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Intravoxel Incoherent Motion Imaging Using Steady-State Free Precession

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IVIM MR imaging is a method which generates images of diffusion and perfusion *in vivo*. Until now, *i*ntravoxel *i*ncoherent *m*otion (IVIM) images have been obtained using spin-echo sequences with extragradient pulses, resulting in long acquisition times (typically 2 × 8 min 32 s). A new method is proposed here, using *s*teady-*s*tate *f*ree *p*recession (SSFP), which allows IVIM images to be obtained in a couple of minutes. Phantom studies showed that the sensitivity of SSFP to IVIMs is much greater than that of spin echoes. *In vivo* images are shown. © 1988 Academic Press, Inc.

INTRODUCTION

IVIM (*i*ntra*v*oxel *i*ncoherent *m*otion) imaging is a method which delivers images of microscopic translational motions occurring in each image voxel (*1*). In biological tissues, these motions essentially are molecular diffusion; microcirculation of blood in the capillary network (perfusion); and nonuniform slow flows, such as cerebrospinal fluid (CSF) flow. Molecular diffusion effects in the presence of magnetic field gradients were demonstrated by Hahn in 1950 (*2*) in spin echoes, and Stejskal and Tanner were able to measure diffusion coefficients in liquids using strong gradient pulses added to a spin-echo sequence (*3*). Therefore, until now, IVIM and diffusion images have been generated using appropriate spin-echo sequences with additional gradient pulses to increase their sensitivity to microscopic motion (*1, 4, 5*). However, the strength of these gradient pulses is limited on conventional MR units, so that their duration must be quite long (typically 2 × 35 ms in our experiments) to produce an effect from IVIMs, thus increasing the echo time (TE = 140 ms) (*1*). To limit a decrease in the signal-to-noise ratio which results from long TE, a long repetition time is needed (typically TR = 1000 ms), and the acquisition time of such a sequence is 8 min 32 s (256 × 256 data set, two excitations). Pairs of sequences, with and without these additional gradient pulses, are needed to eliminate T1 and T2 effects in IVIM images (*1*), resulting in a total acquisition time of 17 min. Although regular T2 images and different slices are also obtained by the end of this period, such a long amount of time may be a problem in clinical practice. On the other hand, it has been pointed out that sequences using *s*teady-*s*tate *f*ree *p*recession (SSFP), which allows very short acquisition times (*6, 7*) to be reached, are very sensitive to phase coherence and slow flow, especially when a transverse magnetization steady state is involved in the presence of magnetic field gradients (*8*). In particular, the effect of gradient strength on sensitivity of SSFP

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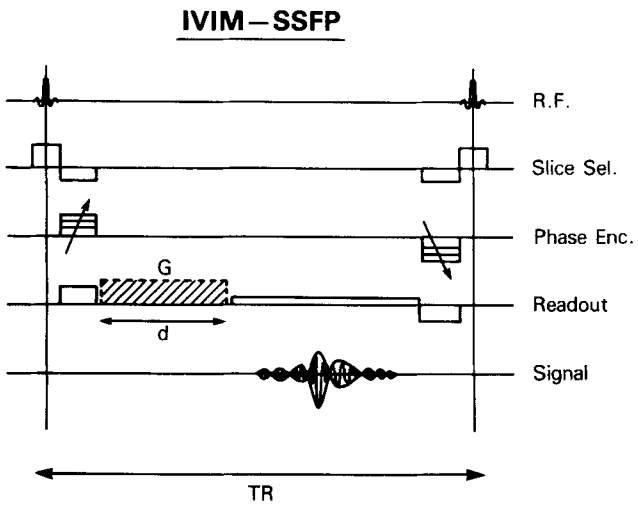


FIG. 1. Diagram of the pulse program used for IVIM-SSFP imaging. The SSFP sequence is sensitized to IVIMs by an additional gradient pulse (strength G, duration d). IVIM images are generated from twin sequences differing only by the presence or absence of the gradient G.

to slow flow has been shown by Patz *et al.* (*9, 10*). Short acquisition time and high sensitivity to phase shifts make SSFP an ideal method for IVIM imaging.

MATERIALS AND METHODS

All experiments were performed on a Thomson-CGR Magniscan 5000 whole-body MR imaging system operating at a field strength of 0.5 T corresponding to 21 MHz proton resonance frequency. The pulse sequence for the IVIM-SSFP experiment is demonstrated in Fig. 1. To generate an IVIM image, two sequences, differing only by the presence or absence of the gradient pulse G, the duration of which is d, are used. The configuration of the gradient pulses on the readout axis is designed in such a way that the signal (pseudo-echo) preceding each RF pulse is monitored while the FID is destroyed by the first gradient pulse as previously suggested (*11, 12*). A symmetric

TABLE 1

Acquisition Parameters and Diffusion Coefficients—IVIM-SSFP Method

G (mG/cm)	200	300	400	400	400	500
d (ms)	15	15	15	15	15	20
TR (ms)	80	70	90	70	80	80
Acq. time	1 min 22 s	1 min 12 s	1 min 32 s	1 min 12 s	1 min 22 s	1 min 22 s
D acetone/D water[a]	1.84	1.96	1.90	1.85	1.93	1.92
$(b_2 - b_1)$[b] (s/mm^2)	81	123	168	170	180	252

Note. The flip angle was 45°.

[a] The diffusion coefficient ratio was calculated by D acetone/D water = [Log(M_1/M_2)] acetone/[Log(M_1/M_2)] water.

[b] The gradient factors b were calculated using Eq. [1] assuming that the ADC of water is the diffusion coefficient measured using the IVIM spin-echo method (Table 2): $b_2 - b_1$ = [Log(M_1/M_2)]/D.

TABLE 2

Diffusion Coefficients—IVIM Spin-Echo Method[a]

Acetone	4.44 ± 0.10	10^{-3} mm²/s
Water	2.31 ± 0.05	10^{-3} mm²/s
D acetone/*D* water	1.92 ± 0.08	

[a] TE = 140 ms, TR = 1000 ms (2 × 8 min 32 s acquisition time), $b_2 - b_1 = 95$ s/mm² ($G = 400$ mG/cm, $d = 2 \times 35$ ms).

disposition of the gradient pulses on the slice-selective and phase-encoding axes is aimed at enforcing transverse magnetization coherence (*11*).

IVIM images were calculated on a pixel-by-pixel basis as previously described for IVIM imaging using spin echoes (*1*) with an *a*pparent *d*iffusion *c*oefficient (ADC) which reflects not only diffusion but also other incoherent motions present in each voxel,

$$\text{ADC} = [\text{Log}(M_1/M_2)]/[b_2 - b_1], \quad [1]$$

where M_1 and M_2 are the transverse magnetization amplitudes in the first and second sequences, respectively, and b_1 and b_2 are factors depending only on the gradient pulses used (*1*). The use of the M_1/M_2 ratio should allow T1 and T2 effects to be canceled in IVIM images, at least when TR ≪ T1, T2. Images were acquired in a high-resolution mode (256 × 256) using four excitations. The acquisition parameters are shown in Table 1.

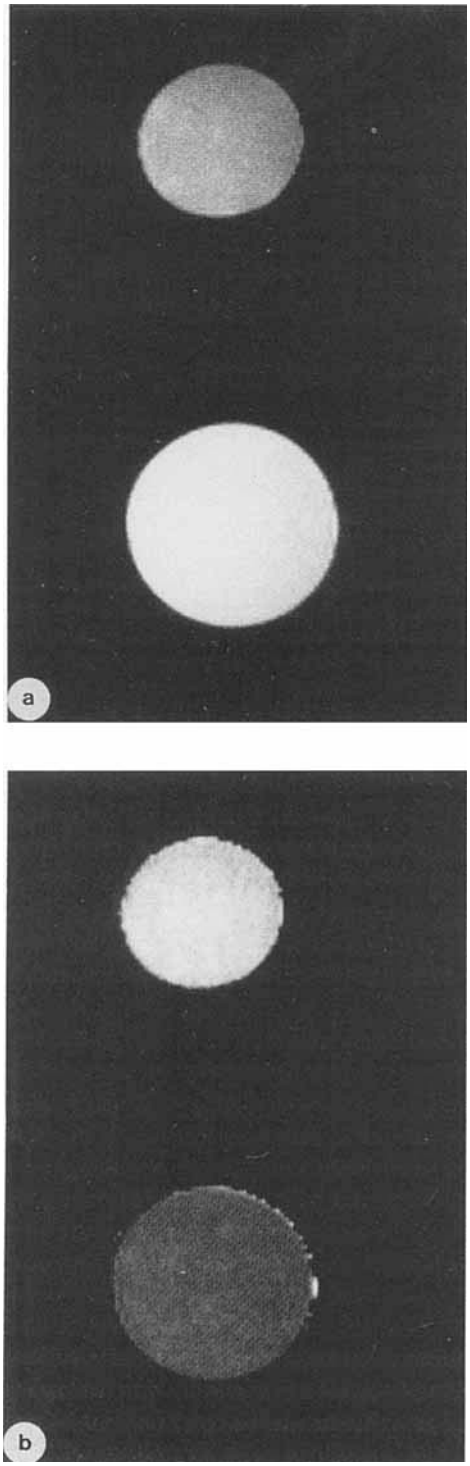
RESULTS

The method was first applied to a phantom made of two bottles, one containing acetone and the other containing water, at 25°C in which the diffusion coefficients were previously determined with the IVIM imaging method using spin echoes (Table 2, Fig. 2).

As shown in Table 1, the relative diffusion coefficient of acetone to water obtained with SSFP agreed very well with those obtained with the spin-echo method. The gradient factor b was determined experimentally from the diffusion coefficient of water using Eq. [1], because its direct calculation from gradient pulses may not be done in SSFP using the relation established from spin echoes (*1*). When compared to the IVIM spin-echo sequence, the IVIM-SSFP appeared to be much more sensitive, similar values for $(b_2 - b_1)$ being reached for a smaller gradient strength (200 mG/cm instead of 400 mG/cm) and a shorter duration (15 ms instead of 2 × 35 ms). The acquisition time is obviously particularly short (2 × 1 min 22 s instead of 2 × 8 min 32 s).

The method was then applied to a normal volunteer. Figure 3 shows a 10-mm-thick slice in a transverse orientation of the brain. The IVIM-SSFP image demonstrates that the diffusion coefficient is higher in structures containing CSF where the apparent diffusion coefficient has been shown to be equal to the diffusion coefficient of pure

FIG. 2. Phantom images (top, acetone; bottom, water): 256 × 256 row data, four excitations, 45° flip angle, 10-mm slice thickness. (a) SSFP image (TR = 70 ms, TE = 22 ms, 1-min 12-s acquisition time). (b) IVIM-SSFP image ($G = 400$ mG/cm, $d = 15$ ms). The diffusion coefficient of acetone is 1.93 times higher than that of water.


a
b

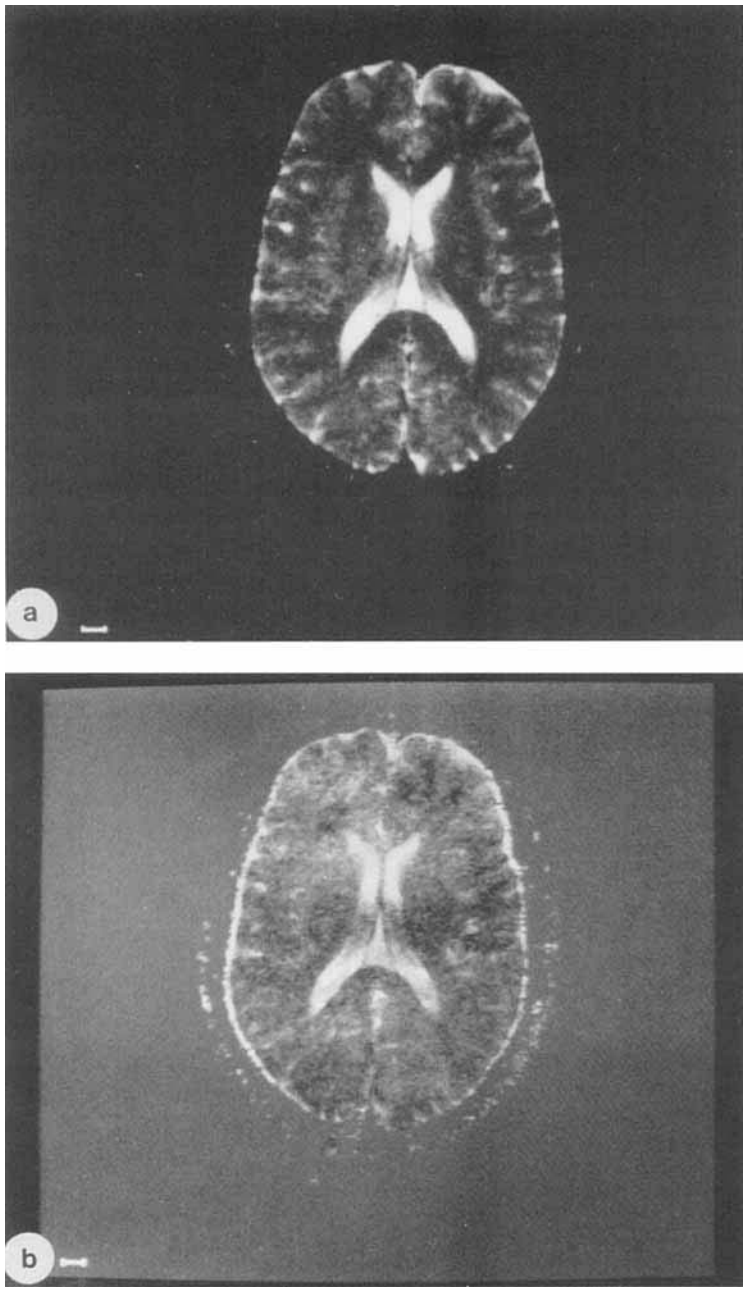


FIG. 3. Normal brain image (10-mm slice thickness, transverse orientation). (a) SSFP image (TR = 60 ms, TE = 20 ms, 25° flip angle). (b) IVIM-SSFP image of the same slice. The acquisition time was 2 × 1 min 12 s (G = 500 mG/cm, d = 15 ms). The apparent diffusion coefficient is higher in structures containing CSF where its value is close to that of pure water and greater in areas of incoherent flow. The apparent diffusion coefficient in gray and white matter is lower, reflecting restricted diffusion and perfusion in these tissues.

water or greater than it in the presence of flow (*1, 13*). The apparent diffusion coefficient in gray and white matter is low. It reflects both molecular diffusion of water and perfusion in these tissues as previously reported (*1, 13, 14*).

DISCUSSION

Interest in molecular diffusion and perfusion has been recently highlighted in tissue characterization and functional studies (*13, 14, 15*). To perform IVIM imaging as part of a clinical routine examination, one aims at using acquisition times that are as short as possible, not only for patient comfort but also to minimize the occurrence of motion artifact to which IVIM sequences are very sensitive (*1*). The high sensitivity of SSFP to phase shifts and the possibility of significantly reducing the acquisition time are very promising for IVIM imaging. A possible application of the method would be to separate perfusion from diffusion using a third sequence in the manner proposed for spin echoes (*13, 14*). As far as perfusion is concerned short acquisition times should allow dynamic studies such as those of brain activation to be performed. Even though more work is needed to optimize the signal-to-noise ratio (significant improvement has recently been obtained by implementing the sequence on a 1.5-T unit, Signa, General Electric) and to establish a direct relation between the gradient factor b and the gradient pulse diagram (so that no diffusion coefficient reference is needed), the usefulness of this IVIM-SSFP imaging method in clinical practice is already evident. A theoretical analysis of the IVIM-SSFP sequence is under way and will be presented later in a more comprehensive report of this work. IVIM images can now be obtained in a couple of minutes using SSFP, which has much better sensitivity than spin-echo sequences.

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