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(54) Title: METHOD AND APPARATUS FOR USING MAGNETIC RESONANCE IMAGING FOR CARTILAGE ASSESSMENT AND MONITORING

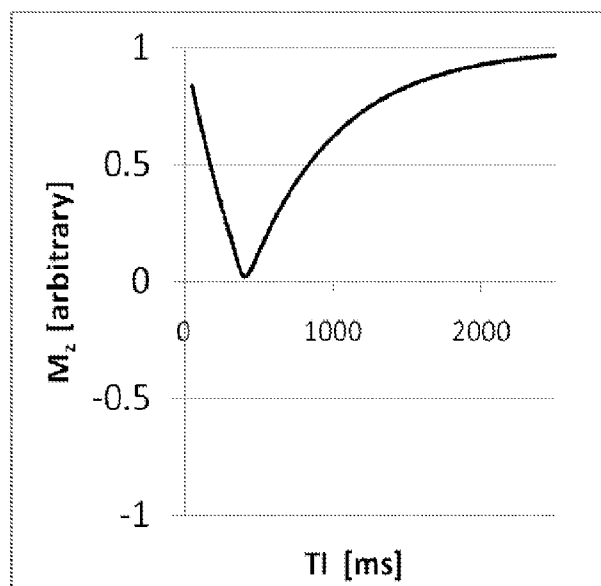


FIG. 1B

(57) Abstract: Embodiments herein provide T1-mapping using a phase-sensitive inversion-recovery (IR) method. The method may use phase information of IR sequence data to restore the polarity of the IR sequence data. Restoring the polarity effectively doubles the dynamic range of the IR sequence data, providing for higher accuracy of T1-mapping. The technique may also allow a smaller number of inversion time (TI) intervals to be used for accurate T1-mapping, thereby reducing data acquisition time.

Method and Apparatus for Using Magnetic Resonance Imaging for Cartilage Assessment and Monitoring

Cross Reference to Related Applications

[0001] The present application claims priority to U.S. Provisional Patent Application No. 61/482,552, filed May 4, 2011, entitled "T1-Mapping Using Phase-Sensitive Inversion-Recovery Method," the entire disclosure of which is hereby incorporated by reference in its entirety.

Technical Field

[0002] Embodiments herein relate to the field of medical imaging, and, more specifically, to a phase-sensitive inversion-recovery method for T1-mapping.

Background

[0003] It is widely accepted, and supported by the result of numerous basic and clinical research studies, that the mechanical properties of cartilage are strongly influenced by the concentration of Glycosaminoglycans (GAGs). In-vivo non-invasive assessment of GAG concentration therefore is valuable for assessing and monitoring cartilage degeneration, regeneration, adaptation and repair. Several techniques have been proposed to assess GAG concentration in cartilage including T1ρ-mapping, sodium imaging and T1- mapping using delayed Gadolinium-Enhanced Magnetic Resonance Imaging (MRI) of Cartilage (DGEMRIC or dGEMRIC). Of these techniques, the DGEMRIC technique has shown the most promise for assessing concentration of glycosaminoglycan (GAG) in cartilage in vivo. Loss of GAG in cartilage is typically an initiating event in osteoarthritis. T1-mapping of DGEMRIC image data has the potential to non-invasively assess the integrity of articular cartilage and recognize early stages of osteoarthritis. This capability offers the possibility of diagnosing, monitoring, and assessing therapies of an array of cartilage disorders. However, low reliability and long

data acquisition times prevent widespread use of the DGEMRIC technique for assessing cartilage integrity.

[0004] Typical implementation of the DGEMRIC technique involves application of an inversion-recovery (IR) sequence, wherein a series of images are acquired with varying inversion-times (TI) to allow probing of a T1 relaxation recovery curve. Standard methods use a reconstruction algorithm that fits the modulus (i.e., magnitude) of the image data for each pixel to a theoretical T1 recovery curve. This approach effectively halves the original dynamic range of the IR signal which in turn contributes to errors in T1 value estimates. It has been demonstrated that signal of IR images can be recovered using a full phase sensitive reconstruction algorithm which can improved detectability in low signal-to-noise ratio MRI images and improve tissue contrast. For example this approach is commercially available in methods for detecting myocardial infarction. Related to such, while particularly valuable for the knee, the described technology could improve dGEMRIC measurements in smaller joints such as hip or ankle that would allow an acquisition of thinner slices with lower signal-to-noise ratio.

Brief Description of the Drawings

[0005] Embodiments will be readily understood by the following detailed description in conjunction with the accompanying drawings and the appended claims. Embodiments are illustrated by way of example and not by way of limitation in the figures of the accompanying drawings.

[0006] Figures 1A and 1B illustrate T1 recovery curves for phase-sensitive and modulus data, respectively, in accordance with various embodiments;

[0007] Figures 2A-C illustrate T1-maps using the DGEMRIC technique calculated with the phase-sensitive reconstruction algorithm for: (A) a patient post osteochondral allograft transplant (OAT); (B) a normal volunteer; and (C) an asymptomatic volunteer with decreased glycosaminoglycan in the cartilage, in accordance with various embodiments;

[0008] Figure 3A shows a linear comparison of T1 values using phase-sensitive and modulus data, in accordance with various embodiments;

[0009] Figure 3B shows a scatter plot of T1 values from fitting phase-sensitive data using four TI intervals, in accordance with various embodiments;

[0010] Figure 3C shows a scatter plot of T1 values from fitting modulus data using four TI intervals, in accordance with various embodiments;

[0011] Figure 4A shows a T1 map generated from the phase-sensitive data using seven TI intervals, in accordance with various embodiments; and

[0012] Figure 4A shows a T1 map generated from the phase-sensitive data using four TI intervals, in accordance with various embodiments.

Detailed Description of Disclosed Embodiments

[0013] In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which are shown by way of illustration embodiments that may be practiced. It is to be understood that other embodiments may be utilized and structural or logical changes may be made without departing from the scope. Therefore, the following detailed description is not to be taken in a limiting sense, and the scope of embodiments is defined by the appended claims and their equivalents.

[0014] Various operations may be described as multiple discrete operations in turn, in a manner that may be helpful in understanding embodiments; however, the order of description should not be construed to imply that these operations are order dependent.

[0015] The description may use perspective-based descriptions such as up/down, back/front, and top/bottom. Such descriptions are merely used to facilitate the discussion and are not intended to restrict the application of disclosed embodiments.

[0016] The terms “coupled” and “connected,” along with their derivatives, may be used. It should be understood that these terms are not intended as synonyms for each other. Rather, in particular embodiments, “connected” may be used to indicate that two or more elements are in direct physical or electrical contact with each other. “Coupled” may mean that two or more elements are in direct physical or electrical contact. However, “coupled” may also mean that two or more elements are not in direct contact with each other, but yet still cooperate or interact with each other.

[0017] For the purposes of the description, a phrase in the form “A/B” or in the form “A and/or B” means (A), (B), or (A and B). For the purposes of the description, a phrase in the form “at least one of A, B, and C” means (A), (B), (C), (A and B), (A and C), (B and C), or (A, B and C). For the purposes of the description, a phrase in the form “(A)B” means (B) or (AB) that is, A is an optional element.

[0018] The description may use the terms “embodiment” or “embodiments,” which may each refer to one or more of the same or different embodiments. Furthermore, the terms “comprising,” “including,” “having,” and the like, as used with respect to embodiments, are synonymous, and are generally intended as “open” terms (e.g., the term “including” should be interpreted as “including but not limited to,” the term “having” should be interpreted as “having at least,” the term “includes” should be interpreted as “includes but is not limited to,” etc.).

[0019] With respect to the use of any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations may be expressly set forth herein for sake of clarity.

[0020] In various embodiments, methods, apparatuses, and systems for T1-mapping using a phase-sensitive inversion-recovery method are provided. In exemplary embodiments, a computing device may be endowed with one or more components of the disclosed apparatuses and/or systems and may be employed to perform one or more methods as disclosed herein.

[0021] Embodiments herein provide T1-mapping using a phase-sensitive inversion-recovery (IR) method. The method may use phase information of IR sequence data to restore the polarity of the IR sequence data. Restoring the polarity effectively doubles the dynamic range of the IR sequence data, providing for higher accuracy of T1-mapping. The technique may also allow a smaller number of inversion time (TI) intervals to be used for accurate T1-mapping, thereby reducing data acquisition time.

[0022] Various embodiments include acquiring an IR sequence, processing the data in the IR sequence using a phase-sensitive reconstruction algorithm, and

calculating T1 values from the processed data. The T1 values may be used to create a T1 map.

[0023] The IR sequence may be a three-dimensional (3D) data set or a two dimensional (2D) data set. The IR sequence may include a number, N, of magnetic resonance imaging (MRI) images, each acquired using a different TI interval. In some embodiments, one or more of the images may be acquired with the same TI interval. At least one of the images may be acquired with a TI interval longer than a threshold value that substantially ensures that all spins have a positive magnetization along a measuring axis. This image may be referred to herein as the reference image. The typical threshold value may be about 1500 to 2500 milliseconds. The particular TI value will depend on the field strength of the MRI scanner and the specific implementations and parameters of IR sequence such as repetition time (TR) and flip angle. In various examples provided herein, TI threshold value was set at 2200ms.

[0024] In various embodiments, the IR sequence may be modified based on phase information in the reference image data, using the reconstruction algorithm, to form a phase-corrected IR sequence. The reconstruction algorithm may restore the polarity in the phase-corrected IR sequence, thereby doubling the dynamic range of the phase-corrected IR sequence data compared with the non-phase-corrected (i.e., modulus) IR sequence data. The phase-corrected IR sequence may be used to calculate T1 values and/or create a T1 map. The phase-corrected IR sequence data may provide greater accuracy and/or allow fewer TI intervals to be used in the IR sequence.

[0025] For example, T1 mapping uses a series of 3D-IR image data sets with N (N>3) different TI times. T1 relaxation times are typically extracted from a 3-parameter (Z_0 , A, T1) fit using equation for signal Z in the IR sequence,

$$Z \propto Z_0 \cdot [1 - Ae^{-(TI/T1)} + e^{-(TR/T1)}],$$
 where Z_0 is a scaling factor, A accounts for spatial imperfections of the 180 degree inversion pulse and T1 is the spin-lattice relaxation time. All currently used reconstruction methods utilize modulus of the available complex signal Z.

[0026] Additionally, for example, in a 3D IR sequence, each 3D image may include a plurality of slices along a z-axis, and each slice may include a plurality of data

points in an x-y plane. An IR signal at a location, x,y, in a slice, l, of a k-th 3D image encoded with a TI value, TI_k, may be represented by a complex function Z_{lk}(x,y):

$$Z_{lk} = M_{lk}(x,y)\exp[\Theta_{lk}(x,y) + \Phi_{lk}(x,y)],$$

where M_{lk} is a magnitude of complex signal Z_{lk}, Θ_{lk} is a phase component of complex signal Z_{lk}, and Φ_{lk} is a phase factor of complex signal Z_{lk}. The phase component of complex signal Z_{lk} may depend on one or more factors, such as B0 and B1 field inhomogeneity, signal delays, mis-centering of an echo in an acquisition window, and/or other factors. The phase factor Φ_{lk} may be related to a state of initial magnetization being positive or negative along the z-axis. In some embodiments, the phase factor, Φ_{lk}, of complex signal Z_{lk} may assume only two phase values, e.g., 0 or π.

[0027] In various embodiments, at least one of the 3D images in the series, referred to herein as the reference image, may be acquired with a value of TI longer than a threshold TI value to substantially guarantee that all spins have a positive initial magnetization along the z-axis. In some embodiments, the images may be acquired in order of increasing TI values, and the reference image may be the last image (i.e., when k equals N). Thus, the phase factor can be dropped from the complex function, Z_{IN}, representing the IR signal for the reference image, meaning the IR signal for the reference image may be written as:

$$Z_{IN} = M_{IN}(x,y)\exp\Theta_{IN}(x,y)$$

[0028] The complex function, Z_{lk}, representing the IR signal for the IR sequence may then be phase corrected using the phase information of the reference image, Z_{IN}. To simplify the description, the indexes annotating the slice, l, and pixel coordinates, x,y, are not included in the equations below. Multiplying the complex function, Z_k, for the series of 3D data sets by the complex conjugate, Z^{*}_N, of the complex function for the reference image yields:

$$Z_k Z_N^* = M_k M_N \exp(\Phi_k),$$

where M_k and M_N are the magnitudes of signals Z_k and Z_N , respectively. A phase corrected function, Z'_k , may then be written as:

$$Z'_k = M_k \exp(\Phi_k) = (Z_k Z_N^*) / M_N$$

Accordingly, the signal polarity of the IR signal may be restored by making the magnitude, M_k , of the IR signal negative if the phase factor, Φ_k , is π and keeping the magnitude positive if the phase factor is zero, resulting in a phase-corrected IR sequence. Thus, the reconstruction algorithm for signal polarity restoration may be represented by the substitution:

$$\begin{aligned} M_k &= M_k & \text{if } \Phi_k &= 0 \\ M_k &= -M_k & \text{if } \Phi_k &= \pi \end{aligned}$$

[0029] In various embodiments, a T1 map may then be calculated by fitting the phase-corrected IR sequence data to a theoretical T1 recovery curve, such as by a least-square fit method. In an embodiment, the magnitude, M_k , of the phase-corrected IR sequence data may be fit to the equation:

$$M_k = D [1 - A \exp(-Tl_k/T1) + \exp(-TR/T1)]$$

where A, D, and T1 are the parameters to be fitted. A is a parameter that reflects B1 field inhomogeneity, D is a scaling parameter, and T1 is spin-lattice relaxation time. In some embodiments, the fitting may be done using a least-square fit, with initial estimates of $A = 2$, and $D = M_N$.

[0030] An example of the theoretical T1 recovery curve to be fitted with the phase corrected IR sequence data is shown in **Figure 1A**. Using the fitted parameters, a T1 value may be calculated for each data point in the 3D image. A T1 map may then be created. In some embodiments, the T1 map may be color coded according to the T1 value at each data point. In some embodiments, the cartilage of the patient may be outlined using a mask image, and the mask image may be used to calculate the T1 values for the cartilage. The T1 map may be overlaid over an image. T1 maps can be

calculated over full FOV. The cartilage mask is used to limit calculations to pixels included in the mask only. This allows the speed of calculations to be increased.

[0031] In contrast, a theoretical T1 recovery curve for non-phase corrected IR sequence data (i.e., using the modulus of the IR signal) is shown in **Figure 1B**. This non-phase corrected T1 recovery curve is based on the equation:

$$M_k = D \text{ abs}\{[1 - A \exp(-Tl_k/T1) + \exp(-TR/T1)]\}$$

In accordance with a first method, the first equation is used on the type of data shown in **Figure 1A**. In accordance with a second method, the second equation is used on data presented in **Figure 1B**.

[0032] As shown in **Figures 1A-B**, the phase-sensitive inversion-recovery method restores the signal polarity in the IR sequence data, thereby doubling the dynamic range of data used to fit the T1 curve. The increased dynamic range may decrease the number of faulty fits, thereby improving the accuracy and/or reliability of T1 relaxation time fits to an inversion-recovery function.

[0033] The phase-sensitive inversion-recovery method may be applied to any 2D or 3D IR sequence. The method may be used in conjunction with the DGEMRIC technique to assess the integrity of cartilage. The method provides increased accuracy of T1-mapping for 3.0T MRI magnetic fields, and may be extended to be applied on any field strength scanners using similar methodology. In embodiments, lower field scanners may require larger number of TI time sets or a different selection of TI_N threshold value as indicated above.

Experimental Results

Experiment 1

[0034] A study was performed to validate the phase-sensitive inversion-recovery method described above using the DGEMRIC technique to assess glycosaminoglycan (GAG) concentration in cartilage in vivo. Loss of GAG in cartilage is typically an initiating event in osteoarthritis, and non-invasive assessment of GAG concentration has

potential to become a biomarker for cartilage degeneration, regeneration, adaptation, and repair.

[0035] In the study, the reconstruction algorithm was implemented using Matlab (Mathworks, Natick, MA, USA) software. The reconstruction algorithm was applied with 3D IR gradient-echo sequence for T1 mapping and validated in a phantom study. Additionally, T1-map calculations were performed in human subjects, including post osteochondral allograft transplant (OAT) patients and non-symptomatic volunteers, using the reconstruction method.

[0036] Subjects enrolled in this study were injected with 0.2mmol/kg gadolinium (Gd) contrast (Magnevist) and allowed to exercise following the protocol outlined by Burstein et al. (See Burstein D., et al: MRM 2001, 45:36-41). Imaging studies on a Philips 3T MRI scanner using 8-channel knee coil were started 60-80 minutes post Gd injection. Standard T1 and T2 with fat suppression series were acquired in axial, coronal, and sagittal planes. For T1-mapping, a 3D IR FFE sequence was used with TR/TE 5.1/2.6, 52 shots, shot interval 2800, flip 15, FOV 180x160, matrix 256x200, recon voxel 0.5x0.5x1.5, 62mm slab, bandwidth 434 Hz/pixel, resulting in scanning time of 2:26 minutes per inversion time TI. TI series included 40, 100, 300, 600, 1000, 1500, and 2200 milliseconds (ms). To assure consistency of the data sequence, sequence tuning was turned off between the series. Magnitude, real, imaginary, and phase images were reconstructed and used in the reconstruction algorithm to calculate T1-maps.

[0037] **Figures 2A-C** show examples of T1-maps generated with the DGEMRIC technique calculated using the reconstruction algorithm. **Figure 2A** shows a subject with a osteochondral allograft transplant (OAT), **Figure 2B** shows a normal volunteer, and **Figure 2C** shows an asymptomatic volunteer with decreased GAG in the cartilage. As demonstrated in the study, the phase-sensitive inversion-recovery method restores signal polarity in the IR sequence and therefore doubles the dynamic range of data to be used in T1 curve fitting. The method significantly improves reliability of T1 relaxation time fits to an inversion-recovery function and may be applied to any 2D or 3D IR acquisition sequence used in conjunction with the dGEMRIC technique. Additionally, the method allows for a reduced number of inversion recovery TI points resulting in

substantially shorter acquisition times. In an embodiment, it has been shown that using a 3T scanner, the number of TI times may be reduced from seven to four without reducing accuracy of T1 fits. This constitutes a 43% reduction in total scanning time.

Experiment 2

[0038] In a second study, the phase-sensitive inversion-recovery method was used with an IR sequence having a reduced number of TI points, demonstrating that the method may allow the data acquisition time to be reduced.

[0039] The DGEMRIC technique has potential to quantitatively measure the fixed-charge density (FCD) of proteoglycan aggregates. Multiple DGEMRIC sequences have been developed to generate T1 maps, which in turn can be used to assess cartilage integrity. Among the methods used for T1-mapping, the inversion recovery (IR) based methods are the most reliable, however, at the expense of long data acquisition times. Time constraints associated with image acquisition and post processing make routine DGEMRIC exams clinically unattractive. One factor contributing to the long scan time of DGEMRIC IR is the number of inversion times (TI's).

[0040] The phase-sensitive inversion-recovery method described herein doubles the dynamic range of image data available for T1 fitting and therefore may potentially allow for a smaller number of TI points needed for accurate T1-mapping. In this study, it is demonstrated that using this phase-sensitive algorithm, the number of TI's can be reduced to four, leading to a total exam time of less than 10 minutes, without sacrificing T1-fit accuracy compared with previous methods.

[0041] In the study, 3D IR DGEMRIC images were acquired on a Philips 3.0 Tesla MRI scanner using an 8-channel knee coil with following sequence parameters: TR/TE 5.1/2.6, 52 shots, shot interval 2800, flip 15, FOV 180x160, matrix 256x200, recon voxel 0.5x0.5x1.5, 62mm slab, bandwidth 434 Hz/pixel, resulting in scanning time of 2:26 min per inversion time TI. 3D IR series included a set of seven IR times: 40, 100, 300, 600, 1000, 1500, 2200 ms.

[0042] The phase-sensitive algorithm was applied to sagittal post-Gd IR images using custom software developed in MATLAB (Mathworks, Natick, MA, USA). Phase-

sensitive and standard modulus data were fit to the following equation: $I_z(TI) = I_0[1 - A \cdot \exp(-TI/T1) + \exp(-TR/T1)]$. T1 values calculated from fitting seven TI's were designated as controls. Subsets of three, four, or five TI's were chosen for curve fitting using a least-square fit method. The fitting routine was adjusted to flag bad pixels when the R-squared (R2) fit statistics was less than 0.95.

[0043] Results of analysis of 12,406 T1 values from fitting three, four, or five T1 intervals are shown in Table 1 below. As shown, Trial 2 had the strongest correlation to the controls. At the same time the modulus data produced a large number of bad pixels (R2=0.98-0.97, RMSE=27-30, N=12,406). Modulus data of trial 2 produced 1010 bad pixels while phase-corrected data of trial 2 produced 133 (N=12,406).

Trial	Inversion Times (ms)	Bad Pixels		Trendline R ²		Root Mean Square Error (RMSE)	
		Phase	Modulus	Phase	Modulus	Phase	Modulus
1	40, 600, 2200	120	764	0.92	0.93	53	49
2	40, 300, 1000, 2200	133	1010	0.98	0.97	27	30
3	40, 100, 300, 1500, 2200	134	864	0.96	0.97	38	33
4	40, 300, 600, 1000, 2200	89	784	0.97	0.97	33	31

Table 1

[0044] Additionally, **Figure 3A** shows a linear comparison of the phase-sensitive and modulus controls. **Figures 3B** and **3C** show scatter plots of T1 values from fitting four TI for phase-sensitive data and modulus data, respectively.

[0045] **Figures 4A-B** show T1 maps generated from the phase-sensitive data using seven TI intervals (**Figure 4A**) and four TI intervals (**Figure 4B**).

[0046] The study demonstrated that decreasing the number of inversion times to four and applying a phase-sensitive reconstruction algorithm allows reliable calculation of T1 relaxation maps. In contrast to phase-sensitive IR data, a significant number of pixels processed using a modulus of the equation failed curve fitting. These results suggest that optimization of the current 3D IR DGEMRIC protocol with four instead of seven TI intervals would decrease clinical acquisition times to less than 10 minutes.

Additional Embodiments and Experiments

[0047] Experiments were carried out on 3T MRI scanner (Achieva, Philips medical Systems, Netherlands). A standard phantom to that described in the literature was constructed consisted of nine cylindrical tubes filled with physiological saline doped with Gd(DTPA) (Magnevist, Berlix Imaging, Wayne, NJ, USA) at concentrations of 0.06, 0.125, 0.18, 0.25, 0.37, 0.5, 0.75, 1.0, 1.5 mM. Data were acquired with an 8-channel receive only head coil. The phantom was placed on top of a 500mL saline bag to improve loading of the coil.

[0048] For T1-mapping, a standard 3D-IR TFE sequence available on the scanner was used with TR/TE 5.1/2.6, echo train 100, interval for slice loop 2800, FOV 180x160, slice 3mm, matrix 256x200, reconstructed to 41 slices with voxel dimensions of 0.5mmx0.5mmx1.5mm, 62mm slab and bandwidth 434 Hz/pixel. TI series included seven times: 40, 100, 300, 600, 1000, 1500, 2200 ms. Low to high order of phase encoding was used and the time interval for slice loop constant for all TI times with resulting scan times of 2:26 min per inversion time TI was kept.

[0049] To assure data consistency in acquisition sequences all tuning steps were applied prior to the first series only and then turned off for all remaining series. Magnitude, real, imaginary, and phase images were reconstructed and used in the algorithm/techniques describe herein to calculate T1-maps. This sequence was applied with flip angles of 10, 15, 20 and 30 degrees to establish the flip angle that matches the 2D-IR FSE sequence; considered to be a gold-standard for T1 mapping.

[0050] The 2D-IR FSE single slice sequence was collected with TR/TE 2200/15 ms, echo train 5, slice 3mm, FOV 180x160, matrix 256x200, bandwidth 138hz/pixel and

series of inversion times of 50, 100, 300, 600, 1000, 1500, 2100ms. The slice chosen for 2D imaging was selected from the middle of image stacks used for 3D acquisitions.

[0051] Part of the design of the inversion recovery signal polarity restoration algorithm is an assumption that all tissue of interest will have positive z-magnetization during the readout period of the longest T1 time. Injection of a contrast agent will shorten relaxation times in any given tissue, therefore an estimate of the longest z-magnetization zero crossing prior to contrast injection was made.

[0052] Before Gadolinium injection, the signal of synovial fluid is characterized by the longest T1 relaxation time among all tissues (fat, bone marrow, ligament, cartilage, menisci) typically present in knee images. The T1 of synovial fluid ($T1_{syn}$) in several subjects before Gadolinium injection was measured and an average value of $T1_{syn} \leq 3600\text{ms}$ was obtained. Substituting $T1_{syn}$ into signal Z equation showed the synovial fluid z-magnetization zero crossing to be approximately 1200ms. In our 3D-IR TFE series the longest inversion time is 2200ms. This assures that all magnetizations of interest are positive during data readout for both pre-Gadolinium and post-Gadolinium scans.

[0053] Phantom experiments demonstrated that flip angles of 15 degrees in the 3D-IR TFE sequence provided the best correlation to T1 values from the 2D-IR FSE sequence. This 15 degree flip angle was used in all 3D experiments. Because of a relatively strong SNR in the phantom there was no difference between modulus based reconstruction and the method described herein for T1 calculations in this phantom.

[0054] The dGEMRIC Technique was tested in human subjects via study protocol that was reviewed and approved by the Institutional Review Board and all participants consented to the study. Eight subjects (5 male, 3 female), average age 40.9 years (range 17-66) received single OCA transplants for grade 4 International Cartilage Repair Society articular cartilage defects of the femoral condyle were included in the study. All grafts were stored at 4°C and obtained from the Joint Restoration Foundation (Centennial, CO), a tissue bank approved by the American Association of Tissue Banks. Subjects were evaluated arthroscopically and underwent dowel graft OCA implantation using the press-fit technique.

[0055] At 1 year post OCA implantation subjects were imaged on a 3T Achieva MRI scanner (Philips medical Systems, Netherlands) using an 8-channel knee coil in two imaging sessions: first prior to contrast injection and second after contrast injection. In the pre-contrast session standard T1, T2 series with fat suppression in axial, coronal and sagittal planes, followed by the above 3D-IR TFE sequence in the sagittal plane using the same sequence parameters as in phantom experiments were acquired.

[0056] Following a protocol previously described by Burstein in the literature, the subjects were injected with 0.2mmol/kg Gd-DTPA contrast and allowed to exercise after initial scanning. The subjects returned for the Post-Gadolinium imaging session approximately 60-80 minutes post injection and the 3D-IR TFE sequence was applied 20 minutes into the imaging session. Care was taken to ensure identical positioning of the subject in the knee coil and sequence parameters for the 3D-IR TFE remained the same. Consistency between pre- and post-Gadolinium imaging allowed calculation of dGEMRIC metrics used for analyzing the quality of transplanted cartilage.

[0057] Custom built software, implemented in MATLAB®, allowed a user to define Regions of Interest (ROI) over selected areas of cartilage and calculate descriptive statistics like: mean T1, standard deviation of T1 values, maximum T1, and minimum T1. Additionally T1 values were color mapped to corresponding RGB values and displayed for user review, flagged pixels were identified by assigning RGB values of 0 (white). A trained orthopaedic resident used the T1 2200 image, other MRI sequences, and the patient's chart to draw multiple ROIs over control and repair cartilage. In congruence with previous studies, the ROI were later used to calculate the following dGEMRIC metrics: $R1_{pre}$, $R1_{post}$, and $\Delta R1$ ($R1_{post} - R1_{pre}$). This was accomplished by ensuring the locations and pixel volumes of individual ROI between pre- and post-Gadolinium slices were consistent.

[0058] After drawing multiple Regions of Interest in post-Gadolinium images from 8 patients, 12,450 pixels were analyzed. When fitting seven T1 according to the techniques described herein, the numbers of flagged pixels are significantly reduced when the signal polarity of images are corrected. *Phase* data generated 2 flagged pixels and *Modulus* data had 396 flagged pixels when the R^2 fit statistic was less than 0.95. However there was no statistical difference between the T1 values of *Phase* and

Modulus data when using seven inversion times in the fitting routine (PPMCC=0.996). The major difference between *Phase* and *Modulus* data, when fitting seven TI, is that confidence in the goodness of fit (R^2) is consistently closer to 1 for *Phase* data.

[0059] Using Sagittal post-Gadolinium 3D-IR TFE images from all 8 subjects who received Osteochondral Allograft transplants, ROIs were drawn over grafted and native cartilage as identified on the TI=2200 T1-weighted image. Pixels from each ROI were fit according to the techniques described herein using seven TIs and trials of subsets of four or five as indicated in Table 2 below.

Table 2

Phase and Modulus T1 vales compared to the control T1 values. (n=12,450 pixels)

Tri al	Inversion Times, ms	T1 start value = 200ms				T1 start value = 400ms				T1 start value = 600ms			
		PPMCC		RMSE		PPMCC		RMSE		PPMCC		RMSE	
		<i>Ph</i> <i>ase</i>	<i>Mod</i> <i>ulus</i>	<i>Ph</i> <i>ase</i>	<i>Mod</i> <i>ulus</i>	<i>Phas</i> <i>e</i>	<i>Mod</i> <i>ulus</i>	<i>Pha</i> <i>se</i>	<i>Mod</i> <i>ulus</i>	<i>Phas</i> <i>e</i>	<i>Mod</i> <i>ulus</i>	<i>Phas</i> <i>e</i>	<i>Mod</i> <i>ulus</i>
A	40, 100, 1500, 2200	0.7 28	0.65 8	19 0	209	0.751	0.77 2	188	182	0.73 4	0.74 4	171	168
B	40, 300, 1000, 2200	0.9 89	0.48 7	34	147	0.984	0.32 3	39	127	0.99 3	0.83 1	27	101
C	40, 100, 600, 1500, 2200	0.9 91	0.91 2	31	119	0.995	0.99 6	21	20	0.99 1	0.99 2	30	27
D	40, 300, 600, 1000, 2200	0.9 93	0.97 5	29	54	0.994	0.99 1	23	23	0.99 7	0.98 9	18	34
E	40, 100, 300, 1500, 2200	0.9 37	0.22 1	86	119	0.950	0.18 7	75	130	0.96 1	0.33 2	64	204

Abbreviations: PPMCC, Pearson product-moment correlation coefficient. RMSE, Root-mean-square error of the linear regression line.

[0060] It has been suggested that fitting the modulus of the IR signal to the Z signal equation using a Non-linear Least Squares algorithm proves difficult. The Trust Region fitting algorithm may inadvertently converge on a local minimum and not the global minimum when fitting the modulus of the signal, therefore causing an error in T1 value calculation. In exponential models, convergence of the function to a local minimum can be caused by poor estimation of initial start parameters. To test this the experiment for each trial with three different T1 start values: 200, 400 and 600ms was run. The input start value for "A" was set to 1.8 and Z_0 was set equal to the signal intensity of the last inversion sequence (TI=2200ms).

[0061] T1 values calculated from fitting seven TIs to the Z signal equation described herein were designated controls. The trial data obtained from calculating T1 times using the modulus of the IR image were designated *Modulus* and trial data

processed using the signal restoration algorithm were designated *Phase*. T1 values calculated for each trial using *Phase* data were compared to T1 values from *Phase* controls. Similarly, T1 values for each trial using *Modulus* data were compared to T1 values from *Modulus* controls. A linear analysis of the data was performed and the Pearson product-moment correlation coefficient (PPMCC) between controls and each trial was calculated. This analysis included calculation of the Root-mean-square error of the linear regression line fitted for each trial as compared to controls.

[0062] The results of the signal simulation study are presented in Table 2. The table contains the results of PPMCC and linear regression RMSE calculations for 5 different trials (A-E), three different T1 start values (200, 400, 600ms), and two different fitting functions (*Modulus* and *Phase*). In all trials, fits based on *Phase* data performed consistently better than fits based on *Modulus* data. Results demonstrate the feasibility of decreasing the number of inversion times to four while preserving the fidelity of T1 calculations using the signal polarity restoration algorithm techniques described herein. Additionally, it was found the T1 start value has a strong influence on the quality of T1 calculation for *Modulus* data but does not affect T1 calculation based on phase corrected data. For all T1 start values, *Modulus* data for Trial B had a poor correlation to controls and a high RMSE. However, *Phase* data from Trial B showed a strong correlation and low RMSE at all T1 start values. Interestingly, Trial A was more inferior relative to Trial B suggesting that the calculation of T1 value depends on the selection of inversion times. Moreover, having more inversion times may not necessarily provide a better fit using *Modulus* data as indicated in Trial E.

[0063] Previous dGEMRIC studies using various 2D and 3D Inversion recovery sequences have not experimented with the possibility of decreasing the number of TI times used in curve fitting. Many studies using inversion recovery sequences have used five, six, seven, and twelve inversion times. Details on total acquisition time have only been reported with newer sequences. Current scan times for 3D dGEMRIC sequences are: 4–12 min for 3D-VFA, approximately 10 min for 3D-LL, and 17–20 minutes for 3D-IR TFE. By decreasing the TI intervals from seven to four, the total acquisition time for one scan, using the above mentioned 3D-IR TFE sequence, can be reduced from

17min to 10min while preserving the fidelity of T1 calculations, provided the fit utilizes the full dynamic range of the data.

[0064] Results of the signal simulation study show the selection of inversion times and initial estimation of T1 start values influence calculated T1 values. The initial estimation of the T1 start value strongly affected the *Modulus* data and had little effect on *Phase* data, indicating the robustness of the techniques described herein. The poor performance of *Modulus* data in Trial B compared to *Phase* data is a strong example of how T1 start values influence the final T1. When fitting *Modulus* data in Trial B at all T1 start values the correlation coefficient is consistently lower and the RMSE of the linear regression line is higher. In addition, comparing Trial B to Trial E shows fitting 4 inversion times results in more accurate T1 value calculations than fitting 5 inversion times for all T1 start values. A possible explanation to this observation is the well known fact that multiple minima exist when using Non-linear Least Squares algorithms to fit data to exponential models. Fitting *Modulus* data to the Z equation with a Non-linear Least Squares algorithm is more sensitive to convergence at a local minimum. To compensate for this disparity, multiple start values could be estimated to isolate the global minimum.

[0065] Restoring the signal polarity of 3D-IR TFE images allows the number of inversion times to be reduced, thus leading to decreased acquisition times without compromising the accuracy of T1 calculations. The techniques can be applied to any 2D or 3D-IR sequence used in dGEMRIC. Moreover, the techniques could improve dGEMRIC measurements in smaller joints such as hip or ankle that would allow an acquisition of thinner slices with lower signal-to-noise ratio.

[0066] Any one or more of various embodiments previously discussed may be incorporated, in part or in whole, into a computing device or a system. A suitable computing device may include one or more processors for obtaining/receiving data, processing data, etc. One or more of the processors may be adapted to perform methods in accordance with various methods as disclosed herein. A computing device may also include one or more computer readable storage media.

[0067] Any one or more of various embodiments as previously discussed or discussed below may be incorporated, in part or in whole, into an article of manufacture.

In various embodiments, an article of manufacture may comprise a computer readable medium (e.g., a hard disk, floppy disk, compact disk, etc.) and a plurality of programming instructions stored in computer readable medium. In various ones of these embodiments, programming instructions may be adapted to program an apparatus, such as an MRI device or a processor within or separate from an MRI device, to enable the apparatus to perform one or more of the previously-discussed.

[0068] Although certain embodiments have been illustrated and described herein, it will be appreciated by those of ordinary skill in the art that a wide variety of alternate and/or equivalent embodiments or implementations calculated to achieve the same purposes may be substituted for the embodiments shown and described without departing from the scope. Those with skill in the art will readily appreciate that embodiments may be implemented in a very wide variety of ways. This application is intended to cover any adaptations or variations of the embodiments discussed herein. Therefore, it is manifestly intended that embodiments be limited only by the claims and the equivalents thereof.

Claims

What is claimed is:

1. A method, comprising:
 - obtaining an inversion recovery (IR) sequence including a plurality of magnetic resonance imaging (MRI) images taken with varying IR times, at least one of the images being a reference image taken with an inversion time (TI) greater than a threshold TI value such that substantially all spins have a positive initial magnetization along a measurement axis; and
 - generating a phase-corrected IR image data from the IR sequence using phase information from the at least one reference image.
2. The method of claim 1, further comprising calculating a T1 map from the phase-corrected IR sequence.
3. The method of claim 2, wherein the calculating comprises fitting the phase-corrected IR sequence to a theoretical T1 recovery curve.
4. The method of claim 1, wherein the plurality of MRI images are taken using a delayed gadolinium-enhanced MRI contrast technique.
5. The method of claim 1, wherein a phase factor at each data point of the IR sequence is either a first value or a second value, and generating the phase-corrected IR sequence comprises switching a polarity of a magnitude of the IR sequence at the data point if the phase factor of the IR sequence at the data point is the second value.
6. The method of claim 1, wherein a phase factor corresponding to a first TI_1 value is used to correct for phase of subsequent images in TI series.

7. An article of manufacture including a computer readable medium having instructions stored thereon that, if executed by a computing device, cause the computing device to perform a method comprising:

obtaining an inversion recovery (IR) sequence including a plurality of magnetic resonance imaging (MRI) images taken with varying IR times, at least one of the images being a reference image taken with an inversion time (TI) greater than a threshold TI value such that substantially all spins have a positive initial magnetization along a measurement axis; and

generating a phase-corrected IR image data from the IR sequence using phase information from the at least one reference image.

8. The article of manufacture of claim 7, further comprising instructions stored thereon that cause the computing device to perform a method further comprising calculating a T1 map from the phase-corrected IR sequence.

9. The article of manufacture of claim 8, wherein the instructions that cause the computing device to perform calculating a T1 map comprises fitting the phase-corrected IR sequence to a theoretical T1 recovery curve.

10. A system comprising:

a computing device configured to receive magnetic resonance (MR) image data, analyze the image data, and report the results of the analysis for display,

wherein analyzing the MR image data comprise

obtaining an inversion recovery (IR) sequence including a plurality of magnetic resonance imaging (MRI) images taken with varying IR times, at least one of the images being a reference image taken with an inversion time (TI) greater than a threshold TI value such that substantially all spins have a positive initial magnetization along a measurement axis; and

generating a phase-corrected IR image data from the IR sequence using phase information from the at least one reference image.

11. The system of claim 10, wherein the computing device is further configured to analyze the image data by further comprising calculating a T1 map from the phase-corrected IR sequence.

12. The system of claim 11, wherein the further calculating a T1 map configuration of the computing device comprises configuration for fitting the phase-corrected IR sequence to a theoretical T1 recovery curve.

13. The system of claim 10, wherein the configuration of the computing device for receiving magnetic resonance (MR) image data is configured to receive a plurality of MRI images taken using a delayed gadolinium-enhanced MRI contrast technique.

14. The system of claim 10, wherein the computing device is configured to obtain the IR sequence wherein a phase factor at each data point of the IR sequence is either a first value or a second value, and the configuration for generating the phase-corrected IR sequence comprises switching a polarity of a magnitude of the IR sequence at the data point if the phase factor of the IR sequence at the data point is the second value.

15. The system of claim 10, wherein a phase factor corresponding to a first $T1$ value is used to correct for phase of subsequent images in TI series in the analyzing the MR image data configuration of the computing device.

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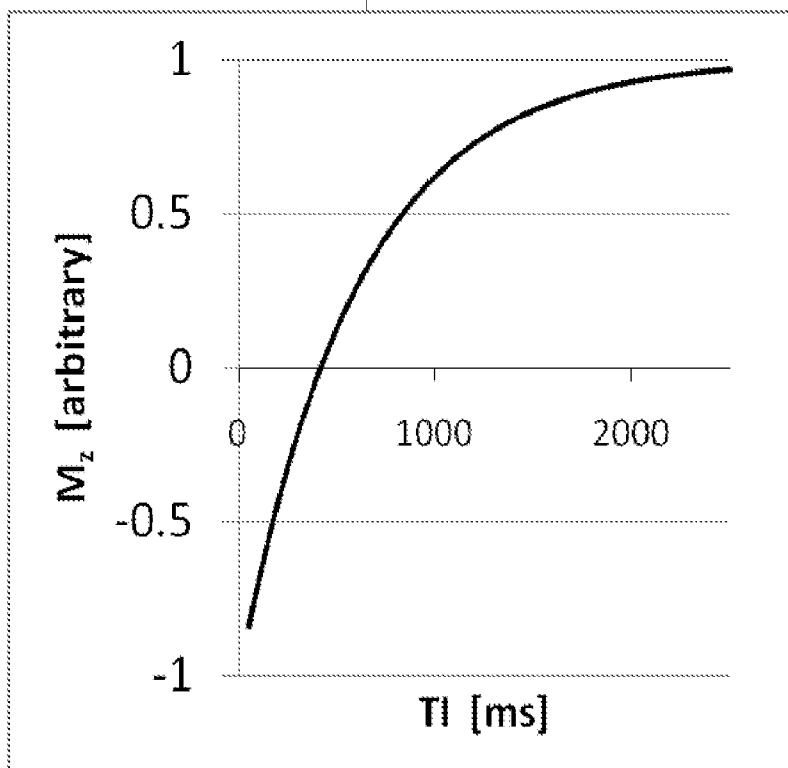
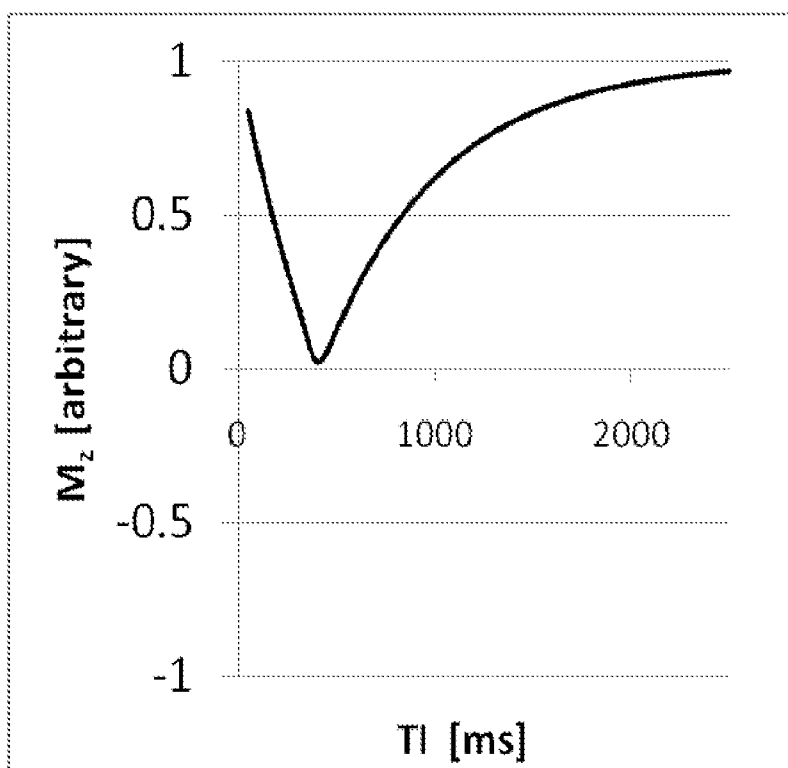
**FIG. 1A****FIG. 1B**



FIG. 2A



FIG. 2B

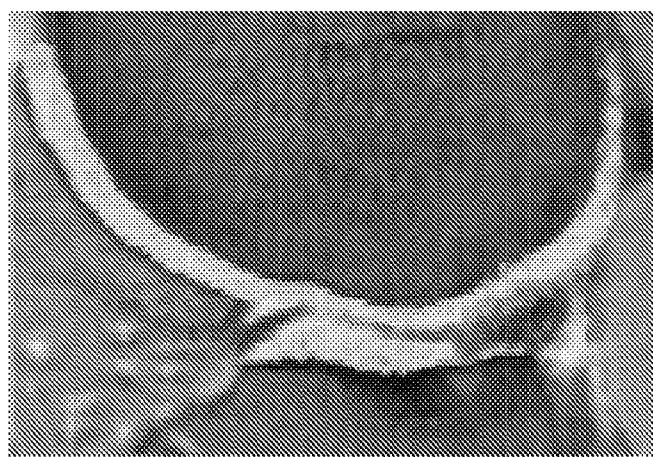
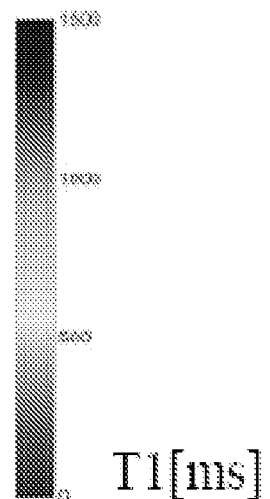
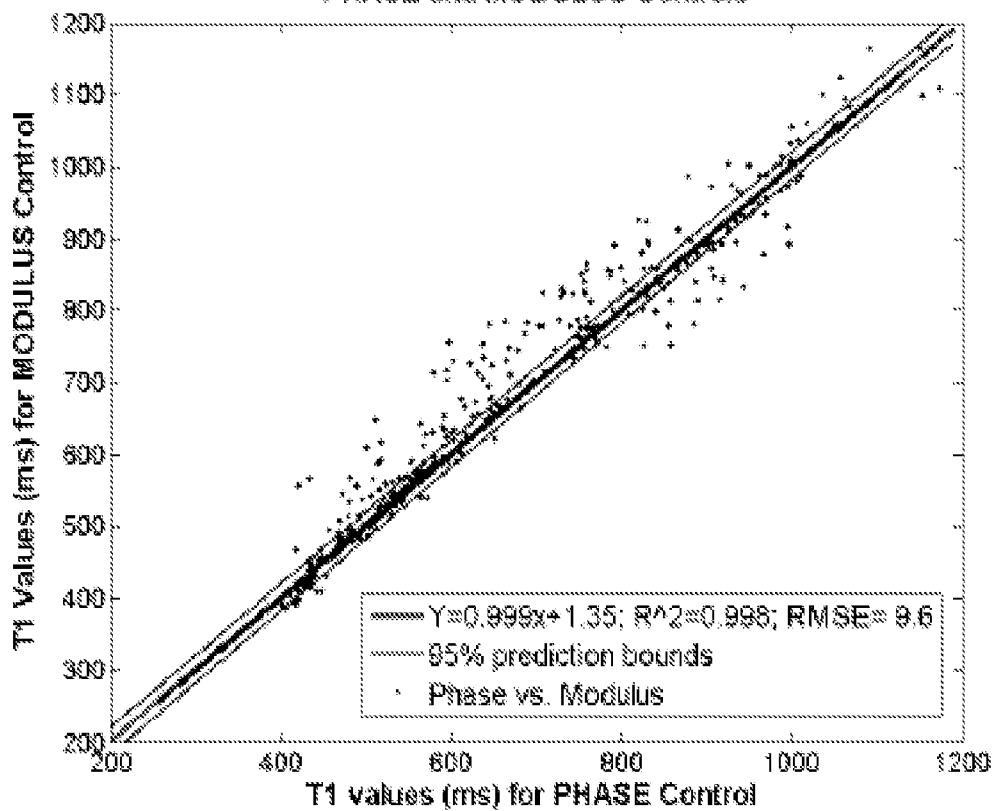


FIG. 2C

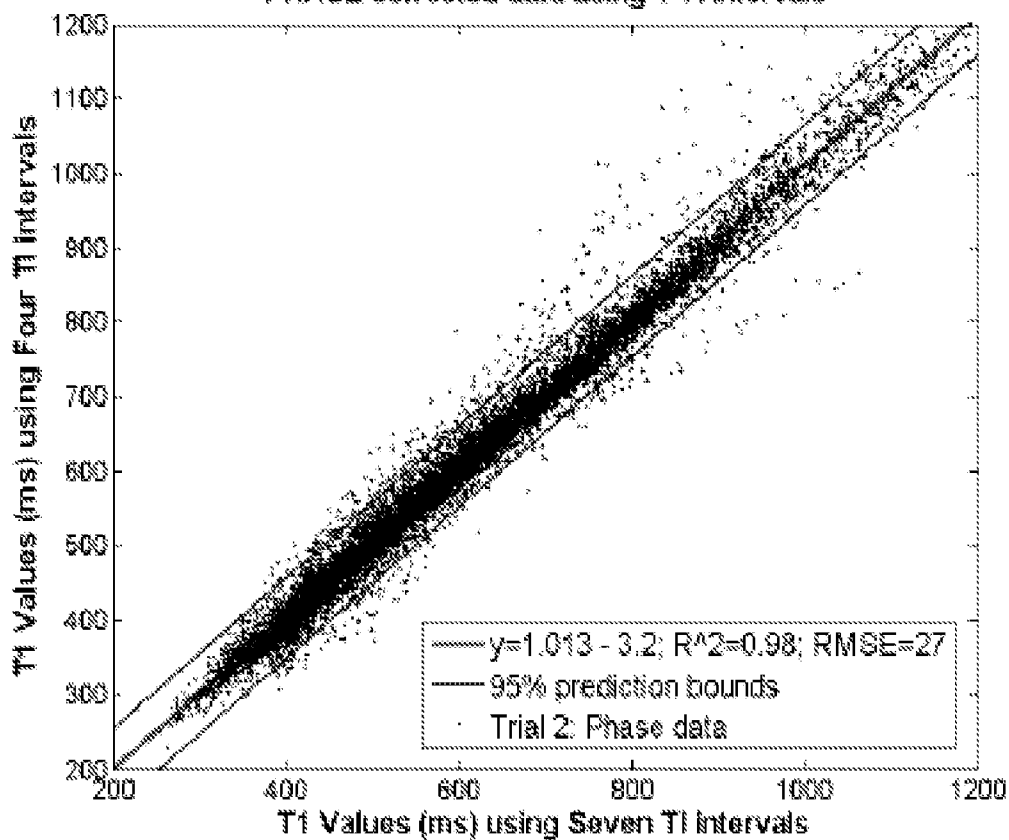


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PHASE and MODULUS Controls

**FIG. 3A**

PHASE corrected data using 4 TI intervals

**FIG. 3B**

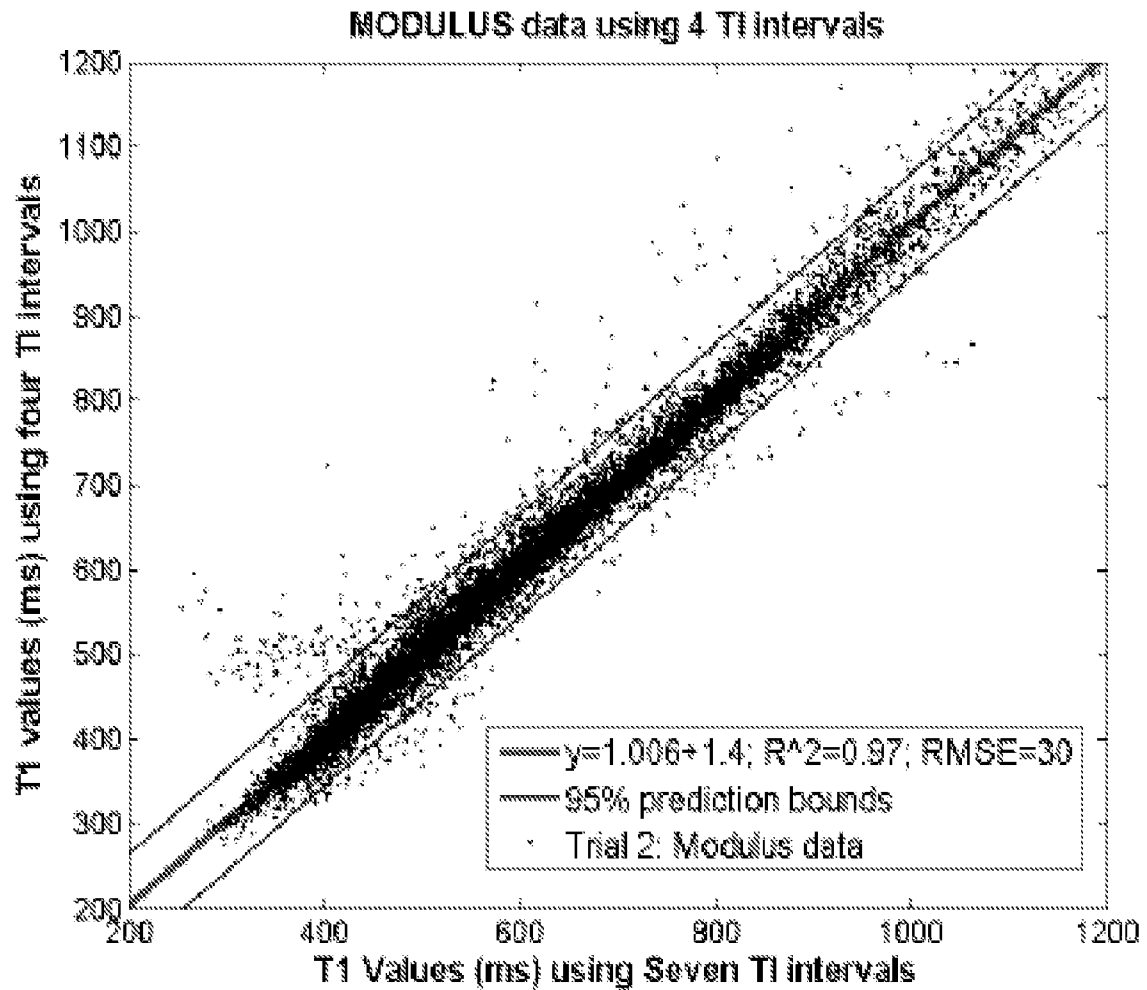
**FIG. 3C**

FIG. 4A**FIG. 4B**