의학물리. 제3권 1호 1992

A Study of Possibility of Improving Cancer Diagnosis by Measuring the Areas of Proton NMR Signals of Human Urine

Yong Jin Kim
Department of Physics, Hanyang Univeristy, Seoul 133-791, Korea.

Abstract

An attempt is made to diagnose cancer of eight persons' urine by measuring the areas of the characteristic proton NMR signals observed in most cancer urine other than by using the previously developed reagent. The results of the attempt show that the former and ther latter give respectively one false diagnosis and four false diagnoses out of the persons' urine tested.

Ⅰ. INTRODUCTION

It has been reported that the characteristic proton NMR signals which correspond to the phenolic compound of tyrosine regarded as a cancer marker are observed between 7 ppm and 8 ppm in most cancer urine. This has also been confirmed by ovserving the urine color reaction by the recently developed reagent for cancer diagnosis. However since the signals are occasionally obsrved even in normal and other diseased urine between the same scales, the reagent sensitivity and specificity can not be enhanced further. In this study an attempt has been made to diagnose cancer by directly measuring the areas under the characteristic signals other than by using the reagent. The results of the attempt show that the direct measurement of the areas gives better diagnoses than the reagent.

Ⅱ. EXPERIMENT

1. Samples

All the urine samples for the present measurement are collected from university hospitals in Seoul. The collected samples are freezed and dried before measuring the proton NMR signals.

2. Measurement

An NMR sample tube is filled with 0.5 c.c. of urine dissolved in D_2O to measure the signals by the Bruker 80 MHz NMR spectrometer. Sodium 2, 2-dimethyl-2-silapentane-5-sulfonate(DSS) is used as an internal reference standard for all chemical shift measurements.

Ⅲ. RESULTS and DISCUSSION

A few exemplary proton NMR signal distributions are taken, for the over-all geometric shape of the characteristic signals of cancer urine is the same. Figs. Ⅰ and Ⅱ show the proton NMR signal distributions of two non-cancer patients' urine. Fig. Ⅲ shows the distribution of a patient's urine of stomach cancer with bilirubinuria. Here it must be noted that the term used for non-cancer urine means normal and other diseased one for simplicity.

In Fig. Ⅰ no characteristic proton NMR signals between the scales of 7 ppm and 8 ppm are shown. When 0.05 c.c. of the reagent indicated in the footnote in Section Ⅰ is added to 3 c.c. of this urine, the characteristic red color reaction which is caused by the excretion of the phenolic compound corresponding to the characteristic signals of cancer urine does not occur. This means that the characteristic excretion can also be identified by the reagent other than by the NMR measurement. In Fig. Ⅱ which is the distribution of the non-cancer urine

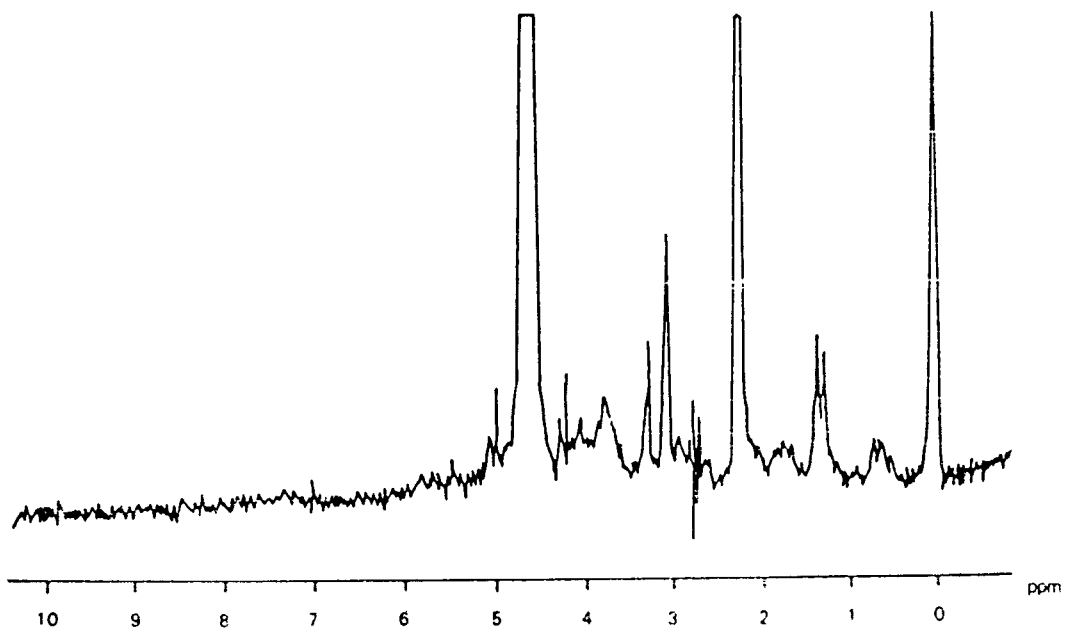

Fig. 1. Oberved proton NMR signal distribution of a non-cancer urine in ppm measured at room temperature.

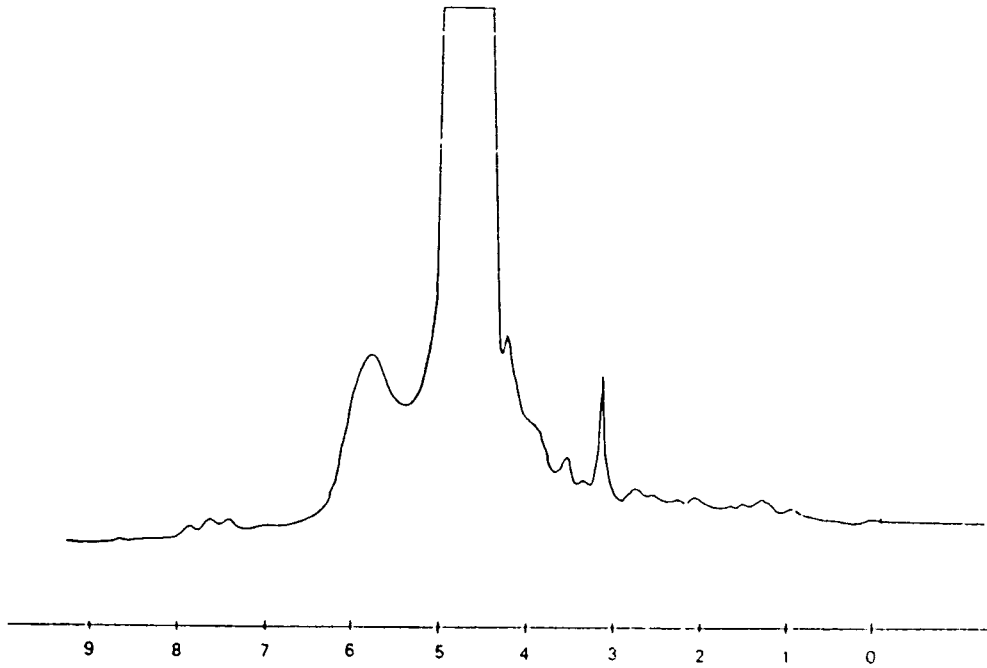

Fig. 2. Oberved proton NMR signal distribution of a non-cancer urine in ppm measured at room temperature.

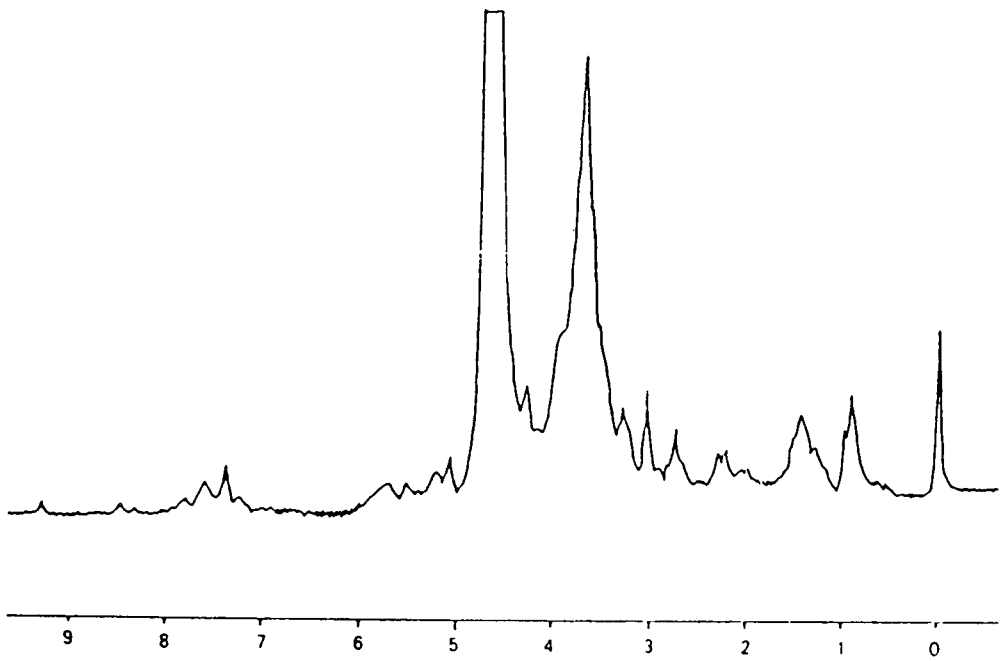

Fig. 3. Oberved proton NMR signal distribution of a stomach cancer patient's urine in ppm measured at room temperature

small ripples appear between the scales. These small ripples are caused by the low excretion concentrations. It is, however, noted that in spite of such low concentrations the urine so sensitively reacts by the reagent that a false diagnosis is obtained from the urine color reaction just mentioned above. In fact this proves that the tyrosine compound normally excrets in human urine, regardless of cancer or non-cancer.[4,5]

When the urine of Fig. Ⅲ reacts by the reagent, the same color reaction is observed like the one of Fig. Ⅱ without distinction, however if the areas under both the ripple signals of Fig. Ⅱ and the signals of Fig. Ⅲ between the scales are measured to differentiate between cancer and non-cancer urine, a definite differentiation is obtained: the two areas measured by use of a planimeter of NO. 3194 made in Japan are 0.23㎡ and 0.88㎡, respectively.

Although the numerical values of the areas under the signals change from time to time, the following table shows the results of the measured areas of typical cancer and non-cancer urine:

Table 1. The areas under the characteristic signals of cancer and non-cancer urine.

Urine	Area(㎠)	Urine color reaction
Carcinoma peritonei	0.60	Red
Colon cancer	0.53	Red
Stomach cancer with bilirubinuria	0.68	Red
Stomach cancer with bilirubinuria	0.88	Red
Non-cancer	0.30	Red
Non-cancer	0.23	Red
Non-cancer	0.28	Red
Normal healthy	0.60	Red

Here Red stands for the positive reaction caused by the excreted phenolic compound.

Except for the last numerical value of the area of normal healthy persons' urine in the table, the areas under the characteristic cancer urine signals are much larger than the ones under the non-cancer urine signals; in the color reaction four false diagnoses out of eight are obtained and in the area measurement one false diagnosis out of eight.

Repeated area measurements of more than the eight persons in the table must be done to confirm the present study by a statistical data, but such a limited number of the measurements is sufficient to meet the present purpose. The reason is that the reagent sensitivity and specificity indicated in the footnote in Section I are the statistical results proven by clinics form the first. Hence it is concluded that the cancer diagnoses by means of the area measurement are much better than the ones by observing the urine color reactions by the reagent.

Reference

1. Yong Jin Kim, The Possible Reagents for a Cancer Diagnosis by a Urine Color Reaction, J. of the Korea Med. & Biol. Eng. 8, 145(1987)
2. Yong Jin Kim, The Possible Discovery of a Reagent for Cancer Diagnosis by Urine NMR Analysis, J. of the Korea Med. & Biol. Eng. 2, 149(1988)
3. Yong Jin Kim, The Study of Possibility of Cancer Diagnosis by the Spectral Analysis of Excretion of Human Urine, J. of the Korea Med. & Biol. Eng. 11, 19(1990)
4. J. J. Emmett and D. V. Witten, Clinical Urography, 2, 3rd ed. p. 1231, W. B. Saunders Co. (1971)
5. D. H. Russell and B. G. M. Durie, in Polyamines as Biochemical Markers of Normal and Malignant Growth, Raven Press (1978)

인뇨의 양성자 NMR신호의 면적측정에 의한 암진단 개선 가능성에 관한 연구

김 영 진
한양대학교 자연과학대학 물리학과

초 록

개발된 암진단 시약을 사용하는 대신에 대부분의 암뇨에서 관측되는 특성 양성자 핵자기공명 신호의 면적측정에 의한 암진단을 시도하였다. 팔명의 뇨에 대하여 암진단을 시도한 결과, 면적측정에 의한 암진단은 팔명중 한개의 오진을 얻게 되었으며, 시약에 의한 암진단은 팔명중 네 개의 오진을 얻게 되었음을 보였다.