Relaxation Time Constants of Nanometals in Human Tissues and Clinical Applications

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ABSTRACT

The metals are in abundance in human body in biofluids, blood, cerebrospinal fluid, saliva, lymph. These metals are found in free and bound forms in each tissue and their amount is tissue specific. The mechanism of major metals and their binding affects their nuclear magnetic resonance relxation times. The longitudinal relaxation (T1) and transverse (T2) time constants are unique signatures in detection and classifying major soft tissue cancers or tissue diseases. We developed a data base of relaxivities of normal and diseased human tissues both soft and solid types. The evaluation of relaxation behavior of major human tissue diseases was made and relaxation time constants of human tissues were measured. The database of tissues is helpful as cheaper technology for quicker tissue characterization. The database also useful in imaging suits as reference guide. In conclusion, database of human tissue tumors and human fluid T1 and T2 relaxation times was developed based on nanometal NMR relaxation signatures.

Key words: relaxation times, nanomaterials, NMR

1 INTRODUCTION

Relaxation times of human tissues is like fingerprints of the specific tissue condition. The protons serve as biomarker of fat-water state of tissue. The water proton spins behave differently than fat proton spins if exposed to high magnetic field. The nuclear magnetic resonance (NMR) technique was developed decades ago to measure and estimate the relaxation constants of different protons in different tissues. Typically two different interactions are experienced by protons in presence of high magnetic field known as longitudinal relaxation (T1) and transverse relaxation (T2). The tissues in the body exhibit and behave distinctly such as soft tissue hard tissue calcification, manganese, iron rich tissue. The NMR behavior (shortening of relaxation constants) of different paramagnetic elements makes them important as imaging contrast agents.

The blood, muscle, fatty tissues and brain tissues are of special mention as they are made of varying proportions of bulk water, bound water, perturbed water as separate water compartments. Similarly the proteins such as enzymes, albumin, and transport protein molecules exhibit distinct behavior as dependent on physiological pH, temperature, protein concentration conditions. These NMR physiological dependence offers an opportunity of distinguishing different tissues as MR-cytomorphic fingerprints.

In present paper, we attempted to measure T1 and T2 relaxation constants of autopsy brain tissue at various physiological conditions of protein concentration, pH, and temperature. As experimental verification, three model proteins hemoglobin, albumin and lysozyme were evaluated. The nanomaterials calcium and manganese salts were studied for their relaxtion times at different concentrations to develop and MR-concentration gray scale.

2 MATERIALS AND METHODS

The relaxation times were measured by inversion recovery methods (for T1) and CPMG (for T2) sequence methods on desk top Mini-Spec 500 Bruker NMR Spectrometer as described elsewhere [1]. The autopsy brain tissues and blood were obtained as leftovers in mortuary from persons died in accident according to the ethical committee (as part of Ph.D dissertation). Calcium carbonate ($CaCO_3$) and manganese chloride ($MnCl_2$) solutions were prepared as model solutions. The model hemoglobin, lysozyme, and bovine serum albumin as standard

compounds were purchased from Sigma Co, St Louis.

3 RESULTS

3.1 Relaxation times of model nanomaterials

The calcium carbonate in solution showed linear relationship of relaxation constants (T1 and T2) at different concentrations shown in Fig 1. However, the manganese chloride did not show linear relationship of T1 at different concentrations but transverse relaxation constants were inversely related at increasing concentrations as shown in Fig 2.

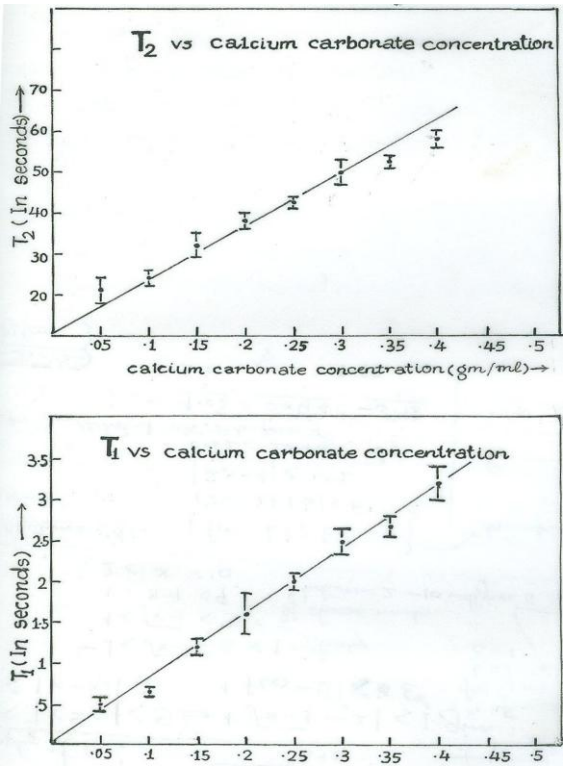

Figure 2: T1 and T2 of calcium carbonate at different concentration

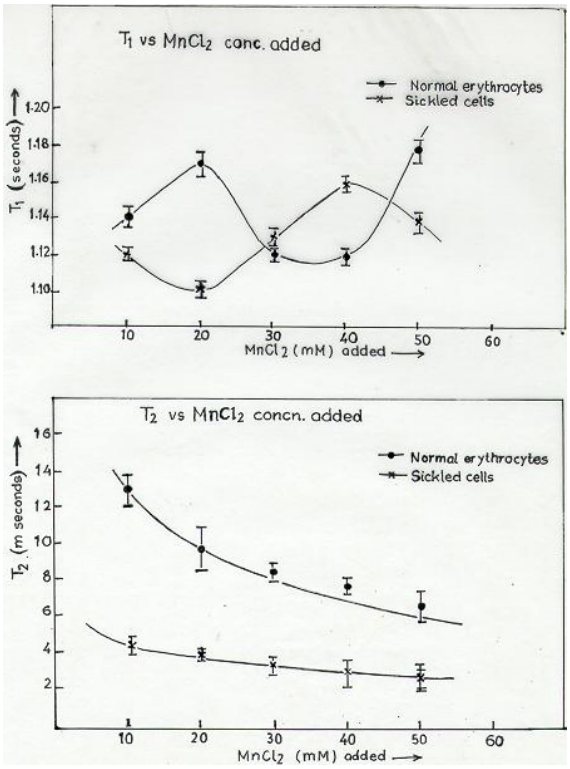

Figure 3:Relaxation constants of MnCl2 at different concentration

3.2 Relaxation constants of different tissues

The T1 and T2 relaxation constants were dependent on water content in the tissues. Basically the proton density of water in tissue was main determinant factor of different relaxation constants. It also serves as marker of tissue density either soft hard or solid and liquid phases in the tissue. The tissues showed distinct T1/T2 constants as shown in following Figures 4a and 4b.

3.3 Relaxation constants of model proteins in solution

The T1 relaxation constants showed a specific pattern of concentration dependence. At low concentrations near physiological condition these proteins showed linear sharp increase in T1 relaxation constants. At high concentrations the concentration dependence was lost as shown in Figure 5. The T2 relaxation constants were less specific.

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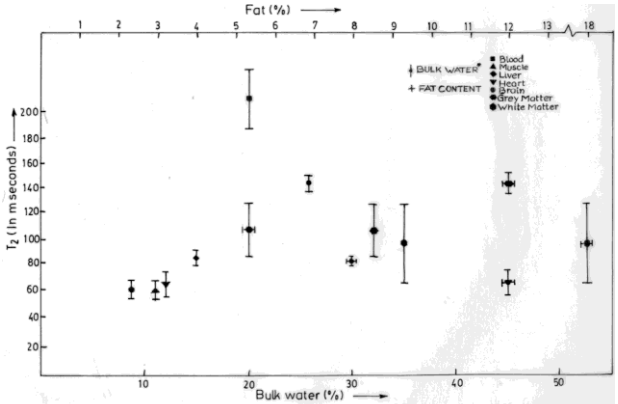

Fig.4 T_2 Relaxation times in blood mucle liver, heart, brain, and their proton density.* mean ±S. D. values of n = 8 samples shown.

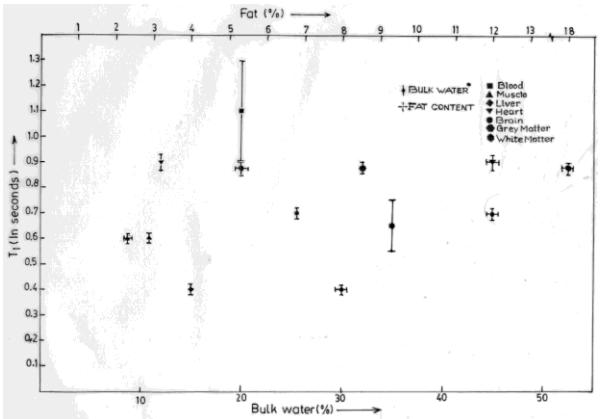

Fig.4 T_1 Relaxation times in blood muscle, liver, heart, brain and their proton density.* mean ±S. D. values of n = 8 samples shown.

3.3 Relaxation constants of model proteins in solution

The T1 relaxation constants showed a specific pattern of concentration dependence. At low concentrations near physiological condition these proteins showed linear sharp increase in T1 relaxation constants. At high concentrations the concentration dependence was lost as shown in Figure 5. The T2 relaxation constants were less specific.

3.4 Relaxation constants of tissues

The T1 relaxation constants showed a specific pattern of concentration dependence. At low concentrations near physiological condition these tissues (brain, liver, muscle and heart) showed linear sharp increase in T1 relaxation constants. At high concentrations the concentration dependence was lost as shown in Figure 6. The T2 relaxation constants were less specific.

4 DISCUSSION

The relaxation constants of different tissues provide a unique opportunity to distinguish them on MRI scanners. However the MRI technique uses image contrast methods which are based on its ability to distinguish to proton density in tissue. The proton density of tissues is best defined by using superparamagnetic elements such as Mn, Ca and other compounds as gadolinium etc. In present study we demonstrated the dependence of concentration of these Mn and Ca on their relaxation constants. The tissues can be defined or separate out on MRI images using similar principles of relaxation constants.

The brain, liver, muscle, and heart tissues differ in their water contents. SO their relaxation constants are distinct and different.

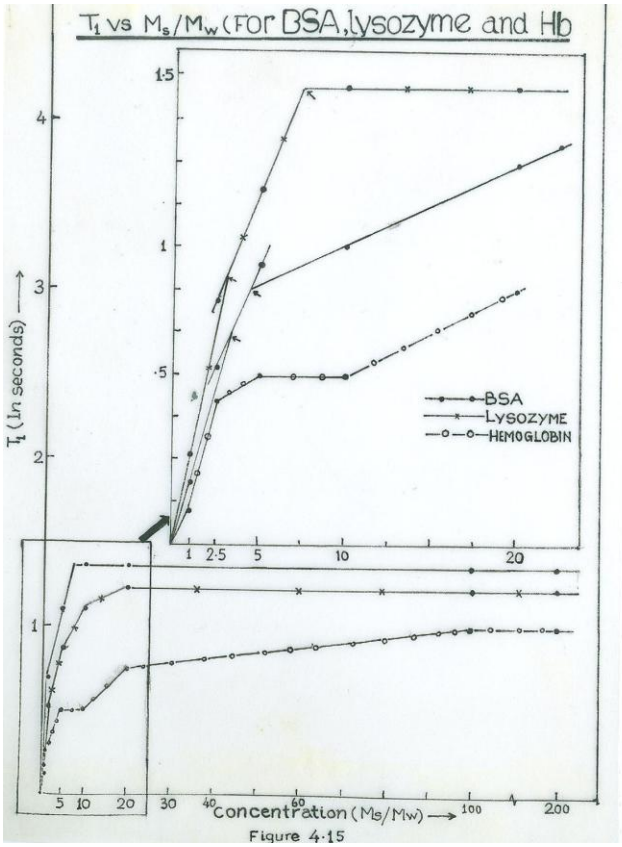

Figure 5: T1 relaxation constants of model proteins and their concentration dependence

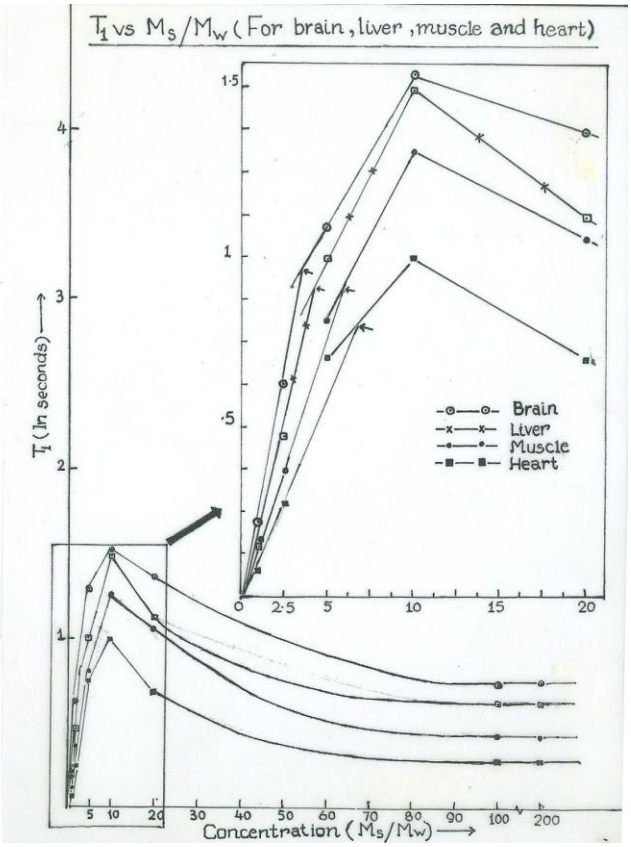

Figure 6: T1 relaxation constants of tissues and their concentration dependence

5 CONCLUSION

Relaxation constants of tissues are distinct and different for each tissue. The relaxation constants are tissue proton density and mass-concentration dependent.

REFERENCES

Sharma R. (1995)The NMR relaxation times of human tissues and biochemical-MR correlation. Ph.D dissertation submitted to Indian Institute of technology, new Delhi