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Investigation of heavy trace elements in neoplastic and non-neoplastic human thyroid tissue: A study by proton – induced X-ray emissions

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ABSTRACT

Background: Within the context of developing techniques to facilitate the diagnosis of the thyroid diseases, the elemental composition of pathological thyroid tissue (neoplastic and non-neoplastic) was investigated by proton induced X-ray emission. The PIXE has been widely used as a sensitive technique for trace elemental analysis in both biological and medical fields.
Materials and Methods: The twenty-eight specimen of thyroid tissue (neoplastic, non-neoplastic and grossly normal tissue) were obtained from operation of 14 patients with different thyroid diseases. Determination of the heavy trace elements distribution (Fe, Co, Ni, Cu, Zn, As, Se, Br, Rb, Mo, I) was carried out by irradiating of the sample surface with a focused proton beam.
Results: Fourteen grossly normal, eleven non-neoplastic and three malignant thyroid neoplasm cases were diagnosed. Trace element contents of the International Atomic Energy Agency (IAEA) MA-B-3/TM Fish tissue was used as standard for calibration of PIXE set up.
Conclusion: The concentration of the heavy trace elements Co, Cu, Zn and Mo in neoplasm of thyroid were higher than other samples. The concentration of the heavy trace elements, Fe, As, Br, Rb, I, are found to be much lower in neoplasm of thyroid than non–malignant and grossly normal thyroid tissue. The concentration of the Se, Co and I in this study is consistent with the others study but there are differences in the concentration of Fe in our study and others works. Iodine concentrations was 11 times lower, on average in neoplasm compared with non-neoplasmic tissue of thyroid. The low levels of I in thyroid neoplasm are correlated to some pathological factors. *Iran. J. Radiat. Res., 2004; 1(4): 211-216*

Keywords: *Thyroid neoplasm, trace element, PIXE analysis.*

INTRODUCTION

The determination of trace elements in human body fluids and tissues has been the subject of numerous investigations (Vatankhah *et al.* 2003). The trace elements, absorbed by the body enter the digestion system, pass through gastrointestinal tract and are deposited in the liver by blood stream.Then, they are carried to different organs from the liver to participate in biochemical reactions.

Usually, the ions of trace elements act as coordination centers to build up the structure of enzymes or proteins (Lindh 1995). Thus, when the concentrations of the trace elements in the body differ from the normal values, many clinical and pathological disorders arise. Low levels of Zn were reported in the human breast malignant tissue (Vatankhah *et al.* 2003), and cancer of kidney (Uda *et al.* 1987). Low ratio of Zn/Mo in urine is also one of the important indication of kidney cancer (Uda *et al.*1987). Decrease in level of serum Zn could be used as a criterion for assessing the severity of bronchogenic carcinoma (Zeng *et al.*1987).

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Direct toxic heavy metal influence on thyrocytes plays a major role in thyroid cancer etiology (Zaichick *et al.* 1995). Thus, the estimation of trace elements and their concentrations in different biological systems shows a promise of becoming a diagnostic tool for monitoring health .

The method of Proton Induced X-ray Emission (PIXE) has been widely used as a technique for trace element analysis in both biological and medical fileds. Further more, it has also been used to determine the elemental distribution profiles in hairs, breast and others tissue, simply by scanning the sample surface with a focused proton beam (Salimi *et al.* 2003). Several authors have reported that PIXE technique has great potential in the estimation of trace elemental concentrations in biological samples (Reddy *et al.* 2002).

The aim of this work is to quantitatively analyze the heavy trace elemental distribution (Mn, Fe, Cu, Zn) in neoplastic, non-neoplastic and grossly normal human thyroid tissue by PIXE method and to compare their results. Irradiating of the sample surface with a focused proton beam carries out this work.

MATERIALS AND METHODS

Sample preparation

The twenty-eight specimen of thyroid tissue (malignant, benign and grossly intact tissue) were obtained from operation of 14 patients with different thyroid disease. Two specimens were taken from each patient, one from grossly pathologic tissue and other one from grossly normal tissue. Fourteen normal, eleven non-malignant diseases and three neoplastic cancer cases were diagnosed.

A thin film of carbon spray coated the samples to make them conductive. These samples were analyzed without any further process as a thick target. IAEA MA-B-3/TM Fish tissue was used for calibration of PIXE set up. The standard target was prepared by pressing 250 mg of powdered standard into a pellet (1.7 cm in diameter) without any addition.

Equipment and measurement

The samples were bombarded using a 3.0 MeV van-de-Graff accelerator at nuclear research center of Atomic Energy Organization of Iran for the PIXE measurement. In the PIXE technique, measurements were carried out in vacuum (10^{-6} torr) with a 2.0 MeV energy proton beam whose spot size is 0.28 cm^2. The Samples were placed at an angle of 90° with respect to the incident beam. Beam currents were around 5nA in order to keep the counting rate below 1000 cps, and the integrated beam current (using a charge integrator in the setup) was 10 µC for each measurement.

Characteristics of X-rays were emitted from the target and detected by a Si (Li) detector at 135°. A 175 µm-thick Mylar absorber was positioned in front of the detector in order to decrease the intense low energy X-rays originating from the low Z elements, while the light elements were detected without absorber. The energy resolution of detector is 175eV at 5.9 keV. The solid angle was limited to be $3.3e^{-3}$ sr that is corrected by one of the available calibration techniques- chosen from amongst the wide variety of techniques for thick specimens using small number of trace elements in standard and known samples (e.g. calculated calcium concentration in the IAEA standard fish tissue serves as a good reference).

Since the spectrums of low Z elements and high Z elements without filter and with Mylar filter were taken in separate run; then, according to sensitivity of detector for calcium and Fe elements for both spectrum sensitivity curve of si (Li) detector in this region are almost flat. Then those two elements were chosen to compare two PIXE spectrum for specific samples. By using this approach and charge correction two spectrums were matched.

RESULTS AND DISCUSSION

The twenty-eight specimen of thyroid tissue (neoplastic, non-neoplastic and grossly normal tissue) were obtained from operation of 14 patients with different thyroid disease. Fourteen grossly normal, 11 non-neoplastic and 3 malignant thyroid neoplasm cases were diagnosed. Determination of the heavy trace elements distribution (Fe, Co, Ni, Cu, Zn, As, Se, Br, Rb, Mo, I) was carried out by PIXE methods.

The PIXE spectrum analysis was performed using the nonlinear least square fitting code AXIL and GUPIX. Data obtained from the computer program were net peak areas of K & L X-Ray; errors are coming from counting statistics and values for the background. Table1 shows the maximum, minimum, mean value, standard deviation (SD) of detected heavy trace elements in neoplastic, non-neoplastic and grossly normal tissue. The absolute and relative analysis is performed for a thick target. All elements from Z=21-53 with high and low value of concentration are expressed in ppm and all elements from z=13-20 are expressed in percent. Figures 1-3 show the typical PIXE spectrum of human thyroid tissues in this study.

Table 1. Type of thyroid tissue and concentration of heavy trace elements.

Type		**Fe**	**Co**	**Ni**	**Cu**	**Zn**	**As**	**Se**	**Br**	**Rb**	**Mo**
	Min	85	0	0	0	28	0	0	0	0	0
Normal	Max	2072	141	13	280	283	173	2310	832	631	764
	Mean	611	17.6	2.93	38	205	22	189	71	73.4	129
	SD	175	10.2	1.14	20	51	15	170	61	47.7	73.2
	Min	137	0	0	0	0	0	0	0	0	0
Non-Neoplasm	Max	9735	56	64	155	682	166	353	387	1740	743
	Mean	1212	15.7	4.92	30	224	17	43.5	44	216	128
	SD	764	5.57	5.12	13	59	13	28.9	32	136	74.3
	Min	166	0	0	0	29	0	0	0	0	0
Neoplasm	Max	723	49	14	0	54	7	181	79	0	0
	Mean	362	23.6	4.66	0	42	2.3	60.3	40	0	0
	SD	227	17.4	5.71	0	9.7	2.9	73.9	28	0	0

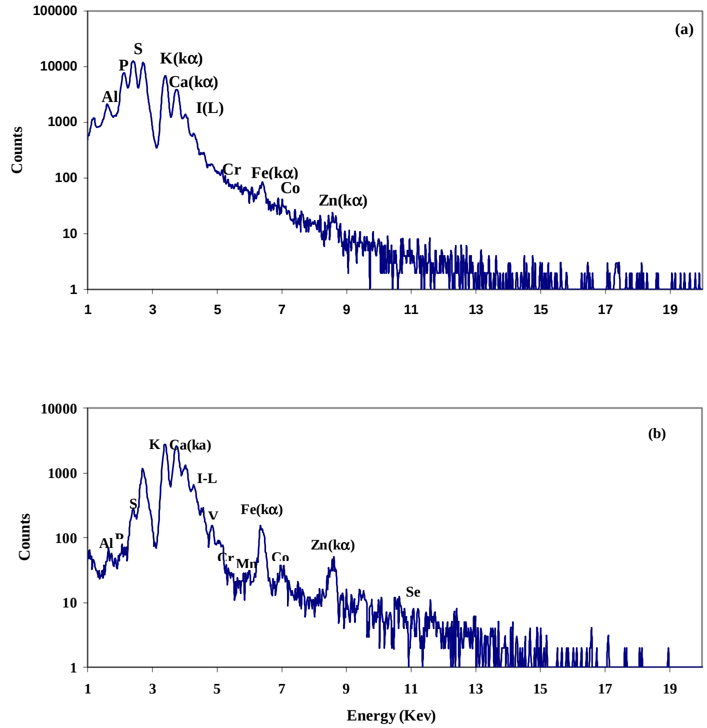

Figure 1. Pixe spectra taken from para-nodular normal tissue of thyroid: (a) without filter and (b) with a 175mm Mylar filter.

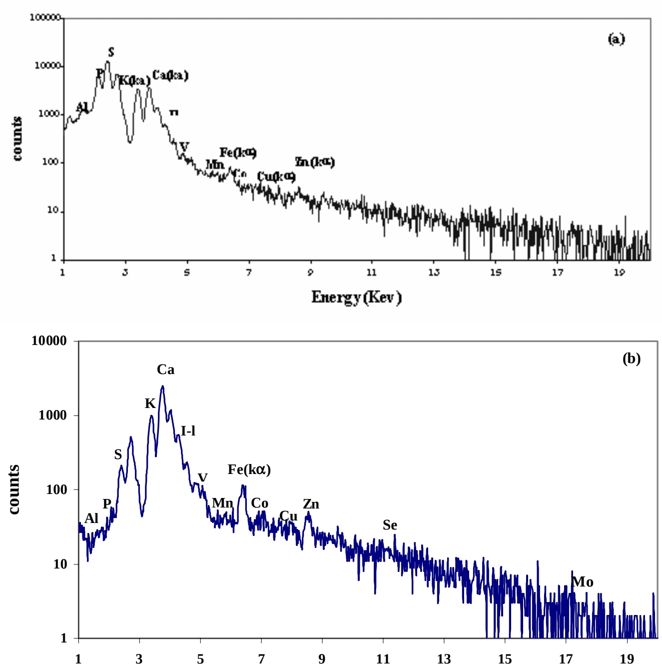

Figure 2. Pixe spectra taken from neoplasmic tissue of thyroid: (a) without filter and (b) with a 175mm Mylar filter.

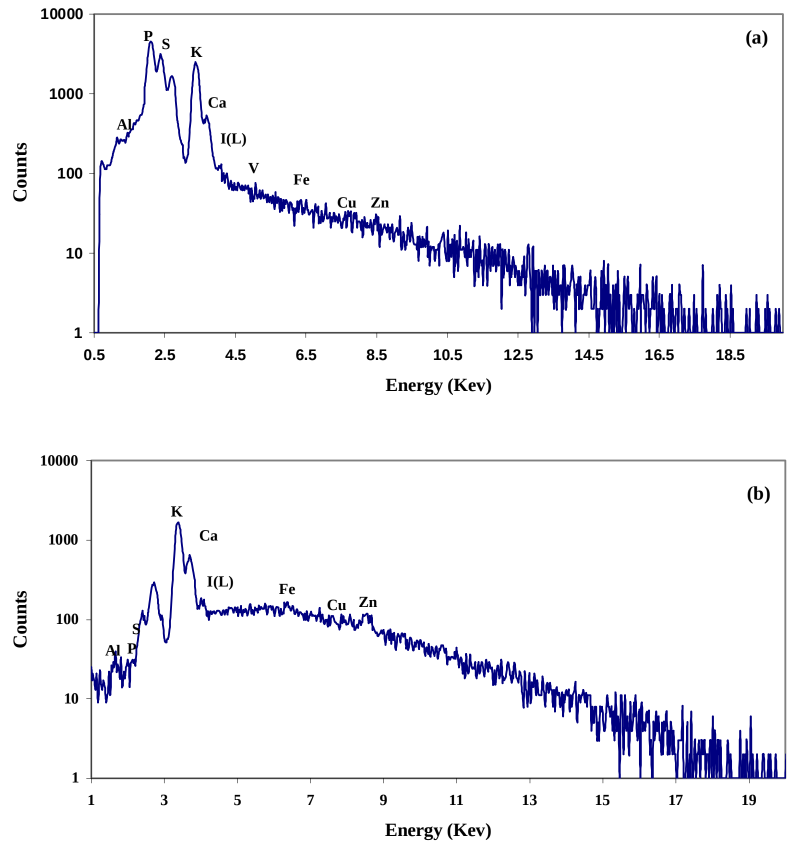

Figure 3. Pixe spectra taken from non-neoplasmic tissue of thyroid: (a) without filter and (b) with a 175mm Mylar filter.

In neoplastic tissue ,the mean value of heavy trace elements Co, Cu, Zn, Mo were greater than non-neoplastic and paranodular normal tissue.The mean value of Fe, As, Br, Rb, I was lower than others tissue.

In non-neoplastic tissue, the mean value of heavy trace elements Fe, Ni, Rb, were greater and mean value of Co, Cu, Se, Mo was lower than neoplastic and normal paranodular tissue, respectvely.

In paranodular normal tissue, the mean value of As, Se, Br, I were greater than neoplastic and non-neoplastic tissue and heavy trace elements Ni, Zn were lower than others tissue respectively .

In our study, the concentration of the elements Co, I in normal and thyroid neoplasm is consistent with the concentration observed by other works (Reddy *et al.* 2002, Zaichick *et al.* 1995).We observed lower levels of Fe in neoplasm compared to the normal but one study reported higher levels of Fe and another work reported the same as our results (Reddy *et al.* 2002, Maeda *et al.* 1987).

Inorganic Iodine is absorbed by gland and is used in the production of hormones known as thyroxin and triiodothyronine. These hormones are involved in cellular oxidation, growth, reproduction and the activity of the central and autonomic nervous system. The functioning of the gland may be known from the uptake test of iodine. Zaichick by using the instrumental neutron activation analysis reported Iodine concentrations are 15 times lower, on average, in malignant compared with benign nodules and the ratio between the iodine concentration in nodular and paranodular tissue can be used for *invivo* thyroid cancer diagnostics (Zaichick *et al.* 1995).

Tadros by using X-ray fluorescence and Reddy by PIXE methods reported that the iodine concentration in cancer is lower than that in normal (Reddy *et al.* 2002). The results of our study indicate the similar trend and iodine concentrations were 11 times lower in neoplasm of thyroid compared to non-neoplasm and normal tissues.

CONCLUSION

The concentration of the heavy trace elements Co, Cu, Zn and Mo in carcinoma of thyroid are higher than other samples. High level of Fe, Ni and Rb were observed in non-neoplasm tissue, and grossly normal tissue contains high level of As, Se, Br and I. The concentration of the Se, Co and I in this study is consistent with the other study but there are differences in the concentration of Fe in our study and others, works.

The results of the study have demonstrated that in patients with neoplasm of thyroid there is a significant decrease in concentration of heavy trace elements Fe, As, Br, Rb and I in thyroid trssue. Iodine concentrations are 11 times lower, on average in neoplasm compared with non-neoplasmic tissue of thyroid. The low levels of I in thyroid neoplasm are correlated to some pathological factors.

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