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Magnetization transfer effect on T1 relaxometry on 1.5T vs. 3T

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BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

MAGNETIZATION TRANSFER EFFECT ON T1 RELAXOMETRY ON 1.5T VS. 3T

by

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B.S., Polytechnic Institute of Bucharest, 1985

Submitted in partial fulfillment of the

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DEDICATION

To my family.

ACKNOWLEDGMENTS

First, I am very grateful to be in this great country; offered me a great environment for raising a family and many professional opportunities any time when the wind of change was imperative. This program offered me the opportunity to improve the knowledge of this amazing field that is MRI and I am grateful for our professors who shared their knowledge and passion for MRI with us. I am very thankful to many people that encouraged and supported me during these three years of work, challenges and rewards. Many thanks to Dr. Ronald Killiany, Dr. Kevin Thomas and to my formerly supervisor, Kelly Bergeron for encouraging me to enter in Bioimaging program; also, a huge thank to my co-worker R. Hobbs who constantly changed his schedule to adapt mine to classes and to my supervisors Christine Seay and Mari Engelhardt for accepting these changes for so many years. I am very thankful to Dr. Kevin Thomas for taking the time to read my thesis. Thank you, Dr. Thomas for your support, encouragement and suggestions during all these years.

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MAGNETIZATION TRANSFER EFFECT

ON T1 RELAXOMETRY ON 1.5T VS. 3T

MIHAELA MAIER

ABSTRACT

Purpose: To assess the variability of incidental magnetization transfer effect (MT) by the number of slices and the magnetic field strength.

Methods: Various magnetic resonance images (MRI) were obtained with a phantom containing a series of solutions of gadolinium (Gd) and sucrose in distilled water, agarose gel and two vials with olive oil and distilled water. A diffusion weighted image (DWI) sequence was acquired to determine diffusion coefficient for each component of the phantom. Several inversion recovery (IR) sequences having different TI values were run for single-slice and used to calculate T1 relaxation time with maximum precision and minimizing magnetization transfer effect. The T1 relaxation value resulting from processing IR sequences was used as reference value. The mixed-TSE sequences were used to calculate T1, T2 and PD values and to assess MT effect for single-slice as for multi-slice acquisition. All the DICOM MR images were processed using various algorithms programmed in Mathcad (version 2001i, PTC Needham, MA) by Dr. Hernan Jara. According with the potential of each sequences the programs generated the qMRI maps and values of T1, T2, PD were obtained for all the components of the phantom. Values resulted from Mathcad calculation were used for analysis. All the acquisitions, calculations and measurements were performed for 1.5T and 3T field strength.

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LIST OF ABBREVIATIONS

D..... Diffusion coefficient

DICOM ..... Digital imaging and communications in medicine

DE-TSE..... Dual-echo turbo spin-echo

DF-FSE ..... Dual-echo fast spin echo

DWI..... Diffusion weighted imaging

DTI..... Diffusion tensor imaging

ES..... Echo space

ETL ..... Echo train length

FE..... Frequency encoding

FSE..... Fast spin echo

Gd..... Gadolinium

IR..... Inversion recovery

MRI..... Magnetic resonance imaging

MT..... Magnetization Transfer

MTC..... Magnetization Transfer Contrast

IR..... Inversion recovery

mL..... Milliliter

mm ..... Millimeter

ms..... Millisecond

NEX ..... Number of excitation

NIH ..... National institute of health

PE.....Phase encoding

QI.....Quantitative imaging

qMRI..... Quantitative MR imaging

ROI.....Region of interest

SE.....Spin echo

T.....Tesla

T1.....T1 relaxation time

T2.....T2 relaxation time

TE..... Echo time

TI..... Inversion time

TR.....Repetition time

INTRODUCTION

A Little Bit of History

Magnetization transfer was first described in 1963 by Forsén and Hoffman as a reversible transfer of nuclear spin of hydroxyl protons in a system containing salicylaldehyde and 2-hydroxyacetophenone (Forsén & Hoffman, 1963). Applying nuclear magnetic resonance technique to the abovementioned system the study demonstrated the correlation between T1 relaxation times of hydroxyl in one component and saturation of hydroxyl protons from the other component; the authors called this 'nuclear magnetic double resonance'.

In 1977 Edzes and Samulski showed that cross relaxation between free water and macromolecules is the dominant relaxation mechanism in hydrated collagen (Edzes & Samulski, 1977).

In 1989 Wolff and Balaban first used these principles to create magnetization transfer contrast and make measurements of magnetization exchange between 'free' and 'bounded' hydrogen protons for in vivo kidney and skeletal muscle tissues (Wolff & Balaban, 1989).

Magnetization Transfer

Due to its abundance in the body the hydrogen protons ^{1}H from water are used to generate the MR signal and images. In the biological tissues water can be unrestricted or contained in macromolecules and in the few layers of water surrounding the macromolecules resulting in restricted motion. In the unrestricted water also called 'free' or 'bulk' water molecules have high degree of freedom and rapid rotations; the magnetic

inhomogeneity is reduced and as a result T1 and T2 relaxation are long. As most of the protons in ‘bulk’ water resonate at Larmor frequency its spectral line is very narrow (1-100Hz).

The second pool is formed by water molecules close to macromolecules. The proteins or other large macromolecules interact mechanically and magnetically with water molecules close to them so their mobility is restricted and magnetic inhomogeneity is increased. This pool is called ‘bound’ water, has a faster dephasing rate so shorter T2 values. Water molecules from the ‘bound pool’ are influenced by the magnetic field of neighbor macromolecule differently and their resonant frequency is different resulting in a broad spectrum of resonant frequency. Both ‘free water’ and ‘bound water’ have the same central resonance frequency.

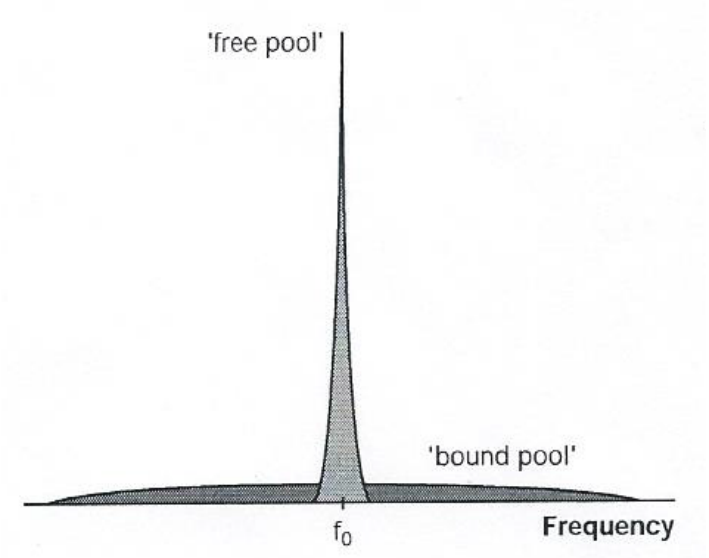


Figure 1: Resonance Frequency of ‘free pool’ and ‘bound pool’.

The two pools of water are in continuous interaction by diffusion so when the ‘bounded water’ is saturated some of its molecules transfer the energy by changing the

spins to some of the ‘free water’ protons (Boer, 1995). The transfer of energy also can be from ‘free water’ protons to ‘bounded’ ones if the RF is applied to the ‘free pool’. This mechanism is known as magnetization transfer and cross-relaxation is considered the most frequent relaxation in biological tissues (Wolff & Balaban, 1989). The direct result of transfer magnetization is a decrease of number of protons adding their spins to generate signal, decrease of signal and apparent reduction of T1 of tissue.

The effects of magnetization transfer can be intrinsic to any MR sequence. For some sequences is desirable to increase MT for better visualization of specific structures as cartilages or muscle using magnetization transfer contrast (MTC) techniques. Magnetization transfer is increased in sequences where off-resonance are reaching ‘untargeted’ protons. The most encountered reasons for MT effect are slice selection RF and refocusing pulses that become ‘off-resonance’ pulses for adjacent slices.

Purpose

Theory and experiments demonstrated that magnetization transfer reduces the effective T1 in tissues containing semisolid pools (Jara, 2013) (Stanisz, et al., 2005) (Henkelman, Stanisz, & Graham, 2014). The purpose of this thesis is to study the correlation between diffusion (quantified by diffusion coefficient) and T1 relaxation time the variability of T1 relative to chemical component and the variability of T1 due to magnetization transfer (MT) for one slice and multiple slices on a phantom composed on multiple types and concentrations of semisolid pools. All the measurements are done for 1.5T and 3T magnetic field strength.

BACKGROUND

Magnetic Resonance Imaging (MRI)

The beginning of NMR can be considered the year 1946 when Felix Bloch and Edward Purcell reported the magnetic resonance phenomenon in condensed matter, for which they received the Nobel Prize in 1952. The immediate application of this discovery was nuclear magnetic spectroscopy used for chemical analysis. In 1971 Raymond Damadian showed that relaxation times of tissues and tumors are different from healthy tissue and stated that MRI can be used to detect cancer ; however, his method was not very accurate and the scanning time was very long being based on 'point-by-point' scanning of the entire body (Damadian, 1971).

In 1973, Paul Lauterbur and Peter Mansfield developed the calculation method and produced the first NMR image using gradients for slice selection reducing drastically the scanning time (Lauterbur & Mansfield, 2008).The increase power of computers along with advent of superconductors transformed the MRI technology in the powerful tool that we know today for imaging in vivo. Clinical MRI scanners were introduced in the early 1980s.

How MRI Images are Generated

The human body is mostly composed of water. Water molecules are formed by oxygen and hydrogen nuclei, protons. Having positive charge and a spin ^{1}H protons act as little magnets and align with machine's magnetic field when the body is placed into the scanner. The MR scanner has three main components: a strong magnet which produces a homogeneous strong main magnetic field, three gradient coils that are electromagnets able

to produce a magnetic field which varies the field strength along a three-orthogonal direction (x, y, z) and radiofrequency (RF) coil which is able to produce and/or receive an electromagnetic wave.

When the body is placed into the scanner ^{1}H start aligning with the scanner's magnetic field, their magnetic fields add-up in z direction, this is $M_z(eq)$. Then an RF pulse with the resonance frequency is transmitted to the body. When the protons are exposed to this RF two phenomena happen: some protons are changing the direction of spin decreasing the magnetization along z-axis or longitudinal magnetization and second all the protons are precessing in phase creating a new magnetization in the x-y plane called transversal magnetization. Then the RF is stopped and the protons orientation. The time required for proton to return to original status is called relaxation time and varies for protons belonging to different tissues. Since there are two planes where the magnetization vector is varying its value there are also two relaxation time: longitudinal or T1 relaxation and transversal or T2 relaxation.

T1 or the longitudinal relaxation time is dictated by the energy exchange or loss to the neighboring tissue. T1 is also known as spin-lattice relaxation time. T1 describes the rate of return of $\mathbf{M_0}$ to its equilibrium value $\mathbf{M_z}(eq)$ after the RF pulse stopped. T1 is influenced by fluctuations of the magnetic fields in the direction of x and y axes ($\mathbf{B_x}$ and $\mathbf{B_y}$). These fluctuations are generated by interactions between spins and surrounding tissue (lipids, proteins, etc. referred as 'lattice') and between spin themselves (spin-spin interaction) due to the molecular motion (the random tumbling of water molecules and diffusion change the angle between $\mathbf{B_0}$ and the line between the spins and influence the

magnetic field in xy plane). The main mechanism of T1 is spin-lattice interaction. The equation describing T1 relaxation is: $Mz(t)= M_0(1-e^{-t/T1})$

T2 is the transverse relaxation time, is a time constant describing the decay of transverse magnetization and is associated with the loss of coherent spin motion (dephasing). When the exciting RF pulse tilts the net magnetization vector M_0 into the xy plane all the spins are rotating in phase at the Larmor frequency but when the RF stops the spins are precessing at different frequencies, the phase coherence is lost and the resulting vector (Mxy) is decaying toward zero value. T2 is the decay time when we use refocusing RF pulses to eliminate the influence of external magnetic inhomogeneities and is the result of interactions between spins. When two spins are adjacent the magnetic field of one proton affects the neighbor proton that will be exposed to a total magnetic field of B0 plus or minus the magnetic field of the first proton; as a result, their precessional frequency will differ accordingly with Larmor equation. This is the mechanism of spin-spin interaction that creates internal magnetic inhomogeneities and is intrinsic to the tissue.

In addition to spin-spin interaction the dephasing process can be induced by variations on external magnetic field. Its effect is called T2' and can be reduced by refocusing pulses.

The combined effect of T2 and T2' is called T2* with formula: 1/T2*=1/T2+1/T2'. The transmitted signal depends by T1 or T2 values and MR images constructed by the computer are the result of differences of T1 and T2 of adjacent tissues.

Signal's spatial localization is accomplished using the three gradients coils for slice selection, frequency encoding and phase encoding. The process composed of RF excitation,

gradient activation and signal reception is repeated by the number of phase and NEX and a whole spectrum of encoded signals is collected and transmitted to the computer. Using Fourier transformation and a complex mathematical algorithm the signal spectrum is translated into physical images of the body (Horowitz, 1995).

MR provides superior tissue contrast and reasonable resolution images for brain, spine, abdomen, and any other soft tissue body parts and is a powerful tool for pathology detection.

Quantitative MRI (qMRI) and T1 Quantification

MR images are a complex result of T1, T2, T2* weightings of the tissue and also depend on external factors as the software and the hardware used (Deoni, 2010). As a result of the mixed input the conventional MR images are qualitative and their interpretation is a subjective process. Subjective analyses of images have low sensitivity and accuracy; small changes in tissue cannot be seen, acquisition parameters influence the image quality. Is well established that the values of T1, T2, T2* are constant for a given tissue and a more accurate interpretation of images is based on measurements of these values, also known as quantitative relaxometry. In MR images pixel value is the signal value, in qMRI pixel value is the measurement value. Quantitative MRI can be used to generate maps for proton density (PD), T1, T1, diffusion and its tensors, spectroscopy and magnetization transfer ratio. The maps generated by quantitative relaxometry provide sensitivity and accuracy and are used for more complex analyses as segmentation, volumetry, structural analyses or even computer simulated MRI (Chang & Jara, 2005).

The standard for T1 mapping is inversion recovery sequence (IR); the sequence is repeated using various inversion times (TI) to produce many samples and T1 is calculated from the generated curve (Cheng, Stikov, Ghugre, & Wright, 2012).

How an IR sequence is produced: two RF pulses are applied at a certain time called inversion time TI; first pulse is an 180^0 and flips the longitudinal magnetization into -z direction; during the TI interval the magnetization is growing back due to T1 relaxation processes, the second pulse is an 90^0 and place the recovered magnetization on the xy (transverse) plane. The equation of T1 recovery is (Chang & Jara, 2005):

$$Mz(t) = \mathrm{M0}(1 - 2e^{t/T1})$$

Equation 1

Taking the logarithm on both sides of this equation results in:

$$\frac{t}{T1} = ln\frac{1}{2}\left(1 + \frac{Mz(t)}{M0}\right)$$

Equation2

The sequence is repeated N times for various TI values and the T1 is the inverse of the slope of equation 2.

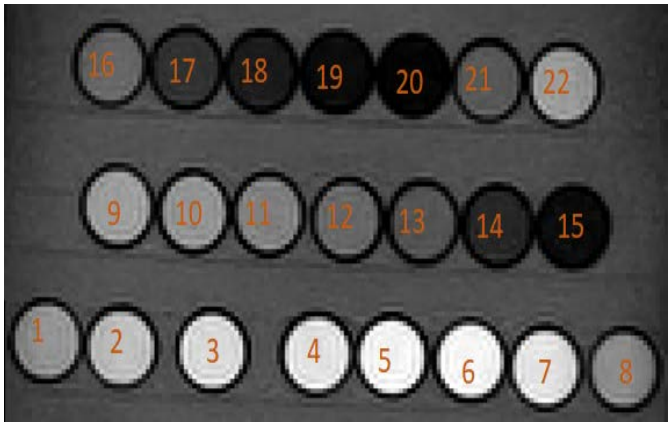
The IR sequences provides the most accurate T1 values and the generated maps were used as reference.

Mixed-TSE is a qMRI pulse sequence that generates T1 and T2 maps in the same acquisition by combining IR and multi echo sampling techniques. The first RF applied is an IR pulse having two inversion times (TI1, TI2) and two effective echo times values ($TE1_{eff}$, $TE2_{eff}$) generating four inversion recovery images for each slice. Due to the combinations of TI and TE_{eff} each image has a different percentage of T1 and T2 weighting

and they are used to calculate the T1 and T2 maps. The interslice cross talking is minimized by using interleaved packages interrogated sequentially.

METHODS AND MATERIALS

A phantom consisting of twenty-two vials containing 15ml of various solutions was used in this study (**Figure.2**)



Tube Number	15 mL Solution of:
1	0.075 microL Gd
2	0.05 microL Gd
3	1.25 microL Gd
4	1.95 microL Gd
5	3.27 microL Gd
6	5.7 microL Gd
7	10.7 microL Gd
8	35.7 microL Gd

Tube Number	15 mL Solution of:
9	3% Sucrose
10	5.9% Sucrose
11	11.3% Sucrose
12	20% Sucrose
13	33% Sucrose
14	50% Sucrose
15	67% Sucrose
16	1% Agarose
17	2% Agarose
18	3% Agarose
19	4% Agarose
20	5% Agarose
21	Olive Oil
22	Distilled Water

Figure 2: Phantom Structure

The first row contains eight vials with solutions of Gd-DTPA in distilled water; the amount of Gd being increased progressively as: 0.075, 0.05,1.25, 1.95, 3.27, 5.7, 10.7, 35.7 microL Gd per vial.

The second row contains seven vials having sucrose solutions; sucrose concentration was increased from vial to vial as: 3%, 5.9%, 11.3%, 20%, 50%, 67%.

The third row contains five vials with agarose gel prepared with distilled water at concentrations: 1%, 2%, 3%, 4%, 5% and two vials with olive oil and distilled water.

The scans were performed using 1.5T clinical scanner (ACHIEVA™, Philips Healthcare, Best, Netherlands) and 3T clinical scanner (INGENIA™, Philips Healthcare). On both scanners 1.5T and 3T the scans were performed using the body coil for RF transmission and a pair of surface coils (Flex-M) for reception. All the calculations were performed using inhouse Mathcad (version 2001i, PTC Needham, MA) programs written by Dr. Hernan Jara. Following sequences were performed in 3T and 1.5T:

1. single-slice DWI was acquired using parameters from **Table 1**.

Parameter	**1.5T**	**3T**
Matrix	224	256
Slice thickness (mm)	5	5
Space between slices (mm)	0.5	0.5
Pixel spacing	0.9765625	0.9765625
Scan percentage	0.8	0.8
'b' values	b1=0; b2=1000	b1=0; b2=1000
SE Repetition time (TR_{SE}) (ms)	6741.0878	6741.0878
IR Repetition time (TR_{IR}) (ms)	7441.0878	7441.0878
Inversion time (TI)(ms)	TI1=700	TI1=700
Effective echo time (TE_{eff}) (ms)	TE1=74; TE2 = 100	TE1=74; TE2 = 100
Echo train length (ETL)	18	18

Table 1. DWI pulse sequence parameters

Diffusion images were loaded into Mathcad and diffusion coefficient was calculated for each component of the phantom (see **Appendix 1**).

2. Single-slice IR-TSE sequence run for various values of TI:
    - for 3T were used 10 values: 50, 75, 100, 200, 300, 600, 1000, 1500, 2000, 3000ms.
    - for 1.5T were used 18 values: 25, 50, 75, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000, 1250, 1500, 1750, 2000, 3000ms.

All the IR sequences were acquired with the same parameters but inversion time (IR).

Parameter	**1.5T**	**3T**
Matrix	288	512
Slice thickness (mm)	5	5
Space between slices (mm)	0.5	0.5
Repetition time (TR) (ms)	8000	8000
Echo space (ES)(ms)	27.88	27.88
Echo time (TE) (ms)	4	4
Echo train length (ETL)	18	18

Table 2. Inversion recovery pulse sequence parameters

The T1 values and qT1 maps were generated using a Mathcad program; measurements were done using ROIs placed in each component of the phantom (see **Appendix 1**).

3. Single slice mixed-TSE was acquired using parameters from **Table 3**.

Parameter	**1.5T**	**3T**
Matrix	192	512
Slice thickness (mm)	5	5
Space between slices (mm)	0.5	0.5
FOV^{FE} x FOV^{PE} x mm^3	180 x 143.438	480 x 382.5
Pixel spacing	0.9375	0. 9375
Scan percentage	0.9	0.9
SE Repetition time (TR_{SE}) (ms)	2556	5789.29
IR Repetition time (TR_{IR}) (ms)	3256	6689.29
Repetition time (TR) (ms)	6512	13378.58
Inversion time (TI)(ms)	TI1=700; TI2=3256	TI1=900; TI2=6689.29
Effective echo time (TE_{eff}) (ms)	TE1=8; TE2 = 100	TE1=7.2; TE2 = 90
Echo train length (ETL)	16	16

Table 3. Mixed-TSE pulse sequence parameters

The T1, T2, PD and corresponding qMRI maps were calculated using an inhouse Mathcad program; measurements were done using ROIs placed in each component of the phantom (see **Appendix 2**).

4. Multi-slice mixed-TSE for 28 slices

This sequence was acquired using the same parameters as single slice mixed-TSE but 28 slices were scanned. The same steps used for single slice mixed-TSE to generate

qMRI maps were applied to determine T1, T2, PD values for middle slice (slice number 14); measurements were done using ROIs placed in each component of the phantom (see **Appendix 3**).

All the calculations and measurements were done for sequences performed in 1.5T and 3T.

According with the two-pool model of transfer magnetization the variation of T1 is correlated with the amount of the magnetization transfer (Boer, 1995) (Henkelman, Stanisz, & Graham, 2014).

We considered T1 values calculated from IR sequences as reference value for T1 and de the differences from single slice mixed-TSE and middle slice of multi slice mixed-TSE an indication of the amount of magnetization transfer.

RESULTS

Correlation Between Diffusion Coefficient and T1

Considering the magnetization transfer is a dynamic process mediated by diffusion we first plotted the variation of T1 reference value by diffusion coefficient. T1 reference is the value calculated from IR sequences.

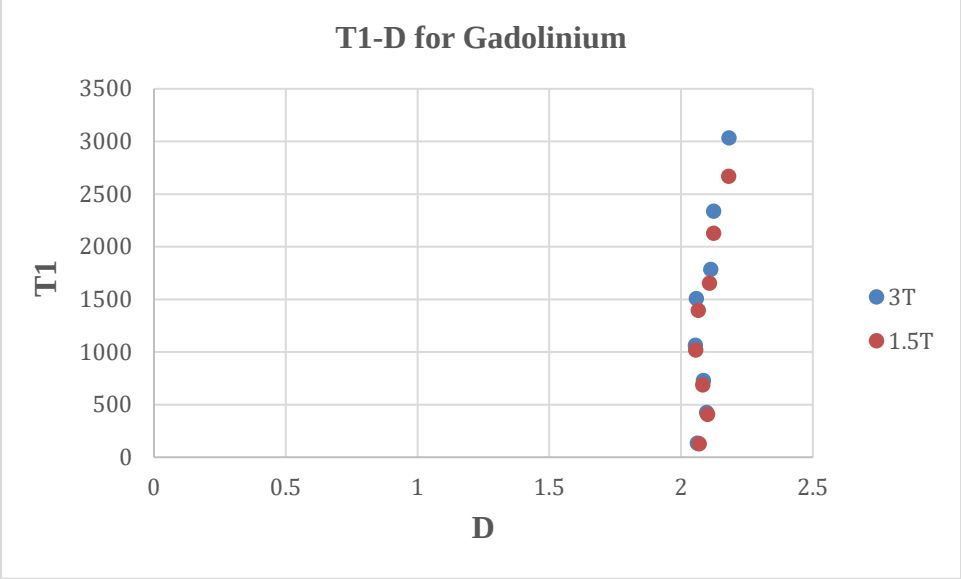


Figure 3. Correlation D-T1 for gadolinium solutions.

Note the very narrow range of D values for various solutions of Gd. For shorter diffusion coefficient T1 values are almost the same for both field strength. Progressively increase of difference of T1 for 3T relatively to 1.5T appears with the increase of diffusion coefficient. Also note that the diffusion coefficient increases when the amount of gadolinium in the solution decreases, the highest diffusion coefficient belongs to the most diluted solution. As expected T1 relaxation is longer in 3T than in 1.5T for the same diffusion coefficient.

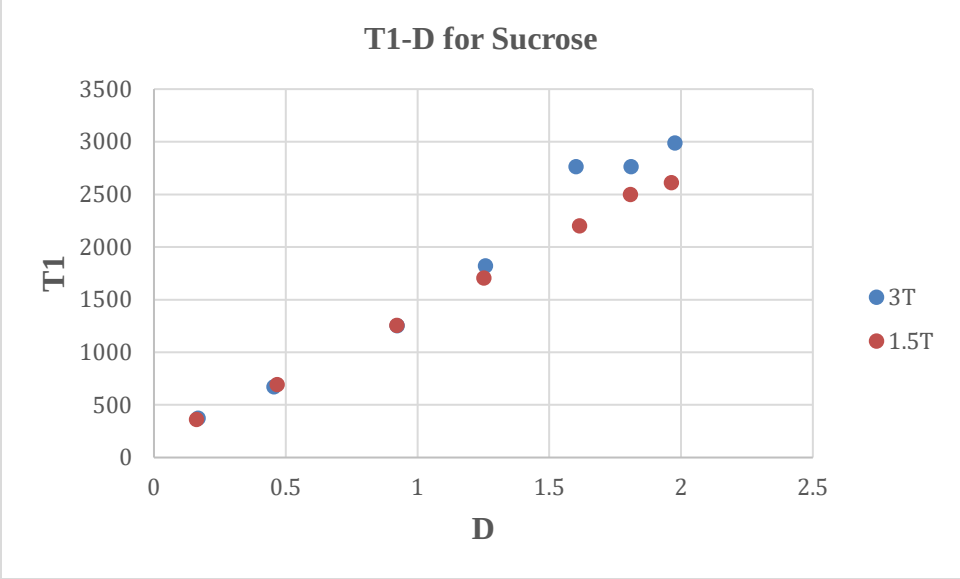


Figure 4. Correlation T1-D for sucrose solutions.

Note the linear correlation D-T1 for 1.5T. Sucrose solutions have a broader range of concentrations (3%-67%) and as a result the diffusion coefficient variation is broader than for gadolinium. Also note that the diffusion coefficient increases when percentage of sucrose decreases, the highest diffusion coefficient belongs to the most diluted solution. For shorter diffusion coefficient T1 values are very close for the two values of the field strength. For lower values of diffusion coefficient so higher concentration solutions, the value of T1 is slightly bigger for 3T than for 1.5T; for higher values of diffusion coefficient the difference between T1 values are notable (between 10.4% and 25.5%) Similarly, with gadolinium solutions T1 relaxation is longer in 3T than in 1.5T for the same diffusion coefficient.

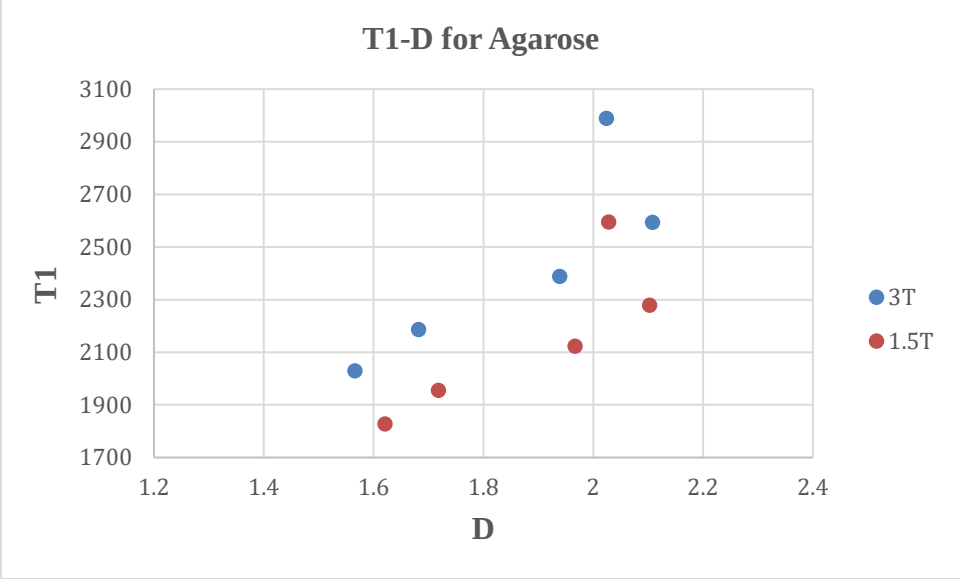


Figure 5. Correlation DCo-T1 for Agarose solutions.

Note that even the small differences in agarose concentration --1% from vial to vial-- produce notable variation of the diffusion coefficient. Similarly, with gadolinium and sucrose solutions the diffusion coefficient increases when percentage of agarose decreases, the highest diffusion coefficient belonging to the most diluted solution. There is an almost linear correlation D-T1 for both field strength, except the most diluted solution. There is a notable difference of T1 for the two field strength relative to diffusion coefficient, always the T1 being significant higher for 3T than for 1.5T (between 10.9% and 15.2%).

T1 Variation for Different Components of the Phantom

Calculating T1 from IR sequences is the gold standard for T1 mapping. We plotted the variation of T1 from IR and mixed-TSE to assess the deviation from reference value for each component of the phantom.

1.5T

3T

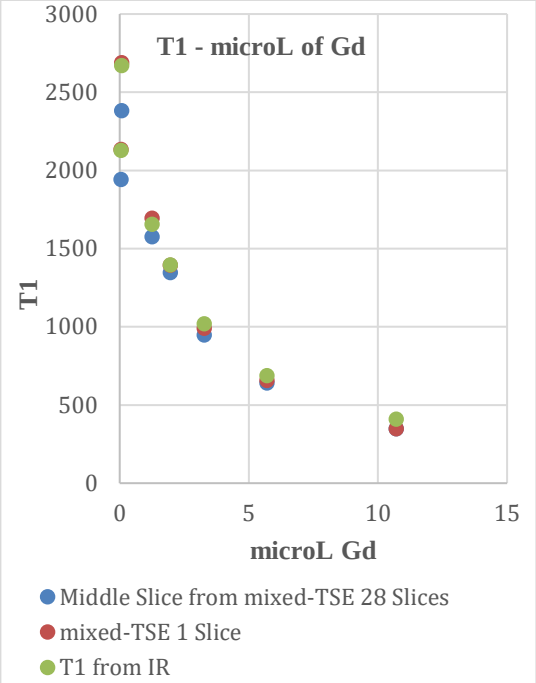
Figure 6. T1 values for different solutions of gadolinium.

All the measured T1 values from IR, single slice and mixed-TSE multi slices decrease with the increase of amount of gadolinium in solution. For lower concentration solutions, there are bigger differences between T1 calculated from the three types of acquisitions: T1 for single slice is longer than T1 reference suggesting an overvaluation of T1 by this sequence; T1 value for multi slice is shorter than T1 reference. For higher concentration solutions T1 for single and multiple slice are almost identical (see

Appendices 2 and **3**) and both are shorter than T1 reference. Note than T1 values are bigger for 3T than for 1.5T for all the measurements.

For a better visualization of T1 variability we removed the highest amount of gadolinium solution from plotted data:

1.5T



3T

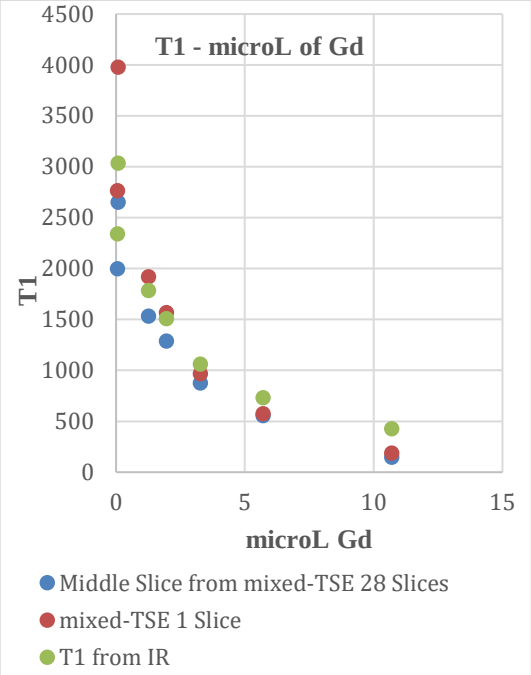


Figure 6b. T1 values for different solutions of gadolinium but the highest concentration. Note that the differences of T1 values are bigger at 3T than at 1.5T.

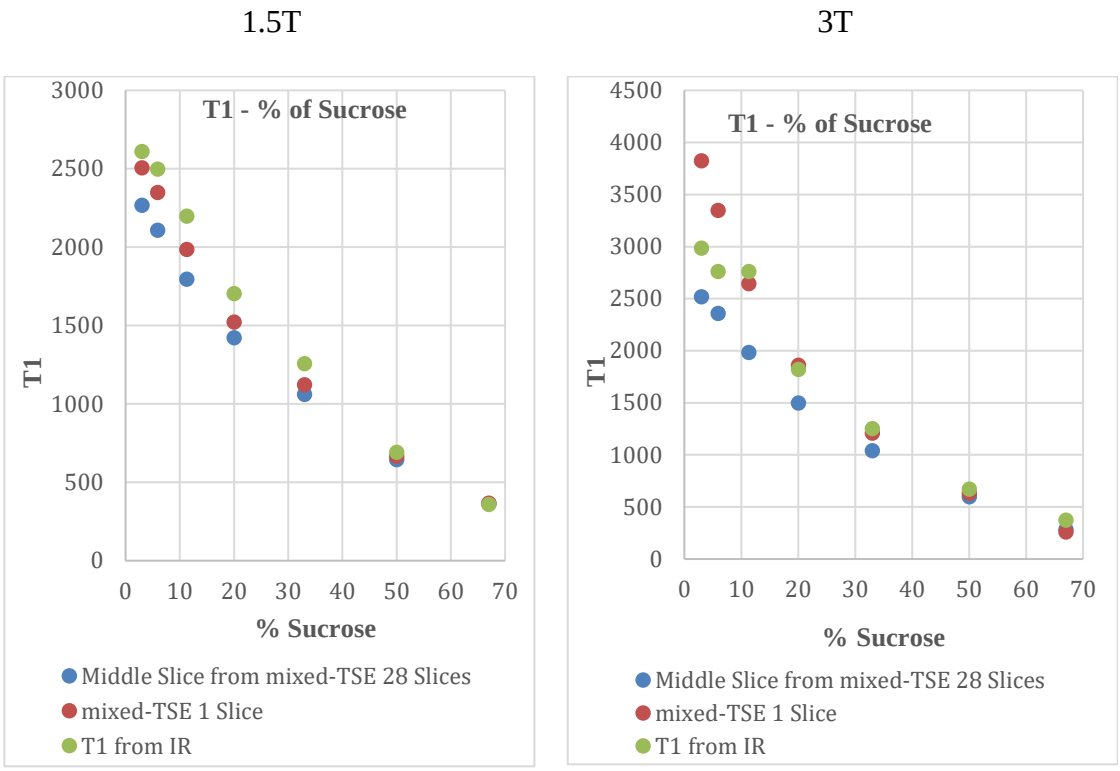


Figure 7. T1 values for different % of sucrose.

All the measured T1 values from IR, mixed-TSE single slice and mixed-TSE multi slices are decreasing with the increase of sucrose concentration in solution. For lower concentration solutions, there are notable differences between T1 calculated from the three types of acquisitions: at 3T the value of T1 for single slice is longer than T1 reference suggesting an overvaluation of T1 by this sequence; at both fields strength T1 value for multi slice is shorter than T1 reference. For higher concentration solutions T1 for single and multiple slice are almost identical (see **Appendices 2** and **3**) and both are shorter than T1 reference. Note than T1 values are bigger for 3T than for 1.5T for all the measurements.

1.5T 3T

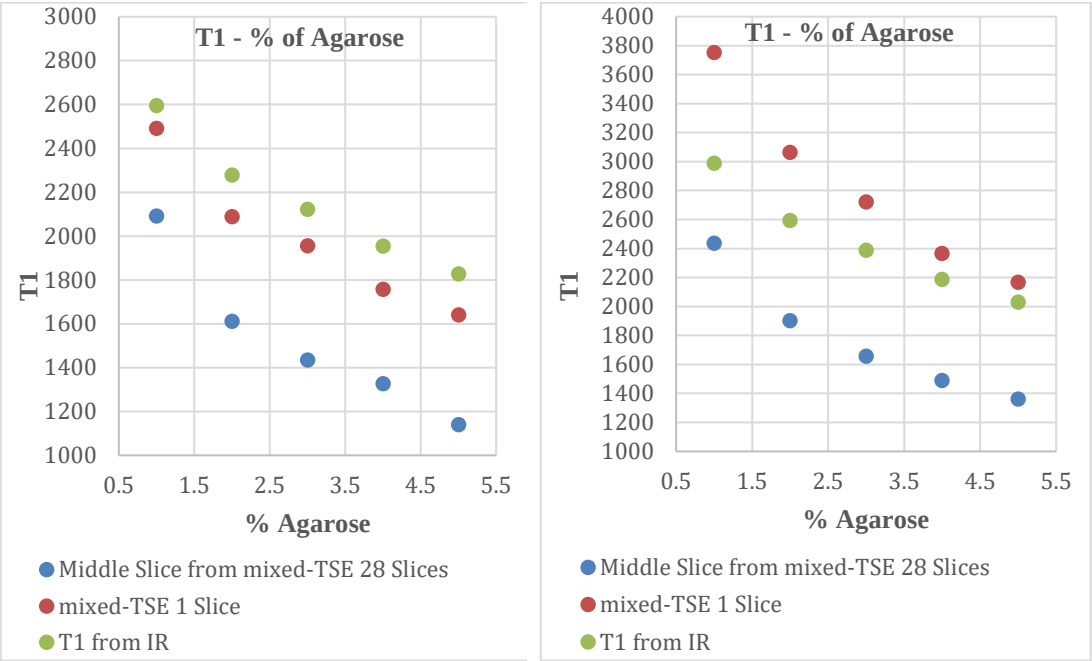


Figure 8. T1 values for different % of agarose.

All the measured T1 values from IR, mixed-TSE single slice and mixed-TSE multi slices are decreasing with the increase of agarose concentration in solution and the correlation is almost linear. At both field strength, there are notable differences between T1 calculated from the three types of acquisitions: at 3T the value of T1 for single slice is longer than T1 reference suggesting an overvaluation of T1 by this sequence; at both fields strength T1 value for multi slice is shorter than T1 reference. Note than T1 values are bigger for 3T than for 1.5T for all the measurements.

T1 Deviation from Reference Value

Plotting the T1 relative to its reference value for each component of the phantom helps to visualize the T1 variability and asses the magnetization transfer effect. We plotted mixed-TSE T1 for single slice and multi slice values relative to T1 calculated from IR sequences considered T1 reference. For a better visualization of T1 deviation from reference value we plotted T1 reference relative to itself and labelled this as 'Identity'.

1.5T 3T

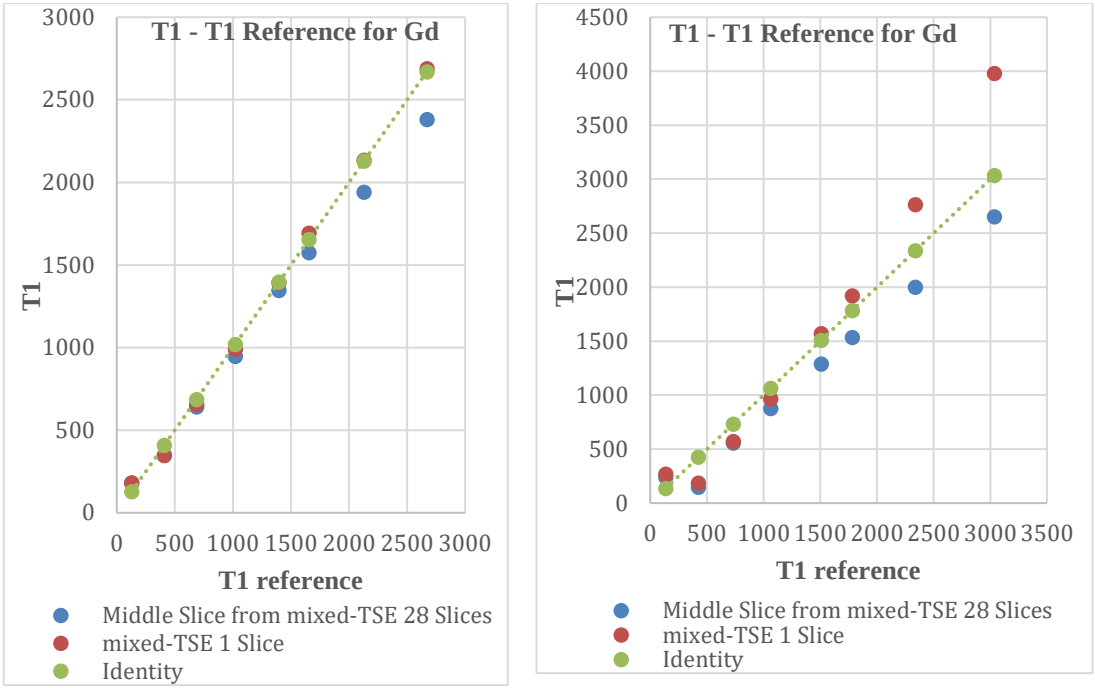


Figure 9. T1 values versus T1 reference for gadolinium.

The measurements of T1 from mixed-TSE single slice and multi slices done at 1.5 T are very close to the T1 reference value suggesting a decreased effect of magnetization transfer; the only notable differences are for the two highest values of T1 multi slices.

Measurements obtained at 3T display a progressive decreasing value for T1 calculated from mixed-TSE multi slices and an inconsistent variability of T1 calculated from mixed-TSE single slice. These results are suggesting an increased MT effect with the increase of number of slices.

1.5T 3T

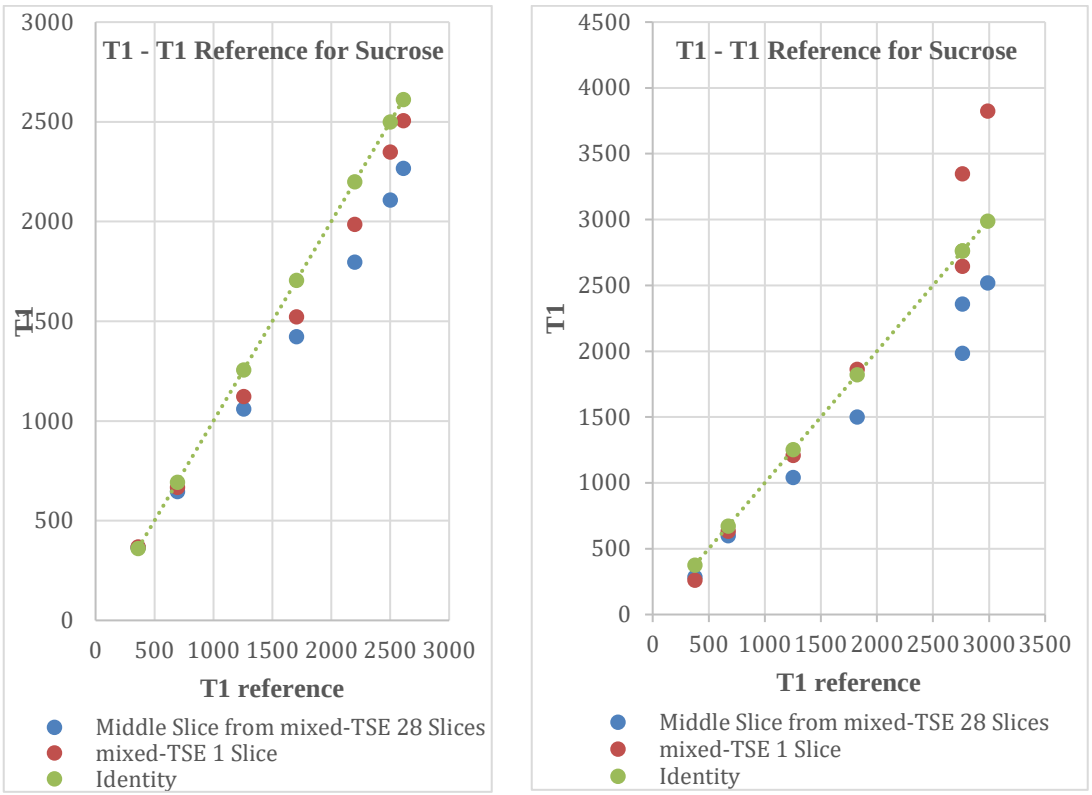


Figure 10. T1 values versus T1 reference for sucrose.

The measurements of T1 from mixed-TSE single slice and multi slices done at 1.5 T show that the T1 are shorter than T1 reference value suggesting a progressive increase effect of magnetization transfer with the increase of T1 value; single slice T1 value are

consistently higher than multi slice T1 value suggesting an increased MT effect with increasing the number of slices.

Measurements done at 3T display a more complex variability of data: for single slice at lower T1 the values are very close to the reference suggesting decreased MT effect but the higher values of T1 are bigger than the reference values suggesting a overvaluation of T1 by mixed-TSE single slice sequence. There is a progressive decreasing value for T1 calculated from mixed-TSE multi slices suggesting an increased MT effect with the increase of number of slices.

1.5T 3T

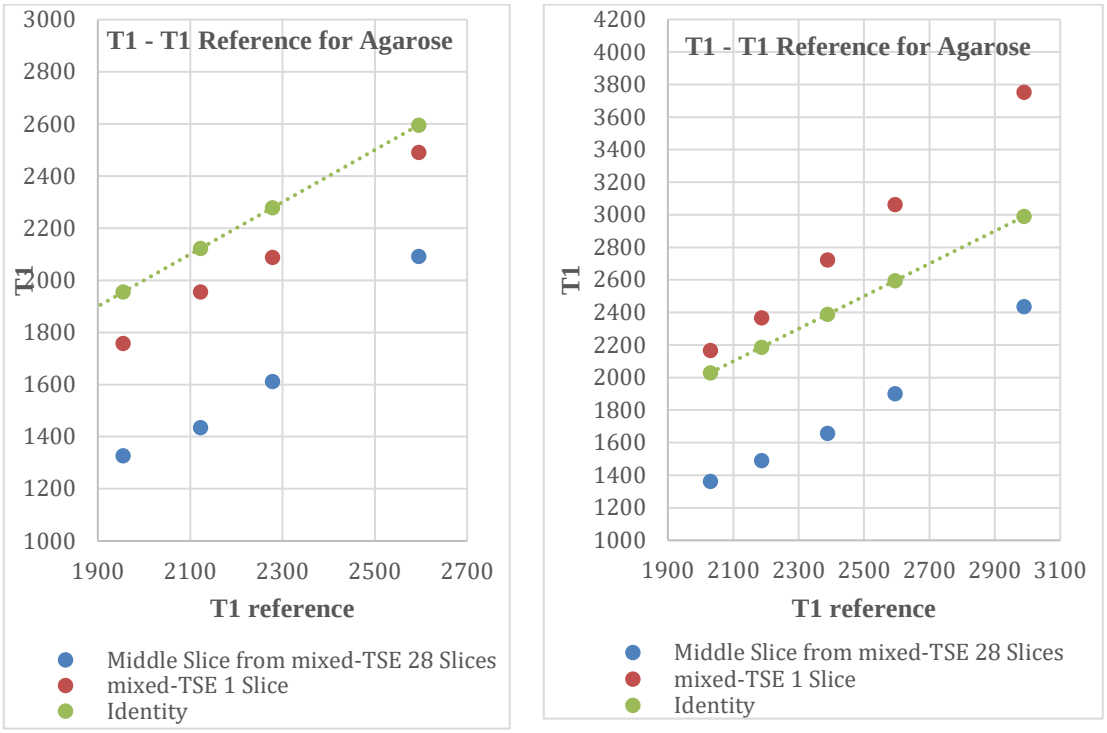


Figure 11. T1 values versus T1 reference for agarose.

The measurements in 1.5T show decreased values of T1 relative to reference from both mixed-TSE single slice and multi slices and always shorter T1 for multi slices than

for single slice. This data suggests a consistent MT effect for both mixed-TSE single slice and multiple slices sequences and also the increasing of MT effect with increasing the number of slices.

Measurements done at 3T show an overvaluation of T1 from mixed-TSE single slice and a progressive decreasing value for T1 calculated from mixed-TSE multi slices suggesting an increased MT effect with the increase of number of slices.

DISCUSSION

All the major components of the phantom display a consistent correlation between T1 and diffusion coefficient: T1 value increases with the increase of diffusion coefficient. T1 reference value was considered for this analysis. For Sucrose and agarose solutions the variation of T1 relative to D is almost linear for both field strength 1.5T and 3T with bigger values of T1 at 3T. Agarose solutions shows the biggest differences of T1 for the two field strength in the range of 10.9% to 15.2%.

The variability of T1 relative to chemical components of the phantom was realized by comparing the values of T1 calculated from three types of acquisition: IR, mixed-TSE single slice and mixed-TSE multi slices (28 slices).

All the measured T1 values from IR, mixed-TSE single slice and mixed-TSE multi slices are decreasing with the increase of amount of gadolinium or concentration of sucrose or agarose in solution.

The agarose solutions present the biggest variation of T1 values relative to concentration and magnetic field strength.

Magnetization transfer effect was evaluated by the reduction of T1 for all the components of the phantom at 1.5T and 3T. The analysis considered the variation of T1 from T1 calculated from IR sequences, considered reference value and values calculated from mixed-TSE for single slice and multiple slices (28 slices) acquisitions.

All the phantom's components presented magnetization transfer effect for mixed-TSE multi slice sequence. The best subject for MT analysis is agarose due to its

consistent and increased variation of T1 values for both single and multiple slices mixed-TSE sequences.

APPENDIX 1 - Diffusion Coefficient, T1 Calculated from IR, T2 Values

Tube Number	15 mL Solution of:	1.5T			3T		
		D	T1	T2	D	T1	T2
1	0.075 microL Gd	2.18	2670	1898	2.182	3034	2713
2	0.05 microL Gd	2.123	2128	1893	2.123	2339	2116
3	1.25 microL Gd	2.108	1655	1444	2.112	1783	1588
4	1.95 microL Gd	2.065	1396	1212	2.058	1508	1313
5	3.27 microL Gd	2.055	1019	866	2.054	1063	916
6	5.7 microL Gd	2.082	686	593	2.085	731	622
7	10.7 microL Gd	2.101	408	346	2.097	425	359
8	35.7 microL Gd	2.069	129	113	2.062	135	118
9	3% Sucrose	1.963	2611	1318	1.977	2987	678
10	5.9% Sucrose	1.808	2499	876	1.81	2762	392
11	11.3% Sucrose	1.615	2199	535	1.601	2762	224
12	20% Sucrose	1.252	1705	317	1.258	1822	143
13	33% Sucrose	0.921	1257	200	0.923	1253	122
14	50% Sucrose	0.468	693	117	0.455	671	111
15	67% Sucrose	0.161	360	72	0.168	374	100
16	1% Agarose	2.028	2595	138	2.024	2989	159
17	2% Agarose	2.103	2278	56	2.108	2594	68
18	3% Agarose	1.967	2123	41	1.939	2388	56
19	4% Agarose	1.718	1955	30	1.682	2186	39
20	5% Agarose	1.621	1828	26	1.566	2030	31
21	Olive Oil	0.021	179	121	0.022	269	140
22	Distilled Water	2.076	2798	2234	2.075	3222	2770

APPENDIX 2 - Mixed-TSE Single Slice Values

Tube Number	15 mL Solution of:	1.5T			3T		
		PD	T1	T2	PD	T1	T2
1	0.075 microL Gd	0.999	2690	2847	0.906	3979	3495
2	0.05 microL Gd	1.054	2134	2840	0.976	2764	3582
3	1.25 microL Gd	1.089	1694	3415	1.013	1921	3438
4	1.95 microL Gd	1.139	1393	2878	1.025	1569	3255
5	3.27 microL Gd	1.132	989	2362	1.033	966	2781
6	5.7 microL Gd	1.107	656	1587	0.989	572	1588
7	10.7 microL Gd	1.084	347	612	0.93	186	620
8	35.7 microL Gd	1.055	181	135	0.802	268	153
9	3% Sucrose	0.902	2506	2462	1.119	3825	2564
10	5.9% Sucrose	0.927	2349	2336	1.103	3349	1046
11	11.3% Sucrose	0.898	1986	1500	1.05	2644	349
12	20% Sucrose	0.896	1522	643	0.991	1862	162
13	33% Sucrose	0.918	1123	300	0.973	1210	102
14	50% Sucrose	0.933	667	150	0.942	633	59
15	67% Sucrose	0.91	368	85	0.838	261	46
16	1% Agarose	0.827	2491	197	0.981	3753	223
17	2% Agarose	0.829	2088	70	0.999	3063	70
18	3% Agarose	0.83	1955	52	0.988	2722	51
19	4% Agarose	0.812	1758	39	0.943	2367	40
20	5% Agarose	0.803	1641	34	0.896	2166	35
21	Olive Oil	0.887	142	113	0.884	251	143
22	Distilled Water	0.851	2884	2813	1.064	4360	3313

APPENDIX 3 - Mixed-TSE 28 Slices Values

Tube Number	15 mL Solution of:	1.5T			3T		
		PD	T1	T2	PD	T1	T2
1	0.075 microL Gd	1.044	2381	2851	0.815	2653	2842
2	0.05 microL Gd	1.142	1941	2777	1.008	1999	2414
3	1.25 microL Gd	1.205	1575	3266	1.048	1533	2668
4	1.95 microL Gd	1.282	1345	3031	1.07	1287	2720
5	3.27 microL Gd	1.295	947	2263	1.106	875	2560
6	5.7 microL Gd	1.29	641	1563	1.085	555	2294
7	10.7 microL Gd	1.291	348	609	1.003	148	1163
8	35.7 microL Gd	1.234	178	135	0.861	240	163
9	3% Sucrose	0.964	2267	2394	0.973	2520	1812
10	5.9% Sucrose	0.993	2108	2056	1.009	2358	1286
11	11.3% Sucrose	0.983	1797	1371	0.995	1985	448
12	20% Sucrose	1.005	1423	614	0.992	1500	197
13	33% Sucrose	1.034	1061	293	1.007	1042	125
14	50% Sucrose	1.074	646	148	0.997	600	72
15	67% Sucrose	1.064	365	84	0.887	285	57
16	1% Agarose	0.82	2091	193	0.82	2436	215
17	2% Agarose	0.753	1611	70	0.811	1901	86
18	3% Agarose	0.717	1435	51	0.784	1658	61
19	4% Agarose	0.688	1327	40	0.751	1490	44
20	5% Agarose	0.655	1140	33	0.725	1362	36
21	Olive Oil	1.053	132	112	0.969	219	147
22	Distilled Water	0.898	2539	2810	0.902	2852	3076

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