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Study of Trace Element Concentrations in Breast Cancer by Neutron Activation Analysis

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Abstract: ***Trace elements are major components of biological structures; however, excessive levels of these elements can be toxic. This study was performed to investigate the influence of cancer of selected trace elements among Egypt patients with confirmed breast cancer. Instrumental Neutron Activation Analysis (INAA) using short and long term irradiation has been employed to determine five minor elements (C1, K, Na, Mg, Al, Br) and 9 trace elements (Se, Zn, Co, Cr, Cs, Rb, Sc, Sr, and Fe) in cancerous and normal breast tissue from 10 patients. The National Cancer Institute of Egypt submits us with 10 samples from 10 patients in the age range 30-65 years are given blood samples breast and one sample from a random person to estimate the concentration values of Na, Al, K, Mn, Mg, Br and Cl. The pneumatic irradiation rabbit system (PIRS) built into the vertical thermal column of the ET-RR-2. The reactor is used for short time irradiation at constant power. Elemental concentrations were estimated from measurements of the gamma-ray spectra of the product short-lived isotopes in the samples. The obtained concentration was calculated using the relative method. The effect of age on chemical element contents in intact breast of 10 apparently healthy 30–65 years was investigated by neutron activation analysis with high resolution spectrometry of short-lived radionuclides. Mean values (SD± Mean) for content (mg/kg, dry weight basis) of chemical elements were: Br–18.84 ± 12.05,As–20.84 ± 17.85, Cl–2.74 ± 2.75, K–1.80 ± 1.85,Co-0.92 ± 0.05,Cs-1.92 ± 1.75,Sc-8.14 ± 5.45,Cr-0.98 ± 1.45,Se-2.04 ± 1.45,Fe-72.34 ± 65.25, Mg–1.25 + 0.47, Mn–0.44 ± 0.10, and Na-3.98 ± 1.75,respectively. A tendency of age-related increase in Na content and decrease in Mn content was observed.***

Keywords: Neutron activation analysis, Trace elements, Breast cancer

1. Introduction

Cancer has recently become one of the most obsessing issues in the world, since both its incidence and impact on the world economy has become enormously huge. This life-threatening disease in its many forms has affected a lot of human lives since it not only disturbs the physical and physiological function of the human cells, but also its effects extend to seriously damage the patient's quality of life breast cancer is a potentially life-threatening malignancy that develops in one or both breasts [1].

For breast cancer many risk factors were reported, namely gender, age, genetic risk factor family history, personal history, abnormal breast biopsy, breast radiation and menstrual periods. The Technique is rapid multi-element analysis of biological samples, which related to medical problems without chemical treatment [2- 4]. This paper gives some information about the change in elementary levels in blood samples of some patients suffering from breast cancer diseases [5- 7].

Comparator Method is based on the simultaneous irradiation of the sample with standards of known quantities of the elements in question in identical positions, followed by measuring the induced intensities of both the standard and the sample in a well-known geometrical position.

A relative standardization can be performed by means of individual mono element standards, or by using synthetic or natural multielement standards. The calculation of the unknown quantity (m) is made according to Equation.

$$m = \frac{I}{I_{sp}}, \quad I_{sp} = \frac{N_{p,st}}{S_{st} \cdot D_{st} \cdot C_{st} \cdot m_{st}};$$

$$I = \frac{N_p}{S \cdot D \cdot C}$$

Trace elements are classified as essential or nonessential, according to whether an organism can grow and complete its life cycle in their absence. Even for essential elements there is always an optimum range of concentration in the diet, below which deficiency symptoms such as stunting of growth occur, and above which symptoms of toxicity begin. There are three main functions for the trace elements, namely inorganic or structural, electrochemical, catalytic and some other unknown functions and miscellaneous [8-10].

2. Methods and Materials

Collection and Preparation of the Blood Samples

This study was carried out on paired samples of 10 breast cancer patients aged 30-65 yr About 15-20 mg of blood samples of different patients suffering from breast cancer were drawn from the patient's at the National Cancer Institute, Egypt and inserted in clean polyethylene vials. The samples were put on ice and then in the refrigerator until the beginning of sample irradiation.

3. Equipments

The pneumatic irradiation rabbit system (PIRS) built into the perpendicular thermic column of the ET-RR-2 reactor

(Inshas, Egypt) was used for short irradiation time. A blood sample was irradiated for a period of for 6m, 10 m, 2 h, 6 h, 1 d and 2 d at 20MW reactor ET-RR-2. Several biological tissue SRMs such as Bovine Liver (1577a) and Oyster Tissue (1566a) from National Institute of Standards and Technology (NIST) US, and Animal Muscle (H-4) from IAEA (Vienna) were used. The measurements of gamma-ray spectra are carried out with P-type coaxial, EG&G Oretic HPGe cylinder with 100% relative efficiency, 1.9 KeV FWHM at 1.3325 MeV of ^{60}Co. Various radionuclides were identified by their characteristic gamma ray energy and half life in case of short lived nuclides. Two random blood samples from the persons are collected, irradiated and it used to test the technique by compare′counting as well as the patients.

4. Results and Discussion

In Table 1 reports the nuclear constants of the elements of interest in the present work photo peak to calculate the efficiency of the detector as a function of ɣ -ray energy. The elemental concentration of one blood sample from a random person is calculated using short irradiation neutron activation technique. Elemental concentrations were calculated using synthetic comparator standard. In some cases, however, SRMs were also used as comparators.

Table 1: Photo peak efficiency of the detector as a function of γ -ray energy

Element	*Efficiency %*	*Gamma abundance %*	*Gamma energy Kev*	*T1/2*	*Isotopic abundance %*	*Barn*	*Nuclear Reaction*
Na	0.246	100	1368.6	14.959 h	100	0.513	23Na(n,ɣ)24Na
Mg	0. 0.318371	71.4 28.6	843.8 1014.4	9.458 m	11.01	0.0372	26Mg(n,ɣ)27Mg
Al	0.193	100	1778.9	2.24 m	100	0.226	27Al(n,ɣ)28Al
Cl	0.208	32.5	1642.4	37.21 m	24.23	0.423	37Cl(n,ɣ)38Cl
Ca	0.0996	91.7	3084.4	8.719 m	0.187	1.12	48Ca(n,ɣ)49Ca
Mn	0.37 0.189	98.9 27.2	846.8 1810.7	2.578 h	100	13.2	55Mn(n,ɣ) 56Mn

Mean concentrations of 10 elements in SRMs along with their certified values are given in Table 2. A comparison of our data with the certified values shows that most elemental concentrations are in agreement within _+10%.

Also, relative standard deviations in most cases are<10%, suggesting a high order of precision. Therefore, it is presumed that all elemental concentrations in tissue samples should be accurate within ±10% and only variations of >20% will be considered for attributing the causative effects.

Table 2: Elemental Concentrations in Biological Standard Reference materials; Values in parenthesis are certified

Elements	*Animal muscle CRM H-4*	*Bovine liver SRM 1577a*	*Oyster tissue SRM 1566a*
Na (mg/g)	2.22 ± 0.16	2.27 ± 0.16	4.17 ± 0.13
K (mg/g)	(16.1 ± 0.58)	(9.96 + 0.07)	7.90± 0.47
Mg (mg/g)	1.03 ± 0.39	0.74 ± 0.11	1.25 ± 0.47
Mn (µg/g)	0.5 ± 0.1	10.4± 1.1	5.9 ± 0.8
Br (µg/g)	4.8 ± 0.5	10.5 ± 2.2	46.5 ± 5.0
Cl (mg/g)	1.84 ± 0.12	2.91 ± 0.18	7.75 ± 0.35
As (ng/g)	6.0 ± 1.0	50 ± 10	--
Co (ng/g)	--	(210 ± 50)	(570 ± 110
Cs (µg/g)	0.09 ± 0.02	0.29 ± 0.03	--
Sc (ng/g)	12.0 ± 2.1	1.5 ± 0.3	51.0 ± 9.0
Rb (µg/g)	18.0 ± 3.1	12.0 ± 0.92	3.47 ± 0.33
Cr (µg/g)	0.52 ± 0.09	0.36 ± 0.08	1.23 ± 0.29
Zn (µg/g)	81.4 ± 7.6	132.0 ± 13.0	799 ± 57
Se (µg/g)	0.63 ± 0.09	0.70 ± 0.06	2.24 ± 0.26
Fe (µg/g)	51.1 _+ 9.1	191 ± 2	485 ± 45

Elemental concentrations and mean values along with standard deviations for normal and cancerous tissues of 10 patients are listed in Table 3. Variations of elemental concentrations showing enhancement or depression with the clinical stage are shown in Figs. 1, 2 and 3. Since all these elements are vital for various biological and enzymatic processes [11- 12].

It has been proposed that minerals of these elements taken as nutrients and food components may accelerate/retard carcinogenic activity, possibly through antioxidant effects in conjunction with antioxidant vitamins.

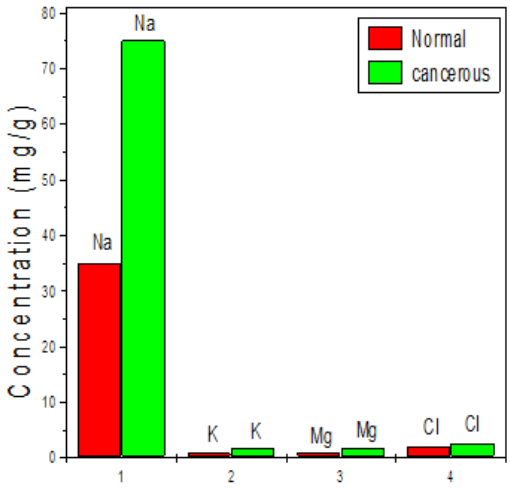

Fig. 1. Comparison of Na, K and Cl concentrations in paired samples of cancerous and normal breast tissues in 10 patients

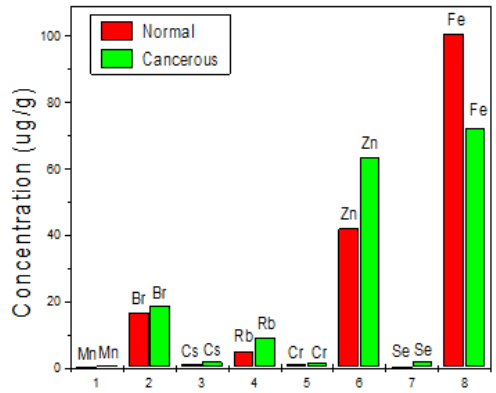

Fig. 2. Comparison of Mn, Br, Cs, Rb, Cr, Zn, Se and Fe concentrations in paired samples of cancerous and normal breast tissues in 10 patients

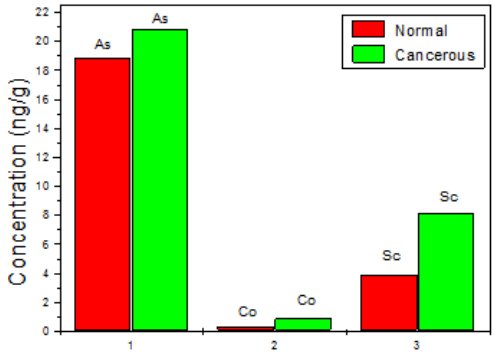

Fig. 3. Comparison of As, Sc and Co concentrations in paired samples of cancerous and normal breast tissues in 10 patients

Elemental concentrations along with standard deviations for normal and cancerous tissues of 10 patients are listed in Table 3. In order to correlate elemental concentrations with the clinical stage of the cancer, mean values for carcinogenic toxic or otherwise significantly important nine elements (As, Br, Co, Cr, Fe, Mn, Rb, Se, and Zn) in normal and cancerous tissues for four stages were calculated.

Histographic variations of elemental concentrations showing enhancement or depression with the clinical stage are shown in Figs. 1, 2 and 3. Several elements, such as Cr, Cd, Fe, Se, and Zn have been under intense scrutiny since they influence carcinogenesis in laboratory animals and humans. It has been proposed that minerals of these elements taken as nutrients and food components may accelerate/retard carcinogenic activity possibly through antioxidant effects in conjunction with antioxidant vitamins Manganese is considered as least toxic to mammals but industrial workers exposed to dust and fumes from mining and smelting may face poisoning characterized by psychiatric disorder. It concentrates in tissues rich in mitochondria but it can also penetrate the blood-brain barrier. It has been suggested that Mn concentration in human tissue remains constant through homeostatic mechanism.

Table 3: Comparison of Elemental concentrations in paired samples of cancerous and normal breast tissue of 10 patients

Normal n=30		*Cancerous n=30*
Elements	*Mean±SD*	*Mean±SD*
Na (mg/g)	2.84 ± 1.35	3.98 ± 1.75
K (mg/g)	0.94 ± 1.45	1.80 ± 1.85
Mg (mg/g)	1.04 ± 0.45	1.74 ± 0.65
Mn (µg/g)	0.54 ± 0.15	0.44 ± 0.10
Br (µg/g)	16.84 ± 10.15	18.84 ± 12.05
Cl (mg/g)	2.14 ± 1.95	2.74 ± 2.75
As (ng/g)	18.84 ± 11.25	20.84 ± 17.85
Co (ng/g)	0.34 ± 0.15	0.92 ± 0.05
Cs (µg/g)	1.24 ± 1.15	1.92 ± 1.75
Sc (ng/g)	3.89 ± 2.45	8.14 ± 5.45
Rb (µg/g)	5.04 ± 1.45	9.12 ± 1.45
Cr (µg/g)	1.24 ± 1.45	0.98 ± 1.45
Zn (µg/g)	42.04 ± 17.15	63.44 ± 28.95
Se (µg/g)	0.61 ± 0.25	2.04 ± 1.45
Fe (µg/g)	100.84 ± 112.45	72.34 ± 65.25

Several elements, such as Fe, Cr, and Mn, all have been considered essential for various biochemical functions in humans. We observed that Fe and Cr concentrations are depressed in cancerous tissue by 35%, whereas Mn is depressed only marginally by 15 Present studies suggest that some elements are incorporated into the normal cell, resulting in blockage of cell metabolism and thus affecting metabolic functions of the body system. In this process, the reduplication of neoplastic growth is enhanced. Inhibition of enzymatic activity by the cancerous cell may induce variation in trace element concentrations resulting into immunological breakdown causing fast dissemination of malignancy in stage IV.

5. Conclusion

Neutron activation analyses employing short and long irradiations and possibly radiochemical procedures sometimes permit the determination of more than 15 elements in normal and cancerous breast tissue. Several minor and trace elements show a definite pattern of enhancement or depression in cancerous tissue, which further depends on the clinical stage of the cancer, suggesting their positive role in the growth of tumor. Considered as a useful method for the determination of trace element concentrations in a variety of matrices such as environmental samples as more accurate and precise

method. The previous methods to analyze liquid samples by using reactor irradiation were carried by immersing a nomination paper by the sample, but in the present work, freezing of samples helps us to keep blood samples for a long time and re irradiation for some other time and overcome the background due to nomination papers. The increasing awareness of the role of trace elements and their interactions in metabolic activities and neoplastic growth has emphasized the need for multielemental micro analytical methods. On the other hand, the short time irradiation and the use with small amounts of biological material 20 mg, reducing the radiation exposure. These experimental techniques using whole blood can be very useful for clinical practices. Which it involves a large number of samples or quantitative analyses of several times. Concentrations of high-Value such as Na, Cl, K showed that it is possible to establish units within the hospitals, which can use closed neutron sources for such analysis. Such studies may be useful to assess the diagnostic and therapeutic aspects.

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