Biol Trace Elem Res
DOI 10.1007/s12011-012-9427-4

Mass Fractions of 52 Trace Elements and Zinc/Trace Element Content Ratios in Intact Human Prostates Investigated by Inductively Coupled Plasma Mass Spectrometry

Sofia Zaichick · Vladimir Zaichick · Sergey Nosenko · Irina Moskvina

Received: 18 February 2012 / Accepted: 13 April 2012

Abstract Contents of 52 trace elements in intact prostate of 64 apparently healthy 13–60-year-old men (mean age 36.5 years) were investigated by inductively coupled plasma mass spectrometry. Mean values (*M* ± SEM) for mass fraction (in milligrams per kilogram, on dry-weight basis) of trace elements were as follows: Ag 0.041±0.005, Al 36±4, Au 0.0039±0.0007, B 0.97±0.13, Be 0.00099±0.00006, Bi 0.021±0.008, Br 29±3, Cd 0.78±0.09, Ce 0.028±0.004, Co 0.035±0.003, Cs 0.034±0.003, Dy 0.0031±0.0005, Er 0.0018±0.0004, Gd 0.0030±0.0005, Hg 0.046±0.006, Ho 0.00056±0.00008, La 0.074±0.015, Li 0.040±0.004, Mn 1.53±0.09, Mo 0.30±0.03, Nb 0.0051±0.0009, Nd 0.013±0.002, Ni 4.3±0.7, Pb 1.8±0.4, Pr 0.0033±0.0004, Rb 15.9±0.6, Sb 0.040±0.005, Se 0.73±0.03, Sm 0.0027±0.0004, Sn 0.25±0.05, Tb 0.00043±0.00009, Th 0.0024±0.0005, Tl 0.0014±0.0001, Tm 0.00030±0.00006, U 0.0049±0.0014, Y 0.019±0.003, Yb 0.0015±0.0002, Zn 782±97, and Zr 0.044±0.009, respectively. The upper limit of mean contents of As, Cr, Eu, Ga, Hf, Ir, Lu, Pd, Pt, Re, Ta, and Ti were the following: As ≤0.018, Cr ≤0.64, Eu ≤0.0006, Ga ≤0.08, Hf ≤0.02, Ir ≤0.0004, Lu ≤0.00028, Pd ≤0.007, Pt ≤0.0009, Re ≤0.0015, Ta ≤0.005, and Ti ≤2.6. In all prostate samples, the content of Te was under detection limit (<0.003). Additionally, ratios of the Zn content to other trace element contents as well as correlations between Zn and trace elements were calculated. Our data indicate that the human prostate accumulates such trace elements as Al, Au, B, Br, Cd, Cr, Ga, Li, Mn, Ni, Pb, U, and Zn. No special relationship between Zn and other trace elements was found.

Keywords Trace elements · Human prostate · ICP-MS

Introduction

The prostate gland may be a source of many health problems in men. One of the most serious problems is prostatic carcinoma (PCa). Globally, PCa is the sixth most common cancer. In Western industrialized countries, it is the third most common cancer in males and the second leading cause of cancer death [1–3]. In North America, it is the most common cancer in males and, except for lung cancer, is the leading cause of death from cancer [4, 5].

Cancer is a multietiological and multifactorial complex disease. Epidemiological and laboratory study provided convincing evidence that genetic factors, diet, lifestyle, and environment are major causative factors of prostate cancer. It is well accepted that genetic variation alone does not explain the observed differences in incidence of PCa [6, 7]. A 120-fold difference in rates of PCa among different countries indicates that there is substantial variation in occurrence of this disease and suggests that dietary and environmental factors, including chemical element intake, are of importance [6–12].

S. Zaichick · V. Zaichick (✉)
Radionuclide Diagnostics Department,
Medical Radiological Research Center,
Koroleva Str. 4,
Obninsk 249036, Kaluga Region, Russia
e-mail: vezai@obninsk.com

S. Zaichick
Department of Immunology and Microbiology,
Northwestern University,
302 East Superior Street, Morton Building,
Chicago, IL 60640, USA

S. Nosenko · I. Moskvina
Institute of Microelectronics,
Technology and High Purity Materials,
Chernogolovka 142432, Russia

Published online: 03 May 2012

Biological systems require not only “bulk” chemical elements but also trace and ultra-trace elements for their functioning. It seems that all chemical elements are more or less involved in various biochemical reactions in cells of the human body [13]. Under normal conditions, the chemical elements are in a state of equilibrium with regard to cellular distribution within tissues. Excessive accumulation, deficiency, or an imbalance of the elements may disturb the cell functions and may result in abnormal cell proliferation and malignant transformation, or in cell degeneration and apoptosis [14–19].

The involvement of trace elements in the etiology of PCa has been debated for almost five decades. It is likely that elevated levels of some metals Ca, Cd, Cr, Cu, Fe, Hg, Mg, Mn, Ni, Pb, V, and Zn and lowered level of Se in prostate tissue possibly initiate and promote PCa [4, 9, 14, 17–28]. The main hypothesis of the molecular mechanisms involved in prostate tumorigenesis is an oxidative DNA damage generated by free radicals of these metals. However, Se compounds have chemopreventive properties for PCa. Metals mentioned above may also be mutagenic through other mechanisms, e.g., by interacting with DNA, and can inhibit zinc finger domains featured in most DNA repair proteins [28–33].

Notably, Zn has been especially highlighted in the literature in relation to PCa. Zn is the second most abundant metal in the human body, serving as a cofactor for more than 300 enzymes with various physiological functions [34]. In the prostate, zinc is accumulated at up to tenfold higher level than in other tissues [35–37] and plays an important role in organ functions [38]. Much of the interest in zinc as an agent for prostate cancer treatment and prevention comes from studies that show a marked reduction of zinc level in prostate cancer tissue versus normal prostate tissue [35, 39]. Proponents of supplemental zinc think that high cellular zinc accumulation is detrimental to the malignant activities of prostate cancer cells. However, at present, there are two diametrically opposite points of view on the role of dietary zinc and supplemental zinc in prostate cancer risk [40].

In our recent study [40], it was shown that not only Zn but also Ca level in the human prostate tissue is almost one order of magnitude higher than in other soft tissues. The unusual high content of Ca in the prostate suggests that Ca may play a role in prostate function and health. The similarity of chemical properties of Ca and rare earth elements (REEs) is well known [40]. Chemical similarity allows ions of REEs to replace not only the ions of Ca and other alkaline earth elements but also transition metal ions such as Fe, Zn, Cu, Mn, Co, Cr, etc. in many macromolecular systems, including enzymes. At the same time, the replacement of REE ions with the ions of alkaline earth elements is impossible. Therefore, the investigation of REE content in the human prostate tissue seems to be especially important.

All current hypotheses that describe the role of trace elements in the etiology of PCa implicate elevated levels of metals in prostate tissue and disturbance in the relationships between elements as the main cause for PCa. Particularly, the focus is on the relationships between trace elements and Zn as well imbalance of trace metals and Se. There is evidence that the complexity of interaction among multiple dietary factors affects the intestinal absorption and assimilation of zinc. For example, the absorption of zinc could be inhibited by iron, calcium, and numerous other ingested micronutrients [40].

In order to confirm or refute these hypotheses, the first step is to investigate the normal levels of trace elements in a healthy prostate and their ratios and correlations with Zn level. To the best of our knowledge, such data are scarce, and the majority of results are based on a nonintact prostate tissue. As a rule, analyzed prostates were obtained from persons who died from different diseases. In some studies, prostatectomy samples were either formalin-fixed or paraffin-embedded. However, there is evidence that these types of tissue treatments lead to loss of some amount of chemical elements [41]. In other studies “histologically normal areas immediately adjacent to tumor” in prostatectomy samples of patients with PCa were used as “healthy” prostate tissues. Moreover, only a few studies used a quality control using certified reference materials for trace element contents.

This work had four aims. The first one was to assess the mass fractions of 52 trace elements in intact prostate of healthy men using inductively coupled plasma mass spectrometry (ICP-MS). The second aim was to evaluate the quality of obtained results. The third aim was to calculate the mean values of the Zn mass fraction/trace element mass fraction ratios for all elements investigated by using individual ratios. The last aim was to estimate the correlations between Zn and other trace elements in normal prostate.

All studies were approved by the Institute of Forensic Medicine, Moscow and the Medical Radiological Research Center, Obninsk Ethical Committees.

Material and Methods

Samples of the human prostate were obtained at postmortems from intact cadavers (64 males, 13–60 years old) within 48 h of death. The majority of deaths were due to traumas. All the deceased were citizens of Moscow. All cadavers had undergone routine autopsy at the Institute of Forensic Medicine, Moscow. Tissue samples were collected from the peripheral zone of prostate dorsal and lateral lobes and then divided into two portions using a titanium scalpel. One of tissue portion was used for morphological study while another was intended for chemical element analysis.

Table 1 The spectrometer parameters and the main parameters of mass-spectrum measurements

Spectrometer parameters	
RF generator power	1,250 W
Nebulizer	Polycon
Spray chamber	cooled at 3°C
Plasma gas flow rate	12 L/min
Auxiliary flow rate	0.9 L/min
Nebuliser flow rate	0.9 L/min
Sample update	0.8 mL/min
Resolution	0.8 atomic mass unit
Parameters of mass-spectrum measurements	
Detector mode	double (pulse counting and analogous)
Scanning mode	Survey scan and peak jumping
Setting for survey scan	
Number of runs	10
Dwell time	0.6 ms
Channels per mass	10
Acquisition duration	13.2 s
Setting for peak jumping	
Sweeps	25
Dwell time	10 ms
Channels per mass	1
Acquisition duration	34 s

A histological examination was used to control the age norm conformity as well as the unavailability of microadenomatosis and latent cancer. None of those who died a sudden death had suffered from any systematic or chronic disorders before.

After the tissue portions intended for chemical element analysis were weighed, they were transferred and stored at −20°C until the day of transportation to the Medical Radiological Research Center (MRRC), Obninsk. In the MRRC, all samples were freeze-dried and homogenized. The sample of homogenized prostate tissue weighing about 50 mg was used for chemical element analysis by ICP-MS.

A concentration of 1.5 mL of HNO_3 (nitric acid 65 %, max. 0.0000005 % Hg, GR, ISO, Merck) and 0.3 mL of H_2O_2 (pure for analysis) were added to prostate tissue samples, placed in one-chamber autoclaves (Ancon-AT2, Ltd., Russia), and then heated for 3 h at 160–200°C to decompose. After autoclaves were cooled to room temperature, 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 prostate tissue samples (only HNO_3 + H_2O_2 + deionized water), and the resultant solutions were used as control samples.

Sample aliquots were used to determine the content of Ag, Al, As, Au, B, Be, Bi, Br, Cd, Ce, Co, Cr, Cs, Dy, Er, Eu, Ga, Gd, Hf, Hg, Ho, Ir, La, Li, Lu, Mn, Mo, Nb, Nd, Ni, Pb, Pd, Pr, Pt, Rb, Re, Sb, Se, Sm, Sn, Ta, Tb, Te, Th, Ti, Tl, Tm, U, Y, Yb, Zn, and Zr by ICP-MS using an ICP-MS Thermo-Fisher “X-7” (Thermo Electron, USA). The measurements were made with the mass-spectrometer parameters shown in Table 1.

The element concentrations in aqueous solutions were determined by the quantitative method using multielemental 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. The next isotope(s) was/were measured and chosen for calculation for each trace element (see Table 2). If an element has several isotopes, the concentration of Li, B, Ti, Ni, Zn, Br, Rb, Mo, Pd, Ag, Cd, Sn, Sb, Te, Nd, Sm, Eu, Gd, Dy, ER, Yb, Hf, Re, Ir, Pt, Hg, Tl, and Pb in a sample was calculated as the mean of the values measured with their different isotopes.

Table 2 The isotope(s) used for determining chemical elements by ICP-MS

Element	Isotope(s)	Element	Isotope(s)	Element	Isotope(s)	Element	Isotope(s)
Li	6, 7	Rb	85	La	139	Lu	175
Be	9	Y	89	Ce	140	Hf	177, 178
B	10, 11	Zr	90, 91	Pr	141	Ta	181
Al	27	Nb	93	Nd	145, 146	Re	185, 187
Ti	47, 50	Mo	95, 98	Sm	147, 149	Ir	191, 193
Mn	55	Pd	104, 105	Eu	151, 153	Pt	194, 195
Co	59	Ag	107, 109	Gd	158, 160	Au	197
Ni	60, 62	Cd	111, 112,114	Tb	159	Hg	201, 202
Zn	66, 68	In	115	Dy	162, 163	Tl	203, 205
Ga	71	Sn	118, 120	Ho	165	Pb	206, 208
As	75	Sb	121, 123	Er	167, 168	Bi	209
Se	82	Te	125, 126	Tm	169	Th	232
Br	79, 81	Cs	133	Yb	173, 174	U	238

Table 3 ICP-MS data of chemical element contents in Certified Reference Materials (M ± SD, mg/kg on dry-weight basis)

Element	Soya Bean Flour (INCT-SBF-4)		Tea Leaves (INCT-TL-1)		Mixed Polish Herbs INCT-MPH-2	
	Certificate	This work	Certificate	This work	Certificate	This work
Ag	–	0.0034±0.0008	–	≤0.0064	–	<0.001(DL)
Al	45.5±3.7	37.1±1.4	2290±280	2248±61	670±111	485±79
As	–	<0.01(DL)	0.11±0.02	0.09±0.03	0.191±0.023	0.160±0.027
Au	–	<0.001(DL)	–	<0.001(DL)	–	<0.001(DL)
B	39.9±4.0	34.5±1.4	26[a]	24.8±1.2	–	28.8±8.1
Be	–	0.0021±0.0019	–	0.020±0.004	–	0.021±0.002
Bi	–	<0.001(DL)	–	0.010±0.002	–	0.07±0.002
Br	2.40±0.17	4.70±0.64	12.3±1.0	6.8±1.6	7.71±0.61	< 7.0 (DL)
Cd	–	0.0208±0.0045	0.030±0.004	0.023±0.004	0.199±0.015	0.194±0.0035
Ce	–	0.0364±0.0057	0.79±0.08	0.74±0.07	1.12±0.10	1.12±0.20
Co	0.096±0.006	0.0908±0.0080	0.39±0.04	0.37±0.04	0.210±0.025	1.92±0.009
Cr	–	≤0.5	1.9±0.2	1.7±0.4	1.69±0.13	1.60±0.37
Cs	0.130±0.004	0.1253±0.0057	3.91±0.37	3.65±0.19	0.076±0.007	0.063±0.005
Dy	–	0.0014±0.0002	–	0.167±0.010	–	0.055±0.008
Er	–	0.0007±0.0001	–	0.098±0.006	–	0.027±0.003
Eu	–	≤0.40	0.050±0.009	0.044±0.002	0.015±0.002	0.014±0.003
Ga	–	≤0.090	–	0.45±0.23	–	0.209±0.008
Gd	–	0.0018±0.0004	–	0.190±0.010	–	0.076±0.018
Hf	–	≤0.014	0.028[a]	0.032±0.019	0.236±0.020	<0.01(DL)
Hg	–	<0.02(DL)	0.005±0.001	≤0.022	0.018±0.002	0.019±0.005
Ho	–	0.0003±0.0001	–	0.032±0.002	–	0.010±0.002
Ir	–	<0.0003(DL)	–	≤0.00021	–	<0.0001(DL)
La	0.019±0.002	0.0144±0.0045	1.00±0.07	0.95±0.05	0.57±0.05	0.54±0.11
Li	–	0.0047±0.0018	–	0.217±0.034	–	0.574±0.044
Lu	–	<0.0001(DL)	0.017±0.002	0.016±0.001	0.009±0.002	0.003±0.001
Mn	32.3±1.1	30.0±1.0	1570±110	1628±145	191±12	197±5
Mo	5.99±0.35	5.66±0.28	–	0.052±0.009	0.52[a]	0.53±0.01
Nb	–	0.0057±0.0023	–	0.044±0.031	–	0.032±0.001
Nd	–	0.0119±0.0036	0.81[a]	0.81±0.06	0.46±0.09	0.47±0.10
Ni	3.12±0.18	2.57±0.20	6.1±0.5	5.3±0.7	1.57±0.16	1.62±0.10
Pb	–	0.068±0.023	1.8±0,2	1.5±0.3	2.16±0.23	2.07±0.32
Pd	–	≤0.077	–	≤0.08	–	<0.01(DL)
Pr	–	0.0027±0.0007	–	0.200±0.013	–	0.124±0.027
Pt	–	<0.0005(DL)	–	<0.0005(DL)	–	<0.001(DL)
Rb	31.7±1.7	30.8±2.8	81.5±6.5	80.9±6.7	10.7±0.07	10.9±0.4
Re	–	<0.001(DL)	–	<0.001(DL)	–	<0.001(DL)
Sb	–	0.0067±0.0044	0.050[a]	0.032±0.011	0.065±0.009	0.053±0.014
Se	–	<0.1(DL)	0.076[a]	≤0.12	–	0.088±0.026
Sm	–	0.0018±0.0006	0.18±0.02	0.17±0.01	0.094±0.008	0.087±0.021
Sn	–	<0.03(DL)	–	0.35±0.06	–	–
Ta	–	≤0.0087	0.008[a]	≤0.0088	0.019±0.002	–
Tb	–	0.00023±0.00004	0.027±0.002	0.028±0.002	0.014±0.001	0.010±0.002
Te	–	<0.002(DL)	–	<0.002(DL)	–	<0.005(DL)
Th	0.007±0.001	0.0069±0.0030	0.034±0.005	0.029±0.011	0.154±0.013	0.136±0.022
Ti	–	0.93±0.15	30[a]	32±6	34[a]	20.7±4.9
Tl	–	0.0011±0.0002	0.063±0.005	0.065±0.003	0.029[a]	0.032±0.002
Tm	–	0.00011±0.00002	0.017[a]	0.015±0.001	–	0.0037±0.0003

Table 3 (continued)

Element	Soya Bean Flour (INCT-SBF-4)		Tea Leaves (INCT-TL-1)		Mixed Polish Herbs INCT-MPH-2	
	Certificate	This work	Certificate	This work	Certificate	This work
U	–	0.0012±0.0007	–	0.009±0.001	0.049[a]	0.038±0.011
Y	–	0.0069±0.0011	–	0.904±0.098	–	0.271±0.032
Yb	–	0.0004±0.0001	0.120±0.013	0.104±0.007	0.053±0.007	0.023±0.002
Zn	52.3±1.3	54.8±6.6	34.7±2.7	36.0±3.7	33.5±2.1	32.0±6.1
Zr	–	0.0295±0.0093	–	0.30±0.12	–	0.400±0.040

M arithmetic mean, *SD* standard deviation, *DL* detection limit

[a] Informative values

The detection limit (DL) was calculated as:

$$\mathrm{DL} = C_\mathrm{i} + 3 \times \mathrm{SD}$$

where C_i is a mean value of the isotope content for measurements in control samples, and SD is a standard deviation of C_i determination in control samples. For elements with several isotopes, the DL was the one corresponding to the most abundant isotope. The relative standard deviation did not exceed 0.05 for elements with $C_\mathrm{i}>5$ DL and did not exceed 0.20 for elements with $C_\mathrm{i}<5$ DL.

Five subsamples of the Institute of Nuclear Chemistry and Technology (INCT, Warszawa, Poland) certified reference material (CRM) INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs were analyzed simultaneously with prostate tissue samples to estimate the precision and accuracy of results. The samples of certified reference materials were treated in the same way as the prostate samples.

Each study specimen was assayed in duplicate using separate weights, and mean values of trace element contents were used in final calculation. Using the Microsoft Office Excel programs, the summary of statistics, arithmetic mean, standard deviation, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels was calculated for trace element contents and ratios. Standard programs were also used for estimation of inter-correlations of trace element contents in prostate tissue.

Results

Table 3 depicts our data for Ag, Al, As, Au, B, Be, Bi, Br, Cd, Ce, Co, Cr, Cs, Dy, Er, Eu, Ga, Gd, Hf, Hg, Ho, Ir, La, Li, Lu, Mn, Mo, Nb, Nd, Ni, Pb, Pd, Pr, Pt, Rb, Re, Sb, Se, Sm, Sn, Ta, Tb, Te, Th, Ti, Tl, Tm, U, Y, Yb, Zn, and Zr mass fractions in five subsamples of INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs certified reference materials and the certified (or informative) values of this material.

Table 4 presents basic 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 Ag, Al, As, Au, B, Be, Bi, Br, Cd, Ce, Co, Cr, Cs, Dy, Er, Eu, Ga, Gd, Hf, Hg, Ho, Ir, La, Li, Lu, Mn, Mo, Nb, Nd, Ni, Pb, Pd, Pr, Pt, Rb, Re, Sb, Se, Sm, Sn, Ta, Tb, Te, Th, Ti, Tl, Tm, U, Y, Yb, Zn, and Zr contents in intact prostate of apparently healthy men.

Basic statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) of Zn mass fraction/trace element mass fraction ratios in intact prostate of apparently healthy men are presented in Table 5.

The comparison of our results with published data [20, 41–56] for the Ag, Al, As, Au, B, Be, Bi, Br, Cd, Ce, Co, Cr, Cs, Dy, Er, Eu, Ga, Gd, Hf, Hg, Ho, Ir, La, Li, Lu, Mn, Mo, Nb, Nd, Ni, Pb, Pd, Pr, Pt, Rb, Re, Sb, Se, Sm, Sn, Ta, Tb, Te, Th, Ti, Tl, Tm, U, Y, Yb, Zn, and Zr contents in the human prostate is shown in Table 6. Because a number of values for chemical element mass fractions was not expressed on a dry-weight basis in the above works, we calculated these values using published data for water (80 %) [57] and ash (1 % on wet weight basis) [58] contents in prostate of adult men.

The differences between the mean of trace element mass fractions in the prostate and in the skeletal muscle, liver, and whole blood of reference man [59, 60] is presented in Table 7. The data of reciprocal relationship (values of *r*, coefficient of correlation) between Zn and other trace element mass fractions are presented in Table 8.

Discussion

Accurate determination of trace element contents by ICP-MS requires the use of a directly matrix-matched standard, with a similar major chemical composition and mineralogical form to the sample. However, no current standard allows for the quantification of chemical elements in

Table 4 Basic statistical parameters of chemical element mass fractions (in milligrams per kilogram dry-weight basis) in intact human prostate

Element	M	SD	SEM	Min	Max	Median	P0.025	P0.975
Ag	0.0413	0.0331	0.0047	0.0070	0.126	0.0290	0.0080	0.113
Al	35.8	23.2	3.7	6.8	121	29	9.5	75.7
As	≤0.018	–	–	<0.01 (DL)	0.162	–	–	–
Au	0.0039	0.0041	0.0007	0.0009	0.0170	0.0020	0.0010	0.0153
B	0.97	0.75	0.13	0.30	3.20	0.70	0.30	3.04
Be	0.00099	0.00039	0.00006	0.00070	0.00260	0.00090	0.00070	0.00186
Bi	0.0209	0.0481	0.0080	0.0010	0.2050	0.0042	0.0014	0.1976
Br	28.7	22.2	3.1	3.0	101	19.7	3.0	89.1
Cd	0.781	0.561	0.089	0.050	2.400	0.640	0.061	1.893
Ce	0.0280	0.0237	0.0038	0.0050	0.0960	0.0190	0.0059	0.0923
Co	0.0347	0.0193	0.0025	0.0135	0.1060	0.0300	0.0147	0.0870
Cr	≤0.64	–	–	<0.5 (DL)	1.9	–	–	–
Cs	0.0342	0.0145	0.0023	0.0100	0.0870	0.0305	0.0149	0.0607
Dy	0.00312	0.00323	0.00052	0.00040	0.01700	0.00189	0.00066	0.00920
Er	0.00181	0.00221	0.00036	0.00016	0.01200	0.00092	0.00032	0.00593
Eu	≤0.0006	–	–	<0.0004 (DL)	0.0020	–	–	–
Ga	≤0.08	–	–	<0.02 (DL)	0.49	–	–	–
Gd	0.00304	0.00305	0.00050	0.00030	0.01600	0.00180	0.00058	0.00906
Hf	≤0.02	–	–	<0.01 (DL)	0.06	–	–	–
Hg	0.0463	0.0444	0.0059	0.0062	0.2650	0.0298	0.0099	0.1564
Ho	0.00056	0.00049	0.00008	0.00009	0.00179	0.00033	0.00009	0.00175
Ir	≤0.0004	–	–	<0.0002 (DL)	0.0010	–	–	–
La	0.0741	0.0943	0.0151	0.0080	0.3240	0.0240	0.0080	0.3012
Li	0.040	0.024	0.004	0.015	0.100	0.030	0.015	0.097
Lu	≤0.00028	–	–	<0.00007 (DL)	0.00200	–	–	–
Mn	1.53	0.56	0.086	0.80	3.10	1.35	0.83	2.80
Mo	0.303	0.185	0.030	0.100	0.850	0.250	0.110	0.698
Nb	0.00511	0.00528	0.00086	0.00100	0.02000	0.00300	0.00100	0.01908
Nd	0.0132	0.0108	0.0018	0.0030	0.0450	0.0090	0.0030	0.0423
Ni	4.31	4.23	0.68	0.20	19.4	3.40	0.20	19.2
Pb	1.76	2.42	0.38	0.19	10.7	0.54	0.25	8.65
Pd	≤0.007	–	–	<0.005 (DL)	0.010	–	–	–
Pr	0.00334	0.00274	0.00044	0.00060	0.01100	0.00230	0.00069	0.01063
Pt	≤0.0009	–	–	<0.0005 (DL)	0.0110	–	–	–
Rb	15.9	4.72	0.60	5.90	26.5	15.9	7.00	25.3
Re	≤0.0015	–	–	<0.0009 (DL)	0.0130	–	–	–
Sb	0.0402	0.0366	0.0047	0.0080	0.1580	0.0255	0.0090	0.1551
Se	0.730	0.245	0.032	0.216	1.300	0.754	0.336	1.198
Sm	0.00268	0.00236	0.00038	0.00050	0.01100	0.00180	0.00050	0.00720
Sn	0.246	0.283	0.045	0.030	1.110	0.120	0.030	1.006
Ta	≤0.005	–	–	<0.004 (DL)	0.013	–	–	–
Tb	0.00043	0.00053	0.00009	0.00007	0.00300	0.00020	0.00007	0.00134
Te	<0.003(DL)	–	–	–	–	–	–	–
Th	0.00243	0.00295	0.00048	0.00050	0.01720	0.00150	0.00050	0.00906
Ti[a]	≤2.6	–	–	<0.4 (DL)	13.7	–	–	–
Tl	0.00141	0.00067	0.00011	0.00020	0.00380	0.00130	0.00048	0.00278
Tm	0.00030	0.00036	0.00006	0.00004	0.00200	0.00016	0.00005	0.00092
U	0.0049	0.0083	0.0014	0.0005	0.0381	0.0024	0.0007	0.0323
Y	0.0192	0.0205	0.0033	0.0020	0.0840	0.0095	0.0029	0.0729
Yb	0.00146	0.00148	0.00024	0.00010	0.00510	0.00070	0.00019	0.00510
Zn	782	776	97	71.6	5868	620	145	1865
Zr	0.0444	0.0515	0.0085	0.0100	0.2500	0.0200	0.0100	0.1690

M arithmetic mean, *SD* standard deviation, *SEM* standard error of mean, *Min* minimum value, *Max* maximum value, *Per. 0.025* percentile with 0.025 level, *Per. 0.975* percentile with 0.975 level, *DL* detection limit

[a] Titanium tools were used for sampling and sample preparation

Table 5 Basic statistical parameters of Zn mass fraction/trace element mass fraction ratios in intact human prostate

Element	*M*	SD	SEM	Min	Max	Median	Per. 0.025	Per. 0.975
Zn/Ag	28,330	26,174	3,818	1,038	108,385	17,260	2,198	95,830
Zn/Al	25.7	23.3	3.8	1.04	114	18.7	1.91	83.1
Zn/Au	308,472	286,017	51,370	7,412	1,199,000	241,111	19,772	886,250
Zn/B	821	635	116	49.7	2,707	604	60.9	2,155
Zn/Be	793,329	538,846	88,586	48,462	2,127,143	687,000	69,286	1,931,714
Zn/Bi	174,671	152,751	26,197	2,514	705,294	157,553	4,012	553,527
Zn/Br	31.7	26.3	3.9	3.30	112	26.1	3.84	98.0
Zn/Cd	22,631	17,040	2,801	2,864	78,368	18,629	4,052	64,632
Zn/Ce	35,720	28,796	4,867	1,537	121,444	27,333	3,696	99,392
Zn/Co	23,658	16,968	2,228	2,864	78,368	19,339	4,196	64,038
Zn/Cs	20,200	12,829	2,081	2,520	60,722	17,200	4,085	46,597
Zn/Dy	371,894	360,087	61,754	7,412	1,383,544	286,372	17,294	1,358,297
Zn/Er	810,332	802,223	133,704	10,500	3,102,083	543,780	26,887	3,030,260
Zn/Gd	346,690	285,356	48,938	7,875	1,150,000	337,077	19,597	1,107,250
Zn/Hg	23,713	19,235	2,570	421	82,722	18,556	2,635	74,116
Zn/Ho	2,367,321	2,377,988	396,331	89,500	8,644,444	1,457,359	90,688	8,318,750
Zn/La	24,499	24,949	4,158	1,375	88,875	12,785	1,404	81,809
Zn/Li	22,253	18,848	3,141	1,909	70,529	15,617	2,557	67,525
Zn/Mn	464	347	54	52.5	1,489	395	63.6	1,385
Zn/Mo	3,060	2,657	431	183	10,838	2,171	343	10,607
Zn/Nb	255,562	233,356	38,893	11,933	869,000	161,000	12,517	730,750
Zn/Nd	81,257	72,689	12,287	2800	306,667	70,429	5,953	278,263
Zn/Ni	217	207	36	6.49	781	146	29.5	755
Zn/Pb	1,031	937	152	50.9	3,097	707	54.5	3,043
Zn/Pr	301,894	246,815	41,719	11,455	993,636	246,500	26,062	906,679
Zn/Rb	43.2	25.1	3.3	5.04	110	38.9	7.90	102
Zn/Sb	26,680	23,144	3,065	2,935	108,385	18,500	3,959	82,155
Zn/Se	913	535	73	138	2,516	795	191	2,032
Zn/Sm	428,851	396,589	66,098	11,455	1,556,000	379,524	22,836	1,438,750
Zn/Sn	5,383	4,771	795	385	19,900	4,785	472	16,283
Zn/Tb	3,357,129	3,290,799	556,247	42,000	11,114,286	2,398,000	125,633	10,957,643
Zn/Th	510,278	481,526	80,254	15,000	2,013,333	324,667	27,006	1,613,167
Zn/Tl	611,416	492,521	80,970	33,158	2,012,857	508,750	61,898	1,840,786
Zn/Tm	4,717,854	4,229,022	704,837	63,000	15,100,000	2,905,052	186,240	13,387,500
Zn/U	403,222	358,104	59,684	28,640	1,345,977	301,189	31,143	1,162,808
Zn/Y	64,763	64,371	11,206	3,768	241,600	45,143	3,934	216,000
Zn/Yb	967,548	963,908	167,795	31,176	3,722,500	635,000	32,272	3,160,500
Zn/Zr	35,541	32,167	5,361	788	120,800	25,700	993	110,738

M arithmetic mean, *SD* standard deviation, *SEM* standard error of mean, *Min* minimum value, *Max* maximum value, *Per. 0.025* percentile with 0.025 level, *Per. 0.975* percentile with 0.975 level, *DL* detection limit

prostate. For this reason, we were forced to evaluate the accuracy of our method using other certified reference materials with the biological matrix, certified for major portion investigated chemical elements—INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs (Table 3). The certified values for Ag, Au, Be, Bi, Dy, Er, Ga, Gd, Ho, Ir, Li, Nb, Pd, Pr, Pt, Re, Se, Sn, Te, Ti, Tm, U, Y, and Zr content were not present in these CRMs only (24 chemical elements from 52).

In 12 (Al, B, Br, Co, Cs, La, Mn, Mo, Ni, Rb, Th, and Zn) of 22 (Al, As, Br, Cd, Ce, Co, Cr, Cs, Eu, Hg, La, Lu, Mn, Ni, Pb, Rb, Sm, Tb, Th, Tl, Yb, and Zn) and of 25 (Al, As, Br, Cd, Ce, Co, Cr, Cs, Eu, Hf, Hg, La, Lu, Mn, Nd, Ni, Pb, Rb, Sb, Sm, Ta, Tb, Th, Yb, and Zn) chemical elements

Table 6 Median, minimum and maximum value of means of chemical element mass fractions (in milligrams per kilogram dry-weight basis) in prostate according to data from the literature in comparison with our results

Element	Published data[a]			This work
	Median of means, (*n*)[b]	Minimum of means M or M ± SD, (*n*)[c]	Maximum of means M or M ± SD, (*n*)[c]	M ± SD, *n*=64
Ag	≤0.1 (2)	<0.05 (48) [42]	0.2 (7) [43]	0.041±0.033
Al	27.7 (3)	13±66 (50) [42]	47 (9) [44]	36±23
As	0.045 (1)	0.045±0.022 (10) [45]	0.045±0.022 (10) [45]	≤0.018
Au	≤1.0 (2)	<0.7 (48) [42]	1.3 (7) [43]	0.0039±0.0007
B	1.2 (2)	<0.47 (50) [42]	1.0 (1) [43]	0.97±0.75
Be	–	–	–	0.00099±0.00039
Bi	<0.09 (1)	<0.09 (50) [42]	<0.09 (50) [42]	0.021±0.048
Br	14.5 (2)	12±8 (4) [46]	17 (12) [47]	29±22
Cd	0.79 (16)	0.06 (129) [48]	427±497 (55) [49]	0.78±0.56
Ce	–	–	–	0.028±0.024
Co	0.55 (3)	<0.09(50) [42]	12 (9) [44]	0.035±0.019
Cr	0.56 (3)	0.042 (50) [42]	1.4 (8) [43]	≤0.64
Cs	<0.47 (2)	0.060±0.075 (6) [50]	2.8 (12) [47]	0.034±0.015
Dy	–	–	–	0.0031±0.0032
Er	–	–	–	0.0018±0.0022
Eu	–	–	–	≤0.0006
Ga	–	–	–	≤0.08
Gd	–	–	–	0.0030±0.0030
Hf	–	–	–	≤0.02
Hg	0.65 (1)	0.65±0.58 (5) [45]	0.65±0.58 (5) [45]	0.046±0.044
Ho	–	–	–	0.00056±0.00049
Ir	–	–	–	≤0.0004
La	–	–	–	0.074±0.094
Li	–	–	–	0.040±0.024
Lu	–	–	–	≤0.00028
Mn	1.0 (6)	<0.47 (12) [47]	7.25±5.00 (4) [51]	1.53±0.56
Mo	1.0 (2)	<0.19 (50) [42]	1.8 (2) [43]	0.30±0.19
Nb	–	–	–	0.0051±0.0053
Nd	–	–	–	0.013±0.011
Ni	<0.47 (4)	0.14 (4) [52]	4.7 (12) [47]	4.31±4.23
Pb	1.0 (11)	0.15 (41) [20]	8 (4) [51]	1.8±2.4
Pd	–	–	–	≤0.007
Pr	–	–	–	0.0033±0.0027
Pt	–	–	–	≤0.0009
Rb	34.5(3)	4.7 (9) [44]	58±33 (4) [51]	15.9±4.7
Re	–	–	–	≤0.0015
Sb	0.42 (1)	0.42±0.56 (10) [45]	0.42±0.56 (10) [45]	0.040±0.037
Se	0.625 (7)	0.27 (129) [48]	1.5 (15) [41]	0.73±0.25
Sm	–	–	–	0.0027±0.0024
Sn	3.3 (4)	0.66 (50) [42]	3.7 (7) [43]	0.25±0.28
Ta	–	–	–	≤0.005
Tb	–	–	–	0.00043±0.00053
Te	164 (1)	164 (2) [51]	164 (2) [51]	<0.0025 DL
Th	–	–	–	0.0024±0.0029
Ti	7.6 (3)	<0.24 (50) [42]	26 (24) [52]	≤2.6[d]
Tl	0.25 (2)	0.0014 (1) [53]	0.5 (1) [43]	0.00141±0.00067

Table 6 (continued)

Element	Published data[a]			This work
	Median of means, (*n*)[b]	Minimum of means M or M ± SD, (*n*)[c]	Maximum of means M or M ± SD, (*n*)[c]	M ± SD, *n*=64
Tm	–	–	–	0.00030±0.00036
U	0.4 (1)	0.4 (1) [54]	0.4 (1) [54]	0.0049±0.0014
Y	<80 (2)	<3.3 (12) [47]	89 (12) [47]	0.019±0.020
Yb	–	–	–	0.0015±0.0015
Zn	482 (48)	111 (–) [55]	2,735 (10) [56]	782±776
Zr	–	–	–	0.044±0.051

M arithmetic mean, *SD* standard deviation, (–) no data

[a] References 20, 41–56

[b] Number of all references

[c] Number of samples

[d] Titanium tools were used for sampling and sample preparation

with certified values for the INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs certified reference material, we determined contents of all 28 certified elements Al, As, B, Br, Cd, Ce, Co, Cr, Cs, Eu, Hf, Hg, La, Lu, Mn, Mo, Nd, Ni, Pb, Rb, Sb, Sm, Ta, Tb, Th, Tl, Yb, and Zn (Table 3). Mean values for Al, As, B, Cd, Ce, Co, Cr, Cs, Eu, Hg, La, Lu, Mn, Mo, Nd, Ni, Pb, Rb, Sb, Sm, Tb, Th, Tl, Yb, and Zn were in the range of 95 % confidence interval. Good agreement with the certified data of CRMs indicates an acceptable accuracy of the results obtained in the study of trace elements of the prostate presented in Tables 4, 5, 6, 7, and 8.

The mean values and all selected statistical parameters were calculated for 39 (Ag, Al, Au, B, Be, Bi, Br, Cd, Ce, Co, Cs, Dy, Er, Gd, Hg, Ho, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Se, Sm, Sn, Tb, Th, Tl, Tm, U, Y, Yb, Zn, and Zr) chemical elements (Table 4). The mass fractions of trace elements were measured in all or a major portion of prostate samples. The content of As, Cr, Eu, Ga, Hf, Ir, Lu, Pd, Pt, Re, Ta, Te, and Ti was determined in a few samples. The possible upper limit of the mean (≤*M*) for these trace elements was calculated as the average mass fraction, using the value of DL instead of the individual value when these latter was found below the DL:

$$\leq M = \left(\sum_{i}^{n_{\mathrm{i}}} C_{\mathrm{i}} + DL \cdot n_{\mathrm{j}} \right) / n$$

where C_{i} is the individual value of trace element mass fraction in *i*-sample, n_{i} is number of samples with the mass fraction higher than the DL, n_{j} is number of samples with the mass fraction lower than the DL, and $n = n_i + n_{\mathrm{j}}$ is number of investigated samples.

The standard deviation obtained for all trace element mass fractions is particularly large (Table 4). This is due to the very wide individual variation of trace element mass fractions in the human prostate.

Mass fraction of such "trace" element as Zn in prostate tissue is much higher than content of all trace elements investigated (Table 5). Zn level in prostate tissue is higher than the content of Al, Br, and Rb (around an order of magnitude), B, Mn, Ni, and Se (around two order of magnitude), Mo, Pb, and Sn (around three order of magnitude), Ag, Cd, Ce, Co, Cs, Hg, La, Li, Nd, Sb, Y, and Zr (around four order of magnitude), Au, Be, Bi, Dy, Er, Gd, Nb, Pr, Sm, Th, Tl, U, and Yb (around five order of magnitude), and Ho, Tb, and Tm (around six order of magnitude).

The obtained means for Ag, Al, As, B, Bi, Br, Cd, Cr, Cs, Mn, Mo, Ni, Pb, Rb, Se, Sn, Ti, Tl, and Zn as shown in Table 6 agree well with the range of values cited by other researches for the human prostate, including samples received from persons who died from different diseases [20, 41–56]. The means for Au, Hg, Sb, U, and Y are one to two orders of magnitude, and the mean for Te, five orders of magnitude lower than previously reported results. No published data referring to the Be, Dy, Er, Eu, Ga, Gd, Hf, Ho, Ir, La, Li, Lu, Nb, Nd, Pd, Pr, Pt, Re, Sm, Ta, Tb, Th, Tm, Yb, and Zr content in human prostate was found.

The obtained values 913±535 (*M*± SD, Table 5) for Zn/Se ratio agrees well with result (*M*=804) published by Sapota et al. [26]. No published data referring to ratio of Zn to other chemical element content in human prostate was found.

In our previous studies, it was shown that Zn and Ca levels in the peripheral zone of dorsal and lateral lobes of prostate are almost one order of magnitude higher than in other soft tissues [35–37, 40]. The obtained mean for Al, Au, B, Br, Cd, Cr, Ga, Li, Mn, Ni, Pb, and U mass fraction in human prostate are more than two times higher than mean

Table 7 The differences between the mean chemical element contents in the prostate and in skeletal muscle, liver, and whole blood of Reference Man (mg/kg, on dry-weight basis)

Element	This work	Median of means for reference man [59, 60]			Ratios		
	Prostate (I)	Muscle (II)	Liver (III)	Whole blood (IV)	I/II	I/III	I/IV
Ag	0.0413	0.15	0.069	0.036	0.28	0.60	1.15
Al	36	1.5	0.0040	0.025	*24*	*9,000*	*1,440*
As	≤0.018	0.014	0.034	0.057	≤1.3	≤0.53	0.32
Au	0.0039	–	0.00018	0.00016	–	*21.7*	*24.4*
B	0.97	0.33	<0.36	0.175	*2.9*	*>2.85*	*5.54*
Be	0.00099	–	–	–	–	–	–
Bi	0.0209	0.033	0.014	0.046	0.64	1.49	0.45
Br	28.7	–	5.2	23.2	–	*5.52*	*4*
Cd	0.781	0.33	4.3	0.0039	*2.4*	0.18	*200*
Ce	0.0280	–	0.21	–	–	0.13	–
Co	0.0347	0.076	0.31	0.0041	0.46	0.11	*8.46*
Cr	≤0.64	0.048	0.097	–	*≤13.3*	*≤6.60*	–
Cs	0.0342	0.14	0.045	0.014	0.24	0.76	*2.44*
Dy	0.00312	–	–	–	–	–	–
Er	0.00181	–	–	–	–	–	–
Eu	≤0.0006	–	–	–	–	–	–
Ga	≤0.08	0.0014	0.0024	–	*≤57*	*≤33.3*	–
Gd	0.00304	–	–	–	–	–	–
Hf	≤0.02	–	–	–	–	–	–
Hg	0.0463	0.33	0.31	0.057	0.14	0.15	0.81
Ho	0.00056	–	–	–	–	–	–
Ir	≤0.0004	–	–	–	–	–	–
La	0.0741	–	0.28	–	–	0.26	–
Li	0.040	0.023	<0.0036	0.0035	1.74	*>11.1*	*11.4*
Lu	≤0.00028	–	–	–	–	–	–
Mn	1.53	0.47	5.4	0.05	*3.26*	0.28	*30.6*
Mo	0.303	–	2.1	0.010	–	0.14	*30.3*
Nb	0.00511	0.14	0.14	–	0.037	0.037	–
Nd	0.0132	–	–	–	–	–	–
Ni	4.31	0.95	0,10	0.015	*4.54*	*43.1*	*287*
Pb	1.76	0.48	1.6	0.52	*3.67*	*1.1*	*3.38*
Pd	≤0.007	–	–	–	–	–	–
Pr	0.00334	–	–	–	–	–	–
Pt	≤0.0009	–	0.11	–	–	–	–
Rb	15.9	28.6	17.2	15.5	0.56	0.92	1.03
Re	≤0.0015	–	–	–	–	–	–
Sb	0.0402	0.14	0.052	–	0.29	0.77	–
Se	0.730	0.81	1.12	0.57	0.90	0.65	1.28
Sm	0.00268	–	–	0.041	–	–	0.065
Sn	0.246	0.52	1.90	–	0.47	0.13	–
Ta	≤0.005	–	–	–	–	–	–
Tb	0.00043	–	–	–	–	–	–
Te	<0.0025 (DL)	3.00	–	0.028	≤0.001	–	0.089
Th	0.00243	–	–	0.0026	–	–	0.93
Tl	0.00141	0.24	0.19	0.0020	0.0059	0.0074	0.705
Tm	0.00030	–	–	–	–	–	–

Table 7 (continued)

Element	This work	Median of means for reference man [59, 60]			Ratios		
	Prostate (I)	Muscle (II)	Liver (III)	Whole blood (IV)	I/II	I/III	I/IV
U	0.0049	0.00095	0.0010	0.000016	*5.12*	*4.9*	*306*
Y	0.0192	0.019	–	0.024	1.01	–	0.80
Yb	0.00146	–	–	–	–	–	–
Zn	782	276	172	33.5	*2.83*	*4.55*	*23.3*
Zr	0.0444	0.095	0.103	0.049	0.47	0.43	0.91

Values in italics are of a ratio >2.0

values of element content in skeletal muscle, liver, and whole blood (Table 7). So, the human prostate accumulates not only for Zn and Ca but also for such trace elements as Al, Au, B, Br, Cd, Cr, Ga, Li, Mn, Ni, Pb, and U. The conclusion for Cd agrees with published data [20, 28, 48, 58].

With the exception of Nb and Rb, we did not find any pronounced correlation between the prostatic zinc and other trace elements (Table 8). This indicates that there is no special relationship between zinc and other trace elements in prostate. The lack of inverse correlation between Zn mass fraction and Cd mass fraction casts doubt on the opinion that Cd has “distinctive agonist effects” with Zn [41, 61, 62]. With the exception of Cd, no published data referring to correlations between Zn and other trace element contents in human prostate were found.

Conclusions

Inductively coupled plasma mass spectrometry is a powerful analytical tool for the determination of chemical element content in the prostate tissue. ICP-MS allows to determine the means of Ag, Al, Au, B, Be, Bi, Br, Cd, Ce, Co, Cs, Dy, Er, Gd, Hg, Ho, La, Li, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Rb, Sb, Se, Sm, Sn, Tb, Th, Tl, Tm, U, Y, Yb, Zn, and Zr (39 elements) and the upper limit of mean for As, Cr, Eu, Ga, Hf, Ir, Lu, Pd, Pt, Re, Ta, Te, and Ti (13 elements). Mean values ($M \pm$ SEM) for mass fraction (in milligrams per kilogram on dry-weight basis) of trace elements were as follows: Ag 0.041±0.005, Al 36±4, Au 0.0039±0.0007, B 0.97±0.13, Be 0.00099±0.00006, Bi 0.021±0.008, Br 29±3, Cd 0.78±0.09, Ce 0.028±0.004, Co 0.035±0.003, Cs 0.034±0.003, Dy 0.0031±0.0005, Er 0.0018±0.0004, Gd 0.0030±0.0005, Hg 0.046±0.006, Ho 0.00056±0.00008, La 0.074±0.015, Li 0.040±0.004, Mn 1.53±0.09, Mo 0.30±0.03, Nb 0.0051±0.0009, Nd 0.013±0.002, Ni 4.3±0.7, Pb 1.8±0.4, Pr 0.0033±0.0004, Rb 15.9±0.6, Sb 0.040±0.005, Se 0.73±0.03, Sm 0.0027±0.0004, Sn 0.25±0.05, Tb 0.00043±0.00009, Th 0.0024±0.0005, Tl 0.0014±0.0001, Tm 0.00030±0.00006, U 0.0049±0.0014, Y 0.019±0.003, Yb 0.0015±0.0002, Zn 782±97, and Zr 0.044±0.009, respectively. The upper limit of mean contents of As, Cr, Eu, Ga, Hf, Ir, Lu, Pd, Pt, Re, Ta, and Ti were the following: As ≤0.018, Cr ≤0.64, Eu ≤0.0006, Ga ≤0.08, Hf ≤0.02, Ir ≤0.0004, Lu ≤0.00028, Pd ≤0.007, Pt ≤0.0009, Re ≤0.0015, Ta ≤0.005, and Ti ≤2.6. In all prostate samples, the content of Te was under detection limit (<0.003).

Our data reveal that the human prostate accumulates such trace elements as Al, Au, B, Br, Cd, Cr, Ga, Li, Mn, Ni, Pb, U, and Zn. There is no a special relationship of zinc with other trace elements investigated in the prostate. The lack of inverse correlation between Zn and Cd mass fractions casts doubt on the opinion that Cd has “distinctive agonist effects” with Zn.

All the deceased were citizens of Moscow. None of those who died a sudden death had suffered from any systematic or chronic disorders before. The normal state of prostates was confirmed by morphological study. Thus, our data for 52 trace element mass fractions in intact human prostate may serve as indicative normal values for urban population of the Russian Central European region.

Table 8 Correlations (r) of Zn mass fractions and other trace element mass fractions in human prostate

Element	r	Element	r	Element	r
Ag	−0.117	Hg	−0.067	Si	−0.266
Au	−0.219	Ho	−0.184	Sm	−0.187
Be	0.003	La	−0.101	Sn	0.032
Bi	0.003	Mo	−0.050	Tb	−0.211
Br	0.096	Nb	0.430*	Th	−0.153
Cd	0.062	Nd	−0.185	Tl	0.202
Ce	−0.137	Ni	0.001	Tm	−0.180
Co	0.250	Pb	0.115	U	0.110
Cs	−0.017	Pr	−0.160	Y	−0.105
Dy	−0.184	Rb	0.328*	Yb	−0.198
Er	−0.201	Sb	−0.084	Zr	−0.174
Gd	−0.204	Se	0.169		

*$p<0.05$ (statistically significant)

Acknowledgments The authors are grateful to Prof. A. A. Zhavoronkov of Institute of Human Morphology, Russian Academy of Medical Sciences, Moscow, for supplying prostate samples, and they acknowledge the support of the Presidium of Russian Academy of Sciences, program for basic research "Creation and improvement of methods of chemical analysis, and investigation of substances and material structure."

References

1. Oliver SE, Gunnell D, Donovan JL (2000) Comparison of trends in prostate-cancer mortality in England and Wales and the USA. Lancet 355:1788–1789
2. Kumar RJ, Barqawi AB, Crawford ED (2004) Epidemiology of prostate cancer. Business Briefing, US Oncology Review, pp 1–6
3. Pischon T, Boeing H, Weikert S, Allen N, Key T, Johnsen NF, Tjonneland A, Severinsen MT, Overvad K, Rohrmann S, Kaaks R, Trichopoulou A, Zoi G, Trichopoulos D, Pala V, Palli D, Tumino R, Sacerdote C, Bueno-de-Mesquita HB, May A, Manjer J, Wallström P, Stattin P, Hallmans G, Buckland G, Larranaga N, Chirlaque MD, Martinez C, Redondo Cornejo ML, Ardanaz E, Bingham S, Khaw K-T, Rinaldi S, Slimani N, Jenab M, Riboli E (2008) Body size and risk of prostate cancer in the European prospective investigation into cancer and nutrition. Cancer Epidemiol Biomark Prev 17:3252–3261
4. Cohen LA (2002) Nutrition and prostate cancer: a review. Ann NY Acad Sci 963:148–155
5. Jones BA, Liu W-L, Araujo AB, Kasl SV, Silvera SN, Soler-Vila H, Curnen MGM, Dubrow R (2008) Explaining the race difference in prostate cancer stage at diagnosis. Cancer Epidemiol Biomark Prev 17:2825–2834
6. Van Patten CL, De Boer JG, Tomlinson Guns ES (2008) Diet and dietary supplement intervention trials for the prevention of prostate cancer recurrence: a review of the randomized controlled trial evidence. J Urol 180:2314–2322
7. Thomas JA (1999) Diet, micronutrients, and the prostate gland. Nutr Rev 57:95–103
8. Giovanucci E, Ascherio A, Rimm E, Stampfer MJ, Colditz GA (1995) Intake of carotenoids and retinol in relation to risk of prostate cancer. J Natl Cancer Inst 87:1767–1776
9. Blumenfeld AJ, Fleshner N, Casselman B, Trachtenberg J (2000) Nutritional aspects of prostate cancer: a review. Can J Urol 7:927–935
10. Yamada K, Araki S, Tamura M, Saka Y, Takahashi M, Kashihara H, Kono S (2000) Epidemiologic determinants of clinically relevant prostate cancer. Int J Cancer 89:259–264
11. Gray MA, Centeno JA, Slaney DP, Ejnik JW, Todorov T, Nacey JN (2005) Environmental exposure to trace elements and prostate cancer in three New Zealand ethnic groups. Int J Environ Res Public Health 2:374–384
12. Rebbeck TR (2006) Conquering cancer disparities: new opportunities for cancer epidemiology, biomarker, and prevention research. Cancer Epidemiol Biomark Prev 15:1569–1571
13. Zaichick V (2006) Medical elementology as a new scientific discipline. J Radioanal Nucl Chem 269:303–309
14. Ide-Ektessabi A, Fujisawa F, Sugiruma K, Kitamura Y, Gotoh A (2002) Quantitative analysis of zinc in prostate cancer tissue using synchrotron radiation microbeams. X-Ray Spectrom 31:7–11
15. Nayak SB, Bhat VR, Upadhyay D, Udupa SL (2003) Copper and ceruloplasmin status in serum of prostate and colon cancer patients. Indian J Physiol Pharmacol 47:108–110
16. Aydin A, Arsova-Sarafinovska Z, Sayal A, Eken A, Erdem O, Erten K, Ozgok Y, Dimovski A (2006) Oxidative stress and antioxidant status in non-metastatic prostate cancer and benign prostatic hyperplasia. Clin Biochem 39:176–179
17. Guntupalli JNR, Padala S, Gummuluri AVRM, Muktineni RK, Byreddy SR, Sreerama L, Kedarisetti PC, Angalakuduru DP, Satti BR, Venkatathri V, Pullela VBRL, Gavarasana S (2007) Trace elemental analysis of normal, benign hypertrophic and cancerous tissues of the prostate gland using the particle-induced X-ray emission technique. Eur J Cancer Prev 16:108–115
18. Silvera SAN, Rohan TE (2007) Trace elements and cancer risk: a review of the epidemiologic evidence. Cancer Causes Control 18:7–27
19. Kiziler AR, Aydemir B, Guzel S, Alici B, Ataus S, Tuna MB, Durak H, Kilic M (2010) May the level and ratio changes of trace elements be utilized in identification of disease progression and grade in prostatic cancer? Trace Elem Electrolytes 27:65–72
20. Oldereid NB, Thomassen Y, Attramadal A, Olaisen B, Purvis K (1993) Concentrations of lead, cadmium and zinc in the tissues of reproductive organs of men. J Reprod Fertil 99:421–425
21. Waalkes MP, Rehm S (1994) Cadmium and prostate cancer. J Toxicol Environ Health 43:251–269
22. Clark LC, Marshall JR (2001) Randomized, controlled chemoprevention trials in populations at very high risk for prostate cancer: elevated prostate-specific antigen and high-grade prostatic intraepithelial neoplasia. Urology 57(4 Suppl 1):185–187
23. Nelson MA, Reid ME, Duffield-Lillico AJ, Marshall JR (2002) Prostate cancer and selenium. Urol Clin North Am 29:67–70
24. Willis MS, Wians FH (2003) The role of nutrition in preventing prostate cancer: a review of the proposed mechanism of action of various dietary substances. Clin Chim Acta 330:57–83
25. Nyman DW, Stratton SM, Kopplin MJ, Dalkin BL, Nagle RB, Gandolfi JA (2004) Selenium and selenomethionine levels in prostate cancer patients. Cancer Detect Prev 28:8–16
26. Sapota A, Daragó A, Taczalski J, Kilanowicz A (2009) Disturbed homeostasis of zinc and other essential elements in the prostate gland dependent on the character of pathological lesions. Biometals 22:1041–1049
27. Sarafanov AG, Todorov TI, Centeno JA, Macias V, Gao W, Liang W-M, Beam C, Gray MA, Kajdacsy-Balla AA (2011) Prostate cancer outcome and tissue levels of metal ions. Prostate 71:1231–1238
28. Guzel S, Kiziler L, Aydemir B, Alici B, Ataus S, Aksu A, Durak H (2012) Association of Pb, Cd, and Se Concentrations and oxidative damage-related markers in different grades of prostate carcinoma. Biol Trace Elem Res 145:23–32
29. Stohs SJ, Baggihi D (1995) Oxidative mechanisms in the toxicity of metal ions. Free Radic Med 18:321–336
30. Witkiewicz-Kucharczyk A, Bal W (2006) Damage of zinc fingers in DNA repair proteins, a novel molecular mechanism in carcinogenesis. Toxicol Lett 162:29–42
31. Beyersmann D, Hartwig A (2008) Carcinogenic metal compounds: recent insight into molecular and cellular mechanisms. Arch Toxicol 82:493–512
32. Salnikow K, Zhitkovich A (2008) Genetic and epigenetic mechanisms in metal carcinogenesis and cocarcinogenesis: nickel, arsenic, and chromium. Chem Res Toxicol 21:28–44
33. Martinez-Zamudio R, Ha HC (2011) Environmental epigenetics in metal exposure. Epigenetics 6:820–827
34. Coleman JE (1992) Zinc proteins: enzymes, storage proteins, transcription factors, and replication proteins. Annu Rev Biochem 61:897–946
35. Zaichick V, Sviridova T, Zaichick S (1997) Zinc in human prostate gland: normal, hyperplastic and cancerous. Int Urol Nephrol 29:565–574
36. Zaichick V, Zaichick S (1999) Role of zinc in prostate cancerogenesis. In: Mengen und Spurenelemente, 19 Arbeitstagung. Friedrich-Schiller-Universitat, Jena, 1999, pp 104–115

37. Zaichick V (2004) INAA and EDXRF applications in the age dynamics assessment of Zn content and distribution in the normal human prostate. J Radioanal Nucl Chem 262:229–234
38. Costello LC, Franklin RB (1998) Novel role of zinc in the regulation of prostate citrate metabolism and its implications in prostate cancer. Prostate 35:285–296
39. Zaichick S, Zaichick V (2012) Trace elements of normal, benign hypertrophic and cancerous tissues of the human prostate gland investigated by neutron activation analysis. Appl Radiat Isot 70:81–87
40. Zaichick V, Nosenko S, Moskvina I (2012) 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. doi:10.1007/S12011-011-9294-4
41. Sarafanov AG, Todorov TI, Kajdacsy-Balla A, Gray MA, Macias V, Centeno JA (2008) Analysis of iron, zinc, selenium and cadmium in paraffin-embedded prostate tissue specimens using inductively coupled plasma mass-spectrometry. J Trace Elem Med Biol 22:305–314
42. Tipton IH, Cook MJ (1963) Trace elements in human tissue. Part II. Adult subjects from the United States. Health Phys 9:103–145
43. Tipton JH, Steiner RL, Foland WD, Mueller J, Stanley M (1954) USAEC-ORNL-Report-CF-54-12-66
44. Stitch SR (1957) Trace elements in human tissue. I. A semi-quantitative spectrographic survey. Biochem J 67:97–103
45. Liebscher K, Smith H (1968) Essential and nonessential trace elements. A method of determining whether an element is essential or nonessential in human tissue. Arch Environ Health 17:882–891
46. Kubo H, Hashimoto S, Ishibashi A, Chiba R, Yokota H (1976) Simultaneous determinations of Fe, Cu, Zn, and Br concentrations in human tissue sections. Med Phys 3:204–209
47. Forssen A (1972) Inorganic elements in the human body. I. occurrence of Ba, Br, Ca, Cd, Cs, Cu, K, Mn, Ni, Sn, Sr, Y and Zn in the human body. Annales medicinae Experimentalis et Biologie (Finland) 50:99–162
48. Schöpfer J, Drasch G, Schrauzer GN (2010) Selenium and cadmium levels and ratios in prostates, livers, and kidneys of nonsmokers and smokers. Biol Trace Elem Res 134:180–187
49. Ogunlewe JO, Osegbe DN (1989) Zinc and cadmium concentrations in indigenous blacks with normal, hypertrophic, and malignant prostate. Cancer 63:1388–1392
50. Yamagata N (1962) The concentration of common cesium and rubidium in human body. J Radiat Res 3:9–30
51. Soman SD, Joseph KT, Raut SJ, Mulay GD, Parameswaran M, Pandey VK (1970) Studies of major and trace element content in human tissues. Health Phys 19:641–656
52. Koch HJ, Smith ER (1956) The determination of copper and zinc in normal and pathologic human thyroid tissue. J Clin Endocrinol 16:123–129
53. Weinig E, Zink P (1967) Über die quantitative massenspektrometrische Bestimmung des normalen Thallium-Geehalts inmenschlichen Organismus. Archiv für Toxikologie 22:255–274
54. Höffken B, Rausch-Stroomann JG (1969) A study of the metabolism of zinc its metalloenzymes in diabetes mellitus. Z Klin Chem Klin Biochem 7:4–7
55. Anspaugh LR, Robinson WL, Martin WH, Lowe OA (1973) Compilation of published information on elemental concentrations in human organs in both normal and diseased states. No. UCRL-51013Pt. 1971-1973, pp. 1–4
56. Jafa A, Mahendra NM, Chowdhury AR, Kamboj VP (1980) Trace elements in prostatic tissue and plasma in prostatic diseases of man. Indian J Cancer 17:34–37
57. Györkey F, Min K-W, Huff JA, Györkey P (1967) Zinc and magnesium in human prostate gland: normal, hyperplastic, and neoplastic. Cancer Res 27:1349–1353
58. Saltzman BE, Gross SB, Yeager DW, Meiners BG, Gartside PS (1990) Total body burdens and tissue concentrations of lead, cadmium, copper, zinc, and ach in 55 human cadavers. Environ Res 52:126–145
59. Iyengar GV, Kollmer WE, Bowen HGM (1978) The elemental composition of human tissues and body fluids. A compilation of values for adults, Verlag Chemie, Weinheim, 151 p
60. Iyengar GV (1998) Reevaluation of the trace element content in reference men. Radiat Phys Chem 51:545–560
61. Feustel A, Wennrich R, Steiniger D, Klauss P (1982) Zinc and cadmium concentration in prostatic carcinoma of different histological grading in comparison to normal prostate tissue and adenofibromyomatosis (BPH). Urol Res 10:301–303
62. Brys M, Nawrocka AD, Miekos E, Zydek C, Foksinski M, Berecki A, Krajewska W (1997) Zinc and cadmium analysis in human prostate neoplasmas. Biol Trace Elem Res 59:145–152