Diffusion Acquisition and Diffusion Weighting

Stefan Skare
Karolinska Institutet, Stockholm, Sweden

Diffusion weighting

Water self-diffusion or random thermal motion (“Brownian motion”) is a microscopic process that within certain limits can be measured in the body by diffusion-weighted MRI (DWI). The random thermal motion of water molecules in different tissue structures is however very complicated. In DWI, we typically have voxel volumes around 10 mm$^3$, wherein multiple tissue compartments having different self-diffusion are averaged together - hence the commonly used name “apparent diffusion coefficient” or ADC.

To produce diffusion-weighted MR images, where the signal intensity in each voxel is largely dependent on the self-diffusion of water molecules, the imaging method (pulse sequence) needs to be sensitized to this microscopic random motion. This is done by inserting two (or more) balanced strong magnetic field gradients (a.k.a. diffusion gradients) between the time the imaging plane is formed (excited) and the MR signal collection (readout) (Fig. 1). We can choose to play out these diffusion gradients in the $x$ (frequency encoding), $y$ (phase encoding), or $z$ (through-plane) direction - or in a linear combination of the three - thereby making the acquired signal dependent on motion along this particular direction. During this diffusion preparation time, which is normally about 30-80 ms long, the magnitude of the MR signal is reduced (“weighted”) in proportion to the amount of water self-diffusion in the voxel. Compared to the gradients used for image encoding (i.e. signal localization), these gradients are large in both amplitude and duration to attenuate the MR signal sufficiently. A quantitative map of diffusion (ADC) is calculated from at least two images, one with and one without diffusion gradients applied, with the gradient duration and amplitude often set to yield a $b$-value of 1000 and 0 by modifying the gradient amplitude), respectively (see Fig. 1).

Apart from affecting the MR signal in a desired manner, the large diffusion gradients makes us also sensitive to other types of motion, such as brain motion and rigid head motion (outside CNS: breathing, etc.). For smaller motion, primarily the phase of the transverse $M_2$ signal is perturbed in a spatially nonlinear fashion across the object. Large bulk motion during the diffusion weighting period, also the magnitude of the signal will be decreased, in some cases up to the point where the magnitude signal over the entire slice has completely vanished, leaving only noise in the image.

The diffusion-weighted image (top left, Fig. 1) is routinely used in the clinical routine, in particular for acute ischemic stroke detection but also to aid in certain differential diagnoses, such as e.g. tumor vs abscess. The ADC image is often used by the radiologist as a complement to the DWI image, as the latter is also subject to some amount of $T_2$-weighted signal dependence (a.k.a. ”$T_2$-shine through”). However, while the ADC is quantitative and solely representing the water diffusion, many lesions of interest show up dark in an ADC image, so also acute ischemic stroke, making it more difficult to detect. For better visualization, the “exponential ADC” (“eADC”, Fig. 1) can be calculated from the ADC map, which is equal to the DWI, but with proton density and $T_2$-weighting information removed.

For research purposes, diffusion (“ADC”) is typically measured in many directions (anywhere between 6 to hundreds) from which a more comprehensive model of diffusion is employed - the simplest being the diffusion tensor imaging (DTI) model. Next, we will focus on the choice of acquisition method (a.k.a pulse sequence) to be used for diffusion imaging, and look into their advantages and disadvantages.

Figure 1

Conventional Cartesian non-diffusion pulse sequences acquire k-space in multiple excitations (a.k.a. shots). As the phase errors originating from motion during the diffusion preparation time are random in nature and large compared to the phase used to spatially encode the image, the use of multi-shot sequences with diffusion gradients is not straightforward, and in most cases severe image ghosting will result.

Single shot diffusion-weighted pulse sequences

A single shot pulse sequence fills the entire k-space after a single excitation and diffusion preparation. Therefore, the spatially nonlinear phase over the object caused by motion appears as a static effect for all k-space lines. Hence, the only effect on the data is that the reconstructed complex image will contain this phase after reconstruction (which is ignored anyway for the magnitude DW images). Because of its high SNR efficiency, single-shot Echo Planar Imaging (ss-EPI) sequence remains the most widely used pulse sequence for diffusion imaging.

The main drawback of ss-EPI is that, because it reads out all k-space lines sequentially along the phase encoding direction, undesired phase (a.k.a. off-resonant spins) from other sources than motion will accumulate during the readout train. This phase accrual will appear large in comparison to the encoding phase induced by the small phase encoding blips in the EPI train, and will result in geometric distortions in two forms. The first type is the nonlinear geometric distortions originating from the static susceptibility gradients (field inhomogeneities) near tissue-air interfaces, and may be up to several centimeters. The second largest source of off-resonances is object independent, namely eddy currents arising from the diffusion gradients. The slowly decaying eddy current terms give rise to an erroneous affine transformation (i.e. some combination of scaling, translation, shear) of the diffusion-weighted image, seldom more than a few millimeters. Although this may not sound as severe, it is a problem because the image warping changes with the diffusion direction played out, resulting in a misregistration across the diffusion-weighted images.

Increasing a) the field strength, b) frequency encoding resolution or c) the phase encoding FOV, makes the off-resonance sensitivity to increase correspondingly. This is why it is hard to achieve high resolution with DW-EPI, in particular at high field strengths.

The so far most successful and widely used way to reduce the off-resonance sensitivity is to reduce the effective phase encoding FOV and unfold it in the reconstruction process via parallel imaging, such as SENSE [1] or GRAPPA [2]. Using e.g. a modern 32-channel head coil, acceleration factors (and hence distortion reduction factors) up to about R≈4-5 become feasible, if the lost SNR from acquiring R times less k-space lines is compensated for by more averages or diffusion directions.

There are also certain DWI applications, such e.g. of the cervical spine [3] or the optic nerve [4], where a narrow final FOV along the phase encoding is suitable because of the shape of the anatomy. For these scenarios, the geometric distortions in DW-ssEPI may be reduced by reducing the final phase FOV, but measures to avoid the aliasing of tissue are needed. The first variant of this was named zonally magnified EPI [5], where the excitation planes of the 90 and the 180 pulses are tilted slightly to end up with a Spin-Echo signal from only a swath of the object‘s anatomy. Alternative methods to avoid aliasing for reduced FOV DW-EPI acquisitions have recently been proposed recently [3, 6, 7].

Other single-shot sequences that have been used for diffusion imaging include line scanning [8], single-shot spiral [9] and SSFSE (a.k.a. HASTE) [10]. Line scanning is a 1D MRI technique, where the previously mentioned phase problem is avoided by skipping phase encoding all together, and stitching together magnitude rods to an image. This is however, in its own way, very sensitive to misregistration between these rods due to motion. Also, as one excitation and diffusion preparation is spent on each column (rather than a 2D image as for EPI), line scanning is an SNR inefficient technique.

Single-shot DW-spiral is, similar to EPI, sensitive to off-resonances, but the phase evolution of these off-resonant spins are now evolving from the center to the periphery of k-space. This gives rise to a blur in the image instead of EPI’s uni-directional displacement (and signal pileup) of the anatomy.

DW-SSFSE comprises of a long readout train with refocusing RF pulses alternated with readout gradients, each collecting one k-space line. The role of the refocusing pulses is to repeatedly reverse the phase evolution from off-resonant spins, thereby making the free from geometric distortions.

However, there are a series of challenges, some of which pertains to the inclusion of the diffusion gradients. First, the sequence itself has a long readout time (some hundred ms), and the image is...
therefore prone to $T_2$-blurring, and a longer TR is needed to cover the same amount of slices, making it less scan time efficient than EPI.

More problematic though, is that the spatially nonlinear random phase following each diffusion preparation period makes it hard to set the RF phase right to meet the Carr-Purcell-Meiboom-Gill (CPMG) condition [11], which is fulfilled in non-diffusion FSE and SSFSE imaging. When the CPMG condition is met, the stimulated echoes (STE), which occur for flip angles $< 180$, end up in phase with the regular spin echoes (SE). As it is hard to produce perfect 180-degree flip angles across the entire slice, signal interferences between the SE and STE occur (Fig. 4). One solution is to insert crusher gradients and remove the non-CPMG component of the signal at the expense of 50% loss in SNR. Another approach is to employ a phase cycling scheme between the refocusing pulses that is much less sensitive to the initial phase following the diffusion preparation and in theory without the previously mentioned loss of SNR [12].

**Multi shot diffusion-weighted pulse sequences**

While the solutions are different, the common rationale for not using single-shot techniques is to achieve higher image resolution with less geometric distortions and/or blurring, at the expense of longer scan times. Mentioned above is that the unreliable phase in DWI makes interleaved multi-shot Cartesian imaging prone to image ghosting. For this reason, non-Cartesian k-space trajectories have been much more successful in this regard.

There have been several variants of diffusion-weighted radial acquisitions [13-15], where one or more radial spokes across a circular k-space are read out after each diffusion preparation. Radial spokes acquired in different TRs (excitations) will be shifted due to the untrustworthy diffusion phase. However, since the radial spokes are all intersecting the k-space center, they are also inherently self-navigated along the radial direction. By Fourier transforming each radial line to the image domain, taking the magnitude of the data, and then Fourier transforming it back to k-space, the peak signals of the radial spokes will all be aligned in the center of k-space. However, as the correction is 1D, it cannot correct for shifts perpendicular to the radial direction.

Another set of diffusion-weighted pulse sequences are PROPELLER [16], Turboprop [17], SAP-EPI [18], and X-PROP [19], which all acquire a central strip, or blade, of k-space after each diffusion preparation (albeit in different ways and with different pros and cons). In subsequent excitations, the blades are rotated to fill the entire k-space. What makes these propeller sequences distinct form standard interleaved multi-shot imaging is that each blade is acquired at full image FOV, making each blade free from ghosting in a similar fashion as ss-EPI. In addition, each blade serves as its own 2D navigator echo, which first allows us to remove all (or just the slowly varying annoying phase) of each image blade separately, similar to be described for radials above, but this time we can correct the undesired translation in the k-space blade (arising from non-zero image phase from e.g. brain motion) in both directions. Second, rigid 2D motion correction can be performed to correct for translations and rotations in the image domain.

In PROPELLER, each blade is read out with RF refocusing pulses similar to SSFSE, why it is free from geometric distortions. The non-CPMG problem still exists however, but is mitigated with good 180 flip angles and by employing an intra-blade phase ordering scheme that puts the even echoes in the center of the blade [20]. This pulse sequence has been successfully implemented on several commercial systems, and is today widely used. Turboprop is a modification of PROPELLER with small EPI trains inserted between the RF refocusing pulses similar to the GRASE sequence, and thereby trading lower SAR and shorter scan times for some limited off-resonance sensitivity. About the same time as Turboprop, diffusion-weighted SAP-EPI was proposed, which uses only an EPI train to read out the blade in k-space. The key in SAP-EPI is that the frequency encoding direction is set along the short-axis of the blade (hence its name), which increases the k-space traversal speed along the phase encoding (long-axis of the blade) and thereby reduces the sensitivity to off-resonances. Because the final gridded image resolution is due to the length of the blade, geometric distortions and image resolution become uncoupled (unlike in ss-EPI, where higher resolution also means more problems). More recently, the X-PROP technique was proposed [19], which is similar to the Turboprop sequence in terms of sequence timing but where the individual EPI echoes between the refocusing pulses are separated into different blades. Thereby, each blade, built up from lines acquired following different refocusing pulses in the readout train, will contain the same phase accrual due to off-resonances, which then can be removed before gridding the blades together.

Another very promising pulse sequence for diffusion imaging is the RS-EPI sequence [21-23]. Sharing the same intra-blade k-space trajectory as SAP-EPI, they are similar in off-resonance sensitivity, but in RS-EPI the blades are put side by side, vertically, in k-space. With all blades having the same phase encoding direction, the residual geometric distortions in the final gridded image are unidirectional too, which has an advantage at very high resolutions ($\sim 480 \times 480$), as SAP-EPI - like any non-Cartesian technique - will be prone to some residual blurring if not all artifacts are completely removed. However, as only one of the vertical blades in the k-space passes through the k-space center, RS-EPI also needs a second blade readout through the k-space center as 2D navigator. This extra readout makes it slightly less scan time efficient compared to SAP-EPI. Both SAP-EPI and RS-EPI benefit largely to be combined with parallel imaging to reduce geometric distortions further.

Diffusion-weighted SNAILS [24], is a multi-shot spiral sequence with a k-space density that increases with its distance from the center. The central portion of k-space is first acquired like a single-shot spiral, every time capturing the low spatial frequencies of the phase, whereas the rest of k-space is read out sparsely in each excitation. Similar to the propeller
sequence family, the fully sampled central portion of k-space for each shot can be used to correct for phase and motion corruption of the data. As each spiral arm is not in its own sub-Cartesian space, the reconstruction and correction becomes more complex than for propeller trajectories, but this has been well explained in Ref [24]. Blurring is, again, however hard to remove completely.

Yet another way to avoid both motion induced phase problems and geometric distortions is to flip the $M_z$ signal after the diffusion preparation back into the longitudinal direction. The new (diffusion-weighted) $M_z$ can then be used to read out multiple k-space lines using a series of small excitation flip angles like in STEAM-DWI [25], where also the TR need to be short between the low-flip angle pulses to avoid too much $T_1$-recovery of non-diffusion-weighted spins. However, in flipping back of the magnetization to $M_z$, half the SNR lost, and further SNR is lost due to the use of the small flip angles.

3D and 3D multi-slab diffusion-weighted pulse sequences

Finally, in this overview of diffusion-weighted pulse sequences is balanced steady-state free precession (bSSFP) [26]. With a new excitation prior to each readout, also bSSFP does not suffer from the geometric distortions encountered in EPI-based imaging. DW-bSSFP differs substantially from the other sequences in that the diffusion-weighting is an accumulated effect over multiple TRs originating from a small diffusion gradient after each readout. Unlike e.g. a classical Stejskal-Tanner diffusion preparation, the b-value in bSSFP is a function of $T_1$, $T_2$ and flip angle. It is therefore in general difficult to use this method for quantification. Moreover, bSSFP is not particular robust against motion. Nevertheless, see e.g. Ref [27] for methods using navigators and cardiac gating with some good DWI examples.

By adding a second EPI readout and a slab phase encoding gradient before the first echo, a GRAPPA accelerated Cartesian EPI sequence may be converted into a 3D multi-slab sequence [28] (a reimplementation of the technique submitted to this year’s ISMRM), where ~15 mm thick slabs are phase encoded in about 10 steps, which after Fourier transformation in the $k_z$ direction and shown also in sagittal and coronal reformats.

Figure 5. 3D-multi-slab DW-EPI (GRAPPA R=3), 160x160, 1.5x1.5x1.5 mm$^3$, scanned axially and shown also in sagittal and coronal reformats

References