Journal of Magnetic Resonance **139,** 74–80 (1999)
Article ID jmre.1999.1757, available online at http://www.idealibrary.com on IDEAL®

Signal Intensities in FLASH-EPI-Hybrid Sequences

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Received August 5, 1998; revised February 24, 1999

Theoretical considerations on the signal-to-noise ratio (SNR) in FLASH-EPI-Hybrid imaging were published previously. The purpose of this work was to investigate *in vivo* the signal intensities in Hybrid images as a function of sequence specific parameters. In detail, the SNR as a function of the number of echoes *m* per RF excitation, the excitation flip angle α, and the dependence on the tissue relaxation times T1 and T2* were studied. In eight healthy subjects brain and abdominal Hybrid images were acquired where *m* and α were changed independently. Signal intensities in human brain, liver, and kidney were evaluated for each Hybrid experiment. Additionally, T1 and T2* values of these tissue types were quantified to allow for a comparison with the theory. An excellent agreement between calculated and measured signal behavior was found. The theory was therefore validated *in vivo* and can thus be used to optimize the signal-to-noise in Hybrid experiments.

Key Words: **rapid MR imaging; multishot EPI; segmented EPI; Hybrid sequence; signal-to-noise ratio.**

INTRODUCTION

FLASH and EPI are two common fast gradient echo recalled MR imaging methods (*1, 2*). Hybrid sequences of both techniques, referred to as multishot, segmented, or interleaved EPI, have been studied recently (*3, 4*). These sequences are based on the acquisition of multiple lines in *k*-space after each RF excitation pulse (*k*-space segmentation). Thus, in comparison to FLASH imaging, Hybrid sequences allow for considerably reduced acquisition times due to a reduced number of excitation pulses and gradient switching steps. In addition, higher excitation angles may be applied because of longer repetition times (TR). This results in an increased signal-to-noise ratio (SNR). In comparison to single-shot EPI, Hybrid imaging provides a better spatial resolution and signal gain because shorter echo trains are less prone to T2* losses.

Typical Hybrid applications, such as cardiac and abdominal studies or functional MR imaging, demonstrate the potential advantages of the Hybrid sequences over the conventional techniques (*5–7*). However, the published studies using the Hybrid approach were focused exclusively on qualitative criteria, e.g., the lesion/adjacent tissue contrast, the overall image quality, the absence of motion artifacts, or the obtainable resolution within a single breath-hold. In almost all these studies only a few segmentation steps were tested (generally a two-, four-, or eight-shot EPI sequence) and the results were compared qualitatively with established techniques (*6, 8, 9*). Hence, today the number of echoes per shot is mostly chosen empirically: About 3 to 5 echoes are used for cardiac investigations, and a higher echo train length for brain imaging.

The purpose of this study was to compare the performance of Hybrid sequences *in vivo* in a quantitative fashion. Thus, signal intensities in Hybrid images were investigated systematically, since the obtainable SNR depends on tissue as well as on imaging parameters. For example, if the transverse relaxation time T2* of a tissue is short, there is a fast decay of the transverse magnetization during the acquisition of the multiple echoes within a Hybrid echo train. This leads to a considerable signal loss of the final echoes and thus to a loss of SNR in the image. Therefore, Hybrid experiments with small echo train length *m* are recommended. If the longitudinal relaxation time T1 of the investigated tissue is long, there is a slower longitudinal relaxation during the repetition time TR. Thus, smaller excitation flip angles α have to be used, which results in a low SNR.

This demonstrates that the SNR and the respective contrast in a Hybrid image for a certain type of tissue depend on two sequence parameters: the number of echoes *m* and the flip angle α. Nonoptimized parameters result in a significant signal loss, which may overcompensate the advantages of the Hybrid technique over FLASH or EPI. This signal loss can be avoided by applying a theoretical approach reported in Ref. (*10*), which describes the signal strength of a Hybrid sequence in dependence on *m* and α. These calculations utilize as input parameters the relaxation times T1 and T2* of the target tissue and imaging parameters of the applied Hybrid sequences. With the knowledge of these input parameters, Hybrid experiments can be simulated first and then performed under optimized conditions, maximizing the SNR within the minimum possible imaging time.

Therefore, the aim of this work was to verify the theory *in vivo* for several organs on a standard clinical scanner and to suggest optimum parameters for Hybrid experiments performed for each anatomical region investigated in this study.

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1090-7807/99 $30.00

THEORY

In Hybrid imaging a series of m echoes with a different degree of phase encoding is acquired after a slice selective RF pulse α, thus covering m distinct lines in k-space. If n echo trains are measured, the total number of phase encoding steps N is given by $N = n \cdot m$. For $m = 1$, the Hybrid sequence corresponds to a FLASH experiment; for $m = N$, to an EPI sequence.

In general, there exists an optimum pair of parameters m and α that provides the maximum SNR for a given tissue. These optimum values can be determined by using the knowledge of the longitudinal relaxation time T1 and the effective transverse relaxation time T2* and by applying a theory reported in Ref. (*10*). This theoretical approach was originally developed for a point source where in the ideal case of no relaxation each sampled k-line has the same contribution to the signal. In the following we summarize the most important results of this theory for completeness:

(a) For a given set of tissue relaxation times T1 and T2* there exists an optimized Hybrid sequence characterized by a set of values (m, α) that maximizes the SNR to a value which is usually higher than the SNR of a FLASH or an EPI sequence.

(b) The influence of T2* is much more pronounced than the influence of T1.

(c) The optimum value of m increases with T2*.

(d) If the optimum values of m and α are chosen, there is no deterioration of the image resolution due to the decay of transverse magnetization during the acquisition of the echo train.

(e) The effect of diffusion may be neglected under standard imaging conditions, but may be considerable for NMR microscopy.

In the original theory two attenuation factors, A_p and B_q, were calculated for each sampled echo, whereby p ($p = 1, \ldots, n$) denotes the respective RF excitation number and q ($q = 1, \ldots, m$) the position of the echo within the echo train. The signal intensity normalized to 1 is weakened by A_p due to T1 relaxation during the course of the acquisition (*11*) and by B_q due to T2* relaxation during the sampling period of an echo train.

For the calculation of the signal attenuation factors A_p the following basic principles have to be assumed: If each RF pulse turns the magnetization by a flip angle α and spoiling is performed at the end of each repetition time, the longitudinal magnetization $M(t)$, which is due directly before the RF excitation performed at time $t = i$ TR ($i = 0, \ldots, n - 1$), approaches a saturation value M_0^*, which is smaller than the equilibrium value M_0. If the spin system is relaxed completely at the beginning of the measurement, the time dependence of the longitudinal magnetization $M(t)$ can be written as (*11*)

$$M(t) = M_0^* + (M_0 - M_0^*)e^{(-t/\mathrm{T1}^*)}, \qquad [1]$$

where the saturation magnetization M_0^* is given by

$$M_0^* = M_0 \frac{1 - e^{-\mathrm{TR/T1}}}{1 - \cos\alpha e^{-\mathrm{TR/T1}}} = M_0 \frac{1 - e^{-\mathrm{TR/T1}}}{1 - e^{-\mathrm{TR/T1}^*}}. \qquad [2]$$

For $\alpha < 90°$ an effective longitudinal relaxation time T1*, which is shorter than T1, is given by

$$\frac{1}{\mathrm{T1}^*} = \frac{1}{\mathrm{T1}} - \frac{1}{\mathrm{TR}} \cdot \ln\cos\alpha. \qquad [3]$$

With a choice of repetition time TR $\ll$ T1 and TR $\ll$ T1*, the saturation magnetization M_0^* can be approximated as

$$M_0^* = M_0 \mathrm{T1}^*/\mathrm{T1}. \qquad [4]$$

The attenuation factor A_p describes the longitudinal magnetization directly before the pth excitation at the time $t = (p - 1)(\mathrm{TR})$ divided by M_0 for normalization to 1. As a result the factor A_p may be written with Eq. [1] as

$$A_p = \frac{1}{M_0}\{M_0^* + (M_0 - M_0^*)e^{-((p-1)\mathrm{TR})/\mathrm{T1}^*}\}. \qquad [5]$$

The B_q factors are calculated using the equation

$$B_q = e^{-(\mathrm{TE}(q))/\mathrm{T2}^*}, \qquad [6]$$

with TE(q) denoted as the echo time of the qth echo of the echo train.

A double sum over the contributions ($A_p \cdot B_q$) of all echoes, multiplied by sinα to take into account that the transverse component of the magnetization is used for imaging, and divided by N for normalization, yields the resulting signal intensity, and thus the achievable SNR in a Hybrid image:

$$S(m, \alpha) = \frac{1}{N} \sum_{p}^{n} A_p \sum_{q}^{m} B_q \sin\alpha. \qquad [7]$$

For known T1 and T2* relaxation times and for a fixed matrix size $N = n \cdot m$, Eq. [7] describes the theoretical signal intensity $S(m, \alpha)$ in a parameter space formed by α and m. This means the signal intensity can be maximized in dependence on α and/or m, where the global maximum can be found by varying both parameters. The parameters α and m of this maximum describe the sequence with optimum SNR for the given T1 and T2* values. It should be noted that the optimum flip angle α is larger than the corresponding Ernst angle, which may be calculated by TR and T1. This is due to the extremely

short duration of the experiments, during which the spins do not reach the steady state.

The theory will be discussed in case of interleaved *k*-space trajectories (*3*) with odd-numbered sampled echoes, since this was the sampling scheme used in our experimental setup.

Furthermore, we assume an object with constant spin density that covers a large portion of the field of view in the phase-encoding direction. For this case the echo data set is weighted by a sinc function that has a sharp maximum at the center of *k*-space. Therefore, we neglect the contribution to the SNR in the final tomogram of all the *k*-space lines but the central *k*-space line ($k_y = 0$).

One thus can use a "mean attenuation factor" to characterize the Hybrid experiment. This is a good approximation to the original theory for two reasons: First, with the applied interleaved *k*-space sampling scheme the excitation of the echo train that contains the central echo ($k_y = 0$) is performed exactly at half of the imaging time. Therefore, the T1* weighting of this echo represents in first-order approximation the mean T1* weighting of all sampled echoes. Second, since an odd number of echoes is sampled within each echo train, the echo with $k_y = 0$ is also positioned exactly in the center of this echo train. Therefore, the T2* weighting of this echo corresponds approximately to the mean T2* weighting of all echoes.

The expected theoretical signal intensities in an interleaved Hybrid sequence for given parameters T1, T2*, TR, m, and α were calculated in the following way: (i) A_p was calculated from Eq. [5] with $p = n/2$. (ii) B_q was calculated from Eq. [6] with $q = (m + 1)/2$. (iii) The normalized signal intensity was then given by $A_p \cdot B_q \cdot \sin \alpha$.

The slice profile of the applied Gaussian-shaped RF pulse in our experiments was taken into consideration by dividing the slice into several subslices with corresponding flip angles α_i. The signal intensity was then calculated as described before for the different α_i and a sum over each value within the slice was performed.

EXPERIMENTAL

All experiments were performed on a clinical 1.5 T MAGNETOM Vision MRI scanner (Siemens Medical Systems, Erlangen, Germany). Hybrid images of the brain and the abdomen of eight healthy volunteers (four each) were acquired stepping m and α independently. The flip angle α was increased successively from 10° to 70° with a 5° increment keeping m constant. These measurements were repeated for $m = 3, 5, 7, 9, 13, 15, 21, 27$ and additionally, in the case of brain imaging, for $m = 31, 41, 85$. These special values of m have been used because they allow experiments to be performed with an odd number of echoes per shot and with nearly equal matrix size, which is necessary to provide comparable SNR measurements.

The matrix size was $(n \cdot m) \times 256$, where n is computable via integer division of 256 by m. Using a sampling bandwidth of ±100 kHz the echo time for the first echo of all Hybrid echo trains was 3.16 ms and the interecho spacing was 2.48 ms. TR depended on the value of m and was given by TR = 7.8 ms + $(m - 1) \cdot 2.48$ ms, where the delay of 7.8 ms includes slice selection, sampling of the first echo, and spoiling of the magnetization with a variable gradient spoiler in slice direction at the end of TR. The resulting scan times were in the range of 635 ms ($m = 85$) to 1035 ms ($m = 3$).

All brain images were acquired with FOV = 250 mm × 250 mm and a slice thickness of 5 mm using the standard head coil. Abdominal imaging was performed with FOV = 350 mm × 350 mm and slice thickness = 8 mm using the body coil, where always four averages were taken to provide sufficient SNR. No fat suppression was applied in any investigation.

To allow for a comparison with the theory, the input parameters T1 and T2* were determined in additional experiments. T1 was quantified as described in Ref. (*11*) by calculating a T1 map from the data acquired in a series of snapshot FLASH images after inversion of the longitudinal magnetization. The coverage of the relaxation curve was improved six-fold by using a segmented version of the original technique. The acquisition parameters were TE = 3.16 ms, TR = 4.66 ms, flip angle 5°, matrix size = 246 × 256, FOV = 250 mm × 250 mm (350 mm × 350 mm), slice thickness = 5 mm (8 mm), 16 images in series, providing a temporal resolution of 194.2 ms, number of averages 4, and total acquisition time = 7 min 14 s.

T2* was measured with a multiecho FLASH sequence: After each excitation a series of 16 echoes was acquired, resulting in 16 images with different TE and different T2* weighting. The parameters were TE (first echo) = 3.8 ms, interecho time = 5 ms, TR = 100 ms, flip angle = 30°, matrix size = 255 × 256, total acquisition time = 26 s. FOV and slice thickness were chosen according to the brain and abdominal studies.

For each subject and each pair of values (m, α) signal intensities S were obtained from regions of white and gray matter in the human brain and from regions of the liver and the kidney in the abdominal images. T1 and T2* values of these regions were taken from the corresponding maps and used to calculate the theoretical signal behavior. The optimum Hybrid parameters (m_{theo}, α_{theo}) for these input values (T1, T2*) can be obtained from the coordinates of the maximum of the function $S(m, \alpha)$.

RESULTS

As an example Figs. 1a–1c show Hybrid images of the human brain from a healthy volunteer acquired with different echo train lengths ($m = 3, 27, 85$) and flip angles ($\alpha = 15°, 40°, 55°$). These flip angles provide maximum SNR in white matter for the chosen m values. To demonstrate the obtained signal changes, Figs. 1a–1c are scaled equally. Figure 1b shows the maximum signal intensity for white matter. Figures

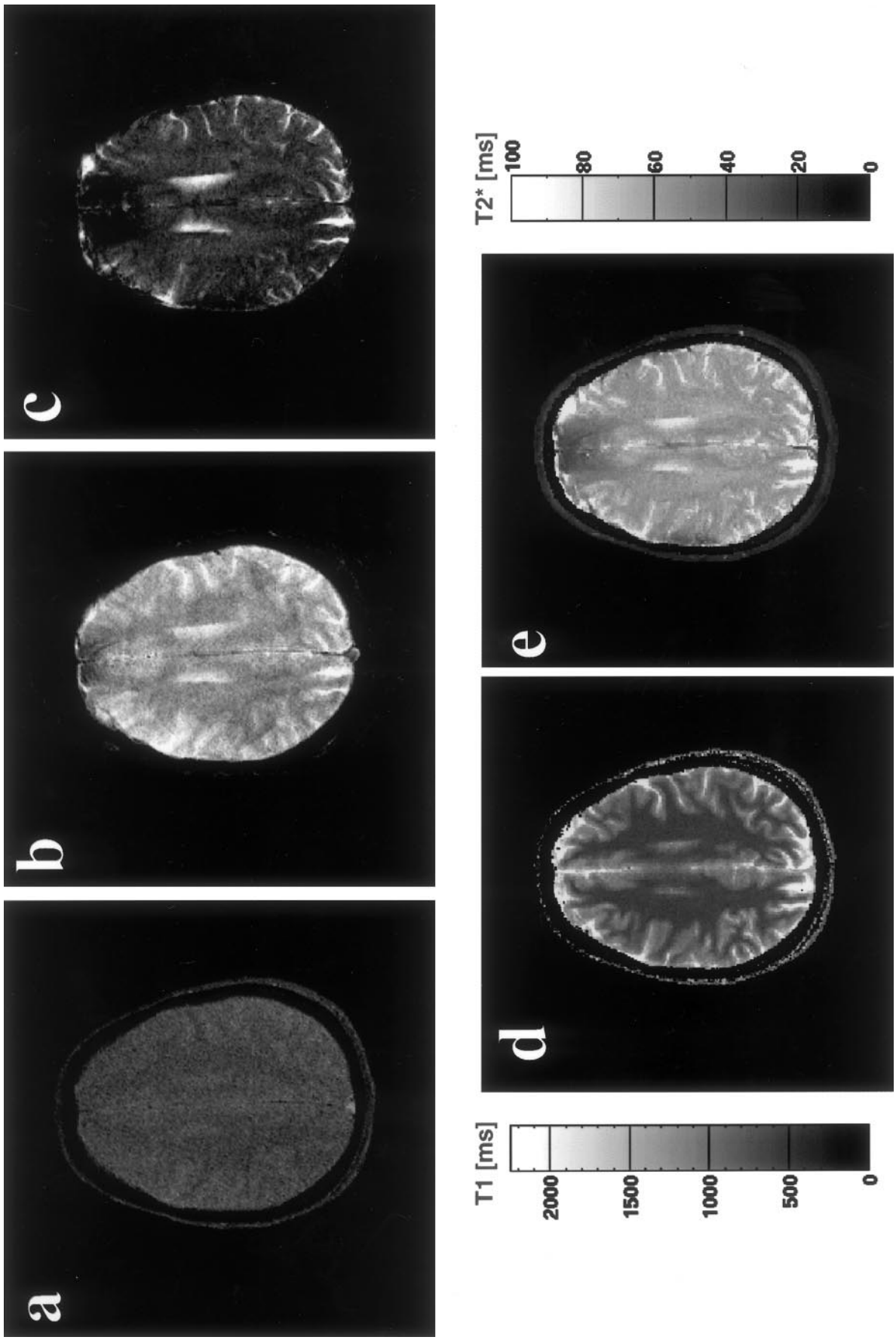

FIG. 1. Selected results of brain imaging experiments of one healthy volunteer. (a) Spin density weighted Hybrid image with $m = 3$, $\alpha = 15°$. (b) Optimal Hybrid image with $m = 27$, $\alpha = 40°$, providing maximum achievable SNR in white matter. (c) Suboptimal Hybrid image with $m = 85$, $\alpha = 55°$. (d) T1 parameter map at the same slice position as (a)–(c). (e) Corresponding T2* map. To allow for comparison of the signal intensities, (a)–(c) are scaled equally.

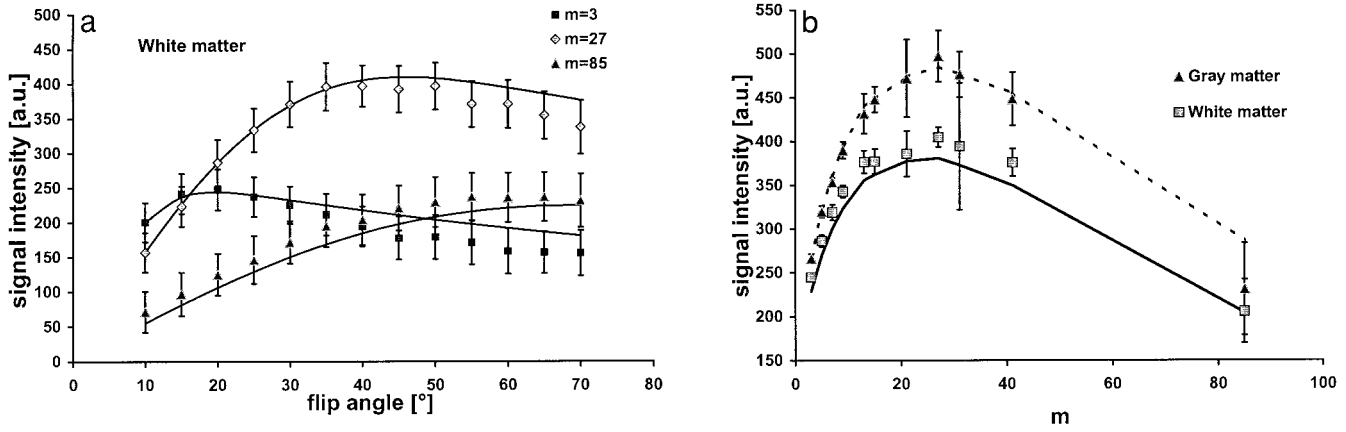

FIG. 2. (a) The plot shows the measured signals and standard deviations (SD) from white matter region as a function of the flip angle α in a single subject. Different values of m are depicted with different symbols. The solid lines are the corresponding theoretical curves. (b) Mean signal intensity (4 subjects) and SD in dependence on the echo train length m in human brain using optimized flip angles α. The corresponding theoretical curves are plotted over the experimental data.

1d and 1e display the corresponding T1 and T2* maps at the same slice position, respectively.

Figure 2a shows the measured signal as a function of the excitation angle α obtained with Hybrid sequences of different echo train length in the white matter region of a single subject. These results demonstrate that there exists an optimum flip angle providing maximum SNR for each Hybrid sequence. This flip angle is larger than the Ernst angle because in most cases saturation conditions are not reached during the acquisition of a single image as a result of the low number of excitations. For smaller values of m, the maximum SNR is found at lower flip angles. An increase of the echo train length shifts the maximum to higher flip angles as expected, since TR increases with m.

The highest signal intensity and the corresponding flip angle was determined for each value of m. In Fig. 2b these signal intensities are plotted as a function of m for white and gray matter averaged over the four subjects. Figures 3a and 3b show equivalent plots to Figs. 2a and 2b for liver (Fig. 3a) and both liver and kidney (Fig. 3b).

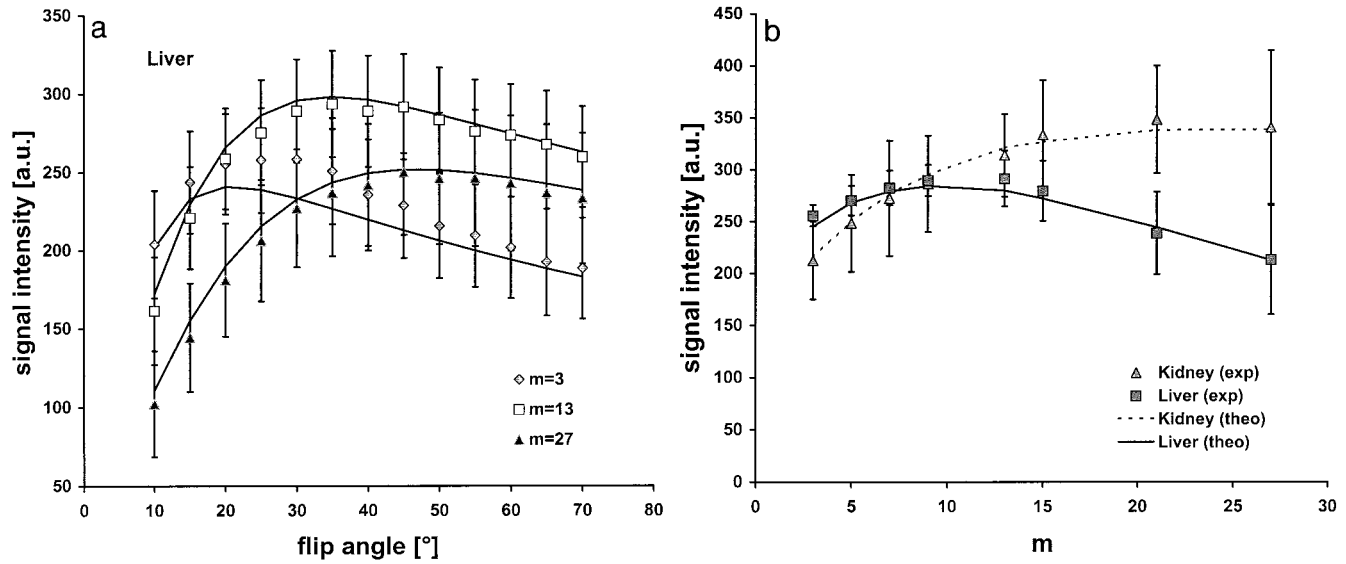

FIG. 3. (a) Signal intensities and SD measured in liver as a function of the flip angle α in a single subject. Different values of m are depicted. The corresponding theoretical curves are plotted as solid lines. (b) Mean signal intensity (4 subjects) and SD and corresponding theoretical curves of liver and kidney tissue in dependence on the echo train length m using optimized flipangles α.

TABLE 1
Experimentally and Theoretically Obtained Results (Mean ± St Dev, 4 Subjects)

Tissue	T1 (ms)	T2* (ms)	m_{exp}	m_{theo}	α_{exp} (°)	α_{theo} (°)
Gray matter	1144 ± 9	73 ± 6	26 ± 3	27 ± 0	39 ± 3	40 ± 0
White matter	605 ± 13	66 ± 4	28 ± 2	26 ± 3	46 ± 5	44 ± 3
Kidney	1319 ± 104	64 ± 15	24 ± 4	24 ± 7	36 ± 8	33 ± 5
Liver	616 ± 5	29 ± 5	13 ± 3	11 ± 2	38 ± 9	33 ± 3

Figures 2b and 3b also demonstrate the existence of an optimum Hybrid experiment with maximum SNR for each type of tissue. The corresponding parameters (m_{exp}, α_{exp}) are summarized in Table 1.

Table 1 also summarizes the measured T1 and T2* values averaged over the four subjects for each selected tissue. In each experiment the average deviation of T1 in the chosen region was less than 10%. The measured values of T1 agree with those reported in literature (*12, 13*). T2* is mainly affected by the local field homogeneity and consequently depends on the shim. Thus, the T2* values for a certain tissue show large variations inter individually in the range of 6 to 23% (Table 1).

The theoretical signal intensities were calculated for the four tissues, averaged, and added to Figs. 2b and 3b. The optimum theoretical results (m_{theo}, α_{theo}) are also summarized in Table 1. Examples for individual calculations are given in Figs. 2a and 3a.

DISCUSSION

Our results, as summarized in Table 1, demonstrate the agreement of theory and experiment: in all investigated tissues the theoretically and experimentally obtained optimum parameters (m_{theo}, α_{theo}) and (m_{exp}, α_{exp}) agree always within their standard deviations.

It is essential for both the experiments and the calculations to determine the relaxation times T1 and T2* as precisely as possible, since the signal behavior in a Hybrid sequence is very sensitive to these parameters. This can be seen, e.g., from the kidney data, where the relaxation times show a large scatter. As a result, the theoretically obtained optimum parameters in this tissue show the largest deviations.

T2* has the main influence on the signal behavior, which can be easily demonstrated with Table 1: In the gray matter, the white matter, and the kidney the optimum echo train length m is almost the same because of the similar T2* values, although there are considerable differences in T1 in the range of 600 to 1300 ms. The increase of T1 causes only a slight decrease of the optimum flip angle as expected, whereas the strong dependence on T2* is clearly demonstrated for the liver with the shortest T2* relaxation time. In this case the number of echoes that deliver the optimum SNR is, because of the short T2*, $m = 11$, and thus it is the smallest value observed in this study.

In Fig. 1 several brain images for flip angles optimized for the chosen echo train lengths are depicted. Clearly a different T2* weighting of the images is observable, since the weighting of the magnetization and thus the contrast changes with the echo train length, which has to be taken into account when using an interleaved *k*-space coverage. Figure 1a shows only spin density contrast for $m = 3$. The image sampled under optimum conditions for white matter ($m = 27$) has maximum SNR in white matter and a moderate T2* contrast (Fig. 1b). Figure 1c ($m = 85$) is strongly T2* weighted because of the long TE of the central echo. This is very pronounced in the sinus region and can be seen in comparison to the T2* map (Fig. 1e). In Fig. 1c, the flip angle $\alpha = 55°$ is optimized for maximum SNR in the case of the applied echo train length $m = 85$, but m and α are larger than the optimum pair of values (m, α), which maximizes the SNR and is given by $m = 27$ and $\alpha = 40°$. Besides a signal loss compared to Fig. 1b, the image resolution is degraded in consequence of the badly chosen parameters as described in the theory.

When performing Hybrid experiments, an evaluation of the theoretical signal intensity given by Eq. [7] should be accomplished first and then the parameters (m, α) optimizing theoretically the SNR should be used for imaging. As an example in the case of white matter imaging, the experimentally determined T1 and T2* values led to an optimum flip angle of 44° and an optimum echo train length of 26 applying the theory (Table 1). Experimentally it was confirmed that these values indeed yielded the maximum signal.

Generally, if the T1 and T2* values of a tissue are known from experiments or literature, they can be used to calculate the optimum parameters (m, α).

It should be noted that the Hybrid sequence that maximizes the SNR in a certain tissue is not necessarily identical to the sequence that provides optimum contrast for the respective application. The theoretical approach not only can be used to optimize the SNR, but may also be applied to maximize the contrast between different types of tissue. The way to proceed is demonstrated for white/gray matter contrast: According to result (d) from Theory, the optimum echo number m_{CNR} should not be longer than the optimum m_{SNR} calculated for any of the two tissues; otherwise, this would lead to losses in spatial resolution. If this condition is fulfilled, the sequence parameters (m_{CNR}, α_{CNR}) providing the maximum difference in the

available signal intensity for both compartments have to be determined theoretically using Eq. [7]. In the case of white matter/gray matter this will be achieved using $m_{CNR} = 7$ and $\alpha_{CNR} = 18°$.

In abdominal imaging we observed a more general problem with Hybrid imaging using high m values ($m > 27$) in tissues with low T2*: the appearance of uncorrectible artifacts due to motion, flow artifacts in large vessels, and susceptibility effects within tissue interfaces. Therefore, imaging with $m > 27$ was not performed in this study.

However, flow artifacts and the effects of T2* may be overcome by applying a center–out k-space trajectory, where the theoretical calculations have only slightly to be modified.

One field of application for Hybrid sequences is fast real-time imaging, e.g., functional, interventional, or perfusion imaging. These measurements are always performed under steady-state conditions. Although the original theory was developed for relaxed spin systems, it may be applied to steady-state measurements after minor modifications: The saturation value of the longitudinal magnetization has to be chosen as the starting value for the recursive calculation algorithm.

CONCLUSION

In summary, we validated successfully a theory for the optimization of the SNR obtainable in a Hybrid image *in vivo*. We suggest using a priori information about the tissue relaxation times before performing Hybrid experiments. This can be realized by performing quantitative T1 and T2* measurements, but in most cases it will be sufficient to know the T1 or T2* values reported in literature. The theory can thus be used to predict the signal intensities in Hybrid imaging or increase significantly the SNR by optimization of the Hybrid parameters m and α. Optimized Hybrid sequences usually yield a higher SNR than standard FLASH or single-shot EPI techniques.

ACKNOWLEDGMENTS

The authors thank Dr. P. M. Jakob for helpful discussions and gratefully acknowledge financial support by the Bundesministerium für Bildung und Forschung (BMBF) grant “Medizin 2000—interdisziplinäres Zentrum für klinische Forschung (Projekt F1).”

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