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Dynamic per slice shimming for simultaneous brain and spinal cord fMRI

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Abstract

Purpose: Simultaneous brain and spinal cord functional MRI is emerging as a new tool to study the central nervous system but is challenging. Poor B_0 homogeneity and small size of the spinal cord are principal obstacles to this nascent technology. Here we extend a dynamic shimming approach, first posed by Finsterbusch, by shimming per slice for both the brain and spinal cord.

Methods: We shim dynamically by a simple and fast optimization of linear field gradients and frequency offset separately for each slice in order to minimize off resonance for both the brain and spinal cord. Simultaneous acquisition of brain and spinal cord fMRI is achieved with high spatial resolution in the spinal cord by means of an echo-planar RF pulse for reduced FOV. Brain slice acquisition is full FOV.

Results: T2*-weighted images of brain and spinal cord are acquired with high clarity and minimal observable image artifacts. Fist-clenching fMRI experiments reveal task-consistent activation in motor cortices, cerebellum, and C6-T1 spinal segments.

Conclusions: High quality functional results are obtained for a sensory-motor task. Consistent activation in both the brain and spinal cord is observed at individual levels, not only at group level. Because reduced FOV excitation is applicable to any spinal cord section, future continuation of these methods holds great potential.

Keywords

dynamic shimming; fMRI; reduced FOV; simultaneous brain and spinal cord fMRI; spinal cord

1 | INTRODUCTION

Human spinal cord transmits bidirectional neural information between brain and body; thus, it performs a critical role in proper sensory, motor, and autonomic functioning. Many studies describe separate fMRI acquisition of brain and spinal cord. Dobek & Beynon et al.¹ studied how music mitigates pain by comparing fMRI activation in participants subject to noxious

thermal stimuli. Khan and Stroman² characterized responses in brain and spinal cord by correlating fMRI activation under noxious heat stimuli to subjective pain ratings. In both studies, brain and spinal cord fMRI data were collected separately. Neither of these works captured temporal interaction between spinal cord, brainstem, and brain.

In this paper, we describe a fast and simple method to perform simultaneous acquisition of brain and spinal cord fMRI images. Simultaneous functional imaging of brain and spinal cord can provide valuable insight into interactions and processing pathways between these organs in normal and abnormal states of spinal cord injury,³ chronic pain,^{4,5} and motor disease.⁶ BOLD fMRI, the most common functional imaging method in MRI, has been extensively adopted for brain study.^{7,8} But, due to seemingly insurmountable challenges, BOLD fMRI has seen little application to spinal cord.^{4,5, 9–11} Consequently, few fMRI studies have been performed on brain and spinal cord simultaneously.

In 2010, Cohen-Adad and Gauthier et al.¹² published the first simultaneous brain and spinal cord fMRI study. Motivated to more fully understand hypercapnia, their slices were centered within each vertebral body so as to minimize B_0 inhomogeneity. Later, in 2013, Finsterbusch and Sprenger et al.¹³ published a shimming technique that adjusts linear x , y , & z shims and frequency offset f -shim *per block* (brain block, spinal cord block). They corrected through-slice off-resonance variation, at k -space origin in the spinal cord, by a slice-specific z -shim gradient moment pulse.¹⁴ Since then, Sprenger and Finsterbusch et al. in 2015,¹⁵ Vahdat and Lungu et al. in 2015,¹⁶ and Tinnermann and Geuter et al. in 2017¹⁷ have published applications of simultaneous brain and spinal cord fMRI.

Finsterbusch and Sprenger's result¹³ inspired us to enhance B_0 correction by adjusting linear gradients *per slice* to shim both the brain and spinal cord. By so doing, the entirety of k -space is corrected by linear x , y , & z shims and frequency offset f -shim that are unique to each slice.

1.1 | Challenges

Principal obstacles to simultaneous brain and spinal cord fMRI are:

- High B_0 inhomogeneity in spine is caused by differences in magnetic susceptibility between the spinal cord and surrounding intervertebral discs. Demagnetization, resulting from geometric differences between upper torso, smaller diameter neck, and larger diameter head, worsens inhomogeneity. B_0 field is more homogeneous in the brain, so a combined brain and spinal cord acquisition cannot be statically shimmed as is typically done when brain is scanned alone.
- Due to the long echo time needed in fMRI to maximize BOLD contrast and the long readout needed to image rapidly with high resolution, B_0 inhomogeneity can lead to signal loss and distortion artifacts. In spinal cord, these artifacts are exacerbated by its small cross-sectional size (≈ 15 mm across at widest¹⁸).

- Spinal cord motion, caused by cardiac and respiratory cycles, is substantially more pronounced than in the brain, producing unwanted signal fluctuation and motion registration problems.

Methods have been developed to mitigate these challenges,^{19,20} of which, B_0 inhomogeneity is the foremost challenge. Static shimming is typically employed for improving homogeneity, but the large range of frequency offsets between the brain and spinal cord requires a dynamic approach.

Our method implements a dynamic shim *per slice* to improve field homogeneity, and uses a 2D echo-planar RF pulse²¹ to excite only the spinal cord and its surrounding structures. This approach allows alias-free reduced field-of-view (**FOV**) imaging.²² Conventional spatial resolution is implemented for brain but a higher resolution for spinal cord. We assess performance of this fMRI method using a sensory-motor fist-clenching task.

1.2 | Previous work: shimming

Conventionally, linear and second-order shim gradients are optimized for an entire imaged volume.^{23,24} This works well for low-order B_0 field variations over small sections (both axially and sagittally) of spinal cord and much of the brain except in proximity to air/tissue interface: the frontal sinus and auditory canal. However, static high-order shimming is inadequate for simultaneous brain and spinal cord fMRI¹³ and cannot address localized field variations such as those caused by the interfaces between spinal cord, vertebral bodies, and cartilaginous intervertebral discs.²⁰ More advanced shim array hardware may be beneficial but is not widely available.²⁵

1.2.1 | Dynamic per block—Finsterbusch and Sprenger et al. introduced optimal shimming *per block* (brain and spinal cord) and slice-specific z -shim gradient moment pulse in the spinal cord. All slices within each block use a fixed set of x , y , z , and f shims. Slice-specific z -shim gradient moment pulses are incorporated for the spinal cord slices to correct through-slice off-resonance variation. The best z -shim moment value is obtained by stepping through a range and then choosing the value that yields the highest spinal cord signal intensity. This repetitive approach increases experiment length. Acquiring multiple images with different shim moments is inefficient and compromises temporal or spatial resolution. Further, one z -shim moment value cannot correct for off-resonance that varies across the field of view.

Because signal nearly everywhere in k -space (except the origin) was not rephased, in Finsterbusch and Sprenger, signal loss and blurring occurred. Since spinal cord is only about 1.5 cm in size, higher spatial resolution is required. Image blurring, consequent to lack of rephasing, competes with high resolution.

1.2.2 | Dynamic per slice—Another approach to shimming is more dynamic; *i.e.*, update linear x , y , z field gradients and center-frequency offset f for each and every slice (*per slice*). This approach was previously demonstrated on brain tissue by Blamire and Rothman et al. in 1996²⁶ and Morrell and Spielman in 1997.²⁷ In the dynamic case, shims are updated in real time as different slices are imaged.

2 | METHODS

We focus on simultaneous imaging of brain, brainstem, and cervical spinal cord including the first thoracic spinal cord segment. To our knowledge, previous works employed field maps only in the x, y dimension. We augment Finsterbusch and Sprenger's work by acquiring one sagittal field map and multiple axial field maps, and by applying per slice shimming to optimize the linear and center-frequency offset shims dynamically for every slice. Sagittal field mapping adds only about three seconds to an experiment, so it is inexpensive to implement. An accurate linear z -shim cannot be calculated with field maps obtained only in the x, y dimension because resolution in the third dimension is then determined by slice spacing. High spatial-resolution field maps in both the x, y dimension (axial) and the z dimension (sagittal) are needed to obtain accurate off-resonance values.

2.1 | Dynamic shim calculation

Our scanner has five static second-order shims with field distributions given approximately by spherical harmonics $xy, yz, xz, x^2 - y^2$, and $z^2 - (x^2 + y^2)/2$. Since these shims have long settling-time due to eddy currents generated by their coupling to the main magnetic field, only one set of static second-order shims can be used for the entire volume (brain and spinal cord). Our scanner also has four dynamic shims: linear x, y, z field gradients and center-frequency offset f that we set per slice.

The dynamic shim calculation, as implemented here, minimizes off-resonance over an imaged volume by least squares to find the linear x, y , and z shims and frequency offset f -shim. This is a linear system that can be written $-o \approx Es(2)$ where o is a vector containing values of off-resonance from the axial field maps, and E is a spatial encoding matrix (1) that specifies dependence (at each voxel position of a generated field) on shim amplitudes in variable vector s . We do not introduce xz and yz terms into encoding matrix E because they are redundant within each axial slice: xz -shim is redundant with x -shim because location z is constant for each slice, yz -shim is similarly redundant with y -shim. Nor is a z term introduced into E because z -shim is calculated using the sagittal field map (5) in a second step of shim calculations. Therefore, vector s contains not only one set of $xy, x^2 - y^2$, and $z^2 - (x^2 + y^2)/2$ shim amplitudes but also contains a distinct set of x, y , and f -shim amplitudes for each slice. (1)

Dynamic per slice shimming computes optimal values of x, y, z , and f -shims in vector s . In the first step of calculations, only axial field maps are included. All shims are computed except the linear z -shim s_z . The f -shim s_f is also computed here, but is later adjusted in a second step where the sagittal field map comes into play.

2.2 | Second-order and linear x, y shims calculation using axial field map

This first step incorporates a total of N (number of slices) 2D field maps covering the brain and spinal cord. Each field map (*slice*) has the general form of a 64×64 matrix of off-resonance values o . Within each field map is a shaped mask of the anatomy whose vectorized length is $M_i, i = 1 \dots N$ and generally different for each mask; i.e., each field map has M_i voxels representing off-resonance within its mask (Figure 3B, $N = 30$ throughout).

The matrix definition below assumes axially oriented slices. Each slice of an imaged volume is stacked in a vector o which represents measured off-resonance values in Hertz. Vectors x , y , z are spatial coordinates of N field maps in centimeters: $[x_{ij}, i = 1 \dots N, j = 1 \dots M_i], i = 1 \dots N, j = 1 \dots M_i, [y_{ij}, i = 1 \dots N, j = 1 \dots M_i], [z_i, i = 1 \dots N]$. For each slice i , unitless f_i is set to 1 in this first step:

In matrix form, E is a thin matrix (more rows than columns):

$$-o \approx Es \quad (2)$$

Vector o is negated because it is a correction to cancel off-resonance. Shim amplitudes, represented by vector s , are not constrained because they rarely exceed the maximum allowed current. In fact, they are fairly small by comparison. Approximation $\approx$ is indicated because vector o is not necessarily in the range of thin matrix E . A best fit, an optimal solution s to minimize $\|o + Es\|_2$, is found by solution to the normal equations²⁸, [§E.0.1]:

$$-E^T o = E^T E s \quad (3)$$

For matrix E of any rank, vector $E^T o$ is always in the range of $E^T E$.

$$\begin{bmatrix} o_{11} \\ \vdots \\ o_{1M_1} \\ o_{21} \\ \vdots \\ o_{2M_2} \\ \vdots \\ o_{N1} \\ \vdots \\ o_{NM_N} \end{bmatrix} \approx \begin{bmatrix} x_{11}y_{11} & x_{11}^2 - y_{11}^2 & z_1^2 - (x_{11}^2 + y_{11}^2)/2 & x_{11} & y_{11} & \Delta f_1 & 0 & 0 & 0 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{1M_1}y_{1M_1} & x_{1M_1}^2 - y_{1M_1}^2 & z_1^2 - (x_{1M_1}^2 + y_{1M_1}^2)/2 & x_{1M_1} & y_{1M_1} & \Delta f_1 & 0 & 0 & 0 & \cdots & 0 & 0 & 0 \\ x_{21}y_{21} & x_{21}^2 - y_{21}^2 & z_2^2 - (x_{21}^2 + y_{21}^2)/2 & 0 & 0 & 0 & x_{21} & y_{21} & \Delta f_2 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{2M_2}y_{2M_2} & x_{2M_2}^2 - y_{2M_2}^2 & z_2^2 - (x_{2M_2}^2 + y_{2M_2}^2)/2 & 0 & 0 & 0 & x_{2M_2} & y_{2M_2} & \Delta f_2 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{N1}y_{N1} & x_{N1}^2 - y_{N1}^2 & z_N^2 - (x_{N1}^2 + y_{N1}^2)/2 & 0 & 0 & 0 & 0 & 0 & 0 & \cdots & x_{N1} & y_{N1} & \Delta f_N \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_{NM_N}y_{NM_N} & x_{NM_N}^2 - y_{NM_N}^2 & z_N^2 - (x_{NM_N}^2 + y_{NM_N}^2)/2 & 0 & 0 & 0 & 0 & 0 & 0 & \cdots & x_{NM_N} & y_{NM_N} & \Delta f_N \end{bmatrix} \begin{bmatrix} s_{xy} \\ s_{x^2-y^2} \\ s_{z^2-(x^2+y^2)/2} \\ s_{x1} \\ s_{y1} \\ s_{\Delta f_1} \\ s_{\Delta f_2} \\ s_{y2} \\ s_{\Delta f_2} \\ \vdots \\ \vdots \\ \vdots \\ s_{xN} \\ s_{yN} \\ s_{\Delta f_N} \end{bmatrix} \quad (1)$$

2.3 | z and f shims calculation using sagittal field map

The second step computes linear z -shim and adjusts offset f -shim computed in the first step. The z component, of B_0 field gradient along spinal cord, suffers severe off-resonance unless compensated. To account for through-slice off-resonance variation, which least squares optimization (1) does not, we fit a quadratic to all voxels within ± 4 cm of each slice in the adjusted sagittal field map after the first step of shim calculations:

$$\Delta f(z) \approx p_1 z^2 + p_2 z + p_3 \quad (4)$$

To calculate z -shim, we evaluate the quadratic's first derivative at the sagittal slice location z_0 ; its negative being the required z -shim value. (Figure 1)

$$s_z = -\frac{d}{dz}\Delta f(z)|_{z_0} \quad (5)$$

This is the z -shim correcting for the z -gradient present at that slice location. To adjust the center-frequency offset shim s_f we need to account for off-resonance as measured by the sagittal field map as well as off-resonance generated by other shim terms: The center-frequency offset shim, from the sagittal field map, is simply estimated as the quadratic evaluated at the sagittal slice location (Figure 2);

$$s_{\Delta f_{\text{sag}}} = \Delta f(z_0) \quad (6)$$

Center-frequency offset generated by the linear z -shim (5) is the derivative (evaluated at that sagittal slice location) multiplied by the sagittal slice location. The shim required $s_{\Delta f_z}$ (8) negates that. Center-frequency offset, generated by the remaining shims, corrects the shim value s_f because f was assigned the value 1 when previously calculated in (1):

$$s_{\Delta f} \leftarrow s_{\Delta f} - s_{\Delta f_{\text{sag}}} + s_{\Delta f_z} \quad (7)$$

where

$$s_{\Delta f_z} = z_0 \frac{d}{dz}\Delta f(z)|_{z_0} \quad (8)$$

Figure 3C shows $\phi + Es$ calculated using optimal shims s . Figure 3D shows measured field maps after shimming.

Figure 4 illustrates calculations of average in-plane off-resonance of field maps corresponding to Figure 3: using auto-shim (Figure 3B), compensated by calculated shims (Figure 3C), and from measurement after shimming (Figure 3D). Solid lines in Figure 4, representing these averages, show that through-slice off-resonance variation has been greatly reduced by the proposed shim optimization method. Figure 4 also compares in-plane field homogeneity, from Figure 3B-D, by calculating the standard deviation of each field map. Shaded bands in Figure 4 illustrate these standard deviations per slice. Only spinal cord enters the mean and standard deviation calculations; otherwise, fat, vertebrae, bone, and

other irrelevant spinal tissue would bias the statistics. The smaller the standard deviation, the more homogeneous a field map. Overall, more than a 50% improvement in homogeneity is attained; ascertained by measurement after shimming.

2.4 | B_0 field maps

All scans were performed on a General Electric Discovery 750 3T scanner using a neurovascular array 8-channel head/neck coil. Axial and sagittal B_0 field maps of brain and spinal cord were collected using a double-echo GRASS sequence with an echo-shift of $TE = 1$ ms corresponding to a field bandwidth $= \pm 0.5$ kHz. Due to a finite number of slices in the axial field map along the z direction, and due to breathing-related variation between slice acquisition, using only axial field maps to compute linear z shims would result in inaccurate z -shim values. A single sagittal field map (Figure 2) through the spinal cord, acquired during approximately 3 s breath holding, is not susceptible to breathing-related B_0 variations and provides for higher resolution along the z direction.

Axial maps were acquired with the following parameters: number of slices = 30 (18 in brain, 12 in spinal cord centered around the C5/C6 vertebrae, Figure 2A), FOV = 22 cm, matrix size = 128×128 . The sagittal field map was acquired with FOV = 30 cm and matrix size = 256×64 (frequency-encode, superior/inferior) $\times$ (phase-encode, anterior/posterior). Field maps are masked to retain only the tissue of interest: i.e., the brain and spinal cord. In axial slices, the region around the spinal cord is retained in the mask in order to accurately estimate the dynamic shims (Figure 3C).

2.5 | Reduced field of view

Saturation bands were utilized by Finsterbusch and Sprenger to reduce the spinal cord FOV and prevent aliasing.¹³ If a spinal cord region of interest (**ROI**) is thoracic or a more inferior section of the cervical spinal cord, then placement of saturation bands may null desired signal in the thoracic spinal cord or brain. By contrast, we implement an echo-planar RF pulse to achieve reduced FOV imaging. This approach avoids both aliasing and signal nulling in the ROI.

2.6 | fMRI Acquisition

Nine healthy human subjects were scanned (with IRB approval and informed consent). T2*-weighted images were collected using an EPI sequence with GRAPPA²⁹ acceleration factor 2, eight fully sampled lines at k -space center, and the following readout parameters: flip-angle θ equals Ernst angle 80° (gray matter $T_1 = 1350$ ms), $TE = 30$ ms, $TR = 2.4$ s, matrix size = 64×64 , readout BW = ± 125 kHz, slice thickness = 4 mm, and slice spacing = 2 mm. Physiological data from a respiratory belt and a pulse oximeter were collected. Although GRAPPA kernels are conventionally estimated by a fully sampled k -space center, we instead used an extra scan to calculate the kernels for interpolation of missing k -space samples; which provides for better reconstruction. The eight fully sampled lines in every T2*-weighted image serve only to increase SNR.

For fMRI acquisition, a 7-minute block-design task (comprising 15 s blocks) alternates between rest and bilateral fist-clenching. Subjects were instructed to clench their fists at

approximately 80% of their maximum strength. This experiment was repeated four times for each subject. This task was used because it gives reliable activation in spinal cord fMRI. Although sustained tasks have yielded good results in the spinal cord,¹⁰ they are reported to yield less activation in the brain.³⁰

2.6.1 | RF excitation sequences—Within a scan of one volume (axial slices for combined brain and spinal cord), there is one pulse sequence applied to the brain but a different sequence for the spinal cord. The spinal cord sequence uses an echo-planar RF pulse providing reduced FOV (8 cm), while the brain (FOV = 22 cm) uses a Hamming-weighted sinc RF pulse.

The echo-planar pulse is selective along the anterior/ posterior (phase-encode) and slice directions. The pulse time-bandwidth of slice excitation is chosen to reduce its sensitivity to off-resonance along the phase-encode direction. Low time-bandwidth increases the likelihood that the spinal cord is excited and confined to the reduced FOV. Figure 5 illustrates the pulse sequence diagrams for the brain and spinal cord.

2.7 | fMRI data processing and analysis

Preprocessing steps included slice-timing correction and cardiac and respiratory noise correction by RETROICOR.³¹ Further preprocessing steps and analyses differed for the brain and spinal cord:

2.7.1 | Brain data—For each subject, the brain image data were analyzed using the **FSL** toolbox.^{32,33} Preprocessing included standard motion correction,³⁴ smoothing by 4 mm-FWHM isotropic Gaussian kernel, highpass filtering via local fit of linear trend (window size = 128 s), and prewhitening.

Preprocessed data were analyzed with a general linear model (**GLM**) in which the task regressor was a boxcar function (corresponding to fist-clenching and rest blocks) convolved with a canonical hemodynamic response function (**HRF**). Nuisance regressors included derivatives of the task regressor (to account for HRF temporal delay and dispersion) and six motion parameters (translation and rotation, in three dimensions, from motion correction preprocessing).

The preceding GLM analysis generated subject-level activation maps. These were registered to MNI space and input into a mixed-effects analysis to compute a group activation map.
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2.7.2 | Spinal cord data—Although we instructed subjects not to change breathing patterns between task and rest, some changes in breathing, heart rate, or involuntary muscle tension may be inevitable due to nature of the task. Because of the nonrigid tissue motion exterior to spinal cord, and the fact that motion registration is performed only on the spinal cord, task-correlated motion artifacts in surrounding tissue are expected.

For each subject, the spinal cord images were motion-corrected in three stages. Each stage of motion correction applies its own stage-dependent vertebral mask^{10,38,39}:

1. The spinal cord time-series images were aligned to the first volume using three-dimensional registration. (A spinal cord mask excludes structures of no interest.)
2. The process in stage 1 was then repeated, but the volumes were aligned to the average volume (over time) from stage 1.
3. Then the time-series images output from stage 2 were aligned to the average image from stage 2 independently for each slice using a two-dimensional registration process.

After motion correction, each subject's spinal cord data were smoothed in-plane with a 2 mm-FWHM Gaussian kernel and smoothed through-plane with a 6 mm kernel. Just as we did for the brain, the spinal cord data were highpass filtered via local fit of linear trend (window size = 128 s) and then prewhitened.

GLM analysis was performed using the same task regressor and task derivatives as for brain data, but the six motion regressors generated from stage 2 of the motion correction procedure were used for the spinal cord. We also included a nuisance regressor that accounted for the mean cerebrospinal fluid signal,⁴⁰ and additional nuisance regressors for outliers (defined by computing a DVARS time series as the RMS variation [*sic*] in successive time frames over the entirety of imaged spinal cord). The outlier threshold was set as the 75th percentile of DVARS range + 1.5 times interquartile DVARS range. Outliers were identified where the DVARS time-series exceeds threshold.⁴¹

GLM analysis generated an activation map for each subject. For the group analysis, the subject-level spinal cord activation maps were straightened and then registered to the MNI-Poly-AMU spinal cord template using the Spinal Cord Toolbox.⁴² Each subject map was first aligned to a high-resolution T2 image, and then to the standard spinal cord template.^{43–45} As for brain data, output from the preceding subject-level spinal cord GLM analyses was input to the same mixed-effects analysis to obtain a group activation map.

3 | RESULTS

Figure 3 demonstrates the effect that shimming has on the field maps. Without the dynamic shim, generally speaking, the B_0 field shows greater variation in the sagittal direction than within an axial slice. In particular, a large and nonlinear gradient exists along the spinal cord (Figure 2B). These variations are largely corrected by dynamic shimming (Figure 3B-D). Sagittal and axial field maps agree where they intersect, ideally, and off-resonance goes to 0 Hz as shimming proceeds. In some slices, a small amount of off-resonance may remain if the discrepancy between axial and sagittal field maps exists where they coincide. Residual field variation also remains in the regions having large localized nonlinear gradients (e.g., frontal sinus, auditory canal, and spinal cord). Off-resonance in those particular regions cannot be adequately shimmed with linear gradients.

Figure 6 displays the T2*-weighted images and axial B_0 maps obtained by the various shimming methods. T2*-weighted images in Figure 6A show distortion caused by field inhomogeneity and inadequate shimming. Field maps collected by GRASS sequence in Figure 6B are immune to image distortion. With conventional shimming, the brain images

show distortion and blurring in Figure 6 columns 1 & 2 primarily along the anterior/posterior (phase-encode) direction under both the static auto-shim method and static second-order shim method. Under conventional shimming, spinal cord images are dominated by noise. The brain images are noise dominated in Figure 6 column 3, but the spinal cord images are best using the static second through zero-order shim. With dynamic per slice shim (Figure 6 col.4), both the brain and spinal cord images are of superior quality.

Figure 7 shows brain slices while Figure 8 shows spinal cord slices, both acquired by 2DFT via GRASS acquisition and by simultaneous T2*-weighted EPI acquisition with dynamic per slice shimming. Unlike EPI, GRASS is immune to off-resonance in the phase-encoding direction and to image distortion. The great resemblance between GRASS and T2*, in both brain and spinal cord regions, attests to the utility of dynamic per slice shimming.

Figure 9 illustrates functional activation maps, from the fist-clenching task, with bilateral activation in the motor cortices, cerebellum, and the C6 through T1 spinal cord segments. Group level analysis reveals robust activation in those regions. In order to highlight the robustness and reproducibility of the proposed method, no spatial mask was applied at subject level to remove activation from outside the spinal cord. We observed activation in tissue exterior to spinal cord; most likely, a result of physiological distress associated with the task. Overall, our results demonstrate that the proposed method indeed allows simultaneous fMRI of the brain and spinal cord in the expected regions.^{46,47}

4 | DISCUSSION

We have developed and implemented an optimization method for simultaneous brain and spinal cord fMRI that combines a reduced FOV imaging method with dynamic per slice shimming. An echo planar RF excitation pulse enables reduced FOV for imaging spinal cord without aliasing, while per slice shimming reduces B_0 field inhomogeneity. Spinal cord slices are acquired with higher resolution than that of the brain to resolve their smaller anatomic features.

Input field-map mask selection plays a critical role in robustness of the dynamic per slice shim calculation. Masking is required to remove nontissue and low-SNR voxels:

4.1 | Brain mask selection

Brain regions having large local field gradients (e.g., those near frontal sinus and auditory canal as well as skull and subcutaneous fat) are removed because those regions cannot be shimmed adequately by available hardware.

4.2 | Spine mask selection

Noise in low-signal regions, like that found in vertebral discs surrounding the spinal cord, can result in nonsmooth field maps. Spinal cord is too small to estimate the linear x and y shims accurately. Although we expect the x -shim to be small due to left/right symmetry, a small mask may erroneously produce a significant x -shim that would adversely affect quality of both the excitation and readout. To estimate the required smooth fields more accurately, we must also include in the mask a significant amount of tissue surrounding the

spinal cord. Thus it is necessary to mask out voxels having low signal intensity or high local field variance anywhere in the surrounding tissue.

The situation is similar with regard to the linear y -shim; except that anterior/posterior symmetry is, comparatively, much less. Still, a significant amount of tissue surrounding the spinal cord must be included in the masking for proper calculation of the y -shim.

4.3 | Dynamic shim parameter estimation

The crucial parameter among the dynamic shim parameters is the z -shim because of the large off-resonance variation along spinal cord (Figure 2B). Hence the acquisition of accurate off-resonance values in the spinal cord, by means of sagittal field mapping, is particularly important. f -shim (*frequency offset shim*) is important for spinal cord since off-resonance is large there. Were the center-frequency not corrected by shimming, then the region excited (by the echo-planar pulse) would shift along the anterior/posterior direction; thus, it could miss the spinal cord. Shims s_x and s_y are less critical to the spinal cord because their values are typically one order of magnitude smaller than the z -shim.

4.4 | Need for sagittal field map

In order to calculate accurate linear z and offset f -shim values, a high resolution sagittal field map along the spinal cord must be acquired. Although dynamic shims might be calculated using only the axial field maps, in principle, respiratory-induced field variation between slices^{48,49} makes reliable calculation of the z and f -shims impractical. A sagittal field map provides previously unavailable voxels, along the z direction in between axial field maps, thus providing a more reliable method for calculating these shims.

4.5 | Sagittal field map sensitivity

In the worst case, there can be significant variation between a sagittal field map that is acquired during a fully inhaled state when compared with a sagittal field map acquired during a fully exhaled state (Figure 10). Yet optimal linear z -shim shows little variation when calculated from these same extreme sagittal maps; i.e., less than 3 Hz difference across a 4 mm slice thickness between breathing states.

In these extreme cases, on the other hand, optimal offset f -shim can vary by as much as 70 Hz in the spinal cord; consistent with previous findings.⁴⁸ Consequent signal loss, due to through-plane off-resonance effects, is negligible even in the worst case.

4.6 | Echo-planar RF pulse sensitivity

B_0 variation has little noticeable effect on the echo-planar RF excitation since its 215 Hz pulse bandwidth along the phase-encode (anterior/posterior) direction is much larger than the ≈ 70 Hz field variation. Indeed, artifacts are not observed in the reconstructed images due to these extreme field variations. The echo-planar pulse is selective along the anterior/posterior (phase-encode) and slice directions. As long as aliasing is confined to regions of no interest exterior to the spinal cord, some aliasing can be tolerated.

5 | CONCLUSION

Simultaneous fMRI of the brain and spinal cord adds vital understanding of intricate ascending and descending pathways and processes within the central nervous system, and it permits exploration of functional connectivity between these organs. This goal was elusive due to the diminutive girth of the spinal cord and poor local B_0 field homogeneity.

Here we developed and implemented an alternative method, incorporating efficient dynamic per slice shimming and reduced FOV imaging, to perform simultaneous fMRI of the brain and spinal cord. As proof of concept we demonstrated causal existence of activation in expected regions of brain and spinal cord^{46,47} during a fist-clenching task.

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FIGURE 1.

A, Masked adjusted sagittal field map after the first-step shim calculations (1). Dashed line at $z = 9$ cm indicates the sagittal slice location z_0 . Red dashed lines indicate ± 4 cm bounds about z_0 . All lines (except red) indicate the slice locations. B, Blue dots represent off-resonance values within the masked spinal cord and within bounds. Red line fits those off-resonance values quadratically. Black line is tangent to the quadratic at z_0 . This quadratic fit is repeated for each and every slice location z_0 over brain and spinal cord

FIGURE 2.

A, Sagittal gradient-echo image with red lines indicating the slice position; spinal slices are centered around the C5/C6 vertebrae. B, Masked sagittal field map using auto-shim. Masks remove tissue of no interest. Masked sagittal field map serves as input to dynamic shim calculation

FIGURE 3.

A, Axial gradient-echo images of brain and spinal cord corresponding to slice locations in Figure 2A. B, Masked axial field maps ϕ using auto-shim. C, Shimmed axial field maps $\phi + E_s$ via (1) (5) (7). D, Field maps measured after per slice shimming, for verification only, are in close agreement with calculated maps in panel C. Bottom row (a*) (b*) (c*) (d*) shows zoomed images of slices indicated by red squares from panels A–D

FIGURE 4.

In-plane mean and standard deviation of off-resonance vs slice for: B, axial field maps ϕ using auto-shim (blue), C, calculated shimmed axial field maps $\phi + E_s$ (red), D, measured axial field maps after proposed per slice shimming (green). Solid line segments (within B, C, D) correspond to mean off-resonance calculated from field maps in Figure 3B–D. Shaded bands B–D correspond to in-plane standard deviation of off-resonance. Average standard deviation over all slices: B, 29.6 Hz, C, 19.2 Hz, D, 12.9 Hz

FIGURE 5.

Pulse sequence diagrams for brain and spinal cord slices. Spinal cord slices used an echo-planar RF pulse: length $T = 18.6$ ms, time-bandwidth product in the frequency-encode direction $TB_{\text{freq}} = 2$, time-bandwidth product in the phase-encode direction $TB_{\text{phase}} = 4$, excitation width $D_{\text{phase}} = 6$ cm, and alias distance $R_{\text{phase}} = 40$ cm. For each slice there is a distinct set of linear x , y , & z shims and center-frequency offset f -shim determined dynamically. (1) The two sequences are combined within a single TR, first scanning entire brain and then entire spinal cord. TE = 30 ms throughout

FIGURE 6.

Comparison of the four shimming methods illustrated by: A, T2*-weighted images, B, corresponding measured field maps. Methods are: column 1: standard static linear and zero-order auto-shim, 2: static second through zero-order shim over both brain and spinal cord, 3: static second through zero-order shim on spinal cord only, 4: proposed dynamic per slice shim is the only method illustrated that incorporates field-map masking. Columns 1 & 2 exhibit image distortion with signal loss in the spinal cord. Column 3 shows nominal performance only in the spinal cord. Column 4 performs better overall. Spinal cord slice 24 in columns 1 & 2 and both brain slices in column 3 contain wrapped field estimates. Wrapping indicates out-of-range field map values, which means greater B_0 inhomogeneity. Dynamic per slice shim produces the most homogeneous B_0 field maps

FIGURE 7.

A, GRASS images of brain, B, corresponding T2*-weighted images acquired by dynamic per slice shimming. Simultaneously acquired T2* spinal cord images are shown in Figure 8B

FIGURE 8.

A, GRASS images of spinal cord, B, corresponding T2*-weighted images acquired by dynamic per slice shimming. Simultaneously acquired T2* brain images are shown in Figure 7B. There is great resemblance between these GRASS and T2* images, suggesting that dynamic shim is effective in both brain and spinal cord regions

FIGURE 9.

A, Brain and B, spinal cord fMRI activation maps from a fist-clenching task. For each subject and group activation map, axial and sagittal slices are shown. Level is indicated by blue lines; spinal cord segments C6 through T1 are illustrated. In brain slices, robust bilateral activation is observed in the motor areas and cerebellum ($p < 1e-6$). Spinal cord map threshold is $p < 0.02$ for subjects S1-S9. Group map threshold is $Z > 2.3$ with corrected cluster threshold $p < 0.01$. C, Activation time series, for subject S9, by averaging voxels in slice 25 (spinal cord) having $Z > 4.5$. High correlation with task is observed between measured and ideal time series

FIGURE 10.

Linear z -shim and offset f -shim calculated from sagittal field maps during (**blue**) a 3 s fully inhaled state and (**red**) a 3 s fully exhaled state. Four maps are collected for each state. A, Optimal z -shim does not vary greatly, between states, both in the brain and spinal cord. Maximum z -shim difference between states is insubstantial: 0.016 mT/m corresponding to 2.73 Hz difference across the 4 mm slice thickness. B, f -shim accounts for frequency offset generated by the z -shim. While z -shim is insensitive to breathing, maximum difference of f -shim between the two breathing states is 70 Hz