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INAA application in the assessment of chemical element mass fractions in adult and geriatric prostate glands

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HIGHLIGHTS

- 37 trace elements were determined in prostate of 65 healthy 21–87 year old males by NAA.
- Co, Fe, Hg, Sc, and Zn contents significantly increase with age.
- Mn content significantly decreases with age.
- All elemental contents in the sixth to ninth decades are near constant level.
- There is a great disturbance of chemical element relationships with age.

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ABSTRACT

The variation with age of the mass fraction of 37 chemical elements in intact nonhyperplastic prostate of 65 healthy 21–87 year old males was investigated by instrumental neutron activation analysis with high resolution spectrometry of short- and long-lived radionuclides. Mean values ($M \pm SEM$) for mass fractions (mg kg^{-1}, dry mass basis) of the chemical elements studied were: Ag—0.055 ± 0.007, Br—33.2 ± 3.3, Ca—2150 ± 118, Cl—13014 ± 703, Co—0.038 ± 0.003, Cr—0.47 ± 0.05, Fe—99.3 ± 6.1, Hg—0.044 ± 0.006, K—11896 ± 356, Mg—1149 ± 68, Mn—1.41 ± 0.07, Na—10886 ± 339, Rb—12.3 ± 0.6, Sb—0.049 ± 0.005, Sc—0.021 ± 0.003, Se—0.65 ± 0.03, and Zn—795 ± 71. The mass fraction of other chemical elements measured in this study were lower than the corresponding detection limits (mg kg^{-1}, dry mass basis): As < 0.1, Au < 0.01, Ba < 100, Cd < 2, Ce < 0.1, Cs < 0.05, Eu < 0.001, Gd < 0.02, Hf < 0.2, La < 0.5, Lu < 0.003, Nd < 0.1, Sm < 0.01, Sr < 3, Ta < 0.01, Tb < 0.03, Th < 0.05, U < 0.07, Yb < 0.03, and Zr < 0.3. This work revealed that there is a significant trend for increase with age in mass fractions of Co ($p < 0.0085$), Fe ($p < 0.037$), Hg ($p < 0.035$), Sc ($p < 0.015$), and Zn ($p < 0.0014$) and for a decrease in the mass fraction of Mn ($p < 0.018$) in prostates, obtained from young adult up to about 60 years, with age. In the nonhyperplastic prostates of males in the sixth to ninth decades, the magnitude of mass fractions of all chemical element were maintained at near constant levels. Our finding of correlation between the prostatic chemical element mass fractions indicates that there is a great variation of chemical element relationships with age.

1. Introduction

Prostate cancer (PCa) is the second most common cause of male cancer-related deaths and the most common male non-cutaneous malignancy in the Western world (Velonas et al., 2013). PCa is the sixth most common type of cancer worldwide (Karimi et al., 2012). According to epidemiological data the greatest risk factor for prostate cancer is increasing age. The prevalence of prostate cancer drastically increases 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). Results of autopsy studies have shown that almost 30% of men over the age of 50 have histological evidence of prostate cancer (Stangelberger et al., 2008).

Aging is a complex process involving biochemical and morphologic changes in single cells, in organs, and in the whole organism. One of the most generally accepted explanations of how aging occurs at the molecular level is the oxidative stress

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hypothesis (Olinski et al., 2007). Reactive oxygen species (ROS) are widely considered to be a causal factor not only in aging but in a number of pathological conditions, including carcinogenesis. Aging, considered as an impairment of body functions over time, 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 ROS scavenging (Minelli et al., 2009). Oxidative damage to cellular macromolecules which induce cancer can also arise through overproduction of ROS and faulty antioxidant and/or DNA repair mechanisms (Klaunig et al., 2010). Overproduction of ROS is associated with inflammation, radiation, and some other factors, including overload of some chemical elements, in both blood and certain tissues, or deficiency of other chemical elements with antioxidant properties (Järup, 2003; Zaichick and Zaichick, 1999; Zaichick, 2004a; Zaichick, 2006; Toyokuni, 2008; Gupte and Mumper, 2009; Lee et al., 2009). Studies have shown that the imbalance in the composition of chemical elements may cause different types of pathology. The importance of appropriate levels of many chemical elements is indisputable, due to their beneficial roles when in specific concentration ranges, while on the other hand they can cause toxic effects with excessively high or low concentrations (Zaichick, 2006).

In our previous studies the high mass fraction of Al, Au, B, Ba, Br, Ca, Cl, Cr, Ga, Li, Mg, Na, Ni, Sr, U, and Zn were observed in nonhyperplastic prostate tissue of adult males when compared with levels in nonprostatic soft tissues of the human body (Zaichick et al., 2012; Zaichick and Zaichick, 2013a, 2013b, 2013c, 2013d). However, some questions about the age-dependence of chemical element mass fraction in prostate glands of adult and, particularly, elderly males ($\geq$61 years old) still remain unanswered. One valuable way to elucidate the situation is to compare the mass fractions of chemical elements in young adult (the norm) with those in older adult and geriatric prostate. Carcinogenesis is considered to have four stages: initiation, promotion, progression, and metastasis. Thus, the findings of the excess or deficiency of prostatic chemical element contents and the perturbations of their relative proportions in nonhyperplastic prostate glands of adult and elderly males, may give an indication of their role in at least two stages of carcinogenesis: initiation and promotion.

The data on chemical element mass fractions in geriatric nonhyperplastic prostate is apparently extremely limited (Hienzsch et al., 1970; Leissner et al., 1980; Tohno et al., 2009). There are many studies regarding chemical element content in prostate of adult males, using chemical techniques and instrumental methods (Tipton et al., 1954; Stitch, 1957; Yamagata, 1962; Tipton and Cook, 1963; Sangen, 1967; Liebscher and Smith, 1968; Höffken and Rausch-Stroomann, 1969; Hienzsch et al., 1970; Schneider et al., 1970; Soman et al., 1970; Forssen, 1972; Kubo et al., 1976; Jafa et al., 1980; Leissner et al., 1980; Tisell et al. 1982; Feustel and Wennrich, 1984; Ogunlewe and Osegbe, 1989; Saltzman et al., 1990; Picurelli et al., 1991; Oldereid et al., 1993; Jaritz et al., 1998; Banaś et al., 2001; Galván-Bobadilla et al. 2005; Guntupalli et al., 2007; Schöpfer et al., 2010; Lopes et al. 2011; Sarafanov et al., 2011; White et al. 2012). However, the majority of these data are based on measurements of processed tissue and in many studies tissue samples are ashed before analysis. In other cases, prostate samples are treated with solvents (distilled water, ethanol etc) and then are dried at a high temperature for many hours. There is evidence that certain quantities of chemical elements are lost as a result of such treatment (Zaichick, 1997; Zaichick, 2004b). Moreover, only a few of these studies employed quality control using certified reference materials (CRM) for determination of the chemical element mass fractions (Oldereid et al., 1993; Schöpfer et al., 2010).

The primary purpose of this study was to determine reference values for the chemical element mass fractions in the intact nonhyperplastic prostate of subjects ranging from young adult males to elderly persons ($\geq$61 years old) using non-destructive instrumental neutron activation analysis (INAA). The second aim was to evaluate the quality of obtained results. The third aim was to compare the chemical element mass fractions in prostate gland of age group 3 (elderly persons, who were aged $\geq$61 years), with those of group 1 (adults aged 21 to 40 years) and group 2 (adults aged 41 to 60 years). The final aim was to estimate the correlations between chemical elements' mass fractions in nonhyperplastic prostate of males in different periods of adult life.

All studies were approved by the Ethical Committee of the Medical Radiological Research Center, Obninsk.

2. Material and methods

2.1. Samples

Samples of the human prostate were obtained from randomly selected autopsy specimens of 65 males (European-Caucasian) aged 21 to 87 years. Age ranges for subjects were divided into three age groups, with group 1, 21–40 years (30.4 $\pm$ 1.1 years, M $\pm$ SEM, n=28), group 2, 41–60 years (49.6 $\pm$ 1.1 years, M $\pm$ SEM, n=27), and group 3, 61–87 years (68.8 $\pm$ 2.7 years, M $\pm$ SEM, n=10). These groups were selected to reflect the condition of prostate tissue in the first (group 1), in the second (group 2) period of adult life, and in old age (group 3). The available clinical data were reviewed for each subject. None of the subjects had a history of an intersex condition, endocrine disorder, neoplasm or other chronic disease that could affect the normal development of the prostate. None of the subjects were receiving medications known to affect prostate morphology or chemical element content. The typical causes of death of most of these patients included acute illness (cardiac insufficiency, stroke, embolism of pulmonary artery, alcohol poisoning) and trauma. All prostate glands were divided (with an anterior–posterior cross-section) into two portions using a titanium scalpel. One tissue portion was reviewed by an anatomical pathologist while the other was used for the chemical element content determination. Only the posterior part of the prostate, including the transitional, central, and peripheral zones, was investigated. A histological examination was used to control the age norm conformity as well as to confirm the absence of any microadenomatosis and/or latent cancer.

2.2. Sample preparation

After the samples intended for chemical element analysis were weighed, they were transferred to an environment with temperature at $-20\,^{\circ}C$ and stored there until the day of transportation to the Medical Radiological Research Center (MRRC), Obninsk. At the MRRC all samples were freeze-dried and homogenized. The pounded sample weighing about 100 mg was used for chemical element measurement by INAA with high resolution spectrometry of short-lived radionuclides (INAA-SLR). The samples for INAA-SLR were sealed separately in thin polyethylene films washed with acetone and rectified alcohol beforehand. The sealed samples were placed in labeled polyethylene ampoules. The pounded sample weighing about 50 mg was used for chemical element measurement by INAA 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 rectified alcohol beforehand and placed in a nitric acid-washed quartz ampoule.

2.3. Standards and certified reference materials

To determine contents of the elements by comparison with known standard, biological synthetic standards (BSS) prepared from phenol-formaldehyde resins were used. Corrected certified