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REVIEW

A Systematic Review of the Nickel Content of the Normal Human Prostate Gland

Vladimir Zaichick *Professor, Dr V. Zaichick Principal Investigator, Department of Radionuclide Diagnostics, Medical Radiological Research Center, Korolyev St.- 4, Obninsk 249036, Kaluga Region, Russia***ABSTRACT**

Introduction: The prostate gland is subject to various disorders. The etiology and pathogenesis of these diseases remain not well understood. Moreover, despite technological advancements, the differential diagnosis of prostate disorders has become progressively more complex and controversial. It was suggested that the nickel (Ni) level in prostatic tissue plays an important role in prostatic carcinogenesis and its measurement may be useful as a cancer biomarker. These suggestions promoted more detailed studies of the Ni content in the prostatic tissue of healthy subjects. **Materials and methods:** The present study evaluated by systematic analysis the published data for Ni content analyzed in prostatic tissue of “normal” glands. This evaluation reviewed 1889 studies, all of which were published in the years from 1921 to 2020 and were located by searching the databases Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science. The articles were analyzed and “Median of Means” and “Range of Means” were used to examine heterogeneity of the measured Ni content in prostates of apparently healthy men. **Results:** The objective analysis was performed on data from the 20 studies, which included 743 subjects. It was found that the range of means of prostatic Ni content reported in the literature for “normal” gland varies widely from 0.030 mg/kg to 4.50 mg/kg with median of means 0.625 mg/kg on a wet mass basis. **Conclusion:** Because of small sample size and high data heterogeneity, we recommend other primary studies be performed

KEYWORDS: : Nickel, Human prostate; Normal prostatic tissue; Biomarkers; Trace elements

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INTRODUCTION

The prostate gland is subject to various disorders and of them chronic prostatitis, benign prostatic hyperplasia (BPH), and prostate cancer (PCa) are extremely common diseases of ageing men [1-3]. The etiology and pathogenesis of these diseases remain not well understood. A better understanding of the etiology and causative risk factors are essential for the primary prevention of these diseases.

In our previous studies the significant involvement of trace elements (TEs) in the function of the prostate was found. [4-15]. It was also shown that levels of TEs in prostatic tissue, including nickel (Ni), can play a significant role in etiology of PCa [16-20]. Moreover, it was demonstrated that the changes of some TE levels and Zn/TE ratios, including Zn/Ni ratio, in prostate tissue can be used as biomarkers [21-27].

It was indicated low levels of Ni in human prostatic tissue (0.48 mg/kg of wet tissue) in study published 66 years ago [28]. However, recently Kwiatek et al. [29] found that the Ni mass fraction in human prostate is one order of

magnitude higher previously published results (4.5 mg/kg of wet tissue). This finding allowed made the inference that the prostate gland accumulates Ni, because the level of metal in prostate was three orders of magnitude higher the blood serum level (<0.001-0.002 mg/L) and two order of magnitude higher the liver level (0.010-0.050 mg/kg of wet tissue) of the Reference Man [30]. In addition, experimental and epidemiological data identified that Ni should be considered as genotoxic carcinogens [31-37]. According to the International Agency for Research on Cancer (IARC) Ni compounds were classified as human carcinogens [38]. These findings promoted more detailed studies of the Ni content of prostatic tissue of healthy subjects, as well as of patients with different prostatic diseases, including BPH and PCa.

The effects of TEs, including Ni, are related to their concentration. Recorded observations range from a deficiency state, through normal function as biologically essential components, to an imbalance, when excess of one element interferes with the function of another, to

pharmacologically active concentrations, and finally to toxic and even life-threatening concentrations [39-41]. In this context, low dose of Ni is an essential nutrient for the humans and animals [42,43]. However significant Ni exposure may result in adverse health effects in different organs or tissues, including malignancy such as cancers of the lung, nasal cavity, paranasal sinus, stomach, breast, as well as PCa [31-38,44]. However, precise molecular mechanisms by which this metal causes healthy cells to transform to malignant states have yet to be fully defined. Multiple mechanisms of carcinogenesis have been proposed involving oxidative stress, DNA damage and genomic instability, and epigenetic modulation [32,34,35]. By now, a few studies have reported the Ni content in tissue of "normal" and affected glands. However, further investigation has been considered necessary to provide a practical reference data of Ni levels in prostate norm and disorders, because the findings of various studies indicate some discrepancies.

The present study addresses the significance of Ni levels in prostatic tissue as a biomarker of the gland's condition. Therefore, we systematically reviewed all the available relevant literature and performed a statistical analysis of Ni content in tissue of "normal" glands, which may provide valuable insight into the etiology and diagnosis of prostate disorders.

MATERIALS AND METHODS

Data sources and search strategy

Aiming at finding the most relevant articles for this review, a thorough comprehensive web search was conducted by consulting the Scopus, PubMed, MEDLINE, ELSEVIER-EMBASE, Cochrane Library, and the Web of Science databases, as well as from the personal archive of the author collected between 1966 to 2020, using the key words: prostatic trace elements, prostatic Ni content, prostatic tissue, and their combinations. For example, the search terms for Ni content were: "Ni mass fraction", "Ni content", "Ni level", "prostatic tissue Ni" and "Ni of prostatic tissue". The language of the article was not restricted. The titles from the search results were evaluated closely and determined to be acceptable for potential inclusion criteria. Also, references from the selected articles were examined as further search tools. Relevant studies noted for the each selected article were also evaluated for inclusion.

Eligibility criteria

Inclusion criteria

Only papers with quantitative data of Ni prostatic content were accepted for further evaluation. Studies were included if the control groups were healthy human males with no history or evidence of urological or other andrological disease and Ni levels were measured in samples of prostatic tissue.

Exclusion criteria

Studies were excluded if they were case reports. Studies involving persons from Ni contaminated area and subjects that were Ni occupational exposed were also excluded.

Data extraction

A standard extraction of data was applied, and the following available variables were extracted from each paper: method of Ni determination, number and ages of healthy persons, sample preparation, mean and median of Ni levels, standard deviations of mean, and range of Ni levels. Abstracts and complete articles were reviewed independently, and if the results were different, the texts were checked once again until the differences were resolved.

Statistical analysis

Studies were combined based on means of Ni levels in prostatic tissue. The articles were analyzed and "Median of Means" and "Range of Means" were used to examine heterogeneity of Ni contents. The objective analysis was performed on data from the 29 studies, with 743 subjects.

RESULTS

Information about Ni levels in prostatic tissue in different prostatic diseases is of obvious interest, not only to understand the etiology and pathogenesis of prostatic diseases more profoundly, but also for their diagnosis, particularly for PCa diagnosis and PCa risk prognosis [27,39]. Thus, it dictates a need for reliable values of the Ni levels in the prostatic tissue of apparently healthy subjects, ranging from young adult males to elderly persons.

Possible publications relevant to the keywords were retrieved and screened. A total of 2010 publications were primarily obtained, of which 1990 irrelevant papers were excluded. Thus, 20 studies were ultimately selected according to eligibility criteria that investigated Ni levels in tissue of normal prostates (Table 1) and these 20 papers [9,13,14,26,28,29,45-58] comprised the material on which the review was based. A number of values for Ni mass fractions were not expressed on a wet mass basis by the authors of the cited references. However, we calculated these values using the medians of published data for water – 83% [59-62] and ash – 1% (on a wet mass basis) contents in normal prostates of adult men [47,61,63,64].

Table 1 summarizes general data from the 20 studies. The retrieved studies involved 743 subjects. The ages of subjects were available for 14 studies and ranged from 0–87 years. Information about the analytical method and sample preparation used was available for 19 studies. All nineteen studies determined Ni levels by destructive (require high temperature drying, ashing, acid digestion, cutting section on a cryomicrotome, and pressing) analytical methods (Table 1): one using X-ray fluorescence (XRF), one – synchrotron radiation-induced X-ray emission (SRIXE), one – proton induced X-ray fluorescence (PIXE), three - atomic emission spectrometry (AES), and thirteen - inductively coupled plasma mass spectrometry (ICPMS).

Figure 1 illustrates the data set of Ni measurements in 20 studies during the period from 1954 to 2020.

Table 1. Reference data of Ni mass fractions (mg/kg wet tissue) in “normal” human prostatic tissue.

Reference	Method	n	Age range	Sample preparation	Ni	
					M±SD	M±SD
Tipton et al. 1954 [28]	AES	4	Adult	D, A	0.48	-
Koch et al. 1956 [45]	AES	4	Adult	AD	~0.03	-
Zakutinsky et al. 1962 [46]	-	-	-	-	<0.1	-
Tipton et al. 1963 [47]	AES	50	Adult	D, A	Median<0.05	-
Forssen 1972 [48]	XRF	12	Adult	A, AD	-	<0.1-1.0
Kwiatek et al. 2005 [29]	SRIXE	1	-	CS (NB)	4.5	-
Guntupalli et al. 2007 [49]	PIXE	27	5338-68)	Pressing	2.40±0.72	-
Zaichick et al. 2012 [50]	ICPMS	64	13-60	AD	0.73±0.72	0.034-33.0
Zaichick et al. 2013 [9]	ICPMS	16	20-30	AD	0.70±0.51	-
Zaichick et al. 2014 [51]	ICPMS	28	21-40	AD	0.68±0.36	0.034-15.6
		27	41-60	AD	0.56±0.48	0.034-16.2
		10	61-87	AD	0.46±0.26	0.17-0.80
Zaichick et al. 2014 [13]	ICPMS	16	20-30	AD	0.66±0.32	-
Zaichick et al. 2014 [14]	ICPMS	50	0-30	AD	0.86±0.69	-
		29	0-13	AD	1.01±0.90	-
		21	14-30	AD	0.70±0.35	-
Zaichick 2015 [52]	ICPMS	65	21-87	AD	0.60±0.39	-
Zaichick et al. 2016 [53]	ICPMS	28	21-40	AD	0.78±0.10	-
		27	41-60	AD	0.73±0.16	-
		10	61-87	AD	0.56±0.12	-
		37	41-87	AD	0.68±0.12	-
Zaichick et al. 2016 [54]	ICPMS	32	44-87	AD	0.53±0.51	-
Zaichick et al. 2016 [55]	ICPMS	37	41-87	AD	0.53±0.52	-
Zaichick et al. 2017 [26]	ICPMS	37	41-87	AD	0.53±0.52	-
Zaichick et al. 2017 [56]	ICPMS	37	41-87	AD	0.65±0,55	0.040-2.12
Zaichick 2017 [57]	ICPMS	37	41-87	AD	0.53±0.42	0.034-16.2
Zaichick et al. 2019 [58]	ICPMS	37	41-87	AD	0.53±0.42	0.034-16.2
Median of means			0.625			
Range of means (M _{min} - M _{max}),			~0.030 – 4.50			
Ratio M _{max} /M _{min}			(4.5/0.03)=150			
All references			20			

M – arithmetic mean, SD – standard deviation of mean,

AES – atomic emission spectrometry, XRF– X-ray fluorescence, SRIXE – synchrotron radiation-induced X-ray emission, PIXE – proton induced X-ray fluorescence, ICPMS – inductively coupled plasma mass spectrometry;

D – drying at high temperature, A – ashing, AD – acid digestion, CS – cut section on a cryomicrotome, NB – needle biopsy.

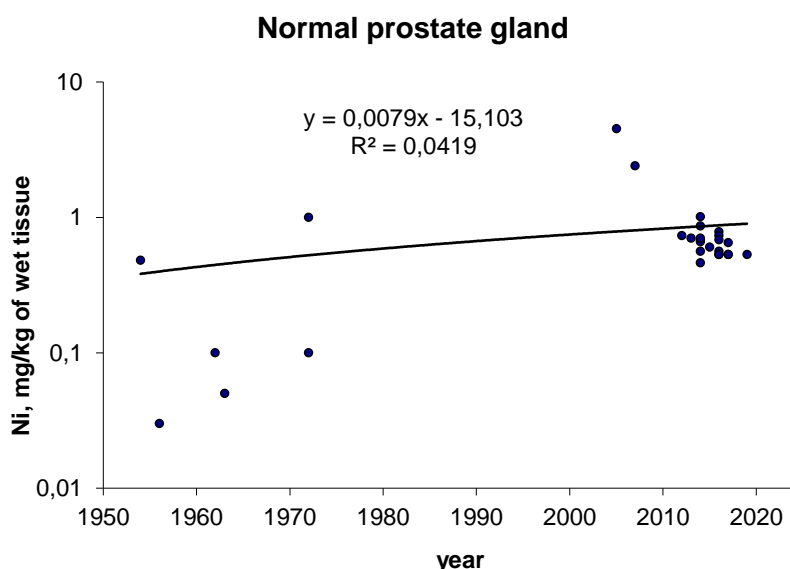


Figure 1. Data on Ni content in normal prostate tissue reported from 1954 to 2020 year.

DISCUSSION

The range of means of Ni mass fractions reported in the literature for “normal” prostatic tissue varies widely from 0.030 mg/kg [27] to 4.5 mg/kg [29] with median of means 0.625 mg/kg of wet tissue (Table 1). The maximal value of mean Ni mass fraction reported [29] was 150 times higher than the median of Ni mass fraction means (Table 1).

This variability of reported mean values can be explained by a dependence of Ni content on many factors, including analytical method imperfections, differences in “normal” prostate definitions, possible non-homogeneous distribution of Ni levels throughout the prostate gland volume, age, ethnicity, diet, smoking, alcohol intake, consuming supplemental Zn and Se, and others. Not all these factors were strictly controlled in the cited studies. For example, in some studies the “normal” prostate means a gland of an apparently healthy man who had died suddenly, but without any morphological confirmation of “normality” of his prostatic tissue. In other studies the “normal” prostate means a non-cancerous prostate (but hyperplastic and inflamed glands were included) and even a visually “normal” prostatic tissue adjacent to a prostatic malignant tumor. In some studies whole glands were used for the investigation while in others the Ni content was measured in pieces of the prostate. However, the very short list of published data does not allowed us to estimate the effect of these factors on Ni content in “normal” prostate tissue.

In our opinion, the leading cause of inter-observer Ni content variability was insufficient quality control of results in published studies. Almost in all reported papers such destructive analytical methods AES and ICPMS were used. These methods require ashing or acid digestion of the samples at a high temperature. There is evidence that use of this treatment causes some quantities of TEs to be lost [39,65,66]. On the other hand, the Ni content of chemicals used for acid digestion can contaminate the prostate samples. Thus, when using destructive analytical methods it is necessary to allow for the losses of TEs, for example when there is complete acid digestion of the sample. Then there are contaminations by TEs during sample decomposition, which require addition of some chemicals. In the case of cutting section on a cryomicrotome (SRIXE method) or pressing (PIXE method) Ni, particularly from prostatic fluid, can be lost during sample preparation. It is possible to avoid these problems by using non-destructive methods, but up to now there are no analytical methods which allow precisely quantify Ni content in “normal” prostate without acid digestion of the samples at a high temperature. It is, therefore, reasonable to conclude that the quality control of results is very important factor for using the Ni content in prostatic tissue as biomarkers.

All natural chemical elements of the Periodic System, including Ni, present in all subjects of biosphere [39,67,68]. During the long evolutionary period intakes of Ni in organisms were more or less stable and organisms were adopted for such environmental conditions. Moreover, organisms, including human body, involved low doses of this element in their functions [42,43]. The situation began to change after the industrial revolution, particularly, over the last 100 years. Several industries involving potential occupational exposure to Ni include mining, metal alloys production such as stainless steel and

superalloys, Ni-contained batteries, and the refinement of this metal. Because Ni increases an alloy's resistance to corrosion and its ability to withstand extreme temperatures, equipment made of Ni-bearing alloys are often used in harsh environments, such as those in chemical plants, petroleum refineries, jet engines, power generation facilities, and offshore installations. Medical equipment, cookware, and cutlery are often made of stainless steel also. Beer kegs, some coins, eyeglass frames, cheap jewellery etc. made of Ni alloys.

Thus, Ni is ubiquitously distributed in environment and food, water, and air everywhere contain this element. In addition to the abundant natural sources of Ni, there are a large number of industrial sources of Ni to the soil (through atmospheric emissions originating from residues from coal, oil, and gas combustion, urban refuse, mine tailings, smelter slag, and waste), water (through irrigation and industrial liquid waste and wastewater sludge application), and air (through atmospheric industrial emissions) contamination. From the polluted environment Ni is subsequently introduced into the food chain [69]. The major routes of nickel intake are dietary ingestion and inhalation. In most individuals, even some who are occupationally exposed, diet constitutes the main source of nickel intake [69-71]. Ni intake in different countries varies and depends on consumption habits [69-71]. However, the human body burden of Ni has increased over the last 100 years due to an increase in global environmental Ni pollution [72]. It is likely that this tendency will continue. Long-term ecological or anthropogenic exposure of humans to Ni via the food chain or work place can lead to chronic diseases or further to mutagenic or cancerogenic changes of different tissues and organs, including prostate [37,69]

Thus, according our study for unpolluted areas there are no information could explain the variability of published means for “normal” prostatic Ni levels from 0.030 mg/kg to 4.50 mg/kg of wet tissue. Moreover, prostate tissue Ni contents showed large variations among individuals, but sources of the variation remain unknown. It is, therefore, reasonable to assume from data of our study that inaccuracy of analytical technologies employed caused so great variability of published means for prostatic Ni levels. This conclusion was supported the fact that the Certified Reference Materials for quality control of results were used only in a very few reported studies.

There are some limitations in our study, which need to be taken into consideration when interpreting the results of this review. The sample size of each study was sometimes relatively small (from 1 to 65), and a total of 743 “normal” prostates were investigated from all 20 studies. As such, it is hard to draw definite conclusions about the reference value of the Ni content in “normal” prostate as well as about the clinical value of the Ni levels in “normal” prostates as a biomarker.

CONCLUSION

The present study is a comprehensive study regarding the determination of Ni content in “normal” human prostates. With this knowledge Ni levels may then be considered as a biomarker for the recognition of prostate disorders. The study has demonstrated that level of Ni in “normal” prostates depends on many unknown factors. Because of

the uncertainties we have outlined, we recommend other primary studies be performed.

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REFERENCES

- [1] Nickel JC. Prostatitis. *Can Urol Assoc J* 2011;5:306–15.
- [2] Lim KB. Epidemiology of clinical benign prostatic hyperplasia. *Asian J Urol* 2017;4:148–51.
- [3] Rawla P. Epidemiology of Prostate Cancer. *World J Oncol* 2019;10(2):63–89.
- [4] Avisyn AP, Dunchik VN, Zhavoronkov AA, Zaichick VE, Sviridova TV. Histological structure of the prostate and content of zinc in it during various age period. *Archiv Anatomy, Gistology, and Ebriology (Leningrad)* 1981;81(11):76–83.
- [5] 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;262:229–34.
- [6] 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. *Appl Radiat Isot* 2013;82:145–51.
- [7] Zaichick V, Zaichick S. INAA application in the assessment of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn mass fraction in pediatric and young adult prostate glands. *J Radioanal Nucl Chem* 2013;298:1559–66.
- [8] 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;156:357–66.
- [9] Zaichick V, Zaichick S. Use of neutron activation analysis and inductively coupled plasma mass spectrometry for the determination of trace elements in pediatric and young adult prostate. *Am J Analyt Chem* 2013;4:696–706.
- [10] Zaichick V, Zaichick S. Relations of bromine, iron, rubidium, strontium, and zinc content to morphometric parameters in pediatric and nonhyperplastic young adult prostate glands. *Biol Trace Elem Res* 2014;157:195–204.
- [11] Zaichick V, Zaichick S. Relations of the neutron activation analysis data to morphometric parameters in pediatric and nonhyperplastic young adult prostate glands. *Advances in Biomedical Science and Engineering* 2014;1:26–42.
- [12] Zaichick V, Zaichick S. Relations of the Al, B, Ba, Br, Ca, Cl, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, and Zn mass fraction to morphometric parameters in pediatric and nonhyperplastic young adult prostate glands. *BioMetals* 2014;27:333–48.
- [13] Zaichick V, Zaichick S. Androgen-dependent chemical elements of prostate gland. *Androl Gynecol: Curr Res* 2014;2:2.
- [14] Zaichick V, Zaichick S. The distribution of 54 trace elements including zinc in pediatric and nonhyperplastic young adult prostate gland tissues. *Journal of Clinical and Laboratory Investigation Updates* 2014;2(1):1–15.
- [15] Zaichick V, Zaichick S. Differences and relationships between morphometric parameters and zinc content in nonhyperplastic and hyperplastic prostate glands. *Br J Med Med Res* 2015;8:692–706.
- [16] Schwartz MK. Role of trace elements in cancer. *Cancer Res* 1975;35:3481–87.
- [17] Soraham T, Waterhouse JA. Cancer of prostate among nickel-cadmium battery workers. *Lancet* 1985 23;1(8426):459.
- [18] Zaichick V., Zaichick S. Role of zinc in prostate cancerogenesis. In: *Mengen und Spurenelemente*. 19. Arbeitstagung. Friedrich-Schiller-Universitat, Jena, 1999, pp 104–115.
- [19] Zaichick V., Zaichick S. Wynchank S. Intracellular zinc excess as one of the main factors in the etiology of prostate cancer. *J Anal Oncol* 2016;5:124–31.
- [20] Zaichick V, Zaichick S, Rossmann M. Intracellular calcium excess as one of the main factors in the etiology of prostate cancer. *AIMS Mol Sci* 2016;3:635–47.
- [21] Dunchik V, Zherbin E, Zaichick V, Leonov A, Sviridova T. Method for differential diagnostics of prostate malignant and benign tumours. Russian patent (Author's Certificate No 764660, priority of invention 27.10.1977). Discoveries, Inventions, Commercial Models, Trade Marks 1980;35:13.
- [22] Zaichick V, Sviridova T, Zaichick S. Zinc in the human prostate gland: normal, hyperplastic and cancerous. *Int Urol Nephrol* 1997;29:565–74.
- [23] Zaichick V, Sviridova T, Zaichick S. Zinc in human prostate gland: normal, hyperplastic and cancerous. *J Radioanal Nucl Chem* 1997;217:157–61.
- [24] Zaichick S, Zaichick V. Trace elements of normal, benign hypertrophic and cancerous tissues of the human prostate gland investigated by neutron activation analysis. *J Appl Radiat Isot* 2012;70:81–7.
- [25] Zaichick V, Zaichick S. Ratios of selected chemical element contents in prostatic tissue as markers of malignancy. *Hematol Med Oncol* 2016;1(2):1–8.
- [26] Zaichick V, Zaichick S. Trace element levels in prostate gland as carcinoma's markers. *J Cancer Ther* 2017;8:131–45
- [27] Zaichick V, Zaichick S. Ratios of Zn/trace element contents in prostate gland as carcinoma's markers. *Cancer Rep Rev* 2017;1(1):1–7.
- [28] Tipton J.H., Steiner R.L., Foland W.D., Mueller J., Stanley M. USAEC-ORNL-Report-CF-54-12-66, 1954.
- [29] Kwiatek WM, Banas A, Gajda M, Gałka M, Pawlicki B, Falkenberg G, et al. Cancerous tissues analyzed by SRIXE. *J Alloys Compd* 2005;401:173–7.
- [30] Iyengar GV. Reevaluation of the trace element content in reference men. *Radiat Phys Chem* 1998;51:545–60.
- [31] Enterline PE, Marsh GM. Mortality among workers in a nickel refinery and alloy manufacturing plant in West Virginia. *J Natl Cancer Inst* 1982;68(6):925–33.
- [32] Sivulka DJ. Assessment of respiratory carcinogenicity associated with exposure to metallic nickel: A review. *Regul Toxicol Pharmacol* 2005;43(2):117–33.
- [33] Grimsrud TK, Peto J. Persisting risk of nickel related lung cancer and nasal cancer among Clydach refiners. *Occup Environ Med* 2006;63(5):365–66.
- [34] Pietruska JR, Liu X, Smith A, McNeil K, Weston P, Zhitkovich A, Hurt R, Kane AB. Bioavailability, intracellular mobilization of nickel, and HIF-1 α activation in human lung epithelial cells exposed to metallic nickel and nickel oxide nanoparticles. *Toxicol Sci* 2011;124(1):138–48.
- [35] Magaye R, Zhao J. Recent progress in studies of metallic nickel and nickel-based nanoparticles' genotoxicity and carcinogenicity. *Environ Toxicol Pharmacol* 2012;34(3):644–50.
- [36] Blanc-Lapierre A, RhaziM, Richard H, Parent M-E. O22-3 Occupational exposure to chromium, nickel and cadmium, and prostate cancer risk and in a population-based case-control study in Montreal, Canada. *Occup Environ Med* 2016;73(Suppl 1):A42.2-A42.

COMPETING INTERESTS

The author declares no competing interests with this case.

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- [37] Chang W-H, Lee C-C, Yen Y-H, Chen H-L. Oxidative damage in patients with benign prostatic hyperplasia and prostate cancer co-exposed to phthalates and to trace elements. *Environ Int* 2018;121(Pt 2):1179-84.
- [38] IARC, International Agency for Research on Cancer. Overall evaluation of carcinogenicity, nickel compounds. Monograph volume 49, 1990.
- [39] Zaichick V. Medical elementology as a new scientific discipline. *J Radioanal Nucl Chem* 2006;269:303-9.
- [40] Hunter P. A toxic brew we cannot live without. Micronutrients give insights into the interplay between geochemistry and evolutionary biology. *EMBO Rep* 2008;9(1):15-18.
- [41] López-Alonso M. Trace Minerals and Livestock: Not Too Much Not Too Little. *International Scholarly Research Notices* 2012;2012:Article ID 704825.
- [42] Anke M, Groppe B, Kronemann H, Grün M. Nickel--an essential element. *IARC Sci Publ* 1984;(53):339-65.
- [43] Spears JW. Boron, chromium, manganese, and nickel in agricultural animal production. *Biol Trace Elem Res.* 2019;188(1):35-44.
- [44] Ionescu JG, Novotny J, Stejskal V, Lätsch A, Blaurock-Busch E, Marita Eisenmann-Klein M. Increased levels of transition metals in breast cancer tissue. *Neuro Endocrinol Lett.* 2006;27(Suppl 1):36-9.
- [45] Koch HJ, Smith ER, Shimp NF, Connor J. Analysis of trace elements in tissue. I. Normal tissue. *Cancer* 1956;9(3):499-511.
- [46] Zakutinsky DI, Parfyenov YuD, Selivanova LN. Data book on the radioactive isotopes toxicology. State Publishing House of Medical Literature, Moscow, 1962.
- [47] Tipton IH, Cook MJ. Trace elements in human tissue. Part II. Adult subjects from the United States. *Health Phys* 1963;9:103-45.
- [48] Forssen A. 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. *Ann Med Exp Biol Fenn (Finland)* 1972;50(3):99-162.
- [49] Guntupalli JNR, Padala S, Gummuluri AVR.M., Muktineni RK, Byreddy SR, Sreerama L, Kedarisetti PC, Angalakuduru DP, Satti BR, Venkatathri V, Pullela VBRL, Gavarasana S. 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* 2007;16(2):108-15.
- [50] Zaichick S, Zaichick V, Nosenko S, Moskvina I. Mass fractions of 52 trace elements and zinc trace element content ratios in intact human prostates investigated by inductively coupled plasma mass spectrometry. *Biol Trace Elem Res* 2012;149:171-83.
- [51] Zaichick V, Zaichick S. Use of INAA and ICP-MS for the assessment of trace element mass fractions in adult and geriatric prostate. *J Radioanal Nucl Chem* 2014;301:383-97.
- [52] Zaichick V. The variation with age of 67 macro- and microelement contents in nonhyperplastic prostate glands of adult and elderly males investigated by nuclear analytical and related methods. *Biol Trace Elem Res* 2015;168:44-60.
- [53] Zaichick V, Zaichick S. Age-related changes in concentration and histological distribution of 54 trace elements in nonhyperplastic prostate of adults. *Int Arch Urol Complic* 2016, 2(2):019.
- [54] Zaichick S, Zaichick V. Prostatic tissue levels of 43 trace elements in patients with BPH. *Br J Med & Med Res* 2016;15(2):1-12.
- [55] Zaichick V, Zaichick S. Prostatic tissue levels of 43 trace elements in patients with prostate adenocarcinoma. *Cancer and Clinical Oncology* 2016;5(1):79-94.
- [56] Zaichick V, Zaichick S. Chemical element contents in normal and benign hyperplastic prostate. *Ann Mens Health Wellness* 2017;1(2):1006.
- [57] Zaichick V. Differences between 66 chemical element contents in normal and cancerous prostate. *J Anal Oncol* 2017;6:37-56.
- [58] Zaichick V, Zaichick S. Comparison of 66 chemical element contents in normal and benign hyperplastic prostate. *Asian J Urol* 2019;6:275-89.
- [59] Isaacs J.T. Prostatic structure and function in relation to the etiology of prostatic cancer. *The Prostate* 1983;4(4):351-66.
- [60] Leissner KM, Fielkegard B, Tisell LE. Concentration and content of zinc in human prostate. *Invest Urol* 1980;18:32-5.
- [61] Woodard HQ, White DR. The composition of body tissues. *Br J Radiol* 1986;59:1209-1218.
- [62] Arnold W.N., Thrasher J.B. Selenium concentration in the prostate. *Biol Trace Elem Res* 2003;91(3):277-80.
- [63] Schroeder HA, Nason AP, Tipton IH, Balassa JJ. Essential trace metals in man: Zinc. Relation to environmental cadmium. *J Chron Dis* 1967;20:179-210.
- [64] Saltzman BE, Gross SB, Yeager DW, Meiners BG, Gartside PS. Total body burdens and tissue concentrations of lead, cadmium, copper, zinc, and ash in 55 human cadavers. *Environ Res* 1990;52:126-45.
- [65] 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, pp 123-133.
- [66] Zaichick V. Losses of chemical elements in biological samples under the dry ashing process. *Trace Elements in Medicine (Moscow)* 2004;5(3):17-22.
- [67] Vernadsky VI. *Living Matter*. Nauka, Moscow, 1978.
- [68] Zaichick V, Ermidou-Pollet S, Pollet S. Medical elementology: a new scientific discipline. *Trace Elem Electroly* 2007;24(2):69-74.
- [69] Anke M, Trüpschuch A, Dorn W, Seifert M, Pilz K, Vormann J, Schäfer U. Intake of nickel in Germany: Risk or normality? *J Trace Microprobe Tech* 2000;18(4):549-56.
- [70] Mania M, Rebeniak M, Postupolski J. Food as a source of exposure to nickel. *Rocz Panstw Zakl Hig* 2019;70(4):393-9.
- [71] Schrenk D, Bignami M, Bodin L, Chipman JK, del Mazo J, Grasl-Kraupp B, Hogstrand C, Hoogenboom L, Leblanc J-C, Nebbia CS, Ntzani E, Petersen A, Sand S, Schwerdtle T, Vleminckx C, Wallace H, Guérin T, Massanyi P, Van Loveren T, Baert K, Gergelova P, Nielsen E. Update of the risk assessment of nickel in food and drinking water. *EFSA J* 2020;18(11):e06268.
- [72] Ahmad MSA, Ashraf M. Essential roles and hazardous effects of nickel in plants. *Rev Environ Contam Toxicol* 2011;214:125-67.