EPISTAR MRI: Multislice Mapping of Cerebral Blood Flow

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A method is described for multislice EPISTAR that perfectly compensates magnetization transfer effects. Inflowing arterial spins are labeled with a 360° adiabatic pulse. Two control tags are applied sequentially at the same location as the labeling pulse, each with a 180° adiabatic pulse so the total RF irradiation, frequency shift, and bandwidth of the labeling and control pulses are identical. Therefore, magnetization transfer effects are the same as for the labeling pulse and cancel with image subtraction for all slices. The method also eliminates tagging of venous spins and concern about asymmetric magnetization transfer effects.

INTRODUCTION

Radiofrequency (RF) pulses can be used to tag inflowing arterial spins for the purpose of mapping cerebral blood flow (CBF). In the original approach, arterial spins were labeled by continuous adiabatic tagging (1). Subsequently, pulsed RF tagging methods were described, such as EPISTAR (2) and FAIR (3, 4). Potentially, spin labeling methods could have clinical uses, for instance to guide the treatment of stroke or to diagnose Alzheimer's disease (5). A key issue for spin labeling techniques is that the tagging RF pulse produces a magnetization transfer (MT) effect on brain tissue (6). The signal change from MT can be comparable to that from blood flow, so it is necessary to compensate. For EPISTAR imaging, a control tag is applied above the slice to balance MT effects from the inversion tag. Unfortunately, the utility of pulsed labeling methods like EPISTAR and FAIR has been limited because only a single slice can be imaged. The reason is that MT effects are only compensated at the center slice of a multislice acquisition. We demonstrate a straightforward modification of EPISTAR that solves this problem and permits multislice mapping of cerebral blood flow.

METHODS

In EPISTAR methods, inflowing arterial spins are labeled by an adiabatic RF pulse, after which an inflow time is permitted to elapse to allow the labeled spins to enter the arterial and capillary beds of the tissue of interest. The spins are imaged with an echo planar acquisition. For arterial labeling, the spins are inverted over a 90-mm region by a 23-ms duration hyperbolic secant inversion pulse (Fig. 1). The labeling pulse is placed below the slice with a slab-selection gradient of 1.8 milliTesla/meter and has a nominal 360° flip angle (7.4 mTesla, peak voltage = 53.30V). An adiabatic pulse will invert the spins as long as the flip angle is greater than or equal to 180°. Use of a larger flip angle than 180° as done here still produces an inversion.

In the original single slice EPISTAR method, a control RF pulse equal in amplitude and thickness to the labeling pulse was applied equidistant above the slice on alternate acquisitions to compensate for MT effects. The unique feature of the new EPISTAR method is in the different way that the control pulse is applied (Fig. 2). Instead of a single 360° pulse, two RF pulses are applied in rapid sequence, each with a 180° flip angle (3.7 mTesla, peak voltage = 26.65V) but otherwise identical to the labeling pulse. A 2-ms spoiler gradient is interposed between the two pulses to eliminate any potential interference of the residual transverse magnetization created by the first 180° pulse. Additionally, the control pulses are applied at the same position as the labeling pulse, rather than above the slice. The first control RF pulse inverts the inflowing spins, while the second RF pulse reinverts them to equilibrium magnetization. As a result, there is negligible labeling of the inflowing spins by the control pulse. Since the frequency shift, slice selection gradient, and total off-resonance RF irradiation absorbed by short T_2 species are identical for the labeling and control pulses, MT effects throughout the brain are exactly identical.

Several phantom experiments have been conducted to evaluate the new approach. First of all, we measured the slice profile of the 180° and 360° pulses to demonstrate that the imperfection of RF slice profiles of these pulses do not contribute to signal variations. Secondly, to confirm that MT effects are identical for the labeling and control pulses, we performed experiments using a phantom made of 3% agarose and 97% water to assess the signal decrease caused by the saturation of macromolecular spins.

Five healthy volunteers were studied (n = 5, 2 male, 3 female, age = 23–32 years, average age = 27.2). For activation studies, they were instructed to perform repeated, rapid apposition of the thumb and fingers of the right hand. The multislice volume was presaturated immediately before each tagging pulse. The slab thickness of the labeling and control pulses was 90 mm; the slabs were positioned 65 mm below the center of the lowest slice in the multislice stack. The section thickness of each slice = 8–10 mm, field of view = 360–380 mm, matrix size = 96 × 128, 6/8 rectangular FOV. The inflow time was 900 ms, with up to a 1-s delay after each readout

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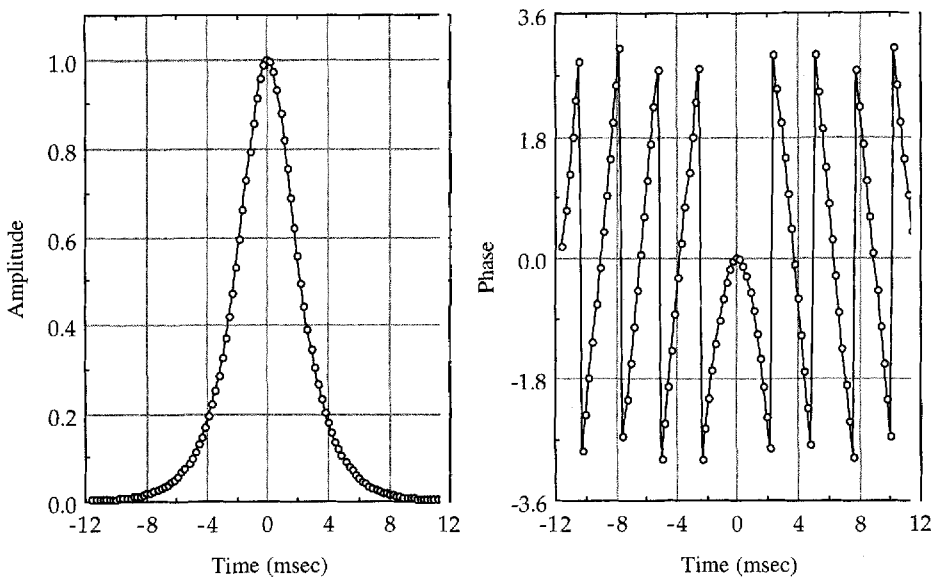

FIG. 1. Hyperbolic secant pulse (b = 600, M = 4.0) used for EPISTAR experiments.

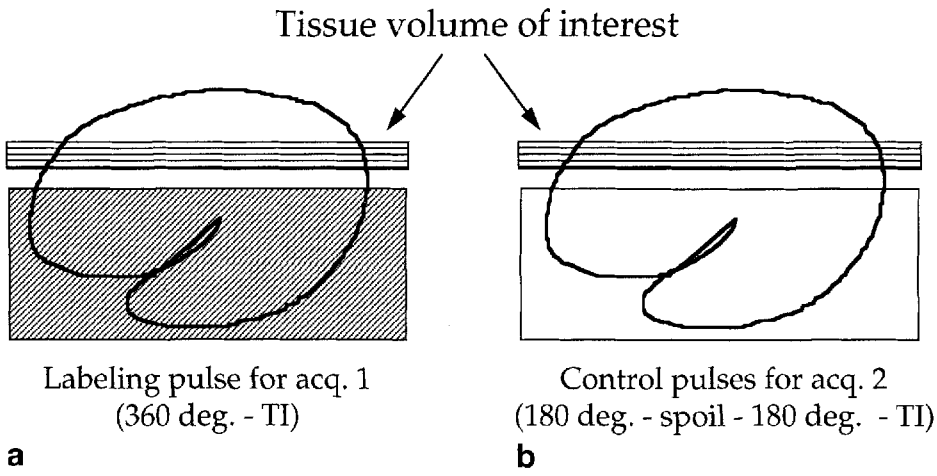

FIG. 2. New EPISTAR method. The labeling pulse (360° flip angle, shaded box) and two control pulses (each with a 180° flip angle, open box) are applied at the same location.

before the next tagging pulse was applied. The actual inflow time varied for each slice, since a total of 95.5 ms was required to acquire each successive image. For instance, in a five-slice study acquired in a top-down order, the inflow time varies from 900 ms for the first (top) slice to 1282 ms for the fifth (bottom) slice.

RESULTS

Using a Siemens resolution phantom made of 1.25 g ($NiSO_4 \times 6\ H_2O$) and 1000 g H_2O (measured T_1 = 301 ± 9 ms and T_2 = 281 ± 2 ms), the control double inversion was seen to produce minimal signal alteration in the tag region as compared with the inversion tag (Fig. 3). Signal was only present along the edges of the tag, where the nutation was less than 180° due to slice profile imperfections. To make sure these imperfections do not interfere with the tissue volume of interest, we have measured the slice profiles of both the 180° and 360° pulses using the same phantom. As demonstrated in Fig. 4, although slice profile imperfections extended from 30 to 60 mm off the center of the inversion slab, these pulses do not affect the spins in the tissue volume of interest. This is because we always place the labeling and control pulses 65 mm below the lowest slice of the multislice stack, thus eliminating their influence to the imaging slices. In addition, there was no observable effect of the slice profile imperfections on CBF maps either.

Figure 5 confirmed our hypothesis that the MT effects are identical using 360° and double 180° pulses. Using phantoms made of 100% water and 97% water/3% agarose, we have evaluated MR signals acquired with 0° (no pulse), 360° and double 180° tagging pulses applied 65 mm below the center of the imag-

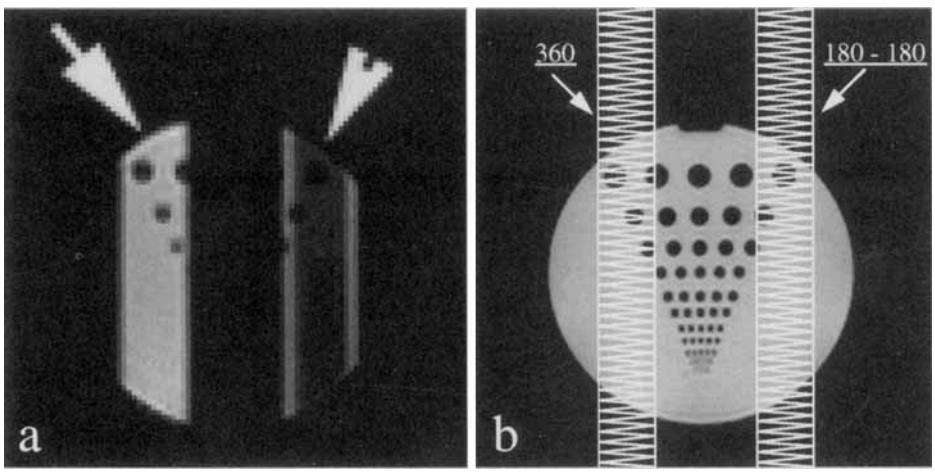

FIG. 3. (a) Resolution phantom imaged with new EPISTAR method using sagittally oriented tags for demonstration purposes. Arrow = 360° inversion tag, arrowhead = double 180° control tag. (b) Reference image of the same phantom showing locations of the tagging pulses.

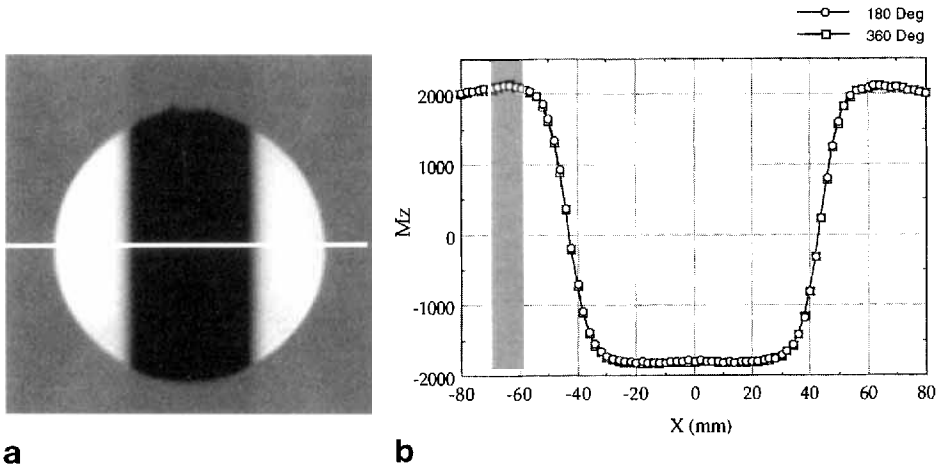

FIG. 4. Measured slice profiles of the 180° and 360° adiabatic inversion pulses. (a) A spherical phantom imaged with the 90-mm pulses applied in the sagittal orientation. (b) Plot of the slice profiles obtained from the experimental data. The patterned bar displays the location of the lowest slice of the multislice stack.

ing slice. Measurements with no tagging pulse were performed twice to assess the signal variations due to system instability. As shown on Fig. 5, no signal difference was detected in the 100% water phantom using any tagging pulses (Fig. 5c), whereas an averaged 4.6% of signal decrease due to MT effects was observed in the 100% water/3% agarose phantom using either 360° or double 180° tagging pulses (Fig. 5d). The MT effects caused by the 360° pulse is identical to that caused by the double 180° pulses within the system errors of the measurements.

In human studies, there was perfect cancellation of MT effects as demonstrated in Fig. 6. For single slice imaging, there was no observable difference in the CBF maps produced by the standard and new EPISTAR methods (Figs. 6a and 6c). Without a control pulse, much of the brain signal intensity in the EPISTAR images was contributed by MT effects (Fig. 6b). Use of two 90° control RF pulses instead of two 180° RF pulses did not eliminate MT effects, as expected (Fig. 6d). One important difference between the old and new EPISTAR methods is the decreased amount of venous tagging when the control pulses are applied below the slice, as evidenced in the reduced amount of signal in the superior sagittal sinus.

Figure 7 shows an example of a six-slice EPISTAR acquisition. The data were collected with 48 excitations over a period of 1 min 45 s. Cortical enhancement is shown on all slices except the top one (upper left), where most enhancement is still in the arteries. No evidence of subtraction artifact or residual magnetization transfer effects are identified. The absence of venous tagging makes it easier to visualize the posterior aspect of the occipital lobes than would be possible with the old EPISTAR method.

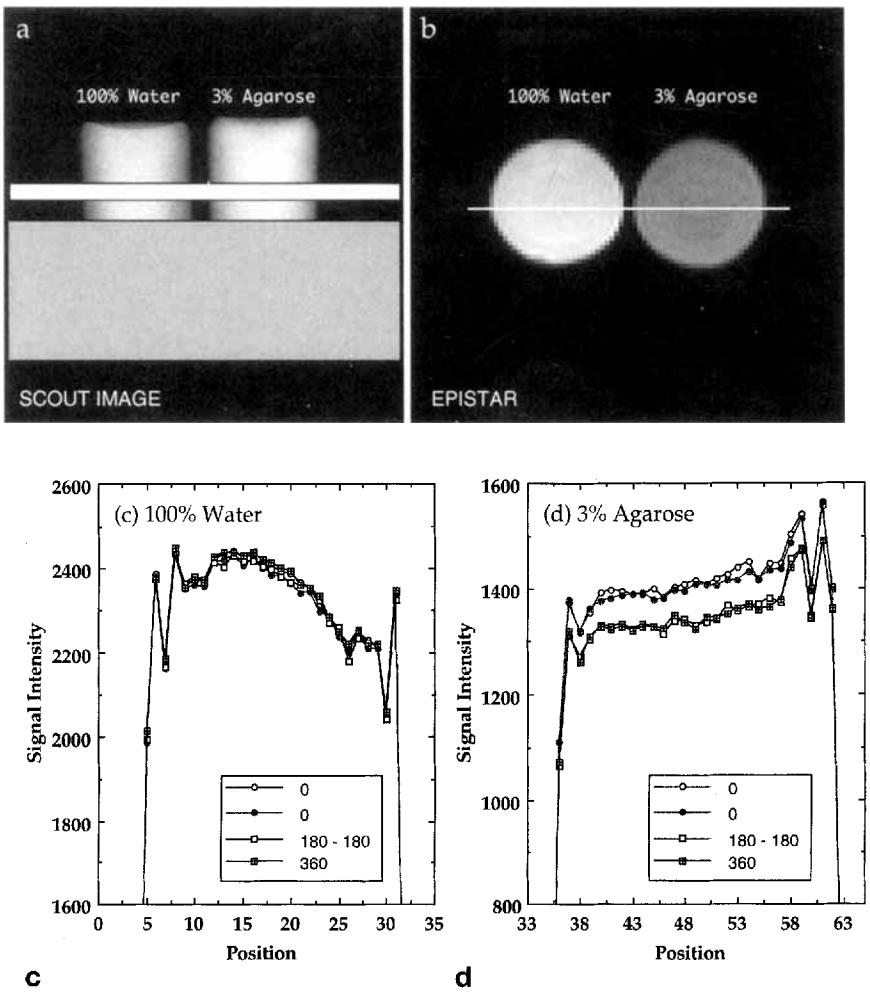

FIG. 5. Evaluation of MT effects from the 360° and double 180° pulses using phantoms made of 100% water and 97% water/3% agarose. (a) Coronal image showing locations of the slice of interest (solid bar) and the tagging pulse (shaded box); (b) acquired EPISTAR image for the two phantoms. The solid line shows the location where profiles of the phantoms are calculated; (c) slice profiles of the 100% water phantom using different tagging pulses. (d) Slice profiles of the 97% water/3% agarose phantom showing MT effects. Notice the MT effect of the 360° pulse is almost identical to that of the double 180° pulses.

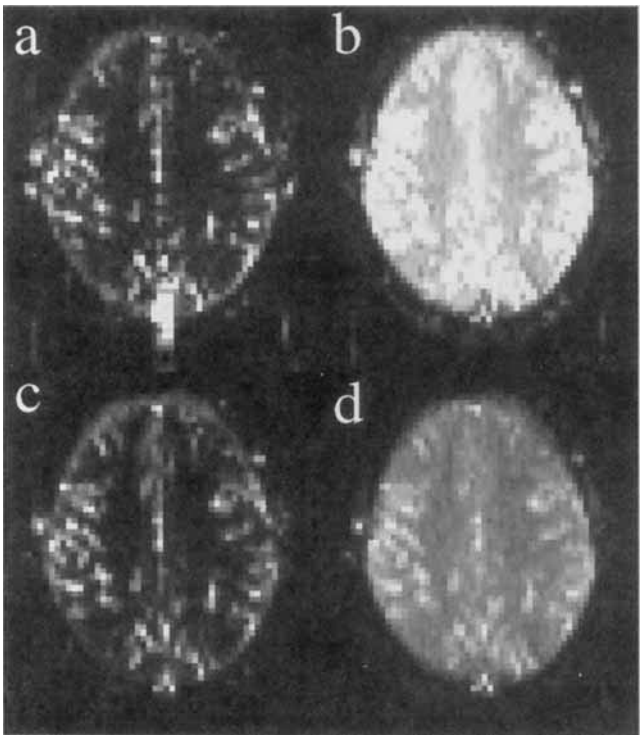

FIG. 6. Perfusion images obtained using (a) conventional single slice EPISTAR method, (b) conventional single slice EPISTAR method without control pulse, (c) new EPISTAR method, and (d) new EPISTAR method with two 90° control pulses. The double inversion (c) eliminates MT effects, whereas the double saturation (d) does not.

Figure 8 shows an example of a five-slice acquisition using a motor activation paradigm. Although only simple subtraction of the (activated-baseline) EPISTAR images was performed, focal CBF changes due to motor cortex activation are seen in all the slices.

DISCUSSION

Several techniques have been proposed for measurement of CBF, but only recently did Alsop show the capability for multislice imaging using the continuous adiabatic tagging method (7). For their control tag, the RF pulse was sinusoidally oscillated at 250 Hz. This produces two narrow bands of inversion located 250 Hz above and below the unmodulated RF frequency. However, continuous tagging techniques are not feasible on all MRI systems, due to the heavy duty cycle requirements for the RF amplifier. Also, this method does not exactly compensate MT effects since the frequency shifts of the inverting band and control bands are not identical.

The technique demonstrated here does not have a high RF duty cycle. Additionally, the cancellation of MT effects is exact, since the labeling and control pulses are applied with the same frequency shift, bandwidth, and total RF irradiation. This exact cancellation of MT effects has been demonstrated using a phantom made of 97% water/3% agarose to show that the signal decrease caused by the 360° pulse is identical to that caused by the double 180° pulses (Fig. 5d). Compared with the original EPISTAR method, other advantages of the new method are the lack of venous tagging by the control pulses, and the elimination of any concern about asymmetric MT effects. Asymmetric MT effects might be a potential concern when the control pulse is placed above the slice, since the frequency shift of this RF pulse is opposite in sign to that of the labeling pulse.

Other multislice imaging methods such as the use of a two-coil system have been proposed previously and used very successfully for assessment of cerebral perfusion (8, 9). The two-coil system consists of one small surface coil for labeling the arterial water spins, and a head coil for MRI that is actively decoupled from the labeling coil. The advantage of using such a method is the complete elimination of MT effects, thus permitting multislice perfusion imaging. However, the need for an extra coil limits the widespread application of such a method at clinical settings.

Frank, Wong, and Buxton have proposed another approach for multislice perfusion imaging (10, 11). Their studies suggested that the main contribution of the off-

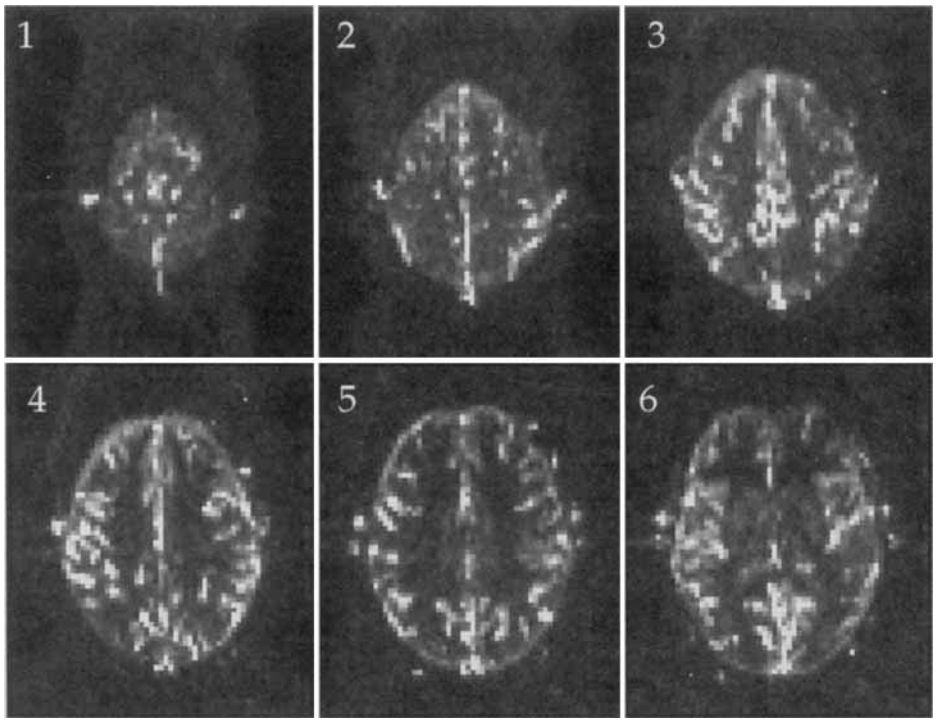

FIG. 7. Perfusion images obtained with new EPISTAR method at six different slice locations.

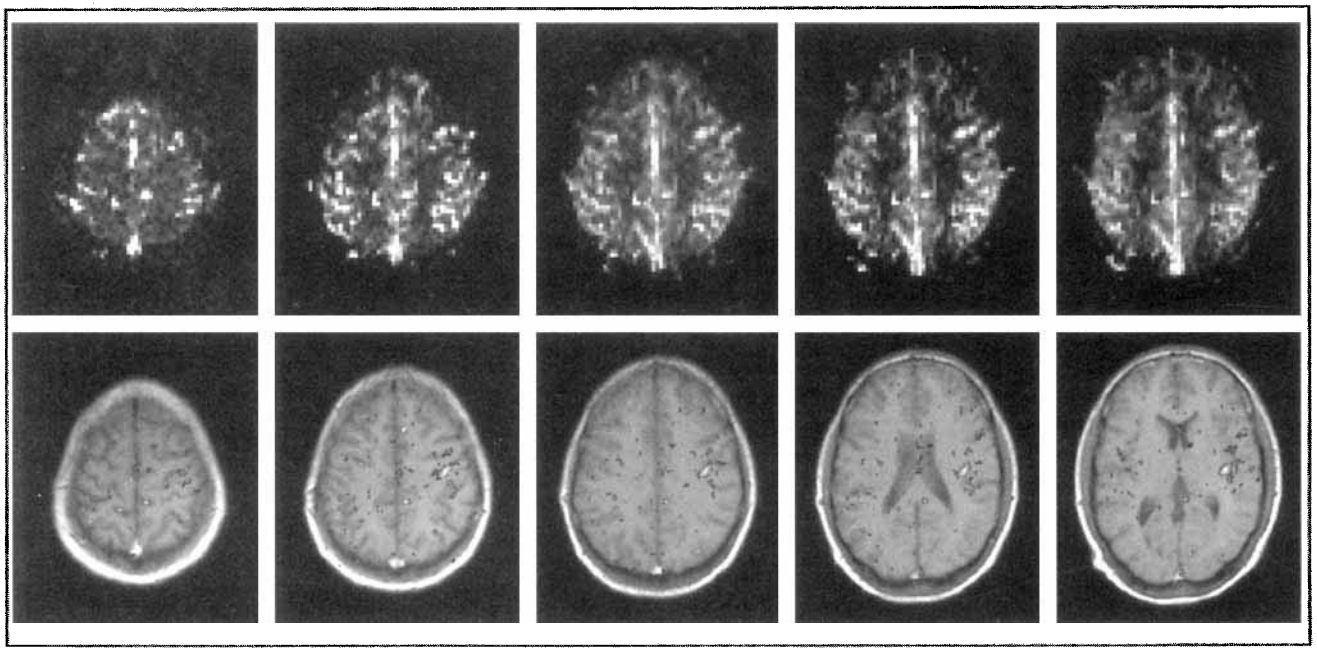

FIG. 8. Motor activation study. Multislice EPISTAR images were acquired at five locations without and then with tapping of the right fingers. Top row: Resting EPISTAR images show distribution of cerebral blood flow without a signal contribution from MT effects. Slice thickness = 8 mm, 40 acquisitions, time of acquisition 1 min 45 s. Bottom row: T_1-weighted spin-echo images obtained at same levels as the EPISTAR images, showing activated regions in the left motor cortex in all five slices.

resonance effects is from the imperfections in the slice profile of the inversion pulses, and the contribution of MT effects from these pulses are negligible. Thus multislice perfusion imaging in their experiments was performed simply by improving the slice profile of the adiabatic inversions and neglecting MT contribution. Compared to our approach, this method could be limited when MT effects cannot be neglected.

It needs to be pointed out, however, that the performance of the double 180° pulses as a perfect control is slightly compromised by slice profile imperfections and motion of arterial water spins. Spins along the edges of the tag will not be reinverted by the second 180° pulse due to the less than 180° nutation in those regions. Some fast-flowing arterial water spins will move out of the tagging slab before experiencing the second 180° pulse. While these factors do not interfere with static spins within the tissue volume of interest, they need to be considered when quantitative perfusion assessment is desired, although the effects are expected to be minor.

Two remaining problems with multislice imaging using either continuous or pulsed arterial labeling methods are (1): that the various slices have different inflow times, and (2) the transit time for the labeled arterial spins from the tag region to the capillary bed will vary for each brain tissue location. The problem of varying inflow times can be ameliorated, but not eliminated, by minimizing the data acquisition period for each slice (e.g., using a reduced number of phase encodes or faster gradients). With the new method for compensating MT effects, it is possible to perform a 3D EPISTAR acquisition. A 3D acquisition ensures that the inflow times are identical throughout the imaging volume (although arterial transit times will still vary). Three-dimensional imaging was not possible with the original EPISTAR method since the control pulse had a different MT effect than the labeling pulse except at the center of the 3D volume. Finally, the new method could be modified to permit quantitation of cerebral blood flow, using approaches such as QUIPPS (11, 12). However, it does not appear applicable to the FAIR technique.

In conclusion, we have described an improved technique for mapping of CBF that permits multislice imaging. The method should be easily implemented on any MRI system capable of EPI and should greatly increase the practical utility of EPISTAR and related quantitative methods for the study of brain function.

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