Sequences for Diffusion MRI

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1. INTRODUCTION: The first half of this presentation discusses the unique challenges to diffusion weighted imaging (DWI) one must considering when choosing and designing pulse sequences. The second half discusses the more common pulse sequences with their relative advantages and challenges.

2. CHALLENGES:

2.1 Bulk Motion Sensitivity. A generic pulse sequence for diffusion-weighted imaging (DWI) adds a bipolar gradient G_{diff}, in some direction, after spin excitation and before readout (Fig. 1). This gradient pair adds a phase to each spin proportional to the difference between its average positions during gradient A and during gradient B of Fig. 1 (A and B are roughly 25 msec apart). To produce a measurable effect from water diffusion (with a standard deviation of displacement on the order of 10μm in 25 msec), a significant spin phase must be produced for this small motion. A typical gradient pair might produce a 90 degree phase shift for a displacement of 10μm in 25msec ≈ .04 cm/sec. Exact values will vary, but this degree of phase sensitivity means that any bulk tissue motion on this order (0.1mm/sec) will add a significant phase shift to the MR signal, which can corrupt the phase used to encode position across multiple TR's (i.e. phase encoding). For brain DWI, very slight rotations can produce significant linear phase shifts across the FOV, translating the center of k-space [1]. For brain DWI, even if the patients skull is completed fixed, internal motion from cardiac-driven pressure waves are problematic [2].

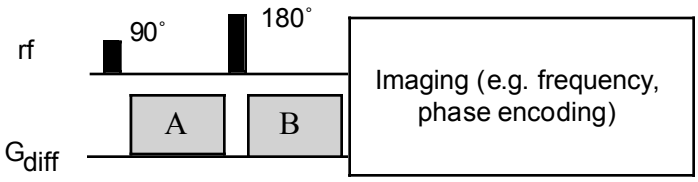

Fig. 1. Typical diffusion sequence, with diffusion weighting gradients (A,B) after excitation and before encoding.

There are several ways to mitigate this motion-related phase, each with their drawbacks. These methods include:

a. Velocity compensated diffusion gradients [3], as shown in Fig. 2, remove all phase sensitivity to constant-velocity patient motion during the diffusion weighting period. A significant drawback is the reduction of b-value to roughly 25% that of the standard gradients shown in Fig. 1 (in the same time).

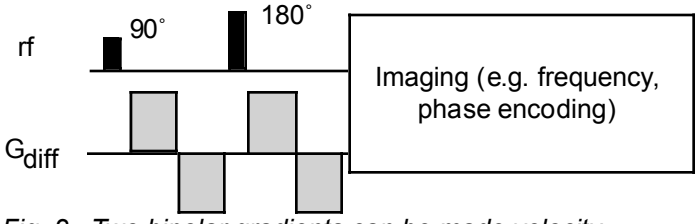

Fig. 2. Two bipolar gradients can be made velocity compensated, with a reduction of b-value.

b. Cardiac gating the pulse sequence minimizes cardiac-related motions [2,4-6], but reduces scan efficiency and can add signal noise due to variable TR.

c. External physical restraints on the patient can be used to reduce gross head motion. In our experience, their effectiveness is highly variable and patient-dependent.

d. One dimensional “Navigator” echoes information can be collected along with imaging data acquisition to estimate rotation motion of the head via the corresponding k-space shift, as well as, to some degree, the nonlinear phase shifts from internal motion [1,5,7,8]. This can then be used to correct or eliminate data. Two dimensional navigation [9] and other methods for data correction have been proposed [10].

e. The most common method for mitigating shot-to-shot phase changes due to non-reproducible motion is to employ single-shot techniques, in which a single application of diffusion weighting gradients is followed by an imaging component that captures all information for creating the desired spatial information. The common examples of 1D (aka “linescan”), 2D Single Shot EPI, and 2D Single Shot FSE are discussed later in this abstract.

2.2. Eddy Currents: The very large diffusion gradients of Fig. 1 carry with them a significant eddy current, which is synergistic because they have the same sign. These eddy currents are problematic for the imaging portion of the sequence that follows, especially for EPI-related sequences. The gradients of Fig. 2 pose much less of a problem due to their net zero-area (long term eddy currents will cancel) [11]. An alternative design which carries nearly the same efficiency (b-value per time) as Fig. 1, and keeps the eddy current immunity of those in Fig. 2 (but loses the velocity compensation) is shown in Fig. 3; these split diffusion gradients work well at reducing long-term eddy currents [12].

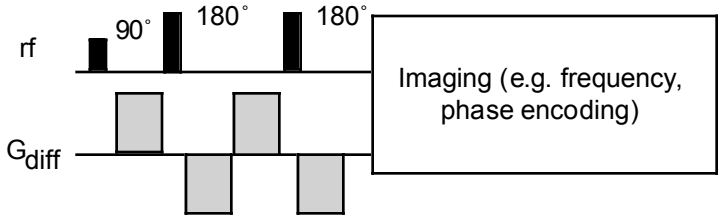

Fig. 3. Split Diffusion gradients reduce eddy currents.

2.3 SNR, time restraints. DWI images have inherently low SNR due to signal reduction from (1) T2 loss during the long TE’s required by diffusion weighting, and (2) signal loss directly from required by - optimized measurement length. Simple models show that for optimal SNR, the echo train length of the imaging part of the sequence in Figs 1-3 should be slightly less than the T2 of the tissue of interest. Longer echo trains measure very low SNR data, and shorter echo trains are inefficient (too much of the scan time is used for diffusion weighting).

Diffusion scans can also require long scan times, due to the multiplicity of diffusion weightings (directions, and b-values) often needed, and also due to the added time of diffusion weighing to each TR. With sufficient SNR, fast single-shot imaging methods can help to mitigate this problem. If SNR is sufficient, “isotropic” diffusion weighting schemes exist which can weight by the average diffusion in one TR instead of the typical 3 TR’s (for weighting by diffusion along X, Y, and Z) [13], thus halving scan time.

2.4. Cross terms. Calculation of the b-value involves the integral of the applied diffusion-weighting gradient over time. In the presence of additional gradients, whether

they applied gradients (e.g. needed for the imaging sequence) or whether they are "background" gradients caused by magnet inhomogeneity and susceptibility differences, these additional terms will affect the true diffusion weighting (b-value) that is applied. For this reason, it is good practice to: (1) keep the imaging gradients compact, e.g. they should have zero net area as much as possible, (2) design diffusion gradients with an alternating or split design (such as Fig. 3) to minimize the effects of background gradients, and (3) go through the exercise of calculating the b-value based on the entire gradient waveforms (diffusion weighting plus imaging gradients) to be aware of the amount of bias added to the intended diffusion weighting.

2.5 Challenges to CPMG FSE. Immediately after the diffusion weighting gradients, the phase of the spins will depend on patient motion, and thus be (a) spatially varying, and (b) generally unpredictable. This makes employing the CPMG condition for FSE sequences very difficult - two basic methods to maintain an echo train are phase cycling methods [14,15] and separating the CPMG component [16,17]. The latter methods may be a bit more robust, however they can result in a significant loss of signal.

2.6 Partial Volume Effects. The encoding of data in MRI commonly results in pixel values which represent contributions from different compartments, a so-called "partial volume" effect. While this is linear in the collected images, the non-linear effects of diffusion weighting and post-processing of DWI images can result in significant bias of synthesized images. The more pronounced effects are that of CSF on the calculated ADC of adjacent tissue, and that of adjacent, non-parallel white matter tracts (or white matter tracts adjacent to CSF) on the calculated fractional anisotropy value.

3. COMMON PULSE SEQUENCE DESIGNS

3.1. Single Shot EPI (SS-EPI) Methods. By far the most common sequence for collecting DWI images is SS-EPI. Although motion during diffusion weighting does create spatially varying phase, it is remains constant throughout the imaging experiment, and thus usually has negligible impact. Because EPI is a rapid method of acquisition, it lessens the time constraints {section 2.3} and keeps the echo train relatively short, helping to retain SNR {section 2.3}. Sensitivity to off-resonance can introduce significant warping and signal pileup artifacts near the skull base, implants, and regions where susceptibility-related gradients are present. The use of split diffusion gradients {Fig. 3, section 2.2} is very beneficial for SS-EPI, since eddy currents from diffusion gradients will geometrically warp the image - since eddy currents will vary between different b-values and directions of diffusion weightings, this warping will vary, making registration of images with different diffusion weightings difficult. A plethora of post-processing methods for removing these warpings exists [an incomplete list is refs. 18-20] and are typically necessary for accurate combination of DWI images using SS-EPI.

Another common artifact seen in SS-EPI comes about from the shifting of k-space from head rotations [1] and the partial k-space acquisition common in SS-EPI. If the rotation-induced shift of data is toward the uncorrected part of k-space, then significant artifacts can appear in the image. For this reason, the uncollected part of k-space should not be

too large (i.e. should be much less than 50% of the "total" phase encodings). Even in this case, it should be noted that a shift of k-space data along the phase encoded direction will change the effective TE and move the center of k-space off of the spin echo, and can change the effective TE, and can therefore create small biases in signal values.

The advent of parallel imaging (SENSE) methods [21] has proven to be very important to SS-EPI DWI [22]. The ability to measure only every Nth phase encoding line reduces geometric warping and eddy current sensitivity by N, speeds up data acquisition, and in many cases improves SNR over the $N^{(-1/2)}$ typically predicted by minimizing T2* losses and making the echo train closer to optimal for SNR {section 2.3}.

3.2 Multi-shot Methods.
Combining data from multiple TR's into one image typically requires some sort of "navigator" information about the phase acquired during each set of diffusion weighting gradients. Multishot methods generally allow for higher matrix sizes and potentially higher SNR (by collecting at the optimal echo train duration), but can often exhibit errors due to uncorrected phase.

3.3. FSE Methods.
Many FSE-based methods have been introduced in the literature. These methods have the advantage of dramatically reduced sensitivity to eddy currents and susceptibility gradients compared to EPI-based methods. They also remove T2* blurring. The biggest obstacle problem of FSE-based DWI is the inability to reliably achieve a CPMG train of refocussing pulses, which can generally degrade the signal after a few echoes. Approaches to this are discussed above {section 2.5}.

FSE methods include single-shot methods [16], which avoid the phase problems of multi-shot. DifRad DWI [23] uses radial encoding to reduce sensitivity to motion. Twin-navigator methods have been proposed for monitoring phase variations [24]. PROPELLER DWI [25] collects imaging data with 'built-in' 2D navigation to facilitate multi-shot phase correction from head rotation and cardiac motion.

3.5 LineScan (1D) Methods. By exciting spins in a column and Fourier encoding in only one direction, linescan methods mitigate the susceptibility and eddy current sensitivity of EPI methods while avoiding the need for multi-shot imaging [2]. These lines of data may be collected contiguous within a desired plane in order to form an image [26]. The challenge to these methods is longer imaging times and reduced SNR.

3.6 Stimulated Echo DWI. One can design stimulated echo DWI experiments [27]. An advantage of these methods is that the diffusion time can be made very long (but not significantly longer than tissue T1, e.g. on the order of 1 second or less), which for periodic motions can significantly reduce the bulk motion sensitivity.

3.7 FLAIR Methods. All of the above methods can be combined, as desired, with FLAIR methods to suppress the CSF signal [28]. While this increases scan time,

removal of the CSF signal has been shown to produce more accurate ADC values and anisotropy maps in areas bordering CSF spaces.

3.8 SSFP Methods. An entire class of methods, which is somewhat separate from the above methods, is based on steady state free precession imaging [e.g. refs 29-31]. Adding small diffusion-sensitive gradients to each TR creates diffusion weighting - these sequences are fast and higher resolution. One of their biggest challenges is the extraction of quantitative diffusion information, since the diffusion weighting depends on the relaxation properties of the tissue, unlike the non-steady-state methods above.

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