Comprehensive Research and Reviews in
Medicine and Dentistry
Journal homepage: https://crrjournals.com/crrmd/
ISSN: 2961-3647 (Online)

(Research Article)

Age dependence of iodine to some trace element content ratios in normal thyroid of females investigated by neutron activation and inductively coupled plasma mass spectrometry

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Comprehensive Research and Reviews in Medicine and Dentistry, 2022, 01(01), 020–031

Publication history: Received on 28 July 2022; revised on 05 September 2022; accepted on 08 September 2022

Article DOI: https://doi.org/10.57219/crrmd.2022.1.1.0018

Abstract

Thyroid diseases rank second among endocrine disorders, and prevalence of the diseases is higher in the elderly as compared to the younger population. An excess or deficiency of trace element (TE) contents in thyroid play important role in goitro- and carcinogenesis of gland. The correlations between age and thirty-eight TE, including I, as well as between age and I/TE content ratios in normal thyroid of 33 females (age range 3.5-87 years) was investigated by two methods: instrumental neutron activation analysis and inductively coupled plasma mass spectrometry. Our data reveal that the Co, Cs, La, Pb, Rb, Sb, Se, Sn, Tl, and Zn contents increase, while I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl, I/Zn content ratios decrease in the normal thyroid of female during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive Co, Cs, La, Pb, Rb, Sb, Se, Sn, Tl, and Zn level in the thyroid of old females, as well as a disturbance in intrathyroidal I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl, I/Zn relationships with increasing age may be assumed.

Keywords: Thyroid; Trace elements; Age-related changes; Neutron activation analysis; Inductively coupled plasma mass spectrometry

1 Introduction

According to the World Health Organization (WHO), thyroid diseases rank second among endocrine disorders after diabetes mellitus. More than 665 million people in the world have endemic goiter or suffer from other thyroid pathologies. Women are affected by thyroid diseases almost ten times more often than men. At the same time, according to the same statistics, the increase in the number of thyroid diseases in the world is 5% per year [1]. It has been suggested that risk factors for the development of thyroid disorders may be numerous factors, including genetics, radiation, autoimmune diseases, as well as adverse environmental factors, such as an increase in the content of various chemicals in the environment [2].

Trace elements (TE) are among these various chemicals, because their levels in the environment have increased significantly over the past hundred years as a result of the industrial revolution and the tremendous technological changes that have taken place in metallurgy, chemical production, electronics, agriculture, food processing and storage, cosmetics, pharmaceuticals and medicine. In connection with these changes, the levels and ratio of TE entering the human body from the outside have been significantly disturbed, compared with the conditions in which human societies have lived for many millennia.

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More than 50 years ago, we formulated the postulate about the somatic TE homeostasis, which is now generally recognized [3]. According to this postulate, under evolutionary environmental conditions, the mechanisms of homeostasis of organisms maintain the levels and ratios of TE in tissues and organs within certain limits. If the content of TE in the environment changes significantly, the mechanisms of somatic homeostasis may respond inadequately. Inadequate response of homeostasis mechanisms leads to changes in TE levels in tissues and organs, which, in turn, can affect their function and lead to the development of pathological conditions. The correctness of this conclusion was illustrated by us earlier on the example of the study of the role of TE in the normal and pathophysiology of the prostate [4-24]. It was shown, in particular, that a special role in the development of pathological transformations of the prostate is played by disturbances in the relationship between TE in the tissue and gland secretion. Moreover, it was found that changes in the relationship between TE can be used as highly informative markers of various prostate diseases, including malignant tumors [25-40]. These findings stimulated our investigations of TE relationships in thyroid tissue in normal and pathological conditions.

There are many studies regarding TE content in human thyroid, using chemical techniques and instrumental methods [41-64]. However, among the published data, no works on the relationship of TE in the normal human thyroid were found.

This work had three aims. The primary purpose of this study was to determine reliable values for the Ag, Al, B, Be, Bi, Cd, Ce, Co, Cr, Cs, Dy, Er, Fe, Ga, Gd, Hg, I, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Sn, Tb, Ti, Tl, U, Y, and Zn mass fractions in the normal thyroid of subjects ranging from children to elderly females using instrumental neutron activation analysis (INAA) combined in consecutive order with destructive inductively coupled plasma mass spectrometry (ICP-MS) and calculate individual values of I/Ag, I/Al, I/B, I/Be, I/Bi, I/Cd, I/Ce, I/Co, I/Cr, I/Cs, I/Dy, I/Er, I/Fe, I/Ga, I/Gd, I/Hg, I/La, I/Li, I/Mn, I/Mo, I/Nb, I/Nd, I/Ni, I/Pb, I/Pr, I/Rb, I/Sb, I/Sc, I/Se, I/Sm, I/Sn, I/Tb, I/Ti, I/Tl, I/U, I/Y, and I/Zn. The second aim was to compare thirty eight TE mass fractions in thyroid gland obtained in the study with published data. The final aim was to estimate the correlations between age and TE contents, as well as between age and I/TE content ratios in normal thyroid of females.

All studies were approved by the Ethical Committees of the Medical Radiological Research Centre, Obninsk. All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments, or with comparable ethical standards.

2 Material and methods

Randomly selected tissue samples of the thyroid gland were obtained from autopsies of 33 practically healthy residents (European-Caucasian nationality) of the Obninsk city, who died suddenly. The age of the deceased women ranged from 3.5 to 87 years. The main causes of sudden death were injuries in car accidents. Several women have died from suicide, alcohol poisoning, stroke, acute heart failure, and pulmonary embolism. Autopsies were carried out in the forensic medical examination department of the city hospital. In the anamnesis of the deceased women there were no chronic diseases, as well as medications or nutritional supplements that affect the development and function of the thyroid gland,

Thyroid tissue samples were taken from the right lobe of the gland using a titanium scalpel [65] and divided into two parts. One part was subjected to histological examination in order to confirm compliance with the age norm, as well as to exclude the presence of microadenomas and latent cancer. The second part was intended to determine the content of TE in it.

Thyroid tissue samples were delivered frozen to the Medical Radiological Research Center, where they were weighed and stored at -20°C. Subsequently, all samples were lyophilized and homogenized [66]. To determine the contents of the TE by comparison with a known standard, aliquots of commercial, chemically pure compounds were used [67]. Ten subsamples of the Certified Reference Material (CRM) produced by the International Atomic Energy Agency (IAEA) IAEA H-4 (Animal Muscle) and IAEA HH-1 (Human Hair), as well as Polish CRM INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs were analyzed to estimate the precision and accuracy of results. The CRM subsamples were prepared in the same way as the samples of dry homogenized thyroid tissue.

The content of I was determined by INAA using short irradiation in a horizontal channel equipped with the pneumatic rabbit system of the WWR-c research nuclear reactor in Obninsk. The neutron flux in the channel was 1.7×10^{13}n cm^{-2} s^{-1}. A vertical channel of nuclear reactor WWR-c with a neutron flux of 1.3×10^{13} n×cm^{-2}×s^{-1} was applied to determine the content of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn by long irradiation. Details of sample preparation and used nuclear reactions, induced radionuclides, gamma-energies and semiconductor spectrometry were presented in our earlier publications concerning TE contents in human scalp hair [68,69]. After non-destructive INAA investigation the thyroid samples were decomposed in autoclaves and used for ICP-MS. The content of Ag, Al, B, Be, Bi, Cd, Ce, Co, Cr, Cs, Dy, Er, Fe, Ga, Gd, Hg, I, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Se, Sm, Sn, Tb, Ti, Tl, U, Y, and Zn was determined by ICP-MS using an ICP-MS Thermo-Fisher "X-7" Spectrometer (Thermo Electron, USA). The TE concentrations in aqueous solutions were determined by the quantitative method using multi elemental calibration solutions ICP-MS-68A and ICP-AM-6-A produced by High-Purity Standards (Charleston, SC 29423, USA). Indium was used as an internal standard in all measurements. Information detailing with the ICP-MS methods used and other details of the analysis was presented in our previous publication concerning TE contents in human prostate [70-73].

A dedicated computer program for INAA mode optimization was used [74]. All thyroid samples were prepared in duplicate, and mean values of TE contents were used in final calculation. The main statistical characteristics of the TE content and the I/TE content ratio of. such as the arithmetic mean, standard deviation, standard error of the mean, minimum and maximum values, median, percentiles with levels of 0.025 and 0.975 were found using Microsoft Office Excel. Pearson's correlation coefficient was used in Microsoft Office Excel to calculate the relationship "age – TE mass fraction" and "age – I/TE mass fraction".

3 Results

Table 1 depicts the similarity of the means of the Ag, Co, Cr, Fe, Hg, Rb, Sb, Se, and Zn mass fractions in the normal thyroid of female determined by both INAA and ICP-MS methods.

Table 1 Comparison of the mean values (M±SEM) of the chemical element mass fractions (mg/kg, on dry-mass basis) in the normal thyroid of females obtained by both INAA -LLR and ICP-MS methods

Element	INAA -LLR M_1	ICP-MS M_2	Δ, %
Ag	0.0140±0.0020	0.0129±0.0041	7.9
Co	0.0505±0.0064	0.0479±0.0069	5.1
Cr	0.573±0.049	0.496±0.057	13.4
Fe	232±22	217±19	6.5
Hg	0.0389±0055	0.0471±0.0087	-21.1
Rb	6.16±0.48	6.38±0.53	-3.6
Sb	0.116±0.012	0.098±0.014	15.5
Se	2.22±0.23	2.16±0.23	0.5
Zn	85.7±7.4	83.2±8.1	2.9

M – arithmetic mean, SEM – standard error of mean, $\Delta=[(M_1 - M_2)/M_1] \cdot 100\%$.

Table 2 Some statistical parameters of 38 trace element mass fraction (mg/kg, dry mass basis) in the normal thyroid of female

Element	M	SD	SEM	Min	Max	Median	P 0.025	P 0.975
Ag	0.0132	0.0092	0.0020	0.0016	0.0331	0.0121	0.00225	0.0321
Al	7.43	4.49	1.24	2.50	17.2	5.50	2.77	16.6
B	0.418	0.257	0.074	0.200	1.00	0.315	0.200	0.890
Be	0.00067	0.00089	0.00028	0.00010	0.0031	0.00035	0.00010	0.00261
Bi	0.0180	0.0300	0.0084	0.00100	0.100	0.0070	0.00106	0.0902
Cd	1.63	1.73	0.48	0.0110	5.84	1.18	0.0443	5.21
Ce	0.00897	0.00785	0.00227	0.00140	0.0253	0.00590	0.00195	0.0251

Co	0.0493	0.0332	0.0066	0.0160	0.140	0.0380	0.0166	0.130
Cr	0.535	0.254	0.051	0.233	1.22	0.456	0.270	1.11
Cs	0.0185	0.0105	0.0029	0.0022	0.0368	0.0182	0.00289	0.0360
Dy	0.00173	0.00328	0.00095	0.00030	0.0121	0.00084	0.00030	0.00913
Er	0.00050	0.00057	0.00017	0.00010	0.00220	0.00032	0.00013	0.00181
Fe	225	98	20	52.0	435	199	64.2	391
Ga	0.0309	0.0209	0.0060	0.0100	0.0810	0.0285	0.0100	0.0725
Gd	0.00147	0.00174	0.00048	0.00040	0.00650	0.00090	0.00040	0.00560
Hg	0.0400	0.0274	0.0057	0.0070	0.100	0.0310	0.0125	0.100
I	1956	1199	219	114	5061	1562	309	4662
La	0.00550	0.00368	0.00106	0.00100	0.0118	0.00450	0.00128	0.0117
Li	0.0153	0.0078	0.0024	0.00150	0.0251	0.0152	0.00300	0.0250
Mn	1.32	0.84	0.22	0.550	4.04	1.10	0.603	3.28
Mo	0.0755	0.0608	0.0169	0.0104	0.252	0.0567	0.0150	0.217
Nb	0.641	0.722	0.200	0.0130	2.21	0.336	0.0130	2.00
Nd	0.0046	0.0042	0.0012	0.00054	0.0165	0.0035	0.00086	0.0139
Ni	0.385	0.192	0.056	0.200	0.890	0.310	0.211	0.810
Pb	0.200	0.110	0.032	0.0230	0.450	0.185	0.0442	0.406
Pr	0.00123	0.00102	0.00028	0.00020	0.00390	0.00090	0.00029	0.00345
Rb	6.27	2.43	0.48	1.21	12.8	6.30	2.50	30.8
Sb	0.107	0.066	0.013	0.0115	0.248	0.090	0.0183	0.247
Sc	0.0086	0.0158	0.0046	0.00020	0.0570	0.00340	0.00034	0.0453
Se	2.19	1.17	0.23	0.320	5.32	2.07	0.745	4.85
Sm	0.00057	0.00046	0.00013	0.00010	0.00140	0.00043	0.00012	0.00140
Sn	0.112	0.093	0.026	0.00900	0.263	0.0621	0.0165	0.260
Tb	0.00020	0.00015	0.00004	0.00008	0.00060	0.00018	0.00009	0.00052
Ti*	3.74	4.20	1.16	0.440	13.6	2.30	0.521	12.8
Tl	0.00070	0.00036	0.00010	0.00010	0.00130	0.00072	0.00016	0.00125
U	0.00060	0.00069	0.00020	0.00010	0.00260	0.00033	0.00012	0.00219
Y	0.00304	0.00282	0.00082	0.00100	0.0110	0.00190	0.00100	0.00930
Zn	84.5	38.9	7.6	7.30	166	83.5	23.0	156

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level, *scalpel made od Ti was used in sample preparation

Tables 2 and 3 represents the main statistical characteristics of the TE mass fractions and of the I/TE mass fraction ratios in normal thyroid of females, respectively.

Table 3 Some statistical parameters of iodine/trace element mass fraction ratios in the normal thyroid of female

Ratio	M	SD	SEM	Min	Max	Median	P 0.025	P 0.975
I/Ag	224504	182005	40698	63689	746875	159136	66916	624859
I/Al	290	208	60	16.3	786	252	26.4	721
I/B	5230	3662	1057	193	14143	3887	557	12322
I/Be	5690275	4768244	1507851	444194	15040000	4142500	1026750	14756500
I/Bi	457046	486287	140379	7770	1377000	313179	9357	1314117
I/Cd	12736	35568	10268	324	125273	946	380	93587
I/Ce	294503	267166	80554	25333	984286	221176	27992	850378
I/Co	51329	33339	6952	7125	137235	41417	7380	123168
I/Cr	4305	2404	501	160	10425	4125	825	8926
I/Cs	154799	176393	50920	25333	626364	74768	27297	542343
I/Dy	2430361	1827158	527455	87692	5303750	1965806	113735	5108385
I/Er	5500119	4325967	1248799	495652	13780000	4553788	635222,8	13198375
I/Fe	11.2	10.2	2.1	2.19	47.0	8.53	2.38	36.1
I/Ga	68612	48865	14106	11400	151536	53653	13952	147758
I/Gd	2086317	1421041	410219	285000	4243000	2267361	299998	4110175
I/Hg	73558	63246	13801	3677	241000	62636	6388	223000
I/La	463210	392348	118297	17538	1378000	355000	32433	1227917
I/Li	201731	269484	85218	12391	918667	96069	17968	774775
I/Mn	1524	878	235	161	3214	1243	182	2999
I/Mo	35718	37426	10804	4419	132500	19662	5044	117355
I/Nb	42530	80234	23162	852	260307	3150	912	220538
I/Nd	652639	698276	201575	71250	2551852	466439	84156	2187764
I/Ni	4651	2630	793	190	9643	3760	790	9055
I/Pb	15306	18800	5668	633	59913	7650	980	55542
I/Pr	2151295	1887095	544758	190000	6890000	1716318	242021	6101414
I/Rb	350	235	48	73,5	811	250	85.4	807
I/Sb	20484	11240	2294	5328	46626	18085	7010	43461
I/Sc	2417541	4137026	1247360	26158	13150000	569048	36069	11670000
I/Se	1075	884	180	180	3903	928	232	3430
I/Sm	4832810	4353189	1312536	407143	13780000	3342222	467857	13251250
I/Sn	37039	43377	12522	1052	153111	22547	2057	131158
I/Tb	10128072	6147451	1774616	1140000	21215000	10965834	1617889	20117750
I/Ti*	1194	1118	323	17.0	3422	871	42.9	3342
I/Tl	3823630	4076128	1228999	237500	13780000	1512658	455564	12279167
I/U	4528971	2840999	820126	407143	7776667	5047143	528611	7774834

I/Y	744338	437931	126420	81429	1378000	773500	114211	1377725
I/Zn	28.9	23.8	4.86	5.66	109	22.7	6.28	93.2

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level, *scalpel made od Ti was used in sample preparation

The comparison of our results with published data for contents of all TE in the human thyroid determined in the present study is shown in Table 4.

Pearson's correlation coefficients in Tables 5 and 6 estimate the effect of age on the TE contents and I/TE content ratios, respectively.

Table 4 Median, minimum and maximum value of means of trace element contents in the normal thyroid according to data from the literature in comparison with our results (mg/kg, dry mass basis)

Element	Published data [Reference]			This work
	Median of means (n)*	**Min of means M or M±SD, (n)****	**Max of means M or M±SD, (n)****	**M±SD**
Ag	0.25 (12)	0.000784 (16) [41]	1.20±1.24 (105) [42]	0.0132±0.0092
Al	33.6 (12)	0.33 (-) [43]	420 (25) [44]	7.43±4.49
B	0.151 (2)	0.084 (1) [49]	0.46 (1) [49]	0.418±0.257
Be	0.042 (3)	0.000924(16) [41]	<0.12 (-) [48]	0.00067±0.00089
Bi	0.126 (4)	0.0339 (16) [41]	<0.4 (-) [48]	0.0180±0.0300
Cd	1.68 (20)	0.12 (131) [45]	47.6±8.0 (16) [50]	1.63±1.73
Ce	0.22 (1)	0.22 (59) [41]	0.22 (59) [41]	0.00897±0.00785
Co	0.306 (25)	0.016 (66) [51]	70.4±40.8 (14) [52]	0.0493±0.0332
Cr	0.69 (17)	0.088 (83) [53]	24.8±2.4 (4) [46]	0.535±0.254
Cs	0.066 (6)	0.0112±0.0109 (14) [54]	0.109±0.370 (48) [55]	0.0185±0.0105
Dy	0.00106 (1)	0.00106 (60) [41]	0.00106 (60) [41]	0.00173±0.00328
Er	0.00068 (1)	0.00068 (60) [41]	0.00068 (60) [41]	0.00050±0.00057
Fe	252 (21)	56 (120) [56]	3360 (25) [44]	225±98
Ga	0.273 (3)	<0.04 (-) [48]	1.7±0.8 (-) [57]	0.0309±0.0209
Gd	0.00256 (1)	0.00256 (59) [41]	0.00256 (59) [41]	0.00147±0.00174
Hg	0.08 (13)	0.0008±0.0002 (10) [47]	396±40 (4) [46]	0.0400±0.0274
I	1888 (95)	159±8 (23) [58]	5772±2708 (50) [59]	1956±1199
La	0.068 (3)	0.052 (59) [41]	<4.0 (-) [48]	0.00550±0.00368
Li	6.3 (2)	0.092 (-) [48]	12.6 (180) [60]	0.0153±0.0078
Mn	1.62 (40)	0.076 (83) [53]	69.2±7.2 (4) [46]	1.32±0.84
Mo	0.40 (11)	0.0288±0.0096 (39) [47]	516±292 (14) [52]	0.0755±0.0608
Nb	<4.0 (1)	<4.0 (-) [48]	<4.0 (-) [48]	0.641±0.722
Nd	0.0108 (1)	0.0108 (60) [41]	0.0108 (60) [41]	0.0046±0.0042
Ni	0.44 (19)	0.0084 (83) [53]	33.6±3.6 (4) [46]	0.385±0.192
Pb	0.58 (25)	0.021 (83) [53]	68.8±6.8 (4) [46]	0.200±0.110

Pr	0.0034 (1)	0.0034 (59) [41]	0.0034 (59) [41]	0.00123±0.00102
Rb	7.8 (9)	≤0.85 (29) [47]	294±191 (14) [52]	6.27±2.43
Sb	0.15 (10)	0.040±0.003 (-) [61]	≤12.4 (-) [48]	0.107±0.066
Sc	0.009 (4)	0.0018±0.0003 (17) [62]	0.0135±0.0045 (10) [47]	0.0086±0.0158
Se	2.32 (21)	0.436 (40) [63]	756±680 (14) [52]	2.19±1.17
Sm	0.00216 (1)	0.00216 (60) [41]	0.00216 (60) [41]	0.00057±0.00046
Sn	0.67 (7)	0.0235 (16) [41]	-≤3.8 (17) [64]	0.112±0.093
Tb	0.000224 (1)	0.000224 (60) [41]	0.000224 (60) [41]	0.00020±0.00015
Ti	1.42 (8)	0.084 (83) [53]	73.6±7.2 (4) [46]	3.74±4.20
Tl	<0.2 (2)	0.00138 (16) [41]	<0.4 (-) [48]	0.00070±0.00036
U	0.0060 (11)	0.00014 (66) [51]	0.428±0.143 (10) [47]	0.00060±0.00069
Y	<2.9 (2)	0.00225 (16) [51]	≤5.9 (17) [64]	0.00304±0.00282
Zn	110 (56)	2.1 (-) [43]	820±204 (14) [52]	84.5±38.9

M –arithmetic mean, SD – standard deviation, Min – minimum, Max – maximum, (n)* – number of all references, (n)** – number of samples.

4 Discussion

A good agreement of our results for the Ag, Al, B, Be, Bi, Cd, Ce, Co, Cr, Cs, Dy, Er, Fe, Ga, Gd, Hg, I, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Sn, Tb, Ti, Tl, U, Y, Zn mass fractions with the certified values of CRM IAEA H-4 (Animal Muscle), IAEA HH-1 (Human Hair), INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs [68-73] as well as the similarity of the means of the Ag, Co, Cr, Fe, Hg, Rb, Sb, Se, and Zn mass fractions in the normal thyroid of female determined by both INAA and ICP-MS methods (Table 1) demonstrates an acceptable precision and accuracy of the results obtained in the study and presented in Tables 2-6.

Table 5 Correlations between age (years) and trace element mass fractions (mg/kg, dry mass basis) in the normal thyroid of female (r – coefficient of correlation)

Element	**Ag**	**Al**	**B**	**Be**	**Bi**	**Cd**	**Ce**	**Co**	**Cr**	**Cs**
r	0.15	0.46	0.26	-0.25	0.26	0.26	0.44	0.56[b]	0.31	0.50[a]
Element	**Dy**	**Er**	**Fe**	**Ga**	**Gd**	**Hg**	**I**	**La**	**Li**	**Mn**
r	0.06	0.07	0.26	0.38	0.19	-0.08	0.08	0.59[a]	0.45	0.16
Element	**Mo**	**Nb**	**Nd**	**Ni**	**Pb**	**Pr**	**Rb**	**Sb**	**Sc**	**Se**
r	0.39	0.32	0.29	0.05	0.74[b]	0.34	0.60[c]	0.51[b]	-0.39	0.50[b]
Element	**Sm**	**Sn**	**Tb**	**Ti**	**Tl**	**U**	**Y**	**Zn**		
r	0.47	0.55[a]	0.18	0.23	0.62[a]	0.14	0.15	0.65[c]		

Statistically significant values: [a] $p \leq 0.05$, [b] $p \leq 0.01$, [c] $p \leq 0.001$.

The content of TE was determined in all or most of the examined samples, which made it possible to calculate the main statistical parameters: the mean value of the mass fraction (M), standard deviation (SD), standard error of the mean (SEM), minimum (Min), maximum (Max), median (Med), and percentiles with levels of 0.025 (P 0.025) and 0.975 (P 0.975), of the Ag, Al, B, Be, Bi, Cd, Ce, Co, Cr, Cs, Dy, Er, Fe, Ga, Gd, Hg, I, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Sn, Tb, Ti, Tl, U, Y, and Zn mass fractions (Table 2), as well as I/Ag, I/Al, I/B, I/Be, I/Bi, I/Cd, I/Ce, I/Co, I/Cr, I/Cs, I/Dy, I/Er, I/Fe, I/Ga, I/Gd, I/Hg, I/La, I/Li, I/Mn, I/Mo, I/Nb, I/Nd, I/Ni, I/Pb, I/Pr, I/Rb, I/Sb, I/Sc, I/Se, I/Sm, I/Sn, I/Tb, I/Ti, I/Tl, I/U, I/Y, and I/Zn mass fraction ratios (Table 3) in normal thyroid of females. The values of M, SD, and SEM can be used to compare data for different groups of samples only under the condition of a normal distribution of the results of determining the content of TE in the samples under study. Statistically reliable identification of the law of distribution of results requires large sample sizes, usually several hundred samples, and therefore is rarely used in biomedical research. In the conducted study, we could not prove or disprove the “normality” of the distribution of the results obtained due to the insufficient number of samples studied. Therefore, in addition to the M, SD, and SEM values, such statistical characteristics as Median, range (Min-Max) and percentiles P 0.025 and P 0.975 were calculated, which are valid for any law of distribution of the results of TE content in thyroid tissue.

Table 6 Correlations between age (years) and iodine/trace element mass fraction ratios in the normal thyroid of female (r – coefficient of correlation)

Element	**I/Ag**	**I/Al**	**I/B**	**I/Be**	**I/Bi**	**I/Cd**	**I/Ce**	**I/Co**	**I/Cr**	**I/Cs**
r	-0.28	-0.39	-0.24	-0.19	-0.52	-0.74[b]	-0.70[a]	-0.33	-0.14	-0.62[a]
Element	**I/Dy**	**I/Er**	**I/Fe**	**I/Ga**	**I/Gd**	**I/Hg**	**I/La**	**I/Li**	**I/Mn**	**I/Mo**
r	-0.45	-0.41	0.21	-0.53	-0.18	0.40	-0.72[a]	-0.72[a]	0.27	-0.69[a]
Element	**I/Nb**	**I/Nd**	**I/Ni**	**I/Pb**	**I/Pr**	**I/Rb**	**I/Sb**	**I/Sc**	**I/Se**	**I/Sm**
r	-0.02	-0.66[a]	-0.25	-0.67[a]	-0.67[a]	-0.19	-0.31	0.06	-0.21	-0.60
Element	**I/Sn**	**I/Tb**	**I/Ti**	**I/Tl**	**I/U**	**I/Y**	**I/Zn**			
r	-0.69[a]	-0.29	-0.36	-0.66[a]	-0.21	-0.42	-0.40[a]			

Statistically significant values: [a] $p \leq 0.05$, [b] $p \leq 0.01$, [c] $p \leq 0.001$.

Values obtained for Al, B, Cd, Cr, Cs, Dy, Er, Fe, Gd, Hg, Mn, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Sc, Se, Sm, Tb, Ti, and Zn contents in the normal human thyroid (Table 4) agree well with median of mean values reported by other researches [41-64]. The obtained means for Ag, Co, Mo, Sn, Y, and U were almost one-three orders of magnitude lower median of previously reported means but inside the range of means (Table 4). The mean obtained for Be, Bi, Ce, Ga, La, Li, and Tl were also one-three orders of magnitude lower than the median of previously reported data and outside the range of previously reported means (under a minimal value of published means).

In some published articles, the values of the mass fractions of TE were presented in terms of ash or wet mass of the thyroid tissue. Therefore, we recalculated these data for dry mass basis using published values of 75% for water [55] and 4.16% for ash [75] in adult thyroids. No published data referring to I/Ag, I/Al, I/B, I/Be, I/Bi, I/Cd, I/Ce, I/Co, I/Cr, I/Cs, I/Dy, I/Er, I/Fe, I/Ga, I/Gd, I/Hg, I/La, I/Li, I/Mn, I/Mo, I/Nb, I/Nd, I/Ni, I/Pb, I/Pr, I/Rb, I/Sb, I/Sc, I/Se, I/Sm, I/Sn, I/Tb, I/Ti, I/Tl, I/U, I/Y, and I/Zn mass fraction ratios in human thyroid was found.

With age, the Co, Cs, La, Pb, Rb, Sb, Se, Sn, Tl, and Zn contents increase (Table 5), while I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl, I/Zn content ratios (Table 6) decrease. All these characteristics can be used to estimate the "biological age" of the female thyroid gland.

Previously, it was shown that an increase in the content of such TE as Co [5], La [76], Pb [11], Sb [7], Sn [14], Tl [22], and Zn [16,24] in the tissues of various organs can lead not only to disruption of their normal functioning, but also be the cause of the development of various pathological conditions, including malignant tumors. Since iodine plays a crucial role in thyroid function, it is especially important to maintain the relationship of this element with other TE contained in the thyroid tissue. Decrease with age in the thyroid gland of women the I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl , I/Zn content ratios indicates that in relation to the iodine content, the levels of TE such as Cd, Ce, Cs, La, Li, Mo, Nd, Pb, Pr, Sn, Tl, and Zn increase. This factor may also play a role in the etiology of goiter and thyroid cancer.

5 Conclusion

The combination of INAA and ICP-MS is a useful analytical tool for the determination of TE contents in the thyroid tissue samples. This method makes it possible to determine the content of at least thirty-eight TE.

Our data reveal that the Co, Cs, La, Pb, Rb, Sb, Se, Sn, Tl, and Zn contents increase, while I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl, I/Zn content ratios decrease in the normal thyroid of female during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive Co, Cs, La, Pb, Rb, Sb, Se, Sn, Tl, and Zn level in the thyroid of old females, as well as a disturbance in intrathyroidal I/Cd, I/Ce, I/Cs, I/La, I/Li, I/Mo, I/Nd, I/Pb, I/Pr, I/Sn, I/Tl, I/Zn relationships with increasing age may be assumed.

Compliance with ethical standards

Acknowledgments

The author is extremely grateful to Dr. Yu. Choporov, Head of the Forensic Medicine Department of City Hospital, Obninsk, for supplying thyroid samples. He is also grateful to Dr. Karandaschev V, Dr. Nosenko S, and Moskvina I from Institute of Microelectronics Technology and High Purity Materials, Chernogolovka, Russia, for their help in ICP-MS analysis.

Submission

The manuscript is not submitted at any other journals.

Disclosure of conflict of interest

There is no any conflict of interest.

Funding

There were no any sources of funding that have supported this work.

Running Head

Age dependence of iodine to trace element content ratios.

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