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Simultaneous Calculation of Flow and Diffusion Sensitivity in Steady-State Free Precession Imaging

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Abstract

In this paper the authors quantitatively evaluate the combined effect of both flow and diffusion in steady-state free precession (SSFP) imaging. A partition analysis (PA) is used to derive a fourth order approximation (in E_2) of the signal in an echo SSFP sequence. The authors also introduce a novel very fast simulation technique, based on a circular convolution, which accurately accounts for both flow and diffusion. A 2D SSFP-echo sequence was implemented to obtain experimental data from a phantom containing three different solutions. Excellent agreement between the theory and the experimental data was found. Then by using the simulation algorithm and experimental measurements of *in vivo* brain motion, the authors estimated the artifacts to be expected in SSFP diffusion imaging of the brain and found them to be comparable with those of pulsed gradient spin echo. Finally, the authors point out the equivalence between the flow sensitivity of SSFP and RF spoiling commonly used in fast imaging.

Keywords

flow; diffusion; SSFP; simulation

INTRODUCTION

The steady-state free precession (SSFP) imaging pulse sequence has long been known for its high sensitivity to flow (1) and diffusion. The diffusion sensitivity of SSFP has been thoroughly investigated (2–6) whereas the sensitivity of SSFP to both flow and diffusion simultaneously has previously only been studied experimentally (7,8). One of the reasons is that the approach used by Kaiser *et al.* (2) to obtain a closed form solution for the diffusion sensitivity is not feasible when bulk flow is added to the model. In this paper we use a partition analysis (PA) to obtain an approximate analytical solution for the simultaneous sensitivity of SSFP to both flow and diffusion. Our approach parallels that of Buxton (9), however, and includes the flow as well as the diffusion; it is a fourth order instead of a second order approximation. We also introduce here a new very fast and accurate simulation technique, based on *conditional random walk* and *circular convolution*, which we then use for cases where the PA is inaccurate as well as simulation of pulsatile flow.

The flow sensitivity of SSFP was first described by Patz and Hawkes (1) in terms of a gradient dependent scale invariant parameter. Patz (10,11) also showed how it is possible to suppress the signal from static spins and make the steady-state signal more sensitive to slowly moving spins by using the moving reference frame (MRF) technique. The MRF method was later used

by Tyszka *et al.* (12–14) to image very slow fluid flow. The flow sensitivity of SSFP has been used for fast imaging of cerebrospinal fluid motion (15) and has also been applied in the study of renal microcirculation. A strong correlation was shown to exist between the signal in a missing pulse SSFP sequence (MP-SSFP) (16), which has a flow sensitivity similar to the SSFP sequence, and the perfusion rate in kidney (17).

Because SSFP is very sensitive to diffusion and has relatively short acquisition times, it has been proposed for diffusion imaging (6,18) as an alternative to method such as echo planar imaging (EPI), which requires specialized hardware, and to the pulsed gradient spin echo (PGSE) method (19), which is relatively slow.

The aim here is to analyze the sensitivity of SSFP to both bulk flow and diffusion. We believe it is important to understand this simplified problem to gain understanding of more complicated situations that are to be expected *in vivo*. Understanding of the flow sensitivity is also essential to maximize or minimize the flow attenuation in SSFP imaging (20,21).

We start by reviewing some of the fundamental concepts of SSFP. Then a PA is used to analyze and approximate the simultaneous flow and diffusion sensitivity. Although the analytical expression obtained from the PA is very complex, it gives a good understanding of the nature of the flow and diffusion sensitivity in SSFP. Next we introduce a novel computer simulation technique based on conditional random walk and circular convolution. The PA analysis is verified by using this simulation method and the difference between the PA and the computer simulation is addressed using an underlying physical model. Then the theoretical results are compared with experimental data obtained from phantoms with a flow sensitive 2D SSFP sequence. Excellent agreement was found between the theory and the experimental data. Computer simulations were then used to qualitatively assess the accuracy of diffusion-weighted SSFP imaging in the brain and compare it with conventional diffusion-weighted PGSE imaging.

Finally, we point out that there is an analogous problem to the flow sensitivity of SSFP, namely the spoiling of transverse magnetization in fast low angle shot (FLASH) imaging (22–25). Hence, understanding the flow sensitivity also provides insight to the effectiveness of RF spoiling used in many fast imaging sequences.

THEORY

The basic equation, which describes the dynamics of an ensemble of uncoupled spin- $\frac{1}{2}$ nuclei, under the influence of relaxation, diffusion, and flow, is the Bloch-Torrey equation (26). The Bloch-Torrey equation has been solved earlier for a free induction decay that results from the application of a RF excitation pulse in combination with a series of 180° refocusing pulses (19). A different approach is needed to obtain the steady-state solution.

One cycle from a general SSFP imaging pulse sequence is shown in Fig. 1. It is possible to acquire both the FID and the echo, but we will only focus on the echo because it is much more sensitive to both flow and diffusion (3).

The Steady State of an Isochromat

By assuming hard and instantaneous RF pulses, the dynamics of the isochromat can be described by a RF-rotation, precession, and relaxation. Figure 2 shows a discrete state model of the Bloch equation for SSFP, where the time increments are TR . The magnetization vector just before the application of the RF pulse (echo) is denoted by $\mathbf{M}^-$ and just after the RF pulse (FID) by $\mathbf{M}^+$. The longitudinal relaxation, $(1 - E_1)$, can be considered as a discrete input to the system, because we are only interested in solving for $\mathbf{M}^+$ and $\mathbf{M}^-$. It is important to realize that

this discrete system is linear and when neither flow nor diffusion is present its response is also time invariant. Due to relaxation, this system is stable and does therefore reach a steady state. The precession, $\mathbf{P}$, and the RF rotation around the x -axis, $\mathbf{R}$, can be calculated using simple matrix multiplication in the rotating reference frame. If we define $\mathbf{M}$ as $\hat{x}M_x + \hat{y}M_y + \hat{z}M_z$, then $\mathbf{P}$ and $\mathbf{R}$ are given by

$$\mathbf{P} = \begin{bmatrix} E_2 \cos \varphi & -E_2 \sin \varphi & 0 \\ E_2 \sin \varphi & E_2 \cos \varphi & 0 \\ 0 & 0 & E_1 \end{bmatrix} \quad [1]$$

$$\mathbf{R} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos \alpha & \sin \alpha \\ 0 & -\sin \alpha & \cos \alpha \end{bmatrix} \quad [2]$$

where α is the flip angle, $E_1 = \exp(-TR/T_1)$, $E_2 = \exp(-TR/T_2)$, and the precession angle is obtained from the Larmor equation, $\varphi = \gamma \mathbf{G}_{\text{eff}} \mathbf{r} TR$. The gyromagnetic ratio is denoted by γ and we define $\mathbf{G}_{\text{eff}}$ as the average gradient strength and $\mathbf{r}$ is the location of the isochromat.

$$\mathbf{G}_{\text{eff}} = \frac{1}{TR} \int_0^{TR} \mathbf{G}(t) dt \quad [3]$$

Given the condition of a steady state we can relate $\mathbf{M}^+$ and $\mathbf{M}^-$ by

$$\begin{aligned} \mathbf{M}^- &= \mathbf{P} \mathbf{M}^+ + \hat{z}(1 - E_1)M_0 \\ \mathbf{M}^+ &= \mathbf{R} \mathbf{M}^- \end{aligned} \quad [4]$$

These two equations can easily be solved to give $\mathbf{M}^- = (\mathbf{I} - \mathbf{P}\mathbf{R})^{-1} \hat{z}(1 - E_1)M_0$ (27,28). In linear gradients the steady state has a periodic spatial dependence due to its dependence on φ through $\mathbf{P}$. The wavelength, λ , is defined by

$$\lambda \gamma |\mathbf{G}_{\text{eff}}| TR = \lambda |\mathbf{k}_{\text{eff}}| = 2\pi \quad [5]$$

The magnetization will reflect the proton density, $\rho(\mathbf{r})$, modulated with the steady state periodic spatial dependence. Because of the periodicity of the magnetization, the transverse magnetization $m_{xy} = M_x + iM_y$ can be written as

$$m_{xy}(\mathbf{r}, t) = \rho(\mathbf{r}) \exp \left[-t \left/ T_2 + i\mathbf{k}(t) \cdot \mathbf{r} \right. \right] \sum_{n=-\infty}^{\infty} A_n e^{in\mathbf{k}_{\text{eff}} \mathbf{r}} \quad [6]$$

where $t \in (0, TR)$ and $\mathbf{k}(t) = \int_0^t \gamma \mathbf{G}(\tau) d\tau$. Expressions for the coefficients, A_n , in the absence of diffusion and flow can be found in ref. 20.

Equation [6] shows that in a SSFP imaging sequence, the pixel intensity will be influenced by the local magnetic field through the precession angle. Remedies to this problem have been suggested and are commonly used in practice. They involve adjusting the effective gradient such that an integer number of SSFP wavelengths exist within each image voxel (29).

Another related subject is the separation between the FID and the echo. Several authors have considered this subject (30–33); however, their mathematical analysis did not consider an inhomogeneous proton density. A much easier and more intuitive approach is to analyze the magnetization in k -space. Zur *et al.* (30) numerically evaluated the relation between the effective gradient and the readout gradient to have uniform pixel intensity. Their analysis is,

however, only exact when physical parameters such as the proton density are uniform over the whole field of view (FOV). As shown in Eq. [6] the magnetization is modulated in space by the SSFP wavelength. The k -space information of the object will therefore be aliased over k -space because of convolution of the spatial frequencies of the object's proton density with the harmonics of the SSFP wave. The separation of these peaks will depend on the effective wave number, k_{eff} , and the amplitude of the harmonics, A_n . Only when k_{eff} is two times larger than the highest spatial frequencies of the object, can the echoes be considered fully separated. Whether this is true will depend on the structure of the object. It is, however, always true that the larger the effective gradient, the better is the separation and uniformity of the pixel intensity. This, however, leads to larger flow and diffusion sensitivity as we will show later.

It has also been shown by Zur *et al.* (20) that it is possible to use phase cycling to separate the higher order echoes in SSFP when using a very small effective gradient. This is desirable if one wants to reduce the flow sensitivity. Their method resembles the technique used in spectroscopy to select a particular quantum coherence order (34). It is a subtraction technique that requires several acquisitions. The number of acquisitions is determined by the size of the harmonics, A_n . In practice as few as six acquisitions are sufficient because both the magnetic field inhomogeneities and diffusion-related attenuation significantly reduce the amplitude of higher order harmonics.

Partition Analysis

We present in this section a partition analysis, which, despite being an approximation, provides good insight into the flow and diffusion sensitivity of SSFP. When either flow or diffusion is present, the previous analysis cannot be used because the precession angle of the isochromat will no longer be constant. Indeed, each isochromat will not reach a steady state. As we will show, the ensemble average of isochromats from a voxel with a uniform distribution of precession angles will still reach a steady state. To approximate the steady state, we exploit the fact that the discrete state model for an isochromat shown in Fig. 2 is linear. The response to each input impulse can therefore be found separately. Each three dimensional vector can be decomposed into a longitudinal and two transverse components. The input vectors are purely longitudinal but the RF pulses tilt them into the transverse plane. The precession then further decomposes the transverse part into two orthogonal transverse components. At the time when the RF pulses are applied, each of these three vector components are “fed back” and will be decomposed into three new components. This partition continues in each cycle and the number of components grows exponentially. The total contribution from each input vector, or its impulse response, can then be found by adding together all the vector components. It is difficult to keep track of all the components; however, it is easy to approximate the signal by limiting the number of “echo pathways.” These echo pathways are shown schematically in Fig. 3. They represent the partition of each input vector into longitudinal and transverse components. The longitudinal components do not precess and are represented by horizontal lines; however, the transverse components that precess are represented by sloped lines. The slope indicates the precession of some particular isochromat and will depend on its location. During each longitudinal pathway, the signal is attenuated by E_1 and E_2 during each transverse pathway.

A fourth order approximation in E_2 of the signal strength can be calculated by adding together the signal from all echo pathways with no more than four transverse pathways:

$$\begin{aligned}
\mathbf{M}^- \approx & L \dots LTT + L \dots LTL \dots LT + L \dots LTTTT \\
& + L \dots LTL \dots LTTT + L \dots LTTL \dots LTT \\
& + L \dots LTTTL \dots LT + L \dots LTL \dots LTL \dots LTT \\
& + L \dots LTL \dots LTTL \dots LT \\
& + L \dots LTTL \dots LTL \dots LT \\
& + L \dots LTL \dots LTL \dots LTL \dots LT,
\end{aligned} \tag{7}$$

where $L \dots L$ represents one or more consecutive longitudinal pathways. Note that we have ignored pathways with an odd number of transverse pathways because according to Fig. 3 they can never have zero phase and therefore do not contribute to the echo. An equivalent mathematical expression that proves this statement is Eq. [A3]. One of the reasons why we have chosen to calculate a fourth order partition approximation instead of a second order approximation is that it is more accurate for a wider range of T_2/TR ratios. But more importantly, the fourth order approximation reflects the behavior of the steady-state signal as a function of E_2 whereas the second order approximation does not. In the second order approximation all the terms are proportional to E_2 and changes therefore only affect the overall amplitude. The fourth order approximation, however, gives more information such as the relation between E_2 and the RF flip angle.

The expression for each component can be found by repeatedly using Eqs. [1] and [2]. Here we will only calculate the magnetization for one type of echo pathway. The calculations are quite tedious but are all “variations on the same theme.” Here we will only consider contributions from all echoes of the type:

$$\begin{array}{ccccccc}
L & \dots & LTL & \dots & LTL & \dots & LTL & \dots & LT \\
\underbrace{\hspace{1.5cm}} & & \underbrace{\hspace{1.5cm}} & & \underbrace{\hspace{1.5cm}} & & \underbrace{\hspace{1.5cm}} & & \\
n & & m & & l & & k & &
\end{array}$$

This is the last term in Eq. [7]. In presence of flow and diffusion, the precession angle will no longer be constant as in Fig. 3. The relation between the precession angles in consecutive cycles is given by

$$\begin{aligned}
\phi(n) = & \phi(n-1) + \gamma G_{\text{eff}} TR [\nu TR + \Delta x(n, D, TR)] \\
& + \Delta \phi(n, D, G, TR)
\end{aligned} \tag{8}$$

The terms in the bracket are the displacement of the isochromat due to the flow velocity, ν , and the random variable Δx is due to the diffusion, D . The random variable $\Delta \phi(D, G, TR)$ denotes an additional change in the precession angle, which depends on the shape of the gradient. If we assume the duration of the gradient is much shorter than the repetition time, this term can easily be ignored.

The expression for the x -component of the magnetization can now be written by using Eqs. [1] and [2].

$$\begin{aligned}
M(n, m, l, k)_x = & M_0 (1 - E_1) (E_1 \cos \alpha)^{n+m+l+k-3} E_1^3 E_2^4 \\
& \cdot \sin^7 \alpha [\cos(\varphi_1) \cos(\varphi_2) \cos(\varphi_3) \sin(\varphi_4)]
\end{aligned} \tag{9}$$

where $\varphi_1, \dots, \varphi_4$ represent the precession angle of each transverse pathway. Note that the physical significance of this is that longer pathways are better preserved for smaller flip angles than for larger flip angles, because $\cos\alpha$ is closer to one.

As pointed out in a previous section, we are interested in the signal from a uniform distribution of precession angles. The probability distribution of all the random variations in the phase due to diffusion also has to be taken into consideration. The average value, which we represent by $\langle \rangle$, is therefore given by

$$\langle M \rangle = \frac{1}{2\pi} \int_0^{2\pi} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} M(\varphi_1, \varphi_2, \varphi_3, \varphi_4) \cdot \Pr(\varphi_1, \varphi_2, \varphi_3, \varphi_4) d\varphi_4 d\varphi_3 d\varphi_2 d\varphi_1 \quad [10]$$

For free diffusion, the particle displacement has a Gaussian distribution and these integrals can therefore be evaluated analytically for Eq. [9]. Unlike the case when only diffusion is present, the flow makes the x -component of Eq. [9] nonzero, because the precession angles $\varphi_1, \dots, \varphi_4$ are no longer all equal. The details of the integration can be found in the Appendix.

One can assume, that to reach a steady state, the system has been excited by infinitely many longitudinal inputs. The transverse signal at any given time can be expressed by adding up all the pathways, from all previous inputs, which are in the transverse plane at the echo time. Hence, the final result for the x -component of the $L \dots LTL \dots LTL \dots LTL \dots LT$ pathways is given by

$$\begin{aligned} \langle M_x \rangle &= \sum_{n=0}^{\infty} \sum_{m=1}^{\infty} \sum_{l=1}^{\infty} \sum_{k=1}^{\infty} \langle M(n, m, l, k)_x \rangle \\ &= M_0 (1 - E_1) \frac{1}{1 - E_1 \cos \alpha} E_1^3 E_2^4 \sin^7 \alpha \\ &\quad \cdot \left[+ \frac{1}{8} \frac{A_D^4 (\sin(4\Delta_\nu) - \sin(3\Delta_\nu) A_D E_1 \cos \alpha)}{D_1^2 (1 - E_1 \cos \alpha)} \right. \\ &\quad - \frac{1}{8} \frac{A_D E_1 \cos \alpha A_D^4 (\sin(3\Delta_\nu) - \sin(2\Delta_\nu) A_D E_1 \cos \alpha)}{D_1^2 (1 - E_1 \cos \alpha)} \\ &\quad + \frac{1}{8} \frac{A_D^{12} (\sin(8\Delta_\nu) - \sin(6\Delta_\nu) A_D^4 E_1 \cos \alpha)}{D_1^2 D_2} \\ &\quad - \frac{2}{8} \frac{A_D E_1 \cos \alpha A_D^{12} (\sin(7\Delta_\nu) - \sin(5\Delta_\nu) A_D^4 E_1 \cos \alpha)}{D_1^2 D_2} \\ &\quad \left. + \frac{1}{8} \frac{A_D^2 E_1^2 \cos^2 \alpha A_D^{12} (\sin(6\Delta_\nu) - \sin(4\Delta_\nu) A_D^4 E_1 \cos \alpha)}{D_1^2 D_2} \right] \quad [11] \end{aligned}$$

where

$$\begin{aligned} D_1 &= (1 - 2 \cos(\Delta_\nu) A_D E_1 \cos \alpha + A_D^2 E_1^2 \cos^2 \alpha) \\ D_2 &= (1 - 2 \cos(2\Delta_\nu) A_D^4 E_1 \cos \alpha + A_D^8 E_1^2 \cos^2 \alpha) \end{aligned} \quad [12]$$

and

$$\Delta_\nu = \gamma G_{\text{eff}} \nu T R^2 \text{ and } A_D = \exp[-bD] \quad [13]$$

where $b = (\gamma G_{\text{eff}} TR)^2 TR$ is the commonly used diffusion factor.

We notice that the steady-state signal has a complex flow dependence and the diffusion attenuation factor, A_D , appears in many different powers. This is because of the fact that the signal is composed of many different pathways that have different time lengths. The flow dependence is obviously periodic because the flow velocity only enters through trigonometric functions. This period can be found from the definition of Δ_v and agrees with earlier definitions of a gradient dependent scale invariant parameter used to quantify the flow sensitivity of SSFP (1,11). As expected, the x -component of the signal vanishes when no flow is present. The expression for the y -component resembles Eq. [11]; however, the flow enters through cosines instead of sinusoids in the nominator. The contribution from the other types of pathways is calculated in exactly the same manner as we have just prescribed.

COMPUTER SIMULATION

We did a computer simulation to verify the PA and to evaluate the flow sensitivity for large T_2/TR ratios, where the PA is inaccurate. It is desirable to have a fast simulation technique for SSFP because the magnetization has to form a steady state and that usually takes several RF cycles. When diffusion and flow are included in the simulation model, the conventional Monte Carlo (MC) and finite difference (FD) methods will usually be very slow (4).

Results from an MC simulation of SSFP in the presence of both diffusion and flow have been published earlier by Tyszka *et al.* (12,14) but they only approximated the effect of diffusion by increasing the transverse relaxation (6). Wu and Buxton (3) have shown that this approximation does not give the correct flip angle dependence of the diffusion sensitivity.

We have developed a new very fast simulation technique, based on a *Conditional random walk* model, which correctly simulates the diffusion and flow without sacrificing computation speed (35,36). This algorithm applies to any pulse sequence and is especially useful in simulating the SSFP sequence or other steady-state sequences such as the missing pulse steady state (MP-SSFP) (16). Not only does the simulation provide the steady-state value but it also shows how the magnetization evolves into the steady state.

Conditional Random Walk

The displacement of freely diffusing spins can be modeled as a “random walk” process. For simulation of SSFP we only need to consider one dimension; along the direction of the effective gradient, however, the following results are readily generalized because contributions to the phase resulting from displacements in orthogonal directions are independent.

We denote the position of the spin by X and its phase by Φ . Then we let x denote the displacement of a spin due to diffusion during time Δt . Similarly we let φ denote the difference in the phase of a freely diffusing spin and a static spin, after some time step Δt . Carr and Purcell (37) showed, by using a random walk model, that x and φ can be written as

$$x = \xi \sum_{j=1}^N a_j \quad \text{and} \quad \varphi = G\gamma\tau\xi \sum_{j=1}^N j a_{(N+1-j)} \quad [14]$$

where ξ is a small instantaneous displacement and $a_i \in (-1, 1)$ is a discrete zero mean random variable that governs the direction of the motion. The time Δt is defined by the very small time step τ and the number of steps N ; that is $\Delta t = N\tau$. The mean of x and φ is zero and their variance is given in ref. 37

$$\sigma_x^2 = \xi^2 N \text{ and } \sigma_\varphi^2 = G^2 \gamma^2 \tau^2 \xi^2 \frac{N(N+1)(2N+1)}{6} \quad [15]$$

For every practical simulation time step, Δt , N will be a large number. By using the well known relation for the diffusion coefficient, $D = \xi^2/(2\tau)$, one obtains

$$\sigma_x^2 = 2D\Delta t \text{ and } \sigma_\varphi^2 = 2\gamma^2 G^2 D\Delta t^3/3 \quad [16]$$

When N is large, both x and φ depend on a sum of a large number of random variables. The *central limit theorem* can then be used to argue that the probability densities $\text{Pr}(x)$ and $\text{Pr}(\varphi)$ are Gaussian and are therefore completely described by their mean and variance.

In a computer simulation both the position and the phase of the spins have to be updated. If we assume the displacement x at time $t + \Delta t$ caused by the diffusion of some particular spin to be known, then we are restricted to a subset of random variables. By using combinatorial analysis (36), we found that the variance and the mean of φ , given the displacement x , can be expressed as

$$\sigma_{\varphi|x}^2 = \frac{1}{4}\sigma_\varphi^2 \text{ and } \overline{\varphi}_{|x} = \gamma G \frac{x}{2} \Delta t \quad [17]$$

One can indeed show that the probability distribution for x and φ , $\text{Pr}(x, \varphi)$, is a joint Gaussian distribution with a correlation coefficient equal to $\sqrt{3}/4$.

Diffusive Attenuation

In the following discussion it is most convenient to use the complex notation, $m_{xy} = M_x + iM_y$. Precession can be calculated by multiplying by $e^{i\gamma G x \Delta t}$ where Δt is the duration of the simulation time step. Spins that move because of diffusion in a linear gradient G will acquire an additional precession angle, φ . The expectation value of the transverse magnetization, m_{xy} , at location X at time $t + \Delta t$ can be described in terms of the magnetization at time t by

$$\overline{m_{xy}(X, t + \Delta t)} = \int_{-\infty}^{\infty} m_{xy}(X - x, t) e^{i\gamma G(X-x)\Delta t} \text{Pr}(x) \int_{-\infty}^{\infty} e^{i\varphi} \text{Pr}(\varphi|x) d\varphi dx \quad [18]$$

This equation explains how the magnetization at X will be influenced by the fraction of magnetization that diffuses from adjacent regions to X . Equation [17] shows that the magnetization from spins that move through a distance x precess as if the velocity was constant but are also attenuated. The attenuation comes from dephasing and is due to the fact that there are many different path trajectories leading to the same displacement x . Mathematically this result is obtained by evaluating the second integral in Eq. [18] and using the fact that $\text{Pr}(\varphi|x)$ is a Gaussian distribution

$$\overline{m_{xy}(X, t + \Delta t)} = \int_{-\infty}^{\infty} m_{xy}(X - x, t) e^{i\gamma G(X-x)\Delta t} \text{Pr}(x) e^{i\gamma G x / 2 \Delta t} dx \cdot e^{-\gamma^2 G^2 D \Delta t^3 / 12} \quad [19]$$

The dephasing term ($e^{(-\gamma^2 G^2 D \Delta t^3)/12}$) represents irreversible relaxation. This result depends on the fact that all the spins experience the same linear gradient. Each spin is statistically equivalent and the system is therefore *ergodic*.

Circular Convolution Method

From Eq. [19] we see that the dynamics of spins in the presence of free diffusion can be simulated correctly by first updating the magnetization using the Bloch equation for static spins and then convolving the magnetization with a diffusion propagator, which we call a *correction-*

kernel, to account for the movements of the spins (36). The correction-kernel is then easily modified to include the effects of bulk flow as well. For a constant magnetic field gradient during some time step Δt the correction-kernel is given by

$$c(x, G, \Delta t) = \frac{1}{\sqrt{2\pi \cdot 2D\Delta t}} \exp \left[\frac{-(x - v\Delta t)^2}{2 \cdot 2D\Delta t} - \frac{\gamma^2 G^2 D \Delta t^3}{12} + i\gamma G \frac{x + v\Delta t}{2} \Delta t \right] \quad [20]$$

As we know from Eq. [6], the magnetization is spatially periodic. We let λ denote the steady-state wavelength which we then discretize with N points. Then we define $m_{xy}[n, t]$ as the transverse magnetization at location $x = n\lambda/N$ at time t and similarly we define $m_z[n, t] = M_z(n\lambda/N, t)$. Although, generally speaking, the spins can diffuse further than one wavelength during the SSFP cycle, we only need to evaluate the magnetization in one wavelength. This is because of the fact that any magnetization that leaves a wavelength-long region from left equals the magnetization that enters from right and *vice versa*. Hence, it is possible to simulate free diffusion by using an N point circular convolution, which will be denoted by $\mathbb{O}$. Between the RF pulses, the simulation algorithm for the transverse magnetization is given by

$$m_{xy}[n, t + TR] = (m_{xy}[n, t] \cdot e^{i2\pi n/N}) \mathbb{O} c[n, G_{\text{eff}}, TR] \cdot E_2 \quad [21]$$

The longitudinal magnetization is updated in the same manner but without any precession

$$m_z[n, t + TR] = m_z[n, t] \mathbb{O} c[n, 0, TR] \cdot E_1 + (1 - E_1)M_0 \quad [22]$$

It is important to point out that these calculations are exact for any large simulation time step Δt (36). In conventional MC and FD methods, however, large simulation time steps cause incorrect phase integration or instability. In practice, both the magnetization and the correction-kernel have to be sampled in space with sufficient density to avoid any aliasing. If we assume the gradient is only on during the first part of the cycle, then two correction-kernels have to be used, the latter with $G = 0$. However, because the magnetization does not precess when the gradient is off, the second simulation step only involves convolution. The two correction-kernels can then be cascaded into a single kernel, that is $c[n, G_{\text{eff}}, TR] = c[n, G, \Delta t] \mathbb{O} c[n, 0, TR - \Delta t]$. This reduces the computation time in simulating SSFP with a pulsed gradient. The RF pulses are calculated by Eq. [2] and the steps in Eqs. [21] and [22] are then repeated between the RF pulses.

Discrete Fourier Transform Implementation

In the SSFP pulse sequence, the effective gradient in each TR cycle is always the same as shown in Fig. 1. This allows us to exploit the spatial periodicity of the magnetization. Before we describe the simulation algorithm, it is useful to define the following N -point discrete Fourier transform (DFT) pairs (38)

$$\begin{aligned} M_{xy}[k, t] &\stackrel{\text{DFT}}{\leftrightarrow} m_{xy}[n, t] \\ M_z[k, t] &\stackrel{\text{DFT}}{\leftrightarrow} m_z[n, t] \\ C[k, G, \Delta t] &\stackrel{\text{DFT}}{\leftrightarrow} c[n, G, \Delta t] \end{aligned} \quad [23]$$

The simulation algorithm represented by Eqs. [21] and [22] can now be written in the Fourier domain as

$$\begin{aligned}
 M_{xy}^{-}[k] &= M_{xy}^{+}[k-1] \cdot C[k, G_{\text{eff}}, TR] \cdot E_2 \\
 M_z^{-}[k] &= M_z^{+}[k] \cdot C[k, 0, TR] \cdot E_1 + N \cdot \delta[k](1 - E_1)
 \end{aligned}
 \tag{24}$$

where $\delta[k]$ is the Kronecker-delta function. The precession simply shifts the spatial harmonics of the magnetization and the convolution is replaced by multiplication. The computation time is much reduced because the number of multiplications is $O(N)$ whereas in convolution the number of multiplications is $O(N^2)$. The expressions for the RF rotation can be found from Eq. [2] and the definition of the DFT (38):

$$\begin{aligned}
 M_{xy}^{+}[k] &= \frac{1 + \cos a}{2} M_{xy}^{-}[k] \\
 &+ \frac{1 - \cos a}{2} M_{xy}^{-*}[-k] + i \cdot \sin a M_z^{-}[k] \\
 M_z^{+}[k] &= \frac{i \cdot \sin a}{2} M_{xy}^{-}[k] - \frac{i \cdot \sin a}{2} M_{xy}^{-*}[-k] + \cos a M_z^{-}[k]
 \end{aligned}
 \tag{25}$$

The asterisk is used to represent the complex conjugate. It should be noted that this DFT simulation algorithm, which is expressed by Eqs. [24] and [25], is in complete harmony with the diagram in Fig. 3. The RF rotation mixes the negative and positive magnetization harmonics and between the RF pulses the precession shifts the harmonics up by one.

In the Fourier domain, the initial condition where the magnetization is in thermal equilibrium is given by

$$M_z[k, 0] = N \cdot \delta[k] \cdot M_0 \text{ and } M_{xy}[k, 0] = 0 \tag{26}$$

The simulation steps in Eqs. [24] and [25] are then repeated until the magnetization reaches its steady state. The detected signal is the average of the zero'th order harmonic, $M_{xy}[0]/N$, because the other harmonics integrate to zero. The higher harmonics, however, contain the amplitudes of the higher order echoes that can be acquired in SSFP (20, 31–33).

PA AND SIMULATION RESULTS

The fourth order partition approximation was evaluated for a range of different parameters. Figure 4 shows how the magnitude of the SSFP echo behaves as a function of flow and diffusion. The flow sensitivity is periodic and symmetrical. We denote the flow period by the aliasing velocity $V_a = \lambda/TR$. The magnitude range of the flow sensitivity is then completely described when the velocity ratio v/V_a ranges from zero to $1/2$. The diffusion sensitivity is then plotted as a function of bD . For the parameters used in Fig. 4, we clearly see that SSFP is more sensitive to flow for a 30° than a 90° flip angle. This is comparable with the diffusion sensitivity (9), which is also higher for smaller flip angles. This can be understood from Eq. [9]. When the flip angle is small, the higher order pathways or stimulated echoes make a significant contribution to the SSFP signal. These echoes are very sensitive to any motion because of their long time path. Hence the steady state is more easily *scrambled* for the smaller flip angles.

We also note that for the 90° flip angle the signal shows a very complex behavior when the diffusion is varied and $v = V_a/2$. At first the signal decreases when the diffusion is increased and reaches a value close to zero. Then, however, increasing diffusion leads to increased signal. Eventually the signal strength will of course start to fall off as the diffusion increases but it is interesting that a certain combination of flow and diffusion causes maximum scrambling of the steady state.

The PA was compared with results from computer simulations. In Fig. 5 we see the agreement is very good for T_2/TR ratios as large as 2. We also note that the match is very good for higher ratios of T_2/TR when the diffusion sensitivity is large. This is similar to our observations on the flip angle behavior. Increasing diffusion decreases the higher order pathways significantly so that their contribution to the signal can be neglected.

EXPERIMENTAL METHODS AND RESULTS

Pulse Sequence with a MRF

A 2D SSFP-echo pulse sequence was implemented on a 1.5T GE Signa imager (General Electric Medical Systems, Milwaukee, WI). The imaging pulse sequence is the same as the one shown in Fig. 1 but without the acquisition of the FID. The flow and diffusion sensitizing gradients therefore followed the RF excitation. In the sequence we also included the moving reference frame (MRF) by varying the phase of the RF pulses (12). For a particular value of the RF flip angle, the steady state of the isochromats is only influenced by the relaxation and the precession. If the magnetization is subject to constant bulk flow, it is easy to see from Eq. [8] that the change in precession angle between subsequent cycles is given by

$$\Delta\phi = \Delta_\nu = 2\pi \frac{V}{V_a} \quad [27]$$

By synchronizing the RF phase with this phase change, it is possible to make those isochromats that are flowing experience the same RF torque as a stationary isochromat does when the RF phase is kept constant. By similar means, the response of a static isochromat in the MRF will equal the response of an isochromat flowing at the opposite velocity, $-\nu$, when the RF phase is kept constant.

In our implementation of the MRF technique, we used the following phase program

$$\begin{aligned} i) \phi_{n+1} &= (\phi_n + \Delta_\nu) \bmod 2\pi \\ ii) \psi_{n+1} &= (\psi_n + \phi_{n+1}) \bmod 2\pi \end{aligned}$$

In this phase program, ϕ_n and ψ_n are used to represent the precession angle and the total accumulated phase in the n th SSFP cycle, respectively.

The phase of the n th RF pulse was set equal to ψ_n ; however, the phase of the receiver followed the phase program of the following RF pulse, ψ_{n+1} . This is easy to understand by “thinking backward in time.” If the phase of the echo did not follow the phase of the following RF pulse, the torque an isochromats experiences from the RF pulses would not be constant and hence there would not be a steady state.

It is worth noting that our imaging sequence is different from the imaging sequence described by Tyszka *et al.* (12) because we acquired the echo (A_{-1}) whereas they used the FID (A_0), which is much less sensitive to flow.

Measurements

The imaging phantom contained three different liquids: water, doped water, and vegetable oil. The longitudinal relaxation, T_1 , was estimated by using a fast spin echo inversion recovery imaging sequence (FSE-IR). Several images were acquired with different inversion time, TI. The implementation of FSE we used acquired four k -lines in each RF excitation. The T_1 values were found by fitting the average image intensity from the three ROIs to the theoretical T_1 saturation curve by using nonlinear least squares. Similarly, the transverse relaxation was

obtained by using SE images with different echo time, TE . For all these measurements TR was set to 9 s. The results for the best fits can be found in Table 1.

To estimate the diffusion constant, a Stejskal-Tanner (39) imaging sequence was used with varied diffusion gradients. The diffusion constant was then estimated from the best least-square fit to the diffusive attenuation as a function of the b value. The diffusion constants for all the ROIs are also given in Table 1.

Instead of using a flow phantom, which can be hard to construct to set up a constant bulk flow, we used the MRF principle described above. By varying the RF phase or the MRF velocity, we could therefore simulate the ideal constant bulk flow for the whole phantom.

Magnitude images with a 20-cm FOV and a 256×256 resolution were reconstructed. Prior to the acquisition, 100 “dummy” cycles were used to allow the magnetization to reach a steady state. For many of the simulated flow rates, low signal intensity was expected. A 1-cm thick slice was therefore used and the number of averages (NEX) ranged from four to eight. The receiver bandwidth was set to be 16 kHz. This was found to be sufficient to make almost all the measured signal intensities well above the noise level, therefore neglecting any possible bias due to the *Rician* distribution of the data (40).

Figure 6 shows how the magnitude of the SSFP echo changes as a function of the flow rate. As expected from the theory, the flow sensitivity is larger (steeper fall off) for the 30° flip angle than for the 90° flip angle. We also see that the water in ROI No. 2 is most sensitive to the flow because it has the longest relaxation times. The absence of the higher order stimulated echoes, which are easily scrambled by the flow, explains the strong flow sensitivity. In the other regions where the relaxation times are smaller, the reduction in the signal due to the flow is less dramatic. Notice the excellent agreement between the experimental data and the theoretical data, which was calculated by a computer simulation. We also see that the experimental data shows the correct symmetry behavior around $v/V_a = 0.5$. In the computer simulation we did not take into consideration the nonidealities of the slice profile. This could easily be done by averaging the theoretical signal over a range of flip angles, using the flip angle distribution of the slice profile. This would result in a slight increase in the flow and diffusion sensitivity (9).

It should be noted that to compare the theoretical and experimental data, the theoretical curve had to be scaled to match with the units of the imager. To do that we used linear least squares to find a single scaling factor that gave the best fit to both the data from the 90° experiment and the 30° experiment. This constant is justified because the amplifier's gain was kept the same for both of the experiments and because the proton density is not subject to change. If each data set had been separately fit, an even better fit could have been obtained, however, it would be a “less honest” fit.

We also analyzed the dependence of the signal as a function of flow with variable diffusion sensitivity. In Fig. 7 we see the results from measurements with two different b factors, 10 s/mm^2 and 50 s/mm^2 . TR was 35 ms and the flip angle was set to 30° . It is clear that in regions with large diffusion, ROI No. 1 and 2, the flow sensitivity changes whereas in ROI No. 3 it is much less affected. Again this agrees very well with what is expected from the theory because the flow response simply tells us how the higher order pathways add together. When the diffusion sensitivity is increased, fewer pathways contribute to the signal and therefore there are less variations in the signal due to changes in the flow velocity.

Pulsatile Flow and Diffusion

In this section we will analyze how the pulsatile motion of the brain, due to cardiac action and respiratory events, influences the measurement of diffusion. It is well known that the brain and cerebrospinal fluid exhibit periodic motion, with peak velocities up to 1 mm/s, in the frequency range of a normal heart rate. The maximum displacement of the brain tissue can therefore be as high as 50 μm (41).

To address the influence of this motion on the diffusion attenuation, we used flow curves, adopted from ref. 41, for of tissue located to the left of the ventricles. Note that the bulk motion in the brain is spatially varying and our reference point is chosen arbitrarily. First we simulated a regular SSFP imaging sequence with hardly any diffusion weighting (DW). We assumed the relaxation parameters of the brain tissue to be $T_1 = 800$ ms, $T_2 = 100$ ms and the diffusion was assumed to be that of water, $D = 2 \mu\text{m}^2/\text{ms}$. To have a uniform pixel intensity, the SSFP wavelength was set to be slightly smaller than a typical voxel size, 24 cm/256. When the repetition time was set to 50 ms, the resulting diffusion sensitivity was close to $bD = 0.01$. Both 30° and 90° flip angles were simulated. The results are shown in Fig. 8 with the corresponding flow curve at the top of the figure. Note that the flow curve has been normalized to the units of the aliasing velocity, V_a , which depends on the SSFP wavelength and the repetition time. The maximum and minimum of the flow are 0.57 mm/s and -0.89 mm/s, respectively. On the plots the time history of the magnitude of the transverse magnetization is shown with a solid line. For a comparison, we also simulated the signal when flow (dashed line) and when both diffusion and flow (dash-dotted line) are ignored. We see that after the magnetization reaches its steady state, there are only very small perturbations from the response of static spins. For the 90° flip angle case, there is no diffusion or flow sensitivity apparent; however, for the 30° flip angle, there is a small attenuation due to diffusion as well as a tiny flow sensitivity. Figure 9 shows the equivalent results when the b factor has been increased to give $bD = 0.2$. Note that this also affects the flow sensitivity, and therefore the flow curve has a different amplitude in units of V_a . Now, we clearly see a very strong diffusion attenuation for both flip angles, and it is also evident that the bulk motion of the tissue causes extra signal loss. This increased signal loss leads to an overestimation of the diffusion attenuation in DW imaging.

One might speculate whether it is possible to reduce the flow sensitivity while maintaining the diffusion sensitivity. The relation $\Delta_v = \sqrt{v^2 \cdot b \cdot TR}$ implies that for a given diffusion sensitivity, b , and flow, v , the flow sensitivity could be minimized by using a small TR . This, however, requires a larger effective gradient to maintain the fixed diffusion sensitivity. We checked this idea by repeating the simulation with a shorter repetition time, $TR = 30$ ms, but keeping the b factor constant and the results are shown in Fig. 10. Our results show that the shorter repetition time not only gives increased flow sensitivity but also diffusion sensitivity especially for the 90° flip angle. This is where one of the complications of SSFP becomes visible, i.e., that the flow and the diffusion sensitivity depend not only on Δ_v and the b factor, respectively, but also on E_1 , and E_2 .

To make the results shown in Figs. 8–10 more quantitative, we calculated the point spread functions (PSF) one would obtain if the last 128 echoes are used in SSFP Fourier imaging. This is simply done by calculating the discrete Fourier transform of the complex SSFP signal. Figure 11 shows the magnitude of the PSFs, in the phase encoding direction, from the simulation with and without flow, for different diffusion sensitivity, TR s and flip angles. The amplitude of the PSF has been normalized with the maximum amplitude of the PSF when both flow and diffusion are ignored. The height of the dashed PSFs is therefore indicative of the theoretical diffusion attenuation. We see from Figs, 11a and 11d that there is only a small distortion from the brain motion in a non-diffusion-weighted SSFP imaging sequence. In Figs, 11b–11f the diffusion sensitivity is $bD = 0.2$ and now it is easy to see the distortion in the PSF. The distortion is more severe for the 30° flip angle in Figs, 11b and 11c than for the 90° flip

angle in Figs. 11e and 11f because smaller flip angles give more sensitivity to diffusion and flow. When the repetition time is 50 ms, as in Figs. 11b and 11e, the overestimation of the diffusion attenuation is 61% and 32% for the 30° and the 90° flip angles, respectively. When the repetition time is decreased to 30 ms, as in Figs. 11c and 11f, the overestimation of the diffusion attenuation is 58% and 33% for 30° and the 90° flip angles, respectively. These results are summarized in Table 2. Thus, for this particular flow curve a reduced repetition time does therefore not reduce the flow sensitivity, if the diffusion sensitivity is kept fixed.

DW-SSFP versus DW-PGSE

We see from Fig. 11 that the overestimation of the diffusion-weighted attenuation is quite severe. It is therefore interesting to compare the artifacts obtained in a DW-SSFP to the artifacts obtained in a diffusion-weighted pulsed gradient spin echo (DW-PGSE) sequence. We assumed the maximum gradient strength to be that of a conventional scanner, 0.01 T/m = 1 G/cm, and we also assumed the separation of the DW gradients to be as small as possible. Given these conditions we used the well known Stejskal-Tanner equation (19) to calculate the necessary gradient duration, to achieve the same diffusion attenuation as in Figs. 11a–11f. From this we estimated the image distortion from the pulsatile bulk flow, in exactly the same manner as we did in the SSFP simulation. To simplify the matter, we ignore phase artifacts from read and phase encoding gradients, which should be relatively small when the diffusion weighting is considerable, i.e., $bD = 0.2$. The peaks of the PSF functions were used as a measure of the diffusion attenuation and from them the error in the estimation was calculated. Both a regular non-gated PGSE and a cardiac gated (ECG) PGSE were considered. For the acquisition of each phase encode, in the non-gated PGSE, we picked an arbitrary flow value from the flow curve in Fig. 8. For the ECG simulation we synchronized the acquisition with the large negative peaks of the flow curve. The results are summarized in Table 2.

Table 2 shows that the errors in DW-PGSE for *in vivo* diffusion assessment are comparable with SSFP despite the more complicated signal dependence of SSFP. By using cardiac gating, however, it is possible to reduce the errors dramatically. This results in longer acquisition time because of the need for a long repetition time, to minimize artifacts that may arise from variable spin lattice relaxation between RF excitations. Because SSFP is a driven equilibrium technique with RF pulses being applied at a constant rate, cardiac gating is not possible. Even with the ECG in PGSE, we are still left with some errors because of the phase variations in the signal. The only way to avoid this problem is to acquire the image in a single-shot, such as in EPI (42). The use of a navigator echo has been suggested (43,44) to reduce the phase artifacts in DW-PGSE. The correction scheme used with these navigators, however, assumes the motion of the brain to be that of a rigid object and cannot take into account the more complicated spatial variations of the brain motion (41).

The Analogy of Flow in SSFP and RF Spoiling

The phase program of the MRF turns out to be identical with the phase pattern commonly used to eliminate the transverse magnetization in many fast low flip angle imaging pulse sequences (22,24) such as FLASH. Constant bulk flow, therefore, causes identical spoiling of transverse magnetization as does RF spoiling. On one hand this tells us that when the SSFP echo signal is totally scrambled because of bulk flow, the SSFP-FID signal equals the theoretical FLASH signal, which is easily calculated from the steady-state solution by setting E_2 equal to zero. On the other hand, the SSFP echo flow curves tell us how effective the spoiling of the transverse magnetization is. A phase change increment of 117° is commonly used to do RF spoiling (22). The effectiveness of the spoiling of the transverse magnetization can be easily seen from Figs. 6 and 7 where $v/V_a = 117^\circ/360^\circ$. Hence by using the pulse sequence with an MRF, described in this paper, one can measure whether adequate spoiling can be achieved. The

figures clearly indicate that the effectiveness of RF spoiling depends on the flip angle, the tissue relaxation parameters, as well as the diffusion coefficient.

CONCLUSION

In this paper we have shown how a partition analysis can be used to obtain an analytical approximation of the simultaneous flow and diffusion sensitivity in SSFP imaging. This approximation was found to be accurate for T_2/TR ratios as large as two and for even larger T_2/TR ratios when diffusion sensitivity is considerable. More significant though is the physical understanding it provides about the signal formation in SSFP. We then introduced a novel discrete Fourier transform simulation technique, based on a conditional random walk model and circular convolution, which allowed us to simulate both flow and diffusion quickly and accurately for cases where the analytical approximation is inaccurate.

A 2D SSFP echo imaging pulse sequence with an MRF was implemented on our imaging system, and we used it to obtain experimental data from a phantom. The MRF technique allowed us to make more accurate comparison between our measurements and the theoretical values because experimental nonidealities due to things such as vortices and laminar flow were avoided. The phantom contained three different solutions with very different relaxation and diffusion properties. An excellent agreement was found between the theory and the experimental data.

Our analysis shows that the flow sensitivity is larger for smaller flip angles than for larger flip angles. An SSFP imaging pulse sequence that is made maximally sensitive to diffusion (9) is also inherently very sensitive to bulk flow as well. Also, if the tissue undergoes bulk movements, whose size is on the order of the SSFP wavelength, the scrambling of the steady state will lead to additional signal loss and therefore an overestimation of the diffusion-related attenuation. This we demonstrated by using experimental data and our simulation algorithm to calculate the simultaneous effect of pulsatile *in vivo* brain motion and diffusion. The overestimation in SSFP was found to be similar to those in a PGSE sequence.

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APPENDIX

By using Eq. [8] the precession angle for each of the four transverse pathways can be written as

$$\begin{aligned}
 \varphi_1 &= \varphi \\
 \varphi_2 &= \varphi + ((m+1)\Delta_v + \delta_m + \delta_1) \\
 \varphi_3 &= \varphi + ((m+l+2)\Delta_v \\
 &\quad + \delta_m + \delta_1 + \delta_l + \delta_2) \\
 \varphi_4 &= \varphi + ((m+l+k+3)\Delta_v \\
 &\quad + \delta_m + \delta_1 + \delta_l + \delta_2 + \delta_k + \delta_3)
 \end{aligned} \tag{A1}$$

where $\Delta_v = \gamma G_{\text{off}} v TR^2$ and in general $\delta = \gamma G_{\text{eff}} TR \Delta x$. The random variables δ_1 , δ_2 , and δ_3 are changes in the precession angle because of diffusion during only one SSFP cycle. The random variables δ_k , δ_l , and δ_m are, however, changes due to k , l , and m SSFP cycles, respectively. The variance of δ_k is therefore k times larger than the variance of δ_1 and so on. According to Eq. [16] the variance of the particle displacement, Δx , during one SSFP cycle is given by $2D TR$. For a zero mean Gaussian probability distribution, we find that

$$\begin{aligned}
 &\frac{1}{2\pi} \int_0^{2\pi} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \left(\prod_{j=1}^4 \cos(\varphi + \Delta_j + \delta_j) \Pr(\delta_j) \right) \\
 &\quad \cdot d\delta_1 d\delta_2 d\delta_3 d\delta_4 d\varphi \\
 &= \frac{1}{8} [\cos(\Delta_1 - \Delta_2 - \Delta_3 + \Delta_4) \exp(-\text{var}(\delta_1 - \delta_2 - \delta_3 + \delta_4)/2) \\
 &\quad + \cos(\Delta_1 - \Delta_2 + \Delta_3 - \Delta_4) \exp(-\text{var}(\delta_1 - \delta_2 + \delta_3 - \delta_4)/2) \\
 &\quad + \cos(\Delta_1 + \Delta_2 - \Delta_3 - \Delta_4) \exp(-\text{var}(\delta_1 + \delta_2 - \delta_3 - \delta_4)/2)]
 \end{aligned} \tag{A2}$$

Note that when there is a uniform distribution of precession angles, the signal from an odd number of transverse pathways is always zero because

$$\frac{1}{2\pi} \int_0^{2\pi} \prod_{i=1}^n \cos(\varphi + \Delta_i) d\varphi = 0 \text{ for } n = 1, 3, 5, \dots \quad [\text{A3}]$$

By using the identity in Eq. [A2], we can evaluate the average magnetization of Eq. [9]. We see from Eqs. [A2] and [9] that we only need to know the mean and the variance of the three different combinations of the four precession angles, $\varphi_1, \dots, \varphi_4$. The mean is only a function of the bulk flow and is deterministic whereas the variance is due to the stochastic nature of the diffusion. Table 3 shows how the mean and the variance add together for the different combinations of the four precession angles. Note that the variances always add, independent of the signs of the angles. Combining Eqs. [9] and [A2] with the results in Table 3 gives

$$\begin{aligned} \langle M(n, m, l, k)_x \rangle &= M_0 (1 - E_1) \\ &\cdot (E_1 \cos \alpha)^{n+m+l+k-3} E_1^3 E_2^4 \sin^7 \alpha \\ &\cdot \left[+\frac{1}{8} (\sin(-m-k)\Delta_\vee) A_D^{m+k+2} \right. \\ &\quad - \sin(-(m+k+2)\Delta_\vee) A_D^{m+k+2} \\ &\quad \left. - \sin(-(m+2l+k+4)\Delta_\vee) A_D^{m+4l+k+6} \right] \end{aligned} \quad [\text{A4}]$$

where $A_D = \exp[-bD]$ and $b = (\gamma G_{\text{eff}} TR)^2 \text{TR}$.

The total transverse signal at any given time can be expressed by adding up all the pathways from all previous inputs, which are in the transverse plane at the echo time. Hence, the final result for the x -component is given by Eq. [11].

FIG. 1.

An SSFP pulse sequence with flow and diffusion sensitivity in all three directions. The effective gradient, which determines the diffusion sensitivity, has to be kept constant in each SSFP cycle to establish a steady state. This is accomplished by rewinding the phase encoding gradient, which amplitude varies from cycle to cycle.

FIG. 2.

A discrete-state model for the Bloch equation in SSFP. Spin-lattice relaxation can be considered as an input, entering the spin system just before each RF excitation.

FIG. 3.

This diagram represents the partition of a single vector impulse that enters the system in Fig. 2. A particular pathway, TTLTT, is shown with a thick line. Between the RF pulses the precession angle, ϕ , increases by $r \cdot k_{eff}$. The RF pulse splits each vector into three new vectors. Pathways that cross the zero phase line represent the parts of the original impulse magnetization vector whose phase is reduced to zero. Only those parts contribute to the echo.

FIG. 4.

The sensitivity of SSFP echo magnitude signal plotted as a function of diffusion (bD) and flow (v/V_a). At left $\alpha = 30^\circ$ and on the right $\alpha = 90^\circ$. $T_1/TR = 10$ and $T_2/TR = 2$.

FIG. 5.

The 4th order partition analysis (PA) compared with results from computer simulation. The solid and dashed lines show the results from the PA without and with diffusion, respectively. The circles and the asterisks represent the corresponding values from the simulation. $T_1/T_2 = 5$ and $\alpha = 60^\circ$.

FIG. 6.

The SSFP echo magnitude signal as a function of the MRF velocity for two different flip angles, 30° and 90°. Theory is shown as a solid line and measurements as asterisks. The signal intensity is in arbitrary imager units and the standard deviation of the measurements is less than the size of the asterisks. $TR = 30$ ms and $b = 10$ s/mm².

FIG. 7.

The SSFP echo magnitude signal as a function of the MRF velocity for two different b values, 10 s/mm^2 and 50 s/mm^2 . Theory is shown as a solid line and measurements as asterisks. The signal intensity is in arbitrary imager units and the standard deviation of the measurements is less than the size of the asterisks. $TR = 35$ ms and the flip angle is 30° .

FIG. 8.

Top: *In vivo* motion of brain tissue to the left of the ventricles, adopted from Maier *et al.* (41). Maximum and minimum flow rates are 0.57 mm/s and -0.89 mm/s respectively. Middle: Results of simulation, showing the magnitude of the transverse magnetization with $T_1 = 800$ ms, $T_2 = 100$ ms, $bD = 0.01$, $TR = 50$ ms, and 30° flip angle. The dot-dashed line shows the results when both diffusion and flow are ignored. The dashed line shows the results when only flow is ignored. The solid line shows the results when both flow and diffusion are taken into account. Bottom: Same as above except for a flip angle of 90° .

FIG. 9.

Same as in Fig. 8 except for a larger b factor, $bD = 0.2$. A 30° flip angle (middle) is compared with a 90° flip angle (bottom).

FIG. 10. Same as in Fig. 9 except for a shorter repetition time, $TR = 30 \text{ ms}$. A 30° flip angle (middle) is compared with a 90° flip angle (bottom).

FIG. 11.

The magnitude of the point spread functions in the phase encoding direction, for the cases considered in Figs. 8 and 9. The dashed line shows the PSF when flow is ignored, and the solid line shows the PSF when both flow and diffusion are considered. The PSFs are normalized by the maximum of the PSF when both flow and diffusion are ignored to show the theoretical diffusion attenuation, (a) $bD = 0.01$, $TR = 50$ ms, and $\alpha = 30^\circ$. (b) $bD = 0.2$, $TR = 50$ ms, and $\alpha = 30^\circ$. (c) $bD = 0.2$, $TR = 30$ ms, and $\alpha = 30^\circ$. (d) $bD = 0.01$, $TR = 50$ ms, and $\alpha = 90^\circ$. (e) $bD = 0.2$, $TR = 50$ ms, and $\alpha = 90^\circ$. (f) $bD = 0.2$, $TR = 30$ ms, and $\alpha = 90^\circ$.

Table 1
Relaxation Times and Diffusion Constants Estimated for the Different ROI in the Phantom

	ROI No. 1	ROI No. 2	ROI No. 3
T_1/ms	90	2500	190
T_2/ms	75	2050	150
$D/(\mu\text{m}^2/\text{ms})$	2.1	2.0	0.02

ROI No. 1 is doped water, ROI No. 2 is water, and ROI No. 3 is vegetable oil.

Table 2

Error in the Estimation of the Diffusion Attenuation Relative to the Theoretical Diffusion Attenuation for the Cases Considered in Fig. 11

PSF No.	DW att.	SSFP err. %	PGSE err. %	ECG-PGSE error %
a)	0.94	7	3	0.5
b)	0.40	61	64	14
c)	0.33	58	72	18
d)	0.98	2	0.5	0.1
e)	0.69	32	25	5
f)	0.62	33	34	7

The SSFP, PGSE, and the cardiac gated PGSE all have the same theoretical diffusion attenuation (DW att.).

Table 3

Mean of the Accumulated Flow Phase and the Total Variance of the Phase Due to Diffusion, Expressed as Function of k , l , and m

	$\phi_1 - \phi_2$	$\phi_1 - \phi_2 - \phi_3 + \phi_4$	$\phi_1 - \phi_2 + \phi_3 - \phi_4$	$\phi_1 + \phi_2 - \phi_3 - \phi_4$
Mean/ Δ_v	$-(m+1)$	$-(m-k)$	$-(m+k+2)$	$-(m+2l+k+4)$
Var/ bD	$m+1$	$M+k+2$	$m+k+2$	$M+4l+k+6$