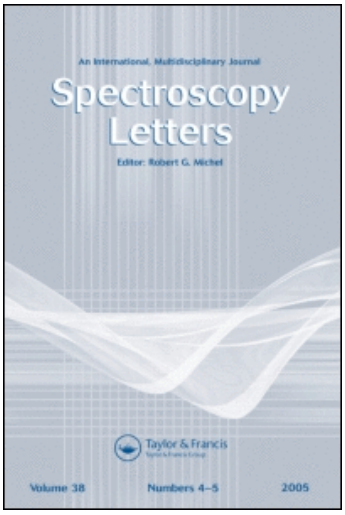

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Comparison of NMR Water Proton T1 Measurements in Healthy and Pathological Blood

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COMPARISON OF NMR WATER PROTON T1 MEASUREMENTS IN HEALTHY AND PATHOLOGICAL BLOOD.

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ABSTRACT

water proton T1 in blood from healthy volunteers and patients with acute leukaemia, lymphoma, iron deficiency anaemia, post hepatitic cirrhosis and tuberculosis, was measured by a FT-NMR spectrometer. Relaxation measurements were performed at 60MHz frequency and a temperature of (20 ± 0.5)C. The T1 measured for each disease correlates strongly with hemoglobin content. The spin-lattice relaxation time in each abnormal group was signaficantly($p<0.001$) elevated over normal group. There is little overlap between the healthy and abnormal groups. On the contrast, T1 ranges obtained for malignant groups and non-malignant diseases do overlap.

INTRODUCTION

The possibility of using nuclear magnetic relaxation times to diagnose cancer and to discriminate between malignant tumors and corresponding benign tissues has received more attention since Damadian first suggested NMR as a diagnostic tool for the detection of

cancer in 1971[1]. A systemic effect of cancer, evidenced by an increased T1 of tumor -bearing tissues, has been demonstrated by several authors[2,3] Furthermore, NMR imaging techniques, developing on this basis, are being used to discriminate the normal and pathological tissues. On the other hand, water-suppressed proton NMR studies on blood plasma have recently suggested that a new convenient diagnostic procedure may be feasible[4-6]. In these papers the mean linewidths of the lipid methyle and methylene resonances of plasma samples from patients with malignant tumors were reported to be narrower than those of the normal and benign tumor-bearing groups. Nevertheless, Utilizing water proton relaxation measurements in blood to diagnose human cancer would be of a great value in clinical use because of a need to a more rapid and more simple diagnostic blood test.

Blood consists of serum and cells. The systemic effect in the sera and cells of the tumor-bearing animals and human beings has been demonstrated by several authors[7-10]. Furthermore, T1 in blood from patients with leukaemia, myelofibrosis and multiple myeloma was found to be longer than that of blood from healthy volunteers[11]. To extend previous results we have examined the T1 measurements in blood from groups with non- malignant diseases , as well as groups of malignant diseases and healthy volunteers.

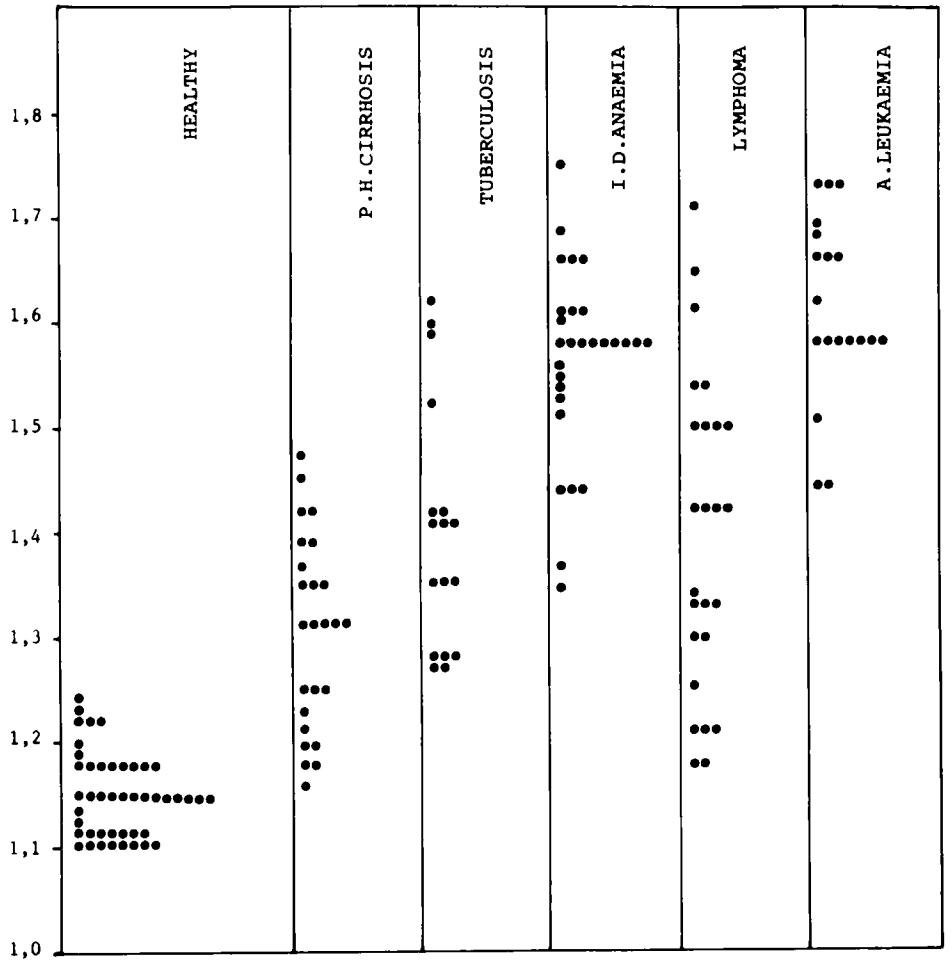

FIG. 1. T1 values of healthy volunteers , patients with non-malignant disease (post hepatitic cirrhosis, tuberculosis and iron deficiency anaemia) and patients with with malignant disease (lymphoma and acute leukaemia).

MATERIAL AND METHOD

Patients for this study were selected by hospital specialists in Internal Medicine Clinic of Dicle University Medicine School. They had a continuously active disease, mostly at advanced stage,and therefore were not in good clinical conditions with regard to healthy ones. Venous blood from untreated patients and healthy volunteers was collected into very little heparin and then used for hemoglobin content(Hb) and NMR measurements.The Hb content of the blood samples was determined by DHB-3 hemoglobinometer(ATAGO,Co,LTD.).

Experiments were conducted on 159 blood specimens; 45 from healthy controls; 44 from patients with malignant diease (acute leukemia and lymphoma); and 70 from patients with non-malignant disease(iron deficiency aneemia , post hepatitic cirrhosis and tuberculosis). Patients distribution is shown in TABLE 1.

T1 measurements were carried out on a JEOL FX-60Q FT-NMR spectrometer operating at 60MHz for proton and 10-mm o.d. NMR tubes,filled with 1.5ml of samples, were used. The inversion recovery pulse sequence was used with pulse spacing , τ , being varied from 0.3 to 2.4 s [11,12]. The peak heights of the magnetization recovery were normalized to the infinite τ , which was 12s. Pulse repitition time was set at 15s. The probe temperature was maintained at (20$\pm$0.5)C by means of a JNM- VT-3C

TABLE 1

Comparison of Whole Blood Relaxation Time T1 of Patients with Active Disease

Groups	T1(s) Mean ± SD	Range	N	Significancy compared with normal
Normal	1.15 ± 0.04	1.13 - 1.17	45	-
Lymphoma	1.40 ± 0.15	1.20 - 1.51	25	P < 0.001
A.Leukaemia	1.61 ± 0.09	1.53 - 1.69	19	P < 0.001
I.D.Anaemia	1.56 ± 0.08	1.51 - 1.61	28	P < 0.001
P.H.Cirrhosis	1.30 ± 0.09	1.24 - 1.36	25	P < 0.001
Tuberculosis	1.40 ± 0.12	1.28 - 1.52	17	P < 0.001

Range = 99% confidence limits of the mean relaxation time T1
N = Number of samples
p = significance of difference between normal and disease

automatic temperature controller unit. The magnetization decay curve was found to be a single exponential [11-14], in agreement with recent reports. The experimental error for T1 was estimated to be about ±0.03s. All measurements were made immediately after blood taken.

Comparisons of the examined groups were made using Student's t test because the distributions of the relaxation times were normal.

RESULTS AND DISCUSSION

The mean values (±SD) of T1 for each group are shown in TABLE 1. The mean T1 value of healthy controls

was Significantly shorter than that of anaemia ($P<0.001$), leukameia($P<0.001$), lymphoma($P<0.001$), cirrhosis($P<0.001$) and tuberculosis($p<0.001$). Furthermore, the mean T1 in healthy controls falls out of the confidence range obtained for the mean T1 of each abnormal group. However, There is little overlap between T1 values in blood from healthy controls and T1 values in blood from patients with lymphoma and cirrhosis. On the contrast, a considerable overlap exists in the range of T1 values measured for each abnormal group.

The correlation coefficients between the spin - lattice relaxation rate , 1/T1, and the Hb contents in each group are shown in TABLE 2. The deviation of the Hb in each group is rather large, and hence the correlations are strong.

A previous studies showed that T1 in blood from patients with malignant blood disease correlates strongly with Hb content [11]. It has also been reported that the 1/T1 in blood from patients with malignant diseases and non-malignant diseases is nearly linearly proportional to the Hb content [15,16]. Therefore, the elevation of T1 in pathological blood is nearly explained by its Hb change. In fact, the strong correlations, given in TABLE 2, imply that the distribution of T1 in each examined group indicates nearly the same thing as its Hb distribution. As is

TABLE 2

Mean Hb Distributions and Correlation of Relaxation Time T1 to Hb for Each Group.

Groups	Hb(g/dl) Mean ± SD	N	r
Normal	13.97 ± 1.60	45	0.86
Lymphoma	9.25 ± 3.11	25	0.99
A.Leukaemia	8.20 ± 2.37	19	0.88
I.D.Anaemia	7.15 ± 1.87	28	0.96
P.H.Cirrhosis	9.36 ± 2.92	25	0.97
Tuberculosis	10.55 ± 5.19	17	0.87

r = The correlation coefficients between relaxation time T1 and Hemoglobin content(Hb).

seen, the Hb deviation from normal range, depending on severity of diseases, is a common charactheristic for both malignant and others diseases studied. Therefore, we conclude that NMR T1 measurements are not a specific marker for malignant tumors, but may recognize pathological disorder like erythrocyte sedimentation rate.

However, recent studies showed that the 1/T1 in serum from healthy subjects can be correlated with total serum iron and total protein [17,18]. It is well known that in many cases, this parameters are changed by diseases. Therefore, NMR T1 measurements in whole blood and its associated serum and packed cells altogether may

represent a valuable approach for distinguishing some pathological disorder.

REFERENCES

1. Damadian R., Tumor detection by NMR. Science 1973; 171 : 1151.

2. Bottomley PA.,Foster TH.,Argersinger RE.,Pfeifer LM., A review of normal tissue hydrogen NMR relaxation times and relaxation mechanisms from 1 - 100 MHz : Dependence tissue type, NMR frequency, temperature, species,excision, and age. Med.Phys.1984; 11 : 425.

3. Bottomley PA., Hardy CJ., Argersinger RE., Allen-Moore A., A review of 1H NMR relaxation in pathology : Are T1 and T2 diagnostic ? Med.Phys.1987; 14 : 1.

4. Fossel ET., Carr JM., McDonagh J., Detection of malignant tumors:Water-suppressed proton NMR Spectroscopy of plasma, N.Eng.J.Med.1986; 315 : 1369.

5. Regan MC, Cottrell C, Detection of Malignant tumors by NMR spectroscopy of plasma(correspondence), N.Eng. J.Med.1987;316 : 1412.

6. Van Blitterswijk WJ.,Detection of malignant tumors by NMR spectroscopy of plasma (correspondence), N.Eng.J. Med.1987;316 : 1413.

7. Hollis DP., Saryan LA., Economou JS., Eggleston JC., Czeisler JL., Morris HP., NMR studies of cancer. V. Appearance and development of a tumor systemic effect in serum and tissues. J.Natl.Cancer Inst.1974;53: 807.

8. Beall PT.,Medina D, Chang DC., Seitz PK.,Hazlewood CF F,Systemic effect of benign and malignant mammary tumors on the spin-lattice relaxation time of water protons in mouse serum, J. Natl.Cancer Inst.1977; 59 : 1431.

9. McLachlan LA., Cancer-induced decreases in human plasma proton NMR relaxation rates, Phys.Med.Biol. 1980;25 : 309.

10. De Certaines J, Bernard AM., Benoist L, Rivet P., Gallier J., Morin P., NMR study of cancer: Systemic effect on the proton relaxation times T1 and T2 of human serum, Cancer Detec. Prevent. 1981;4 : 267.

11.Koivula A, Suominen K, Timonen T, and Kivinitty K, The spin-lattice relaxation time in the blood of healthy subjects and patients with malignant blood disease, Phys.Med.Biol.1982; 27 : 937.

12.Ekstrand KE., Dixon RL., Raben M, Ferree CR., Proton NMR relaxation times in the peripheral blood of cancer patients, Phys.Med.Biol.1977; 22 : 925.

13.Brooks RA., Battocletti JH., Sances A., Larson SJ., Bowman RL., Kudravcev V, Nuclear magnetic relaxation in blood. IEEE Trans.Bio-Med.Eng.1975;BME-22 : 12

14.Koenig SH., Spiller M., Brown III RD., Wolf GL., Relaxation of water protons in the intra- and extra-cellular regions of blood containing Gd(DTPA). Mag. Reson.Med.1986;3 : 791.

15.Singer JR., Crooks LE., Some magnetic studies of normal and leukemic blood, J.Clin.Eng.1978;3 : 237.

16.Yılmaz A., and Balcı K., Determination of factors affecting the spin - lattice relaxation time T1 of pathological blood by FT - NMR spectrometer. In: Proceedings of the II International Conference on Applications of Physics to Medicine and Biology,Bajzer Z, Baxa P and Franconi C eds., Singapore, World Scientific Publ. Co.: 555-556.

17.Kang YS., Gore JC., Armitage IM., Studies of factors affecting the design of NMR contrast agents: Manganese in blood as a model system. Mag.Reson.Med.1984;1 : 396

18.Yılmaz A., Chu SC., Osmanoglu Ş, Dependence of the solvent proton 1/T1 on the iron content in normal human serum, Mag.Reson.Med.1988,7 : 337.

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