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Determination of iodine concentration in aqueous solutions by proton activation analysis: preliminary results for digested human thyroids

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Abstract The aim of our studies is to check the possibilities of using proton activation analysis as a competitive method over other analytical techniques applied for iodine determination. It is well known that long-term irradiation of biological samples leads to their decomposition and formation of gaseous radiolysis products, which increase the pressure inside the sample container. In case of using proton beam another problem with liquid samples appears. It is the production of ^{7}Be via spallation reactions ^{16}O(p, spall)^{7}Be. The Compton effect from ^{7}Be γ-line increases the detection limits for isotopes with low-energy γ-lines. AIC-144 cyclotron at The Niewodniczański Institute of Nuclear Physics Polish Academy of Science can accelerate protons up to energy of 60 MeV which is sufficient for (p,5n) reaction needed to obtain ^{123}I ($T_{1/2} = 13.27$ h, $E\gamma = 159$ keV, $I = 83\%$) from stable ^{127}I, thus the Compton effect from ^{7}Be was the main factor perturbing the analysis. Separation and removal of ^{7}Be is required to improve the detection limit. The paper presents a method and an example of its application to the determination of iodine concentration in digested fragments of human thyroids obtained during surgical treatment of patients with different types of thyroid tumor.

Keywords Proton activation analysis · Iodine determination · Iodine concentration · ^{123}I · Human thyroid · Beryllium separation

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Introduction

Proton activation analysis is a well known analytical technique useful for performing both qualitative and quantitative multielemental analysis of major, minor and trace elements without or with chemical separation. Charged particle activation analysis (CPAA), essentially due to its inherent complexity, has predominant applications in the determination of light elements inaccessible to neutron activation analysis (NAA). Nevertheless, after appropriate optimization procedures, proton activation analysis can be highly effective in simultaneous quantitative determination of medium-heavy trace elements in biological samples [1]. Samples, which come under irradiation, usually are pulverized and formed into a small disc. In case of biological samples in principle routinely lyophilization is applied. This procedure ensures the homogeneity of studied material and facilitates dissolution, especially if the analysis is performed using radiochemical separation of activation products. There are at least two reasons why the application of the freeze-dried samples is reasonable. Firstly, it is well known that long-term irradiation of biological samples leads to their decomposition and formation of gaseous radiolysis products such as H_2, H_2O_2 and O_2 which increase the pressure inside the sample container approximately proportionally to the sample mass

and radiation doses [2]. It requires implementation of some cooling system. Another problem arises in case of using proton beam and liquid samples. It is the production of ^{7}Be via spallation reactions ^{16}O(p, spall)^{7}Be [3]. The Compton effect from this isotope ($T_{1/2} = 53.12$ d, $E\gamma = 478$ keV, $I = 10.52\%$) substantially increases the background in analyzed γ-spectrum and simultaneously the detection limits (LLD) for isotopes with low-energy γ-lines. However, these two impediments can be eliminated through the application of relatively small beam currents during the irradiation and subsequent radiochemical separation of beryllium. The purpose of this work is to show the possibility of using proton activation analysis as a competitive method over other analytical techniques applied routinely for iodine determination in biological samples, especially in human thyroids. So far, from a technical point of view, iodine has been determined in thyroids using neutron activation analysis (NAA) [4–9], X-ray fluorescent analysis (XRF) [9–12] and the spectroscopic method based on the Sandell–Kolthoff reaction [13, 14]. All this methods have their strengths but on the other hand they grapple with some problems. The mean values of total thyroid iodine content and its concentrations vary greatly. The iodine level in the thyroid depends on iodine intake and function of the thyroid. Hou et al. [15, 16] have reported the concentration of iodine in normal human thyroid of ca. 1 mg/g wet mass and 0.2–7.2 mg/g dry mass in samples from China and Belarus.

Experimental

Sample preparation

Selected fragments of human thyroids were collected during a surgical treatment of patients with different types of thyroid tumor (total or near total thyroidectomy)—who presented to the 3rd Department of General Surgery Collegium Medicum Jagiellonian University (Kraków, Poland)—and kept frozen at −20 °C until analysis. Thyroid samples were weighted and dried in a vacuum dryer for about 2 days to obtain a dry mass. Afterward, they were homogenized in agate mortar, transferred into a 7 mL polypropylene vial and weighted again. Digestion of samples and certified reference materials was performed using 5 mL 3 M potassium or lithium hydroxide together with the application of ultrasonic cleaner and vortex before the irradiation. All employed reagents of analytical grade were purchased from POCH (Poland). Standard reference materials were obtained from the National Institute of Standards and Technology (NIST), USA. A working standard solution with 1.0 µg iodine (in I^{-} form) per mL was prepared by dissolving high purity KI with deionized water. 5 mL of above iodine solution was used as a comparative standard solution. The accuracy of the method was also planned to be checked by analyzing the oyster tissue (1566a and b) and sea lettuce (BCR 279) certified reference material, because there are no thyroid gland or similar tissue certified reference materials commercially available with certified iodine content. Radiochemical separation of beryllium was used after irradiation and was based on ion-exchange chromatography as follows: digested samples were put into a glass container with ice. They were neutralized by adding 2 M HNO_3 and then acidified to pH < 2 with 0.1 M HNO_3. Such prepared samples were passed through a small polyethylene cation exchange column (7 mm in diameter, 30 mm in height). The resin (BE Resin (DIPEX™, 100–150 mesh) purchased from Eichrom, USA) in the column was previously purified by 0.1 M HNO_3. After loading, the column was washed with 20 mL of 4 M HNO_3 to remove beryllium.

Instruments

AIC-144 isochronous cyclotron designed and constructed at The Niewodniczański Institute of Nuclear Physics Polish Academy of Science can accelerate protons up to energy of 60 MeV (internal proton current in the range of a dozen nA) [17]. Due to the application of the rotating target holder, samples and standards situated in plastic vials have been irradiated simultaneously for 2.5–5 h. The rotating target holder [19] supporting up to eight samples were mounted at the end of beam line. As the disk rotates, each sample was brought in front of the beam spot, just for the time resulting from the rotation speed (about 60 rpm). An external beam current during the irradiation was in the range 25–40 nA, however it was not needed to determine it precisely since the irradiation of samples and standards were done in the same average activation field assured by rotation of targets. Measurements were performed after about 13 h of the cooling time and lasted from 1 to 8 h. In this study gamma spectra were collected using ultra-low level gamma spectrometric system [18] consisting of High Purity Germanium (HPGe) detector with aluminium free cryostat. The shield consist of active (a multiwire proportional chamber) and passive shield (from outside—10 cm of paraffin, 10 cm of standard lead, 2 mm cadmium, 5 cm of 2,500 year old lead, 1 cm of pure copper). Spectrometer was calibrated using multi-isotopic source FP 40/10 (POLATOM, Poland) which has the same geometrical properties as measured samples. The nuclear parameters of the radioisotopes measured in this work are summarized in Table 1. In sample activity calculations necessary corrections for decay and counting times were applied.

Table 1 The nuclear parameters of the main radioisotopes measured in this work

Reaction	Half life	Emitted gamma-lines (keV)	Intensity (%)
^{127}I(p,5n)^{123}Xe	2.08 h	149.90	49
$^{123}\text{Xe} \xrightarrow{\beta^+} {}^{123}\text{I}$	13.27 h	158.97	83
^{16}O(p, spall)^{7}Be	53.12 days	477.60	10.52

The half-lifes of produced radionuclides and the energy of the gamma-lines chosen for detection are taken from Lund/LBNL Nuclear Data Search

Results and discussion

It was confirmed, that our proton beam was sufficient for (p,5n) reaction needed to obtain ^{123}I ($T_{1/2}$ = 13.27 h) from stable ^{127}I. ^{123}I produced as a result of the decay of ^{123}Xe nuclei can be detected using high resolution gamma-ray spectrometer (HPGe detector). Since we used a proton beam which energy is higher than typically used in proton activation analysis we actually manage with mixed radiation field during the irradiation. Consequently, apart from ^{123}I, we could observe a formation of ^{126}I ($T_{1/2}$ = 13.11 days) as a product of neutron activation of ^{127}I [(n,2n) reaction].

Determination of iodine using conventional instrumental proton activation analysis is critically limited by strong matrix radioactivities of ^{7}Be so that after irradiation post-irradiation separation has to be used to eliminate these interferences. Our set-up was tested using KI solutions in the range from 10^{-1} to 10^{-7} M. Sample preparation, irradiation and measurements conditions are described elsewhere [19].

The concentration of iodine in samples was calculated comparing the intensities of the lines deriving from standard solution. The results as well as the experimental conditions for each irradiation of human thyroid are given in Table 2. The mean value of iodine concentration in analyzed samples amounted to 0.590 ± 0.301 (SD) mg/g. Figure 1 shows gamma-ray spectra of an activated sample of the thyroid X13 before and after separation of ^{7}Be.

To investigate the origin of observed 159 keV gamma line the measurements were repeated several times. It eliminated unambiguously the possibility of interference coming from ^{47}Sc ($T_{1/2}$ = 3.35 days) which is a product of the activation of calcium. Figure 2 presents the results of these measurements for sample X13. The sensitivity of presented technique was also checked in these experiments calculating the detection limits as 4.65 times background area, as defined by Currie [20].

SRM 1566a and b (Oyster tissue) which were originally chosen for data validation turned out to be not appropriate in our experimental conditions because of the activation of iron which leads to the formation of ^{52}Fe ($T_{1/2}$ = 8.28 h, $E\gamma$ = 168.69 keV, I = 89.2%). Application of these standard reference materials requires not only a removal of ^{7}Be but also ^{52}Fe, which on the other hand causes the losses of other, important elements, which are also of our interest. That is why we finally decided to use BCR 279 (Sea lettuce)—certificate reference material with considerably higher iodine content in comparison with iron content—for the validation of the presented method. The concentration of iodine in this certificate reference material was found 154 ± 13 mg/kg (mean ± standard deviation), which is in very good agreement with the indicative value 151 ± 6 mg/kg.[1]

The human thyroids were easy to digest completely, since only a small volume of 3 M KOH or LiOH was required with the ultrasonic cleaner treatment. A vacuum dryer can be used interchangeably with a freeze dryer because no losses of elements of interests during sample preparations have been observed.

In such irradiation conditions, as presented above, there were no significant problems with emerging gaseous products and any cooling system associated with the rotating target holder was not needed. However, application of such system could reduce the costs of analysis since it would allow us to use higher beam currents and reduce irradiation times. At present the minimal duration of irradiation cannot be shorter than 2 h while the beam current exceeds 25 nA. The Compton effect from ^{7}Be is the main factor perturbing the analysis even when ultra-low level gamma spectrometric system with HPGe detector is used. Separation and removal of ^{7}Be can significantly improve the detection limit due to reducing of the Compton continuum. It can be done by using Eichrom BE Resin which is highly effective in this radiochemical procedure. The only factor which can somewhat decrease the accuracy of this method is the loss of iodine during this radiochemical procedures when sample is transferred from one container to another one.

To summarize, this pilot study on application of proton activation analysis to determination of iodine in thyroid samples yielded some drawbacks and hence also practical suggestions for future studies. The advantages of the method are as follows: (1) the irradiation conditions need not be reproducible or presumptive as samples and standards, situated in the rotating target holder, are irradiated simultaneously; this technique compensates also for errors owing to geometry with an overall gain in quality; (2) time of irradiation (2.5–5 h) and cooling time (13 h) are relatively short which provides satisfactory analytical

[1] http://www.irmm.jrc.be/html/reference_materials_catalogue/catalogue/attachements/BCR-279_report.pdf.

Table 2 Results of the determination of iodine concentrations in analyzed thyroids by gamma-spectrometry

Sample ID	Sex	Age	Irradiation time (h)	Beam current (nA)	Sample weight (mg)	Iodine concentration (mg/g) in dry tissue
X29	F	48	4.50	25	35.4 ± 0.1	0.891 ± 0.060
X13	F	51	5.00	25	73.0 ± 0.1	0.637 ± 0.071
Y1	M	68	2.50	30	52.3 ± 0.1	0.494 ± 0.029
X8	F	75	4.33	30	37.7 ± 0.1	0.802 ± 0.072
X19	F	37	4.33	30	40.4 ± 0.1	0.125 ± 0.040

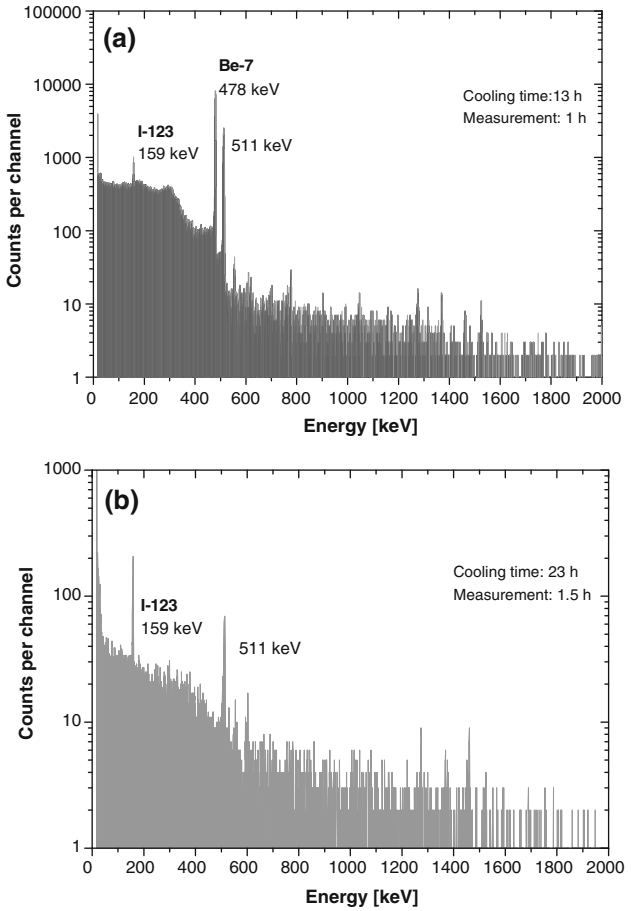

Fig. 1 Gamma-ray spectra of an activated sample of the thyroid X13 before (**a**) and after (**b**) separation of ^{7}Be

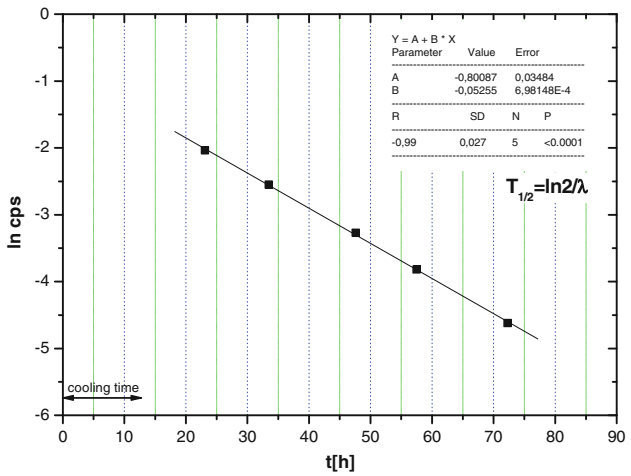

Fig. 2 Decline in the activity of ^{123}I in analyzed human thyroid X13. Statistical errors were smaller than the point dimension and therefore not shown

throughput; (3) despite greatly different matrix composition, the iodine concentration obtained for CRM showed no significant bias; (4) sample pretreatment is relatively short and easy; (5) detection limit of iodine (10^{-6} M) is sufficiently low and ensures reliable measurements in thyroids; (6) instrumental proton activation analysis is sufficient for these samples where the concentration of iodine is 10^{-6} M (and higher). Disadvantages: (1) the main problem is matrix interference caused by ^{7}Be, and the need to use radiochemical separation for its elimination; (2) the detection limit is still too high for more demanding analyses, e.g. determination of iodine in serum for diagnostic purposes; however, lower detection limits could be achieved with slightly longer irradiation and counting times and improvement of ^{7}Be elimination; (3) the availability of proper certified material containing iodine is limited.

At present, we are investigating the possibilities of iodine determination, but other trace elements (Se, Cu, Zn, Fe, Rb, Br, Sr) are also considered for future studies. In principle, this method should be applicable to other real samples originating e.g. from experiments on animals conducted to assess the impact of different diets and stress conditions on element redistribution in the organism.

Conclusions

We presented relatively new alternative approach for the determination of iodine in biological samples, but this is only initial work, and not a ready-to-use method, with many areas still needing improvements. Although preliminary results obtained for iodine are promising, further experiments are needed to conduct full validation procedure and check the applicability of this method to the determination of other elements.

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