

**(12) PATENT**  
**(19) AUSTRALIAN PATENT OFFICE**

**(11) Application No. AU 200065185 B2**  
**(10) Patent No. 773421**

(54) Title  
Methods and apparatus for mapping internal and bulk motion of an object with phase labeling in magnetic resonance imaging

(51) <sup>6</sup> International Patent Classification(s)  
G01R 033/483 G01R 033/563

(21) Application No: 200065185 (22) Application Date: 2000.08.04

(87) WIPO No: WO01/11380

(30) Priority Data

(31) Number	(32) Date	(33) Country
60/147314	1999.08.05	US
60/165564	1999.11.15	US
60/201056	2000.05.01	US

(43) Publication Date : 2001.03.05

(43) Publication Journal Date : 2001.05.10

(44) Accepted Journal Date : 2004.05.27

(71) Applicant(s)  
The Government of The United States of America as represented by The Secretary, Department of Health and Human Services

(72) Inventor(s)  
Anthony H. Aletras; Han Wen

(74) Agent/Attorney  
Griffith Hack, GPO Box 1285K, MELBOURNE VIC 3001

(56) Related Art  
EP 0561628  
US 4797615

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
15 February 2001 (15.02.2001)

PCT

(10) International Publication Number  
**WO 01/11380 A2**

(51) International Patent Classification<sup>7</sup>: **G01R 33/483, 33/563**

(72) Inventors; and

(21) International Application Number: **PCT/US00/21299**

(75) Inventors/Applicants (for US only): **ALETRAS, Anthony, H. [US/US]; Apartment 201, 256 Congressional Lane, Rockville, MD 20852 (US). WEN, Han [US/US]; Apartment 301, 437 West Drive, Gaithersburg, MD 20878 (US).**

(22) International Filing Date: **4 August 2000 (04.08.2000)**

(74) Agent: **NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Whinston, L.L.P., Suite 1600 - One World Trade Center, 121 S.W. Salmon Street, Portland, OR 97204 (US).**

(25) Filing Language: **English**

(74) Agent: **NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Whinston, L.L.P., Suite 1600 - One World Trade Center, 121 S.W. Salmon Street, Portland, OR 97204 (US).**

(26) Publication Language: **English**

(74) Agent: **NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Whinston, L.L.P., Suite 1600 - One World Trade Center, 121 S.W. Salmon Street, Portland, OR 97204 (US).**

(30) Priority Data:

60/147,314 5 August 1999 (05.08.1999) US  
60/165,564 15 November 1999 (15.11.1999) US  
60/201,056 1 May 2000 (01.05.2000) US

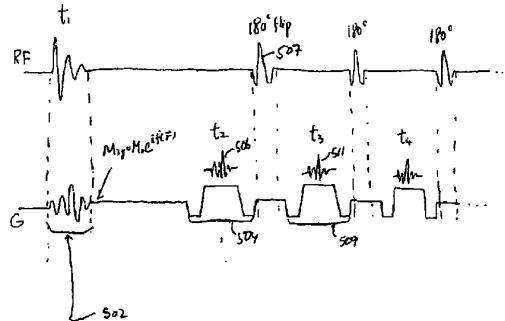
(81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**

(71) Applicant (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES OF AMERICA as represented by THE SECRETARY, DEPARTMENT OF HEALTH & HUMAN SERVICES [US/US]; The National Institute of Health, Office of Technology Transfer, Suite 325, 601 Executive Boulevard, Rockville, MD 20852 (US).**

(84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,**

*[Continued on next page]*

(54) Title: **METHODS AND APPARATUS FOR MAPPING INTERNAL AND BULK MOTION OF AN OBJECT WITH PHASE LABELING IN MAGNETIC RESONANCE IMAGING**



**WO 01/11380 A2**

(57) Abstract: Magnetic resonance imaging method and apparatus are provided for mapping the internal or bulk motion of an object by labeling the phase of a specimen magnetization with a selected spatial function and measuring changes in the phase of the magnetization. The special function is selectable to provide magnetization phase modulation corresponding to displacements in a selected direction, such as a radial or azimuthal direction. Methods and apparatus for producing images based on magnetization phase modulation acquire image data based on stimulated echos and stimulated anti-echos. In an embodiment, a series of 180 degree pulses produces alternating stimulated and stimulated anti-echos that are measured and assigned to respective images.

**METHODS AND APPARATUS FOR MAPPING INTERNAL AND BULK  
MOTION OF AN OBJECT WITH PHASE LABELING IN MAGNETIC  
RESONANCE IMAGING**

5

**Field of the Invention**

The invention pertains to methods and apparatus for magnetic resonance imaging.

**Background**

Magnetic resonance imaging ("MRI") is a noninvasive imaging method widely used for medical diagnostics. To date, MRI methods for tracking the motion 10 of an object over relatively long periods of time have been based on spatially modulating magnitude of the specimen magnetization according to a specific grid pattern, and observing the deformation of this grid pattern as motion occurs. In order to quantify the displacement vector of any small volume element (voxel), the positions of the grid lines and their intersection points are precisely defined. This 15 usually requires human assistance, and precision is limited by image resolution or voxel size. The motion of voxels between grid lines cannot be measured directly, and interpolation methods are used to estimate motion.

Other MRI methods measure voxel velocity by subjecting the transverse magnetization to a biphasic gradient pulse before readout, so that stationary spins do 20 not accumulate a net phase change, while spins with nonzero velocity components along the gradient direction accumulate a phase change. By measuring such phase changes, one or more velocity components can be derived. While phase-contrast velocity mapping generally provides high spatial resolution and simple data processing, it is generally unsuitable for motion tracking, as it requires integration of 25 velocity vectors from multiple measurements and mathematically tracking voxel positions. These integrations and voxel position tracking are difficult and prone to error.

**Summary**

According to one aspect of the present invention, there is provided a magnetic resonance imaging system, comprising:

- 5        a magnet that applies at least one magnetic field to a specimen;
- a radio-frequency transmitter that applies a radio-frequency pulse to the specimen, wherein the magnetic field and the radio-frequency pulse are configured to
- 10      label a phase of a magnetization of the specimen based on a function of position at or near a first time point;
- a radio-frequency receiver that detects magnetic resonance signals from the specimen; and
- a processor that produces an image of the specimen
- 15      based on the magnetic resonance signals, wherein the image includes spatial variations in the phase of the magnetization of the specimen accumulated in a mixing time subsequent to the first time point.

According to a further aspect of the present invention, there is provided a method of reducing free induction decay contributions to a magnetic resonance image in phase-labeled displacement imaging, the method comprising:

- selecting a time interval;
- 25      applying a radio-frequency (RF) pulse to a specimen at a time point within the time interval, wherein the time point is selected to reduce a contribution to a magnetic resonance signal from free induction decay.

According to a further aspect of the present invention, there is provided a method of mapping motion of a specimen with magnetic resonance, imaging, the method comprising:

- (a) applying a spatially varying phase based on a function  $f(r)$  to a specimen magnetization;
- 35      (b) applying a 180 degree RF pulse to the specimen;

- (c) applying a spatially varying phase that is approximately opposite to the spatially varying phase based on the function  $f(r)$  to the specimen magnetization;
- (d) measuring a spatially varying phase of the specimen magnetization;
- 5 (e) producing a specimen image based on the measured phase of the specimen magnetization; and
- (f) repeating steps (a)-(e).

According to a further aspect of the present  
10 invention, there is provided a method of magnetic resonance imaging a specimen having a moving axis, the method comprising:  
measuring a location of the axis at a first time;  
phase encoding a specimen magnetization as a function  
15 of specimen position based on a location of the axis at the first time;  
measuring a location of the axis at a second time;  
phase decoding the specimen magnetization at the second time based on the location of the axis at the  
20 second time; and  
producing an image of the specimen based on the phase-decoded specimen magnetization.

According to a further aspect of the present invention, there is provided a magnetic resonance imaging  
25 method for producing an image based on displacements of a specimen, comprising:  
selecting a direction of displacement;  
phase labeling a magnetization of the specimen based on displacements in the selected direction; and  
30 producing an image of the specimen from measurements of a phase of the magnetization.

According to a further aspect of the present invention, there is provided a method of acquiring phase-encoded displacement data in magnetic resonance imaging,  
35 comprising:  
applying at least one 180 degree radio-frequency pulse to a specimen;

receiving signals corresponding to a stimulated echo and a stimulated anti-echo produced by the 180 degree radio-frequency pulse; and

5 processing the signals to obtain said phase-encoded displacement data.

According to a further aspect of the present invention, there is provided a dual echo magnetic resonance imaging method, comprising:

10 phase labeling a specimen magnetization;  
storing at least a portion of the phase-labeled magnetization along a longitudinal axis;  
rotating at least a portion of the stored magnetization into a transverse plane;  
applying an RF-gradient pulse combination to the  
15 rotated magnetization to produce a magnetization having a first decoded phase to produce a first echo;  
obtaining a first set of image data based on the first echo;  
applying additional RF-gradient pulse combinations to  
20 produce a second echo corresponding to a magnetization having a second decoded phase that is opposite the first decoded phase; and  
obtaining a second set of image data based on the second echo.

25 According to a further aspect of the present invention, there is provided a magnetic resonance imaging method, comprising:  
storing a phase labeled magnetization by rotating a portion of the phase labeled magnetization to be directed  
30 along a longitudinal axis defined by an axial magnetic field;  
rotating a portion of the stored magnetization into a transverse plane;  
applying a gradient pulse to at least the portion of  
35 the stored magnetization in the transverse plane to compensate phase dispersion; and

rotating a portion of a longitudinal component of magnetization to the transverse plane to compensate decay in the labeled magnetization.

According to a further aspect of the present

5 invention, there is provided a method of magnetic resonance imaging of displacements of a heart, comprising:

- selecting a displacement direction;
- providing a function of position corresponding to the selected displacement direction;

10 applying phase modulation to a magnetization of the heart using the function of position at an initial time;

- forming an image of the heart based on changes in magnetization phase with respect to the phase modulation applied at the initial time.

15 According to a further aspect of the present invention, there is provided a method of displaying strain data, comprising:

- displaying a strain magnitudes at image positions as a grayscale value or a color; and

20 displaying strain axes at the image positions as orthogonal line segments.

According to a further aspect of the present invention, there is provided a method of correcting phase wrap around in phase labeled magnetic resonance imaging,

25 comprising:

- locating an image boundary corresponding to a phase discontinuity; and
- adjusting a phase on a side of the boundary to eliminate the phase discontinuity.

30 Brief Description of the Drawings

FIG. 1 is a schematic block diagram of a magnetic resonance (MR) imaging system.

35 FIGS. 2A-2B illustrate volume element ("voxel") phase labeling based on a function  $f(r)$ .

- 2d -

FIGS. 3A-3C illustrate phase labeling of a longitudinal and transverse magnetization based on a function  $f(r)$ .

FIGS. 4A-4C illustrate phase labeling of a longitudinal and transverse magnetization based on a function  $f(r)$ .

FIG. 5 illustrates RF and gradient (G) pulses applied in a fast spin-echo readout of a phase labeled transverse magnetization.

10

68  
14  
48  
68

8  
9  
8

FIG. 6 illustrates RF and gradient (G) pulses applied in a fast spin-echo readout of a phase labeled longitudinal magnetization.

FIG. 7 is an illustration of k-space regions corresponding to phase factors of a transverse magnetization.

5 FIG. 8 illustrates voxel motion with respect to a non-stationary coordinate system.

FIG. 9 illustrates RF and gradient pulses applied to produce a signal (rx) from a phase labeled specimen, wherein the signal corresponds to a stimulated echo or stimulated anti-echo.

10 FIG. 10 is a block diagram of a dual echo imaging method.

FIG. 11A illustrates RF and gradient pulses applied to an image of a phase labeled specimen in an alternating dual echo imaging method.

FIG. 11B illustrates RF and gradient pulses applied to an image of a phase labeled specimen in a simultaneous dual echo imaging method.

15 FIG. 12 illustrates a magnetization spin wheel.

FIG. 13 is a diagram of a sequence of RF and gradient pulses applied according to an embodiment of a rotating wheel method of acquiring phase labeled data.

20 FIG. 14 illustrates RF and gradient pulses of a dual-echo method configured to reduce free induction decay.

#### Detailed Description

FIG. 1 is a schematic block diagram of a magnetic resonance imaging (MRI) system 100 that provides images of a specimen. The MRI system 100 includes a controller 102 that is typically programmed by a clinician with a series of commands corresponding to a particular imaging sequence. The command sequences can be entered with a keyboard, a pointing device such as a mouse, or other input device. Command sequences can be stored by the controller 102 for retrieval from a hard disk, floppy disk, or other computer readable media and can be selected from a

menu, so that a clinician can easily select among an imaging protocol from various command sequences.

The MRI system 100 includes an axial magnet controller 104 that controls the spatial homogeneity of an axial magnetic field  $B_0$  with an axial field coil 105.

5 As used herein, the axial magnetic field  $B_0$  is directed along a +z-axis in a xyz coordinate system. A plane parallel to an xy-plane (perpendicular to the z-axis) is referred to as a transverse plane. A gradient controller 106 activates gradient coils 107-109 that produce a magnetic field gradients  $G_x$ ,  $G_y$ ,  $G_z$ . For convenience, the magnetic field gradients  $G_x$ ,  $G_y$ ,  $G_z$  are represented generically as  $G$ . The magnetic field gradients are typically applied as pulses.

10 A radio-frequency (RF) transmitter 110 is configured to generate RF pulses that are applied to a transmitter coil 112 to produce a pulsed magnetic field. A receiver coil 114 detects changes in magnetization in the specimen and communicates the detected magnetization changes to an RF receiver 116. The RF receiver 116 processes the detected magnetization changes and provides image data to the controller 102 based on these changes.

15 A specimen to be imaged is exposed to the axial magnetic field  $B_0$  and a field gradient  $G$  selected by the controller 102. An RF pulse is applied to produce a change in magnetization that is detected by the receiver coil 114 and processed by the RF receiver 116. The RF pulse is typically represented as product of a pulse envelope  $B_1$  and a complex exponential  $\exp(i\omega_{RF}t)$ , wherein  $t$  is time,  $i$  is the square root of -1, and  $\omega_{RF}$  is an excitation carrier frequency. The excitation frequency  $\omega_{RF}$  is generally selected to be approximately equal to a resonance frequency of one or more constituents of the specimen. The resonance frequency  $\omega_0$  is proportional to a product of a gyromagnetic ratio  $\gamma$  (a material constant) and a magnitude of the axial field  $B_0$ . By applying a field gradient  $G$  with the gradient coils 107-109 so that the specimen is exposed to a non-uniform magnetic field, slices of the specimen can be selected for imaging. Within a selected slice, the resonance frequency  $\omega_{RF}$  is sufficiently constant so that the RF receiver 116 can reject magnetization changes in non-selected slices by rejecting frequency components corresponding to the non-selected slices. Detecting changes in magnetization slice by slice permits image formation.

With only the axial magnetic field  $B_0$  applied, some magnetic dipoles of sample constituents align with the axial magnetic field  $B_0$  to produce an equilibrium magnetization  $M_0$  that generally has only a +z-directed component. The specimen includes individual magnetic dipoles of dipole moment  $\mu$  that precess about the

5 direction of  $B_0$  (the z-axis) at the frequency  $\omega_0 = \gamma B_0$  that is also referred to as the Larmor frequency. Changes in magnetization are generally described with reference to an xyz coordinate system that rotates about the axial direction at the Larmor frequency. The z-axis of such a rotating coordinate system is the same as the z-axis of a stationary coordinate system while the x-axis and y-axis of the rotating

10 coordinate system rotate in a transverse plane.

Application of a selected RF pulse can rotate a magnetization or one or more components thereof. An RF pulse of duration and magnitude sufficient to produce a 180 degree rotation is referred to as a 180 degree pulse and an RF pulse sufficient to produce a 90 degree rotation is referred to as a 90 degree pulse. In general, an RF

15 pulse sufficient to produce a rotation  $\alpha$  is referred to as an  $\alpha$  pulse. The axis of rotation of such pulses can be selected based on the direction in which the corresponding pulse magnetic field is applied.

Vector quantities are expressed herein in boldface. A transverse component  $M_{xy}$  of a (vector) magnetization  $\mathbf{M}$  (i.e., a component of the magnetization  $\mathbf{M}$  in the 20 xy-plane) is expressed as  $M e^{i\theta}$ , wherein an x-component is a real part of  $M e^{i\theta}$ , a y-component is an imaginary part of  $M e^{i\theta}$ , and  $M$  is a magnitude of the magnetization  $\mathbf{M}$ .

#### Phase Labeling

25 In some specimens, some volume elements ("voxels") are moving and experience a displacement between an initial time  $t_1$  and a subsequent time  $t_2$ . For example, a portion of a specimen moving parallel to the x-axis acquires an x-directed displacement. The magnetization  $\mathbf{M}$  can be encoded (i.e., modulated) based upon such displacements. Such a modulation can be a function of position and can

30 be generally expressed as  $f(r(t_2)) - f(r(t_1))$ , wherein  $r(t_2)$  and  $r(t_1)$  are positions of a voxel at times  $t_2$  and  $t_1$ , respectively, and  $f(r)$  is an arbitrary function of position  $r$ .

Modulation of the magnetization based on displacements permits imaging based upon displacement.

The magnetization can be amplitude modulated, frequency modulated, or phase modulated. Phase modulation can be accomplished by modulating the magnetization  $\mathbf{M}$  or a component of the magnetization  $\mathbf{M}$  with a phase factor  $e^{i\mathbf{f}(\mathbf{r})}$  at a time  $t_1$ , producing a phase modulated magnetization. A phase factor such as  $e^{i\mathbf{f}(\mathbf{r})}$  is referred to herein as a "phase label." The phase modulated magnetization can be preserved until a time  $t_2$ , when an MR image is acquired based on the phase modulation. A voxel that is displaced to a position  $\mathbf{r}(t_2)$  retains a phase factor based on  $\mathbf{f}(\mathbf{r}(t_1))$  and can be further modulated or demodulated with a phase factor based on  $\mathbf{f}(\mathbf{r}(t_2))$  to produce an image based on  $\mathbf{f}(\mathbf{r}(t_2)) - \mathbf{f}(\mathbf{r}(t_1))$ . RF and gradient pulses that provide a selected modulation or phase labeling can be selected to provide phase modulation according to a function  $\mathbf{f}(\mathbf{r})$ .

FIGS. 2A-2B illustrate phase labeling based on a function  $\mathbf{f}(\mathbf{r}) = kr$ , wherein  $r$  is a radial coordinate in a cylindrical  $(r, \theta, z)$  coordinate system and  $k$  is a constant. A corresponding phase label is  $e^{ikr}$ . With such a phase label, a voxel acquires a phase proportional to a change in radial coordinate between times  $t_1$  and  $t_2$ , i.e., a change in distance between the voxel and an origin of the cylindrical coordinate system. At time  $t_1$ , a phase proportional to  $kr$  is applied so that voxel phase as a function of the radial coordinate is  $\mathbf{f}(\mathbf{r}) = kr$  with a corresponding phase label  $e^{ikr}$ . At time  $t_2$ , voxels are displaced from voxel positions at time  $t_1$  and the voxel phase label is  $e^{i\mathbf{f}(\mathbf{r})}$ . The phase  $\phi(r)$  is produced by a combination of the initial phase labeling with  $e^{ikr}$  and changes in the phase as a function of position produced by displacements. A radial displacement  $\Delta r$  of a voxel can be obtained from a measurement of the phase  $\phi(r)$  as  $\Delta r = r - \phi(r)/k$  and a radial coordinate of a voxel at time  $t_2$  is  $\phi(r)/k$ .

In a Cartesian  $(x, y, z)$  coordinate system, the magnetization  $\mathbf{M}$  includes a longitudinal component  $M_z$  and a transverse component  $M_{xy}$  and can be phase labeled in several ways. The longitudinal component  $M_z$  can be phase labeled using RF and gradient pulses to apply a modulation  $m(r)e^{i\mathbf{f}(\mathbf{r})}$ , wherein  $m(r)$  is a real function of position  $\mathbf{r}$ , and  $\mathbf{f}(\mathbf{r})$  is a phase-labeling function. Because the longitudinal magnetization  $M_z$  is a scalar, and therefore a real number, the

longitudinal magnetization  $M_z$  also contains a complex conjugate term  $m(r)e^{-i\tilde{f}(r)}$ . Alternatively, the transverse component  $M_{xy}$  can be labeled with a combination of RF and gradient pulses to include modulations corresponding to  $m(r)e^{i\tilde{f}(r)}$ ,  $m(r)e^{-i\tilde{f}(r)}$ , or a combination of both. In addition, both the longitudinal and transverse

5 components can be labeled to include phase-labeled terms such as  $e^{i\tilde{f}(r)}$ ,  $e^{-i\tilde{f}(r)}$ , or both.

To produce a transverse magnetization having a selected phase modulation according to a function  $\tilde{f}(r)$ , the equilibrium magnetization  $M_0$  is typically rotated into the transverse plane with a combination of RF and gradient pulses. Such a

10 pulse combination can be determined based on the following equations for rates of change of  $M_{xy}$  and  $M_z$  found in, for example, Pauly et al., J. Magn. Resonan. 81:43-56 (1989):

$$\begin{aligned}\dot{M}_{xy} &= -i\gamma\mathbf{G}\cdot\mathbf{r}M_{xy} + i\gamma B_1 M_z, \\ \dot{M}_z &= -\gamma \langle M_{xy} \cdot iB_1 \rangle,\end{aligned}$$

where  $\mathbf{G}$  represents an applied magnetic field gradient and  $B_1$  is an amplitude of the RF pulse. By integrating these equations,  $M_{xy}$  can be determined as a function of position  $\mathbf{r}$  and time  $t$ :

$$M_{xy}(\mathbf{r}, t) = i\gamma M_0 \int_0^t B_1(\tau) e^{i\tau\mathbf{k}(\tau)} d\tau + i\gamma^2 \int_0^t d\tau B_1(\tau) e^{i\tau\mathbf{k}(\tau)} \int_0^\tau \langle M_{xy}(\mathbf{r}, s) \cdot iB_1(s) \rangle ds,$$

wherein  $\mathbf{k}(t)$  is a k-space trajectory driven by the gradient  $\mathbf{G}$  as defined in Pauly et al. If the RF-gradient pulse combination is to produce  $M_{xy}(\mathbf{r}, T) = m(r)e^{i\tilde{f}(r)}$  at a time

20  $T$  corresponding to the conclusion of the RF-gradient pulse combination, then the RF pulse can be selected so that

$$\int_0^t B_1(\tau) e^{i\tau\mathbf{k}(\tau)} d\tau = -\frac{i}{\gamma M_0} M_{xy}(\mathbf{r}, T) - \frac{\gamma}{M_0} \int_0^T d\tau B_1(\tau) e^{i\tau\mathbf{k}(\tau)} \int_0^\tau \langle M_{xy}(\mathbf{r}, s) \cdot iB_1(s) \rangle ds.$$

If  $m(r)$  is small compared to the magnetization  $M_0$ , the small-tip-angle

25 approximation of Pauly et al. can be used and  $B_1(t)$  calculated by neglecting the second term in the above equation. For phase labeling in motion/displacement imaging,  $m(r)$  is preferably substantially equal to the magnetization  $M_0$  to improve signal-to-noise ratio ("SNR") in phase-label measurements (and to avoid signal contributions from unlabeled magnetization components), and the small-tip-angle

approximation is generally not sufficient.  $M_{xy}$  and  $B_1$  can be obtained from a series expansion, wherein a zeroth order term of  $B_1$  is obtained from the small tip angle approximation, and higher order terms are obtained from lower order terms as follows:

$$5 \quad \int_0^T B_{1,n}(t) e^{i\pi k(t)} dt = -\frac{\gamma}{M_0} \sum_{j+l+m=n-1} \int_0^T d\tau B_{1,j}(\tau) e^{i\pi k(\tau)} \int_0^\tau \langle M_{xy,l}(\tau, s) \cdot iB_{1,m}(s) \rangle ds,$$

$$M_{xy,n}(\mathbf{r}, t) = i\gamma M_0 \int_0^t B_{1,n}(\tau) e^{i\pi k(\tau)} d\tau + i\gamma^2 \sum_{j+l+m=n-1} \int_0^t d\tau_1 B_{1,j}(\tau_1) e^{i\pi k(\tau_1)} \int_0^{\tau_1} d\tau_2 \langle M_{xy,l}(\tau_1, s) \cdot iB_{1,m}(s) \rangle ds,$$

wherein  $j$ ,  $l$ ,  $m$ , and  $n$  are nonnegative integers, and  $n$  is the order of the term obtained, i.e.,  $B_{1,n}$  and  $M_{xy,n}$  are  $n$ th order contributions to  $B_1$  and  $M_{xy}$ , respectively. For a specified function  $m(\mathbf{r})e^{i\pi k(\mathbf{r})}$ , the series expansion can be calculated numerically

10 until  $M_{xy,n}(\mathbf{r}, t)/M_0 < 1$ , and the RF-gradient pulse combination is sufficiently approximated to produce a selected transverse magnetization  $M_{xy}(\mathbf{r}, T) = m(\mathbf{r})e^{i\pi k(\mathbf{r})}$ .

Although phase labeling is described herein generally with respect to phase labeling with a single function  $f(\mathbf{r})$ , multiple phase labels can be used to obtain a transverse magnetization  $M_{xy}(\mathbf{r}, T) = m_1(\mathbf{r})e^{i\pi f_1(\mathbf{r})} + m_2(\mathbf{r})e^{i\pi f_2(\mathbf{r})} + m_3(\mathbf{r})e^{i\pi f_3(\mathbf{r})} + \dots + m_N(\mathbf{r})e^{i\pi f_N(\mathbf{r})}$  that is phase-labeled with respective functions  $f_1(\mathbf{r})$ ,  $f_2(\mathbf{r})$ ,  $f_3(\mathbf{r})$ ,  $\dots$ ,  $f_N(\mathbf{r})$ .

The longitudinal magnetization  $M_z$  can be phase-labeled in several ways.

For example, a transverse magnetization  $M_{xy}(\mathbf{r}) = m(\mathbf{r})e^{i\pi k(\mathbf{r})}$  can be produced with an RF-gradient pulse combination as described above, and a second RF pulse such as a 20 90 degree pulse or other RF pulse applied along the  $y$ -axis. In this example, a 90 degree pulse is used and, for improved SNR,  $m(\mathbf{r})$  is configured to be substantially equal to the magnetization  $M_0$  and the resulting longitudinal magnetization is  $M_z = [m(\mathbf{r})e^{i\pi k(\mathbf{r})} + m(\mathbf{r})e^{-i\pi k(\mathbf{r})}]/2$ .

FIGS. 3A-3C illustrate phase labeling of longitudinal and transverse magnetizations with a specified function  $f(\mathbf{r})$ . The initial magnetization is the axial magnetization  $M_0$  as shown in FIG. 3A. An RF-gradient pulse combination is applied to rotate the magnetization  $M_0$  into the transverse plane and produce a transverse magnetization  $M_{xy} = M_0 e^{i\pi f(\mathbf{r})}$  as shown in FIG. 3B, leaving only a small (or no)  $z$ -component. A 90° RF pulse is applied along the  $y$ -axis, and an  $x$ -

component of the magnetization is rotated into the  $yz$ -plane. The resulting longitudinal and transverse magnetizations, illustrated in FIG. 3C, are:

$$M_z = [e^{i\tilde{f}(r)} + e^{-i\tilde{f}(r)}]M_0/2, \text{ and}$$

$$M_{xy} = [e^{i\tilde{f}(r)} - e^{-i\tilde{f}(r)}]M_0/(2i), \text{ respectively,}$$

5 and are both phase-labeled based on the function  $f(r)$ .

Another method of producing phase-labeled terms  $m(r)e^{i\tilde{f}(r)}$  or  $m(r)e^{-i\tilde{f}(r)}$  in the longitudinal magnetization  $M_z$  is to apply an RF-gradient pulse combination based on Pauly et al.'s small-tip-angle approximation.

Generally the RF-gradient pulse combinations produce phase modulations of 10 the form  $m(r)e^{i\tilde{f}(r)}$  and  $m(r)e^{-i\tilde{f}(r)}$  on both the transverse and longitudinal magnetizations. As shown in FIG. 4A, an RF-gradient pulse combination is applied to rotate the magnetization  $M_0$  into the  $xy$ -plane and produce a transverse magnetization  $M_{xy} = M_0e^{i\tilde{f}(r)}$  and no axial magnetization. As shown in FIG. 4B, a 90° RF pulse is applied about an axis AX at an angle  $\phi$  from the x-axis. A 15 component of  $M_{xy}$  perpendicular to the axis AX is rotated into a vertical plane at an angle  $\phi$  relative to the x-axis and a component of  $M_{xy}$  parallel to the axis AX remains in the  $xy$ -plane along the axis AX. The longitudinal and transverse magnetizations, illustrated in FIG. 4C, are  $M_z = M_0\{e^{i[\tilde{f}(r)+\phi]} - e^{-i[\tilde{f}(r)+\phi]}\}/(2i)$ , and  $M_{xy} = M_0\{e^{i[\tilde{f}(r)+\phi]} + e^{-i[\tilde{f}(r)+\phi]}\}e^{i\phi}/2$ . The presence of the phase angle  $\phi$  in the terms 20  $e^{i[\tilde{f}(r)+\phi]}$  and  $e^{-i[\tilde{f}(r)+\phi]}$  provides a method for separating these terms, i.e., by subtracting MRI signals that are acquired with  $\phi = \phi_1$  and  $\phi = \phi_2$ .

#### Examples of Phase Labeling

In a first example, the selected function of displacement is equal to a 25 Cartesian component of voxel displacement. For example, if the x-component is selected, the phase difference is proportional to  $\tilde{f}(r(t_2)) - \tilde{f}(r(t_1)) = k(x(t_2) - x(t_1))$ , wherein  $k$  is a nonzero constant. The corresponding phase label is the function  $e^{ikx}$  and a transverse magnetization modulated with this phase label is produced by applying a 90° RF pulse (either slice-selective or volumetric) along the x-axis, followed by a gradient pulse along the x-axis and having an area corresponding to  $k$ . 30 The resulting transverse magnetization is  $M_{xy} = M_0e^{ikx}$ . Another 90° RF pulse is

applied along the axis AX at an angle  $\phi$  from the x-axis so that both  $M_z$  and  $M_{xy}$  include phase-labeled terms:

$$M_z = M_0[e^{i(kx-\phi)} - e^{-i(kx-\phi)}]/(2i), \text{ and}$$

$$M_{xy} = M_0[e^{i(kx-\phi)} + e^{-i(kx-\phi)}]/2.$$

5 Such phase labeling is readily configurable to phase modulate corresponding to a projection of the displacement vector along an arbitrary direction.

The function  $f(r)$  can also be specified in cylindrical, spherical, or other coordinates. As a second example, voxels can be phase labeled based on a radial displacement  $r$  in cylindrical coordinates with a function  $f(r) = kr$ , wherein  $k$  is a constant. The series expansion described above can be used to determine an appropriate RF-gradient pulse combination to produce  $M_{xy} = m(r)e^{ikr}$ . The resulting transverse magnetization  $M_{xy}$  can be configured so that  $m(r) = 0$  for  $r = 0$  so that the Fourier transform of  $M_{xy}$  is well defined and the series expansion for the RF-gradient pulse combination converges. As with the function  $kx$  in Cartesian

10 coordinates, a 90° RF pulse is applied about an axis AX at an angle  $\phi$  from the x axis after producing the transverse magnetization  $M_{xy} = m(r)e^{ikr}$  so that both  $M_z$  and  $M_{xy}$  are phase-labeled:

$$M_z = M_0[e^{i(kr-\phi)} - e^{-i(kr-\phi)}]/(2i), \text{ and}$$

$$M_{xy} = M_0[e^{i(kr-\phi)} + e^{-i(kr-\phi)}]/2.$$

15 20 Such phase-labeling is especially useful for mapping changes in the diameter or size of an object relative to a central axis, such as measuring a radial contraction or dilation of a left ventricle of a heart.

The function  $f(r)$  can also be selected to be a function of the  $\theta$ -coordinate (azimuthal angle) in a cylindrical coordinate system to label angular displacements,

25 25 i.e.,  $\theta(t_2) - \theta(t_1)$ . In a third example, a representative phase labeling function is  $f(r) = n\theta$ , wherein  $n$  is a nonzero integer. Phase-labeling is performed as above except the RF-gradient pulse combination is determined using the function  $m(r)e^{in\theta}$ . This function is useful for mapping rotations, about a central axis. For example, such a function can be used in MRI of a cross-section of a left ventricle of the heart to

30 30 produce images based on rotations of the left ventricle and angular changes in segments of the left ventricle.

**Mapping the Time-Evolution of a Phase Label**

The evolution of voxel phase after an initial phase labeling at time  $t_1$  can be determined by detecting voxel phase at a subsequent time  $t_2$ . If the phase label is applied to the transverse magnetization as  $M_{xy} = m(r)e^{i\theta(r)}$ , and the time period

5 between  $t_1$  and  $t_2$  is short enough so that the transverse magnetization  $M_{xy}$  does not entirely decay due to spin relaxation processes such as  $T_2^*$  relaxation, then at time  $t_2$  an image based on the transverse magnetization  $M_{xy}$  can be directly acquired with standard gradient-recalled-echo (GRE) or spin-echo readout (SPE) methods, or variants such as spoiled gradient-recalled echo, fast-spin-echo, echo-planar, echo-train, k-space spiral scan, true free imaging in steady precession (FISP), and others.

10 The spatial distribution of the phase of the transverse magnetization  $M_{xy}$  corresponds to the phase label.

FIG. 5 illustrates acquisition of image data based on a phase-labeled transverse magnetization  $M_{xy}$  using a fast spin-echo readout in which the transverse magnetization  $M_{xy}$  is acquired at a series of times  $t_n$ . At a time  $t_1$ , an RF-gradient pulse combination 502 produces a transverse magnetization  $M_{xy} = M_0e^{i\theta(r)}$  that is sampled at time  $t_2$  by applying a fully balanced readout gradient pulse 504 to produce a first echo 506. The balanced readout gradient pulse 504 is compensated to produce no net phase shift. A 180° RF pulse 507 is then applied, followed by

15 balanced readout gradient pulse 509, producing a second echo 511. The 180 degree RF pulse and the balanced readout gradient pulse are repeated, producing additional echoes.

Various exemplary acquisition methods are described herein that are suitable for measuring phase labeled transverse or longitudinal magnetizations (or both) that

20 contain phase labels such as  $e^{i\theta(r)}$  and  $e^{i\theta(r)}$ . A phase-labeled longitudinal magnetization  $M_z = [m(r)e^{i\theta(r)+\phi} - m(r)e^{-i\theta(r)+\phi}]/(2i)$  at time  $t_1$  can be detected by applying an RF-gradient pulse combination at a time  $t_2$  to produce a spatial phase distribution  $A(r) = a(r)e^{-i\theta(r)}$ , wherein  $a(r)$  is a real function of position  $r$ . The spatial phase distribution  $A(r)$  provided by the RF-gradient pulse combination is selected to

25 correspond to the phase-label applied at time  $t_1$ . Such RF-gradient pulse combinations can be selected using the series expansion described above. The resulting transverse magnetization is:

$$M_{xy}(r) = a(r) \{ m(r') e^{i[f(r(1))-f(r(2))\cdot r]} - m(r') e^{i[f(r(1))+f(r(2))\cdot r]} \} / (2i).$$

For some phase-labeling functions  $f(r)$ , the two terms in the above equation have little overlap in Fourier transform space ("k-space"), and data corresponding to the first term can be isolated by acquiring  $M_{xy}(r)$  over a k-space region encompassing primarily the first term. The acquisition can be of any of the standard gradient-recalled echo or spin-echo schemes, or variants thereof. The phase of the first term in  $M_{xy}$  includes  $f(r') \cdot f(r)$ . The RF-gradient pulse combination that produces  $A(r)$  is referred to as a "decoding pulse."

FIG. 6 illustrates data acquisition using a decoding pulse and a fast spin-echo readout. At time  $t_1$ , an RF-gradient pulse combination 602 produces a phase-labeled transverse magnetization  $M_z = [e^{i\pi(r)} - e^{-i\pi(r)}]M_0/(2i)$ . A spoiler gradient pulse 604 is applied to dephase the coherent transverse magnetization. At time  $t_2$ , an RF-gradient decoding pulse 606 produces a tip angle of the spatial distribution  $a_0 e^{-i\pi(r)}$ . The resulting transverse magnetization is:

$$15 \quad M_{xy}(r) = a_0 M_0 \{ e^{i[f(r(1))-f(r(2))]} - e^{-i[f(r(1))+f(r(2))]} \} / (2i).$$

This magnetization is then sampled with a fully balanced readout gradient pulse 608 to produce an echo 610. A 180° RF pulse 612 is applied, changing the sign of the phase factors in the transverse magnetization so that  $M_{xy}(r)$  is:

$$M_{xy}(r) = a_0 M_0 \{ e^{-i[f(r(1))-f(r(2))]} - e^{i[f(r(1))+f(r(2))]} \} / (2i)$$

20 and the balanced readout gradient pulse/180° RF pulse sequence is repeated. If the two terms in  $M_{xy}$  have little k-space overlap, only the area of k-space encompassing the first term is sampled. To compensate for sign changes of the phase factors produced by 180° RF pulses, a complex conjugate of data from every other readout period is obtained and assigned to an opposite location in k-space.

25 As shown in FIG. 6, between times  $t_1$  and  $t_2$ , the spoiler pulse 604 is applied to destroy the coherence in  $M_{xy}$  left by the RF-gradient pulse combinations at time  $t_1$ . Alternatively, if the time period between  $t_1$  and  $t_2$  is sufficiently long so that the coherence in  $M_{xy}$  decays to negligible levels, then such a spoiler gradient pulse is unnecessary.

30 This acquisition method can be further illustrated with the example of the phase-labeling function  $f(r) = kr$ , in cylindrical coordinates. After the decoding RF-gradient pulse combination that produces  $A(r)$  is applied, the terms in  $M_{xy}$  have

phase factors  $e^{i[k(r(t_1)-r(t_2))\phi]}$  and  $e^{i[k(r(t_1)+r(t_2))\phi]}$ . If the specimen does not experience large or abrupt deformations or displacements, changes, but a continuous or gradual deformation, the second term oscillates radially at a high spatial frequency of approximately  $2k$ , while the first term has a nearly zero frequency oscillation.

5 Referring to FIG. 7, the Fourier transform of the first term is concentrated at  $k = 0$  in a region 702, while the Fourier transform of the second term is at a distance greater than or equal to  $2k$  from the origin in a region 704. If  $k$  is sufficiently large, these two regions have little or no overlap in  $k$ -space. In MRI, sampling  $M_{xy}(\mathbf{r})$  with a series of readout gradients is equivalent to sampling the Fourier transform of  $M_{xy}(\mathbf{r})$

10 in  $k$ -space. Therefore,  $M_{xy}(\mathbf{r})$  can be sampled in  $k$ -space near the origin ( $k = 0$ ) to include contributions from the term having phase factor  $e^{i[k(r(t_1)-r(t_2))\phi]}$ . After an inverse Fourier transform, the corresponding image includes contributions based on  $k(r(t_2)-r(t_1))$ .

15 Generally, by using an RF-gradient pulse combination  $A(\mathbf{r})$  to tip the magnetization  $M_z$  onto the  $xy$  plane and selecting a phase of  $A(\mathbf{r})$  to have a sign opposite that of one of the phase-labeled terms in  $M_z$ , the phase of a magnetization tipped onto the transverse plane contains  $f(r(t_2))-f(r(t_1))$ . By acquiring data corresponding to this term, images based on  $f(r(t_2))-f(r(t_1))$  can be produced.

20 In the above example,  $k(r(t_2)-r(t_1))$  is proportional to the radial distance change between the voxel and the central axis. In certain applications, such as mapping the radial contraction and dilation of the left ventricle relative to a long axis of the left ventricle, the position of the long axis generally changes with time as is illustrated in FIG. 8. In this case, a prior MRI scan can be used to locate ventricle positions 801, 803 at times  $t_1$  and  $t_2$ , respectively. Then, the RF-gradient pulse

25 combination that applies the selected phase label can be calculated with respect to the axis position at the initial time  $t_1$ , while the decoding RF-gradient pulse combination can be calculated with respect to the axis position at the time of decoding. Then,  $r(t_1)$  and  $r(t_2)$  are radial distances to the long axis of the left ventricle at times  $t_1$  and  $t_2$  points from the same voxel of the myocardium, and

30  $k(r(t_2)-r(t_1))$  represents radial dilation/contraction regardless of the translational movement of the heart.

Data can also be acquired based on a phase-labeled longitudinal magnetization, such as  $M_z = \{m(r)e^{i(f(r)-\phi)} - m(r)e^{-i(f(r)-\phi)}\}/(2i)$ . Between times  $t_1$  and  $t_2$ , a series of spoiler gradient pulses (or a single spoiler pulse) is applied to reduce or eliminate coherence in the transverse magnetization left by the encoding RF gradient pulse combination at  $t_1$ . Alternatively, if the time period between  $t_1$  and  $t_2$  is sufficiently long so that the coherence in  $M_{xy}$  decays to negligible levels, then the spoiler gradient pulses are not needed. At time  $t_2$ , a standard MRI sequence (e.g., GRE or SPE) is used to acquire an image based on the transverse magnetization of  $M_{xy}$ . Then another phase labeling is performed with a different phase constant  $\phi'$  by changing the direction of the RF pulses and another image based on the transverse magnetization  $M_{xy}$  is acquired the same way. Denoting the original voxel position as  $r(t_1) = r'$ , then

$$M_{xy}(r) = \{m(r')e^{i(f(r')+\phi)} - m(r')e^{-i(f(r')+\phi)}\}/(2i) \text{ and}$$

$$M_{xy,2}(r) = \{m(r')e^{i(f(r')+\phi)} - m(r')e^{-i(f(r')+\phi)}\}/(2i).$$

Based on these equations,  $m(r')e^{i(f(r'))}$  can be determined as

$$m(r')e^{i(f(r'))} = [M_{xy,2}(r)e^{i\phi} - M_{xy}(r)e^{i\phi}]/\sin(\phi - \phi'),$$

and therefore the phase-label function  $f(r')$  can be obtained as the phase of  $m(r')e^{i(f(r'))}$  and the function of displacement  $f(r') - f(r)$  can also be obtained. This method is particularly suited to phase labels such as  $e^{i\pi\theta}$  for which modulations corresponding to the phase labels  $e^{-i(f(r))}$  and  $e^{i(f(r))}$  are not well separated in k-space.

#### Phase-labeled Longitudinal Magnetization Acquisition Method

The longitudinal magnetization can be phase labeled to be  $M_z = \{m(r)e^{i(f(r)-\phi)} - m(r)e^{-i(f(r)-\phi)}\}/(2i)$  at time  $t_1$ . Between times  $t_1$  and  $t_2$ , a series of spoiler gradient pulses can be applied to destroy the coherence in  $M_{xy}$  left by the encoding pulses at  $t_1$ . Alternatively, if the time period between  $t_1$  and  $t_2$  is sufficiently long so that the coherence in  $M_{xy}$  decays to negligible levels, then the spoiler gradient pulses are not needed. If the two terms in  $M_z$  have little overlap in k-space, as for example in  $f(r) = k_x x + k_y y$  where  $k_x$  and  $k_y$  are large, then at time  $t_2$ , a standard GRE or SPE method or their variants can be used to acquire a region in k-space that encompasses both terms. The two terms are then reconstructed from their respective regions in k-space. The phase factor  $e^{i(f(r))}$  can then be obtained from

either one of two terms, or from the phase difference between the two terms. Once  $f(r')$  is known, the desired function of displacement  $f(r') - f(r)$  is obtained. The two phase-labeled terms  $m(r)e^{i\theta(r)}$  and  $m(r)e^{-i\theta(r)}$  are conventionally called a stimulated echo (STE) and a stimulated anti-echo (STAE).

5 If the two terms in  $M_z$  are sufficiently separated in  $k$ -space, a gradient-recalled echo method or a modified spin-echo readout method, or their variants, can also be used to collect only the region in  $k$ -space that corresponds to one of the two terms. The phase of this single term then contains  $f(r')$ , and the desired function  $f(r') - f(r)$  can be obtained.

10

#### Example Mapping of Phase Label Time Evolution

Phase labels can be mapped as a function of time to track motion tracking over a period of time. At each time point after the initial phase labeling, a fraction of the longitudinal magnetization is tipped onto the transverse plane, and the 15 resulting transverse magnetization is detected with any of the methods described herein. After data acquisition, the remaining transverse magnetization can be destroyed with gradient spoiler pulses, and this procedure repeated again. The process can be repeated until the phase-labeled longitudinal magnetization is expended. To ensure that only a fraction of the phase-labeled  $M_z$  is used each time, 20 the tip angle of the decoding RF-gradient pulses preferably small compared to  $90^\circ$ , e.g.,  $30^\circ$ .

For such motion tracking, the phase labeling is performed with a  $90^\circ$  RF pulse, a gradient pulse along the  $x$  direction, and a second  $90^\circ$  pulse. This creates the longitudinal magnetization  $M_z = (e^{ikx} - e^{-ikx})M_0/(2i)$ . A spoiler gradient pulse is 25 then applied to destroy the coherent transverse magnetization. At time  $t_2$ , a small flip angle  $\alpha$  pulse tips a portion of the longitudinal magnetization into the transverse plane, where it is sampled repeatedly with a fast spin-echo readout scheme. The readout gradient waveforms of the fast spin-echo scheme are fully balanced to avoid any phase addition to the phase-label function. Then a spoiler gradient can be 30 applied to crush any residual transverse magnetization, before this process is repeated again for the next time point. This process is repeated for a series of time points, until the phase-labeled terms in the longitudinal magnetization are exhausted.

Example Mapping of Displacement with Phase Labeling

A specific example of phase labeling is described with reference to cardiac functional imaging based on displacement encoding with stimulated echoes ("DENSE"). A phase labeling function  $f(\mathbf{r})$  is selected that is a dot product of  $\mathbf{r}$  and a vector  $\mathbf{k}$  such that the phase-labeling function is  $f(\mathbf{r}) = k_x x + k_y y + k_z z$ , wherein  $k_x$ ,  $k_y$ , and  $k_z$  are constants. Phase-labeled terms corresponding to  $m(\mathbf{r})e^{if(\mathbf{r})}$  and  $m(\mathbf{r})e^{-if(\mathbf{r})}$  are referred to as a stimulated echo ("STE") and a stimulated anti-echo ("STAE"). A stimulated echo is generally compensated for phase shifts caused by magnetic field inhomogeneity, chemical shifts, and off-resonance effects and is nearly equivalent to a spin-echo except for the signal loss due to  $T_1$  during a mixing time ("TM"). In order to acquire an STE, two gradient field pulses of equal gradient moment and of the same polarity are used during the echo time ("TE"). In contrast, a stimulated anti-echo (STAE) can be produced with gradient pulses of opposite polarities. An STAE resembles a gradient-recalled echo instead of a spin-echo and carries phase accumulated due to magnetic field inhomogeneities, chemical shifts, and off-resonance effects.

Referring to FIG. 9, a magnetization vector  $\mathbf{M}$  is first tipped onto the transverse plane with a first 90° pulse 901. The magnetization  $\mathbf{M}$  is described in a complex representation as:

$$20 \quad M[\cos(\phi) + i \sin(\phi)] = Me^{i\phi} \quad [1]$$

wherein  $M$  is an amplitude and  $\phi$  a phase of the magnetization  $\mathbf{M}$  as it precesses onto the  $xy$ -plane. In the laboratory frame of reference, the phase  $\phi$  in is given by:

$$25 \quad \phi = \gamma B_0 t + \omega_{OFF} t + \Delta B_0 t + m r \quad [2]$$

wherein  $\omega_{OFF}$  is the off-resonance offset,  $\Delta B_0$  is an inhomogeneity in  $B_0$ , and  $m$  is a gradient field moment or area. In this example, the gradient field moment is defined as  $m = G t_G$  wherein  $G$  is the amplitude of an equivalent rectangular gradient pulse and  $t_G$  is a pulse duration of the equivalent pulse. In the rotating frame of reference,  $\gamma B_0 t$  is zero. Off-resonance, main field inhomogeneity and chemical shift phase accumulations have similar time dependence and a total  $S$  of these phase shifts is:

$$30 \quad S = \omega_{OFF} t + \Delta B_0 t. \quad [3]$$

Therefore, in the rotating frame of reference, the total phase is:

$$\phi = S + \gamma mr. \quad [4]$$

During STEAM imaging, all 90° pulses are applied along the same axis (for example along +y), during the first half 902 of an echo time (TE/2) and a phase

$$\varphi_1 = S_1 + \gamma m_1 r, \quad [5]$$

5 accumulates. A second 90° pulse 903 rotates a component of magnetization perpendicular to  $B_1$ , (the x-component) back to the z-axis. Gradient spoiler pulses (not shown in FIG. 9) applied during the mixing time TM scramble components of magnetization remaining in the transverse plane. Because the gradient pulse 910 during the first half of the echo time TE distributes the magnetization components  
10 evenly between the real (x) and the imaginary (y) axes, one half of the magnetization is lost. The magnetization relaxes with time constant  $T_1$ . In addition, the phase of the scrambled portion is lost, and a direction of precession of the magnetization can no longer be uniquely determined. If an imaginary part of the magnetization is  
15 scrambled and lost (i.e., a y-component), only  $M \cos(\varphi_1) = M \cos(S_1 + \gamma m_1 r)$  is restored onto the transverse plane following a third 90° RF pulse 905. This magnetization can be written as

$$\begin{aligned} M \cos(\varphi_1) &= \frac{M}{2} e^{i\varphi_1} + \frac{M}{2} e^{-i\varphi_1} = \\ &= \frac{M}{2} [\cos(\varphi_1) + i \sin(\varphi_1)] + \frac{M}{2} [\cos(-\varphi_1) + i \sin(-\varphi_1)] \end{aligned} \quad [6]$$

The nonscrambled real portion of the signal along the x-axis can be considered as the sum of two vectors precessing at the same rate, but in opposite directions. Each  
20 of them has half the amplitude of the original magnetization vector.

The magnetization described by Equation 6 is missing phase imparted to the spins by the 90° pulses. For this description of STEAM, the second and third 90° pulses in the RF pulsing scheme (90°<sub>y</sub> - 90°<sub>y</sub> - 90°<sub>y</sub>) behave as a 180° pulse because the magnetization rotates 180° as a result of their application. A 180° pulse changes  
25 the sign of the phase since the signal is multiplied by  $e^{i\pi}$ . After the application of a 180° pulse, the resulting magnetization is the complex conjugate of the original magnetization, i.e., its phase changes sign. For an RF pulse scheme 90°<sub>y</sub> - 90°<sub>y</sub> - 90°<sub>y</sub>, there is no sign change. After the 90° pulse 905, the phase of the magnetization is:

$$\varphi_1 = -S_1 - \gamma m_1 r_1 \quad [6a]$$

During the second half 904 of the echo time TE an additional phase  $\varphi_2$  accumulates, wherein

$$\varphi_2 = +S_2 + \gamma m_2 r_2. \quad [7]$$

5 At a center of an acquisition window 906, the transverse magnetization is:

$$\begin{aligned} M \cos(\varphi_1) e^{i\varphi_2} = \\ \left\{ \frac{M}{2} e^{i\varphi_1} + \frac{M}{2} e^{-i\varphi_1} \right\} e^{i\varphi_2} = \frac{M}{2} e^{i(\varphi_1+\varphi_2)} + \frac{M}{2} e^{i(-\varphi_1+\varphi_2)} = \\ \frac{M}{2} [\cos(\varphi_1 + \varphi_2) + i \sin(\varphi_1 + \varphi_2)] + \frac{M}{2} [\cos(-\varphi_1 + \varphi_2) + i \sin(-\varphi_1 + \varphi_2)] \end{aligned} \quad [8]$$

Gradient pulses 910, 912 are characterized by respective amplitudes  $m_1, m_2$  and a duration  $t_G$ . Typically,  $m_1=m_2$  and  $S_1=S_2$  since the echo interval TE is divided into two equal parts. Therefore, for stationary spins,  $\phi_1+\phi_2=0$  and (-

10  $\phi_1+\phi_2)=2S_1+2\gamma m_1 r_1$ . The detected signal is obtained from the magnetization

$$\frac{M}{2} + \frac{M}{2} [\cos(2S_1 + 2\gamma m_1 r_1) + i \sin(2S_1 + 2\gamma m_1 r_1)] \quad [9]$$

The signal consists of two parts. The first part corresponds to an STE since no residual phase exists as a result of the time-dependent terms described by S and resembles a spin-echo. The second part is modulated by twice the phase imparted

15 by the gradient moment  $m_1$ . In imaging experiments,  $m_1$  is typically large enough to shift this component outside the region of k-space sampled to create an image.

Otherwise, banding artifacts can appear. For non-stationary spins ( $r_2 = r_1 + \delta$ ), then  $\phi_1+\phi_2 = \gamma m_1 \delta$  and  $(-\phi_1+\phi_2) = 2S_1 + 2\gamma m_1 r_1 + \gamma m_1 \delta$ . Therefore, the detected signal consists of a DENSE signal and an  $m_1$  modulated component that is filtered out.

20 The DENSE signal is:

$$\frac{M}{2} [\cos(\gamma m_1 \delta) + i \sin(\gamma m_1 \delta)] = \frac{M}{2} e^{i\gamma m_1 \delta}. \quad [10]$$

On the other hand, if two gradient pulses 910, 914 of opposite signs are applied, the signal changes. With stationary spins  $m_1 = -m_2$ , and  $S_1 = S_2$ , then  $\phi_1+\phi_2 = -2\gamma m_1 r_1$  and  $(-\phi_1+\phi_2) = 2S_1$ . Therefore, the signal detected is an STAЕ and corresponds to:

$$25 \quad \frac{M}{2} [\cos(-2\gamma m_1 r_1) + i \sin(-2\gamma m_1 r_1)] + \frac{M}{2} [\cos(2S_1) + i \sin(2S_1)]. \quad [11]$$

A filter prior to a Fourier transform removes signal contributions modulated by  $m_1$ .

The remaining signal portion is modulated by the time-varying terms ( $S$ ) such as field inhomogeneity, etc., and is similar to a gradient-echo. If the spins are not stationary ( $r_2=r_1+\delta$ ), then  $\phi_1+\phi_2=-2\gamma m_1 r_1 - \gamma m_1 \delta$ , and  $(-\phi_1+\phi_2)=2S_1 - \gamma m_1 \delta$ . Thus,

5 the signal portion that is passed by the Fourier transform filter is an STAE and corresponds to:

$$\frac{M}{2} [\cos(2S_1 - \gamma m_1 \delta) + i \sin(2S_1 - \gamma m_1 \delta)] = \frac{M}{2} e^{i(2S_1 - \gamma m_1 \delta)}. \quad [12]$$

The STAE in a DENSE experiment reflects displacement  $\delta$  that occurs between the two gradient pulses in the TE period but it is contaminated by the time varying terms

10 ( $S$ ). This is the reason for selecting the STE not the STAE as the STEAM signal when performing such measurements. The STE is not totally free of influence by the time-varying terms. Because the spins move, the contributions of these terms during the first half 902 of TE are not equal to those during the second half 904 of TE. In a more accurate description,  $S_1 \neq S_2$ .

15 To describe phase label measurements, phases of two components of the signal magnetization can be written as ordered pairs. For example, the signal stored along the longitudinal axis after the second 90° pulse, as described by Equations 5 and 6, can be expressed as

$$\{\phi_1, -\phi_1\} = \{S_1 + \gamma m_1 r_1, -S_1 - \gamma m_1 r_1\} \quad [12a]$$

20 Referring to FIG. 9, the signal magnetization after the gradient pulse 912 is described by Equation 9 and can be written as  $\{0, 2S_1 + 2\gamma m_1 r_1\}$ . In the case of moving spins, where  $S_1 \neq S_2$  and  $r_2 = r_1 + \delta$ , the STE can be written as:

$$\{-S_1 + S_2 + \gamma m_1 \delta_1, S_1 + S_2 + \gamma m_1 \delta + 2\gamma m_1 r_1\} \quad [13]$$

As discussed previously, only the first term is detectable while the second is

25 modulated by  $2\gamma m_1 r_1$  and is filtered out before the Fourier transform. The detected portion corresponds to an STE. A more complete description of a STEAM signal in the presence of motion and gradient pulses of opposite polarity is:

$$\{-S_1 + S_2 - 2\gamma m_1 r_1 - \gamma m_1 \delta, S_1 + S_2 - \gamma m_1 \delta\} \quad [14]$$

The first term is undetectable since it is modulated by  $\gamma m_1 r_1$ , while the second term 30 corresponds to an STAE.

The fast spin echo (FSE) measurement shown in FIG. 9 can cause severe image artifacts when used to rapidly sample a STEAM signal because the signal phase changes sign with every 180° pulse. These image artifacts can be avoided with a dual echo method.

5 FIG. 10 is a block diagram of a dual echo method of displacement imaging. An axial magnetic field  $B_0$  is established in a step 1002 to produce a +z-directed magnetization  $M_0$ . In a step 1004, a 90 degree pulse is applied with the y-axis as the axis of rotation, rotating the magnetization  $M_0$  to the x-axis. A magnetic field gradient  $+G_x$  is applied in a step 1006 for a duration  $t_G$ , shifting the Larmor

10 frequency by  $\gamma G_x x$ . This frequency shift produces a phase shift proportional to  $\gamma G_x t_G x = \gamma m_1 x_1$  where  $m_1 = G_x t_G$ , and rotates the magnetization  $M_0$  from the x-axis by an angle  $\gamma m_1 x_1$ . In addition, during  $t_G$  an additional time-dependent phase shift  $S_1$  is produced by an off-resonance frequency offset  $\omega_{off}$ , and the inhomogeneity  $\Delta B_0$  in the axial field  $B_0$  and the phase shift  $S_1 = \omega_{off} t_G/2 + \gamma \Delta B_0 t_G/2$ . Upon

15 completion of the step 1006, the magnetization is in the transverse plane and is represented as  $M_0 \exp[i(\gamma m_1 x_1 + S_1)]$ . In a step 1008, a second 90 degree pulse is applied along the y-axis to rotate an x-component (i.e., the real part) of the magnetization  $M_0 \exp[i(\gamma m_1 x_1 + S_1)]$  to the z-axis and a y-component of the magnetization is unchanged. Typically, the y-component decays rapidly with a time

20 constant referred to as  $T_2^*$ . As a result of the second 90 degree pulse and the decay of the y-component of magnetization, the remaining magnetization is z-directed with a magnitude that is proportional to  $M_0 \cos(\gamma m_1 x_1 + S_1)$ . For convenience,  $\cos(\phi_1 + S_1)$  can be expressed as a sum of complex exponentials so that the magnetization is  $M_0 [\exp(i(\phi_1 + S_1)) + \exp(-i(\phi_1 + S_1))/2]$ .

25 In a step 1010, a mixing time  $T_M$  is provided in which no additional magnetic fields are applied. During the mixing time  $T_M$ , dipole moments associated with moving voxels of the sample experience displacements. After the mixing time  $T_M$ , a third 90 pulse is applied in a step 1012, rotating the magnetization vector back into the transverse plane. A first compensation interval of duration  $t_2/2$  is provided in a

30 step 1014. During the first compensation interval, no additional magnetic fields are applied but a phase shift  $S_2$  is produced by the off-resonance frequency offset  $\omega_{off}$

and the magnetic field inhomogeneity  $\Delta B_0$ . The phase shift  $S_2 = \omega_{OFF} t_2/2 + \gamma \Delta B_0 t_2/2$ .

A 180 degree pulse is applied in a step 1016, rotating the magnetization in the xy-plane such that the x-component experiences a 180° phase shift. A magnetic field gradient of magnitude  $-G$  is then applied for a duration  $t_G$  in a step 1018 and produces a phase shift proportional to  $-Gt_Gx = -\gamma m_2 x_2$ . A second compensation interval  $t_2/2$  is provided in a step 1020. An echo is detected in a step 1022 and data are processed in a step 1024.

In a step 1026, a compensation interval  $t_2/2$  is provided and in a step 1028 a gradient  $+G$  is applied for a duration  $t_G$ . Steps 1026, 1028, 1018, 1020 are repeated to provide additional echos in order to form an image. The number of echos is limited by  $T_2$  relaxation.

Table 1 illustrates the phase shifts produced by the method of FIG. 10, wherein  $\cos\phi$  is represented as a sum of  $\exp(-i\phi)$  and  $\exp(i\phi)$ .

15

Table 1. Phase shifts associated with the method of FIG. 10 for  $m_1 = m_2$ .

Step No.	Phase Source	-phase term	+phase term
1012	90 degree pulse	$-S_1 - \gamma m_1 x_1$	$S_1 + \gamma m_1 x_1$
1014	$t_2/2$	$-S_1 + S_2 - \gamma m_1 x_1$	$S_1 + S_2 + \gamma m_1 x_1$
1016	180 degree pulse	$S_1 - S_2 + \gamma m_1 x_1$	$-S_1 - S_2 - \gamma m_1 x_1$
1018	-gradient	$S_1 - S_2 - \gamma m \delta$	$-S_1 - S_2 - \gamma m \delta - 2\gamma m x$
1020	$t_2/2$	$S_1 - \gamma m \delta$	$-S_1 + \gamma m \delta - 2\gamma m x_2$
1022		Echo	
1026	$t_2/2$	$S_1 + S_2 - \gamma m \delta$	$-S_1 + S_2 + \gamma m \delta - 2\gamma m x_2$
1028	+gradient	$S_1 + S_2 + \gamma m x_1$	$-S_1 + S_2 - \gamma m x_1$
1016	180 degree pulse	$-S_1 - S_2 - \gamma m x_1$	$S_1 - S_2 + \gamma m x_1$
1018	-gradient	$-S_1 - S_2 + \gamma m \delta - 2\gamma m x_2$	$S_1 - S_2 - \gamma m \delta$
1020	$t_2/2$	$-S_1 + \gamma m \delta - 2\gamma m x_2$	$S_1 - \gamma m \delta$
1022			Echo

While the echos are contaminated by  $S_1$ , the  $S_2$  contributions are cancelled. The procedure of Table 1 and FIG. 10 continues until limited by a transverse

relaxation time  $T_2$  or other relaxation time. In the step 1022, the echo is associated with either the  $+i\phi$  or  $-i\phi$  phase terms and added to a corresponding image.

**Simultaneous Dual-Echo Readout for STEAM**

5        The readout scheme presented above has the advantage of utilizing the full extent of the available magnetization for collecting data by sampling either the STE or the STAE at any given acquisition window. In addition, it requires no special post-processing tools when compared to existing slower versions of DENSE. However, this scheme lacks the ability of simultaneously sampling both components

10      (STE and STAE) of the signal. By eliminating the second gradient encoding pulse (see FIG. 11B), both components can be sampled within the same acquisition window. The two components are separated in k-space by a distance of  $2\gamma m_1 r_1$ . Therefore, the acquisition window is extended to accommodate both components. Its actual duration will depend on the desired imaging parameters (such as field of

15      view ("FOV"), sampling speed, image resolution) and the encoding strength utilized. Since both components are rephased off-center within the acquisition period, a linear phase gradient will exist across the FOV of the image reconstructed from either component. In order to estimate this phase gradient and compensate for its effects via the image reconstruction algorithm, the gradient moment  $m_1$  is preferably

20      compared to the area of the readout gradient pulse contained between two successive sampled points. Since this area of  $G_x/BW$  corresponds to a maximum of  $2\pi$  phase evolution, the overall phase gradient across the FOV can be estimated and corrected for. However, in practice, hardware limitations can cause additional phase gradients across the FOV and therefore it is preferable to measure the phase gradient from an

25      immobile structure within the image, such as a representation of the liver margin, and adjust the correction factor accordingly. Once the phase gradient has been corrected in both images acquired from the two signal components (STE and STAE), the displacement information can be combined to yield a single dataset that possesses a higher signal-to-noise ratio. The resulting dataset will be contaminated

30      by the time varying phase terms,  $S_1$ , by twice as much when compared to the STE alone.

**Decoupling Overlapping STE and STAE in the Acquisition Window**

In both acquisition schemes described above, it is assumed that the two echoes (STE and STAE) are separated in k-space adequately by means of the encoding gradient moment,  $m_1$ , in order to avoid overlap of the two signal components. Such overlap can result in high-frequency content contamination during signal sampling and therefore diminished edge definition in the images. Unless such a penalty is acceptable, the two echoes are preferably separated by at least  $\gamma N_x G_x / \text{BW}$ , where  $N_x$  is the number of points along the x-direction. This translates to utilizing encoding gradient strengths (measured in mm/ $\pi$ ) of less than half the pixel size. This is true because the encoding gradient strength,  $Enc$ , is described by

$$Enc = \frac{1}{m_1 \cdot 2 \cdot 4250 \cdot 10^{-7}}$$

while the pixel size,  $p$ , is

$$p = \frac{1}{m_{READ} \cdot 4250 \cdot 10^{-7}}$$

15 and

$$m_1 \geq m_{READ}$$

With some encoding schemes, it is not always possible to utilize encoding pulses that will lead to such clear separation between the two components of the signal. A mechanism for distinguishing the two components in such cases is 20 described below. For this description, it is assumed that the free induction decay ("FID") has been suppressed.

For example, with the STEAM pulse sequence, the application of the gradient encoding pulse, with moment  $m_1$ , results in imparting phase to the spins according to their position in space. As such, the net  $M_{XY}$  magnetization is 25 scrambled across the xy-plane on both the x and y-axes. As a result, the second 90° RF pulse can only nutate back to the longitudinal axis half of the signal, i.e., either  $M_x$  or  $M_y$  but not both. Since the total signal on the xy-plane is  $M_{xy} = M_x + iM_y$ , the phase of the second 90° pulse determines whether the real or the imaginary part of the signal is preserved for imaging later in the sequence. Assuming that a second

90° RF pulse along the same axis as the first preserves the real part, then one can write this portion of the magnetization as

$$M_x = \frac{M_x + iM_y}{2} + \frac{M_x - iM_y}{2} = \frac{1}{2}(M_{xy} + M_{xy}^*)$$

In other words, the real part of the signal can be described as the sum of the total signal plus its complex conjugate. Similarly, if a second experiment is carried out with the second RF pulse applied with a 90° phase relative to the first RF pulse then the imaginary part of the signal is preserved. This can be written as

$$M_y = i \cdot \frac{M_x + iM_y}{2} - i \cdot \frac{M_x - iM_y}{2} = \frac{i}{2}(M_{xy} - M_{xy}^*)$$

The imaginary part of the signal can be written as the difference between the total signal and its complex conjugate. By acquiring  $M_x$  and  $M_y$  by means of two measurements, the individual  $M_{xy}$  and  $M_{xy}^*$ , which correspond to the STE and STAE, respectively, can be decoupled from one another without the limits of the above equations. FID suppression can be accomplished as well by acquiring data from a third experiment with the phase of the third 90° pulse modified accordingly.

15

#### Rotating Wheel Method

In phase-labeled imaging, phase-labeled components of magnetization decay or lose coherence via several processes that are conventionally characterized by time constants  $T_1$ ,  $T_2$ , and  $T_2^*$ . Many of the limitations imposed by these decay processes can be overcome as follows, with a rotating wheel method illustrated in FIG. 13. Such a method permits voxel motion to be tracked at a series of times. For a magnetization that, at time  $t_1$ , is phase-labeled so that

$$M_z = \{m(r)e^{i(f(r)\phi)} - m(r)e^{-i(f(r)\phi)}\}/(2i), M_{xy} = \{m(r)e^{i(f(r)\phi)} + m(r)e^{-i(f(r)\phi)}\}/2$$

and the initial coherence in  $M_{xy}$  is retained for a substantial period of time, both  $M_z$  and  $M_{xy}$  are used for data acquisition. Data is acquired at a series of time points  $t_n$  after the initial phase labeling using a series of RF pulses and readout schemes that satisfies three conditions: (a) at each time point  $t_n$ , readout-induced phase dispersion in  $M_{xy}$  is refocused with gradient pulses before the next time point; (b) at some time points  $t_n$ , a portion of  $M_z$  is tipped onto the transverse plane to replenish magnetization losses due to decay in  $M_{xy}$  due to various relaxation processes, while

a portion of the refocused  $M_{xy}$  is tipped into the longitudinal axis for storage; and (c) at least some adjacent RF pulses produce a nearly  $180^\circ$  flip, so that phase dispersion due to field inhomogeneities in  $B_0$  are compensated, and the decay of the transverse component  $M_{xy}$  follows approximately the  $1/T_2$  rate. When these three conditions

5 are satisfied, the phase-labeled transverse magnetization acquired at the time points decays at roughly the rate of  $1/T_2$ , while it is continuously or intermittently replenished by the labeled terms in the longitudinal magnetization that decay at the slower  $1/T_1$  rate in most biological samples. An advantage of this method is that the labeled terms in  $M_{xy}$  are used to improve SNR, while the available acquisition time

10 is increased by continuously or intermittently storing part of  $M_{xy}$  on the longitudinal axis and replenishing  $M_{xy}$  with a portion of the phase-labeled magnetization  $M_z$ . By adjusting the RF pulse flip angles, the amount of  $M_z$  tipped into the transverse plane at each time point is controlled, and therefore the total time available for data acquisition is controlled. Generally, there exists a tradeoff between the data

15 acquisition time and the SNR at each time point, and one can choose a suitable balance between the two by adjusting the RF pulses, as well as how frequently  $M_z$  is tipped in the transverse plane to replenish  $M_{xy}$ .

In one example of phase labeling, the magnetizations of all voxels in a region of interest form spokes of a wheel in a plane perpendicular to the  $xy$  plane, after

20 phase labeling as shown in FIG. 12. The axis of the wheel is in the  $xy$  plane at an angle  $\phi + \pi/2$  from the  $x$  axis. At time  $t_2$ , a gradient-balanced RF pulse combination of flip angle  $\alpha$  is applied along this direction (the direction perpendicular to the direction of the last  $90^\circ$  pulse in the phase labeling). This pulse turns the wheel around its axis by angle  $\alpha$  as shown in FIG. 12, so that the longitudinal and

25 transverse magnetizations are

$$M_z = m(r') \{e^{i[f(r') \phi - \pi/2 - \alpha]} + m(r) e^{-i[f(r') \phi - \pi/2 - \alpha]}\}/2,$$

$$M_{xy} = m(r') \{e^{i[f(r') \phi + \alpha]} + m(r) * e^{-i[f(r') \phi + \alpha]}\}/2,$$

wherein  $r' = r(t_1)$ . One or more of the readout methods described above can be used to acquire  $M_{xy}$  and isolate the phase-label function  $f(r')$ . All gradients used during

30 the readout period are rewound so that  $M_{xy}$  is restored to the form above.

At time  $t_3$ , a gradient-balanced  $\alpha$  RF pulse is applied along the direction  $\phi + \pi/2$ . The magnetizations are then:

$$M_z = m(r') \{ e^{i(f(r')-\phi-\pi/2-2\alpha)} + m(r) * e^{-i(f(r')-\phi-\pi/2-2\alpha)} \} / 2,$$

$$M_{xy} = m(r') \{ e^{i(f(r')-\phi-2\alpha)} + m(r) * e^{-i(f(r')-\phi-2\alpha)} \} / 2.$$

The readout and gradient rewinding process done at  $t_1$  is performed again to acquire  $M_{xy}$ .

5        This process can be repeated for the series of time points: At each time  $t_n$ , an  $\alpha$  RF pulse tips part of the longitudinal magnetization  $M_z$  onto the  $xy$ -plane and restores part of the  $M_{xy}$  along the  $z$ -axis. Mathematically, this is reflected as adding and subtracting  $\alpha$  to the phases of the two terms in  $M_z$  and  $M_{xy}$ . FIG. 13 is a schematic diagram representation of such a pulse sequence, where the readout after

10      each  $\alpha$  pulse is a gradient-recalled-echo readout. On average, the magnetization vector of a voxel spends equal times in the transverse plane and along the main field. Thus, the coherence of the magnetization decays at roughly half the rate of its relaxation in the transverse plane (assuming the relaxation rate along the longitudinal direction is much lower). Because several consecutive  $\alpha$  pulses

15      approach a  $180^\circ$  RF pulse, any phase dispersion of the transverse magnetization due to  $B_0$  inhomogeneity is refocused after several  $\alpha$  pulses.

FIG. 13 illustrates one embodiment of the rotating-wheel acquisition method for mapping an  $x$ -component of the displacement at multiple time points. The phase-labeling segment consists of a  $90^\circ$  RF pulse followed by a gradient pulse, and then another  $90^\circ$  flip along the  $x$ -axis. This creates a spin wheel, with  $M_z = (e^{ikx} - e^{-ikx}) M_0 / (2i)$ ,  $M_{xy} = (e^{ikx} + e^{-ikx}) M_0 / 2$ . A fully balanced readout gradient is preferably applied to sample both terms of the transverse magnetization  $M_{xy}$  simultaneously, as represented by the two echoes above the readout period. The magnetization is returned to the above spin-wheel form after the balanced readout.

20      Then, at time  $t_1 + \Delta t$ , an RF pulse of  $\alpha$  flip angle is preferably applied around the  $y$ -axis, and the balanced readout is repeated. At time  $t_1 + 2\Delta t$ , this process is repeated again. During each readout period, the gradient waveforms are fully balanced (net time integral of the gradient waveforms is zero), so as not to add additional phase to the magnetization. This process is repeated for a series of time points  $t_1 + n\Delta t$ .

25      Each RF pulse in this sequence, including the  $90^\circ$  pulses in the phase-labeling section, are fully balanced so as not to leave residual phase dispersion on

the magnetization vectors, regardless of the initial orientation of the magnetization vector. A fully balanced slice-selective RF pulse 1302 in the form of a sinc function is illustrated in FIG. 13. The gradient area  $G$  under the slice-select gradient pulse is balanced by two gradient pulses of opposite sign and half the area ( $G/2$ ), one applied 5 immediately before the slice-select gradient pulse, the other immediately after the slice-select gradient pulse.

In biological samples, usually  $T_1 \gg T_2$ , so the MR signal in this method lasts approximately twice  $T_2$ , during which the desired function  $f(r(t_n)) - f(r(t_1))$  is repeatedly mapped to form a history of motion.

10 The RF pulses at the time points  $t_n$  need not have the same flip angle. As long as the flip angle for each pulse is known, the phase offsets brought about by the RF pulse to the terms in  $M_z$  and  $M_{xy}$  are known and preferably compensated for during image reconstruction. In cases where the flip angle is not exactly uniform in the region of interest, for example, with slice profile imperfections in slice-selective 15 RF pulses, this flexibility allows several RF pulses to be used in one direction of spin rotation, and then an equal number of pulses in the other direction to compensate for the imperfections. In the pulse sequence of FIG. 13, this is implemented by replacing the series of  $\alpha$  pulses with a series of  $+\alpha$  and  $-\alpha$  pulses, e.g.,  $(+\alpha, +\alpha, +\alpha, +\alpha, -\alpha, -\alpha, -\alpha, +\alpha, +\alpha, +\alpha, -\alpha, -\alpha, -\alpha, -\alpha, -\alpha, \dots)$ .

20 This analysis leads to other embodiments in which the RF pulses for the time series alternate between  $180^\circ - \alpha$  and  $-(180^\circ - \alpha)$ ,  $\alpha$  being a small angle (e.g.,  $30^\circ$ ). Since each RF flip is about  $180^\circ$ , it refocuses most of the phase dispersions in  $M_{xy}$  due to  $B_0$  inhomogeneities. In the meantime, with each RF pulse a  $1-\cos(\alpha)$  portion of the longitudinal magnetization  $M_z$  is preferably brought into the transverse plane 25 to replenish  $M_{xy}$ , while a  $1-\cos(\alpha)$  portion of the transverse magnetization  $M_{xy}$  is brought back to the  $z$  axis for storage. By reducing the angle  $\alpha$ , the sustainable acquisition time approaches  $T_1$ , while SNR at each time point is reduced. Raising  $\alpha$  has the opposite effect.

30 In other embodiments, one can replace the  $\alpha$ -pulse train in FIG. 13 with a repeating segment consisting of an even number of alternating  $180^\circ$  and  $-180^\circ$  pulses followed by a small tip angle  $\alpha$  pulse, i.e.,  $(180, -180, 180, -180, \alpha, 180, -180, 180, -180, \alpha, \dots)$ . In each segment, the series of  $180$  pulses repeatedly refocus as the

transverse magnetization  $M_{xy}$  for readout, and then the  $\alpha$  pulse tips a portion of the longitudinal magnetization into the transverse plane to replenish  $M_{xy}$  in preparation for data acquisition in the next segment.

Further embodiments include reading the transverse phase-encoded magnetization with a train of 180-degree pulses, right after the phase label has been applied. The signal sampled during the series of 180-degree pulses can be used to form images, which possess phase-labeled information at different time points. The length of this readout period will be limited by  $T_2$  relaxation. Once the transverse magnetization has decayed and is no longer useful for creating images, it is crushed by gradient pulses. Following this, a 90-degree pulse can be utilized to bring the longitudinal magnetization onto the transverse plane. This part of the magnetization has experienced  $T_1$  relaxation ( $T_1 \gg T_2$ ) and, as such, has not decayed significantly. Imaging can now resume with a train of 180-degree pulses as mentioned above, to collect data from more time points.

There are many other possible embodiments of this general method in using a combination of other RF pulse series and readout schemes. If the RF pulses are slice selective, then the slice selective gradient needs to be fully balanced to avoid unwanted phase dispersion in the through-slice direction. FIG. 13 illustrates such a fully balanced slice selective pulse.

This method is called the rotating-wheel method because the magnetization vectors form a vertical wheel in the spin space after phase labeling, and the wheel rotates around its axis during data acquisition (See FIG. 12).

A cycling between imaging and storing magnetization along the z-axis can be maintained by applying a series of gradient-balanced 90° RF pulses. In this series, the phase of the 90° RF pulses can be changed by 180° after every four such pulses. By doing so, for every eight RF pulses, any deviations from a true 90° rotation are compensated for. In addition, both halves of the magnetization spend equal time along the longitudinal axis and the transverse plane. As a result they decay according to the same decay-rate, which is approximately two times  $T_2$ . Field inhomogeneity is compensated for by the RF-train phase cycling scheme since the spins spend equal time along both positive and negative directions on the XY-plane. Since for half the time the magnetization is protected from  $T_2$  decay by storage

along the Z-axis, the decay rate due to spin-spin relaxation is  $2T_2$ . This is true only when  $T_1 \gg T_2$ , which is the case for non-contrast-enhanced specimens. For the portion of the magnetization being imaged, either one or both of the STE and STAE can be sampled as described previously. Since all RF pulses used are slice-selective,

5 through-plane motion may cause significant signal loss, especially for later acquisition windows. Increasing the slice-thickness of the pulses in the RF pulse series that follows the position-encoding gradient can provide slice tracking in order to avoid undesired signal loss. However, out-of-slice free induction decay (FID) contributions can degrade image quality. In cases of significant through-slice

10 motion, this problem can be solved by placing out-of-slice saturation pulses immediately before the position-encoding segment.

The acquisition methods can be adapted for mapping phase labels at a series of time points to track motion. At each time point after the initial phase labeling, a fraction of the longitudinal magnetization is tipped onto the transverse plane, and

15 data corresponding to the resulting transverse magnetization is acquired as described above. After data acquisition, the remaining transverse magnetization can be destroyed with gradient spoiler pulses, and this procedure repeated until the phase-labeled longitudinal magnetization is exhausted. To ensure that only a fraction of the phase-labeled longitudinal magnetization  $M_z$  is used each time, the tip angle of

20 the decoding RF-gradient waveform is preferably much less than  $90^\circ$ , e.g.,  $30^\circ$ .

#### Free Induction Decay Suppression

FIG. 14 illustrates a DENSE measurement method. Referring to FIG. 14, during a time period  $TM$  between a second 90 degree pulse 1402 and a third 90 degree pulse 1404, the magnetization relaxes due to energy dissipation onto the

25 lattice according to  $T_1$  to produce a contribution  $M_{FID}$  to the z-component of the magnetization. In the presence of an axial magnetic field  $B_0$  that establishes an equilibrium +z-directed magnetization  $M_z$  (in the absence of RF pulses), a magnetization of magnitude  $M_{initial} < M_z$  decays to form a z-component of magnetization  $M(t)$ , wherein  $M(t) = M_z + (M_{initial} - M_z) \exp(-t/T_1)$ .

30 After a first 90 degree pulse 1406, the unlabeled transverse magnetization has a zero z-component so that  $M_{FID} = M_z [1 - \exp(-\tau_1/T_1)]$  at a time  $\tau_1$ , wherein  $T_1$  is a

longitudinal magnetization relaxation time. A 180 degree pulse 1404 flips  $M_{FID}$  to be directed along the -z axis, i.e.,  $M_{FID} = -M_{FID}$ . This flipped magnetization relaxes to produce a z-component of magnetization  $M(\tau_2)$  at a selected time  $\tau_2$  and has a magnitude that can be determined by assigning  $M_{initial}$  the value of  $M_{FID}$  so that

5  $M(\tau_2) = M_z + [-M_z(1-\exp(-\tau_1/T_1)) - M_z] \exp(-\tau_2/T_1)$ . The durations  $\tau_1$  and  $\tau_2$  can be selected so that at time  $\tau_2$ ,  $M(\tau_2) = 0$  by selecting  $\tau_2 = T_1 \ln[2/(1 + \exp(-T_M/T_1))]$ . As a representative example, for a mixing time  $T_M = 300$  ms and a longitudinal relaxation time  $T_1 = 300$  ms,  $\tau_1 = 262.2$  ms and  $\tau_2 = 138.8$  ms.

Selection of  $\tau_1$  and  $\tau_2$  for FID suppression depends on the longitudinal relaxation time  $T_1$  and because  $T_1$  is generally material dependent. For example, for myocardial tissue  $T_1$  is approximately 850 ms while for fat tissue,  $T_1$  is approximately 200 ms. However, FID associated with two time constants can be suppressed by providing an additional 180 degree pulse and corresponding time intervals.

10

15

**Reduction of Phase Errors by Interleaved Data Acquisition**

Phase-labeled terms acquired during readout contain the phase-label function as well as other additional phase contributions from eddy currents,  $B_0$  inhomogeneities, etc.. These contributions bring errors into the measurement. One 20 method of removing these phase errors is to acquire two data sets that are phase-labeled with different functions,  $a\mathbf{f}(\mathbf{r})$  and  $b\mathbf{f}(\mathbf{r})$ , where  $a$  and  $b$  are different constants. These two data sets share the same unknown phase contributions. By subtracting their respective results, we obtain  $(a-b)[\mathbf{f}(\mathbf{r}')-\mathbf{f}(\mathbf{r})]$ , and the common phase errors are removed. These two data sets can be acquired under the same 25 condition of motion, preferably in an interleaved fashion, to reduce errors from small changes in the position and movement of the object.

**Resolving Phase Ambiguities**

The phase of an MRI signal is normally expressed in the range of 0 to  $2\pi$  radians. When a specified phase-label function exceeds this range, the acquired 30 phase-label distribution contains step-like jumps of  $2\pi$  magnitude. This phenomenon is called "phase wrap-around." Phase wrap-around is corrected by first

locating the discontinuous boundaries where this jump occurs, and then, for each boundary, the phase of the voxels on one side of the boundary is added or subtracted with an integer multiple of  $2\pi$ , such that the discontinuity is removed. This procedure is generally effective. In some specimens, a bulk motion of an isolated region needs to be measured in relation to other regions and phase differences between these regions are ambiguous. In diagnostic imaging, the purpose of motion tracking is usually to characterize the internal movements of a contiguous area, where phase unwrapping is sufficient to resolve the ambiguity. In certain applications, measurements of local tissue deformation are needed, such as the strain in the myocardium. For these applications, it is not necessary to unwrap the phase for the entire region of interest as a whole, but rather it is sufficient to phase-unwrap each small area encompassing a group of neighboring voxels, and obtain the local deformation in this area.

#### Strain Data Display

15 In certain applications of MRI motion tracking, it is advantageous to quantify the deformation of a region by computing material strain. An example is strain mapping in the myocardium. In a two-dimensional (2D) plane, such as a 2D image through the long axis of the left ventricle, strain tensor maps can be calculated once the in-plane components of displacement vectors are mapped with one or more of 20 the methods described in the previous sections. The strain tensor at each voxel is represented by the strain values (negative for compression and positive for stretching) along two orthogonal directions, called principal axes of strain. Both the strain values and the principal axes contain useful information in many cases. The strain values can be displayed using short, thick line segments of uniform length to 25 represent the principal axes at each voxel, while the color or a grayscale intensity of the line segments represent the strain values. The strain data can be presented in two strain images, each containing strain values of a particular sign, so that one map presents the axes and strain values for compression, while the other presents the axes and strain values for stretching. The color or grayscale intensity in each map 30 represents the absolute value of the positive or negative strain. If a voxel has the

same sign of strain for both principal axes, then in one map, two orthogonal line segments appear in its position, while in the other map the line segments are absent.

Alternatively, the strain data can be separated into  
5 two maps containing the higher and lower strain values, respectively. Then, each voxel in a map contains one line segment, whose color or grayscale intensity represents the corresponding strain value. Since each map may contain both positive and negative strain values, the color scale  
10 or gray intensity scale may need to represent a range of values from negative to positive, and a mixture of color and gray-intensity scale can be used for this purpose.

Strain data can also be displayed in a single image by providing each voxel with orthogonal line segments of  
15 uniform length to represent the principal axes of strain. The color or grayscale intensity of each line segment represents the corresponding strain value. A mixture of color scale and gray intensity scale can be used to cover a range of values including both negative and positive  
20 numbers.

Example embodiments of the invention are described above. It will be appreciated that these embodiments can be modified in arrangement and detail without departing from the scope of the invention.

25 It is to be understood that, if any prior art publication is referred to herein, such reference does not constitute an admission that the publication forms a part of the common general knowledge in the art, in Australia or any other country.

30 In the claims which follow and in the preceding description of the invention, except where the context requires otherwise due to express language or necessary implication, the word "comprise" or variations such as "comprises" or "comprising" is used in an inclusive sense,  
35 i.e. to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A magnetic resonance imaging system, comprising:
  - a magnet that applies at least one magnetic field to
  - 5 a specimen;
  - a radio-frequency transmitter that applies a radio-frequency pulse to the specimen, wherein the magnetic field and the radio-frequency pulse are configured to label a phase of a magnetization of the specimen based on
  - 10 a function of position at or near a first time point;
  - a radio-frequency receiver that detects magnetic resonance signals from the specimen; and
  - a processor that produces an image of the specimen based on the magnetic resonance signals, wherein the image
  - 15 includes spatial variations in the phase of the magnetization of the specimen accumulated in a mixing time subsequent to the first time point.
2. The magnetic resonance imaging system of claim 1,
  - 20 wherein the radio frequency transmitter is configured to produce a radio-frequency pulse that stores a portion of the phase-labeled magnetization along a storage axis.
3. A method of reducing free induction decay
  - 25 contributions to a magnetic resonance image in phase-labeled displacement imaging, the method comprising:
    - selecting a time interval;
    - applying a radio-frequency (RF) pulse to a specimen at a time point within the time interval, wherein the time
    - 30 point is selected to reduce a contribution to a magnetic resonance signal from free induction decay.
4. The method of claim 3, wherein the time point divides the time interval into a first interval of duration  $t_1$  and
  - 35 a second interval of duration  $t_2$ , such that  $t_2 = T_1 \ln[2/(1 + \exp(-T_M/T_1))]$ , wherein  $T_1$  is a longitudinal decay time and  $T_M = t_1 + t_2$

5. The method of claim 3, further comprising applying a 180 degree pulse at an end of the time interval of duration  $t_1$ .

5 6. A method of mapping motion of a specimen with magnetic resonance, imaging, the method comprising:

- (a) applying a spatially varying phase based on a function  $f(r)$  to a specimen magnetization;
- (b) applying a 180 degree RF pulse to the specimen;
- 10 (c) applying a spatially varying phase that is approximately opposite to the spatially varying phase based on the function  $f(r)$  to the specimen magnetization;
- (d) measuring a spatially varying phase of the specimen magnetization;
- 15 (e) producing a specimen image based on the measured phase of the specimen magnetization; and
- (f) repeating steps (a)-(e).

10 7. The method of claim 6, wherein the image is based on 20 a difference between the measured phase and the labeled phase.

15 8. The method of claim 7, wherein a longitudinal component  $M_z$  of the magnetization of the specimen is phase-labeled based on the function of position  $f(r)$  such that  $M_z$  25  $= [m(r)e^{if(r)} + m(r)e^{-if(r)}]/2$ , wherein  $m(r)$  is a real function of position, and further comprising applying an RF-gradient pulse combination to transform at least of portion of the longitudinal component  $M_z$  into a transverse component  $M_{xy}$  that is proportional to  $e^{if(r)}$ .

20 9. The method of claim 7, further comprising applying an RF pulse to produce longitudinal and transverse components of 30 the specimen magnetization that are proportional to  $[e^{if(r)} + e^{-if(r)}]$  and  $[e^{if(r)} - e^{-if(r)}]/(2i)$ , respectively.

10. The method of claim 7, wherein the phase of the magnetization is labeled based on a plurality of functions of position.

5 11. The method of claim 10, wherein a transverse component of the magnetization of the specimen is proportional to  $m_1(r)e^{if_1(r)} + m_2(r)e^{if_2(r)} + \dots + m_N(r)e^{if_N(r)}$ , wherein  $f_1(r), \dots, f_N(r)$  are functions of position,  $m_1, \dots, m_N$  are constants, and  $N$  is an integer.

10

12. A method of magnetic resonance imaging a specimen having a moving axis, the method comprising:

measuring a location of the axis at a first time;  
phase encoding a specimen magnetization as a function

15 of specimen position based on a location of the axis at the first time;

measuring a location of the axis at a second time;  
phase decoding the specimen magnetization at the

20 second time based on the location of the axis at the second time; and

producing an image of the specimen based on the phase-decoded specimen magnetization.

10  
11  
12  
13  
14  
15

13. A magnetic resonance imaging method for producing an image based on displacements of a specimen, comprising:

25 selecting a direction of displacement;  
phase labeling a magnetization of the specimen based on displacements in the selected direction; and

30 producing an image of the specimen from measurements of a phase of the magnetization.

16  
17  
18  
19  
20

14. The method of claim 13, wherein the selected direction of displacement is radial direction.

35 15. The method of claim 13, wherein the selected direction of displacement is an azimuthal direction.

16. A method of acquiring phase-encoded displacement data in magnetic resonance imaging, comprising:  
    applying at least one 180 degree radio-frequency pulse to a specimen;  
5    receiving signals corresponding to a stimulated echo and a stimulated anti-echo produced by the 180 degree radio-frequency pulse; and  
    processing the signals to obtain said phase-encoded displacement data.

10 17. A dual echo magnetic resonance imaging method, comprising:  
    phase labeling a specimen magnetization;  
    storing at least a portion of the phase-labeled  
15 magnetization along a longitudinal axis;  
    rotating at least a portion of the stored magnetization into a transverse plane;  
    applying an RF-gradient pulse combination to the rotated magnetization to produce a magnetization having a  
20 first decoded phase to produce a first echo;  
    obtaining a first set of image data based on the first echo;  
    applying additional RF-gradient pulse combinations to produce a second echo corresponding to a magnetization  
25 having a second decoded phase that is opposite the first decoded phase; and  
    obtaining a second set of image data based on the second echo.

30 18. The method of claim 17, wherein the first and second echos are acquired in a single acquisition window.

19. The method of claim 17, further comprising forming an image with the first and second sets of image data by  
35 subtracting the first and second sets of image data.

20. A magnetic resonance imaging method, comprising:

storing a phase labeled magnetization by rotating a portion of the phase labeled magnetization to be directed along a longitudinal axis defined by an axial magnetic field;

- 5       rotating a portion of the stored magnetization into a transverse plane;
- applying a gradient pulse to at least the portion of the stored magnetization in the transverse plane to compensate phase dispersion; and
- 10      rotating a portion of a longitudinal component of magnetization to the transverse plane to compensate decay in the labeled magnetization.

21. A method of magnetic resonance imaging of displacements of a heart, comprising:
  - 15    selecting a displacement direction;
  - providing a function of position corresponding to the selected displacement direction;
  - applying phase modulation to a magnetization of the heart using the function of position at an initial time;
  - 20    forming an image of the heart based on changes in magnetization phase with respect to the phase modulation applied at the initial time.

- 25    22. A method of displaying strain data, comprising:
  - displaying a strain magnitudes at image positions as a grayscale value or a color; and
  - displaying strain axes at the image positions as orthogonal line segments.

- 30    23. A method of correcting phase wrap around in phase labeled magnetic resonance imaging, comprising:
  - locating an image boundary corresponding to a phase discontinuity; and
  - 35    adjusting a phase on a side of the boundary to eliminate the phase discontinuity.

24. The method of claim 12, further comprising selecting the phase encoding based on a selected displacement direction.

5 25. The method of claim 24, wherein the selected displacement direction is a radial direction.

26. The method of claim 24, wherein the selected displacement direction is an azimuthal direction.

10

27. A system as claimed in claim 1 or claim 2, and substantially as herein described with reference to the accompanying drawings.

15

28. A method as claimed in any one of claims 3 to 23, and substantially as herein described with reference to the accompanying drawings.

20 Dated this 4th day of March 2004

THE GOVERNMENT OF THE UNITED STATES OF AMERICA AS  
REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH & HUMAN  
SERVICES

By their Patent Attorneys

25 GRIFFITH HACK

Fellows Institute of Patent and  
Trade Mark Attorneys of Australia

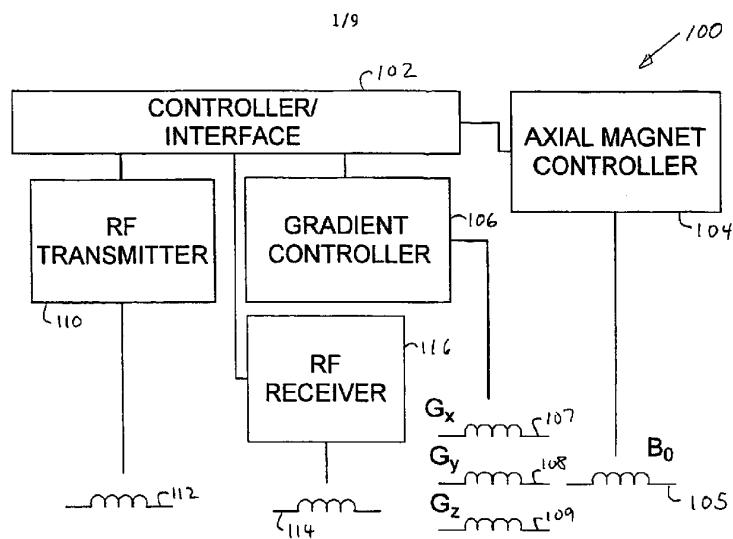


FIG. 1

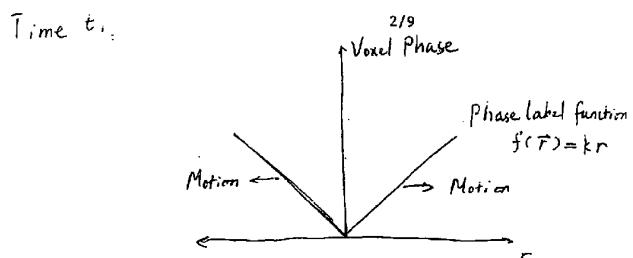


FIG. 2A

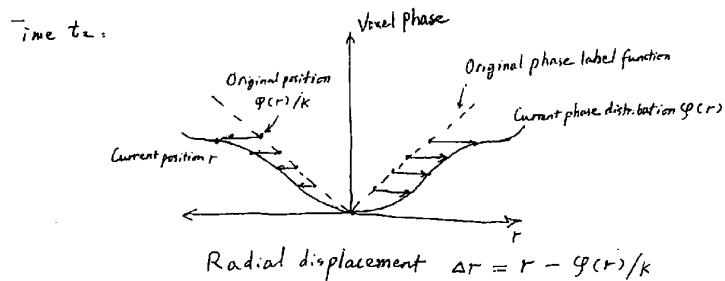


FIG. 2B

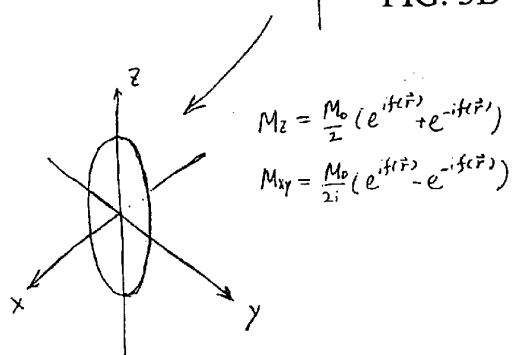
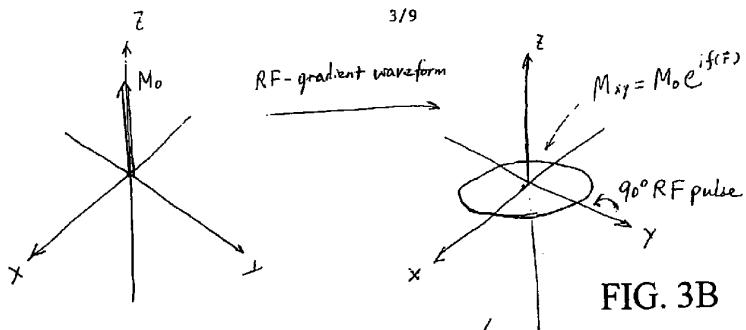


FIG. 3C

4/9

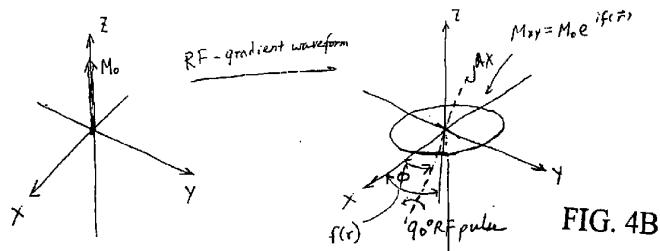


FIG. 4A

FIG. 4B

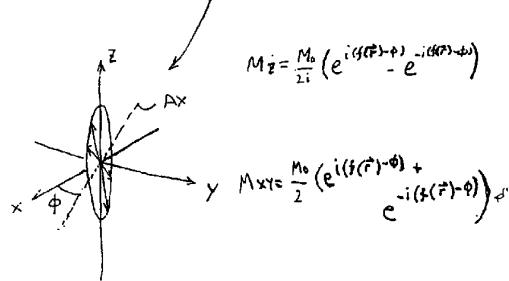


FIG. 4C

5/9

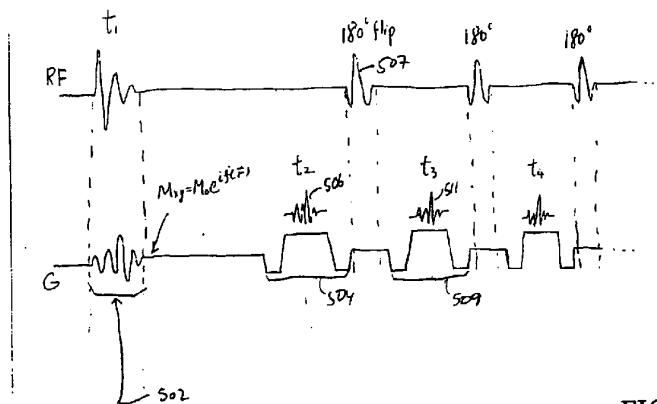


FIG. 5

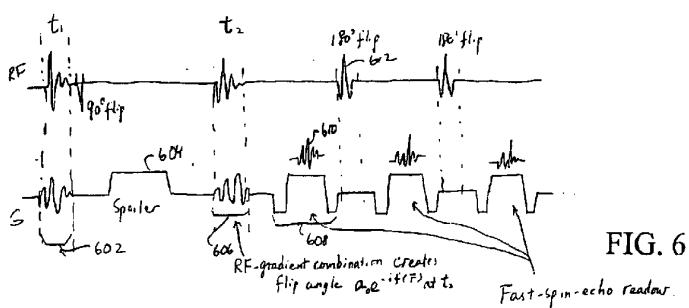


FIG. 6

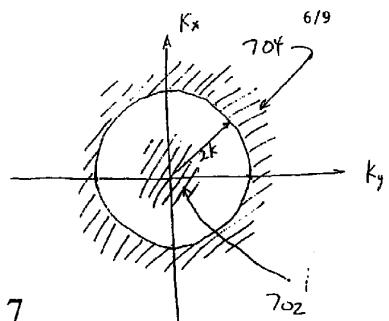


FIG. 7

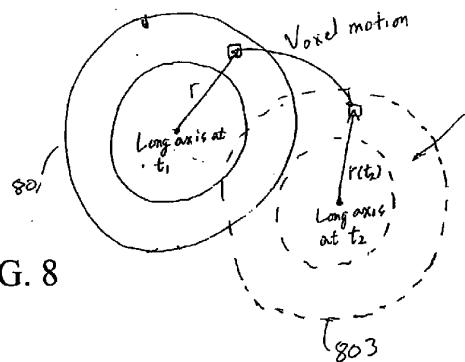


FIG. 8

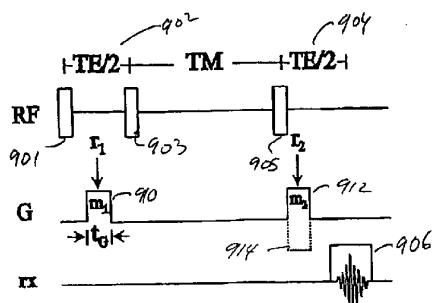


FIG. 9

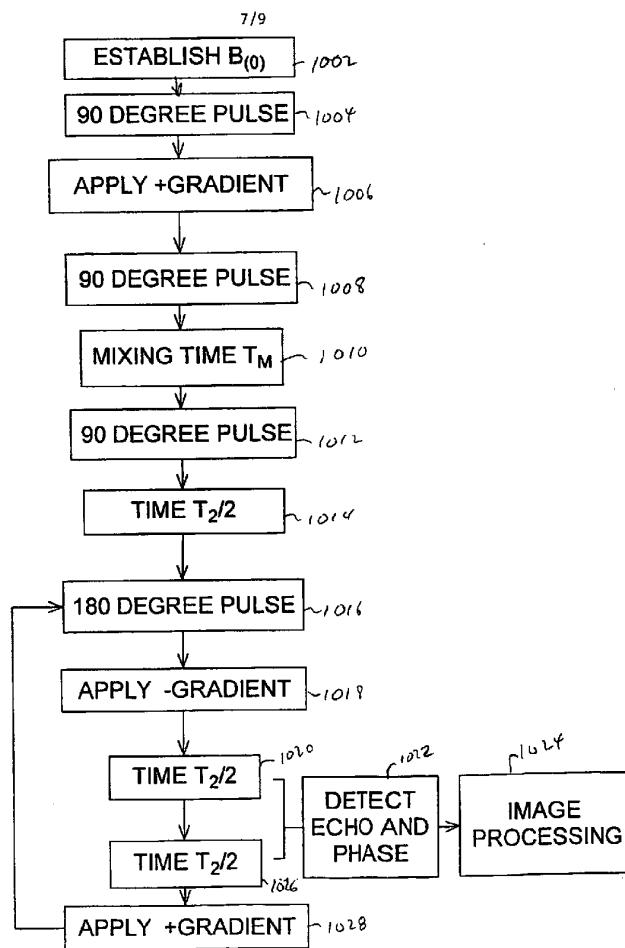


FIG. 10

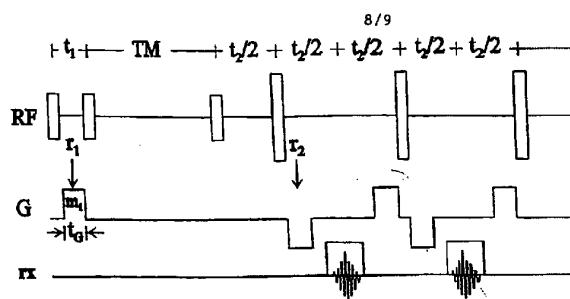


FIG. 11A

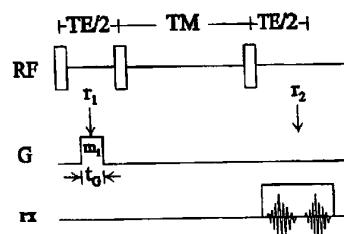


FIG. 11B

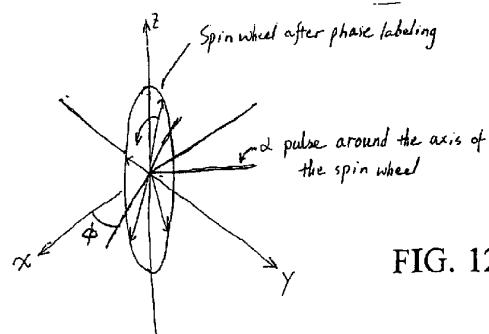


FIG. 12

9/9

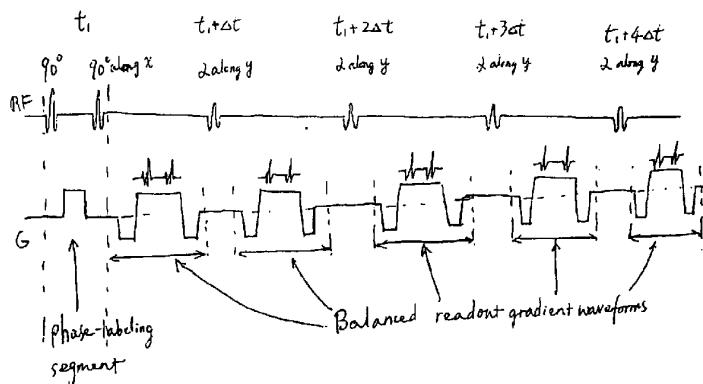


FIG. 13

Balanced slice-selective RF pulse:

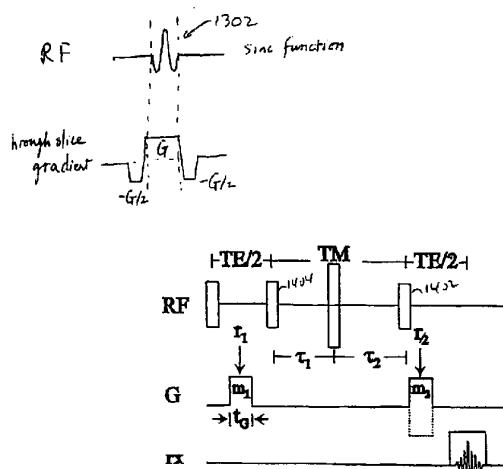


FIG. 14