



ORIGINAL PAPER

Zuzanna Bober ^{1(ABG)}, David Aebisher ^{2(ABDGF)}, Adrian Truskiewicz ^{1(ABG)},
Łukasz Ożóg ^{3(ABG)}, Dorota Bartusik-Aebisher ^{4(ABDGF)}

The usefulness of relaxation time using MRI measurements

¹ Department of Electroradiology, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland

² Department of Human Immunology, Faculty of Medicine, University of Rzeszów, Rzeszów, Poland

³ Center for Innovative Research in Medical and Natural Sciences, Faculty of Medicine,
University of Rzeszów, Rzeszów, Poland

⁴ Department of Experimental and Clinical Pharmacology, Faculty of Medicine,
University of Rzeszów, Rzeszów, Poland

ABSTRACT

Introduction. Magnetic Resonance Imaging methods are now frequently used for the analysis of the diseased tissue. These methods are based on the fact that the spin-lattice, T_1 , and the spin-spin, T_2 , relaxation times are different in diseased tissue as compared to that of normal tissue.

Aim. Here we present measurements of spin-lattice relaxation time T_1 on a Magnetic Resonance Imaging scanner with field strength 1.5 Tesla.

Material and methods. Measurements of T_1 relaxation time and analysis of literature.

Results. We provide procedure for measurements of T_1 relaxation time with field strength 1.5 Tesla and present a discussion of current applications.

Keywords. Magnetic Resonance Imaging; T_1 relaxation; field strength 1.5 Tesla

Introduction

Magnetic Resonance Imaging (MRI) has been shown to be very useful tool for imaging of anatomy and morphology as well as the chemical composition of tissue. MRI is based on hydrogen nuclei, and does not involve emission of weak ionizing radiation as in Computed Tomography (CT) techniques. MRI is most commonly used for samples containing ^1H nuclei in high concentration in magnetic fields that range between 0.05 – 14 Tesla. Brief-

ly, MRI evaluates the physical properties of the sample area relative to neighboring areas. MRI *in vivo* is mainly used to image anatomical and morphological changes in the human body. The main applications of MRI *in vitro* are monitoring of water and other solvents, controlled release of dosage forms, hydration and diffusion. Currently, MRI is used as a standard test in central nervous system, heart, muscle, or soft tissue imaging. MRI is one of the most popular diagnostic methods available

Corresponding author: Dorota Bartusik-Aebisher, E-mail: dbartusik-aebisher@ur.edu.pl

Participation of co-authors: A – Author of the concept and objectives of paper; B – collection of data; C – implementation of research; D – elaborate, analysis and interpretation of data; E – statistical analysis; F – preparation of a manuscript; G – working out the literature; H – obtaining funds

Received: 10.07.2018 | Accepted: 23.08.2018

Publication date: September 2018

to modern medicine and, in addition, with high sensitivity and specificity, it is considered to be the most accurate method of medical imaging. In the opinion of clinicians and researchers, MRI is one of the most accurate noninvasive imaging methods available.¹ This method allows one to make sections in any plane of both living organisms and non-anatomical structures. The signal that we receive in MRI is dependent on the object being tested and its properties, but also on the individual protocol created.² In MRI, we have the ability to obtain data with morphological, functional and metabolic information. This allows one to see changes in the chemical composition of tumor tissue and then make a diagnosis of whether a drug works properly. For a sample placed in a strong magnetic field, you can operate with radio frequencies of a specific frequency. The nucleus absorbs the energy of the transmitted waves, rendering it to emit waves of the same frequency.³ In MRI there are two relaxation times which strongly depend upon the local molecular environment: the first is T_1 (the spin lattice relaxation time) and the second T_2 (the spin-spin relaxation time). T_1 describes the exponential recovery of the equilibrium longitudinal magnetization that is aligned with the applied magnetic field. T_2 describes the exponential decay of the precessing component of the magnetization, and hence also the decay of the MR signal.⁴ In our work presented here we optimized sequence and measured T_1 and T_2 relaxation times on a 1.5 Tesla General Electric Healthcare MRI scanner. For the phantoms we used a solution of CuSO_4 and sugar.

Material and Method

Measurements of T_1 relaxation time were made using a 1.5 Tesla Magnetic Resonance Imager (Optima MR360 Advance, General Electric Healthcare). Three prepared containers with a solution of CuSO_4 and water at a concentration of 0.1 %, 0.2 %, 0.4 % and a mixture of sugar and water at a concentration of 2.5%, 5% and 10% were placed in the magnet. The samples were then scanned using Fast Spin Echo sequences with a coronal projection using a 4 channel small flex coil with a matrix size of 320×224 , a field of view of $10 \text{ cm} \times 10 \text{ cm}$, and a slice thickness of 2 mm. The T_1 relaxation time was measured using the saturation recovery method with a TE of 3 ms and TR values of 30 ms to 15000 ms. Based on the generated image sequence, the MR signal was read from the region of interest that covered the same area in each sample.

In the next step, sparkling Vitamin C tablets from Efferta Sp. z o.o. with a weight of 4g containing 80 mg of vitamin C was used. A minimum amount of water was given to the container in which the tablet was placed, then measurements were made using magnetic resonance field with a 1.5 Tesla Optima MR360 model from General Electric Healthcare. In addition, the composi-

tion of the tablets were acidity regulators: citric acid and sodium carbonates, glucose, flavors, sweeteners: aspartame, saccharine and riboflavin. The relaxation time T_1 was then measured. A sample was prepared with a dissolved vitamin C tablet in 5 ml of water, then placed in a magnet and the sample was scanned using the FSE sequence in a coronal projection using a 4-channel small flex coil with a 320×224 size matrix, a $10 \text{ cm} \times 10 \text{ cm}$ field of view and a distance between layers of 1 mm. The relaxation time T_1 was determined at a constant echo time $\text{TE} = 3 \text{ ms}$ and TR values from 50 ms to 15000 ms. Measurements were made for three successive layers.

Results

The relaxation times of all the mixtures of CuSO_4 and water are plotted in Figure 1 and mixtures of sugar and water are presented in Figure 2. Figures show the effect of the CuSO_4 and sugar concentrations on the T_1 relaxation time. The T_1 relaxation time decreased as the CuSO_4 and sugar concentration increases.

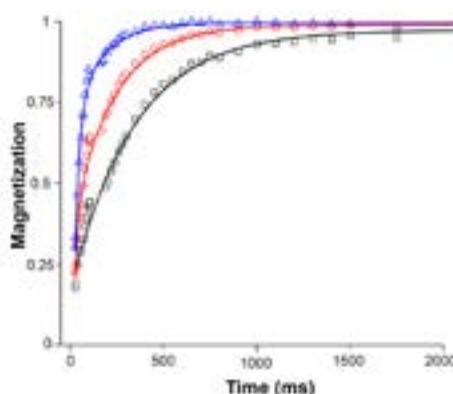


Fig. 1. T_1 relaxation curves for water solution with CuSO_4 concentration of 0.1% (black square), 0.2% (red circle) and 0.4% (blue triangle)

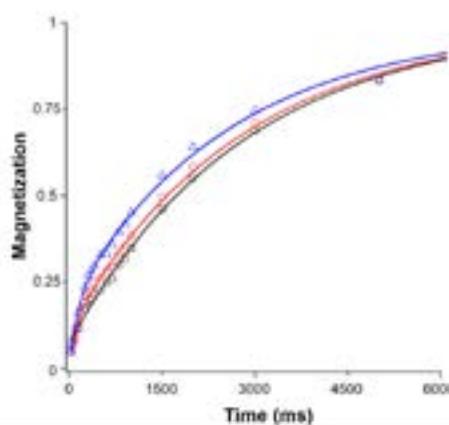


Fig. 2. T_1 relaxation curves for water solution with sugar concentration of 2.5% (black square), 5% (red circle) and 10% (blue triangle)

In Table 1 are listed results of T_1 time measurement for CuSO_4 at concentrations of 0.1%; 0.2%; 0.4% and results for sugar mixtures with water of various concentration.

Table 1. Relaxation time T_1 results for CuSO_4 and sugar solution

		CuSO_4 in H_2O			
Concentration (%)	0	0.1 ±	0.2	0.4	
T_1 (ms)	3100 ± 15	250 ± 4	155 ± 10	59 ± 4	
		Sugar in H_2O			
Concentration (%)	0	2.5	5	10	
T_1 (ms)	3100 ± 12	2950 ± 7	2450 ± 10	2150 ± 12	

The obtained results showed that an increase of both sugar and CuSO_4 in solution causes T_1 shortening. The initial concentration of CuSO_4 was 0.1% and for this solution we measured a 250 ms relaxation time. When concentrations of CuSO_4 increased two-fold, T_1 decreased about 38%. When concentrations of CuSO_4 increased four-fold to 0.4%, the decrease of T_1 was 76.4%. We observed a consistent relation between increased concentration of CuSO_4 agent and measured T_1 .

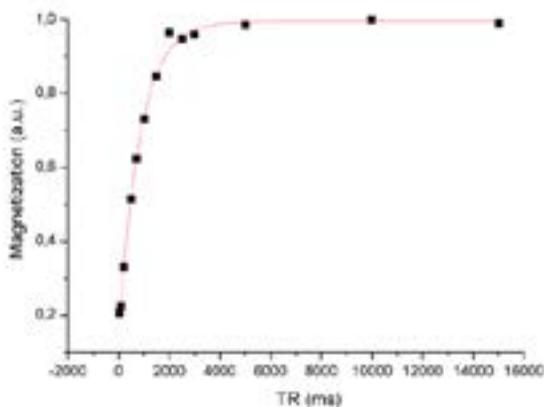


Fig. 3. Relaxation curve T_1 for water solution of vitamin C (tablet + 5ml of water) On the basis of the relaxation curve T_1 , the longitudinal relaxation time $T_1 = 710.86$ ms was determined

We used solution of sugar in H_2O to confirm the sensitivity of T_1 measurements to concentration. When sugar concentration in H_2O was increased from 2.5% to 5%, T_1 decreased about 17%, and for a concentration at 10%, we measured a 28% decrease of T_1 , when compared to solution of concentration 2.5%. In the next step we carefully revised all quantitative measurements of T_1 done at 1.5 T. We found that quantitative MRI measurements have been used in several studies to investigate vegetal tissues.⁵ The transverse relaxation time T_2 is known to be related to the water status in cell compart-

ments which encompasses water content, water mobility and interactions between water and macromolecules.⁶ In general, the lower the molecular mobility, the shorter the T_2 relaxation time, so that the signal from water bound within a polymer matrix decays away faster (1-100 ms) than that from free water. In solids, the signal decays away in less than 100 μs and this is usually not sufficient for spatial encoding to be applied.

Measurements of the relaxation curve T_1 were made for water solutions of vitamin C (tablet + 5 ml of water, Fig. 3). On the basis of the relaxation curve T_1 , the longitudinal relaxation time $T_1 = 710.86$ ms was determined.

Current applications

T_1 and T_2 relaxation times have been measured on human tissue samples of adipose, muscle, bone marrow and osteolytic skeletal metastases at temperatures ranging from +37°C to -10°C.⁷ Relative signal intensities for T_1 , proton density and T_2 -weighted imaging sequences were also calculated. T_1 and T_2 of adipose tissue decreased almost linearly with decreasing temperature while for muscle, bone marrow and metastases T_1 and T_2 decreased slightly to moderately, with temperature reduction to about -5 °C at which temperature a sudden marked decrease occurred.^{ref} Calculated signal intensities showed a decrease in image contrast with temperature reduction and reversal of contrast between adipose tissue and the other tested tissues with all imaging sequences at temperatures around 0°C.⁷ The aim of the study was to examine the validity and reliability of a quantifiable measure of inflammation using magnetic resonance imaging (MRI) in children with juvenile dermatomyositis (JDM). Ten children with active JDM, 10 with inactive JDM and 20 healthy children completed the study. There was no significant difference in ages between the three groups. The MRI T_2 relaxation times were significantly increased in active JDM compared with inactive JDM and healthy children ($P = 0.05$), indicating a detectable increase in inflammation within the muscles. There were also good correlations between the MRI scores and the measures of muscle strength and function; however, there was no correlation between the MRI and muscle enzymes. The MRI T_2 relaxation time can be used as a quantitative measure of muscle inflammation and it has good correlations with other measures of disease activity.⁸ To pool and summarize published data from magnetic resonance longitudinal relaxation measurements of the human lung at 1.5 T to provide a reliable basis of T_1 relaxation time constants of healthy lung tissue both under respiration of room air and of pure oxygen were measured. In particular, the oxygen-induced shortening of T_1 was evaluated.⁹

Several circumstances may explain the great variation in reported proton T_1 and T_2 relaxation times usual-

Table 2. Relaxation time

CLINICAL scanners				
Relaxation Time			a magnetic field	Ref
T_1	2300 to 3100 ms	H ₂ O	1.5 T	Kjaer 1987
T_1	1520 ms	H ₂ O, after distillation	1.5 T	Jerome 2016
T_1	1321.5 ms ± 2.14%,	mean tissue water	3 T	Knight-Scott 2016
T_2	65.2 ms ± 2.45%,	mean tissue water	3 T	Knight-Scott 2016
T_1	2950 ms (20° C)	Oxygen-free water		Simpson 1958
T_1	1377 ± 37.1	Water in soleus muscle	3 T	Krššák 2004
T_1	1387 ± 12.3	tibialis anterior	3 T	Krššák 2004
T_2	31,3 ± 1.2	Water in soleus muscle	3 T	Krššák 2004
T_2	28,4 ± 0.7	tibialis anterior	3 T	Krššák 2004
EXPERIMENTAL				
Relaxation Time			a magnetic field	Ref
T_1	3905 ± 311.3	H ₂ O	400MHz Bruker spectrometr	Kamaly, 2010
T_1	Fraction of Water 0ml: 1537	H ₂ O/D ₂ O mixtures with and without 0.2 g of albumin.	BRUKER AVANCE-400 MHZ proton NMRspectrometer operating at 400.132 MHz.	Bilgin Zengin, 2012
T_1	3300	95% H ₂ O	Bruker DRX 500 MHz spectrometer	Eykyn 2005

ly seen. This study was designed to evaluate the accuracy of relaxation time measurements by magnetic resonance imaging (MRI) operating at 1.5 Tesla. Using a phantom of nine boxes with different concentrations of CuSO₄ and correlating the calculated T_1 and T_2 values with reference values obtained by two spectrometers (corrected to MRI-proton frequency = 64 MHz) we found a maximum deviation of about 10 per cent. Measurements performed on a large water phantom in order to evaluate the homogeneity in the imaging plane showed a variation of less than 10 per cent within 10 cm from the center of the magnet in all three imaging planes. Changing the gradient field strength apparently had no influence on the T_2 values recorded. Consequently, diffusion processes seem without significance. It is concluded that proton T_1 and T_2 relaxation times covering the majority of the biologic range can be measured by MRI with an overall accuracy of 5 to 10 per cent.

Conclusion

T_1 and T_2 relaxation times are determined largely by the macromolecular environment of hydrogen nuclei. The more macromolecules in sample, the shorter T_1 . Diseased tissues tend to have longer T_1 and T_2 values, and higher spin-densities, than normal tissues.

Acknowledgments

Dorota Bartusik-Aebischer acknowledges support from the National Center of Science NCN (New drug delivery systems-MRI study, Grant OPUS-13 number 2017/25/B/ST4/02481).

References

1. Arbab A, Yocum G, Kalish H, et al. Efficient magnetic cell labeling with protamine sulfate complexed to ferumoxides for cellular MRI. *Blood J.* 2004;104:1217.
2. McKinney JR, Sussman MS, Moineddin R, Amirabadi A, Rayner T, Doria AS. Accuracy of magnetic resonance imaging for measuring maturing cartilage: A phantom study. *Clinics (Sao Paulo).* 2016;71(7):404-411.
3. Jerome NP, Papoutsaki MV, Orton MR, et al. Development of a temperature-controlled phantom for magnetic resonance quality assurance of diffusion, dynamic, and relaxation measurements. *Med Phys.* 2016;43(6):2998-3007.
4. Richardson JC, Bowtell R, Mäder K, Melia C. Pharmaceutical applications of magnetic resonance imaging (MRI). *Adv Drug Deliv Rev.* 2005;57:1191.
5. Hills BP, Clark CJ. Quality assessment of horticultural products by NMR. *Ann Rep NMR Spec.* 2003;50:75-120.
6. Van As H, Scheenen T, Vergeldt F. MRI of intact plants. *Photosynth. Res.* 2009;102(2-3):213.
7. Petrén-Mallmin M, Ericsson A, Rauschnig W, Hemmingsson A. The effect of temperature on MR relaxation times and signal intensities for human tissues. *Magma* 1993;1:176-184.
8. Maillard SM, Jones R, Owens C, et al. Quantitative assessment of MRI T_2 relaxation time of thigh muscles in juvenile dermatomyositis. *Rheumatology (Oxford).* 2004;43(5):603-608.
9. Dietrich O, Gaass T, Reiser MF. T_1 relaxation time constants, influence of oxygen, and the oxygen transfer function of the human lung at 1.5T-A meta-analysis. *Eur J Radiol.* 2017;86:252-260.