

# The Possibility of Cancer Diagnosis by Human Serum NMR Measurement

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— Abstract —

A characteristic proton NMR signal is found in human cancer serums. The signal is given by  $6.43 \pm 0.06$  ppm on average. An attempt is made to find a certain correlation between the appearance of the signal and the amounts of CEA and AFP in the serums.

## 1. Introduction

The urine NMR measurements<sup>1-4)</sup> have been made to find a possible method for the differential diagnosis between the cancer and non-cancer patients. From the measurements the characteristic cancer urine NMR signals corresponding to amino acid with a phenolic compound were obtained.

In this paper an attempt for the serum proton NMR measurements of the cervix and endometrial cancer patients and the patients of tubal pregnancy, myoma and ectopic pregnancy has been made to find certain characteristic NMR signals which can be used for cancer diagnosis. The results of the attempt are compared with those obtained by Phadebas CEA (carcino embryonic antigen) PRIST and the GAMMADAB(I-125) AFP (alpha-feto-protein)

Radioimmunoassay to seek a certain correlation between them.

## 2. Experiment

### A. Samples

The urine samples of cervix, endometrial, tubal pregnancy, myoma and ectopic pregnancy patients are furnished by the obstetrics department of Hanyang University Hospital in Seoul. All the samples\* are evaporated and kept in a freezer so as not to be decomposed before measuring the urine proton NMR signals.

### B. Measurement

D<sub>2</sub>O is used as a solvent. The NMR sample tube is filled with 0.5 c. c. of the solvent mixed with the evaporated serums to measure the proton NMR frequency-shift signals using the Varian EM-360 60 MHz high resolution NMR spectrometer. TMS (tetramethylsilane) is used as a reference standard which is taken to be 0 ppm for the measurement.

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\* The Samples were collected by Dr. Yong oh Lee's help in the department.

\*\* The determinations can be made by Dr. Hae Ran Moon's help in Green Cross Clinical Examination Center.

## 3. Results and Discussion

Distinctive proton NMR signals among the va-

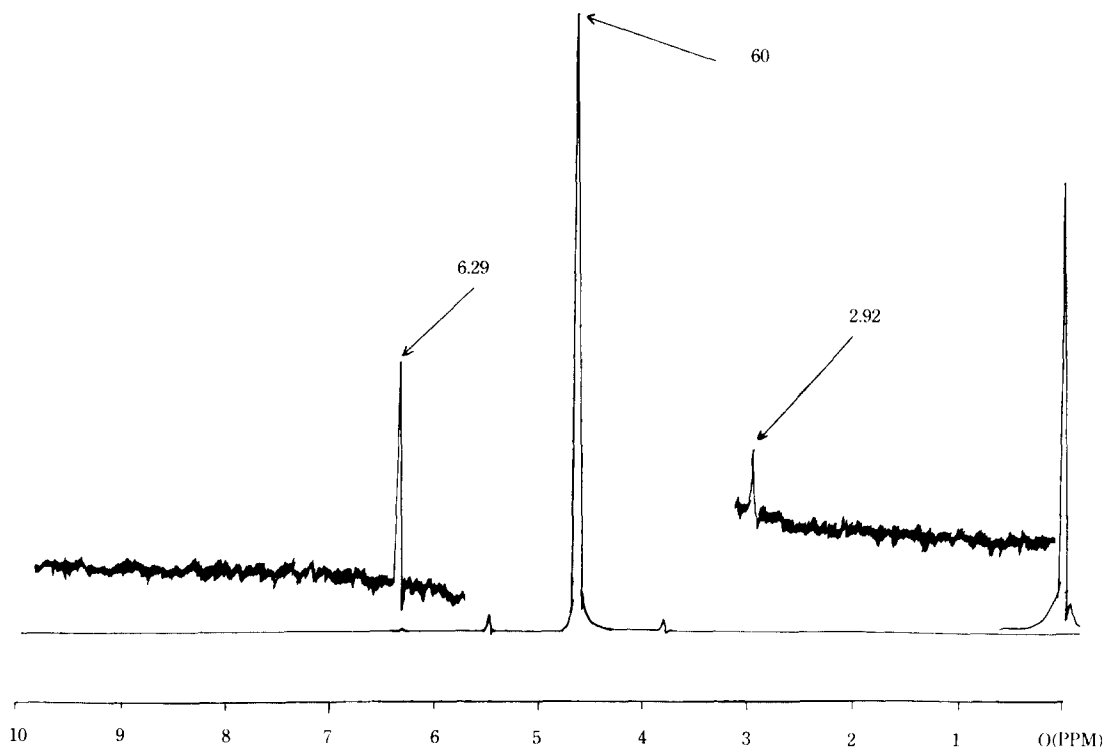
**Table 1.** Experimentally obtained NMR signals of the cancer and non-cancer sera at room temperature.

Serum	d(ppm)	0	1	2	3	4	5	6	Range of error(ppm)
			1.13						
Cervix cancer	0.77		1.27		3.76	4.56	5.62	6.42	$\pm 0.06$
			1.93						
			1.11						
Cervix cancer	0.75		1.25		3.77	4.57	5.63	6.41	$\pm 0.06$
			1.91						
			1.12						
Endometrial cancer	0.78		1.28		3.76	4.59	5.62	6.42	$\pm 0.06$
			1.94						
			1.23						
Tubal pregnancy (non-cancer)	0.87		1.33		3.80	4.60	5.67		$\pm 0.06$
	0.90		1.87						
			1.20						
Myoma (non-cancer)	0.86		1.33		3.81	4.58	5.74		$\pm 0.06$
	0.89		1.85						
			1.21						
Ectopic pregnancy (non-cancer)	0.85		1.34		3.79	4.61	5.77		$\pm 0.06$
	0.87		1.88						
Column		A	B	C	D	E	F	G	

rious signals are selected and listed in Table 1 so as not to confuse noise signals with the true ones.

It is noticed that all the signals distributions are roughly the same if the signals of  $6.42 \pm 0.06$  ppm,  $6.41 \pm 0.06$  ppm and  $6.45 \pm 0.06$  ppm shown in Column G are disregarded. The signals in Column E of the table are the proton NMR signals of the solvent of  $D_2O$ . The signals shown in Column A and B are supposed to represent those of the methylene group<sup>5)</sup> in the sera. The signals in Column D and F show those of the NH and OH compound elements<sup>6)</sup>. Up to this point the signals (or the average signal in Column G,  $6.45 \pm 0.06$  ppm) in Column G in the table seem to be the characteristic cancer serum proton NMR signals by which a cancer diagnosis can possibly be made. However the cancer patients in the Hospital mentioned earlier have been treated by the anti-cancer agents<sup>7)</sup> of

methotrexate, adriamycin, bleomycin, vinblastine, and cisplatin. The first cancer patient shown on the left-hand side of the table has been treated by the first two agents just mentioned above and the second and third patients in the table have been treated by the rest of them. It is known that the agents used are mostly excreted in urine<sup>7)</sup>. It is ascertained that the serums are also affected by the agents. Hence the following possibilities of causing the signals in Column G must be considered and examined: Since methotrexate is composed of amide<sup>7)</sup> and since the proton NMR signal of NH of amide lies within the range of 6.50 ppm to 5.50 ppm<sup>5,6)</sup>, it may be considered that the signals in the column are caused by the agent. Since the proton NMR signal of OH of bleomycin(or adriamycin) is  $6.29 \pm 0.06$  ppm as shown in Fig. I, the average signal of the column,  $6.43 \pm 0.06$  ppm, may



**Fig. 1** Proton NMR signal distribution of bleomycin observed by 100 x 3 of sepectrum amplitude at room temperature.

be caused by it. One reason for supporting this is that a certain dissolved substance in a solvent can usually have a few frequency-signal shift from the original signal of the pure substance which was not in the dissolved state due to a shielding effect on an externally applied magnetic field caused by other neighboring substances(or other neighboring nuclei<sup>5, 6)</sup>). However such presumption can not be accepted unless it is experimentally shown. Therefore the signals in the column may be the characteristic ones which can be utilized for the cancer diagnosis, although the NMR results are obtained from a small number of people who are in particular diseases.

A further attempt for the quantitative determinations\*\* of CEA and AFP in the patients sera has been made to find a certain correlation with the

NMR results. The results of the attempt are listed in Table 2. As shown in the table, there are some numerical differences between the cancer and non-cancer patients. If the numerical differences are

**Table 2.** The results obtained from the quantitative determinations of CEA and AFP in human serums.

Serum	CEA (ng/ml)	AFP (ng/ml)
Cervix cancer	0.5	1.8
Cervix cancer	0.5	2.0
Endometrial cancer	0.7	2.6
Tubal pregnancy(non-cancer)	0.6	1.7
Myoma (non-cancer)	0.2	1.5
Ectopic pregnancy (non-cancer)	0.2	2.4

practically adopted for the diagnosis, then the average proton NMR signal can indirectly be correlated with them. However this does not mean the signal corresponding to either of the numerical values of them. Since the allowed numerical values of CEA and AFP are 0 to 0.3 ng/ml and 0 to 0.2 ng/ml, no decisive difference between the cancer and non-cancer sera can be found except for small numerical deviations. If this were so, the characteristic signals in the cancer sera might be caused by the treated medicines.

However, as indicated in Section 3, since the overall standard deviation is  $\pm 0.06$  ppm, the average NMR signal of human serum which is given by 6.43 ppm is not resulted from bleomycin medicated whose NMR signal is 6.29 ppm. Hence it is concluded that the above signal is certainly a characteristic one of the cancer serum regarded as a cancer marker. Furthermore it is also concluded that the NMR cancer diagnosis seems much more prevailed than any diagnostic methods such as CEA FRIST and AFP Radioimmunoassay.

## Reference

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