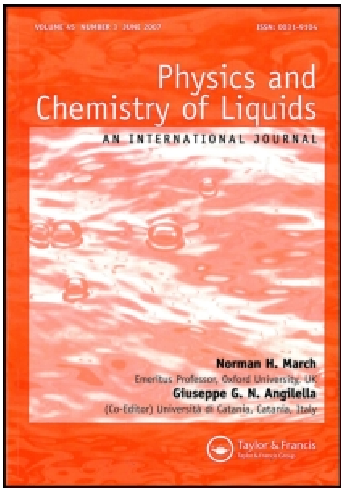

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A. Mikusińska-Planner[a]; J. GĄgalska[a]; M. Pochylski[a]; M. M. Kaczmarek[a]
[a] Optics Laboratory, Institute of Physics, Adam Mickiewicz University, Umultowska 85, 61-614 Poznań, Poland

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X-Ray method of detection of neoplasmic changes

A. MIKUSIŃSKA-PLANNER*, J. GĄGALSKA,
M. POCHYLSKI and M.M. KACZMAREK

Optics Laboratory, Institute of Physics, Adam Mickiewicz University,
Umultowska 85, 61-614 Poznań, Poland

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The article presents an X-ray method of detection of neoplasmic changes in people based on measurements from human blood serum. A new X-ray marker Ω_{rtg} is defined and determined directly from the experimental angular distributions of radiation scattered by human blood serum samples. The numerical values of the marker Ω_{rtg} are related directly to the character of the angular distribution of the scattered radiation intensity. The values of Ω_{rtg} markers obtained for cancer patients were compared with the levels of the PSA marker. Statistical computer analysis of the correlation between the markers Ω_{rtg} and PSA was made with the use of Statistica software by the method of classification trees. The threshold value of the Ω_{rtg} marker, allowing distinction between the healthy and neoplasmically changed blood serum, was determined.

Keywords: X-Ray diffraction patterns; Human serum; Neoplasmic diseases

1. Introduction

The high rate of incidence of neoplasmic diseases has become an increasingly important problem in contemporary medicine. Success of treatment of this disease critically depends on its early diagnosis. Of great importance can also be the method of diagnosis and the use of non-invasive techniques. The proposed method is absolutely non-invasive as it is based on X-ray measurements of human blood serum. It is also a simple and direct method as the angular intensity distribution depends directly on the molecular arrangement in a sample studied. This arrangement is determined by the structure of water studied in [1–4], water accounting for over 90% of blood serum [5]. Blood serum contains anions, cations (it is an electrolyte) and some amount of proteins mainly albumins, α- and β-globulins [6,7]. These components are randomly distributed in the blood serum bulk. In blood serum from healthy people the presence of these components does not disturb the structure of water but on the

*Corresponding author. Fax: +48-61-8257-758. Email: annap@main.amu.edu.pl

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contrary – stabilises it [8,10]. The character of the angular distribution of scattered intensity is then comparable with that of pure water [5]. It has been established that in patients with neoplasmic changes or in pregnant women the angular distributions measured in blood serum are different [9,10]. The regularities noted in the changes of the angular intensity in the range of the so-called secondary maximum [8,9] permitted defining an X-ray marker Ω_{rtg}.

2. Method

The human blood serum samples to be studied were placed in a flat cell, figure 1, designed by our group and constructed at our university workshop. The cell was mounted on a holder e (figure 1) of a goniometer and fastened to it with a screw c. The ring a (figure 1) determined the thickness of the sample s equal to $d = 0.1 \times 10^{-2}$ m. The ring b ensured the tightness of the cell. The centre of the sample was at the axis of the goniometer f (figure 1). A layer of the liquid studied restricted by mica windows was placed between the source of monochromatic X-rays MoKα and a counter probe. The pulses were counted within 120 s, in the angular range $2° \leq \Theta \leq 50°$, with an accuracy of $0.005° \leq \Delta\Theta \leq 0.1°$. A scheme of the measuring set is presented in figure 2. The samples of blood plasma from blood donors were

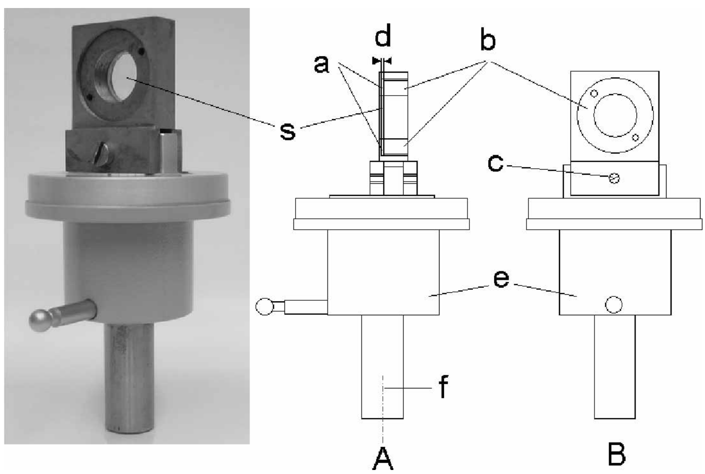

Figure 1. The new type of cell designed and constructed for the purpose of our study. On the right – A – the projection of the cell in the plane perpendicular to the face of B of the cell.

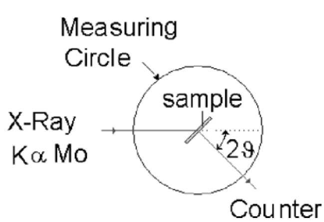

Figure 2. A scheme of the measuring apparatus.

obtained from centrifuged blood, characterised by standard analytical procedures [11]. Pure water was three times distilled and deionised, while the samples of serum were defrosted prior to the measurement. The study was conducted on 174 samples of human blood serum collected from men diagnosed with prostate cancer, prostate adenoma and men over 50 years of age at increased risk of developing prostate cancer.

3. Definition of the new X-ray marker Ω_{rtg}

The X-ray marker Ω_{rtg} has been defined on the basis of the experimental angular distributions of X-ray radiation intensity scattered by the blood serum samples studied. The angular distributions of scattered radiation intensity show the main maximum and a secondary maximum being more or less pronounced. For pure water this secondary maximum is clearly seen at $\Theta \approx 9.5°$; figure 3, which proves an arrangement of the water molecules similar to that in ice [4,12]. The experimental curve (circles in figure 3) can be approximated analytically by the function $f(\Theta)$ being a sum of two Lorentz type functions:

$$f(\Theta) = \sum_{i=1}^{2} a_i \Big/ \left\{1 + [(\Theta - \Theta_{0i})/b_i]^2\right\}, \tag{1}$$

where a_i – is the height at the maximum, b_i – half width, Θ_{0i} – the maximum position.

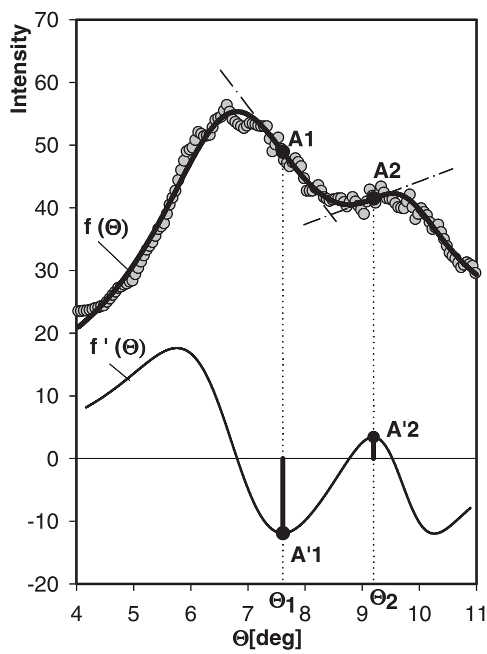

Figure 3. The function $f(\Theta)$ describing the angular distribution of the scattered radiation intensity and its derivative $f'(\Theta)$ for pure water.

The fit of the function $f(\Theta)$ to the experimental curve (circles in figure 3) has been made at the correlation coefficient $R = 0.997$. Figure 3 also shows (solid line) the derivative $f'(\Theta)$ – as the curve whose extremes at A_1' and A_2' are the inflection points of the function $f(\Theta)$ that is A_1 and A_2. At these points the tangents to the curves have been drawn – marked by dash-dot lines (figure 3), whose slopes are equal to the values of the derivative $f'(\Theta)$ at Θ_1 and Θ_2 that is $\mathrm{tg}\,\alpha_1 = f'(\Theta_1)$ and $\mathrm{tg}\,\alpha_2 = f'(\Theta_2)$. The values of these derivatives (sections in figure 3) have been used to define a coefficient:

$$\Omega = \frac{f'(\Theta_2)}{f'(\Theta_1)}, \tag{2}$$

which is sensitive to a change in the course of the function $f(\Theta)$ in the angular range $7.5^\circ \leq \Theta \geq 9.5^\circ$. Taking into account the fact that the character of the angular functions of scattered radiation intensity obtained for healthy people is comparable to that of the function for pure water [6,7], being a reference standard, a relative coefficient Ω_{rtg} was defined:

$$\Omega_{\mathrm{rtg}} = \frac{\Omega}{\Omega_w}, \tag{3}$$

further called the X-ray marker. The value $\Omega_w = -0.29$ is a constant calculated for pure water.

4. X-ray marker Ω_{rtg} for the samples studied

Figure 4 presents angular distributions of scattered radiation intensity for pure water, for samples from healthy subjects (lines: 14, 101, 74, 31, 3, 98), for patients with prostate adenoma (lines: 126, 127, 142, 133, 152) and for those with prostate cancer (lines: 173, 174, 170, 157, 161).

The curves given in figure 3 are denoted with numbers labelling particular blood serum samples for which the results are given in table 1. For the sake of clarity, figure 4 shows only the curves for a limited angular range $4^\circ \leq \Theta \geq 12^\circ$. Table 1 also gives the values of PSA marker characterising the health status of prostate [6,13,14]. The health status of prostate is also diagnosed by ultrasonographic study and cytological methods [15]. A sufficiently diagnosed health condition is described by the so-called disease symbol, e.g. N40 stands for a diagnosis of prostate adenoma, and C61-prostate cancer. A block letter H means no changes in the prostate condition.

The samples of blood serum studied, together with the PSA level values and disease number were provided by the hospital unit specialised in prostate cancer treatment.

5. Discussion

For 174 human blood serum samples the values of Ω_{rtg}, calculated from the experimental results have been compared with the PSA level determined for the same samples.

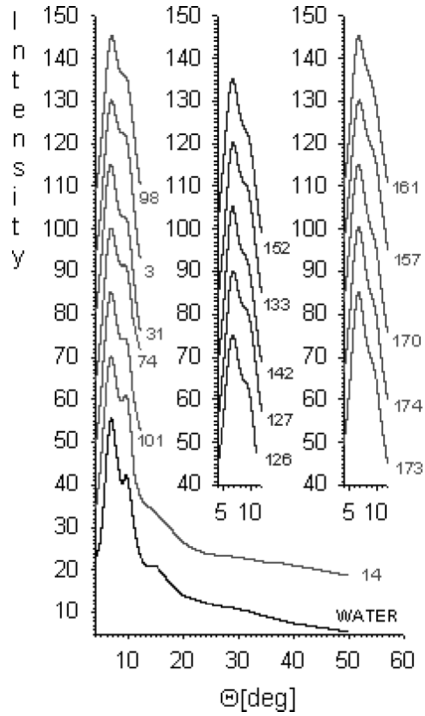

Figure 4. The angular distributions of the scattered radiation intensity for pure water and for selected samples of blood serum of healthy subjects and cancer patients.

According to the literature data [6,16–19] the correct PSA level in human blood serum ranges from 0 to 4 ng/mL, its value in the range 4–10 ng/mL indicates high risk of neoplasmic disease. The PSA value is always positive and increases with increasing risk of cancer. The values of the X-ray marker decrease with increasing risk of prostate cancer.

Statistical comparative analysis of the correlation between PSA and the X-ray marker was made by Statistica software [20] using the method of classification trees with the ordering variable being Ω_{rtg} and the dependent variables are the PSA level, and diagnosis expressed by the disease symbol. Figure 5 presents the scheme of the classification trees that allowed for a determination of the threshold value of Ω_{rtg}.

As follows from the statistical analysis the threshold value of the X-ray marker allowing a distinction of neoplasmic changes is $\Omega_{rtg} = -0.75$.

Table 2 presents the percent of samples for which the X-ray marker value was lower than the threshold value $\Omega_{rtg} < -0.75$.

As follows from figure 5 and table 2, the samples of all cancer patients (C61) and about 79% of patients with prostate adenoma (N40) were characterised by the X-ray marker values $\Omega_{rtg} < -0.75$. Moreover, the samples of 26% of healthy subjects (H) not diagnosed with prostate condition were also characterised by the X-ray marker values from the range below −0.75. However, it cannot be excluded that these people classified as healthy may suffer from other forms of neoplasmic changes. The value $\Omega_{rtg} = -0.75$ has been assumed to be the threshold and the values below the threshold indicate neoplasmic changes.

Table 1. The values of the X-ray marker Ω_{rtg} determined for the samples studied, the PSA level in these samples and disease symbols.

No	Ω_{rtg}	PSA	Disease symbol	No	Ω_{rtg}	PSA	Disease symbol	No	Ω_{rtg}	PSA	Disease symbol
1	−0.87	0.15	H	59	−1.46	1.03	H	117	−0.93	2.44	N40
2	0.12	0.25	H	60	−0.60	1.06	H	118	−0.18	2.5	H
3	−0.08	0.25	H	61	−0.17	1.13	H	119	−0.53	2.61	H
4	−0.57	0.36	H	62	−0.90	1.13	H	120	−0.63	2.63	H
5	−1.04	0.42	H	63	−0.54	1.15	H	121	−0.23	2.82	H
6	−0.50	0.40	H	64	−0.45	1.16	H	122	−1.00	2.85	N40
7	−0.33	0.40	H	65	−0.31	1.16	H	123	0.14	2.77	H
8	0.22	0.42	H	66	−0.63	1.21	H	124	−0.40	2.62	N40
9	−0.5	0.43	H	67	−0.46	1.22	H	125	−0.20	2.92	N40
10	−1.15	0.44	H	68	−1.00	1.24	H	126	−0.47	2.96	N40
11	−0.49	0.41	H	69	−1.01	1.25	H	127	−0.65	3.04	N40
12	−0.32	0.44	H	70	−0.83	1.27	N40	128	−1.46	3.09	N40
13	−0.16	0.46	H	71	−0.96	1.27	N40	129	−0.90	3.29	N40
14	0.43	0.46	H	72	−1.11	1.28	H	130	−0.71	3.41	H
15	−0.97	0.49	H	73	−0.48	1.28	H	131	−0.92	3.55	N40
16	−0.54	0.54	H	74	0.22	1.28	H	132	−0.52	3.58	H
17	−1.01	0.54	H	75	−0.43	1.29	H	133	−0.71	3.64	N40
18	−0.5	0.54	H	76	−0.61	1.33	H	134	−0.62	3.81	H
19	−1.13	0.55	H	77	−1.37	1.35	N40	135	−1.05	3.93	N40
20	−0.47	0.56	H	78	−0.31	1.37	H	136	−0.99	4	N40
21	−1.07	0.57	H	79	−0.48	1.38	H	137	−1.05	4.11	N40
22	−0.28	0.57	H	80	−0.58	1.41	H	138	−1.29	4.12	N40
23	−0.55	0.59	H	81	−0.37	1.42	H	139	−0.98	4.4	H
24	−1.33	0.61	H	82	−0.65	1.43	H	140	−1.43	4.56	C61
25	−0.69	0.62	H	83	−0.67	1.45	H	141	−0.96	4.96	C61
26	−0.32	0.62	H	84	−0.59	1.45	H	142	−0.75	5.07	N40
27	−0.67	0.63	H	85	−1.12	1.47	H	143	−0.71	5.45	N40
28	−0.49	0.63	H	86	−0.32	1.47	H	144	−1.02	5.7	C61
29	−0.91	0.63	H	87	−0.01	1.47	H	145	−1.33	5.71	C61
30	0.13	0.62	H	88	−1.04	1.5	N40	146	−0.82	5.98	C61
31	0.09	0.66	H	89	−1.40	1.53	H	147	−0.92	6.04	C61
32	0.04	0.66	H	90	−0.52	1.5	H	148	−1.17	6.09	C61
33	−1.01	0.67	H	91	−0.41	1.56	H	149	−0.81	6.81	N40
34	−0.35	0.68	H	92	−0.84	1.6	H	150	−1.04	6.96	C61
35	−0.23	0.69	H	93	−0.02	1.7	H	151	−0.79	7.01	N40
36	−0.59	0.69	H	94	−0.70	1.76	H	152	−0.78	7.02	N40
37	−0.54	0.70	H	95	−0.36	1.65	H	153	−1.09	7.13	C61
38	−0.85	0.70	H	96	−0.99	1.62	H	154	−0.13	7.31	N40
39	−0.74	0.77	H	97	−0.72	1.87	H	155	−1.26	7.62	C61
40	−0.48	0.79	H	98	−0.23	1.95	H	156	−1.20	7.75	C61
41	−0.99	0.79	H	99	−0.41	1.92	H	157	−1.90	8.51	C61
42	−0.57	0.79	H	100	−1.19	1.96	H	158	−0.63	8.47	N40
43	−0.62	0.79	H	101	0.21	1.96	H	159	−0.96	9.36	C61
44	−0.11	0.79	H	102	−0.28	2.01	H	160	−1.17	10.97	N40
45	−0.44	0.79	H	103	−0.33	2.05	H	161	−2.33	11.04	C61
46	−0.66	0.80	H	104	−0.94	2.05	H	162	−0.83	12.38	C61
47	0.02	0.83	H	105	−0.45	2.05	H	163	−1.14	12.4	C61
48	−0.19	0.85	H	106	−0.90	2.06	H	164	−1.09	13.85	C61
49	−0.38	0.89	H	107	−0.58	2.07	H	165	−1.00	15.64	C61
50	−0.47	0.90	H	108	−0.55	2.14	H	166	−1.00	18.75	C61
51	−1.02	0.93	H	109	−0.86	2.15	H	167	−1.18	18.81	C61
52	−1.25	0.95	H	110	−0.46	2.17	H	168	−1.10	53.9	C61
53	−0.47	0.98	H	111	−0.07	2.19	H	169	−0.94	71	C61
54	0.05	0.98	H	112	−0.64	2.21	H	170	−1.41	30.02	C61
55	−0.67	0.98	H	113	−0.57	2.23	H	171	−1.06	31.25	C61
56	−0.31	1.01	H	114	−0.80	2.29	N40	172	−1.19	100	C61
57	−1.28	1.02	H	115	−0.64	2.37	H	173	−1.20	48	C61
58	−0.37	1.02	H	116	−0.35	2.41	H	174	−1.40	78	C61

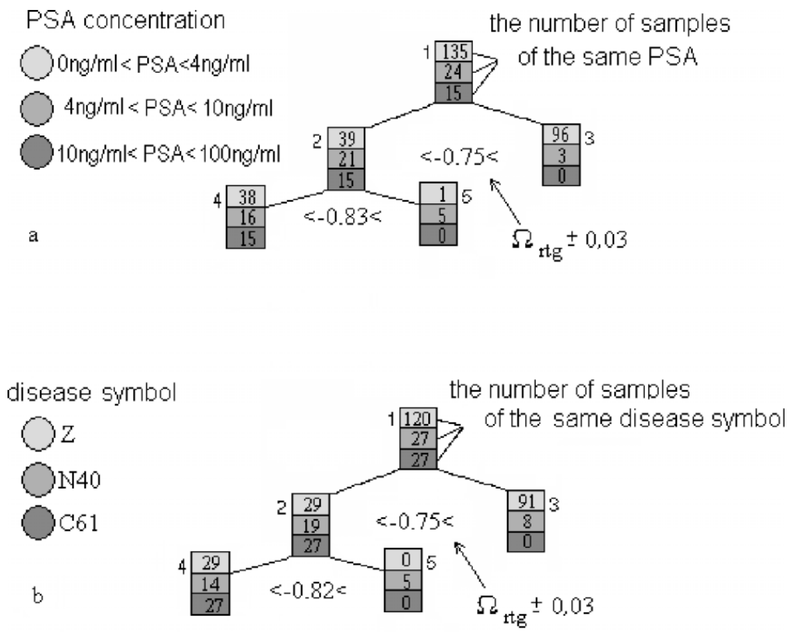

Figure 5. A scheme of the classification trees – the ordering variable is Ω_{rtg} and the dependent variables are (a) PSA level and (b) diagnosis expressed by the disease symbol.

Table 2. The percent of samples studied for which $\Omega_{rtg} < -0.75$.

Dependent variable		Percent of samples with $\Omega_{rtg} < -0.75$
PSA (ng/mL)	0–4	29
	4–10	88
	10–100	100
Disease symbol	H	24
	N40	70
	C61	100

6. Conclusions

It has been established that changes in the blood serum caused by development of neoplasmic condition can be detected early by the X-ray method. The results of the X-ray method study are sensitive to changes in the angular distribution of the scattered radiation intensity in a certain angular range and can be expressed by the newly defined X-ray marker Ω_{rtg}.

The X-ray method giving the marker value is simple and cheap relative to the other diagnostic methods, so it seems promising in medical diagnosis. For the X-ray marker to become of common use and supply reliable information, it is still required to perform similar analyses on a greater number of patients. In future the method can be automated and preliminary diagnosis could be reached within 30 min.

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References

[1] D. Bernal, P. Fowler, *J. Chem. Phys.*, **1**, 515 (1933).
[2] S. Katzoff, *J. Chem. Phys.*, **2**, 841 (1934).
[3] J. Morgan, B.E. Warren, *J. Chem. Phys.*, **6**, 666 (1938).
[4] M.D. Danford, H.A. Levy, *J. Am. Chem. Soc.*, **84**, 3965 (1962).
[5] C.A. Villee, *Biology*, W.B. Saunders, Philadelphia, PA (1977).
[6] F. Kokot, S. Kokot, *Laboratory Analysis, the Standards and Interpretation*, PZWL Warszawa (1997).
[7] S. Angielski, *Clinical Biochemistry and Chemical Analysis*, PZWL Warszawa (1990).
[8] A. Mikusińska-Planner, M. Surma, *Spectrochimica Acta,* Part *A* **56**, 1835 (2000).
[9] J. Gągalska, A. Mikusińska-Planner, *Phys. Chem. Liq.*, **41**, 133 (2003).
[10] A. Mikusińska-Planner, J. Gągalska, *Phys. Chem. Liq.*, **14**, 155 (2003).
[11] R.K. Murray, D.K. Granner, P.A. Mayes, V.W. Rodwell, *Harper's Biochemistry*, translated from English issue 22 and 23, as *Biochemia Harpera*, F. Kokot (Ed.), Copyring for the Polish Edition by PZWL., Warszawa (1964).
[12] J.L. Kavanau V, *Water and Solute Water Interactions*, Holden-Day, San Francisco (1964).
[13] A. Christenson, C.B. Laurell, H. Lilija, *Eur. J. Biochem.*, **194**, 755 (1990).
[14] T.A. Stamey, *Urology*, **45**, 173 (1995).
[15] M. Macyszyn, *Medical Hand-book*, PWL Warszawa (2002).
[16] J.E. Osterling, *Hematol. Oncol. Clin. N. Amer.*, **8**, 555 (1994).
[17] T.A. Stamey, N. Yang, A.R. Hay *et al.*, *New. Engl. J. Med.*, **317**, 909 (1987).
[18] U.H. Stenman, J. Leinonen, W.H. Zhang, *Eur. J. Clin. Chem. Clin. Biochem.*, **34**, 735 (1996).
[19] J. Zhang, N. Leoninen, B. Kalkkinen, U.H. Dowell, *Clin. Chem.*, **41**, 1567 (1995).
[20] Statistica software Inc. Statistica, Version 6 (2003).