Some New Observations on Pulse Sequence Dependent Diffusion Related Edge Enhancement in MR Microscopy

Zang-Hee Cho, In-Ki Hong, Yong-Man Ro

Self-diffusion of nuclear spins has been suggested to cause edge enhancement in images especially on a microscopic scale. According to previously published work, theory suggests that edge enhancement is caused by motional narrowing due to the boundaries and spin self-diffusion during the data acquisition period. More careful examination reveals that edge enhancement due to motional narrowing develops only under a few specific conditions. This lack of generality of motional narrowing theory, as well as experimental observations, indicates that edge enhancement due to effects other than motional narrowing alone can exist. It is found that edge enhancement depends greatly on the data acquisition mode; therefore, the images obtained are different depending on the pulse sequence employed. For example, excessive attenuation of DC components due to diffusion can result in edge enhancement in the spin echo signal. However, in the case of FID-like signals, DC components are preserved while positive high frequency parts are attenuated, thereby degrading resolution. The new phenomenon observed has been termed selective spectral suppression since the observed edge enhancement results from the selective attenuation of certain frequency components in the nuclear signals due to diffusion-dependent signal attenuation for a given pulse sequence.

Key words: diffusion-dependent edge-enhancement in MR microscopy; MR microscopy; pulse sequence-dependent edge-enhancement in MR microscopy.

INTRODUCTION

Recently, there have been increasing demands for very high resolution imaging in vivo for the inspection of small biological samples such as embryos, and many different kinds of microscopes, such as optical and electron microscopes, have been employed for this purpose. These microscopes, however, have many inherent limitations for the study of living objects in vivo. During the last several years, however, many successful attempts in the field of NMR imaging for the study of small biological objects in vivo have been made, and resolutions down to a few microns have been achieved (1–9). At present, an image resolution of only 4 μm can be acquired when a sufficiently thick sample is imaged (1, 10–13). If indeed in vivo microscopy of only a few-micron resolutions is feasible, much useful information can be obtained from biological samples; for instance, the understanding of cell lineage or cell development in the early stage of an embryo (2, 8). Micron-resolution NMR microscopy, however, suffers from a low signal-to-noise ratio (SNR), as well as from several small artifacts, such as the diffusion effect (14–16). As attempts are made to improve spatial resolution, the diffusion effect increases due to the increased gradient strength. The diffusion effect, therefore, appears to be the major factor that limits the spatial resolution on a microscopic scale (14–16). However, more recent studies suggest that the diffusion effect can lead to an edge enhancement (19–23). Such an effect has been observed experimentally (20–26).

As is well known, each molecule in a liquid state diffuses to a different position by random Brownian motion. Therefore, the related phases of the spins will be different from the original spins because of the different gradient fields experienced by the spins. As time progresses, the spins will have a quite different phase distribution. Since the total magnetization or resultant signal is the vector sum of the nuclear spins over the voxel, the signal (magnetization) also decreases over time.

The effect of diffusion on an NMR signal in a homogeneous magnetic field has been studied for a long time; the work of Hahn is the most well known. According to Hahn’s formula, the echo signal decays as exp(–Dg²G²τ/3) where D and G are the diffusion coefficient and the magnitude of the magnetic field gradient, respectively, and τ is the data acquisition period (17). This formula implies that the echo signal is strongly affected by the gradient field as well as by the data acquisition time (18). As is known, the gradient field in NMR microscopic imaging is relatively high; therefore, the diffusion effect is particularly noticeable. Generally, there are two important diffusion effects on NMR image resolution, namely, the finite phase variation due to the Brownian motion of the spins under the applied gradient field and the signal attenuation due to the diffusion and its eventual line broadening effect on the image (14). More recently, however, a controversial edge enhancement by the diffusion effect was reported by Pitz et al. (19, 20), Lauterbur et al. (21–23), and Callaghan et al. (24) and is known as the edge enhancement effect due to motional narrowing (19, 21). Callaghan et al., however, argued that there could be another edge enhancement effect due to diffusion, the diffusion relaxation effect (24). Recently, we observed a similar edge enhancement effect, which appears to be affected by frequency selective attenuation or the pulse sequence; that is, the edge enhancement was dependent on whether the acquired nuclear signals are echo signals or FID. For example, in the spin echo sequence, selective attenuation of the DC and the positive high-frequency components of the echo signal, which lie far beyond the negative high frequency components, results in a relative enhancement of those components of the collected data.


From the Department of Radiological Sciences, University of California, Irvine, California (Z.H.C.); the Department of Information and Communication, Korea Advanced Institute of Science (Z.H.C., I.K.H.), and the Department of Computer Engineering, Taepjon University (Y.M.R.), Taejon, Korea. Address correspondence to: Z. H. Cho, Ph.D., Department of Radiologic Sciences, University of California, Irvine, CA 92717.

Received December 29, 1995; revised February 26, 1996; accepted April 2, 1996.

0740-3194/96 $3.00
Copyright © 1996 by Williams & Wilkins
All rights of reproduction in any form reserved.
(see Fig. 3 for definitions) (26). This effect, as reported here, appears to significantly alter the image resolution and, in some cases, improve the edges of the images.

THEORY AND SIMULATIONS
Motional Narrowing (19–21, 25)

By examining the effects of diffusion within the microscopic compartments, one can predict a distortion or uneven distribution of the excited spins within the volume due to the well-known “motional narrowing.” In NMR imaging, a diffusing spin does not precess at the same Larmor frequency as the one at the original position, but rather experiences new local fields along its diffusion path, and thereby precesses (encodes) with a different frequency. The frequency spectrum observed in imaging after the phase encoding, therefore, reflects the diffusive movements of the spins. A consequence of the diffusion effect is, therefore, that the observed magnetization, or signal, carries only the average frequency of the magnetized spins during the data collection period. In Fig. 1, various trajectories of the bounded spins at different positions as a function of time for three different diffusion coefficients are visualized. In the figure, the diffusion trajectories have been drawn for a time interval of ΔT, which is comparable to a period of one spin precession. In case of slow diffusion (see Fig. 1a), the mean positions (shown with broken lines) of the diffusing spin trajectories remain close to the original positions over the entire time period, including those spins at the boundary regions. However, in the case of large diffusion, the mean positions of the rebounded spins at the boundaries tend to push more toward the center. As a result, the average resonance frequencies of the spins over a time interval of ΔT tend to be shifted toward the center frequency as shown in Fig. 1c. This phenomenon is more clearly seen in the following study.

Let’s assume that the readout gradient is the dominant gradient. Then each spin magnetization in the 1D imaging case can be written as

\[ M_s(x, t) = A e^{i \gamma G x \omega t} \tag{1} \]

where \( M_s(x, t) \), \( \gamma \), \( G \), \( A \), and \( x \) are the transverse magnetization, the gyromagnetic ratio, the readout gradient, the magnitude of the spin signal, and the position of the spin, respectively. Each spin remains at the original position if diffusive motions of the spins do not exist; i.e., if \( D = 0 \), \( x \) will be a constant. However, if \( x \) is a time variant due to the diffusion effect, it can be taken as \( x(t) \). In the case of no diffusion, i.e., no spin motion, and assuming that the \( G \) is a constant gradient, Eq. [1] can be rewritten as

\[ M_s(x, t) = A e^{i \gamma G x(t) \omega t} \tag{2} \]

However, if diffusive spin motion is included, Eq. [1] can be rewritten as

\[ M_s(x, t) = A e^{i \gamma G \overline{x}(t) \omega t} \tag{3} \]

where \( \overline{x}(t) \) is the time-averaged spin position due to the diffusive motion. Obviously, when the diffusive motion is small, \( \overline{x}(t) \) will become \( x \) and Eq. [3] will become Eq. [2]. However, if the diffusion effect is large, \( \overline{x}(t) \) will behave differently as time evolves. The evolution of the spin distribution according to the diffusional motion during the data acquisition is calculated and is plotted in Fig. 2. Figures 2a–2f show the data with progressively increasing diffusion effect. A set of 32 distributions is given for a diffusion coefficient, and each distribution represents the resulting instantaneous magnetized spin distribution within a short time interval Δt, a short po-

**Effect of Motional Narrowing**

![Diagram](https://via.placeholder.com/150)

**FIG. 1.** Simplified illustration of the motional narrowing of bounded spins. (a) to (c) are sketches of the spin diffusion paths in a one-dimensional space as a function of time for three different diffusion coefficients. The spin paths are shown as solid lines while their average positions are shown by dashed (vertical) lines. The rate of diffusion increases from (a) to (c): (a) \( D \ll \Delta L^2/\Delta T \), (b) \( D = \Delta L^2/\Delta T \), and (c) \( D \gg \Delta L^2/\Delta T \) where \( \Delta L \) is the length of the spacing (19).

Equation [3] then can be written as

\[ M_s(x, t) = A e^{i \gamma G \overline{x}(t) \omega t} \tag{4} \]
Pulse Sequence-Dependent Edge Enhancement MR Microscopy

Spin Evolution due to Motional Narrowing

![Spin Density Distributions](image)

(a) D = 5x10^{-6} cm^2/sec  
(b) D = 5x10^{-5} cm^2/sec  
(c) D = 5x10^{-4} cm^2/sec  
(d) D = 2x10^{-3} cm^2/sec  
(e) D = 5x10^{-3} cm^2/sec  
(f) D = 5x10^{-2} cm^2/sec

FIG. 2. Distributions of the instantaneous spin density due to motional narrowing effect over the passage of time for several values of the diffusion coefficients. The rate of diffusion increases from (a) to (f). As shown, the edge enhancement effect occurs only on a few occasions, such as the cases with D = 5 \times 10^{-5} to D = 5 \times 10^{-4} cm^2/s.

First let us observe the bounded spin case, and then we will look at the unbounded spin case. When each spin distribution within a short time interval n\Delta t (each x directional line data) represents a sampled instantaneous spin distribution during the data acquisition period n\Delta t, a series of spin distributions will result as time evolves (see Fig. 2). Note here that the y direction is also the time axis and that one data acquisition period is divided into 32 time intervals with each interval representing an instantaneous spin distribution. These results, due to purely motional narrowing, imply that the dynamics of the spin densities are markedly different, not only as a function of the value of the diffusion coefficient, but also as a function of the time of spin evolution. As shown in Fig. 2, at some points in time with specific conditions, e.g., D = 5 \times 10^{-5} and 5 \times 10^{-4} cm^2/s, the edge enhancement is clearly visible as time evolves. However, edge enhancement lessens as diffusion coefficients become either smaller than or larger than the specific values mentioned (D = 5 \times 10^{-5} - 5 \times 10^{-4} cm^2/s). That is, it is visible only in this specific range of diffusion coefficients and at a few specific time limits.

Pulse Sequence and Selective Spectral Suppression Effect

If these spin distributions are translated into the NMR signal by solving the Bloch equation classically and us-
FIG. 3. The spin echo and the DRG pulse sequences used for the study and their typical nuclear signals. (a) The spin echo pulse sequence and (b) a typical echo signal. From the left, the negative high-frequency parts, the DC parts at the center, and the positive high-frequency are shown with arrows. As time progresses, diffusion attenuation becomes larger; i.e., while the negative high-frequency parts experience the least attenuation, the DC and the positive high-frequency parts suffer the largest attenuation. (c) DRG pulse sequence and (d) a typical FID-like DRG echo signal. From the left, the DC parts and positive high-frequency parts are shown. As is known, there are no negative high-frequency parts in the DRG sequence.

FIG. 4. The spin echo signals with selective spectral suppression effect and their corresponding 1D images for bounded spins. (a) The spin echo signals of different diffusion coefficients and (b) 1D images reconstructed from the above echo signals.
Pulse Sequence-Dependent Edge Enhancement MR Microscopy

results are obtained. First, with the spin echo sequence showing the imaging sequence shown in Fig. 3, the following located at the left or the beginning of the echo signal, parts: one being the negative high-frequency components located at the right. Another pulse sequence known as the DRG sequence shown in Fig. 3a, a typical echo signal will be obtained as shown in Fig. 3b. As shown, the frequency distribution of the generated spin echo signal can be divided into three parts: one being the DC components at the center, and the last part being the positive high-frequency components located at the right. Another pulse sequence known as the DRG sequence (1) is shown in Fig. 3c with its signal shown in Fig. 3d. With the latter, as shown in Fig. 3, one can obtain FID-like echo signals.

In Fig. 4a, spin echo signals obtained with three different diffusion coefficients, namely $D = 1 \times 10^{-6}$, $1 \times 10^{-5}$, and $2.5 \times 10^{-5}$ cm$^2$/s, are shown. The diffusive motions of spins have two consequences, namely the diffusive motion that distorts the spin distribution from the original one (see Fig. 2) and the spin phase dispersion that results in spin phase incoherency within a voxel that leads to a signal attenuation. The latter, which is often referred to as diffusive attenuation, attenuates the signal similar to $T_2^*$ attenuation.

Now let us first look at the bounded spin case as shown in Fig. 4. In this case, the results show markedly enhanced edges in the reconstructed images. Figure 4a show how the spin echo signals are attenuated due to the diffusion effect as a function of time for several different values of the diffusion coefficients. Although it is difficult to visualize clearly from these figures, trends of the unequal spectral attenuation are clearly visible: e.g., the positive high-frequency parts and, to a lesser extent, the DC parts of each spectrum at $t = TE + \pi/2$ and $t = TE$ are severely attenuated compared with the negative high-frequency parts at $t = TE - \pi/2$, especially with large diffusion coefficients ($D > 2.5 \times 10^{-5}$ cm$^2$/s). An obvious reflection of this result is seen in the reconstructed images shown in Fig. 4b. As noticed, the edge enhancement effect becomes more pronounced with increasing diffusion coefficient while the attenuation of the DC components (middle part of the image) becomes more severe as the diffusion coefficient increases. Although some portion of the edge enhancement could be due to motional narrowing, it seems to be mostly due to selective spectral suppression, that is, attenuation of the DC components and the positive high frequency parts. However, it is not yet clear from this study alone whether the edge enhancement is due to motional narrowing or selective spectral suppression, since it is a bounded spin case.

To clarify this edge enhancement effect, especially to determine whether it is due to motional narrowing or otherwise, we have simulated a spin echo imaging with unbounded spins and obtained the results as shown in Fig. 5. To our surprise, nearly the same results as those observed with the bounded spin case were obtained (compare with Fig. 4). This led us to reexamine the whole diffusion-dependent edge enhancement hypotheses, since edge enhancement still persists as shown in Fig. 5b,
in spite of the fact that the spins are now unbounded. The latter cannot be explained by motional narrowing effect. The results of Fig. 5, therefore, clearly imply that edge enhancement is due to some other effect, such as the selective spectral suppression we are proposing in this paper and also implied by Callaghan et al. (24). In other words, in spin echo sequence the positive high-frequency parts of the echo signal and, to a lesser extent, the DC parts at the center are attenuated more severely by diffusion attenuation than by the negative high-frequency parts. Note that the negative high-frequency parts are also responsible for the edge enhancement.

Strictly speaking, the spin density of the edge is not enhanced, but the negative high-frequency terms are unattenuated and remain at the same magnitude, while the DC, as well as the positive high-frequency components (these parts are equally responsible for the edge enhancement), are severely attenuated. (Although the positive high-frequency components are attenuated most severely there is no significant effect on the image resolution since the negative high-frequency components still exist.) Main edge enhancement is also due to the reduction of the DC components, which in turn reduce the flat middle part of the image, thereby appearing as if the edges are enhanced.

Selective spectral attenuation in the domain of the nuclear signal (in the echo signal as well as FID) due to diffusion attenuation seems mostly responsible for edge enhancement in microscopic imaging rather than the motional narrowing effect as previously thought. This is a new result not previously postulated by Pütz et al. (19), Lauterbur et al. (21), and Callaghan et al. (24). Although Callaghan et al. have postulated a diffusive relaxation effect, the specifics of the result were not discussed. These results are similar to that of Callaghan et al. given in ref. 24. All those previous results, however, suggested (see Fig. 2) that the edge enhancement is likely to occur only at a few specific values of the diffusion coefficients, that is, only approximately $D = 5 \times 10^{-3}$ to $5 \times 10^{-4}$ cm$^2$/s. Diffusion coefficients, larger or smaller than those values, tend to have quite different shapes or distributions. The edge enhancement effect of the image, therefore, may not be only due to motional narrowing. From these observations, we can conclude that edge enhancement, which is likely to be observed in microscopic imaging, is largely due to the selective attenuation of the spectral components of the nuclear signals and that the motional narrowing appears to play only a minor role. The edge enhancement effect is, therefore, dependent on the pulse sequence employed, i.e., whether the signal obtained is spin echo or FID.

To further confirm the above selective spectral suppression hypotheses, we have simulated an FID-like pulse sequence known as the DRG sequence (Figs. 3c and 3d),
whose results are shown in Figs. 6a and 6b. In this DRG sequence, DC parts are conserved while the positive high-frequency parts are attenuated; therefore, edge resolution is expected to be degraded in all cases, i.e., in both unbounded and bounded cases. As expected, in the case of unbounded spins, the resolution is degraded for all cases due to the loss of the positive high-frequency components (Fig. 6a). It is also noted that the flat middle portions of the images are nearly unattenuated and remain the same, suggesting that the DC components are unattenuated. For the bounded spins, however, we observe some edge enhancements, as shown in Fig. 6b. This can be explained by the fact that, with large diffusion coefficients (ranging from $3 \times 10^{-5}$ to $3 \times 10^{-5} \text{ cm}^2/\text{s}$), the motional narrowing effect becomes relatively large; therefore, the edge enhancement effect begins to be seen. These results clearly confirm that selective spectral suppression plays the dominant role in edge enhancement. As shown in Fig. 6, in DRG sequence for both cases (bounded and unbounded spins) due to excessive loss of the positive high-frequency components, edges are always degraded except for bounded cases with large diffusion coefficients where some edge enhancements are visible due to the motional narrowing effect by diffusion (see and compare with Fig. 4b). Also, note that the intensity at the middle portion of the image is not reduced, as in the cases of the spin echo signals, as shown in Figs. 4b and 5b.

**DISCUSSION AND CONCLUSIONS**

We have observed a new phenomenon that is due to selective spectral suppression of frequency components in the nuclear signals by the diffusion attenuation. From this observation, one can conclude that the edge enhancement effect is dependent on the pulse sequence employed. For example, in the spin echo sequence, the DC and the positive high-frequency components are severely suppressed while the negative high-frequency components are nearly unattenuated, thereby enhancing the edges of the images. This relative attenuation and preservation of the various frequency components in relation to the diffusion-dependent signal attenuation appears to be the dominant factor in edge enhancement rather than the motional narrowing effect as previously believed. Along similar lines of thought, the results obtained using the DRG sequence (FID-like signal) support the proposed hypothesis and demonstrate that edge enhancement is largely due to selective spectral suppression, except for the few cases of bounded spins with large diffusion coefficients. The latter, for the bounded spins, is due to motional narrowing rather than selective spectral suppression, and appears only with large diffusion coefficients.

**REFERENCES**