Pulse Sequence Modules II: Tagging, Labeling, Diffusion Sensitization & MT

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Highlights

- Motion in the body can be probed over a very wide range of scales using MRI, from molecular motion through magnetization transfer, to diffusion, to blood flow and cardiac motion.
- Motion encoding methods can be usefully categorized into those that modulate longitudinal magnetization, and those that modulate transverse magnetization.

Objectives

- To understand precisely what information is (and is not) provided by each method, so that the methods can be selected and interpreted objectively.
- To understand the capabilities and limitations of each method, so that each can be prescribed with optimal utility and realistic expectations.

Introduction to Motion Encoding

In most MRI imaging methods, linear gradient fields provide the primary means of obtaining spatial information from which to reconstruct the image. Other spatial encoding methods include the use of inhomogeneous RF reception fields in RF coil arrays, along with parallel imaging reconstruction methods.

The application of linear gradients can be though of as a means of moving about K-space, thereby generating Fourier coefficients to be detected by the RF receive coils. We consider here the further use of gradient fields as well as other pulse sequence modifications for the generation of motion related image contrast.

Gradients fields only operate on transverse magnetization. They change the local Larmour frequency, and thereby the local phase of spins. When used in conjunction with RF pulses to nutate magnetization, Mxy and/or Mz can be modulated using gradient pulses.
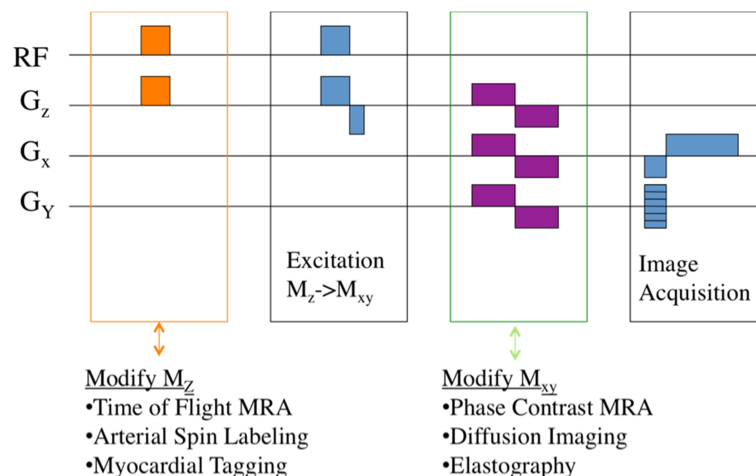
A prototypical pulse sequence shown schematically above. The portion that deals

directly with excitation and spatial encoding is show in blue, and has two phases. The first uses a combination of RF and gradient pulses to excite spins, converting longitudinal magnetization to observable transverse magnetization, and the second uses additional imaging gradient pulses to spatially encode the magnetization for signal detection and image reconstruction.

Prior to the excitation phase, there is an opportunity to modify the spatial distribution of longitudinal magnetization to generate motion related contrast. Examples of methods in this category include: time-of-flight MR angiography; arterial spin labeling; and myocardial tagging.

After excitation but before data acquisition, existing transverse magnetization can be manipulated using only gradient pulses to provide another source of motion contrast. Methods in this category include: phase contrast MR angiography; diffusion imaging; and elastography.

Motion in the Body

The scale and key properties of relevant classes of motion in the body are tabulated below.

Mechanism	Scale	Characteristics
Self Diffusion	$50\mu m\sqrt{t}$ for t in seconds	Mean displacement is zero Can be anisotropic
Blood Flow	1mm/s – 1m/s	Unidirectional on the sub-second scale Can be plug, laminar, turbulent
Externally applied (elastography)	Typically 1mm/s	Frequency can be accurately controlled Typically ~50μm displacement at 200Hz
Cardiac Motion	0-10cm/s	Complex but approximately periodic (~1Hz)

Motion Contrast using modification of Mz:

In these methods, the basic principle is the use of a combination of RF and gradient pulses to create a spatial modulation of longitudinal magnetization, and observe the effects of the transport of these 'tagged' spins from one location to another. Because they are based on modulation of Mz, the time constant for the decay of the generated tag is T_1, which then determines the maximum time scale for these methods.

Time of Flight MRA: In this method, the goal is to maximize the conspicuity of vessels by manipulating the imaging parameters in a conventional imaging sequence. A fast gradient echo sequence is used with a large flip angle and short TR, such that the steady state magnetization in static spins in the imaging volume is low. Blood flow continually transports relaxed blood spins into the imaging volume, and the blood flowing inside the vessels therefore tends to have larger longitudinal magnetization (and MR signal) than surrounding static tissue. Simple image processing methods such as Maximum Intensity Projection then serve to exclude non-flowing spins from the final image.

Arterial Spin Labeling: This class of methods is similar in principle to time of flight

MRA in that spatially selective RF pulses are used to generate a difference in Mz between upstream blood and the tissue of interest. In the case of MRA, the pulses that generate the contrast are the imaging pulses themselves, and the contrast is between relaxed inflowing blood and saturated tissue spins. In ASL, upstream blood is 'labeled', typically using inversion pulses, and a delay is inserted into the sequence to allow for the tagged blood to reach the target tissue. In this case, the goal is not to resolve the vessels themselves, but to measure the amount of tagged blood delivered to the tissue, and to calculate tissue perfusion from this measurement. Because the focus is often on quantitation of tissue perfusion, most ASL pulse sequences carefully control the dimensions of the bolus of magnetically tagged blood, insert long pulse sequence delays to allow for complete inflow of tagged blood into the region of interest, and incorporate signal calibration methods to quantify the absolute amount of blood delivered.

Myocardial Tagging: Measuring the mechanics of myocardial contraction is of great diagnostic value in many diseases of the heart. In this class of methods, a spatial modulation of the longitudinal magnetization of the myocardium is generated, typically in a radial or rectangular grid, using combinations of RF and gradient pulses. After the heart proceeds to a different phase of the cardiac cycle, an image is acquired in which the pattern of magnetization that has been 'painted' into the myocardium is still visible. From these images the local displacements of the myocardium can be visualized and/or calculated.

Motion Contrast using modification of Mxy:

In the presence of a gradient field G(t), the phase $\phi(t)$ of a spin at location r(t) can be described by:

$$\phi(t) = \int_0^t \gamma \vec{G}(\tau) \bullet \vec{r}(\tau) d\tau$$
$$= \int_0^t \gamma \vec{G}(\tau)(\vec{r}_0 + \vec{V}\tau + ...) d\tau$$
$$= \vec{r}_0 \bullet \vec{M}_0(t) + \vec{V} \bullet \vec{M}_1(t) + ...$$

where

$$\vec{M}_0(t) = \vec{k}(t) \equiv \int_0^t \gamma \vec{G}(\tau) d\tau$$
and
$$\vec{M}_1(t) \equiv \int_0^t \gamma \vec{G}(\tau) \tau d\tau$$

and V is the local velocity. Acceleration and higher order terms have been ignored.

M_0, or the zeroth moment of the gradient, is also known as a displacement in K-space. It is the time integral of the gradient (times γ) and is used to sample the Fourier coefficients of the object for basic image formation.

M_1, or the first moment of the gradient, produces a phase shift that is proportional to the velocity.

Motion Encoding Gradients

The basic gradient waveform for providing motion sensitivity is the bipolar gradient pulse:

The key property of this pulse is that M_1 is large, while M_0 is zero. This allows this pulse to be inserted into an imaging sequence, generating
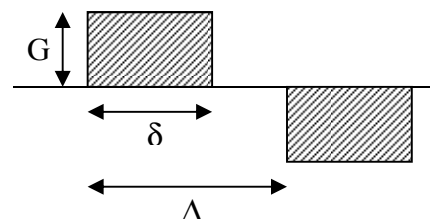
motion related phase shifts, but with nominally no effect on image acquisition. The first half of this pulse generates a linear phase modulation in the direction of the gradient vector, and the second reverses this modulation. If motion along the gradient occurs during the pulse, then the phase modulation is incompletely unwound, leaving a residual phase shift. For this pulse, $M_1=\gamma G\delta\Delta$, and the phase shift is $\phi=M_1V=\gamma G\delta\Delta V$.

As an example, consider a bipolar gradient pulse with an amplitude that is typical for the peak gradient in a modern scanner, a duration that is small compared to the T_2 of most tissues, and a velocity that is typical of arterial flow:

For G=4G/cm, δ=1ms, Δ=2ms, V=10cm/s, $\phi\approx$120 degrees

Thus, for velocities on this order, using gradient pulses that result in minimal additional T2 decay, it is straightforward to generate large and easily measured phase shifts.

Phase Shift Based Motion Sensitive MR imaging Methods:

In these methods, the basic effect is the generation of phase shifts from motion along gradients. Because the contrast comes from phase shifts in transverse magnetization, the time scale for the generation of contrast is limited by T_2 decay.

Diffusion Imaging: In this application, bipolar gradients are used to produce motion related phase shifts in individual spins. However, because the net movement of a group of spins due to diffusion is zero, there is no net phase shift in the MR signal of a group of spins. Instead, phase dispersion across the spins causes signal attenuation, and the local diffusion coefficient can be calculated from this measured attenuation. The attenuation S/S_0 is related to the diffusion coefficient D by $S/S_0 = e^{-bD}$, where b is a pulse sequence dependent diffusion weighting factor. For the bipolar gradient shown above, $b = \gamma^2 G^2 \delta^2 \left(\Delta - \delta/3\right)$. Note that b has a higher order dependence on both time and gradient amplitude than the flow moment M_1. One can calculate from these expressions the gradient pulses required to generate a particular level of diffusion related attenuation, but the order of the effect can be appreciated from the flow moment. For the example bipolar gradient shown above, the duration is 2ms, and the RMS diffusion related displacement is approximately $\sqrt{\langle x^2 \rangle} = \sqrt{2Dt} \approx 2\mu m$ for brain tissue where D=10^{-3}mm^2/s. This gives an average velocity of 2μm/2ms=0.1cm/s, and a phase shift of (0.1/10)*120degrees=1.2 degrees, which is not enough to generate significant attenuation from phase dispersion. Thus, diffusion weighting gradients typically need to be 1-2 orders of magnitude larger than flow weighting gradients in order to generate measurable signal attenuation. For this reason, diffusion imaging often requires echo times that are longer than desired for image contrast, and pushes gradient hardware to the limits.

Phase Contrast MRA: This method is a straightforward application of motion encoding gradients within an imaging sequence. Bipolar gradients are typically added to a fast gradient recalled imaging sequence, and the phase of the image is directly proportional to the local velocity. Only the component of velocity that is along the direction of the applied gradient is measured in each image. Taking phase contrast MRA a step further, one can apply a range of flow encoding gradients, thereby inducing a range of flow related phase shifts. A Fourier transform across flow encoding steps then resolves a spectrum of velocities for each voxel.

MR Elastography: In this relatively new imaging method, acoustic shear waves are introduced into the body using an external apparatus with carefully controlled frequency and phase. These produce standing waves in the body, and the local wavelength provides an indication of the local shear modulus. This parameter has been shown to be of diagnostic value in several clinical applications. The standing waves are imaged using the principles of phase contrast MRA, but because the displacement is periodic rather than uni-directional, one can apply periodic motion encoding gradients, tuned to the vibration frequency, and thereby selectively sensitize the sequence to the applied vibrations, while filtering out other sources of motion.

Magnetization Transfer

The MR signal that is detected in MR imaging comes almost exclusively from hydrogen nuclei residing in water and fat molecules in the body. There are also many hydrogen atoms residing in macromolecules in most tissues, but the restricted motion of the macromolecular environment results in rapid transverse relaxation, with T2 values that are typically less than 1ms. Water molecules that are tightly bound to macromolecules can also experience restricted motion and rapid transverse relaxation. These nuclei are typically not observed by MRI because their T2 values are much shorter than TE for most imaging methods. However, even without observing the signal from these nuclei directly, the presence of these macromolecules can be detected, and converted into image contrast through magnetization transfer (MT). To generate MT contrast, macromolecular spins are saturated by RF irradiation, but not observed directly. Instead, time is allowed for magnetization to transfer between macromolecules and water, through a group of mechanisms collectively known as saturation transfer. The modulation of the longitudinal magnetization of water is observed, producing image contrast that is dependent upon the size of the macromolecular pool, and exchange properties between this and the water pool. Selective saturation of the macromolecular pool is possible because the width of the frequency spectrum of the macromolecular spins, which is inversely proportional to T2, is much broader than that of the free water spins, and off-resonance RF irradiation can therefore selectively saturate macromolecular spins without directly perturbing free water spins. A typical MT experiment involves a period of off-resonance RF irradiation, followed by a waiting period for saturation transfer, and then a conventional MRI pulse sequence that measures the prepared magnetization. Examples of applications for MT contrast include discrimination between pathological tissues with different macromolecular content, and selective saturation of background signals in MR angiography, where the tissue of interest (blood) has much lower MT effects than the background tissue.