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Optimization of Survey Protocols for MRI

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Abstract

A method for evaluating the sensitivity of MRI protocols to changes in an arbitrary number of tissue parameters over a broad range of parameter values is presented. This analysis is useful for choosing an optimal basis set of images for either a “survey” protocol or tissue segmentation algorithms. A survey protocol is required when searching for a lesion of unknown type or location. Segmentation requires unique signal signatures for tissues that may cover a broad range of tissue parameter values. Data acquisition is modeled as a mapping of a domain of tissue parameter values into a signal manifold in a signal strength space defined by the MRI protocol. The efficacy of the protocol is evaluated by investigating the characteristics of the signal manifold. A figure of merit which maximizes the probability of discriminating each point in the domain of tissue parameters from all others is developed.

1. INTRODUCTION

Magnetic resonance imaging (MRI) offers unique potential as a diagnostic tool because it is sensitive to changes in many different tissue parameters. While this multivariate information increases the power of the technique, the corresponding increase in complexity necessitates a sophisticated method for optimizing the data acquisition (1-7). Choosing the set of images for the optimal MRI protocol requires balancing increasing sensitivity to changes in one tissue parameter with a concurrent decrease in sensitivity to changes in another parameter.

If the clinical problem requires an answer to a simple question, such as the presence or absence of a specific lesion, then a priori information about the potential lesion and the possible background tissues can be used to choose the optimal MRI protocol (8,9). If the clinical problem is less specific such that the nature of the suspected lesion is unknown, then the optimal MRI protocol will be a “survey” technique (10). The method for determining this survey protocol is the topic of this paper.

The optimal survey protocol must have good sensitivity to changes in tissue parameter values over a broad range of these parameters. Another requirement is sensitivity to both correlated and uncorrelated changes in the tissue parameters, such as T_1 and T_2 relaxation times and proton density, $N(H)$. The goal of the survey protocol is to provide a basis set of images which meets these criteria.

2. DEFINITION OF AN MRI PROTOCOL

Differences in tissue parameter values form the basis from which all tissue discrimination using MRI signals is obtained. In this analysis, a volume of homogeneous tissue is described by an

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N -tuple of parameter values, such as T_1 , T_2 , and $N(H)$, and can, therefore, be represented by a point in tissue parameter space (T -space).

An MRI protocol consists of one or more scans of the same portion of the patient. If N_s scans are obtained for each slice in a study, each voxel is represented by N_s signal values. Therefore, the N_s scans form the basis set of a N_s -dimensional signal space (S -space). For this analysis, the MRI protocol is modeled by a mapping from the T -space to the S -space (9) where the mapping is determined by the signal strength equations. Formally, the mapping is written

$$S_i = \psi_i(X_1, X_2, \dots, X_{N_p}; \text{TR, TE, TI, } \alpha, \dots), \quad i = 1, 2, \dots, N_s, \quad [1]$$

where ψ_i is the signal strength function for the i th pulse sequence, the X_j are the tissue parameters, and TR, TE, ... are the pulse sequence parameters. With this mapping, N_p -dimensional points in the T -space ($X_1, X_2, \dots, X_{N_p}$) are mapped to N_s -dimensional points in the S -space ($S_1, S_2, \dots, S_{N_s}$). The tissue parameters X_j are the independent variables in the expression; the machine parameters (TR, TE, ...) are treated as constants for a particular pulse sequences. The optimization problem is to determine which combination of pulse sequences ψ_i is the best, and what values the constants (TR, TE, ...) should have.

A simple mapping from a two-dimensional T -space to a two-dimensional S -space is shown in Fig. 1. The T -space is the $T_1 \times T_2$ plane; the basis set in the S -space is composed of a T_1 -weighted, T_2 -weighted pair of spin-echo images. In the nomenclature of Eq. [1] this mapping is written

$$S_1 = \text{SE}(T_1, T_2; \text{TR} = 500 \text{ ms, TE} = 20 \text{ ms, } \alpha = 90^\circ) \quad [2a]$$

$$S_2 = \text{SE}(T_1, T_2; \text{TR} = 2000 \text{ ms, TE} = 60 \text{ ms, } \alpha = 90^\circ). \quad [2b]$$

It is clear from Fig. 1 that a one-to-one mapping is achieved between a large domain of interest ($200 < T_1 < 1000 \text{ ms}$, $20 < T_2 < 100 \text{ ms}$) and the corresponding range in the S -space.

The dimension of T -space is established by the number of tissue parameters included. Possible basis vectors for the T -space other than T_1 and T_2 are $N(H)$, chemical shift, diffusion, perfusion, magnetic susceptibility, and flow velocity. The dimension of the S -space is set by the number of scans (i.e., basis images) performed on each slice. In Fig. 1 the domain of interest in the T -space is mapped to a two-dimensional signal manifold in the S -space. If a third scan were added to this protocol, this two-dimensional signal manifold would be lifted away from the $S_1 \times S_2$ plane into a three-dimensional space. The signal manifold, however, would still be parameterized only by T_1 and T_2 and would remain a two-dimensional surface. Adding the third pulse sequence to the protocol stretches the signal manifold, but it does not affect its intrinsic dimension.

Image noise is readily included in this model of MRI protocols. Noise in MR images is spatially invariant, has a flat power spectrum, and follows a Gaussian probability density function (PDF) (11). Therefore, in the S -space the noise is represented by an N_s -dimensional Gaussian PDF. A simple method of including noise is to scale each basis vector in the S -space so that its unit of length is equivalent to the root-mean-square-deviation (RMSD) in the corresponding image. When this is done, the Euclidean distance in the S -space is measured in fundamental units of the signal-difference-to-noise ratio (SDNR). The signal values in Fig. 1 are plotted this way assuming that the intrinsic signal-to-noise ratio (SNR) (12,13) is 100 at the required spatial resolution.

For any point on the signal manifold, the optimization task is to find a mapping (i.e., an imaging protocol) that maximizes the separation of this point from the neighboring points on the

manifold. This is equivalent to stretching the signal manifold in the S -space which can be achieved in two ways: (1) by signal averaging for any sequence to decrease the RMSD on that axis of S -space; or (2) by adding a new sequence to increase the dimension of S -space and stretch the manifold in a new direction. The optimal protocol will give maximal isotropic stretching around all points on the manifold. Evaluation of the performance of a protocol in achieving this goal is the topic of the next section.

3. EVALUATION OF THE SENSITIVITY OF A PROTOCOL

The sensitivity of a pulse sequence to a change in a single tissue parameter is not difficult to envisage. The pulse sequence that produces the maximum sensitivity has the maximum rate of change of signal strength with respect to change in the parameter; i.e., $\partial S / \partial X_j$, is a maximum (14,15). In a multidimensional T -space, however, the sensitivity is proportional to the directional derivative of the signal strength and can be evaluated in an infinite number of directions. By definition, a survey protocol is a set of pulse sequences that provides good sensitivity in all possible directions over a large domain in the T -space.

3.1. Visualization of the Sensitivity at a Point in T-Space

Consideration of multiple directions in the optimization process requires a “sensitivity profile” which plots values of differential signal changes as a function of direction. As an example, the point $T_1 = 750$ ms, $T_2 = 75$ ms, $N(H) = 0.8$ in the T -space is chosen as the operating point, $\mathbf{r}_0$. Differential distances along the basis in T -space are arbitrarily defined as $\frac{1}{2}$ % of the estimated full range of the parameter values (i.e., $\Delta(H) = 0.005$, $\Delta T_1 = 10$ ms, $\Delta T_2 = 1$ ms) for the purpose of visualizing the sensitivity profile. With these basis distances chosen, a differential in any direction can be defined as shown in Fig. 2. For each direction (value of θ and ϕ) the magnitude of the signal difference $|\Delta S|$ is calculated between the operating point $\mathbf{r}_0$ and the point $\mathbf{r}_0 + \Delta \mathbf{r}(\theta, \phi)$. If $\mathbf{r}_0 = (T_1, T_2, N(H))$ then the function $\Delta \mathbf{r}(\theta, \phi)$ is given by

$$\Delta \mathbf{r}(\theta, \phi) = (\delta T_1, \delta T_2, \delta N(H)), \quad [3a]$$

where

$$\delta T_1 = \Delta r \sin \theta \cos \phi \quad [3b]$$

$$\delta T_2 = \Delta r \sin \theta \sin \phi \quad [3c]$$

$$\delta N(H) = \Delta r \cos \theta. \quad [3d]$$

In this way the sensitivity profile of the protocol, $|\Delta S(\theta, \phi)|$, is calculated. Because of the symmetry through the operating point in this local first-order analysis ($\Delta \mathbf{r}$ is small), only 27π steradians need to be covered by θ and ϕ to investigate the sensitivity profile and the r dependence of ΔS can be dropped.

Figure 3 shows $|\Delta S(\theta, \phi)|$ from four protocols for $0 \leq \theta \leq \pi/2$ and $0 \leq \phi \leq 2\pi$ (this corresponds to the 2π steradians of the top of a sphere). Figure 3a is the result of a T_1 -weighted sequence SE (TR = 375, TE = 20), Fig. 3b is from a T_2 -weighted sequence SE (TR = 1100, TE = 80), and Fig. 3c is from an $N(H)$ -weighted sequence SE (TR = 1100, TE = 20). The solid arrows in Fig. 3a show ΔS in the direction of the basis vectors T_1 , T_2 , and $N(H)$. In each case, the partial derivative, $\partial S / \partial X_j$ with respect to the weighted parameter X_j is maximized per root scan time (14) assuming a minimum available TE of 20 ms. Note that the sensitivity in all three cases collapses entirely ($|\Delta S| = 0$) over a locus of directions; i.e., there exist major “blind spots” in the sensitivity profile. This is because at least three sequences are required to obtain a nonsingular mapping to S -space from a three-dimensional T -space.

Figure 3d is the sensitivity profile from a protocol which consists of all three of the pulse sequences (a), (b), and (c), with the imaging time held constant. By combination of the individual pulse sequences into a three-sequence protocol, the blind spots have been removed, but these sequences still may not be the optimal basis images for isotropic sensitivity. These plots do illustrate why the derivative method fails in optimizing MRI protocols and has had little clinical application. The function $\Delta S(\theta, \phi)$ helps visualize the changes in sensitivity with direction but determining the optimal survey protocol requires a metric that balances the tradeoffs between increasing sensitivity in one direction and the concurrent loss of sensitivity in another direction. This balance is best achieved with a probabilistic model which remains sensitive to blind spots where $\Delta S \cong 0$.

3.2. Calculating the Optimal Survey Protocol at a Point in T-Space

The goal of the optimum survey protocol is to provide a set of images that differentiates points in the T -space. For a single operating point in T -space, this implies that the probability of distinguishing that point from all other points in the T -space is maximized. This probability has an analytical form which we use to develop an optimization criterion. The extension of this analysis to a domain of interest in the T -space is shown in Section 3.3.

Consider an operating point in T -space defined by the vector $\mathbf{r}_0$. For an ideal detector (16) the probability of distinguishing $\mathbf{r}_0$ from a neighboring point displaced from $\mathbf{r}_0$ by the vector $\mathbf{r}$ in the T -space is given by (17)

$$P(\mathbf{r}_0, \mathbf{r}) = \frac{1}{2} \left(1 + \operatorname{erf} \left(\frac{\Delta S(\mathbf{r}_0, \mathbf{r})}{\sqrt{2}} \right) \right), \quad [4a]$$

where

$$\operatorname{erf}(x) = \frac{2}{\sqrt{\pi}} \int_0^x \exp(-u^2) du \quad [4b]$$

and $\Delta S(\mathbf{r}_0, \mathbf{r})$ is the Euclidean distance (in units of RMSD) between the points $\mathbf{r}_0$ and $\mathbf{r}$ after they have been mapped to the S -space by the protocol. A one-dimensional example of $P(\mathbf{r}_0, \mathbf{r})$ is shown in Fig. 4a.

The probability of distinguishing $\mathbf{r}_0$ from all other points of T -space in independent trials is the product of the individual probabilities. The assumption of independent trials is required if no a priori information is used when distinguishing $\mathbf{r}_0$ from the other points. The total probability is maximized when the integral over all T -space

$$\int \ln(P(\mathbf{r}_0, \mathbf{r})) d\mathbf{r} \quad [5]$$

is maximized. This integral, which is always negative, will be a maximum when the stippled area shown in Fig. 4b for a one-dimensional example is a minimum. In this one-dimensional example, therefore, the integral will be a maximum when $\partial S / \partial T_1 | T_{10}$ is a maximum, unless $\Delta S(T_{10}, T_1)$ is highly nonlinear and the probability criterion is not really needed. However, in a T -space of higher dimension, the optimal survey protocol will be that which produces the most isotropic stretching of the signal manifold. The criterion of Eq. [5] determines how that stretching should be done and is particularly sensitive to blind spots. If the derivative in a given direction, $\mathbf{v}$, is zero (i.e., the signal manifold collapses in that direction), then $P(\mathbf{r}_0, r_v) = 0.5$ for all r_v and the integral in Eq. [5] does not converge.

The optimization procedure consists of searching through all possible MRI protocols for that which produces the function $\Delta S(\mathbf{r}_0, \mathbf{r})$ in Eq. [4a] which maximizes the integral in Eq. [5]. Because of the insensitivity of the pulse sequence equations to small changes in pulse sequences, the global maximum is usually fairly broad, and the search is not hindered by local maxima. A specific example in Section 4 shows these properties.

3.3. Calculating the Optimal Survey Protocol over a Region of T-Space

For a survey technique, sensitivity to the presence of a lesion in a number of back-ground tissues is required. Similarly, when deriving a basis set of images for tissue segmentation, the protocol must span a large region of T -space to produce unique signal signatures for a large number of tissues. The probability criterion is well suited to these tasks. It allows not only tradeoffs between sensitivity in different directions of T -space but also tradeoffs at different points of T -space. A nonuniform distribution of background tissues in T -space is accommodated by adjusting the limits of integration in Eq. [5].

The probability of distinguishing every point in some region R of T -space from all other points is obtained by integrating Eq. [5] and is proportional to the exponential of

$$\iint_R \ln(P(\mathbf{r}_o, \mathbf{r})) d\mathbf{r} d\mathbf{r}_o. \quad [6]$$

The optimal protocol for the region R in T -space maximizes this integral.

4. AN EXAMPLE CALCULATION

In this example the optimal image set for tissue differentiation in the brain at a field strength of 1.5 T is derived. This example permits comparison to previous work and to empirical clinical knowledge while illustrating the incorporation of practical imaging constraints. The T -space chosen is $T_1 \times T_2 \times N(H)$, and the domain of interest in the T -space is $500 < T_1 < 1000$ ms, $50 < T_2 < 100$ ms, and $0.8 < N(H) < 1.0$; this domain includes most normal tissues in the brain (18) except CSF, but differentiating CSF is not difficult.

The first consideration in the optimization procedure is to determine the constraints imposed on the protocol by clinical circumstances and imager capabilities. To survey the entire volume of the brain, approximately 15 cm must be covered with axial slices. This imposes a limit on the time which can be spent collecting echoes on each excitation. To eliminate the problem of optimizing TE, we assume that a sufficient number of echoes can be collected in this time to cover all of the T_2 decay curve available. We also assume a fixed sampling window and sampling rate (12,19,20), a minimum available TE of 20 ms, and a fixed scanning time. For this example we optimize TR only in the individual pulse sequences of the protocol. In a more general optimization, all of these parameters would be included.

As a starting point in the search for the optimal protocol, an attempt is made to span the three-dimensional T -space with the T_1 - T_2 - $N(H)$ -weighted triplet shown in Fig. 3. Because the T_2 -weighted and $N(H)$ -weighted images can be obtained from the same multiecho pulse sequence, the intervening echoes (TE = 40,60) are added to the protocol; this increases performance with no cost in imaging time, although specific absorption rate restrictions must be observed (21). This gives a five-image protocol derived from two pulse sequences.

Equation [6] may be used as the figure of merit in the optimization. However, under conditions of high SNR, a simplification can be made when maximizing the probability of discriminating a point from the rest of T -space. If the function $\Delta S(\mathbf{r}_o, \mathbf{r})$ of Eq. [4] can be approximated to first order over all regions in which the function $\ln(P(\mathbf{r}_o, \mathbf{r}))$ has significant value, relative values of the integral in Eq. [5] become essentially independent of the transform $\ln(P(\mathbf{r}_o, \mathbf{r}))$ and the analysis can be done using $\Delta S(\mathbf{r}_o, \mathbf{r})$ only. The search for the optimal TR for the T_1 -weighted sequence and the optimal TR for the T_2 -weighted sequence can be performed using a metric outlined in the Appendix which is derived from this simplification. In the Appendix it is shown that for a three-dimensional T -space

$$-\iint \ln(P(\mathbf{r}_o, \mathbf{r})) d\mathbf{r} \cong K \int_{\theta} \int_{\phi} \left| \partial S / \partial r \right|_{\theta, \phi}^{-3} \sin \theta d\theta d\phi \quad [7]$$

and that the optimal protocol will minimize the integral on the right. In order to evaluate the integral on the right with computer methods, $\partial S/\partial r$ is approximated with $\Delta S/\Delta r$. Because $|\Delta r|$ is invariant with respect to θ and ϕ , the optimal protocol minimizes the integral

$$\int_0^\pi \int_0^{2\pi} |\Delta S(\theta, \phi)|^{-3} \sin \theta \, d\theta d\phi. \quad [8]$$

This result is pleasing for its simplicity and is easily evaluated on a computer. The integrand of Eq. [8] from the optimal protocol is shown in Fig. 5 as a function of θ and ϕ at the point $T_1 = 750$ ms, $T_2 = 75$ ms. The peaks indicate the directions in which this protocol has weak sensitivity. The optimal protocol at this point minimizes the volume under the surface. The figure displays $0 \leq \theta \leq \pi$ and $0 \leq \phi \leq 2\pi$ but only one-half of this domain is required in the calculation because of the symmetry $\Delta S(\theta, \phi) = \Delta S(\theta + \pi/2, \phi + \pi)$.

The optimization over the region of interest in the T -space is accomplished by integrating the function of Eq. [8] over the domain of interest. We call this the figure of merit (FM); the optimal protocol minimizes the FM. Equation [8] was evaluated on a grid of $T_1 \times T_2$ values using a cubic spline integration subroutine (22). (Because the signal strengths are linearly proportional to $N(H)$ for these pulse sequences, the integration of Eq. [8] need be done only for one value of $N(H)$.) The magnitude of the integral of Eq. [8] increases with increasing T_1 and T_2 values of the point in T -space, but the shape of the function shown in Fig. 5 is fairly constant. Thus, points in the T -space with high T_1 and T_2 values influence the optimization more than the lower T_1 and T_2 points where high sensitivity is easily achieved. The ability to calculate this weighting is an advantage of this optimization technique.

The optimal survey protocol for a single slice with constant imaging time consists of two sequences, an SE (TR1 = 400, TE = 20, 1 echo) and a multiecho SE (TR2 = 2250, TE = 20, 4 echoes). This protocol agrees with current clinical practice, which is an empirical form of optimization, but differs significantly from that obtained by combining sequences that have maximum partial derivatives $\partial S/\partial X_j$ as shown in Fig. 3. Figure 6 shows the relative value of the FM as a function of TR1 and TR2 for constant imaging time. These plots show smooth functions with TR2 having a broad minimum, which allows considerable flexibility when designing a multislice protocol.

The short TR of the T_1 -weighted sequence presents a problem for optimizing the multislice protocol. If thirty 0.5-cm slices are required to scan the brain volume, then the T_1 -weighted sequence must be performed in three sections, with 10 slices per section. This divides the time spent on the T_1 -weighted image by one-third, which decreases the SNR. A more practical alternative is to use TR1 = 600 ms and to cover the volume in two sections, with 15 slices per section. In this case the imaging time spent on the T_1 -weighted image is only split in two. This choice between discrete alternatives can be made only after the required number of slices is defined.

Figure 7 shows the relative changes in the value of the FM as a function of the fraction of the imaging time spent on the T_2 - $N(H)$ -weighted sequence. This plot shows that about two-thirds of the total imaging time should be spent on this sequence, and about one-third spent on the T_1 -weighted sequence. Again, the minimum is fairly broad, which gives flexibility in the implementation of this protocol.

Other T_1 -weighted sequences, such as inversion recovery and STEAM (23,24), do not improve the performance of the protocol when used as replacements for the T_1 -weighted spin-echo sequence. This does not imply that these sequences are not useful in other contexts. Also, no improvement was found by dividing the scanning time into more than two TR values.

The FM used in this example is dependent on the linearity of the function $\Delta S(\mathbf{r}_0, \mathbf{r})$ in a local region of T -space, a condition tested in Fig. 8 which plots ΔS as a function of Δr for the most nonlinear direction and position. Assuming an intrinsic SNR for the desired resolution to be 100, the points deviate from a linear relationship only well beyond $\Delta S = 5$.

5. DISCUSSION AND CONCLUSIONS

This method maximizes the probability of distinguishing points in T -space from each other. In particular, loss of sensitivity in any direction will be reflected in the figure of merit. The preceding example showed clearly that maximizing the derivative along each of the axes in T -space fails to produce the optimal basis images for the survey protocol. This is because sensitivity to correlated changes in the tissue parameters must be evaluated in the optimization, a task which is difficult to do analytically, but which is straightforward with computer methods. The agreement of the calculated brain survey protocol with current practice is not surprising; it confirms the clinical applicability of this method and, conversely, provides a theoretical basis for the empirical, clinical optimization.

A major advantage of this technique is that any number of tissue parameters and pulse sequences can be included in the optimization. Increasing the number of tissue parameters increases the dimension of the signal manifold. This increases the complexity of the calculation because more directions must be probed, but this only requires more computer resources. Increasing the number of images in the protocol is trivial; this increases the dimension of the S -space, but the Euclidean distance is easily calculated for any dimension. Thus, this method should find application to complex clinical imaging problems.

The ability to incorporate multiple tissue parameters in the optimization can be important. For example, if the $N(H)$ dependence of the SE sequences is ignored (i.e., the integration in Eq. [8] is performed only over ϕ , with θ set to $\pi/2$), the solution to the example in Section 4 is significantly different. Without $N(H)$ dependence, the optimization is in the two-dimensional T -space $T_1 \times T_2$, and the optimal protocol is found to be a single multiecho SE sequence, with $TR = 750$ and four echoes ($TE = 20$). Correlated increases in T_1 and $N(H)$ would not be separated and are only resolved with the true optimal protocol combining the long TR and short TR sequences.

The simplification of the optimization criterion to a local analysis is possible only with sufficient SNR. If clinical conditions require very high resolution or very fast imaging times, the local analysis may not be adequate. In this case Eq. [6] must be evaluated explicitly as the figure of merit, a requirement for more computer resource. The possibility of the manifold folding back on itself also exists. This perverse circumstance can be avoided provided a subset of the protocol constitutes a one-to-one mapping from T -space to S -space. When the SNR is high enough, however, the “local” metric of Eq. [8] derived in the Appendix is very convenient.

The optimization procedure outlined here assumes that signal differences in any direction in the S -space are equally valuable. This implies that the clinician must be provided with the ability to view these directions through mathematical combinations of the basis images collected. Such combinations can be made in a variety of ways (25-28) depending on the goals of the viewer. One possibility would use a position and a direction of desired sensitivity in T -space as input parameters. This direction of sensitivity in the T -space is mapped by the protocol to an associated direction in the S -space and the image displayed would be a weighted sum of the basis images, calculated to have maximum sensitivity in the defined direction. This corresponds to a rotation of the S -space coordinates such that one of the basis vectors is parallel to the desired direction of sensitivity.

A number of image analysis techniques such as cluster analysis (29), principal component analysis (27,28), and eigenimage construction (30) have been applied to MRI but optimizing the image data to feed these algorithms has not been done. Maximizing the ability to differentiate points on the signal manifold with our optimization method will provide the best basis set for image processing algorithms that attempt to discriminate using measures of separation in a signal space.

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APPENDIX

A simplified optimization criterion can be derived from Eq. [5] and can be written in one dimension as

$$\int \ln\left(\frac{1}{2}\left(1 + \operatorname{erf}\left(\frac{|\Delta S(x_0, x)|}{\sqrt{2}}\right)\right)\right) dx, \quad [\text{A1}]$$

where x_0 is the operating point and therefore $\Delta S(x_0, x_0) = 0$. Changing the terminology so that $\ln\left(\frac{1}{2}\left(1 + \operatorname{erf}\left(\frac{|\Delta S(x_0, x)|}{\sqrt{2}}\right)\right)\right) \equiv f(\Delta S(x_0, x))$ we can write Eq. [5] as

$$\int f(\Delta S(x_0, x)) dx. \quad [\text{A2}]$$

If this integral obtains most of its value over a local region of the T -space, that is,

$$\int_{-\infty}^{\infty} f(\Delta S(x_0, x)) dx \approx \int_{x_0-x_1}^{x_0+x_1} f(\Delta S(x_0, x)) dx \quad [\text{A3}]$$

and the function $\Delta S(x_0, x)$ can be approximated to first order in the interval (x_0-x_1, x_0+x_1) then a simplification can be made. In these circumstances we can write

$$\int_{x_0}^{\infty} f(\Delta S(x_0, x)) dx \approx \int_{x_0}^{\infty} f\left(\left|\frac{\partial S}{\partial x}\right|_{x_0} (x - x_0)\right) dx = \int_0^{\infty} f\left(\left|\frac{\partial S}{\partial x}\right|_{x_0} |x|\right) dx, \quad [\text{A4}]$$

where we have considered only the part of the integral in the direction of increasing x . The other direction is treated similarly. Now substituting $u = \left|\frac{\partial S}{\partial x}\right|_{x_0} |x|$ the integral becomes

$$\left|\frac{\partial S}{\partial x}\right|_{x_0}^{-1} \int_0^{\infty} f(u) du. \quad [\text{A5}]$$

Because $\int f(u) du$ is a constant which is independent of the protocol, the integral in Eq. [A5] is linearly proportional to $\left|\frac{\partial S}{\partial x}\right|_{x_0}^{-1}$. In a fashion similar to this the result for two- and three-dimensional T -spaces can be derived.

If we define the constant $K = \int f(u) du$, the result for a two-dimensional T -space in polar coordinates is

$$K \int_{\theta} \left|\frac{\partial S}{\partial r}\right|_{\theta}^{-2} d\theta, \quad [\text{A6}]$$

where $\partial S/\partial r$ is the radial derivative of the signal strength. In three dimensions the result is expressed in spherical polar coordinates as

$$K \int_{\theta} \int_{\phi} \left|\frac{\partial S}{\partial r}\right|_{\theta, \phi}^{-3} \sin \theta d\theta d\phi. \quad [\text{A7}]$$

These results imply that the important value for calculating tradeoffs is the *inverse* of the derivative. In multidimensional T -spaces, the radial derivative at an operating point can be used to evaluate sensitivity in all directions around that point. Maximum overall sensitivity at the point is achieved when the integral of $|(\partial S/\partial r)|^{-N_p}$ over all directions is minimized.

This result is valid only if the function $\Delta S(\mathbf{r}_o, \mathbf{r})$ can be approximated with a linear expansion in the region of space in which the integral obtains the major fraction of its value. For our purposes this implies that the function $\Delta S(\mathbf{r}_o, \mathbf{r})$ is linear over the region in which $\Delta S < 4$, (i.e., the SDNR is less than 4). Outside this region there is a high probability that the point $\mathbf{r}_o + \mathbf{r}$ will be distinguished from the operating point $\mathbf{r}_o$, and the function $\ln\left(\frac{1}{2}\left(1 + \operatorname{erf}\left(\left|\Delta S(\mathbf{r}_o, \mathbf{r})\right|\right)\right)\right)$ is nearly zero.

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FIG. 1. A mapping from the two-dimensional T -space, $T_1 \times T_2$, to a two-dimensional S -space, $SE(500, 15) \times SE(2000, 60)$.

FIG. 2.
Spherical polar coordinates defined at the operating point.

FIG. 3.

The sensitivity profile $|\Delta S(\theta, \phi)|$ at $T_1 = 750$ ms, $T_2 = 75$ ms, $N(H) = 0.8$, plotted for four protocols with equivalent imaging times. (a) A T_1 -weighted sequence SE(375, 20). TE = 20 was chosen as the minimum TE available. (b) A T_2 -weighted sequence multiecho SE(1100, 80). TE = 80 was the optimal TE consistent with the multiecho pulse sequence and multislice constraints. (c) An $N(H)$ -weighted sequence multiecho SE(1100, 20). (d) The profile of a protocol that is composed of the three sequences (a), (b), and (c), with the imaging time held constant.

FIG. 4.

(a) The function $P(T_{10}, T_1)$ from Eq. [4] for $T_{10} = 750$ ms. The pulse sequence is SE(375, 20); the SNR is assumed to be 100. (b) The function $\ln(P(T_{10}, T))$. The stippled area is the magnitude of the integral given in Eq. [5].

FIG. 5. A plot of the function $|\Delta S(\theta, \phi)|^{-3} \sin \theta$. The peaks in the function show directions of lower sensitivity.

FIG. 6. Plots of the figure of merit vs TR1 and TR2 with all other parameters fixed at the optimal protocol values. (a) The figure of merit vs TR1. (b) The figure of merit vs TR2.

FIG. 7.

The figure of merit as a function of the fraction of imaging time spent on the T_2 - $N(H)$ -weighted multiecho SE pulse sequence.

FIG. 8.

A plot of $|\Delta S(\mathbf{r}_0, \mathbf{r})|$ (solid line) for the direction of changing T_1 . The position in T -space is $T_1 = 750$ ms, $T_2 = 50$ ms, and the dashed line is the tangent to $\Delta S(T_{10}, T_1)$ at that point. The function $\Delta S(T_{10}, T_1)$ is approximately linear for a large range of ΔS values.