Published in final edited form as:

Magn Reson Med. 2019 May ; 81(5): 3314–3329. doi:10.1002/mrm.27613.

Motion-Robust Diffusion Compartment Imaging using Simultaneous Multi-Slice Acquisition

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Abstract

Purpose.—To achieve motion-robust diffusion compartment imaging (DCI) in near continuously moving subjects based on simultaneous multi-slice, diffusion-weighted brain MRI.

Methods.—Simultaneous multi-slice (SMS) acquisition enables fast and dense sampling of k - and q -space. We propose to achieve motion-robust DCI via slice-level motion correction by exploiting the rigid coupling between simultaneously acquired slices. This coupling provides 3-D coverage of the anatomy that substantially constraints the slice-to-volume alignment problem. This is incorporated into an explicit model of motion dynamics that handles continuous and large subject motion in robust DCI reconstruction.

Results.—We applied the proposed technique, called Motion Tracking based on Simultaneous Multislice Registration (MT-SMR) to multi b-value SMS diffusion-weighted brain MRI of healthy volunteers and motion-corrupted scans of 20 pediatric subjects. Quantitative and qualitative evaluation based on fractional anisotropy in unidirectional fiber regions, and DCI in crossing-fiber regions show robust reconstruction in the presence of motion.

Conclusion.—The proposed approach has the potential to extend routine use of SMS DCI in very challenging populations such as young children, newborns, and non-cooperative patients.

Keywords

Motion-Robust; Motion Correction; Diffusion-Compartment Imaging; Diffusion-Weighted MRI; Simultaneous Multi-Slice; Intra-Volume Motion; Slice Registration; Motion Tracking; Image-Based Self-Navigation; Image-based Navigation

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Introduction

Diffusion-weighted magnetic resonance imaging (DW-MRI or DWI) (1, 2) is one of the main imaging techniques for *in-vivo* and *ex-vivo* analysis of neural microstructure and structural connectivity of the brain (3, 4, 5, 6, 7, 8). While a diffusion tensor imaging (DTI) (9) model was widely used to describe major fiber bundles and tractography (10, 11, 12), models and techniques have evolved to characterize the complex structure of neural anatomy including crossing fibers, fanning fibers, and free and restricted water diffusion compartments (13, 14, 15, 16, 17, 18, 19, 20, 21) in techniques that we refer to as Diffusion Compartment Imaging (DCI) (20). Fitting more complex models in DCI requires relatively dense q-space sampling (18, 22) which can be extremely time consuming to acquire. Acceleration through simultaneous multi-slice (SMS) acquisition and controlled aliasing (23) has played a significant role in routine use of these techniques in large-scale projects such as the human connectome project (7, 8).

The primary goal of SMS-DWI has been accelerated imaging which has effectively pushed the limits on spatial resolution, signal-to-noise ratio, and accuracy of brain micro-structural modeling through reasonably short, *in-vivo*, dense q-space sampling. But SMS-DWI has also the potential to facilitate fast and robust slice-level motion tracking in imaging moving subjects, as shown in our preliminary work (24). Slice-level motion tracking through state-space estimation was first introduced in (25), which, as an extension of previous efforts on using slice-to-volume registration for motion-robust imaging (26, 27, 28, 29, 30, 31, 32), incorporated an explicit model of motion dynamics into motion-robust DTI reconstruction. It was shown that in the case of continuous intermittent subject movements, slice-level motion tracking, correction, and robust reconstruction (25) (MT-SVR in this article) led to significantly more accurate DTI results than the state-of-the-art volume-to-volume registration methods such as those discussed in (33). Slice-level motion tracking is achieved through robust slice-to-volume registration (25) due to the high sampling rate of slice acquisitions in DWI, a framework for detecting and filtering motion-corrupted slice data, and a state-space estimation method based on (34). As a method that solely relies on imaging data rather than prospectively-designed intrinsic or extrinsic motion navigators, this technique has been successfully adopted and used in extremely challenging applications such as fetal DTI (35) where motion effects are complex. It has also shown significant value in restoring useful information through retrospective processing of previously acquired motion-corrupted DWI scans (36).

In this paper we extend a framework based on slice-level motion correction by exploiting the rigid coupling between simultaneously acquired slices for robust reconstruction in DCI. Without loss of generality, we build our reconstruction framework based upon the DIAMOND model (20) which performed well compared to other models in a recent multi-group comparison of DCI models (21). Compared to the ball-and-stick model (13) considered in (24), DIAMOND provides a much better model of brain microstructure as it simultaneously estimates the number of compartments and fits a statistical distribution of diffusion tensors for each compartment, effectively allowing characterization of diffusivity rate for each fascicle while accounting for the microstructural heterogeneity. In designing the motion correction component, we take advantage of the rigid coupling between

simultaneously acquired slices in the SMS sequences routinely used for DCI for both intra-slice motion detection and slice-level motion tracking. Fast intra-slice motion disrupts slice acquisitions and unaliasing, and corrupts the signal received in all simultaneously excited slices. After unaliasing, simultaneously acquired slices that are not corrupted by motion, cover distant positions of the imaged anatomy. These SMS-acquisition slices provide excellent coverage of the 3D anatomy thus can be effectively used as intrinsic 3D image-based navigators. They can be used for retrospective image-based motion correction or as self-navigators in prospective motion correction. The use of a robust state estimation approach is crucial as intervals of intra-slice motion can lead to significant data loss which can adversely affect a non-robust motion tracking method. The output of the motion correction algorithm is not motion corrected DWI, but is model-based reconstruction of DTI or DCI. From the computed DCI or DTI, one can then generate motion-corrected DWI. We present experimental evaluation results of the proposed motion-robust SMS DCI, which we call MT-SMR (for Motion-Tracking based on Simultaneous Multi-slice Registration), on volunteer experiments with controlled motion, and in the analysis of motion-corrupted DCI scans of 20 pediatric subjects. The results indicate robust DCI reconstruction in the presence of extensive subject movements, and the feasibility of restoring useful information from previously-acquired motion-corrupted DWI data. This can significantly enhance advanced magnetic resonance imaging in challenging populations such as newborns and young children. Following three sections describe the methods, experimental results, and a discussion and conclusion.

Methods

An SMS DWI scan is acquired using interleaved 2D echo-planar imaging with M slices excited simultaneously. At each signal-acquisition step, k-space data for M slices is concurrently acquired from multiple receiver coils and unaliased to reconstruct slices (23). Motion that happens during slice acquisitions results in signal loss or distortion in all M simultaneously acquired slices (see Figure 1). If fast motion is intermittent, some good-quality slices are also acquired; but inter-slice motion presents in data. The approach presented here accounts for inter-slice motion and is robust to signal loss caused by intra-slice motion. We accomplish this by tracking slice-level motion dynamics through image registration and automatically rejecting slices that are corrupted by intra-slice motion. The following subsections describe the specifics of our approach, including motion-correction methods and the diffusion compartment model reconstruction.

Motion Tracking

For slice-level motion tracking and estimation in this work, we extend the robust state-space slice-to-volume registration method in (25) to DWI with SMS acquisition. To this end, we take advantage of slice timing and of the 3D anatomy coverage provided by simultaneously acquired slices. As opposed to motion tracking based on 3D registration of a single slice, which is intrinsically ill-posed due to singleplane (2D) coverage of the anatomy, SMS slices are distant from each other and rigidly coupled. They provide 3D coverage of the anatomy at distant planes thus better constrain the registration problem. This is particularly helpful in brain boundaries, where boundary slices may not have sufficient image features for reliable

registration. In SMS DWI, these boundary slices are coupled with slices in the middle of the brain that are rich in features. Consequently, this significantly boosts the registration accuracy. Following (25) we formulate motion-tracking as a dynamic state-space model estimation where multiple SMS slices are used as observations to estimate motion parameters modeled as hidden states.

Given the set of simultaneously acquired slices $\mathbf{y}_k = \{y_1, y_2, \dots, y_M\}$ at a time step k , the position of the head at time k is denoted by the hidden state $\mathbf{x}_k$ – a 6-element vector of rigid transformation parameters. With a finite sequence of observations (SMS slices), we aim to estimate the states $\mathbf{x}_k$ of motion dynamics using the stochastic equations: $\mathbf{x}_k = \mathbf{x}_{k-1} + \omega_{k-1}$, and $\mathbf{y}_k = \mathbf{H}(\mathbf{x}_k) + \nu_k$; where ω_k is the process noise in the modeling of motion dynamics and ν_k is the measurement noise. $\mathbf{H}(\cdot)$ is a non-linear function that maps $\mathbf{x}_k$ to the measurements $\mathbf{y}_k$; $\mathbf{H}(\cdot)$ can be thought of as a generative function for the SMS slices $\mathbf{y}_k$ acquired at time step k when head position is described by $\mathbf{x}_k$.

We solve this problem through Kalman filtering for state estimation (25). We separate the nonlinear output model from the filtering process which leads to $\mathbf{z}_k = \mathbf{x}_k + \nu_k$, where image registration is used to estimate $\mathbf{z}_k$. This is performed via matching the observations (as target) and the reference image (as source) transformed by $\mathbf{p}$; i.e. $\mathbf{z}_k = \arg\max_{\mathbf{p}} \text{Sim}(\mathbf{H}(\mathbf{p}), \mathbf{y}_k)$, where

$\text{Sim}(\cdot)$ is a matching metric between the set of M slices ($\mathbf{y}_k$) and the transformed source image. Image registration based on the set of simultaneously acquired slices ($\mathbf{y}_k$) is more robust than slice-to-volume registration based on a single slice because sampling from multiple slices separated in different planes results in more robust, locally convex similarity metric functions for registration compared to those generated by a single slice. The output of image registration is $\mathbf{z}_k$, which is used in state estimation. The reference (source) image is a $b = 0$ image reconstructed from all $b = 0$ images through slice motion correction and volume reconstruction (30, 37).

Intra-slice motion can cause signal loss in a number of subsequent slices, leading to mis-registration, and outliers, error and missing values in observations for the Kalman filter. As such, the Gaussian distribution assumption for measurement noise is not valid. To address this issue we use a state estimation method for heavy-tailed noise as formulated in (34). This outlier-robust Kalman filtering approach still assumes a Gaussian distribution with a fixed covariance matrix $\mathbf{Q}$ for the process noise, i.e. $\omega_k \sim \mathcal{N}(0, \mathbf{Q})$, but relaxes the assumption on the distribution of the measurement noise. The measurement noise in this method is not fixed *a priori*. It is assumed to have the form $\nu_k \sim \mathcal{N}(0, \mathbf{S}_k)$ and is updated based on sequential observations through estimating its covariance $\mathbf{S}_k$ at any time step k . Algorithm 1 shows the pseudo code of the proposed slice-level motion tracking and estimation algorithm adopted from (25) for SMS acquisition. $\mathbf{P}_k^-$ and $\mathbf{P}_k$ are *a priori* and *a posteriori* estimates of the error covariance, respectively; $\mathbf{K}_k$ is the Kalman gain; and $\mathbf{R}$ is the covariance of the measurement noise where $\mathbf{S}_k^{-1} \sim \mathcal{W}(\mathbf{R}^{-1}/s, s)$ which is a Wishart distribution with s degrees of freedom and precision matrix $\Lambda_k = \mathbf{R}^{-1}/s$. With the updates on $\mathbf{K}_k$, Λ_k , and $\mathbf{P}_k$ robust state estimation in the presence of outliers (heavy-tailed noise) is achieved (34).

Algorithm 1

Pseudo-code of the slice-level motion estimation algorithm based on (25) which has been extended here for simultaneously acquired slices in $\mathbf{y}_k$. $\hat{\mathbf{x}}_k$ is the posterior estimate of the motion states (transformation parameters) at time k .

Input: $\mathbf{H}, \mathbf{y}_k = \{y_1, y_2, \dots, y_M\}, \hat{\mathbf{x}}_{k-1}$

Output: $\hat{\mathbf{x}}_k$

- 1: *Register volumetric source to simultaneously acquired slices:* $z_k \leftarrow \max_p \text{Sim}(\mathbf{H}(p), \mathbf{y}_k); p_0 = \hat{\mathbf{x}}_{k-1}$
- 2: *predict states:* $\hat{\mathbf{x}}_k^- \leftarrow \hat{\mathbf{x}}_{k-1}, \hat{\mathbf{x}}_k \leftarrow \hat{\mathbf{x}}_k^-; \mathbf{P}_k^- \leftarrow \mathbf{P}_{k-1} + \mathbf{Q}, \mathbf{P}_k \leftarrow \mathbf{P}_k^-$
- 3: **repeat**
- 4: *update noise:* $\delta = z_k - \hat{\mathbf{x}}_k; \Lambda_k = (s\mathbf{R} + \delta\delta^T + \mathbf{P}_k)/(s+1)$
- 5: *update states:* $\mathbf{K}_k = (\mathbf{P}_k^- + \Lambda_k)^{-1} \mathbf{P}_k^-; \hat{\mathbf{x}}_k = \hat{\mathbf{x}}_k^- + \mathbf{K}_k^T (z_k - \hat{\mathbf{x}}_k^-)$
- 6: $\mathbf{P}_k = \mathbf{K}_k^T \Lambda_k \mathbf{K}_k + (\mathbf{H} - \mathbf{K}_k)^T \mathbf{P}_k^- (\mathbf{H} - \mathbf{K}_k)$
- 7: **until** converged
- 8: **return** $\hat{\mathbf{x}}_k$

Intra-Slice Motion Detection and Outlier Rejection

Intra-slice motion results in distortion and signal loss within all the slices acquired simultaneously at time step k . Figure 1(a) shows an example of these artifacts in a 2-band, 2-interleaved DWI sequence. In order to automatically detect the slices that are corrupted by intra-slice motion, we exploit the fact that SMS DWI slices are acquired in an interleaved manner (to minimize slice cross-talk) so fast intra-slice motion, that occurs intermittently, causes inter-slice intensity discontinuity (38). Intensity discontinuity can be detected. To do this, we first compute a filtered version of the image by applying a morphological closing filter. Subsequently, we subtract the filtered image from the source image to compute a difference image I_d . We then use robust statistics to detect intra-slice motion: the set of simultaneously acquired slices $\mathbf{y}_k$ is deemed affected by intra-slice motion if the average of their median in I_d is greater than 0 or their mean is an outlier (Figure 1(b)). When intra-slice motion is detected at time k , all slices acquired at k are rejected, registration is considered invalid, and the state remains unchanged until the next valid observation is obtained.

Model Reconstruction from Motion-Corrected Data

The output of Algorithm 1 and the intra-slice motion filtering process discussed in the previous section is a set of slices $\mathbf{y}_k$ and their corresponding estimated states $\hat{\mathbf{x}}_k$ that define the relative 3D position (rigid transformation) of DW slices with respect to a reference, target $b=0$ image. In this study, we aimed to use this data to estimate a diffusion model that accounts for the intra-voxel orientation heterogeneity and allows delineation of crossing white matter fascicles, believed to occur in 60 to 90% of brain white matter voxels (39).

Without loss of generality, we formulate the problem based on the DIAMOND (20) approach which performed well in a recent comparison of several state-of-the-art DW-MRI models (21). DIAMOND is a hybrid biophysical and statistical diffusion model that allows characterization of fascicle-specific diffusion characteristics while also modeling the intra-compartment heterogeneity. This is achieved by considering the presence of a finite number of compartments in slow exchange in voxels, and by modeling the signal arising from each compartment with a statistical distribution of diffusion tensors. Given the non-diffusion weighted signal S_0 and diffusion-weighted signal $S_k(b_k \neq 0)$ with gradients g_k and b-values b_k , the analytical expression of DIAMOND is (20):

$$S_k = S_0 \sum_{i=1}^N f_i \left(1 + \frac{-b_k g_k^T D_i g_k}{\kappa_i} \right)^{-\kappa_i}, \quad (1)$$

where N is the number of compartments and f_i is the relative volumic fraction of occupancy of compartment i . D_i is the expectation of the distribution of diffusion tensors i . It is a tensor that describes the average 3-D diffusivity of the compartment i , from which fascicle-specific diffusion characteristics can be assessed such as the fascicle fractional anisotropy (fFA), fascicle mean diffusivity (fMD), fascicle radial diffusivity (fRD) and fascicle axial diffusivity (fAD). κ_i is a scalar that describes the concentration of the statistical distribution. High values of κ_i indicate a narrow distribution and therefore a low intra-compartment heterogeneity. In contrast, low values of κ_i indicate a broad distribution and therefore a high intra-compartment heterogeneity.

To estimate model parameters, we use maximum a posteriori (MAP) estimation at the voxel level, i.e. $\{\hat{L}, \hat{f}\} = \arg\max_{L, f} p(L, f | S_i)$, where $L = (\log(D_1), \dots, \log(D_N))$ and $f = (f_1, \dots, f_N)$ is the vector of the compartment fractions. To ensure that the intermediate estimates of diffusion tensors remain symmetric positive definite, the diffusion tensors are log-transformed. It is well known that motion during a DWI acquisition requires reorientation of the diffusion gradients for each volume when volume-to-volume registration is used (40). In the case of slice-level motion correction, the diffusion gradients must be reoriented for each individual slice (using the estimated slice motion parameters $\hat{x}_k$). This leads to a complex scattered data problem and to a different sampling of q-space at every voxel. We constructed at each voxel v of the target image a data structure that synthesizes the scattered data in a neighborhood $\mathcal{N}(v)$ of v from all the realigned slices. It contains the list of corrected gradient vectors, b-values, diffusion attenuations C_i and corrected physical coordinates of the voxels in $\mathcal{N}(v)$. We assume that the observed data $\{C_k, k = 1, \dots, M_v\}$ at each voxel are i.i.d and normally distributed around the unknown modeled signals $\{S_k, k = 1, \dots, M_v\}$ with variance σ^2 , so that:

$$P(C|L, f) = \prod_{v \in V_0} \frac{1}{\sigma\sqrt{2\pi}} \exp \left(-\frac{\sum_{k=1}^{M_v} w_k \left\| S_k \left(e^{\mathbf{L}_v}, \kappa_v, f_v \right) - C_k \right\|^2}{2\sigma^2} \right), \quad (2)$$

where M_v is the number of voxels in $\mathcal{N}(v)$. The weights w_k s are calculated by the spatial distance between the neighborhood voxels and the reference voxel using a Gaussian kernel that models the point-spread-function of the DWI slice acquisition. In our experiments we used a kernel with radius of one voxel. The parameters were estimated using the BOBYQA (41) numerical optimization algorithm with an approach similar to that in (20).

Quantitative Evaluation Methods

Quantitative evaluation was performed based on volunteer subject experiments, in which adult volunteer subjects complied with our request to stay completely still during a number of scans used to establish reference standard and randomly moved their head in other scans. Random head movements resulted in different patterns and amount (up to approximately 30°) of head movement. We quantified the extent of motion using $d = \sqrt{x^2 + y^2 + z^2 + (cr)^2}$, where x , y and z represent the three translation parameters, r represents the Euler angle (rotational component) of measured motion and is computed using the three angles of rotation based on the Euler's rotation formula, and c is a hyper-parameter set to $50mm$ to adjust the relative contribution of translation and rotation towards d metric computation.

We quantitatively evaluated different methods for both DTI and DCI models. For the DTI model, we evaluated the difference in DTI-derived scalars between the DTIs reconstructed using the proposed motion-correction approach and the reference standard that was acquired under no-motion. This analysis was possible since we were able to acquire same-session no-motion scans in volunteer subject experiments. The differences in DTI scalars were obtained by probing the DTI obtained using various motion-correction strategies, i.e. Volume-to-Volume Registration (VVR), Slice-to-Volume Registration (SVR) initialized using VVR, Motion-Tracking based on Slice-to-Volume Registration (MT-SVR) (25), and Motion-Tracking based on Simultaneous Multi-slice Registration (MT-SMR), against DTI obtained without motion correction (Uncorrected) and reference standard (Reference). For each of these scenarios we calculated the following metrics in specific regions-of-interest (ROIs): (i) difference in FA values (Δ_{FA}), (ii) rotation between the principal eigenvectors of the tensors (Δ_{Angle}), (iii) the Frobenius norm of the difference tensor (Δ_{FN}), and (iv) the difference in the mean diffusivity (Δ_{MD}) between each motion-correction approach (and the uncorrected image) with the reference standard using the formulas given below:

$$\Delta_{FA}(S^a, S^b) = \sqrt{\frac{1}{n_x} \sum_{i=1}^{n_x} (FA(S_i^a) - FA(S_i^b))^2} \quad (3)$$

$$\Delta_{\text{Angle}}(S^a, S^b) = \frac{1}{n_x} \sum_{i=1}^{n_x} (1 - |e_i^a \cdot e_i^b|) \quad (4)$$

$$\Delta_{\text{FN}}(S^a, S^b) = \sqrt{\frac{1}{n_x} \sum_{i=1}^{n_x} \|S_i^a - S_i^b\|_F^2} \quad (5)$$

$$\Delta_{\text{MD}}(S^a, S^b) = \sqrt{\frac{1}{n_x} \sum_{i=1}^{n_x} (\text{MD}(S_i^a) - \text{MD}(S_i^b))} \quad (6)$$

where a and b are two DTIs being compared, n_x is the number of voxels in the region-of-interest (ROI), $\text{FA}(S_i^a)$ is the FA value of i^{th} tensor within ROI in a , e_i^a is the principal eigenvector of i^{th} tensor in a , and $\|\cdot\|_F$ represents the Frobenius norm.

To quantitatively evaluate the DCI models obtained from different motion correction methods we evaluated both angular errors between estimated fascicles and tensor error metrics to assess the discrepancy in estimated fascicle parameters. This was achieved by computing the Average Minimum Angle (AMA) and Minimum Log-Euclidean Metric (MLED) (42) defined by:

$$\text{AMA}(D^a, D^b) = \frac{1}{N} \sum_{i=1}^N \min_j \left\{ \arccos \left[(e_i^a)^T e_j^b \right] \right\} \quad (7)$$

$$\text{MLED}(D^a, D^b) = \min_{j \in \{1 \dots N\}} \left\{ \sum_{i=1}^N (D_i^a, D_{j(i)}^b)_{LE} \right\}; j = P(1 \dots N) \quad (8)$$

where D^a and D^b are two sets of tensors each comprising N tensors, each tensor describing the average compartment-specific diffusivity (see Eq. 1), e_i^a is the principal eigenvector of i^{th} tensor in D^a , $(S_1, S_2)_{LE} = \|e^{\log(S_1)} - \log(S_2)\|_F$ is the log-euclidean distance between two tensors S_1 and S_2 , and $\|\cdot\|_F$ represents the Frobenius norm. The subscript j represents an ordered set obtained by permuting the index set $[1 \dots N]$ and $j(i)$ represents the i^{th} element of set j . To compute MLED, we added pairwise distances between tensors in D^a and D^b over number of tensors (N) and took the minimum of the aggregate distances computed for all possible ordering (permutations) of tensors in D^b . We also evaluated the impact of the different motion correction techniques on the estimated number of fascicles at each voxel.

Imaging

All imaging was performed at Boston Children's Hospital (BCH) using 3T Siemens Skyra scanners (Siemens Healthineers, Erlangen, Germany) using 32-channel head coils (additional experiments, reported in the supporting information, were performed using a Siemens Prisma scanner). DWI acquisitions for DCI were performed using a cube and sphere (CUSP) q-space sampling scheme (42) with 13 $b=0$ images and 78 diffusion-sensitive ($b > 0$) images with b values in the range of 400 — 3000 s/mm^2 , with $TR = 9000$ — 13200, $TE = 88$ ms, flip angle = 90° , in-plane and out-of-plane resolution = 2 mm, a SMS factor of 2, matrix size = 128×128 , and field-of-view of 256 mm. In addition, DWI acquisitions were performed on adult volunteers for DTI model fitting. These acquisitions involved 30 diffusion directions with 6 $b = 0$ images and were also performed with SMS factor of 2 (in two experiments involved SMS factors of 3 and 4), where the volunteers were asked to stay completely still during reference motion-free scans, and performed a range of slow, fast, and continuous motion to the largest possible extents within the head coil in several motion experiments. Supporting Information Video S1 shows sample DWI scan of one of the main volunteer subject experiments with SMS factor of 2 on a Skyra scanner, and Supporting Information Videos S2 to S4 show sample DWI scans with SMS factors of 2, 3, and 4, respectively, obtained from a volunteer subject in motion experiments performed on the Prisma scanner. These videos show the extent of motion and their effects on SMS DWI acquisitions. All DWI scans were performed with Siemens product sequences using EPI based calibration; interleaved slice acquisition; 6/8 partial Fourier; twice-refocused spin echoes to reduce eddy current artifacts (43); parallel imaging with GRAPPA factor of 2; and standard shim to reduce susceptibility-induced geometric distortion.

Experiments involved 15 adult volunteer research DWI scans and DCI scans of 20 pediatric subjects (between 3 and 14 years old) who moved during DWI scans. The study was approved by the BCH Institutional Review Board (IRB) Committee and a written informed consent was obtained from all participants (or an adult guardian for children). We processed the images with our proposed MT-SMR method as well as the VVR, SVR, and MT-SVR (25) methods. We used the Normalized Cross Correlation (NCC) metric for slice-to-volume registration in DWI images (including $b = 0$ and $b > 0$ images), and the Mattes Mutual Information (MI) metric (44) for volume-to-volume registration. Intra-slice motion was detected using the algorithm explained in the Methods section, and the corresponding motion-corrupted slices were excluded in the MT-SVR and MT-SMR techniques. All volumes with more than 20% motion-corrupted slices were excluded in all reconstruction algorithms. For DTI model, we fit a single tensor model using Weighted Linear Least Squares (WLLS) method (45, 46, 47) based on the formulation in (25). For the DCI model, we fitted DIAMOND with maximum number of compartments $N = 3$.

Results

DTI - Adult Volunteers

Figure 2 shows representative color Fractional Anisotropy (FA) images obtained from DTI reconstructed using different motion correction strategies, i.e. VVR, SVR, MT-SVR, and MT-SMR against DTI obtained without motion correction (Uncorrected) and reference

standard (Reference). We then calculated DTI evaluation metrics in Equations (3) to (6) in three ROIs with dominantly unidirectional dense fibers: Corpus Callosum (CC), Cingulum (Cg), and Limbs of the Internal Capsule (LIC); as well as the Lateral Ventricles (LV). The results have been tabulated in Table 1. In this evaluation, lowest errors in comparison metrics were consistently observed for DTIs computed using MT-SMR compared to other methods. The results of MT-SVR and SVR were generally better than VVR and all were much better than uncorrected scans. The results obtained using VVR and SVR were fairly close for two metrics, MD and FA . Additionally, we evaluated FA in the CC and Cg ROIs against the amount-of-motion metric (d) in Figure 3. In these plots, we observed that MT-SMR consistently resulted in lowest errors across the range of motion. Further, error obtained using all but MT-SMR method appeared to increase with the extent of motion. This figure suggests that MT-SMR is able to robustly adjust for motion in computing the DTIs and is nearly unaffected by the extent of intra-volume motion. An example result of DTI reconstruction for an experiment with SMS acceleration factor of 3 is shown in the Supporting Information Figure S1.

DCI - Adult Volunteers

Through adult volunteer experiments with controlled motion, we assessed the impact of motion-correction on model selection during DCI estimation and on the coherence between estimated fascicles orientations. We compared motion-free DCI to motion-corrupted DCI corrected using various motion-correction strategies.

Figure 4 shows the result of the estimated number of fascicles at each voxel in a scan with motion (uncorrected) and after motion correction using VVR, SVR, MT-SVR, and MT-SMR. For comparison, the estimated fiber count in the reference standard, motion-free scan is also shown. The bottom row in Figure 4 compares the estimated crossing fibers in part of corona radiata, overlaid on the corresponding T1-weighted image. We observed that motion-correction using VVR resulted in erroneously low voxel counts with cyan color (3 fibers-per-voxel), whereas in comparison, slice-to-volume registration methods (SVR, MT-SVR, and MT-SMR) enabled reconstruction of 3 fibers in a significantly larger portion of the image, with MT-SMR resulting in a fiber-count distribution that qualitatively appears closer to the reference standard than the SVR and MT-SVR results.

The AMA and MLED metrics (Equations 7 and 8) calculated between reference standard DCI and DCI obtained using motion-correction methods have been reported in Table 2. These metrics were computed in a ROI manually defined in corona radiata on the reference image. In these comparisons, we observed that MT-SMR resulted in lowest AMA and MLED. Metrics obtained using MT-SVR and SVR were close to MT-SMR, although in a paired-sample t-test a p-value < 0.001 was observed suggesting statistically significant differences.

DCI and DTI - Pediatric Subjects

We applied our developed motion correction and reconstruction technique (MT-SMR) to fit DCI and DTI models of DWI scans (CUSP90, SMS=2) of 20 pediatric subjects who moved during DWI acquisitions. Figure 5 shows DTI and DCI results, as well as DCI model

selection maps of a ten-year-old subject processed with VVR, SVR, MT-SVR, and MT-SMR. The color FA for the DTI model has been shown in the first row, and crossing fibers obtained from the DCI model in a zoomed area shown by the white square in the first row, are shown in the second row. The model selection maps given in the third row show the number of compartments automatically selected by the DCI model reconstructed by each method. The colors (black, green, pink, and cyan) in the model selection map show the estimated number of compartments (i.e. 0, 1, 2, and 3, respectively). The model selection map obtained from MT-SMR best matches our knowledge of brain microstructural anatomy in this area that involves three major crossing fiber bundles. These fibers were reconstructed and detected by the MT-SMR approach for DCI model fitting.

We also evaluated the trends in estimated motion parameters (rotation and translation) over acquisition time. A representative plot of three rotation and three translation parameters estimated using VVR, SVR, MT-SVR, and MT-SMR methods for the ten-year-old subject is shown in Figure 6. This figure shows that robust state-space motion-tracking with rigidly-coupled SMS registration corrects the registration error and captures motion parameters that appear more plausible than the motion parameters captured by SVR and MT-SVR.

Compared to the MT-SMR plot (bottom row), the SVR plot shows significant presence of jitter in the motion parameters, and the MT-SVR plot shows jitter in the boundary slices of the head. Smooth and robust motion tracking was achieved as MT-SMR factored in multiple distant slices that were simultaneously acquired into the registration process. The presence of spatially distributed data resulted in a smoother cost-optimization landscape during registration compared to SVR, and the maximum distance between coupled slices resulted in accurate registration-based motion tracking compared to MT-SVR, which did not perform well in the boundary slices. Figures 5 and 6 together offer strong evidence in favor of MT-SMR for motion-correction among the options considered.

For further quantitative evaluation of MT-SMR motion correction in pediatric subjects (in the absence of reference standard per subject), we analyzed diffusion measures based on the DTI model fitted to this data, where we focused on regions of mainly unidirectional fiber pathways. These regions included the corpus callosum (CC), cingulum (Cin), limbs of the internal capsule (LIC), and pons. Figure 7 compares the statistics of FA values using box plots in these four regions for the Uncorrected data, VVR, SVR, MT-SVR, and MT-SMR methods. Uncorrected motion and sub-optimal reconstruction resulted in image blur and thus reduced FA values in these dense fiber regions, whereas with motion-robust reconstruction we observed high FA values in these regions as expected. To this end, Figure 7 indicates that the best reconstructions were obtained from MT-SMR, where the highest FA values were obtained in all four regions. We then analyzed the effect of the amount of motion on FA values in these regions. Figure 8 shows plots of the FA values and their trend as a function of the amount of motion in 20 subjects for the Uncorrected, VVR, SVR, MT-SVR, and MT-SMR methods. These results 1) confirm that the best values (highest FAs in these regions) were almost always obtained from MT-SMR, and 2) MT-SMR performed robustly regardless of the amount of motion, whereas uncorrected data and VVR, in particular, showed a strong decreasing trend with increased amount of motion.

Discussion

DWI of children, fetuses, and un-cooperating patients requires accelerated sequences for image acquisition and motion-robust post-processing of data. Long acquisitions required for DCI, in particular, cannot be used in practice without acceleration. The simultaneous multi-slice (SMS) acquisition with unaliasing scheme (23) is the current technique-of-choice for DCI acceleration. We developed and evaluated a motion-tracking framework based on simultaneous multi-slice registration (called MT-SMR) for SMS DCI reconstruction. While SMS accelerates DCI acquisitions by a factor of two or more, these scans are still time-consuming and generate loud noise and vibrations that are not easily tolerated by children and newborns. Our proposed approach benefits from SMS while integrating several key components including simultaneous multi-slice registration and Kalman-filter based motion-tracking with a powerful DCI model that enables modeling multiple fascicles per voxel and tissue heterogeneity within each voxel in challenging populations. We also note that slice-level outlier-detection within the MT-SMR approach, that detects partial signal loss, plays a significant role in dynamic motion-tracking based on SMS registration. This along with weighted linear least squares estimation in DIAMOND model reconstruction effectively removed all intra-slice and intra-volume motion artifacts and generated reliable estimates of diffusion properties and crossing fibers.

Extensive research has been done on motion-robust sequences and motion correction techniques in MRI (48), but the use of these techniques has been limited by the type and amount of motion that can be corrected, and the challenges in implementation or setup. Motion correction in DWI is currently performed at the volume level either retrospectively using image registration (33) or prospectively using navigators (49). These techniques are slow and do not perform well in continuous and fast motion. The key components developed in this study address these challenges; the MT-SMR framework itself is modular and can be used with any tensor modeling approach. In our approach model estimation is performed on image grid directly from scattered motion-corrected data with iterative refinement that results in more accurate estimation of tensors compared to methods that resample data in the target space before tensor computation.

We tested our proposed method for robustness to motion and the extent of motion using different datasets. In Figure 2 we showed that MT-SMR based DTI reconstruction was nearly identical to motion-free reference standard DTI. In evaluating the robustness to the extent of motion, we observed that MT-SMR resulted in consistently low FA in corpus callosum and cingulum over the quantified amount of motion (d), Figure 3. MT-SMR also led to lowest errors in frequently-used DTI-derived metrics such as FA and MD in four sampled ROIs (Table 1). This is particularly useful for group analysis studies that require most accurate representation of DTI-derived scalars to reduce errors in group-level inferences. We showed that in the absence of slice-level motion correction and robust reconstruction, FA values computed from DTI scans of 20 pediatric patients, decreased as the amount of motion increased (Figure 8). This trend was not seen when we used our MT-SMR for DTI analysis, which shows robustness of MT-SMR to motion.

Ultimately, our goal was to model multiple fascicles and their heterogeneity within every voxel. The process of recovering multiple crossing fibers is challenging and typically involves DWI acquisition at multiple b-values with a high number of gradient directions. In the presence of uncontrolled motion, resolving crossing fibers becomes even more challenging. In our evaluation, MT-SMR based DCI led to estimated fiber population that appeared most similar to the reference standard DCI computed using scans acquired under no movement (Figure 4). This was further validated in quantitative comparisons where we achieved lowest errors measured in terms of AMA and MLED metrics (Table 2 using MT-SMR based DCI).

In clinical MRI, unconstrained motion is frequently observed in pediatric MR imaging (50). Accurate representation of neural architecture in developing subjects is particularly important as fascicles continue to develop and alter in their arrangement. In order to evaluate applicability of our approach to account for motion during MRI of children, we observed the fiber crossings in the corona radiata region. We found that MT-SMR based DCI preserved the crossing fiber pathways better than other approaches (VVR, SVR) as shown in Figure 5, and resulted in jitter-free estimation of motion trajectories based on slice-level image registration (Figure 6). These results suggest that MT-SMR based DCI leads to most accurate tractography under the presence of motion compared to traditional VVR or SVR based motion-correction strategies. All experiments showed that MT-SMR also outperformed MT-SVR (25) which incorporated slice timing in interleaved DWI slice acquisition schemes to regularize motion tracking in the absence of SMS acquisitions. Interleaved slice DWI acquisitions regularize and improve motion tracking using MT-SVR (25) as they provide distant sampling of anatomy at slices that are acquired in short time intervals; however the performance of MT-SVR is still inferior to MT-SMR which takes advantage of rigidly-coupled, simultaneously-acquired slices that cover the anatomy at maximum distances. Significant boost in performance by MT-SMR is achieved in motion tracking using slices near the boundaries of the anatomy where image features are sparse.

Modeling diffusion tensors and multiple fascicles in the brain is a challenging task under the influence of subject motion and requires an analysis pipeline that specifically accounts for motion in an integrated approach. This is a key requirement for longitudinal studies where the same subject may or may not move in subsequent scans as well as in population studies where different subjects have different levels of tolerance for staying still during MRI acquisition. The high degree of complexity and inter-subject variability cannot be effectively captured if motion is incorrectly or implausibly accounted (as is the case using VVR and SVR-based approaches). Beginning from motion-corrupted DWI, our proposed approach estimates individual slice-level motion with tracking, computes DCIs in standard orientation directly from scattered data (without resampling DWIs) in an iterative manner, and delineates multiple fascicles within a voxel while computing their individual heterogeneity. This approach resulted in DCIs that were most similar to the reference standard among the approaches considered here, and estimated plausible motion trajectories.

The SMS calibration scheme appeared to be fairly robust in practice. In our imaging data, fast intra-slice motion resulted in signal loss in all simultaneously acquired slices, but we did not see any increased ghost or aliasing artifacts due to potential failure of the SMS

calibration scheme despite experimenting with the largest possible extents of motion within a head coil (up to 30 degrees) (Supporting Information Video S1). An SMS acquisition with M bands reduces the time of a non-SMS acquisition by a factor of M . If subject motion is considered a stationary stochastic process, motion-induced signal loss affects similar number of slices in SMS and non-SMS acquisitions, showing no clear advantage for one against the other. However, most non-cooperative subjects tend to move more with longer acquisitions. Newborns may wake up and startle with the loud noise and vibration from DWI scans (51). SMS acquisitions are being increasingly used due to their time saving, faster acquisitions and patient comfort, especially in longer MRI acquisitions such as DCI. In this study we presented a framework that takes advantage of SMS acquisition properties for motion-robust DCI reconstruction in the presence of near-continuous motion.

In our institution, research and clinical DWI scans are currently performed with SMS acceleration factor of 2 and parallel imaging with GRAPPA factor of 2. In our volunteer experiments in this study, we tested SMS factors of 2, 3, and 4 and observed SNR loss at higher SMS factors, which is attributed to the g-factor noise penalty (7, 8). The results shown in Supporting Information Figure S1 demonstrate successful application of our proposed motion tracking and model reconstruction method to data acquired with SMS factor of 3. Supporting Information Figure S2 and Supporting Information Figure S3 compare DTI characteristics obtained from different DWI acquisitions with different SMS factors on two different scanners (Siemens Skyra and Prisma scanners, respectively); where we estimated and compared local average SNR using the optimized blockwise nonlocal means approach (52). Our registration-based motion tracking technique is robust and its performance improves by improved 3D coverage of the anatomy by an increased number of satisfactory quality simultaneously-acquired slices. In choosing SMS and parallel imaging acceleration factors, however, one should consider the g-factor penalties, the achievable level of SNR especially for DCI at high b values, and the potential interactions that have been reported between SMS unaliasing and inplane undersampling in the phase encoding direction (8). For a recent review of technical developments in DWI including considerations on SNR and acceleration methods we refer to (53). We also acknowledge that recent works on superior artifact correction, such as (54), may facilitate effective use of higher SMS factors. Our proposed method can readily be used with any acceptable quality SMS acquisition for improved motion-robust DCI reconstruction.

Echo-Planar Imaging (EPI), used in DWI for DCI, is one of the fastest MRI acquisition schemes. This fast imaging scheme, however, is affected by geometric distortion artifacts caused by eddy currents and susceptibility-induced magnetic field in-homogeneity. In this study, we used twice-refocused spin echoes to control eddy currents (43), and standard shim and a GRAPPA factor of 2 to reduce susceptibility-induced geometric distortions. Our motion tracking and correction techniques do not require any specific pulse sequence modification and can be readily used along with any other scheme that is compatible with SMS EPI. It can be used, for instance, with dual-echo reversed blips for susceptibility-induced geometric distortion correction (55).

Conclusion

We developed a slice-level motion tracking and estimation technique that takes advantage of the 3D coverage of the anatomy at multiple image planes provided by the simultaneously acquired slices in SMS DWI for diffusion compartment imaging. By analyzing model selection maps, diffusion properties in crossing fiber regions, and estimated motion trajectories, we showed that our proposed technique outperforms slice-to-volume registration as it performs 3D registration based on data from multiple planes rather than a single plane. This technique also outperforms the current routinely-used volume-to-volume registration techniques as it enables faster motion tracking which results in more efficient use of DWI data. In this work, we reported retrospective analysis of motion-corrupted data, but our motion tracking and estimation system is causal, therefore, with sufficient computation power and appropriate, optimized implementation it can be used in real-time for prospective motion tracking and correction. This technique can extend the use of SMS DCI to populations that move near continuously during long DCI acquisitions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

This work was supported in part by the McKnight Foundation through a Technological Innovations in Neuroscience Award; Intel IPCC; and the National Institutes of Health (NIH) grants R01 EB018988, R01 EB019483, R01 NS079788, U01 NS082320, U54 NS092090. The Developmental Synaptopathies Consortium (U54 NS092090) is part of the NCATS Rare Diseases Clinical Research Network (RDCRN). RDCRN is an initiative of the Office of Rare Diseases Research (ORDR), NCATS, funded through collaboration between NCATS, NIMH, NINDS, and NICHD. The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of the NIH or the McKnight Foundation.

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Figure 1:

(a) Arrows point at intra-slice motion artifacts seen in simultaneously acquired slices in an interleaved, 2-band axial SMS DWI: fast motion happened at two time points (arrows of different colors) during this SMS DWI acquisition, and each time it affected four slices (two distant coupled slices and their subsequent coupled slices that appear one slice away from the first couple due to the interleaved acquisition scheme). Partial signal loss is observed in a corrupted axial slice on the right. (b) Outliers of the proposed mean and median metrics on a difference filtered image are used to detect intra-slice motion (x-axis is the slice number). This outlier detection framework is also strengthened by the interleaved acquisition scheme which reduces slice cross-talk and the correlation of motion-induced intra-slice distortion. As compared to a single slice, two rigidly-coupled slices in an SMS sequence provide a multi-plane 3D coverage of the anatomy, therefore they mitigate the ill-posed problem of slice-to-volume registration. This is particularly useful in brain boundaries where single slices do not have sufficient image features to guide registration. Simultaneously acquired slices in an SMS sequence are distant from each other, thus a slice in the brain boundary, that has limited anatomical features to guide registration, is coupled with a slice in the middle of the brain that is rich in content, and can regulate the registration process for self-navigated motion tracking.

Figure 2:

Axial (top), coronal (middle) and sagittal (bottom) views of the color FA maps obtained from DTIs of an adult volunteer. Our proposed method, MT-SMR, generated color FA nearly identical to the motion-free reference standard. VVR, SVR, and MT-SVR correction strategies show differences in color FA to a varying extent.

Figure 3:

FA value differences (Δ_{FA}) between the reference standard and each motion-correction method in the CC and Cg ROIs based on the extend of motion (mm). Regardless of the extend of motion, MT-SMR generated less errors in most experiments.

Figure 4:

The model selection map in an axial view (top row) and crossing fibers overlaid on the T1-weighted image in a coronal view (bottom row) of corona radiata where three major fiber pathways (callosal and corticospinal tracts, and the superior longitudinal fasciculus) intersect. The model selection map shows the number of estimated crossing fibers: cyan, tan, green and black colors represent 3, 2, 1, and 0 crossing fibers, respectively. The proposed method, MT-SMR, generated results that were most similar to the reference standard. The results were quantitatively evaluated in Table 2.

Figure 5:

DTI and DCI reconstruction results for DWI scan of a 10-years-old child. Similar regularization parameters were used in all DCI reconstructions. Comparing DTI (first row), DCI (second row), and model selection maps showing number of computed crossing fibers (third row) for five reconstructions: (a) Uncorrected, (b) VVR, (c) SVR, (d) MT-SVR, and (e) MT-SMR. Uncorrected and VVR are missing many crossing fibers because of motion. As can be seen inside the circle in the second row, estimated jittering motion parameters in SVR (second row in Figure 6) results in disordered crossing fiber estimation compared to MT-SVR and MT-SMR. Different colors in the model selection map show the estimated number of crossing fibers in this highlighted region of the brain where three major fiber bundles cross. Black, green, pink, and cyan correspond to 0, 1, 2, and 3 crossing fibers respectively. The model selection map obtained from MT-SMR reveals fiber microstructure that best matches our knowledge of anatomy among all compared reconstructions. The average number of estimated crossing fibers obtained from MT-SMR is larger than the other methods in this figure also confirming the results in Table 2.

Figure 6:

Estimated motion, rotation (a) and translation (b) parameters over time (only 19 volumes are shown) in a 10-years-old subject using VVR, SVR, MT-SVR and MT-SMR methods. The proposed method, MT-SMR, achieves accurate and smooth motion tracking through the registration of simultaneously-acquired distant slices and robust state-space estimation.

Figure 7:

The analysis of FA values obtained from five algorithms (Uncorrected, VVR, SVR, MT-SVR, and MT-SMR) in four regions-of-interest containing mainly unidirectional fiber pathways in pediatric patients. Boxplots show the median, maximum, minimum and inter-quartile ranges of FA values among 20 subjects. CC, Cin, LIC, and Pons refer to corpus callosum, cingulum, limbs of the internal capsule, and pons, respectively. Uncompensated motion results in image blur which lowers the FA values in these regions. The highest FA values in all regions were obtained from the proposed method (MT-SMR), which indicates motion-robust reconstruction.

Figure 8:

Comparing FA values obtained from Uncorrected data, VVR, SVR, MT-SVR, and MT-SMR methods in four regions (CC, Cin, LIC, and pons) in 20 pediatric subjects as a function of the amount of motion estimated for these cases. These results show that 1) the highest FA values in all these regions were almost always obtained from MT-SMR, while the values obtained from Uncorrected and VVR were low, and 2) FA values obtained from Uncorrected and VVR strongly decreased with increased motion. This was not the case for SVR, MT-SVR, and MT-SMR. This analysis shows that MT-SMR, in particular, was robust to motion.

The mean of FA, Angle, FN and MD error metrics in Corpus Callosum (CC), Cingulum (Cg), Limbs of the Internal Capsule (LIC) and Lateral Ventricles (LV) regions. Error metrics computed using motion-uncorrected DTIs are shown under column 'U'. VVR refers to reconstruction with volume-to-volume registration, SVR refers to reconstruction with slice-to-volume registration, MT-SVR refers to reconstruction using motion-tracking based on slice-to-volume registration (25), and MT-SMR refers to reconstruction using motion-tracking based simultaneous multi-slice registration. The proposed method, MT-SMR, consistently generated the lowest errors in all probed ROIs. Other than cases marked with [−] the difference between MT-SMR and MT-SVR/SVR/VVR/Uncorrected was statistically significant ($p < 0.001$ in a paired-sample t -test with $\alpha = 0.05$).

Table 1:

	FA				Angle				FN($\times 10^3$)				MD($\times 10^3$)			
	U	VVR	SVR	MT-SVR	U	VVR	SVR	MT-SVR	U	VVR	SVR	MT-SVR	U	VVR	SVR	MT-SVR
CC	0.35	0.16	0.15	0.14	0.12	0.68	0.38	0.36	0.33	0.30	1.01	0.56	0.56	0.53	0.50	0.17 [−]
Cin	0.33	0.17	0.18	0.16	0.12	0.85	0.51	0.53	0.44	0.36	0.86	0.53	0.59	0.49	0.38	0.15
LIC	0.24	0.14	0.11 [−]	0.11 [−]	0.10	0.50	0.33	0.30	0.29	0.27	0.61	0.38	0.33 [−]	0.32 [−]	0.31	0.08 [−]
Vent	0.12	0.10	0.08 [−]	0.08 [−]	0.07	0.86	0.85	0.83 [−]	0.83 [−]	0.82	1.66	0.89	0.75 [−]	0.76 [−]	0.68	0.27

Table 2:

Quantitative comparison of the DCI reconstruction in volunteer motion studies. The difference between MT-SMR and MT-SVR/SVR/VVR/Uncorrected is statistically significant ($p < 0.001$) in a paired-sample t -test with $\alpha = 0.05$.

	AMA					MLED				
	Uncorrected	VVR	SVR	MT-SVR	MT-SMR	Uncorrected	VVR	SVR	MT-SVR	MT-SMR
motion 1	50.3±17.4	29.7±12.0	15.7±11.4	14.1±10.3	11.7±9.0	1.40±0.39	0.96±0.31	0.62±0.31	0.57±0.29	0.49±0.25
motion 2	42.0±17.0	29.7±12.4	14.8±10.6	13.0±9.2	11.1±8.0	1.25±0.40	1.00±0.32	0.59±0.29	0.54 ±0.27	0.48±0.25