SMGroup

SM Gerontology and Geriatric Research

Research Article

Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males

Zaichick Vladimir[1]* and Zaichick Sofia[2]

[1]*Department of Radionuclide Diagnostics, Medical Radiological Research Centre, Russia*
[2]*Laboratory of Dr. Gabriela CaraveoPiso, Feinberg School of Medicine, Northwestern University, Chicago, USA*

Article Information

Received date: Apr 24, 2018
Accepted date: May 16, 2018
Published date: May 21, 2018

Corresponding author(s)

Zaichick Vladimir, Department of Radionuclide Diagnostics, Medical Radiological Research Centre, Korolyev St. 4, MRRC, Obninsk 249036, Russia,
Fax: +7 (495) 956 1440;
Tel: +7 (48439) 60289;
Email(s): vezai@obninsk.com; vzaichick@gmail.com

Keywords Thyroid; Age-related changes; Chemical element contents; Neutron activation analysis; Inductively coupled plasma atomic emission spectrometry

Abbreviations ROS: Reactive Oxygen Species; CRM/SRM: Certified/Standard Reference Materials; INAA-SLR: Instrumental Neutron Activation Analysis With High Resolution Spectrometry of Short-Lived Radionuclides; ICP-AES: Inductively Coupled Plasma Atomic Emission Spectrometry; BSS: Biological Synthetic Standards; IAEA: International Atomic Energy Agency; INCT: Institute of Nuclear Chemistry and Technology (Warszawa, Poland)

Article DOI 10.36876/smggr.1014

OPEN ACCESS

ISSN: 2576-5434

Abstract

The prevalence of thyroid dysfunction is higher in the older adults as compared to the younger population. An excess or deficiency of chemical element contents in thyroid plays an important role in goitro- and carcinogenesis of gland. The variation with age of the mass fraction of twenty chemical elements in intact thyroid of 72 males (mean age 37.8 years, range 2-80 years) was investigated. Measurements were performed using neutron activation analysis and inductively coupled plasma atomic emission spectrometry. Tissue samples were divided into two portions. One was used for morphological study while the other was intended for chemical element analysis. This work revealed that there is a statistically significant increase in Ca and I mass fraction, as well as a decrease in Al, B, Ba, K, Li, Mn, and P mass fraction in the normal thyroid of male during a lifespan. Results of the study showed that for older males there is a goitrogenic and carcinogenic association with inadequate levels of the thyroid parenchymal chemical elements as Al, B, Ba, Ca, I, K, Li, Mn, and P, some of which can increase intra-thyroidal oxidative stress.

Introduction

The endocrine organs, including the thyroid gland, undergo important functional changes during aging and a prevalence of thyroid dysfunction is higher in the older adults as compared to the younger population [1,2]. Advancing age is known to influence the formation of adenomatous goiter and thyroid cancer [3]. The prevalence of thyroid nodules is increased in the older adults, reaching a frequency of nearly 50% by the age of 65 [4]. Both prevalence and aggressiveness of thyroid cancer increase with age [2]. Women are affected by thyroid nodule and cancer two to five times more often than men, but in age over 65 years a prevalence of thyroid cancer may be higher in men [2-4, 5].

Aging is characterized by progressive impairment of body functions caused by the accumulation of molecular damage in DNA, proteins and lipids, is also characterized by an increase in intracellular oxidative stress due to the progressive decrease of the intracellular reactive oxygen species (ROS) scavenging [6,7]. Oxidative damage to cellular macromolecules which induce age-related diseases, including cancer, can also arise through overproduction of ROS and faulty antioxidant and/or DNA repair mechanisms [8]. Overproduction of ROS is associated with stress, inflammation, radiation, and some other factors, including overload of certain chemical elements, in both blood and certain tissues, or deficiency of other chemical elements with antioxidant properties [9-15]. The imbalance in the composition of chemical elements in cells, tissues and organs may cause different types of pathology. The importance of appropriate levels of many chemical elements is indisputable, due to their beneficial roles when present in specific concentration ranges, while on the other hand they can cause harmful effects with excessively high or low concentrations [12].

In our previous studies [16-24] the high mass fraction of iodine and some other chemical element were observed in intact human thyroid gland when compared with their levels in non-thyroid soft tissues of the human body. However, the age-dependence of chemical element mass fraction in thyroid of adult and, particularly, older males is still need to be evaluated. One valuable way to elucidate the situation is to compare the mass fractions of chemical elements in young adult (the control group) with those in older adult and geriatric thyroid. The other way is to calculate a correlation between age and chemical element content in thyroid. The findings of the excess or deficiency of chemical element contents in thyroid and the perturbations of their relative proportions in glands of adult and older males may indicate their roles in a higher prevalence of thyroid dysfunction in the older adults.

The reliable data on chemical element mass fractions in normal geriatric thyroid is apparently extremely limited. There are a few studies reporting chemical element content in human thyroid, using chemical techniques and instrumental methods [25-45]. However majority of the analytical

methods currently used and validated for the determination of major and trace elements in thyroid and other human organs are based on techniques requiring sample digestion. The most frequently used digestion procedures are the traditional dry ashing and high-pressure wet digestion that cause destruction of organic matter of the sample. Sample digestion is a critical step in elemental analysis and due to the risk of contamination and analytes loss, a digestion step contributes to the systematic uncontrolled analysis errors [46-48]. Moreover, only a few of the previous studies employed quality control using certified/standard reference materials (CRM/SRM) for determination of the chemical element mass fractions. Herein, in published papers there is no data on the age effect on chemical element contents in normal human thyroid.

Therefore, sample-nondestructive technique such as instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) combined in consecutive order with destructive inductively coupled plasma atomic emission spectrometry (ICP-AES)is good alternatives for multi-element determination in the samples of thyroid parenchyma. This combination provides a possibility of data quality assurance using a comparison of results obtained for some elements by both methods.

There were three aims in this study. The primary purpose of the study was to determine reliable values for chemical element mass fractions in the normal (intact) thyroid of subjects ranging from children to older males using INAA-SLR and ICP-AES. The second aim was to compare the chemical mass fractions determined in thyroid gland of age group 2 (adults and elderly persons aged 36 to 80 years), with those of group 1 (from 20 to 35 years). The final aim was to find the correlations between age and chemical element contents.

Materials and Methods

Ethics approval

The study plan was submitted to the Ethical Committee of the Medical Radiological Research Centre, Obninsk, Russia for approval prior to starting the study, as required by local regulatory provisions, and the Declaration of Helsinki.

Samples

Samples of the human thyroid were obtained from randomly selected autopsy specimens of 72 males (European-Caucasian) aged 2 to 80 years. All the deceased were citizens of Obninsk and had undergone routine autopsy at the Forensic Medicine Department of City Hospital, Obninsk. From all subjects were selected two age groups, group 1 with 20-35 years (26.0±1.0 years, M±SEM, n=27) and group 2 with 36–80 years (53.3±2.5 years, M±SEM, n=36). These groups were selected to reflect the condition of thyroid tissue in the young adults and first period of adult life (group 1) and in the second period of adult life as well as in old age (group 2). The available clinical data were reviewed for each subject. None of the subjects had a history of an intersex condition, endocrine disorder, or other chronic disease that could affect the normal development of the thyroid. None of the subjects were receiving medications or used any supplements known to affect thyroid chemical element contents. The typical causes of sudden death of most of these subjects included trauma or suicide and also acute illness (cardiac insufficiency, stroke, embolism of pulmonary artery, alcohol poisoning).

Sample preparation

All right lobes of thyroid glands were divided into two portions using a titanium scalpel [49]. One tissue portion was reviewed by an anatomical pathologist while the other was used for the chemical element content determination. A histological examination was used to control the age norm conformity as well as the unavailability of microadenomatosis and latent cancer.

After the samples intended for chemical element analysis were weighed, they were transferred to -20°C and stored until the day of transportation in the Medical Radiological Research Center, Obninsk, where all samples were freeze-dried and homogenized [50-52].

The sample weighing about 100 mg was used for chemical element measurement by INAA-SLR. The samples for INAA-SLR were sealed separately in thin polyethylene films washed beforehand with acetone and rectified alcohol. The sealed samples were placed in labeled polyethylene ampoules. Biological synthetic standards (BSS) prepared from phenol-formaldehyde resins were used as standards [53]. In addition to BSS, aliquots of commercially available pure compounds were also used.

After NAA-SLR investigation the thyroid samples were taken out from the polyethylene ampoules and used for ICP-AES. The samples were decomposed in autoclaves; 1.5 mL of concentrated HNO3 (nitric acid at 65 %, maximum (max) of 0.0000005 % Hg; GR, ISO, Merck Darmstadt, Germany) and 0.3 mL of H2O2 (pure for analysis) were added to thyroid samples, placed in one-chamber autoclaves (Ancon-AT2, Ltd., Moscow, Russia) and then heated for 3 h at 160-200 °C. After autoclaving, they were cooled to room temperature and solutions from the decomposed samples were diluted with deionized water (up to 20 mL) and transferred to plastic measuring bottles. Simultaneously, the same procedure was performed in autoclaves without tissue samples (only HNO3+H2O2+ deionized water), and the resultant solutions were used as control samples.

Certified Reference Materials

For quality control, ten subsamples of the certified reference materials IAEA H-4 Animal Muscle from the International Atomic Energy Agency (IAEA), and also five sub-samples INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves and INCT-MPH-2 Mixed Polish Herbs from the Institute of Nuclear Chemistry and Technology (INCT, Warszawa, Poland) were analyzed simultaneously with the investigated thyroid tissue samples. All samples of CRM were treated in the same way as the thyroid tissue samples. Detailed results of this quality assurance program were presented in earlier publications [54-56].

Instrumentation and methods

A horizontal channel equipped with the pneumatic rabbit system of the WWR-C research nuclear reactor was applied to determine the mass fraction of Br, Ca, K, Mg, Mn, and Na by INAA-SLR. The neutron flux in the channel was 1.7×10^{13}n $cm^{-2}s^{-1}$. Ampoules with thyroid samples, BSS, intra laboratory-made standards, and CRM were put into polyethylene rabbits and then irradiated separately for 180s. Copper foils were used to assess neutron flux. The measurement of each sample was made twice, 1 and 120 min after irradiation. The duration of the first and second measurements was 10 and 20 min,

Table 1: Comparison of the mean values (M±SEM) of the chemical element mass fractions (mg/kg, on dry-mass basis) in the thyroid of males obtained by both NAA-SLR and ICP-AES methods.

Element	NAA-SLR M_1	ICP-AES M_2	Δ, %
Ca	1703±131	1647±118	3.3
K	6289±329	7071±299	-12.4
Mg	306±19	326±19	-6.5
Mn	1.31±0.07	1.23±0.07	6.1
Na	6820±214	7368±231	-8.0

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

respectively. The gamma spectrometer included the 100 cm^3Ge (Li) detector and on-line computer-based MCA system. The spectrometer provided a resolution of 1.9 keV on the ^{60}Co 1332 keV line.

Sample aliquots were used to determine the Al, B, Ba, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions by ICP-AES using the Spectrometer ICAP-61 (Thermo Jarrell Ash, USA). The determination of the trace element content in aqueous solutions was made by the quantitative method using calibration solutions (High Purity Standards, USA) of 0.5 and 10 mg/L of each element. The calculations of the trace element content in the probe were carried out using software of a spectrometer (ThermoSPEC, version 4.1).

Table 2: Some statistical parameters of Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P,S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in thyroid of male (n=72).

Element	M	SD	SEM	Min	Max	Median	P 0.025	P 0.975
Al	11.3	14.9	2.2	0.800	69.3	6.40	1.12	58.6
B	0.491	0.473	0.071	0.200	2.30	0.300	0.200	2.03
Ba	1.03	1.08	0.16	0.050	4.70	0.570	0.141	4.08
Br	13.7	7.8	1.0	1.90	32.3	10.2	2.50	30.7
Ca	1675	979	122	373	5582	1458	429	4163
Cl	3449	1450	219	1030	5920	3470	1262	5657
Cu	4.07	1.41	0.19	1.10	11.0	4.00	1.93	6.21
Fe	223	95	12	52.0	489	215	77.5	445
I	1786	940	118	220	4205	1742	239	3808
K	6680	2352	299	3698	15293	6060	3734	12355
Li	0.0225	0.0168	0.0028	0.0040	0.0977	0.0179	0.0046	0.0547
Mg	316	136	18	99.0	930	287	118	572
Mn	1.27	0.47	0.06	0.0470	2.30	1.16	0.534	2.21
Na	7094	1709	206	3700	13453	6882	4003	11350
P	4414	1366	204	2127	8996	4227	2305	6858
S	8745	1478	220	5066	11377	8806	5925	11326
Si	43.6	41.1	6.1	5.70	180	32.7	7.45	163
Sr	3.96	2.98	0.39	0.100	12.6	2.95	0.443	11.7
V	0.104	0.033	0.005	0.0510	0.200	0.100	0.0591	0.179
Zn	95.4	39.8	5.1	34.0	237	87.6	45.2	199

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.

Information detailing with the NAA-SLR and ICP-AES methods used and other details of the analysis was presented in our previous [54-58].

Computer programs and statistic

A dedicated computer program for INAA mode optimization was used [59]. All thyroid samples were prepared in duplicate and mean values of chemical element contents were used in final calculation. Using Microsoft Office Excel, a summary of the statistics, including, arithmetic mean, and standard deviation, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels was calculated for chemical element contents. The difference in the results between two age groups was evaluated by the parametric Student's t-test and non-parametric Wilcoxon-Mann-Whitney U-test. For the construction of "age -chemical element mass fraction" diagrams (including lines of trend with age) and the estimation of the Pearson correlation coefficient between age and chemical element mass fraction the Microsoft Office Excel programs were also used. To identify the trend of the age dependency of chemical element contents, we applied approximation methods using exponential, linear, polynomial, logarithmic and power function. The maximum of corresponding values of R^2 parameter, reflecting the accuracy of approximation, was used for the selection of function.

Table 3: Median, minimum and maximum value of means Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn contents in the normal thyroid according to data from the literature in comparison with our results (mg/kg, dry mass basis).

	Published data [Reference]			This work
	Median of means (n)*	Minimum of means M or M±SD, (n)**	Maximum of means M or M±SD, (n)**	M±SD
Al	33.6 (12)	0.33 (-) [25]	420 (25) [26]	11.3±14.9
B	0.151 (2)	0.084 (3) [27]	0.46 (3) [27]	0.491±0.473
Ba	0.67 (7)	0.0084 (83) [28]	≤5.0 (16) [29]	1.03±1.08
Br	18.1 (11)	5.12 (44) [30]	284±44 (14) [31]	13.7±7.8
Ca	1600 (17)	840±240 (10) [32]	3800±320 (29) [32]	1675±979
Cl	6800 (5)	804±80 (4) [33]	8000 (-) [34]	3449±1450
Cu	6.1 (57)	1.42 (120) [35]	220±22 (10) [33]	4.07±1.41
Fe	252 (21)	56 (120) [35]	2444±700 (14) [31]	223±95
I	1888 (95)	159±8 (23) [36]	5772±2708 (50) [37]	1786±940
K	4400 (17)	46.4±4.8 (4) [33]	6090 (17) [29]	6680±2352
Li	6.3 (2)	0.092 (-) [38]	12.6 (180) [39]	0.0225±0.0168
Mg	390 (16)	3.5 (-) [25]	840±400 (14) [40]	316±136
Mn	1.82 (36)	0.44±11 (12) [41]	69.2±7.2 (4) [33]	1.27±0.47
Na	8000 (9)	438 (-) [42]	10000±5000 (11) [40]	7094±1709
P	3200 (10)	16 (7) [43]	7520 (60) [30]	4414±1366
S	11000 (3)	4000 (-) [34]	11800 (44) [30]	8745±1478
Si	16.0 (3)	0.97 (-) [25]	143±6 (40) [44]	43.6±41.1
Sr	0.73 (9)	0.55±0.26 (21) [27]	46.8±4.8(4) [33]	3.96±2.98
V	0.042 (6)	0.012 (2) [45]	18±2 (4) [33]	0.104±0.033
Zn	118 (51)	32(120) [35]	820±204 (14) [31]	95.4±39.8

M -arithmetic mean, SD - standard deviation, (n)* - number of all references, (n)** - number of samples.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

Results

The comparison of our results for the Ca, K, Mg, Mn, and Na mass fractions (mg/kg, dry mass basis)in the normal thyroid of male obtained by both NAA-SLR and ICP-AES methods is shown in Table 1.

Table 2 represents certain statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) of the Al, B, Ba, Br,Ca, Cl, Cu, Fe,I, K,Li, Mg, Mn, Na, P,S, Si,Sr, V, and Zn mass fractions in intact (normal) thyroid of males.

The comparison of our results with published data for the Al, B, Ba, Br,Ca, Cl, Cu, Fe,I, K,Li, Mg, Mn, Na, P,S, Si, Sr, V, and Zn contents in the human thyroid is shown in Table 3.

Table 4 indicates some statistical parameters of Al, B, Ba, Br,Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P,S, Si,Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in intact male thyroid of two age groups 20-35 and 36-80 years.

Table 4: Some statistical parameters of Al, B, Ba, Br,Ca, Cl, Cu, Fe,I, K,Li, Mg, Mn, Na, P,S, Si,Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in male thyroid of two age groups 20-35 and 36-80 years.

Age	Element	M	SD	SEM	Min	Max	Median	P 0.025	P 0.975
20-35	Al	12.3	16.6	3.7	1.10	60.3	4.50	1.20	52.0
years	B	0.630	0.622	0.139	0.200	2.300	0.340	0.200	2.21
n=27	Ba	1.21	1.08	0.25	0.140	4.10	0.57	0.235	3.65
	Br	12.0	8.3	1.9	1.90	32.3	10.0	2.19	28.1
	Ca	1567	528	104	414	2880	1484	599	2457
	Cl	3135	1489	413	1260	5660	2230	1359	5462
	Cu	3.80	0.91	0.19	2.30	5.60	3.90	2.35	5.44
	Fe	212	114	23	77.0	489	169	81.8	482
	I	1703	899	192	220	4205	1743	220	3526
	K	7073	1505	307	4490	10509	6812	4980	9854
	Li	0.0289	0.0221	0.0057	0.0106	0.0977	0.0215	0.0109	0.0810
	Mg	327	100	21	168	522	294	169	509
	Mn	1.43	0.45	0.10	0.870	2.20	1.35	0.886	2.18
	Na	7246	1393	268	3700	10900	7216	4787	9819
	P	4500	1368	306	2127	6876	4167	2371	6769
	S	9329	1304	292	7507	11377	9217	7510	11370
	Si	44.5	38.2	8.5	5.70	168	36.3	7.36	133
	Sr	3.39	2.33	0.47	0.500	10.8	2.80	0.713	9.54
	V	0.106	0.038	0.009	0.0510	0.200	0.100	0.0596	0.191
	Zn	82.2	22.8	4.6	47.1	140	80.2	47.3	132
36-80	Al	7.50	6.74	1.51	0.800	25.4	6.50	1.13	24.1
years	B	0.286	0.112	0.026	0.200	0.600	0.200	0.200	0.510
n=36	Ba	0.568	0.354	0.079	0.050	1.30	0.485	0.102	1.30
	Br	15.0	7.5	1.3	4.50	31.1	13.6	4.58	30.4
	Ca	1880	1218	212	440	5582	1461	528	4796
	Cl	3478	1418	273	1030	5620	3500	1199	5594
	Cu	4.10	1.09	0.205	1.70	6.40	4.05	2.24	6.06
	Fe	224	79	15	52.0	389	233	69.6	367
	I	1930	970	169	254	4098	1994	262	3676
	K	6030	2379	414	3698	13300	5444	3724	11860
	Li	0.0150	0.0078	0.0019	0.0040	0.0335	0.0164	0.0043	0.0298
	Mg	296	165	31	99.0	930	261	104	707
	Mn	1.10	0.38	0.07	0.530	2.21	1.07	0.537	1.87
	Na	6872	1604	267	3930	12400	6719	4335	9970
	P	3964	909	203	2272	5676	4030	2428	5537
	S	8489	1479	331	5066	11000	8526	5470	10857
	Si	34.1	43.0	9.6	7.40	180	20.8	7.64	150
	Sr	4.58	3.52	0.68	0.100	12.6	3.70	0.750	12.3
	V	0.100	0.032	0.007	0.0590	0.170	0.095	0.0595	0.165
	Zn	95.2	33.6	6.4	34.0	176	87.6	44.3	167

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.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

Table 5: Differences between mean values (M±SEM) of Al, B, Ba, Br,Ca, Cl, Cu, Fe,I, K,Li, Mg, Mn, Na, P,S, Si,Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in normal male thyroid of two age groups (AG1 and AG2).

Element	Male thyroid tissue				Ratio
	AG1 20-35 years n=27	AG2 36-80 years n=36	t-test *p*≤	U-test p	AG2 to AG1
Al	12.3±16.6	7.50±1.51	0.243	>0.05	0.61
B	0.630±0.622	0.286±0.026	**0.024**	**≤0.01**	0.45
Ba	1.21±1.08	0.568±0.079	**0.023**	**≤0.01**	0.47
Br	12.0±8.3	15.0±1.3	0.190	>0.05	1.25
Ca	1567±528	1880±212	0.192	>0.05	1.20
Cl	3135±1489	3478±273	0.494	>0.05	1.11
Cu	3.80±0.91	4.10±0.21	0.293	>0.05	1.08
Fe	212±114	224±15	0.656	>0.05	1.06
I	1703±899	1930±169	0.378	>0.05	1.13
K	7073±1505	6030±414	**0.048**	**≤0.01**	0.85
Li	0.0289±0.0221	0.0150±0.0019	**0.033**	**≤0.01**	0.52
Mg	327±100	296±31	0.419	>0.05	0.91
Mn	1.43±0.45	1.10±0.07	**0.009**	**≤0.01**	0.79
Na	7246±1393	6872±267	0.327	>0.05	0.95
P	4500±1368	3964±203	0.154	>0.05	0.88
S	9329±1304	8489±331	0.064	>0.05	0.91
Si	44.5±38.2	34.1±9.6	0.424	>0.05	0.77
Sr	3.39±2.33	4.58±0.68	0.158	>0.05	1.35
V	0.106±0.038	0.100±0.007	0.577	>0.05	0.94
Zn	82.2±22.8	95.2±6.4	0.053	>0.05	1.16

M – Arithmetic mean, SEM – standard error of mean, *t*-test - Student's *t*-test, U-test - Wilcoxon-Mann-Whitney *U*-test, statistically significant values are in **bold**.

To estimate the effect of age on the chemical element contents we examined two age groups, described above (Table 5). In addition, the Pearson correlation coefficient between age and chemical element mass fraction was calculated (Table 6). Figure 1 shows the individual data sets for the individual Al, B, Ba, Ca, I, K, Li, Mn, and P mass fraction in all samples of thyroid, and also lines of trend with age. Since the age dependency of these element contents was best described by a polynomial function, this approximation was reflected in Figure 1.

Discussion

Precision and accuracy of results

A good agreement of our results for the Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions with the certified values of CRM IAEA H-4 Animal Muscle, INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2Mixed Polish Herbs[54-56] as well as the similarity of the means of the Ca, K, Mg, Mn, and Na mass fractions in the normal thyroid of male determined by both NAA-SLR and ICP-AES methods (Table 1) demonstrates an acceptable precision and accuracy of the results obtained in the study and presented in Tables 2-6 and Figure 1.

Comparison with published data

The obtained means for Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction, as shown in Table 3, agree well with the medians of mean values reported by other researches for the human thyroid, including samples received from persons who died from different non-thyroid diseases [25-45]. The obtained mean for Li is two orders of magnitude lower the median of previously reported data. Moreover, it is outside the range of previously reported means. A number of values for chemical element mass fractions were not expressed on a dry mass basis by the authors of the cited references. Hence we calculated these values using published data for water 75% [60] and ash 4.16% on dry mass basis [61] contents in thyroid of adults.

Effect of age on chemical element contents

A statistically significant age-related decrease in B, Ba, K, Li, and Mn mass fraction was observed in thyroid of males when two age groups were compared (Table 5). In second group of males with mean age 53.3 years the mean of B, Ba, K, Li, and Mn mass fraction in thyroids were 55%, 53%, 15%, 48%, and 21%, respectively, lower than in thyroids of the first age group (mean age 26.0 years). A statistically significant decrease in B, Ba, K, Li, and Mn mass fraction with age was confirmed by the Pearson's coefficient of correlation between age and mass fractions of these elements (Table 6). Moreover, a statistically significant increase in Ca and I content accompanied by a decrease in Al and P was shown by the Pearson's coefficient of correlation between age and mass fractions of these elements (Table 6, Figure 1).

Thus, both positive (increase with age) and negative (decrease with age) correlations were observed for chemical element contents in the normal male thyroid. The Al, B, Ba, K, Li, Mn, and P contents (Figure 1) were declining with age. The rate of the decrease was clearly larger for Al, B, and Ba than for K, Li, Mn, and P (Figure 1). The decrease of Al, B, Ba, K, Li, and P content was fast during the first four-five decades, after which the changes in mass fractions of these elements were rather limited. However, the Mn mass fraction showed a progressive slow decrease with age in range from 2 to 80 years. Ca and I, in contrast, are accumulated during lifespan (Figure 1). Herein, elemental contents remain fairly stable until the fifth decade, after which a strong but variable accumulation takes place. Ca and I mass fractions are about doubled from age 40 until age 80(Figure 1). As per author's current information, no published data referring to age-related changes of Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions in human thyroid is available.

Table 6: Correlations between age (years) and chemical element mass fractions (mg/kg, dry mass basis) in the normal thyroid of male (*r* - coefficient of correlation).

Element	Al	B	Ba	Br	Ca	Cl	Cu	Fe	I	K
r	-0.29[a]	-0.37[a]	-0.41[b]	0.11	0.45[c]	0.11	-0.09	-0.11	0.32[a]	-0.32[a]
Element	Li	Mg	Mn	Na	P	S	Si	Sr	V	Zn
r	-0.31[a]	0.08	-0.35[a]	-0.10	-0.30[a]	-0.14	-0.24	0.09	-0.02	-0.10

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

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

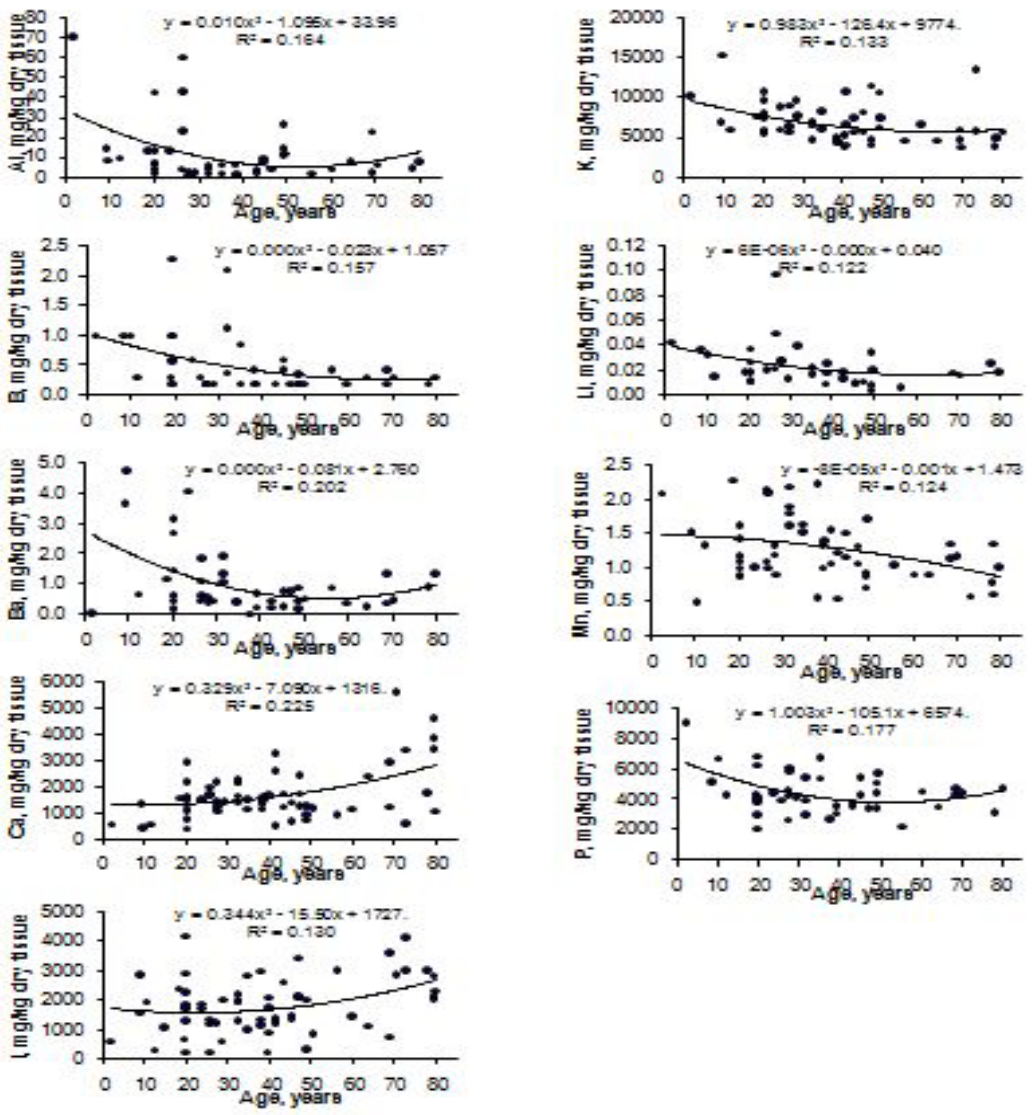

Figure 1: Data sets of individual Al, B, Ba, Ca, I, K, Li, Mn, and P mass fraction values in the normal thyroid of males and their trend lines.

Role of chemical elements in malignant transformation of the thyroid

Calcium: Ca content increases with age in many organs of human body [62-70]. This natural phenomenon is probably a common occurrence for all organs and soft tissues, except for bone. An age-related increase and excess in Ca mass fractions in thyroid tissue may contribute to harmful effects on the gland. There are good reasons for such speculations since many reviews and numerous papers raise the concern about role of Ca in the prostate, breast, lung and other organ malignant transformation [62-72]. Calcium ions Ca^{2}+ are central to both cell proliferation and cell death [64]. Changes in cytosolic Ca^{2}+ trigger events critical for tumorigenesis, such as cellular motility, proliferation and apoptosis [66]. An increased growth rate of cells is correlated with an increase in the intracellular calcium pool content [62,63]. Moreover, increases in cytosolic free Ca^{2}+ represent a ubiquitous signaling mechanism that controls a variety of cellular processes, including not only proliferation, but also cell metabolism and gene transcription [65]. Indeed, an increased level of Ca content in the thyroid tissue of old males reflects an increase in the intracellular calcium pool. Thus, an increase of Ca content in tissue and organs with age is a key feature in etiology of many benign and malignant tumors, including thyroid goiter and cancer.

Iodine: The endocrine organs, including the thyroid gland, undergo important functional changes during aging. The prevalence of subclinical hypothyroidism, which is characterized by normal free thyroxine and increased thyrotropin (TSH) levels, increases with aging. Therefore, subclinical hypothyroidism is frequently seen in old people [73]. In this, probably, the intra-thyroidaliodine levels are elevated in old men with increased TSH level. However, it is well known that excess in I mass fractions in thyroid tissue may contribute to harmful effects on the gland, including malignant transformation [19-21, 74-77].

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

Aluminum: Trace element Al is not described as essential, because no biochemical function has been directly connected to it. At this stage of our knowledge, no doubt that the Al overload negatively impacts human health [78]. Why Al content in normal male thyroid decrease with age and how it acts on thyroid are still to be cleared.

Boron: Trace element B is known to influence the activity of many enzymes [79]. Numerous studies have demonstrated beneficial effects of B on human health, including anti-inflammatory stimulus - reduces levels of inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor α (TNF-α); as well as raises levels of antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase [80]. Moreover, B helps the conversion of the storage form of thyroid hormone, T4, to T3, the active form. In normal situations B deficiency does not occur in humans, as most of the dietary sources are rich in this nutrient, but older adults are at greater risk for nutritional deficiencies than are younger adults. Thus, the age-related decrease of B content in normal male thyroid can be associated with a decrease in B dietary intake.

Barium: Trace element Ba has been shown to affect thyroid function in occupationally exposed persons. Urinary Ba content was associated with decreased T_4 and T_3 level in blood serum [81]. Why Ba content in normal male thyroid decrease with age are still to be cleared.

Potassium: K is a ubiquitous, intracellular element essential to more than one metabolic pathway. Low K levels in the blood and tissue, known as hypokalemia, is particularly common in the elderly for various age-related reasons. A deficiency in potassium is not immediately evident and develops gradually over time in most people [82]. Thus, the age-related decrease of K content in normal male thyroid reflects the process of hypokalemia development in senior citizens. From the other hand, because K+ is mainly an intracellular electrolyte, a decreased level of K content in the thyroid tissue of old males might indicate an age-related decrease of ratio "thyroid cell mass -follicular colloid mass". Herein, mass fraction of Na does not change during a lifespan (Table 5). From this it follows that an intracellular Na+: K+ ratio in thyroid of old males may be higher normal level. In turn, increasing intracellular Na+: K+ ratio is associated with a depolarization of the cell membrane [83]. The sustained depolarization of the cell membrane results in an increased rate of cell division and in that way with an increased risk of goiter, benign and malignant tumor of thyroid.

Lithium: Li has been used for decades to treat bipolar disorders. Impaired thyroid function is a common side effect of Li medication. Recent data indicate that Li exposure through drinking water, although providing much lower doses than the medication, may also affect thyroid hormone levels. The inhibition of thyroid hormone secretion results in decreased serum T4 and T3 concentrations [84]. From the other hand, the results of lifelong lithium-poor nutrition of animals show that lithium is essential to the fauna, and thus, to humans as well. It was shown that lithium-poor nutrition has a negative influence on feed intake, organism growth, skin properties, reproduction performance, milk production, mortality, and on some enzyme activity, mainly the enzymes of the citrate cycle, glycolysis, and of nitrogen metabolism [85]. Thus, Li is an ambivalent element for which further studies are necessary to determine the likely narrow range of content in thyroid with beneficial effects.

The Li intake by adult humans with mixed diets was systematically investigated in 10 test populations from different regions of Germany [86]. Adults of both genders with mixed diets consumed significantly more Li with increasing age. On average, seniors consumed 30-46% more Li. If Li dietary intake by Russian population is similar to the situation in Germany, mechanisms of the age-related decrease of Li content in normal male thyroid can't be completely elucidated. In our previous study significant age-related decrease in Li content in prostate gland was observed [85].

Manganese: Trace element Mn is a cofactor for numerous enzymes, playing many functional roles in living organisms. The Mn-containing enzyme, manganese superoxide dismutase (Mn-SOD), is the principal antioxidant enzyme which neutralizes the toxic effects of reactive oxygen species. It has been speculated that Mn interferes with thyroid hormone binding, transport, and activity at the tissue level [87]. There is opinion that Mn deficiencies in humans are rare and humans maintain stable tissue levels of this trace element [88]. This contradicts the observed age-related decrease of Mn content in normal male thyroid parenchyma.

It was reported that intracellular Mn content was positively correlated with manganese-containing superoxide dismutase (Mn-SOD), suggesting that the intracellular Mn level is associated with Mn-SOD activity [89]. Thus, a decrease of Mn content in thyroid parenchyma with age indicates the deficiency of antioxidant enzymes in the gland of old males.

A number of nutritional deficiencies are known to develop in subclinical hypothyroidism, including mineral deficiency: P, Mn, K and others [90]. At the current state of knowledge, it is impossible to reach definite conclusion of the cause- and -effect relation between subclinical hypothyroidism and deficiency of P, Mn, Kas well as some others chemical elements in old male thyroid. However, if the intra-thyroidal contents of chemical element in the first period of male life (<36 years) accept as normal levels, we can conclude that in the thyroid of old men there is at least deficiency of P, Mn, and K.

Study Limitations

This study has two limitations. Firstly, analytical techniques employed in this study measure only twenty trace element (Al, B, Ba, Br,Ca, Cl, Cu, Fe,I, K,Li, Mg, Mn, Na, P,S, Si,Sr, V, and Zn) mass fractions. Future studies should be directed toward using other analytical methods which will extend the list of chemical elements investigated in thyroid tissue. Secondly, generalization of our results may be limited to Russian population. Despite these limitations, this study provides evidence on tissue Al, B, Ba, Ca, I, K, Li, Mn, and P level alteration with age and shows the necessity the need to continue age-dependence research of chemical element contents in male thyroid.

Conclusion

Our data elucidate that there is a statistically significant increase in Ca and I mass fraction, as well as a decrease in Al, B, Ba, K, Li, Mn, and P mass fraction in the normal thyroid of male during a lifespan. Thus, from results of our study, a goitrogenic and carcinogenic effect of inadequate Al, B, Ba, Ca, I, K, Li, Mn, and P levels in the thyroids of older malesis shown to be a very likely consequence.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

Acknowledgements

We are grateful to Dr. Yu Choporov, Head of the Forensic Medicine Department of City Hospital, Obninsk, for supplying thyroid samples. We are also grateful to Dr. Karandas chev V, Dr. Nosenko S, and Moskvina I, Institute of Microelectronics Technology and High Purity Materials, Chernogolovka, Russia, for their help in ICP-MS analysis.

References

1. Gesing A. The thyroid gland and the process of aging. Thyroid Res. 2015; 8: A8.
2. Mitrou P, Raptis SA, Dimitriadis G. Thyroid disease in older people. Maturitas. 2011; 70: 5-9.
3. Kwong N, Medici M, Angell TE, Liu X, Marqusee E, Cibas ES, et al. The influence of patient age on thyroid nodule formation, multinodularity, and thyroid cancer risk. J Clin Endocrinol Metab. 2015; 100: 4434-4440.
4. Mazzaferri E. Management of a solitary thyroid nodule. NEJM. 1993; 328: 553-559.
5. Smailyte G, Miseikyte-Kaubriene E, Kurtinaitis J. Increasing thyroid cancer incidence in Lithuania in 1978-2003. BMC Cancer. 2006; 11: 284.
6. Olinski R, Siomek A, Rozalski R, Gackowski D, Foksinski M,Guz J, et al. Oxidative damage to DNA and antioxidant status in aging and age-related diseases. Acta Biochim Pol. 2007; 54: 11-26.
7. Minelli A, Bellezza I, Conte C, Culig Z. Oxidative stress-related aging: A role for prostate cancer? BiochimBiophys Acta. 2009; 1795: 83-91.
8. Klaunig JE, Kamendulis LM,Hocevar BA. Oxidative stress and oxidative damage in carcinogenesis. ToxicolPathol. 2010; 38: 96-109.
9. Järup L. Hazards of heavy metal contamination. Br Med Bull. 2003; 68: 167-182.
10. Zaichick V, Zaichick S. Role of zinc in prostate cancerogenesis. In: Mengen und Spurenelemente, 19 Arbeitstagung, Friedrich-Schiller-Universität, Jena, 1999; 104-115.
11. Zaichick V. INAA and EDXRF applications in the age dynamics assessment of Zn content and distribution in the normal human prostate. J Radioanal Nucl Chem. 2004; 262: 229-234.
12. Zaichick V. Medical elementology as a new scientific discipline. J Radioanal Nucl Chem. 2006; 269: 303-309.
13. Toyokuni S. Molecular mechanisms of oxidative stress-induced carcinogenesis: from epidemiology to oxygenomics. IUBMB Life.2008; 60: 441-447.
14. Gupte A, Mumper RJ. Elevated copper and oxidative stress in cancer cells as a target for cancer treatment. Cancer Treat Rev. 2009; 35: 32-46.
15. Lee JD, Wu SM, Lu LY, Yang YT, Jeng SY. Cadmium concentration and Metallothionein expression in prostate cancer and benign prostatic hyperplasia of humans. Taiwan yizhi. 2009; 108: 554-559.
16. Zaichick V, Tsyb A, Vtyurin BM. Trace elements and thyroid cancer. Analyst. 1995; 120: 817-821.
17. Zaichick V, Choporov Yu. Determination of the natural level of human intra-thyroid iodine by instrumental neutron activation analysis. J RadioanalNucl Chem. 1996; 207: 153-161.
18. Zaichick V, Zaichick S. Normal human intrathyroidal iodine. Sci Total Environ.1997; 206: 39-56.
19. Zaichick V. Iodine excess and thyroid cancer. J Trace Elem Exp Med. 1998; 11: 508-509.
20. Zaichick V. In vivo and in vitro application of energy-dispersive XRF in clinical investigations: experience and the future. J Trace Elem Exp Med. 1998; 11: 509-510.
21. Zaichick V, Iljina T. Dietary iodine supplementation effect on the rat thyroid 131I blastomogenic action. In: Mengen und Spurenelemente, 18 Arbeitstagung, Friedrich-Schiller-Universität, Jena, 1998; 294-306.
22. Zaichick V, Zaichick S. Energy-dispersive X-ray fluorescence of iodine in thyroid punctures biopsy specimens. J Trace Microprobe Tech.1999; 17: 219-232.
23. Zaichick V. Human intrathyroidal iodine in health and non-thyroidal disease. In: New aspects of trace element research. Smith-Gordon and Nishimura. 1999; 114-119.
24. Zaichick V. Relevance of and potentiality for in vivo intrathyroidal iodine determination. Ann NYAcad Sci. 2000; 904: 630-631.
25. Kortev AI, Dontsov G, Lyascheva AP. Bio-elements in human pathology, Middle-Ural publishing-house, Sverdlovsk, Russia, 1972.
26. Kamenev VF. Trace element contents in the thyroid gland of adult person. In: Trace elements in agriculture and medicine. Ulan-Ude, Russia, 1963; 12-16.
27. Tipton IH, Cook MJ. Trace elements in human tissue. Part II. Adult subjects from the United States. Health Phys. 1963; 9: 103-145.
28. Reytblat MA, Kropacheyv AM. Some trace elements in the normal thyroid of Perm Prikam'e inhabitants. Proceedings of Perm Medical Institute. 1967; 78: 157-164.
29. Forssen A. Inorganic elements in the human body. Ann Med ExpBiolFenn. 1972; 50: 99-162.
30. Zhu H, Wang N, Zhang Y, Wu Q, Chen R, Gao J, et al. Element contents in organs and tissues of Chinese adult men. Chin Med Sci J. 2007; 22: 71-82.
31. Salimi J, Moosavi K,Vatankhah S,Yaghoobi A. Investigation of heavy trace elements in neoplastic and non-neoplastic human thyroid tissue: A study by proton - induced X-ray emissions. Iran J Radiat Res. 2004; 1: 211-216.
32. Boulyga SF, Zhuk IV, LomonosovaEM, Kievetz MK, Denschlag HO, Zauner S, et al. Determination of microelements in thyroids of the inhabitants of Belarus by neutron activation analysis using the k0-method. J RadioanalNucl Chem. 1997; 222: 11-14.
33. Reddy SB, Charles MJ, Kumar MR, Reddy BS, AnjaneyuluCh, Raju GJN, et al. Trace elemental analysis of adenoma and carcinoma thyroid by PIXE method. Nucl Instrum Methods Phys Res B. 2002; 196: 333-339.
34. Woodard HQ, White DR. The composition of body tissues. Brit J Radiol. 1986; 708: 1209-1218.
35. Zaichick V, Zaichick S. Age-related changes of manganese, cobalt, coper, zinc, and iron contents in the endocrine glands of females. J Gerontol Geriatr Med. 2017; 3: 015.
36. Mato A, Gippini A, Peino R, Gayoso P, Uriel B. Differentiated carcinoma of the thyroid gland in an area of endemic goiter. An Med Interna. 1996 Nov; 13: 537-540.
37. Zabala J, Carrion N, Murillo M, Quintana M, Chirinos J, Seijas N, et al. Determination of normal human intrathyroidal iodine in Caracas population. J Trace Elem Med Biol. 2009; 23: 9-14.
38. Zakutinskiy DI, ParfeynovUyD, Selivanova LN. Handbook on the toxicology of radioisotopes, MedicinskayaLiteratura, Moscow, 1962.
39. Remis AM. Endemic goiter and trace elements in Kabardino-Balkaria, in: Proceedings of the fifth congress of Northern Caucasia surgeons. Rostov-on-Don. 1962; 276-278.
40. Soman SD, Joseph KT, Raut SJ, Mulay CD, Parameshwaran M, Panday VK. Studies of major and trace element content in human tissues. Health Phys. 1970; 19: 641-656.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

41. Teraoka H. Distribution of 24 elements in the internal organs of normal males and the metallic workers in Japan. Arch Environ Health. 1981; 36:155-165.

42. Boulyga SF, Becker JS, Malenchenko AF, Dietze H-J. Application of ICP-MS for multielement analysis in small sample amounts of pathological thyroid tissue. Microchim Acta. 2000; 134:215-222.

43. Novikov GV, Vlasova ZA. Some organism functions in connection with the iodine content in human diet and experimental animal fodders. In: Biological role of trace elements and their use in agriculture and medicine, Vol. 2. Nauka, Leningrad, 1970; 6-7.

44. Bredichin LM, Soroka VP. Trace element metabolism in patients with thyroid goiter under treatment. Vrachebnoe Delo. 1969; 51: 81-84.

45. Byrne AR, Kosta L. Vanadium in foods and in human body fluids and tissues. Sci Total Environ.1978; 10: 17-30.

46. Zaichick V. Sampling, sample storage and preparation of biomaterials for INAA in clinical medicine, occupational and environmental health. In: Harmonization of Health-Related Environmental Measurements Using Nuclear and Isotopic Techniques, IAEA, Vienna, 1997; 123-133.

47. Zaichick V. Losses of chemical elements in biological samples under the dry ashing process. Microelementi v Medicine. 2004; 5: 17-22.

48. Zaichick V, Zaichick S. INAA applied to halogen (Br and I) stability in long-term storage of lyophilized biological materials. J RadioanalNucl Chem.2000; 244: 279-281.

49. Zaichick V, Zaichick S. Instrumental effect on the contamination of biomedical samples in the course of sampling. The Journal of Analytical Chemistry. 1996; 51: 1200-1205.

50. Zaichick V, TsislyakYuV. A simple device for bio-sample lyophilic drying, Laboratornoe Delo. 1978; 2: 109-110.

51. Zaichick V, TsislyakYu V. A modified adsorptive and cryogenic lyophilizer for biosample concentrations. Laboratornoe Delo. 1981; 2: 100-101.

52. Zaichick V, Zaichick S. A search for losses of chemical elements during freeze-drying of biological materials. J Radioanal Nucl Chem.1997; 218: 249-253.

53. Zaichick V. Applications of synthetic reference materials in the medical Radiological Research Centre. Fresen J Anal Chem.1995; 352: 219-223.

54. Zaichick V, Nosenko S, Moskvina I. The effect of age on 12 chemical element contents in intact prostate of adult men investigated by inductively coupled plasma atomic emission spectrometry. Biol Trace Elem Res. 2012; 147: 49-58.

55. Zaichick V, Zaichick S. NAA-SLR and ICP-AES Application in the assessment of mass fraction of 19 chemical elements in pediatric and young adult prostate glands. Biol Trace Elem Res.2013; 156: 357-366.

56. Zaichick V, Zaichick S. Determination of trace elements in adults and geriatric prostate combining neutron activation with inductively coupled plasma atomic emission spectrometry. Open J Biochem. 2014; 2:16-33.

57. Zaichick S, Zaichick V. INAA application in the age dynamics assessment of Br, Ca, Cl, K, Mg, Mn, and Na content in the normal human prostate. J Radioanal Nucl Chem. 2011; 288: 197-202.

58. Zaichick V, Zaichick S. The effect of age on Br, Ca, Cl, K, Mg, Mn, and Na mass fraction in pediatric and young adult prostate glands investigated by neutron activation analysis. J Appl Radiat Isot. 2013; 82: 145-151.

59. Korelo AM, Zaichick V. Software to optimize the multi-elemental INAA of medical and environmental samples. In: Activation Analysis in Environment Protection. Joint Institute for Nuclear Research, Dubna, Russia, 1993; 326-332.

60. Katoh Y, Sato T, Yamamoto Y. Determination of multielement concentrations in normal human organs from the Japanese. Biol Trace Elem Res. 2002; 90: 57-70.

61. Schroeder HA, Tipton IH, Nason AP. Trace metals in man: strontium and barium. J Chron Dis. 1972; 25: 491-517.

62. Legrand G, Humez S, Slomianny C, Dewailly E, VandenAbeele F, Mariot P, et al. Ca2+ pools and cell growth. Evidence for sarcoendoplasmic Ca2+-ATPases 2B involvement in human prostate cancer cell growth control. J Biol Chem. 2001; 276: 47608-47614.

63. Munarov L. Calcium signalling and control of cell proliferation by tyrosine kinase receptors (Review). Int J Mol Med. 2002; 10: 671-676.

64. Capiod T, Shuba Y, Skryma R, Prevarskaya N. Calcium signalling and cancer cell growth. Calcium Signalling and Disease. Subcell Biochem. 2007; 45: 405-427.

65. Roderick HL, Cook SJ. Ca2+ signalling checkpoints in cancer: remodelling Ca2+ for cancer cell proliferation and survival. Nat Rev Cancer. 2008; 8: 361-375.

66. Flourakis M, Prevarskaya N. Insights into Ca2+ homeostasis of advanced prostate cancer cells. Biochim Biophys Acta. 2009; 1793: 1105-1109.

67. Yang H, Zhang Q, He J, Lu W. Regulation of calcium signaling in lung cancer. J Thorac Dis.2010; 2: 52-56.

68. Mc Andrew D, Grice DM, Peters AA, Davis FM, Stewart T, Rice M, et al. ORAI1-mediated calcium influx in lactation and in breast cancer. Mol Cancer Ther. 2011; 10: 448-460.

69. Zaichick V, Zaichick S. INAA application in the assessment of chemical element mass fractions in adult and geriatric prostate glands. J Appl Radiat Isot. 2014; 90: 62-73.

70. Zaichick V, Zaichick S, Davydov G. Differences between chemical element contents in hyperplastic and nonhyperplastic prostate glands investigated by neutron activation analysis. Biol Trace Elem Res. 2015; 164: 25-35.

71. Zaichick V, Zaichick S. Age-related changes in concentration and histological distribution of Br, Ca, Cl, K, Mg, Mn, and Na in nonhyperplastic prostate of adults. EJBMSR. 2016; 4: 31-48.

72. Zaichick V, Zaichick S, Rossmann M. Intracellular calcium excess as one of the main factors in the etiology of prostate cancer, AIMS Molecular Science. 2016; 3: 635-647.

73. Khan MA, Ahsan T, Rehman UL, Jabeen R, Farouq S. Subclinical hypothyroidism: frequency, clinical presentations and treatment indications. Pak J Med Sci. 2017; 33: 818-822.

74. Camargo RYA, Tomimori EK, Neves SC, Rubio GS, Galrão AL, Knobel M, et al. Thyroid and the environment: exposure to excessive nutritional iodine increases the prevalence of thyroid disorders in São Paulo, Brazil. Eur J Endocrinol. 2008; 159: 293-299.

75. Sun X, Shan Z, Teng W. Effects of increased iodine intake on thyroid disorders. Endocrinol Metab (Seoul). 2014; 29: 240-247.

76. Miranda DMC, Massom JN, Catarino RM, Santos RTM, Toyoda SS, Marone MMS, et al. Impact of nutritional iodine optimization on rates of thyroid hypoechogenicity and autoimmune thyroiditis: A cross-sectional, comparative study. Thyroid. 2015; 25: 118-124.

77. Shan Z, Chen L, Lian X, Liu C, Shi B, Shi L, et al. Iodine status and prevalence of thyroid disorders after introduction of mandatory universal salt iodization for 16 years in China: A cross-sectional study in 10 cities. Thyroid. 2016; 26: 1125-1130.

78. Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, et al. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. J Toxicol Environ Health Part B. 2007; 10: 1-269.

79. Naghii MR, Mofid M, Asgari AR, Hedayati M, Daneshpour MS. Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines. J Trace Elem Med Biol. 2011; 25: 54-58.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014

80. Pizzorno L. Nothing boring about boron. Integr Med (Encinitas). 2015; 14: 35-48.

81. Yorita Christensen KL. Metals in blood and urine, and thyroid function among adults in the United States 2007-2008. Int J Hyg Environ Health. 2013; 216: 624-632.

82. Martin A. Apportsnutritionnelsconseilles pour la population Française. Third edition, Tec & Doc Editions, Paris, 2000.

83. Nagy I, Lustyik G, Lukács G, Nagy V, Balázs G. Correlation of malignancy with the intracellular Na+:K+ ratio in human thyroid tumors. Cancer Res.1983; 43: 5395-5402.

84. Harari F, Bottai M, Casimiro E, Palm B, Vahter M. Exposure to lithium and cesium through drinking water and thyroid function during pregnancy: A prospective cohort study. Thyroid. 2015; 25: 1199-1208.

85. Zaichick S, Zaichick V, Karandashev V, Nosenko C,Ermidou-Pollet S, Pollet S. The effect of age on the lithium content in prostate of healthy men. In: Interaction of Neutrons with Nuclei. Joint Institute for Nuclear Research, Dubna, Russia, 2011; 337-341.

86. Anke M, Arnhold W, Groppel B, Kräuter U. Die biologische Bedeutung des Lithiums als Spurenelement. Erfahrungsheilkunde. 1991; 10: 656-664.

87. Soldin OP, Aschner M. Effects of manganese on thyroid hormone homeostasis. Neurotoxicology. 2007; 28: 951-956.

88. Aschner JL, Aschner M. Nutritional aspects of manganese homeostasis. Mol Aspects Med. 2005; 26: 353-362.

89. Hasegawa S, Koshikawa M, Takahashi I, Hachiya M, Furukawa T, Akashi M, et al. Alterations in manganese, copper, and zinc contents, and intracellular status of the metal-containing superoxide dismutase in human mesothelioma cells. J Trace Elem Med Biol. 2008; 22: 248-255.

90. Watts DL. The nutritional relationships of the thyroid. J Orthomol Med. 1989; 4: 165-169.

Citation: Zaichick V and Zaichick S. Association between Age and Twenty Chemical Element Contents in Intact Thyroid of Males. SM Gerontol Geriatr Res. 2018; 2(1): 1014.
https://dx.doi.org/10.36876/smggr.1014