer fit to the cortical surface.

Second, comparing the results at two statistical control levels (i)-(ii), we observed a smaller discrepancy between the activation maps obtained when static and up-to-the-first-order dynamic field terms are corrected. This suggests that at a given false positive rate the sensitivity to the BOLD contrast is increased and that the results are not merely biased by false positives.

These qualitative findings are supported by the figures reported in Table 3 , which summarizes the systematic gain in the number of activated voxels and maximum z-score values when  $B_0$  field imperfections are corrected (strategy (f)): The number of activated voxels extracted using the thresholding alternative (i) (resp, (ii)) is on average  $43.3\% \pm 17.2\%$  (resp,  $159.3\% \pm 38.6\%$ ) larger. The greater boost in effect size when an FDR control is applied suggests once again a higher prevalence of true positives over false positives in the corrected fMRI scans. The reported figures are consistent between the first and third participants. V#2, however, reveals fewer activated voxels, notably after applying FDR control. This is likely due to larger head movement amplitudes as shown in Figure S3 in Supporting Information Section S5 where the time course of motion regressors of the translation over the z-axis are depicted.

### 4.5 | More accurate BOLD phase maps

Figure 5 depicts the BOLD phase maps derived from uncorrected and corrected fMRI volumes on selected axial views. Firstly, we noticed a larger spatial extent of the BOLD phase maps when  $B_0$  field imperfections are corrected. Second, the maps shown are in better agreement with the prior knowledge about the projection of the visual field onto the occipital cortex. A zoomed-in example is shown for V#1 as she/he was the most compliant volunteer: We clearly observe that the two visual hemifields project onto the contra-lateral hemispheres in the occipital cortex, a well-known mirroring feature of the primary visual cortex. Furthermore, and without ambiguity, the top (resp., bottom) parts of the visual field project onto the

bottom (resp. top) parts of the occipital cortex. In comparison, the BOLD phase map yielded by the uncorrected data seems noisy and matches the expected gradient only partially.

To gain a better insight, the BOLD phase maps ought to be projected on the cortical surface as shown in Figure 6 (A) (qPhase1). In the first column, we observe significantly enhanced BOLD phase maps when  $B_0$  imperfections are corrected: A poor retinotopic organization is retrieved when no field term is corrected whereas an improved one can be inferred when they are. Furthermore, estimating the BOLD phase maps using an ROI defined using a p-value of 0.05 with FDR control (alternative (ii)) has a considerable demeaning effect on the phase maps yielded by the uncorrected fMRI volumes. However, the degradation is almost imperceptible on BOLD phase maps obtained from the corrected fMRI volumes.

Additionally, we compared in Figure 6 (B) the BOLD phase maps derived from raw corrected (strategy(f)) and smoothed uncorrected (strategy(a)) fMRI volumes. Two distinct isotropic 3D Gaussian kernels (FWHM=1.1mm and FWHM=1.5mm) were used to smooth the raw fMRI volumes before performing a GLM analysis. FWHM=1.1mm was tested because, all else being equal, it corresponds to an increase in tSNR of about 33%, which roughly corresponds to the maximum gain in tSNR we claim is possible to achieve using our protocol. Firstly, we observed that the smoothed uncorrected volumes yield BOLD phase maps with lower quality than the raw corrected scans. Secondly, we noticed that smoothing the images at FWHM=1.5mm does not recover the lost signal, whereas correcting  $B_0$  field imperfections does (zoomed-in region in the left hemisphere). Furthermore, while it is true that we recover more spatially extended BOLD phase maps on the right hemisphere when smoothing the images, this map remains less spatially specific than in the raw corrected volumes. We conclude that the increase in median tSNR observed when correcting  $B_0$  imperfections yields an increase in sensitivity that exceeds the expected improvement if we choose to degrade the spatial resolution to increase the tSNR.

## 5 | DISCUSSION

In this work, the impact of static  $B_0$  field inhomogeneities and dynamic  $B_0$  field fluctuations retrospective correction on fMRI volumes has been assessed.

### 5.1 | Main findings

Through the application of a suitable external spoiling gradient, we have first demonstrated that it is possible to use the field camera outside its standard experimental setting, which requires a quite long  $TR_{probe}$  with respect to the  $TR_{shot}$  in

fMRI, and accurately estimate up-to-the-first-order dynamic field fluctuations. Second, on resting-state fMRI data, we have proved that  $B_0$  field imperfections correction has a hugely beneficial impact on 3D-SPARKLING image quality as well as tSNR: Up to 30% increase in median tSNR was quantified. Finally, a rather exhaustive evaluation of the impact on the fMRI volumes demonstrated a significant improvement in the sensitivity and quality of the BOLD phase maps.

### 5.2 | Improved tSNR and detection of evoked brain activations

Our findings provide qualitative and quantitative evidence of a systematic gain in tSNR on average as demonstrated using resting-state fMRI data. This is generally in accordance with previous studies. In<sup>19</sup>, the same field camera was used to correct field fluctuations in 2D-EPI fMRI acquisitions at 3T. The authors note that the increase in tSNR is most notable in the occipital lobe which is consistent with Figure 3 (B). Furthermore, they demonstrate that the gain in tSNR is mainly due to the correction of hardware-related fluctuations. At 7T and in 3D acquisitions, physiological fluctuations impact the signal more severely: In<sup>27</sup>, the authors observed up to 14.3% (resp., 35.6%) relative gain in the mean tSNR over the brain when performing forced breathing (resp., hand-to-chin movement) for 1mm<sup>3</sup> 3D-EPI fMRI (20 repetitions) data at 7T. Upon comparison with 2mm<sup>3</sup> fMRI data, they showed that the gain in tSNR is more significant at higher spatial resolution, i.e., 1mm<sup>3</sup>. The differences in the reported numbers arise from the experimental conditions (2D vs 3D, 3T vs 7T, number of repetitions, volunteer's movement).

To the best of our knowledge, no existing study in the literature using a field camera pushed the comparison up to the statistical analysis. The increase in sensitivity associated with  $B_0$  field imperfections correction we observed remains notable at stricter statistical thresholding levels as demonstrated by criteria QActiv1: The recovery of lost signal plays a major role in retrieving true positives. The enhanced image quality is also expected to yield better spatial specificity as blurring is extremely reduced. Such a claim is supported by the projections of the retinotopic maps onto the cortical surface for V#1.

The BOLD phase maps obtained from the corrected volumes were not merely better than those produced by the uncorrected ones, but their quality also exceeded that of those yielded by smoothing (using either FWHM=1.1mm or FWHM=1.5mm) uncorrected volumes: In fact, when  $B_0$  field imperfections correction is performed, confounding factors due to the participant's physiological movement and the system's instabilities and drifts are eliminated prior to pre-processing and statistical analysis whilst larger voxel sizes



only help in aggregating more signal within a voxel without effectively minimizing the effects of such confounding factors.

### 5.3 | Is it relevant to go beyond first-order dynamic field fluctuations correction?

It is worth noting that our protocol is feasible and has proved without ambiguity that static and up-to-the-first-order dynamic  $B_0$  field imperfections correction is beneficial for 3D-SPARKLING fMRI statistical analysis by illustrating the gain in image quality, tSNR, and accuracy of the retonotopic mapping. Nevertheless, it is essential to keep in mind that data collected from 16 probes was used to estimate four unknown terms for each time point  $t$ , namely one zeroth-order term ( $k_0(t)$ ), and three terms translating the first-order field fluctuations ( $\delta\mathbf{k}(t) = (\delta k_x(t), \delta k_y(t), \delta k_z(t))$ ). This means that the lower SNR of the probes expected from using a shorter  $TR_{probe}$  is compensated with data redundancy.

A further step would be to correct the higher-order field terms<sup>33</sup> during MR image reconstruction. However, it involves an additional and heavy computational burden during image reconstruction, especially in the non-Cartesian setting. Depending on the encoding scheme, it would be necessary to consider the higher order terms<sup>34</sup> or not<sup>26,4</sup>. In our case, the compromise between the possible benefit and computational load of such a strategy could be further investigated. Furthermore, additional investigation will be required to prove that the SNR at the levels of the probes remains high enough to estimate higher-order terms accurately as well.

### 5.4 | Limitations and perspectives

In the literature, several Cartesian and non-Cartesian methods<sup>3,27,35,4</sup> seem to yield improved image quality compared to that reported in this work. However, it is actually challenging to perform relevant and fair comparisons as different experimental setups are used in the competing studies<sup>3,27,35,4</sup> in terms of brain coverage, number of shots, 2D vs. 3D acquisitions, etc. In a former work<sup>36</sup>, we performed an extensive comparison in fMRI between 3D-EPI and 3D-SPARKLING for similar acquisition parameters (same spatiotemporal resolution  $-1\text{mm}^3$  and  $2.4\text{s-TR}$  – and  $\text{FOV}=192\times 192\times 128\text{mm}^3$ , same  $\text{TE/TR}_{shot}=20/50\text{ms}$  and similar  $T_{obs}$ ). In this previous study, the dynamic field fluctuations were not corrected in 3D-SPARKLING fMRI volumes, and we found a poorer image quality as compared to 3D-EPI. This is likely due to the fact that 3D-SPARKLING is more sensitive to the acquisition's imperfections than 3D-EPI. Indeed, in contrast to 3D-EPI where the same readout is repeated along the k-space planes, the random nature of 3D-SPARKLING trajectories make imperfections due to  $B_0$  or motion accumulated along

different orientations (cf Fig. S4 in Supporting Information, section S6). This effect directly translates into more complex artifacts in the image domain. However, we demonstrated in<sup>36</sup> that despite a poorer image quality the sensitivity/specificity statistical trade-off for the detection of evoked brain activity based on the BOLD contrast is, on average over six volunteers, similar for both techniques (3D-SPARKLING vs. 3D-EPI). With the addition of dynamic field perturbations correction, we believe that we further improve the image quality for 3D-SPARKLING.

As demonstrated by our findings on resting-state fMRI data collected for the FB and HC scenarios, the fact that head movements are not corrected hinders the efficiency of the correction performed for the most extreme cases. In contrast, in typical cases of involuntary moderate movement such as for V#2, the findings showcase undeniable benefits. In<sup>37</sup>, the authors present an experimental protocol for using the field camera for motion monitoring in anatomical imaging. Such a solution should work for fMRI as well. However, it is beyond the scope of this paper.

In this work, we resort to external measurements of the dynamic field fluctuations, overlooking the fact that each shot crosses the center of the k-space in 3D-SPARKLING. In fact, such a feature enables self-navigation and the estimation of an average zeroth-order dynamic term  $\Delta B_{0,dyn}$  per shot, similarly to the solution proposed for TURBINE in<sup>35</sup>. Nevertheless, such estimates may not be as accurate as the field camera measurements. In any case, it would be interesting to implement such a strategy and to compare its estimates with external measurements.

Furthermore, we consider that the static and dynamic field terms evolve independently from each other since such an approximation is easy to implement and remains accurate enough. Nevertheless, it does not reflect the MR physics of the experiment faithfully. In fact, a truthful model would consider static and dynamic  $B_0$  imperfections as evolving jointly: A  $\Delta B_0$  map would be estimated for each volume in this case analogously to what is proposed in<sup>38,39</sup>. As demonstrated in<sup>29</sup>, it would actually be possible to estimate a volume-wise  $\Delta B_0$  map from 3D-SPARKLING data. Such a solution would also avoid any possible inconsistencies between an external  $\Delta B_0$  map and the fMRI volumes in case of patient movement for instance. However, the pipeline in<sup>29</sup> was conceptualized for anatomical scans and would need further tuning for fMRI data since, to date, it does not produce good estimates of  $\Delta B_0$  maps from highly accelerated fMRI data.

## 6 | CONCLUSIONS

In this work, we demonstrated a systematic and significant benefit in image quality, tSNR, and in terms of effect size and accuracy of the brain activity detection and localization when

static and dynamic  $B_0$  field imperfections are corrected retrospectively during MR image reconstruction: In fact, using retinotopic fMRI data, we have noted an increase in sensitivity, notably at a stricter false positive rate control level, and more accurate BOLD phase maps. This study was conducted using a field camera in an alternative setting challenging its  $TR_{probe}$  constraint to monitor up-to-the-first-order dynamic  $B_0$  field fluctuations.

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**TABLE 1** Specifications of the different sequences used in each participant: 3D-SPARKLING was used to acquire the functional data at  $1\text{mm}^3$ ,  $2.4\text{s-TR}_v$  resolution and with a readout duration of 26.88ms. 120 volumes were collected for each retinotopic run (either clockwise or counter-clockwise), whereas one resting-state run consisted of 125 volumes. The GRE sequence used had three echoes: Raw data of the full dataset (3 echoes) and raw data from only the first echo were used to estimate the  $\Delta B_0$  and sensitivity maps, respectively. The estimated maps were interpolated to match the 3D FOV and resolution of the fMRI scans. The XFL sequence was used for  $B_1^+$  mapping and calibration. The MP2RAGE sequence was used to acquire an anatomical  $T_1$  w scan.

	TE(ms)	$TR_{shot}$ (ms)	Volumetric TR(s)	Spatial resolution	FOV(mm)	Number of repetitions
3D-SPARKLING	20	50	2.4	1mm iso	(192,192,128)	120 125
GRE 3D	1.8, 3.06, 5.10	20	58	3mm iso	(192,192,132)	1
XFL	3.06	2000	44	4mm iso	(256,256,88)	1
MP2RAGE	3.29	5000	347	1mm iso	(192,192,128)	1

**FIGURE 1** Example of the NMR signal decay from one probe of the field camera over 96 FIDs with/out an external spoiling gradient for a  $TR_{shot} = TR_{probe} = 50\text{ms}$ : Stimulated echoes prevent steady-state in the absence of an external spoiling gradient whereas a  $470\text{mT}\cdot\text{ms/m}$  spoiling gradient ensures a steady-state at the level of the probes.

**FIGURE 2** Comparison of the mean image of resting-state fMRI scans collected from V#1 reconstructed using strategies (a) to (f). From left to right, the top row (resp., bottom row) depicts the mean images yielded by the images reconstructed using strategies (a) to (c) (resp., (d) to (f)). The overall contrast is enhanced, the lost signal is better recovered, and anatomical details are better reconstructed as illustrated by the blue, orange, and green arrows, respectively.

**FIGURE 3** Comparison of the (A) mean images and (B) tSNR maps yielded by the resting-state fMRI scans sequence collected in the three volunteers and using the different physiological movement scenarios reconstructed using strategies (a) and (f). The improved image quality when strategy (f) is used is reproducible across volunteers.

**TABLE 2** Gain in % of median tSNR in corrected data (strategies (b) to (f)) relative to the native tSNR (uncorrected data, i.e. strategy (a)) computed over the brain mask. The highest figures (in bold) are retrieved when strategy (f) is used.

Terms corrected	Volunteer	Gain in % of median tSNR					
		#1 NB	#2 NB	#3 NB	Average NB	#3 FB	#3 HC
(b) $\Delta B_{0,dyn}$		+20	+11	+22	+18	+24	+24
(c) $\Delta B_{0,dyn}$ & $\delta\mathbf{k}$		+26	+13	+23	+21	+27	+26
(d) $\Delta B_{0,stat}$		+5	+6	+4	+5	+5	+5
(e) $\Delta B_{0,stat}$ & $\Delta B_{0,dyn}$		+28	+18	<b>+29</b>	+25	+32	+31
(f) $\Delta B_{0,stat}$ & $\Delta B_{0,dyn}$ & $\delta\mathbf{k}$		<b>+34</b>	<b>+20</b>	<b>+29</b>	<b>+28</b>	<b>+34</b>	<b>+33</b>

**FIGURE 4** Comparison of the activation maps at the subject level for V#1-V#3 yielded by the retinotopic data reconstructed without and with static and up-to-the-first order field terms correction. The activation maps on the left (resp., right) panel were produced by thresholding the z-score maps corresponding to the global effects of interests using a p-value of 0.001 without multiple comparisons correction (resp., 0.05 with FDR control).

**FIGURE 5** Comparison of the BOLD phase maps over an ROI defined using the thresholding alternative (i) yielded by retinotopic fMRI scans reconstructed without and with static and up-to-the-first order dynamic field terms correction.

**TABLE 3** Number of activated voxels and the maximum z-score values extracted from task-based fMRI volumes with/out correcting  $\Delta B_0$  imperfections. The activated voxels are defined using two distinct statistical significance levels: a p-value of 0.001 without multiple comparisons correction and a p-value of 0.05 with FDR control. The highest figures (in bold) are obtained when strategy (f) -Full Correction- is used. V#2 reveals the lowest statistical significance.

Volunteer	#Activated voxels $p < 0.001$ uncorrected for multiple comparisons		#Activated voxels $p < 0.05$ with FDR correction		Maximum z-score value	
	No correction	Full Correction	No correction	Full Correction	No correction	Full Correction
	#1	6456	<b>9506</b>	3253	<b>7722</b>	8.02
#2	4367	<b>7405</b>	1059	<b>2204</b>	6.75	<b>7.59</b>
#3	8529	<b>10823</b>	2503	<b>7745</b>	10.83	<b>12.08</b>
Average	6450.67	<b>9244.67</b>	2271.67	<b>5890.34</b>	8.54	<b>9.87</b>

**FIGURE 6** (A) BOLD phase maps yielded by the data collected from V#1 and reconstructed without/with  $B_0$  field imperfections correction and their projections on the cortical surface. (B) Projected BOLD phase maps yielded by the data collected from V#1 and yielded by the smoothed (using a Gaussian kernel with FWHM=1.1mm and FWHM=1.5mm)  $B_0$ -uncorrected data and the raw  $B_0$ -corrected data.

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