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Trace elements of normal, benign hypertrophic and cancerous tissues of the Human prostate gland investigated by neutron activation analysis

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ABSTRACT

The Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn contents in normal ($n=37$), benign hypertrophic ($n=43$), and cancerous tissues ($n=60$) of the human prostate gland were investigated by neutron activation analysis. Mean values (M $\pm$ SEM) for content (mg/kg, dry weight basis) of trace elements in the normal tissue were: Ag—0.048 $\pm$ 0.009, Co—0.045 $\pm$ 0.004, Cr—0.53 $\pm$ 0.08, Fe—111 $\pm$ 9, Hg—0.056 $\pm$ 0.011, Rb—12.7 $\pm$ 0.9, Sb—0.045 $\pm$ 0.007, Sc—0.029 $\pm$ 0.005, Se—0.70 $\pm$ 0.04, and Zn—1000 $\pm$ 110, respectively. It was observed that in benign hypertrophic tissues the contents of Co, Cr, Hg, Sb, and Se were higher than in normal tissues, with statistically significant differences. The contents of Co, Rb, Sc, and Zn were significantly lower and those of Ag, Cr, Fe, Hg, and Sb were significantly higher in cancerous tissues than in normal tissues.

1. Introduction

The prostate gland may be a source of many health problems in men past middle age, the most common being benign prostatic hypertrophy (BPH), and prostatic carcinoma (PCa). BPH is a non-cancerous enlargement of the prostate gland leading to obstruction of the urethra. Globally, prostate cancer is the sixth most common cancer, and the third most common cancer in males in Western industrialized countries (Kumar et al., 2004; Pischon et al., 2008). In North America, it is the most common cancer in males and, except for lung cancer, is the leading cause of death from cancer (Cohen, 2002; Jones et al., 2008; Van Patten et al., 2008). Although the etiology of PCa is unknown, several risk factors including age and diet (Ca, Zn and some other nutrients) have been well identified (Yamada et al., 2000; Rebbeck, 2006). It is also reported that the risk of having PCa drastically increase with age, being three orders of magnitude higher for the age group 40–79 years than for those younger than 39 years (Jemal et al., 2003; Rebbeck, 2006).

Trace elements have essential physiological functions such as maintenance and regulation of cell function, gene regulation, activation or inhibition of enzymatic reactions, and regulation of membrane function. Essential or toxic (mutagenic, carcinogenic) properties of trace elements depend on tissue-specific need or tolerance, respectively (Zaichick, 2006). Excessive accumulation or an imbalance of the trace elements may disturb the cell functions and may result in cellular degeneration or death (Ektessabi et al., 2001; Yoshida et al., 2001).

In our previous study a significant positive correlation between the age and Zn mass fraction in the prostate was observed (Zaichick and Zaichick, 1999; Zaichick, 2004,). High intraprostatic zinc concentrations are probably one of the main factors acting in both initiation and promotion stages of prostate carcinogenesis (Leitzmann et al., 2003; Zaichick and Zaichick, 1999; Zaichick, 2004). A significant tendency of age-related increase in Co, Fe, Hg, and Sc mass fraction in the prostate was recently demonstrated by us (Zaichick and Zaichick, 2011a). Hence it is possible that besides Zn, such trace elements as Co, Fe, Hg, and Sc also play a role in the pathophysiology of the prostate.

This work had three aims. The first was to assess the Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, Zn contents in intact prostate of healthy men aged over 40 years using non-destructive instrumental neutron activation analysis. The second aim was to compare the levels of trace elements in the prostate gland of age-matched patients, who had either BPH or PCa, and the third was to evaluate trace element content to aid diagnosis of prostate cancer.

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

2. Material and methods

2.1. Samples

All patients studied ($n=103$) were hospitalized in the Urological Department of the Medical Radiological Research Center. Transrectal puncture biopsy of suspicious indurated regions of the

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prostate was performed for every patient, to permit morphological study of prostatic tissue at these sites and to estimate their chemical element contents. In all cases the diagnosis has been confirmed by clinical and morphological results obtained during studies of biopsy and resected materials. The age of 43 patients with BPH ranged from 38 to 83 years, the mean being 66 ± 8 years ($M \pm SD$). The 60 patients aged 40–79 suffered from PCa. Their mean age was 65 ± 10 years. Intact prostates were removed at necropsy from 37 men (mean age 55 ± 11 years, range 41–87) who had died suddenly. The majority of deaths were due to trauma. Tissue samples were collected from the peripheral zone of dorsal and lateral lobes of their prostates, within 2 days of death and then the samples were divided into two portions. One was used for morphological study while the other was intended for chemical element analysis. A histological examination was used to control the age norm conformity, as well as to confirm the absence of microadenomatosis and latent cancer (Zaichick and Zaichick, 2011a).

2.2. Sample preparation

After the samples intended for chemical element analysis were weighed, they were freeze-dried and homogenized. The sample weighing about 10 mg (for biopsy materials) and 50 mg (for resected materials) was used for chemical element measurement by instrumental neutron activation analysis with high resolution spectrometry of long-lived radionuclides (INAA–LLR). The samples for INAA–LLR were wrapped separately in a high-purity aluminum foil washed with double rectified alcohol beforehand and placed in a nitric acid-washed quartz ampoule.

2.3. Instrumentation, methods and certified reference materials

Ten sub-samples of certified reference material (CRM) IAEA H-4 (animal muscle) and ten sub-samples of CRM IAEA HH-1 (human hair) weighing 50–100 mg were treated and analyzed under exactly the same conditions as the prostate samples, to allow estimation of the precision and accuracy of results.

The vertical channel of a nuclear reactor was used to determine the samples' content of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn by INAA–LLR. The quartz ampoule containing prostate samples, standards, and certified reference materials was soldered, positioned in an aluminum transport container and exposed to a 24 h neutron irradiation in the vertical channel with a neutron flux of $1.3 \cdot 10^{13}$ n cm^{-2} s^{-1}. Ten days after the irradiation samples were reweighed and repacked.

Details of the relevant nuclear reactions, radionuclides, gamma energies, methods of analysis and the results of quality control were presented in our earlier publications concerning the chemical elements of intact human prostate tissue (Zaichick and Zaichick, 2011a).

2.4. Computer programs and statistic

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

Table 1
Some statistical parameters of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn mass fractions (mg kg^{-1}, dry weight basis) in normal, benign hypertrophic, and cancerous prostate tissue.

Tissue element	Mean	SD	SEM	Min	Max	Median	Per. 0.025	Per. 0.975
Normal (n=37)								
Ag	0.0477	0.0456	0.0089	0.0100	0.223	0.0344	0.0100	0.156
Co	0.0452	0.0237	0.0043	0.0165	0.106	0.0400	0.0169	0.0988
Cr	0.532	0.422	0.081	0.030	1.814	0.392	0.030	1.55
Fe	111	51.1	9.0	35.0	267	100	35.8	221
Hg	0.0557	0.0569	0.0110	0.0077	0.242	0.0320	0.0114	0.216
Rb	12.7	5.05	0.86	4.70	25.3	12.0	5.69	24.6
Sb	0.0445	0.0374	0.0067	0.0046	0.158	0.0380	0.0087	0.154
Sc	0.0294	0.0236	0.0053	0.0046	0.0771	0.0200	0.0066	0.0768
Se	0.696	0.240	0.044	0.318	1.43	0.691	0.346	1.15
Zn	1001	664	109	231	3513	915	252	2184
BPH (n=43)								
Ag	0.0346	0.0273	0.0060	0.0050	0.132	0.0288	0.0080	0.0975
Co	0.0716	0.0422	0.0097	0.0246	0.170	0.0500	0.0291	0.162
Cr	1.073	0.530	0.119	0.046	2.268	1.000	0.262	2.21
Fe	139	59.5	10.1	56.0	370	130	61.1	265
Hg	0.232	0.144	0.030	0.053	0.520	0.184	0.058	0.517
Rb	14.8	4.56	0.78	6.60	23.1	14.7	7.34	22.8
Sb	0.163	0.113	0.025	0.0131	0.447	0.148	0.0169	0.404
Sc	0.0257	0.0156	0.0040	0.0039	0.0543	0.0213	0.0051	0.0536
Se	1.243	0.379	0.079	0.430	1.771	1.321	0.529	1.72
Zn	1101	582	79	312	2515	1035	316	2479
PCa (n=60)								
Ag	0.236	0.150	0.028	0.0237	0.527	0.220	0.0326	0.516
Co	0.0326	0.0199	0.0037	0.0049	0.102	0.0289	0.0065	0.0778
Cr	2.35	1.96	0.37	0.165	6.48	1.46	0.286	6.27
Fe	165	105	15	15.0	427	126	36.0	403
Hg	0.118	0.103	0.019	0.016	0.496	0.084	0.022	0.402
Rb	8.94	5.09	0.71	1.00	22.3	7.50	1.88	20.2
Sb	0.468	0.309	0.051	0.015	1.40	0.430	0.045	1.07
Sc	0.0116	0.0082	0.0015	0.0001	0.0438	0.0103	0.0017	0.0275
Se	0.576	0.434	0.078	0.063	1.54	0.438	0.076	1.52
Zn	140	78.2	9.9	20.0	385	127	23.7	309

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, *n*—number of samples.