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A Method to Correct the Voxel Size in PRESS Localized NMR Spectroscopy

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Abstract

Two techniques commonly used on human magnetic resonance spectroscopy systems to obtain spectra from localized volumes in the brain are point resolved spectroscopy (PRESS) and stimulated echo acquisition mode (STEAM) spectroscopy. PRESS gives a signal twice as large as that obtained with STEAM, but suffers from longer minimum echo times. While STEAM must be used to detect species with short spin-spin relaxation times, PRESS can be used for species with longer relaxation times to give a spectrum with a better signal to noise ratio. Only STEAM was provided for the GE Omega 4.7 T small animal imager used in this laboratory. Therefore, a PRESS pulse program was written for this instrument. With the standard sequence, the sampled voxel is smaller than the prescribed voxel. A larger voxel can be prescribed to increase the sampled volume. A different approach, involving the modification of the gradient strength, has been used in this laboratory. The resulting pulse sequence, with representative profiles, is discussed.

Introduction

A phosphorus-31 spectrum of muscle introduced *in vivo* nuclear magnetic resonance (NMR) spectroscopy in 1980 (Cady, 1990). An *in vivo* spectrum from rat brain followed in 1983. By 1986, several techniques for obtaining *in vivo* spectra had been developed [Bottomley, 1986]. Two popular techniques for obtaining *in vivo* proton NMR spectra are point resolved spectroscopy (PRESS), which was introduced in 1984 (Bottomley, 1984; Ordidge, et. al., 1985), and a similar technique, stimulated acquisition mode (STEAM) spectroscopy, which was described in a 1987 publication (Frahm, et. al., 1987). Both of these techniques are used with commercial magnetic resonance imagers. They are not as routinely used with small animal imagers.

Theory

Nuclei precess in a magnetic field at the Larmor frequency, which depends on the magnetic field strength:

$$\omega_0 = \gamma B_0, \quad (1)$$

where ω_0 is the frequency, γ is the magnetogyric ratio, and B_0 is the magnetic field strength. The magnetogyric ratio for a given nucleus must be determined experimentally.

In the field, a small excess of the nuclei align themselves so that the z components of their magnetic vectors are coaxial with the field. The system has a net magnetic moment,

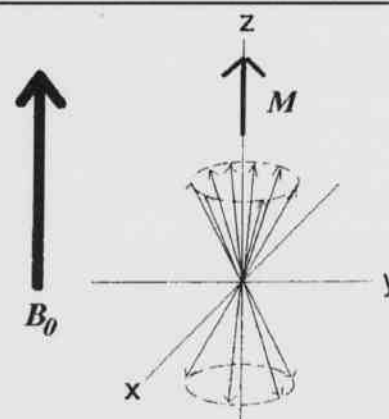


Fig. 1. In an ensemble of spins, a small majority is in the lower energy state. This results in a net magnetic moment, \mathbf{M} , aligned with the main magnetic field, \mathbf{B}_0 .

\mathbf{M} , which is aligned with the external \mathbf{B}_0 field, as shown in Fig. 1.

If an additional field, \mathbf{B}_1 , is introduced into the system, a new effective field, \mathbf{B}_{eff} , is generated. At equilibrium, the net magnetic moment will align itself with \mathbf{B}_{eff} and the individual nuclei will precess at a frequency given by

$$\omega = -\gamma B_{\text{eff}}, \quad (2)$$

where B_{eff} is the magnitude of \mathbf{B}_{eff} .

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Let B_1 oscillate at the Larmor frequency, ω_0 , and introduce new coordinate axes which rotate at the same frequency. The new axes are denoted x' , y' , and z' and are related to the stationary axes as follows: the z and z' axes are coincident, while x' and y' rotate about z . In this rotating frame of reference, B_1 appears stationary and the B_0 field disappears (Farrar and Becker, 1971). In the rotating frame, the net magnetic moment rotates about the B_1 field.

For example, let B_0 be oriented along the z -axis and let B_1 coincide with the x -axis. In the rotating frame, M will experience a torque from the B_1 field and rotate onto the negative y axis, as shown in Fig. 2.

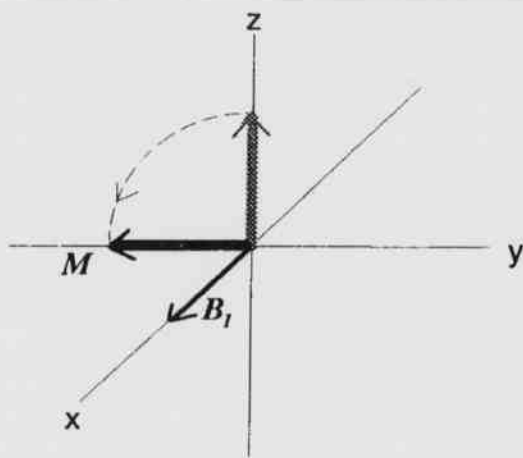


Fig. 2. A B_1 field oscillating at the Larmor frequency is applied along the x -axis. M rotates around the x -axis as long as the B_1 field is applied. Here, M has rotated 90° .

In the rotating frame, the angle through which the magnetization rotates is given by

$$\theta = \omega t = \gamma B_1 t \quad (3)$$

where t is the length of time the field is present and B_1 is its magnitude. A pulse of radio frequency (RF) energy at the Larmor frequency provides the B_1 field. If the pulse is long enough to rotate M by 90° , it is called a 90° pulse. Any desired flip angle can be generated by varying the time for which the RF energy is applied.

After M has been tipped into the xy plane and the B_1 field is removed, the spins return to their original alignment along the z axis. This process is called relaxation. There are two time constants associated with relaxation: the spin-lattice relaxation time, T_1 , and the spin-spin relaxation time, T_2 . The spin-lattice relaxation time is a measure of how long it takes for magnetization along the z axis to recover; the spin-spin relaxation time is a measure of how long magnetization persists in the xy plane. In general, T_1 refers to exponential growth and T_2 refers to exponential decay of the rel-

evant magnetization.

A potential problem with NMR is that the pulse excites a range of frequencies. Theory shows that the bandwidth of a simple on-off pulse is approximately equal to the inverse of the pulse length (Farrar and Becker, 1971). If the pulse length is very short, the bandwidth is broad and spins with largely differing Larmor frequencies are excited. If the pulse is very long, spins with only a narrow distribution of Larmor frequencies will be excited. In *in vivo* spectroscopy, the distribution of frequencies is used to achieve spatial localization.

The frequency response of a pulse is approximated by the Fourier transform of its shape in the time domain. The Fourier transform of a rectangular pulse is a sinc function centered at the RF frequency of the pulse. Other frequencies, contained in the middle and side lobes of the response, are also excited. For many purposes, such a broad excitation is undesirable. To excite a plane of spins, for example, the frequency response should be a well-defined rectangular function.

One of many approaches to defining the frequency response is to Fourier transform the desired response. The resulting function is then used to modulate the RF pulse. Since the transform of a rectangular function is a sinc function, a sinc shaped RF pulse gives a more nearly rectangular excitation.

When shaped RF pulses are used, the flip angle is adjusted by changing the power of the pulse. This corresponds to altering the amplitude of the B_1 field. A 90° power level, rather than a 90° pulse width, is defined.

Localization

Localized NMR experiments must include some means of identifying the position from which the signal originates. Gradients are used in conjunction with the RF pulse to localize the signal.

A gradient is a linearly varying magnetic field that is applied in addition to the B_1 and B_0 fields. Let the strength of this gradient be represented as kx , for a gradient along the x axis of magnitude k . The effective field strength is given by

$$B_{\text{eff}} = B_0 + B_1 + kx \quad (4)$$

Since $\omega = \gamma B_{\text{eff}}$, the Larmor frequency now is proportional to kx . Spins at different x locations will have different Larmor frequencies. Only those spins with Larmor frequencies in the bandwidth of the RF pulse will be affected. Since frequency now depends on position, bandwidth now corresponds to a range of x values.

Consider a gradient for which k is 1 gauss/cm (G/cm), as shown in Fig. 3. Let γ for the nucleus of interest be 4

kHz/G and suppose a 1 ms hard pulse is applied. The bandwidth is then 1/1 ms or 1 kHz. Spins with frequencies ± 1 kHz from the center frequency will be excited. The gradient corresponds to a frequency change of 4 kHz/cm, so the pulse excites a 0.5 cm length of spins along x . Since the object to be imaged is three dimensional, a 0.5 cm thick plane of spins perpendicular to the x -axis has been selected.

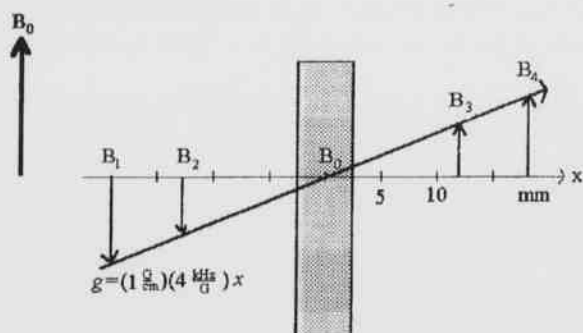


Fig. 3. A 1 ms pulse in the presence of a 1 G/cm x gradient is applied to a system with a magnetogyric ratio of 4 kHz/G. Since the slope of the gradient is 4 kHz/cm, the +1 kHz of excited frequencies centered about $\omega_0 = -\gamma B_0$ is mapped into a slab of spins 0.5 cm thick. The shading represents the area of excited spins.

If a gradient subsequently is applied in the y direction, with a concurrent RF pulse, two planes of spins will be excited. Only along the intersection of those planes will the spins have experienced both pulses. Applying a third gradient along z , with a simultaneous RF pulse, will selectively excite the intersection of three planes. Figure 4 illustrates this intersection, or voxel.

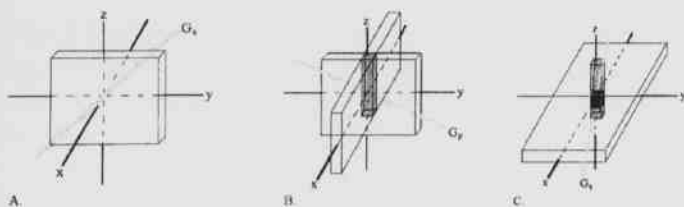


Fig. 4. A. Use of only the x gradient to select a slab of spins. B. Addition of the y gradient selects a column of spins, as indicated by the shaded region. C. Addition of the z gradient selects a box, as shown by the black region in the center. The x and y planes have been omitted for clarity. In all cases, the direction of the gradient is indicated by the dotted line.

The signal collected after the final RF pulse can be Fourier transformed to give a spectrum from the excited voxel. However, spins outside the voxel may contribute to the magnetization in the xy plane at the end of the experiment. Additional gradient pulses are needed to isolate the voxel.

Any sequence that uses multiple RF pulses generates a series of echoes. Hahn showed that, for a sequence of three pulses, a total of five echoes may be generated (Hahn, 1950). Two sequences that utilize these echoes are stimulated echo acquisition mode (STEAM) spectroscopy and point resolved spectroscopy (PRESS).

STEAM uses three 90° pulses to localize the voxel and, therefore, acquires a stimulated echo (Hahn, 1950). PRESS uses a 90° pulse followed by two 180° pulses and acquires a spin echo. The stimulated echo is only half as large as a spin echo acquired from the same region [Hahn, 1950], but the STEAM sequence is preferable for collecting spectra from species with short T_2 's. PRESS, however, is the preferred sequence if some T_2 relaxation is permissible in the experiment.

Point Resolved Spectroscopy

Point resolved spectroscopy uses three RF pulses and three gradients to choose a voxel. Figure 5 is a timing diagram for the sequence. The length of time between the first two pulses determines the echo time (TE), which is the interval between the center of the first RF pulse and the start of data acquisition.

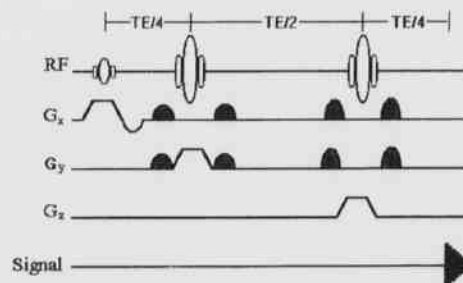


Fig. 5. The PRESS timing diagram.

The first RF pulse is a sinc shaped 90° pulse, which is applied with an x gradient. This causes the spins within a plane perpendicular to the x axis to rotate onto the negative y axis. During $TE/4$, the interval between the first two pulses, the spins dephase by an amount $(\Delta\omega)(TE/4)$, where $\Delta\omega$ is the frequency difference between the frequency of the RF

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pulse and the precessional frequency of a given spin. A 180° pulse, with its associated y gradient, is then applied and flips the spins 180° about the y axis, without changing the direction in which they rotate. The phase of the spins continues to change, but since the spins that were ahead of ω_0 are now behind ω_0 , as seen in Fig. 6, the spins will rephase and form a spin echo $TE/4$ after the pulse.

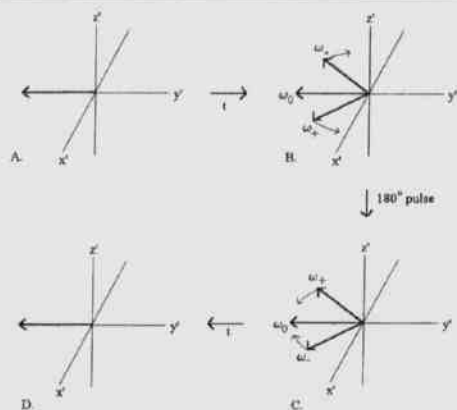


Fig. 6. All diagrams use the rotating frame. A. The spins are in phase in the transverse plane after the 90° pulse. B. The spins have dephased during time t . The center frequency, ω_0 , appears stationary, while other spins rotate at the frequencies ω_+ and ω_- . The differing frequencies cause the spins to spread out in the transverse plane. C. After the 180° pulse is applied along the y' axis, the spins exchange places. D. The spins rephase after a further delay, t .

Finally, the third 180° pulse is applied $TE/2$ after the second pulse, which allows the spins to dephase after forming the echo. This pulse again reverses the spins, but only in the voxel, since there is a simultaneous gradient in the z direction. The rephased spins form a spin echo $TE/4$ after the last pulse.

Although the entire echo can be sampled, in practice, only the second half of the echo is acquired. The primary reason for this delay is the potential for distortion of the echo due to eddy currents from the switched gradients. The second half of the echo, since it occurs later in time, is less likely to be so distorted. Fourier transformation of the sampled data yields the spectrum.

There are several problems with this sequence, most of which arise from imperfect RF pulses. Ideally, each of the 180° pulses causes the transverse spins in the intersection to rephase while simply inverting longitudinal magnetization. However, some of the longitudinal magnetization actually is rotated into the transverse plane (Jung, 1996). This unwanted

ed magnetization contributes to the final signal and must be eliminated.

"Crusher" gradients are used to destroy the unwanted transverse magnetization. If a gradient is applied after a pulse, it dephases the spins in the transverse plane. Crusher gradients are applied after each 180° pulse to dephase the unwanted xy magnetization. However, these gradients also destroy the signal from the voxel. To preserve that signal, an equal but opposite gradient must be applied, but only to the spins in the voxel.

Let C2 be the gradient immediately after the 180° pulse and let its slope be k . In the rotating frame, this gradient causes spins in the transverse plane to dephase by

$$\Delta\theta = 2\pi\gamma kxt, \quad (5)$$

where x is the coordinate of the spin, t is the duration of C2, and $\Delta\theta$ is the phase difference with respect to $x=0$.

If a gradient identical to C2 is applied immediately prior to the 180° pulse, the transverse magnetization will dephase by $\Delta\theta$. The spins in the voxel change places after the 180° pulse and will rephase when C2 is applied, while any new transverse magnetization is dephased. This is identical to Fig. 6, except that now a gradient is used to dephase and rephase the spins, rather than a delay time, t . Therefore, to preserve the spin echo, the crusher gradients must be applied symmetrically around the 180° pulse.

The equations which describe the effects of an RF pulse are nonlinear and, for large tip angles, the simple inverse relationship between bandwidth and pulse duration is no longer applicable (Ernst, et. al., 1987; Yan, et. al., 1987; Yan and Gore, 1987a; Yan and Gore, 1987b). The nonlinearity of the response causes a smaller frequency range to be excited for the 180° pulse than for the 90° pulse (Yan, et. al., 1987; Yan and Gore, 1987a; Yan and Gore, 1987b), which results in narrower planes of excited spins. This is shown in Fig. 7. The profiles were obtained using the standard PRESS sequence and correspond to the width of the plane selected by each pulse.



Fig. 7. Profiles obtained using the unmodified PRESS sequence. A. Profile in the x direction using a 90° pulse. B. Profile in the y direction from a 180° pulse. C. Profile in the z direction.

There are three ways to correct the voxel size: prescribe a larger voxel than is actually desired, increase the bandwidth of the 180° pulses, or reduce the gradient strengths which are applied with those pulses (Jung, 1996; Moonen, et. al., 1989). While prescribing a larger voxel is the simplest solution, it requires the operator to make an accurate estimate of the necessary increase in size. Increasing the bandwidth is undesirable because it makes programming and optimizing the sequence timing difficult. For example, increasing the pulse length or number of lobes in the 180° sinc pulse would increase the bandwidth, but then the power for the pulse would not be related easily to the power for the 90° pulse. By keeping the two pulse shapes identical, the power level for the 180° pulse is just twice that of the 90° pulse. The third alternative is the best solution because the reduction in gradient strength is constant for a given system.

For our system, a GE Omega CSI 4.7 T instrument controlled by a Sun 3/160 workstation, the gradients applied with the 180° pulses need to be reduced by 30% to achieve the correct voxel size at half maximum. This reduction is achieved by multiplying the calculated gradient strength by a scaling factor of 0.7.

The apparent gradient strength, using the Fourier transform approximation, is given by

$$G_{app} = \text{sinc}l / (\text{sinc}l \cdot st) \quad (6)$$

where G_{app} is the apparent gradient strength, $\text{sinc}l$ is the number of lobes in the sinc pulse, $\text{sinc}l$ is the length of time for which the pulse is applied, and st is the desired slice thickness. The actual gradient strength used is given by

$$G_{act} = sf \cdot G_{app} \quad (7)$$

where sf is the scaling factor.

Profiles obtained from the PRESS sequence using the default scaling factor of 0.7 are shown in Fig. 8. Empirical measurements with this system have shown that a scaling factor of 0.7 gives the desired voxel size. A scaling factor of 0.775 was required for a similar instrument (Moonen et. al., 1989). Since the scaling factor is constant, it can be evaluated once and programmed into the sequence. Such a default correction allows the operator to prescribe a voxel without having yet another parameter to adjust.

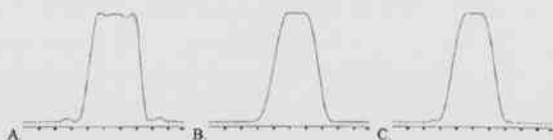


Fig. 8. Profiles from the modified PRESS sequence. A. Profile from the 90° pulse. B. Profile from the first 180° pulse. C. Profile from the second 180° pulse.

The profiles of the 180° planes are not perfectly rectangular. This can be improved by adjusting either the shape of the gradient pulse (Yan and Gore, 1987a), by using multiple RF pulses (Yan and Gore, 1987b), or by using special shaped pulses (Shinnar et. al., 1989a; Shinnar et. al. 1989b). These solutions require either an increase in the complexity of the program or an increase in the duration of the pulse sequence. For some purposes, such increases may be necessary. When they are not, a scaling factor provides a simple means of improving the voxel size.

Conclusion

The PRESS pulse sequence is a good alternative to STEAM for localized *in vivo* NMR spectroscopy. However, it uses 180° pulses, which, due to the nonlinearity of the system, cause unwanted magnetization to contribute to the signal from a voxel that is too small. Careful optimization of the crusher gradients and the slice selection gradients used with these pulses is required. The improper adjustment of the crusher gradients will result in the spin echo being contaminated with signal from outside the voxel. If the slice selection gradients are not adjusted, the sampled voxel will be smaller than desired. Although several methods have been proposed to adjust the voxel size, the simplest method is to multiply the calculated gradient strength by a scaling factor. This scaling factor is constant for a given system, so it can be determined once and incorporated into the pulse program. The operator has one less parameter to adjust, and the program is still easy to implement. The scaling factor is a simple way to make the pulse program both user friendly and accurate.

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