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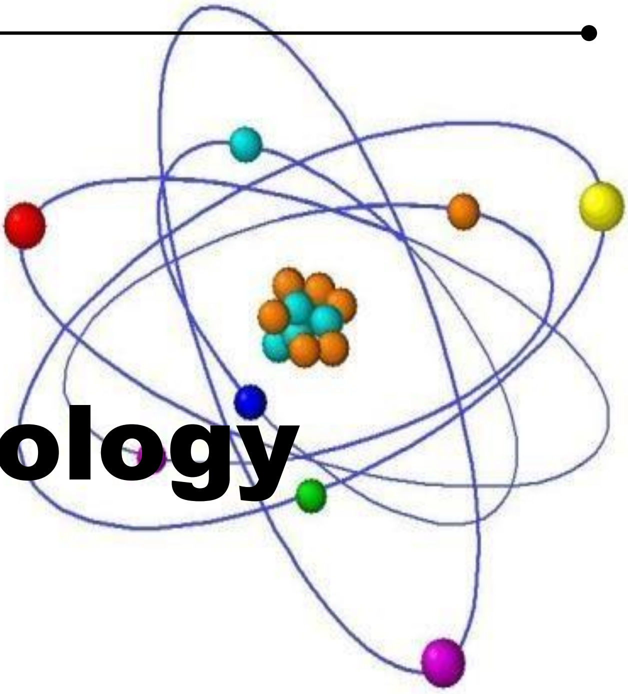

Radiobiology and Radiation safety

The journal "Radiobiology and Radiation safety" publishes scientific articles that reflect the results of radiation and nuclear effects research and the various issues related to radiation safety problems.

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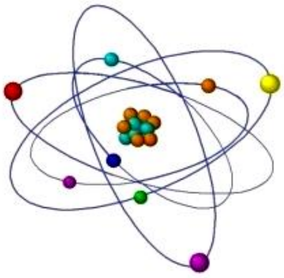

Vassileva J.

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ABSTRACT**:** *Medical use of ionizing radiation is one of the most rapidly developing areas of radiationapplications. Although the access to the medical radiation technologies varies around the world, an important trend is the rapid introduction of new technologies and new techniques linked to the demand of improved diagnosis and treatment outcomes.The technological developments have led to reduction of some of the previously well-established risks, however, new risks emerged linked to the introduction of new modalities with higher doses, easier access to technologies, increased complexity of equipment, as well as the wider group of medical professionals using radiation imaging outside the traditional radiology profession and without proper radiation protection training. The challenges include justification of medical exposure, practical use of approaches for optimization, such as quality control, patient dosimetry, diagnostic reference levels, proper use of imaging in radiotherapy, all linked to the need of improved education and training of health professionals with different professions. Another important area is the need of improved safety culture and team approach to radiation protection, which compliments the safety standards and regulatory actions. Involvement of different key stakeholders is crucial for successful implementation of the international safety standards and recommendations in the medical applications of ionizing radiation.*

Key words: radiation protection, medical uses of radiation, patient protection, justification, optimization

GLOBAL TRENDS IN MEDICAL USES OF IONIZING RADIATION

Medical use of ionizing radiation is one of the most rapidly developing areas of application of radiation. Latest estimates are for around 4.1 billion of X-ray examinations performed worldwide in diagnostic radiology (including dental), 23 million image guided interventional procedures, 40 million nuclear medicine procedures, and 6.2 million radiotherapy procedures [1]. The use of radiation in medicine has brought tremendous benefits to the global population, and because of these benefits, it is expected the number of radiological procedures performed worldwide will continue to increase [2]. Although the access to the medical radiation technologies varies around the world, an important trendisthe rapid introduction of new technologies and new techniques linked to the demand of improved diagnosis and treatment outcomes. Among all modalities used in medicine, the higher dose techniques such as computed tomography (CT), hybrid imaging in nuclear medicine and fluoroscopy guided interventional (FGI) procedures have higher and increasing contribution to the population dose. An important development of medical application is the digitalization of all modalities and their connectivity through the hospital picture archiving and communication systems (PACS), radiology information systems (RIS) and hospital information systems (HIS), introduction of telemedicine and increasing role of artificial intelligence (AI) in all medical applications. An important trend is the use of imaging at different phases of the complex radiotherapy process, from producing the initial plan, performing treatment with high accuracy, and patient follow-up after treatment. All these trends have an impact on radiation protection, which is the focus of this paper. The technological developments have led to reduction of some of the previously well-established risks and radiation protection priorities in the past, such as a better protection of medical staff and reduced individual staff doses, improved awareness andtraining, improved safety features of equipment and access to dose reduction techniques. At the same time however, new risks emerged linked to the introduction of new modalities with higher doses, easier access to technologies, increased complexity of equipment placing demand on the education and training, as well as the wider group of medical professionals using radiation imaging outside the traditional radiology profession, such as cardiologists, surgeons, vascular surgeons, urologists, etc. All these changed in the benefits and risks place some new challenges and issues that require timely actions at international and regional level, which will be shortly described further.

CURRENT CHALLENGES IN RADIATION PROTECTION IN MEDICINE

Justification of medical exposure is one of the areas providing continuous challenges. According to published studies, a significant fraction (20-50%in some areas) of medical imaging procedures is not well justified, meaning performed without net benefit for patient [3]. This unnecessary part of imaging contributes dose and risk to the patient, but not contributing sufficient potential benefit. Since 2007, the IAEA organized a number of technical meetings and consultancies with the Member States, in which the issues related to justification, have been extensively discussed, and actions needed identified. The difficulties are related to the topic being not just radiation protection, but strongly belonging to the medical domain, a complex issue with many contributing factors, that requires a holistic approach and cooperation of many stakeholders – health authorities, professional bodies, radiation protection authorities, health insurance, as well as patients who are in the centre of care. The barriers are linked to the lack of awareness, self-referral or self-presentation, practicing defencing medicine, or a variety of legal, financial and social pressures. The solutions identified include increased awareness, use of referral guidelines for imaging as required by the International Basic Safety Standard (BSS) [4], and use of clinical audit with involvement of professional societies [3,4, 5].

Another important direction of radiation protection work is optimization of radiation protection, which, according to the International BSS, means management of the radiation dose to the patient commensurate with the medical purpose [4]. There is evidence from published literature that much imaging is not optimized, e.g. giving higher dose than necessary, thus contributing dose and risk to the patient unnecessary [6-8]. The international BSS and the accompanying IAEA Safety Guide SSG-46 [5] provide a solid basis for improving optimization through the utilization of different tools: quality assurance and quality programmes, patient dose assessments and establishment and utilization of diagnostic reference levels (DRLs), optimization of clinical protocols by best use of equipment features and dose saving techniques, and integration of optimization into the clinical audits [4, 5].

A key role in optimization plays the clinically qualified medical physicists who are responsible for calibration and dosimetry and should be involved in the clinical optimization team together with medical radiological practitioners and medical radiation technologists (radiographers) [4, 5].

Lack of proper justification and optimization is documented also in the use of image guided radiotherapy (IGRT) as an essential part of the modern therapy, used to delineate targets and normal tissue, in addition to in-room imaging for the purpose of adjusting for target motion or positional uncertainty [9]. While the radiotherapy treatment doses are targeted at the tumour, the doses from imaging are deposited across much larger volumes within the patient and have the potential to give significant cumulative doses to patients and have become a cause for concern. If IGRT is used frequently and the imaging process is not optimised, the doses to organs and tissues outside the planning target volume could be high, and this can also contribute to increase of the dose delivered to the tumour over the course of treatment. Thus, justification and optimization of the use of imaging in radiotherapy are of utmost importance and linked to availability of standards and guidance, as well as appropriate training of radiotherapy staff.

Unintended and accidental exposure of patients happens due to variety of reasons, many linked to human errors but mostly due to systematic problems. Over the last three decades, at least 3000 patients have been affected by radiotherapy incidents and accidents, and the UNSCEAR concluded that radiation accidents involving medical uses have accounted for more deaths and early acute health effects than any other type of accident [1]. The prevention of unintended and accidental medical exposure includes improved procedures and safety rules, use of incidence reporting and learning, and also improved training of staff. The IAEA Safety reporting and learning online systems Safety in Radiation Oncology (SAFRON) (http://rpop.iaea.org/SAFRON) and Safety in Radiological Procedures (SAFRAD) (http://rpop.iaea.org/SAFRAD) provide opportunities for free learning from incidents that happened in other clinics and assessment of risks at introduction of new techniques. Guidance for incident prevention and mitigation in case of incident are provided in a number of IAEA publications [4, 5].

A new issue recently recognised to need more focus and further studies, is the increasing number of patients who undergo frequent imaging. The recent estimatesare for around 0.9 million patients globally who cumulate radiation doses above 100 mSv, where evidence exists for the cancer risk elevation. Recurrent radiological imaging is used for managing various health conditions and chronic diseases such as malignancies, trauma, end-stage kidney disease, cardiovascular diseases, Crohn's disease, urolithiasis, cystic pulmonary disease [10-12]. The solutionto find a balance between the benefit of using imaging for these patients and the associated radiation risks, would be to holistically apply improvement of technologies to reduce individual doses, improve clinical appropriateness and justification pathways, and apply specific optimisation tailored to the clinical condition and patient habitus.Actions on this challenge requires involvement of many different stakeholders.

A big challenge is the lacking regulatory system for radiation protection of patients in line with the international BSS, or when it exists, the week framework for the implementation of the regulatory requirements. The IAEA consultancies revealed a number of areas that need strengthening in this regard, including the need of stronger requirements for involvement of clinically qualified medical physicists and their education, training and certification;implementation of a national strategy for education and training in radiation protection and educational standards; implementation of the concept of DRLs and optimisation in diagnostic and interventional procedures; lack of proper quality control programme and calibration of equipment; improved access to referral guidelines for imaging and improved communication and cooperation between the regulatory bodies, health authorities and professional societies.

CONCLUSIONS

Many elements should be in place to successfully respond to the increasing challenges in radiation protection of patients. They include improved access to modern dose reduction technologies, a robust quality assurance and quality control programme, comprehensive training programmes for all health professionals involved in medical applications of ionizing radiation, proper legislation in line with the international standards and good practices, and improved safety culture and teamwork. Both top-down and down-to-top approach should be practiced with the goal to improve radiation protection of patients and medical staff, and the cooperation at all levels is crucial for the success. The IAEA provides safety standards, guidance, training and information resources to support this process. All these resources are freely available from the publcwebsite of the IAEA on Radiation Protection of Patients, http://rpop.iaea.org.

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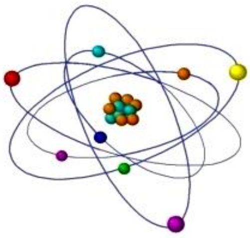
EVALUATION OF DISTRIBUTION OF CARDIAC DOSES IN BREAST CANCER RADIOTHERAPY AND PREDICTION OF PERCENTAGE INCREASE IN CARDIOVASCULAR RISK IN THE GEORGIAN FEMALE POPULATION



(Preliminary Results)

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ABSTRACT: *The purpose of this article is the preliminary Evaluation of cardiac doses distribution in breast cancer radiotherapy and Prediction of Percentage Increase in Cardiovascular Risk in the Georgian Female Population. Patients: The histories of 100 patient cases (40 right breast cancer, 60 left breast cancer) who underwent a course of radiation therapy at the Kutaisi Christina Kiri Cancer Centre in the years 2017-2018, were analysed.*

Dose Evaluation: Patient irradiation program and dose evaluation were performed using conformal 3D and IMRT planning (ZXOX20) and eclipse system based on diagnostic CT scan and virtual simulation (ZXOX30). Total dose 50 Gy, fractional dose 2 Gy, additional dose 10 Gy. MLC blocking was used to protect surrounding tissues. The minimum, maximum and mean dose (MHD) of the heart were recorded.

Data analysis and statistics: Bayesian approach for parameters updating were used to increase the representativeness and accuracy of our survey results. Calculations was performed within hierarchical Bayesian model for a lognormally distributed random value with known variance. As a prior information was used literary data on cardiac doses in breast cancer radiotherapy in EU countries in years 1977-2017. In this case, a posterior distribution function, represents updated with clinical data a prior function, and with crude accuracy can be considered as a dos's distribution in a breast cancer patient in Georgia. The statistical significance of the results was tested with the methods of parametric and non-parametric statistics (ANOVA, Xi2, Shapiro-Wilk test for normality, Grubbs' test and so on).

Results: The mean values of the left and right- sided breast cancer doses and its standard deviations in clinic patients are equal to 2.95 Gy and 2.69, and 1.3Gy, 0.8, respectively. The mean and standard deviation of the normal distribution associated with lognormal approximation of mean heart doses distribution for the left and right sides is equal to 0.87, 0.69 (SW-W = 0.98, p = 0.34) and -0.2328, 0.8236, (SW-W = 0.95, p = 0.07), respectively. The posterior values of the left and right-side doses and their standard deviation are equal respectively to 0.9, 0.08 and -0.2328, 0.12, the mean values of the posterior doses are practically no different from the means of the study cohorts, although their estimation error was reduced practically by 4-7 fold. In the case of doses used in the breast cancer patients of Georgia, the expected total probability of Percentage Increase of Major Adverse Cardiovascular Event Rate is equal to 19% and 6% for the left and right sides, respectively. From the standpoint of the results obtained, the priority areas of our further research are the validation of these results and further refinement of the radiotherapy "benefit-risk" evaluation methodology with consideration of distant tissue effects after radiotherapy

Key words: breast cancer radiotherapy, mean cardiac dose, probability of percentage

INTRODUCTION

According to the World Health Organization, worldwide 2.3 million women were diagnosed with breast cancer worldwide in 2020, of whom 685,000 died. By the end of 2020, there were 7.8 million women alive who had been diagnosed with breast cancer in the last 5 years, making it the most common localization of cancer in the world. Globally, breast cancer is associated with a deterioration in the quality of life associated with disability.

According to the Georgian Cancer Population Register, 29-32% of all cases of malignant neoplasms registered are in women (table 1).

Table 1. Cases of malignant neoplasms registered in women
(Georgian Cancer Population Register) [1]

Number of new cases of breast cancer in Georgia by years 2015-2018				
Years	2015	2016	2017	2018
Total amount	1919	1793	1661	1603

The number of new cases is prevalent in the age group of 50-70 years. At the same time, it should be noted that the incidence of breast cancer in Georgia per 100,000 women, is less than the rate in the European region and the European Union and higher than the average rate in the CIS countries [1]. Radiation therapy is an effective adjunct treatment for many malignant neoplasms, including breast cancer. In fact, over 50% of cancer patients receive radiation therapy. Exposure to radiation causes damage and death of cancer cells, which is the cause of the development of both immediate and distant complications[2].

In the 118 recommendations of the International Commission on Radiological Protection, in the form of an independent radiobiological effect, the so-called long-term tissue reactions [3]. This finding is based on the analysis of long-term complications of radiotherapy in cancer patients and lies in a significant increase in cardiovascular risk. Considering these circumstances, in radiation oncology, it is recommended to take into account the individual factor of the patient's radiosensitivity when selecting the strategy and tactics of therapeutic procedures, especially in the therapy of localizations accompanied by irradiation of the heart muscle and the brain [3,4].

Given the above, and the growth rate of the risk group contingent, the problem of individual and population radiation risk assessment has been made a top priority in modern life sciences and medical sciences, and is currently the subject of large-scale research [5].

Initial and ongoing large-scale population randomized trials will study population dose loads in radiotherapy [4-10], the dependence of the risk of long-term complications on exposure dose, the role of various risk factors, including the role of the development of complications due to irradiation of various functional areas of the heart and concomitant cardiac anomalies, the study of predictors and markers of cardiac risk [11-15]. It should be noted that if in early studies the dose-dependence ratio of cardiological risk was (7.4% 1/Gy) [12], there are data according to which the risk is significantly higher (16% 1/Gy) and its manifestation is within 5 years. They also indicate the presence of a certain limit dose (5 Gy), after which a complication develops - that is, non-linear dependence of the dose-effect. However, according to a number of recent studies, there is no significant increase in cardiac complications [16], the probable explanation for this circumstance is the optimization of radiotherapy procedures and the reduction of the dose range used. There is no unified view on both predictors of distant complications and early markers of complication development.

Finally, the role of individual and population specificity in the risk of cardiac complications is unclear, the role of this factor in terms of both the risk of developing cancer and the effectiveness of its chemotherapeutic and radiotherapeutic interventions [17].

From all the above positions, the study of cardiological risks related to radiotherapy dosage loads and procedure in breast cancer patients is relevant in the population of Georgia: To refine the radiology procedure benefit/risk assessment methodology and to further optimize the strategy and tactics of therapeutic procedures: 1) For evaluations of the flow of cardiac patients related to radiotherapy and combined chemo and radiotherapy of oncological patients and for the optimal treatment of heart diseases олотой. 2) Analysis of population variability of cardiotoxicity of radiotherapy in terms to study its pathogenesis and integration of Georgia into current international studies in this area.

MATERIALS AND METHODS

Patients: The hystories of patients who underwent a course of radiation and combined radiation therapy and chemotherapy at the Kutaisi Christina Kiri Cancer Center in 2017-2018 were analyzed retrospectively.

A total of 1000 patient cases were analyzed (4 right side breast cancer, 60 left side breast cancer). Inclusion criteria: no cardiac complication at the time of irradiation, transmission fraction with echocardiological examination> 50. A potential case of cardiac complication was considered to be a reduction of the delay fraction by about 5–10 units. Information is collected with the consent of patients from their medical history.

Dose Evaluation: Patient irradiation program and dose evaluation were performed using conformal 3D and IMRT planning (ZXOX20) and eclipse system based on diagnostic CT scan and virtual simulation (ZXOX30). Total dose - 50 Gy, fractional dose - 2 Gy, additional dose - 10 Gy. MLC blocking was used to protect surrounding tissues. The minimum, maximum and mean dose (MHD)

Dosage loads in breast cancer radiotherapy:

Variation analysis (ANOVA) was used to assess the statistical reliability of the difference between the mean doses of right and left breast irradiation, and Grubbs' test was used to identify anomalous (outlier) values. Taking into account the asymmetry of the histograms of the dose distribution in patients, the numerical evaluation of the characteristic parameters of the distribution and their comparison with the existing literature data was performed by logarithm-normal distribution:

$$\boldsymbol{Ln(D) = N(\mu, \sigma^2)\ (1),}$$

$$\boldsymbol{P(D|\mu,\rho) = \frac{\sqrt{\rho}}{D\sqrt{2\pi}} * e^{-\frac{\rho}{2}*[ln(D)-\mu]^2}\ ; \qquad \rho = \frac{1}{s^2} \qquad (2)}$$

Where $\boldsymbol{\mu}$ and $\boldsymbol{\sigma}$ are the mean and standard deviations of the normal distributions corresponding to the logarithm-normal distribution. The relationship of these characteristics to the mean of the lognormal distribution ($\boldsymbol{m}$) and the standard deviation **(s)** was established using the following expressions:

$$\boldsymbol{\mu = \ln\left(\frac{m^2}{\sqrt{s^2+m^2}}\right)\ (3)}$$

$$\boldsymbol{\sigma = \sqrt{ln\left[\frac{s^2}{m^2}+1\right]} \quad (4)}$$

The Shapiro-Wilk-test was used to assess the validity of the filtration results.

The Bayesian approach was used to integrate the data obtained by us with the results of various national and international surveys and thus to increase the representativeness and accuracy of our survey results. As a prior information was used [4-10] material published in the works on the distribution of cardiological dose loads in the respective populations. Aposterial dose distributions were considered as the updated probability distribution with the inclusion of a clinical cohort.

We performed the calculations within the Bayesian hierarchical model, approaching the known variance of a logarithmically-normally distributed random quantity. In this approximation, the relationship between the means of posterior and a priori distribution and the accuracy of its becomes simple[18]:

$$\boldsymbol{m' = \frac{mp + n\rho \frac{\sum_{i=1}^{n} ln(D_i)}{n}}{p + n\rho} \; ; \quad p' = p + n\rho} \quad (5)$$

where $\boldsymbol{m'}$ and **p'**; $\boldsymbol{m}$ and $\boldsymbol{p}$ are the means and accuracy of the a posterior and a priori distributions, respectively, ***Di***is the mean dose of cardiac irradiation.Finally, for a posterior distribution we obtained the followingexpression:

$$\boldsymbol{P^{i}_{apost}(D|, m'_i, \sigma_i) = \frac{1}{D\sigma_i\sqrt{2\pi}} * e^{-\frac{1}{2\sigma_i^2}*[ln(D) - m'_i]^2}} \quad (6) \; ;$$

i- Indicates the irradiation side (left-right)
We tested the statistical reliability of the difference between the mean values of the dose distribution characteristics in the a priori, a posteriori, and study cohorts using a ***t***-test.

Assessment of increase of Major Adverse Cardiovascular Event (MACCE) Rate After Breast Cancer Radiotherapy for the Georgian Female Population

The rate of major coronary events was modeled as **Bs(1+KD),** where **Bs** was the rate of major coronary events in the absence of radiotherapy, **D** was the dose of cardiac radiation (**in Gy**),and **K** was the percentage increase in the rate of major coronary events per gray[12].
From these positions, KD represents the percentage increase in major adverse cardiovascular event rate for typical dose loads for Georgia;
The mean value of the K coefficient and its 95% CI was taken [12] from the paper K = 7.4%, (95% CI, 2.9 to 14.5; P <0.001). These values clearly indicate the existence of right asymmetry in the density distribution function of K, which allows us to approximate its lognormal distribution.
By its definition, K can be thought of as a random value whose distribution coincides with the density of the MACCE rate increase (Eff) distribution under the condition D = 1Gy.
With this in mind and simple transformations, it can be shown that the conditional probability of Eff distribution density in the case of D-dose irradiation is described by the following expression:

$$\boldsymbol{P(Eff|, \mu_{Eff}, \sigma_{Eff}, D) = \frac{1}{Eff\sigma_{Eff}\sqrt{2\pi}} * e^{-\frac{1}{2\sigma_{Eff}^2}*[ln(Eff) - (\mu_{Eff} + \ln(D))]^2}} \quad (7) \; ;$$

finally, by combining and integrating the (6) and (7) distributions, we obtain the expected probability of a percentage increase in the major adverse cardiovascular event (MACCE) rate in the left and right sides of the Georgian population.

$$\boldsymbol{P^{i}_{post} = \iint\limits_{Eff,D} Eff \cdot P(Eff|\mu_{Eff}, \sigma_{Eff}, D) \cdot \; P^{i}_{post}(D) \cdot dD \cdot dEff} \qquad (8)$$

RESULTS AND DISCUSSION

Fig. 1 presentsMean values, standard errors, 95% confidentiality intervals and outliers of cardiac doses in radiotherapy of left (l) and right sided (r) breast cancer. The difference between them is statistical significant, however outliers indicate disturbed conditions of normalities of distribution.

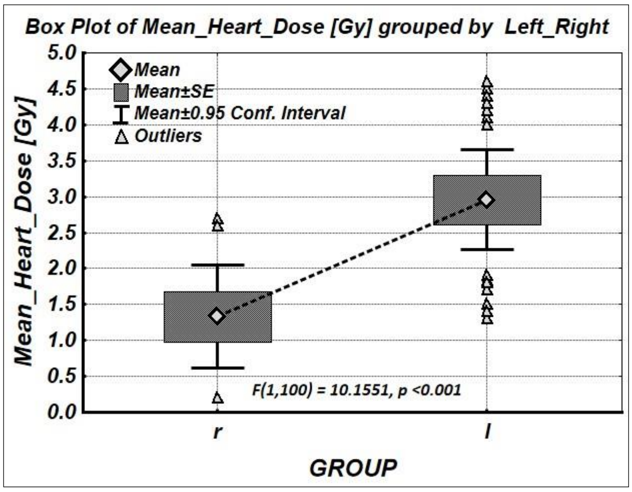

Fig.1. Mean value, standard error, 95% confidentiality interval and outliersof of cardiac doses in radiotherapy of left (l) and right sided (r) breast cancer

Asymmetry in distributions is clearly evident in dose distribution histograms (Fig.2). In order to compare the results of different studies, we considered it expedient to approximate histograms according to parametric theoretical distributions.

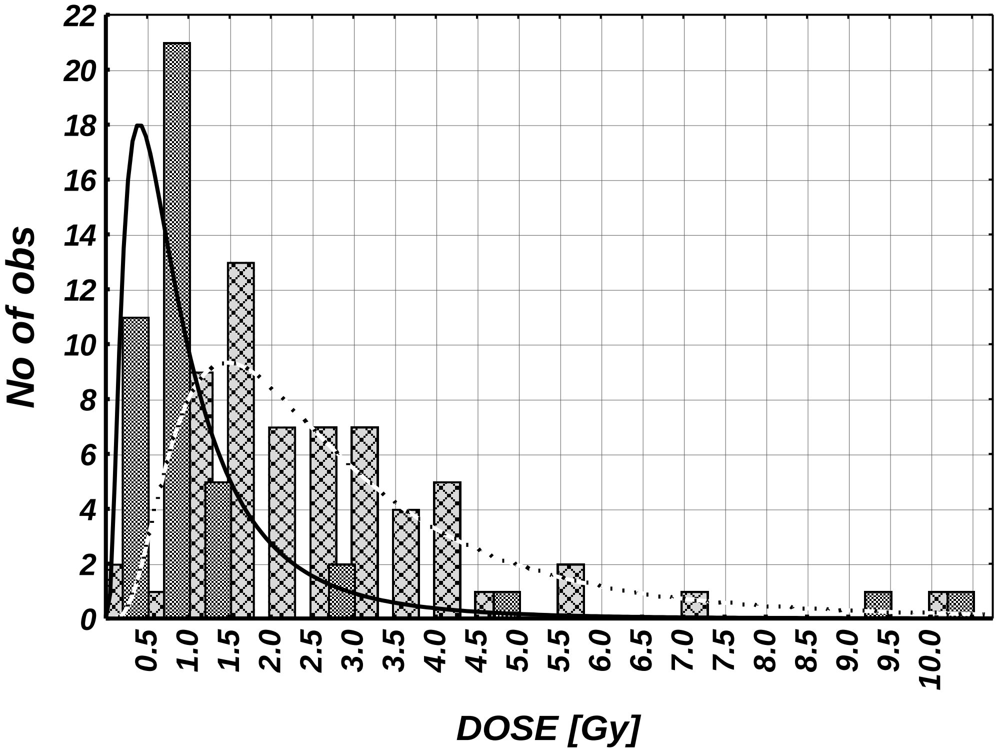

Fig.2. Histograms of cardiac doses distribution and their lognormal approximation in radiotherapy of left (dotted line) and right-sided (solid line) breast cancer

In order to simplify the calculations at this stage and to simplify the interpretation of the results, we considered the logarithmic-normal model to be optimal (Tab.1). The lognormal distribution is one of the important continuous distributions in statistics and due to the fact that it is positively skewed and the effect of a variety of forces working independently on the variability of the lognormal distribution is multiplicative.

Table 1. Meanvalue and standard deviation of distribution of mean heart doses, the mean and standard deviation of the normal distribution associated with lognormal approximation of mean heart doses distribution end value of the Shapiro-Wilk Test of normality

	M	**STD**	**Mean_N**	**Std_N**	**SW-W; p**
Mean Hearth Dose (Left)	2.95	2.69	0.85	0.69	0.97; p=0.33
Mean Hearth Dose (Right)	1.33	2.28	-0.23	0.82	0.95; p=0.07

It should be noted that the asymmetry of the distribution are considered as individual cancer anatomy and its treatment planning [7] and it can reflect both the population-specific aspects of carcinogenesis as well as the specifics of its therapy and in this regard can be used as a criterion for inter-population analysis.However, this is not the subject of this article and we will not discuss it at this point of view. As presented above, a significant proportion of anomalous doses and excesses are observed in the study cohort. Of particular importance in this regard is the assessment of stability, as each new individual case can make significant changes in revealing the patterns of average dose loads for the population and their distribution. Especially if it is based on a study of a limited number of cohorts in one particular clinic. No less important is the question of the representativeness of the cohorts. Considering similar and many other factorsthe US Food and Drug Administration (FDA) has recommended the use of Bayesian statistics in clinical trials of medical devices [21]. Traditional (frequentist) statistical methods may use information from previous studies only at the design stage. In contrast, the Bayesian to formally combine prior information with current information on a quantity of interest. The Bayesian idea is to consider the prior information and the trial results as part of a continual data stream, in which inferences are being updated each time new data become available [21]. In our study, a priori information was taken from data from European Union Countriesabout cardiac dosesIn breast cancer radiotherapy (*Table 2.*)

Table 2.The time range of the examinations selected by us covers the years 1977-2017 and reflects the dynamics of optimization of radiotherapy procedures [4-10]

Country	**Y**	**Side**	**MHD [Gy]**	**STD**
German	1998-2008	*left*	4.6	3.1
German	1998-2008	*right*	1.7	1.2
Danish	1977-1981	*left*	6.1	3.3
Danish	1977-1981	*right*	2.9	1.6
Danish	1982-1988	*left*	5.7	2.3
Danish	1982-1988	*right*	2.9	1.6
Danish	1989-2001`	*left*	5.8	1.2
Danish	1989-2001`	*right*	2.1	0.5
BACCARAT	2015-2017	*left*	2.95	1.49
BACCARAT	2015-2017	*right*	0.46	0.12

There is a clear tendency to reduce cardiac doses, which is explainedwith the introduction of new technologies in radiotherapy. These technologies, such as three-dimensional treatment planning with dose-volume histogram, intensity-modulated radiotherapy (IMRT) image-guided radiotherapy (IGRT), and active breathing controlled (ABC) radiotherapy have the potential to reduce the risk of radiation-related heart problems.

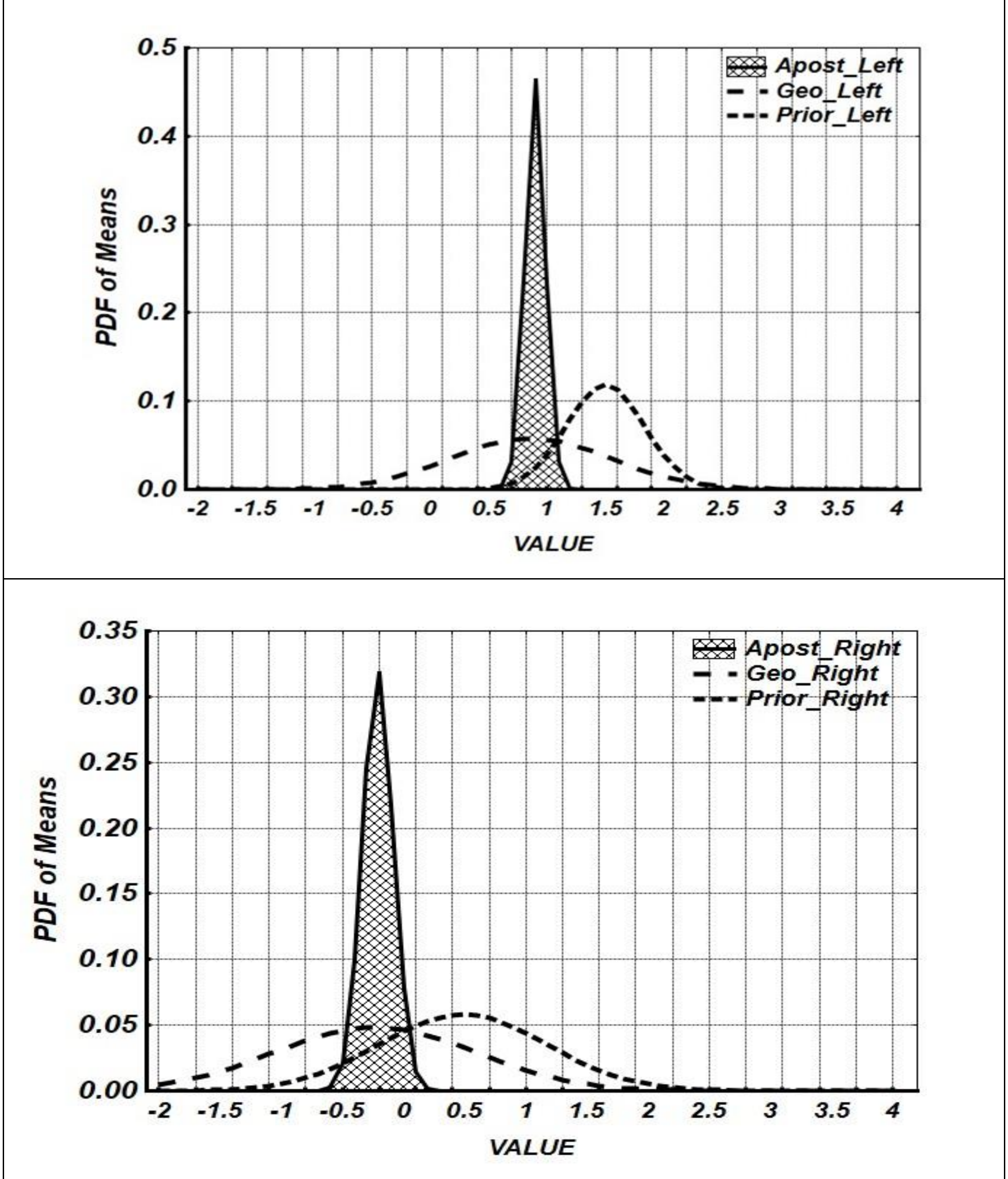

Fig. 3. Probability Density Function of logarithm of prior, cohort and posteriorcardiac doses logarithm distributionin radiotherapy of left and right-sided breast cancer

As shown in Table 2 and Figure 3, the posterior means of the mean heart dose is practically no different from the mean of the cohort, although the mean dispersion and consequently the informational value of the estimate is increased approximately 7-fold

Table 3. Cardiac doses logarithm distribution mean end standard deviation in radiotherapy of left and right sided breast cancer

	Left		Right	
	Mean	STD	Mean	STD
Prior	1.5	0.34	0.48	0.68
Georgian Population	0.86	0.69	-0.23	0.82
Posterior	0.9	0.086	-0.2	0.12

Based on the above, theaverage value of the dose load can be considered as an updated value of the literature and a characteristic of the dose load in the Georgian population in the first approximation. It should be noted that the dose loads on the heart during left-sided radiation in Georgia practically coincide with the results of the latest (BACCARAT) examinations, although the right-sided doses are almost three times higher. Interpretation of this fact requires further analysis.

Figures 4, 5 represents the theoretical function of the dose dependence of conditional probability of percentage increase and dose dependence functions of distribution of this indicator for left and right side radiation in Georgia, calculated by expression (8).

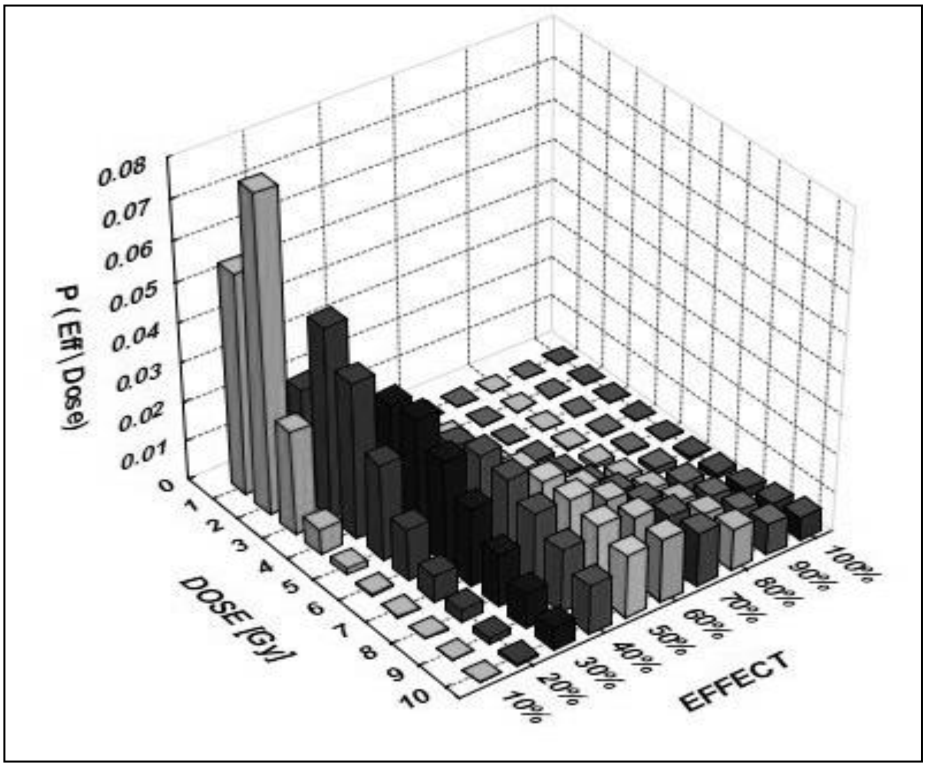

Fig.4Conditional probability density function of Percentage Increase of Major Adverse Cardiovascular Event Rate (EFFECT) for given dose

The conditional probability of percentage increase is characterized by a pronounced peak in the relatively small dose range, while the range of percentage increase varies with increasing dose, indicating a high degree of cardiac risk uncertainty in the high dose range. This complicates the prognosis of cardiac risk in the high-dose radiation range.

By integrating expression (8), we obtain the expected value of major adverse cardiovascular event (MACCE) rate percentage increase in the Georgian population in terms of cardiac dose, it is about 19% for left-sided radiation, and about 6% for right-sided radiation. Left-sided irradiation is Mostly localized in the 10-40% range (dose range 2-4 Gy), while left-sided irradiation is mostly localized in the 5–10% range. These data provide a somewhat remote cardiovascular risk assessment when planning a radiotherapy procedure.

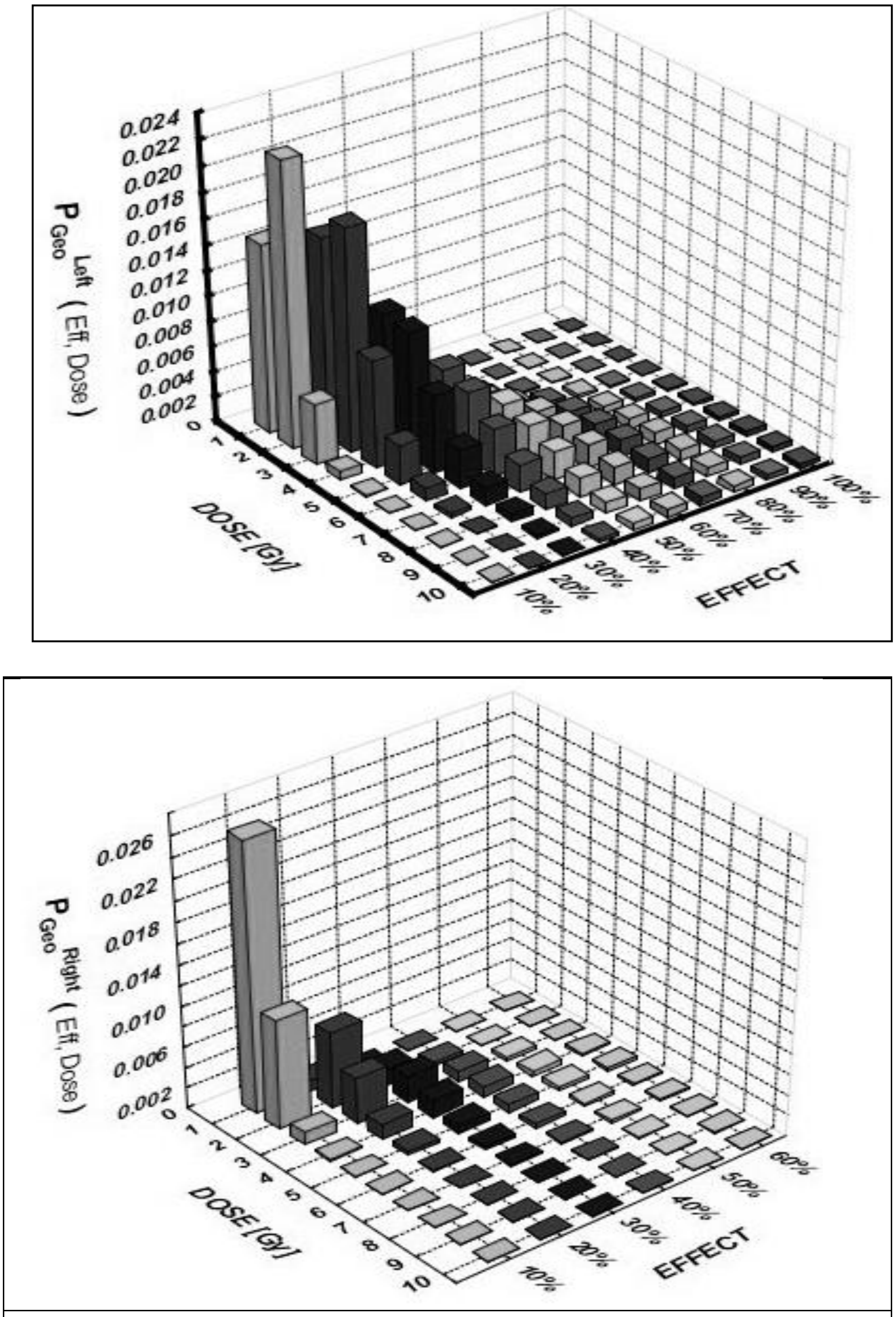

Fig.5. Expected distribution of Probability Density Function of Percentage Increase of Major Adverse Cardiovascular Event Rate (EFFECT) from the dosein Georgian breast cancerpatients

CONCLUSION

From the obtained results, the ways of further optimization of breast cancer radiotherapy are the further clarification of the distant cardiological risk in the relatively small dose range of radiotherapy, further refinement of the radiotherapy "benefit-risk" evaluation methodology with consideration of distant tissue effects after radiotherapeutic effects.

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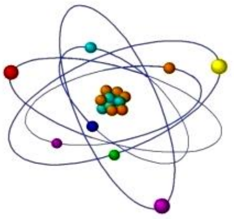
CONSEQUENCES OF RADIOACTIVE AND CHEMICAL CONTAMINATION FOR NATURAL POPULATION OF EARTHWORMS



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ABSTRACT: *The reduced reproduction of A. caliginosaand population densityof lumbricidswas shown at the polluted site. The survival of A. caliginosa after acute γ-irradiation (2270 Gy) was higher at contaminated site ($LD_{50/10}$) than reference site ($LD_{50/6}$).The data obtained indicate the adaptation of inhabiting contaminated site earthworm population to the harsh environmental conditions.*

Key words: radionuclides, earthworms, survival, reproduction, population density

INTRODUCTION

Human industrial activities have left behind a legacy of ecosystems strongly impacted by a wide range of contaminants, including radionuclides. As a rule, the anthropogenic contamination is characterized by the presence of different types of pollutants in the environment. All pollutants, including radionuclides and heavy metals, are deposited in the soil that leads to changes in the state of natural populations of soil fauna. In particular, earthworms are excellent bioindicators of soil pollution because of low migration activity; close contact with contaminated environment.Due to such a set of properties earthworms was chosen as one of the basic reference species in the modern system of the radiation protection of the environment (Larsson, 2008). It is known that radioactive and chemical contamination of soil leads to a wide range of biological effects at different levels of organization of biosystems from molecules and cells to populations and communities. The data about changes in survival (Nakamori et al., 2009; Burgos et al., 2005), reproduction (Krivolutsky, 1987; Anderson et al., 2013), and population density of earthworms (Krivolutskii, 1994) under conditions of radioactive or chemical contamination are widely presented in the literature.

Neverthelessthe combined action of radiation and chemical factors on natural populations of earthworms is poorly studied (Lourenço et al., 2011a; 2011b; 2012; 2013; Mrdakovic Popic et al., 2012). The assessment of chronic radiation or chemical exposure to natural populations, as well as the identification of molecular and cellular mechanisms that allow organisms to sustainably exist in conditions of chronic low-dose exposure to genotoxicants is important challenge (Brechignac et al., 2016; Mothersill et al., 2007).

Therefore, the aim of our study was to investigate the consequences of chronic radiation and chemical exposure for earthworms populations.

MATERIALS AND METHODS

Study area

The earthworms Aporrectodea caliginosa were collected at experimental site near Vodny settlement (Russia) where previously the extraction and production of radium was carried out. This siteis characterized by increasedspecific activities of radionuclides (^{238}U,^{232}Th, ^{230}Th, ^{228}Th,^{226}Ra, ^{210}Po, ^{210}Pb) and concentrations of heavy metals (Cu, Pb, Cd, Zn, Ni, etc.) and As. The ambient dose rate in the air varied from 2.5 to 10.5 μSv/h. The reference sitewas chosen at area without radioactive and chemical contamination of soil. The value of γ–radiation dose rate at reference site was 0.08-0.12 μSv/h.The sites are characterized by similar natural and climatic conditions. The detailed characteristic of sites was presented in our previous articles (Geras'kin et al., 2007; Kaneva et al., 2015; Belykh et al., 2015; Maystrenko et al., 2018; Rybak et al., 2020).

The results of soil radiochemical analysis were presented in figure1. Moreover the total indicator of soil contamination (Z_c) with heavy metals was 108 (dangerous level) and 2 (acceptable level) at contaminated and reference sites, respectively (Revich, 1982).

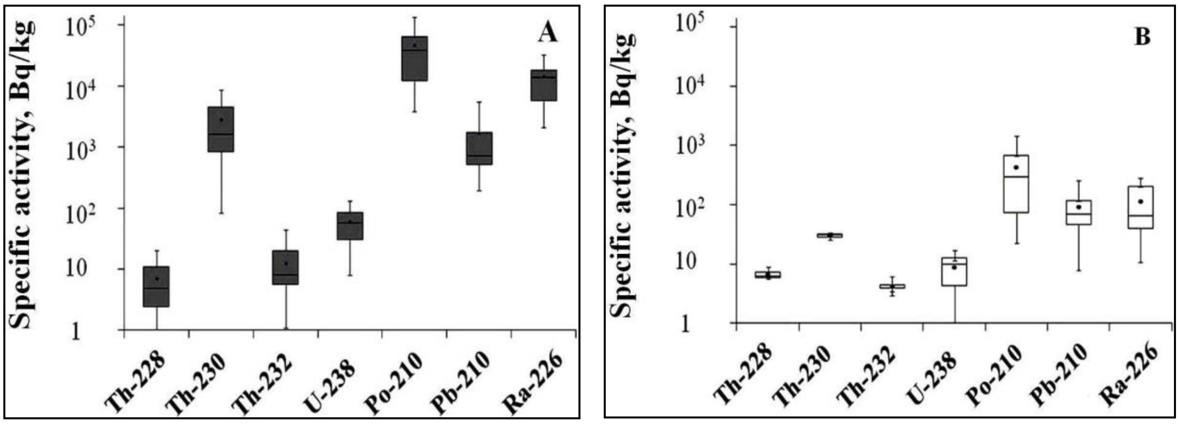

Figure 1 – The box plots of specific activities of radionuclides in soil of contaminated (A) and reference (B) sites

Cultivation of earthworms

The cultivation of earthworms was carried out in plastic containers (14×9×10 cm^3) with 1 kg of wet artificial soil, prepared in laboratory by mixing of natural sand, clay soil (Komi Republic) and neutralized peat (pH = 5.2–6.0) in proportion of 5:4:1, respectively. The acidity of artificial soil was measured before experiment: pH (KCl) = 7.70 ± 0.02. The humidity of soil was 26 ± 1 %(GOST 28268-89). The humidity and food availability were monitored during the experiment.

The specific activities of radionuclides in artificial soil were following: ^{226}Ra - 7.7 ± 1.2, ^{238}U - 94.5 ± 18.9, ^{228}Th - 0.52 ± 0.16, ^{230}Th - 0.38 ± 0.11, ^{232}Th - 0.18 ± 0.05, ^{210}Po - 11.9 ± 11.8, ^{210}Pb - 10.2 ± 1.5 Bg/kg (d.w.). The concentrations of heavy metals and As in artificial soil:Cu - 7 ± 2, Pb - 4 ± 1, Cd - 0.12 ± 0.06, Zn - 20 ± 4, Ni - 16 ± 6, Co - 5 ± 2, Mn - 220 ± 70, Cr - 13 ± 3, Ba - 33 ± 10, As - 3 ± 1, Hg - 0.008 ± 0.004 mg/kg (d.w.). The physical and chemical characteristics of artificial soil: P - 250 ± 80 mg/kg, N - 0.06 ± 0.02 %, C - 2.4 ± 0.4 %, organic matter - 2.8 ± 0.6 %, exchangeable Ca - 5.5 ± 0.4 mmol/100 g, exchangeable Mg - 3.6 ± 0.2 mmol/100 g, K_2O - 105 ±13 mg/kg, Fe_2O_3 - 0.18 ± 0.03 %, Al_2O_3 - 0.14 ± 0.03 %, N-NO_3- - 1.0 ± 0.2 mg/kg, HCO_3 - 170 ± 40 mg/kg, Cl- - 6.4 ± 0.5 mg/kg.

Survival

The survival of adult earthworms A. caliginosa was evaluated after γ-irradiation at 2270 Gy («Issledovatel», USSR, ^{137}Cs, P_γ = 0.7 Gy/min). The distance between the source and biological object was 5 cm.Fiveearthworms were placed into plastic containers with 18 g artificial soil for γ-irradiation (2 replications). After irradiationinvertebrates were cultured inplastic containers with 1 kg of wet artificial soil. Non-irradiated individuals, collected from both sites, were used as control sample (1 replication).The number of surviving earthworms was registered during 30 days after irradiation. Then the cumulative survival curves were constructed using Kaplan–Meier estimator in the program STATISTICA 6.0. The significance of the differences was assessed bythe Mantel Cox test.

Reproduction

Two adult earthworms were placed at plastic container with artificial substrate (m = 1 kg). The estimation was provided for each site using 8-9 replications during 3 months of experiment. The number of produced cocoons was counted 2-3 times a week. The reproductive capacity of earthworms A. caliginosa was evaluated by distribution of the cocoons occurrence frequency per day of parameter registration in all replicationsfor each site (0 – no cocoons, 1-5 – one-five cocoons) and morphometric parameters of coccons (length, diameter, volume). The significance of the differences was assessed with the application of the Mann-Whitney test.

The volume of cocoon (ellipsoid) was calculated using followingequation:

$$V = \frac{4}{3}\pi ab^2,$$

where V – volume of cocoon (cm^3), a – length of coccon (cm), b – diameter ofcoccon (cm).

Population density

The soil monoliths of 0.25×0.25×0.25 m^{3}size from contaminated and reference sites were used to determine the population density of earthworms of Lumbricidae family. The total number of earthworms, selected by hand from soil, was converted into a unit of "individuals per m^2" (ind./m^2). The analysis of relationship between population density and physical and chemical factors was assessed by correlation and regression analysis (Pearson test and linear regression).

RESULTS

Survival after additional acuteγ-irradiation

The long-term living of earthworms A. caliginosa in soil containing increased concentrations of chemicals including naturally occurring radionuclides, could led to pre-adaptation to ionizing radiation exposure and the development of adaptive traitsthat ensure the population existence in conditions of exposure to higher doses of ionizing radiation. Therefore, the survival of A. caliginosa earthworms was studied after acute γ-irradiation with dose 2270 Gy during 30 days of experiment.

The survival of non-irradiated individuals was 100%. The analysis of survival after acute γ-irradiation showed there were no statistically significant differences in resistance of earthworms from polluted and reference sites to high dose of ionizing radiation (Fig. 2A).

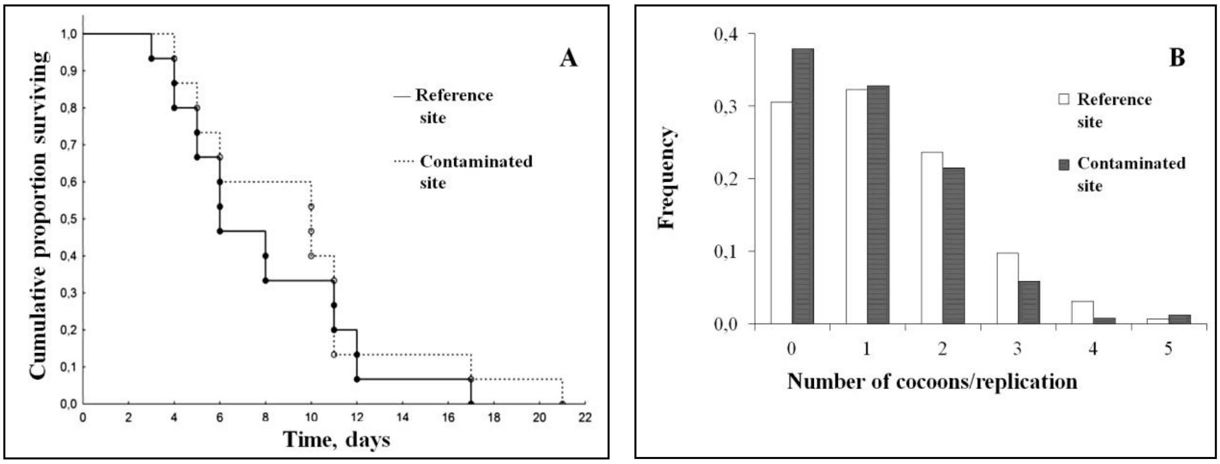

Figure 2 - Survival after γ-irradiation with dose of 2270 Gy (A) and distribution of the cocoons occurrence frequency (B) of A. caliginosa

Despite the lack of evident differences between cumulative survival curves of earthworms from both sites after γ-irradiation, higher survival rate of individuals from polluted site compared to invertebrates from reference site was identified – 21 and 17 days, respectively. After γ-irradiation with dose of 2270 Gy the mortality of 50 % of A. caliginosa from reference site was recorded at 6 day ($LD_{50/6}$), from polluted site – at 10 day of experiment ($LD_{50/10}$). This fact could also indicate the possible adaptation of A. caliginosa earthworms from contaminated site to high doses of ionizing radiation.

Reproduction and population density

Radioactive contamination could inhibit the reproduction, growth and development of organisms. Therefore, we supposed that long-term habitation of A. caliginosa earthworms in soil under conditions of radioactive pollution in the presence of high concentrations of heavy metals can lead to decrease of reproductive potential of organisms as a protective mechanism to ensure a stable existence of population.

The reproductive capacity of earthworms A. caliginosa from reference site, assessed by distribution of the cocoons occurrence frequency in replication during experiment, was significantly higher than the value for invertebrates from contaminated site (p = 0.019) (Fig. 2B). It should be notedthat the absence of cocoons was observed with the greatest frequency in earthworms from polluted site compared to individuals from reference site. But the production of 2-4 cocoons was higher in soil invertebrates from reference site (Fig. 2B). This result indicates the suppression of reproductive function of A. caliginosafrom polluted site, which characterized by high activity concentrations radionuclides and concentrations of heavy metals in soil.

We also assume that the volume of cocoon could be linked with number of individuals in cocoon and the adaptation to living in harsh environment. However, the volumes of cocoons on polluted and reference sites did not significantly differ: 0.2153±0.0017 и 0.2147±0.0019 cm^3.

The population density of earthworms in polluted site was significantly lower than the value for reference site ($p< 0.001$): 51 ± 38 and 178 ± 72 ind./m^2, respectively. In addition, it was shown that the population density of Lumbricidae family linearly depends on pHof soil ($r = –0.67$; $r^2 = 0.4509$, $F = 22.9919$, $p = 0.000049$) and absorbed dose rate ($r = –0.47$; $r^2 = 0.22$, $F = 7.9058$, $p = 0.0089$).Therefore, the increasing values of these factors lead to reducing of population density (Fig. 3). It is important to notethat the influence of other physical and chemical factors (concentrations of heavy metals and main cations and anions) on that biological parameter was not detected.

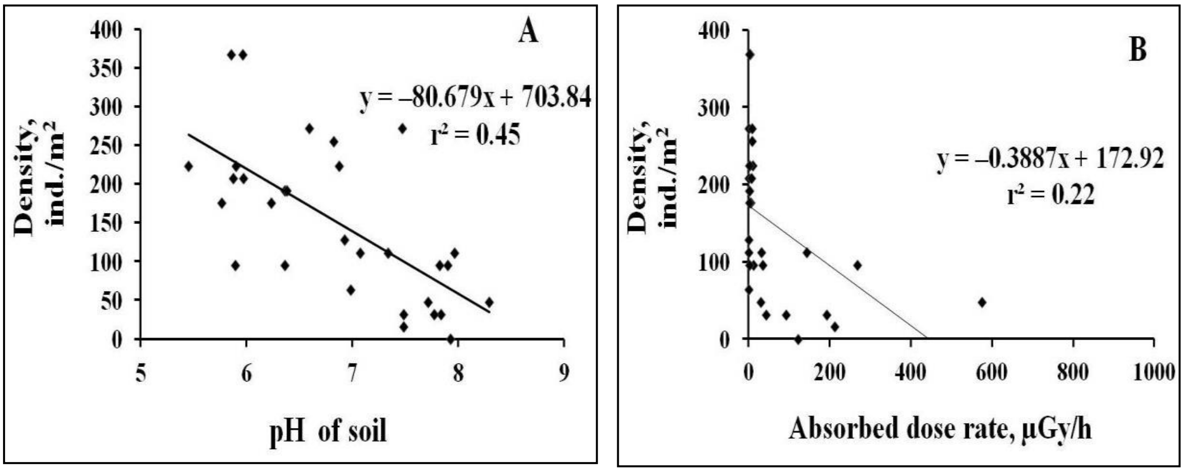

Figure 3- The relationship between population density and pH of soil (A) and absorbed dose rate (B)

DISSCUTION

The maintenance of reproductive capacity of organisms on reduced level is one of the mechanisms of acclimation and population stability to adverse environmental conditions (Sowmithra et al., 2015). In our work the decrease of reproductive potential of A. caliginosa earthworms inhabited contaminated site corresponds to results of investigation (Lourenço et al., 2012). The authors showed that soil contaminated by high concentration of radionuclides (^{234,235,238}U = 163–3696 Bq/kg, ^{230,232}Th = 324–10682 Bq/kg, ^{226}Ra = 1506 Bq/kg, ^{210}Pb = 2318 Bq/kg) and heavy metals (Al = 26440 mg/kg, Ba = 8.5 mg/kg, Be = 50 mg/kg, Cd = 2.6 mg/kg, Fe = 13383 mg/kg, Mn = 3711 mg/kg, Ni = 91.4 mg/kg, Pb = 9.7 mg/kg, Sr = 19.3 mg/kg, U = 215.7 mg/kg, Zn = 511.7 mg/kg) causes negative biological effects associated with the suppression of the growth and reproductive ability of earthworms E. fetida. Ultimately, the reduced reproduction (number, weight, size of cocoons, and number of offspring) is crucial in the survival and stability of the population as a whole (Nakamori et al., 2009; Sowmithra et al., 2015). The increased sensitivity of reproduction capacity compared to other parameters can be explained by the fact that mutations appear immediately after genotoxic exposure and lead to the death of germ cells, thereby reducing the population density of viable individuals in the F1 generation (Nakamori et al., 2009). In addition, the suppression of reproductive function under chronic radioactive and/or chemical contamination also has been shown in studies (Krivolutsky, 1987; Spurgeon et al., 1996; Hertel-Aas et al., 2007; Lourenço et al., 2012; Anderson et al., 2013). This process is usually characterized by a decrease in number of cocoons and juveniles or their complete absence, slowdown in the processes of achieving maturation of juveniles, changes in the size and hatchability of cocoons, etc. In our investigation we identified a statistically significant decrease in the reproductive capacity of A. caliginosa from the contaminated by radionuclides and heavy metals site according to the frequency distribution of a cocoons number ($p = 0.019$). At that, the absence of cocoons was most frequent in individuals from contaminated site, while the number of cocoons from 2 to 4 was more often recorded in earthworms from reference group.

Not only chronic (as was shown above), but also acute radiation exposure causes changes in number, morphological parameters and hatchability of earthworms’s cocoons. For example, the acute γ-irradiation in doses of 1-60 Gy did not lead to influence of cocoon number of E. fetidaearthworms: the number of cocoons varied from 34 to 49 during the experiment (Sowmithra et al., 2015). Nevertheless, the doses of 20-60 Gy induced the decrease of cocoon weight, which became the reason of statistically significant decline of hatchlings number of individuals compared to values for non-irradiated earthworms. Therefore, we expected that combined action of chronic irradiation and chemical pollution on A. caliginosa earthworms from natural population can reduce its reproductive function through volume of cocoons. However, the differences between volumes of A. caliginosa’s cocoons were not found: 0.2153 ± 0.0017 и 0.2147 ± 0.0019 cm^{3}from contaminated and reference sites, respectively. Perhaps, the given result can be explained by the fact that acute irradiation has a more negative impact on the reproductive function than chronic exposure as, for example, it is shown in investigation (Hertal-Aas et al., 2007), where the reproductive function of E. fetida earthworms after acute γ-irradiation turned out to be much more sensitive to radiation stress than after chronic exposure at the same doses. Also morphological changes of cocoons is less sensitive characteristic of organism compared to the level of DNA damages (Kaneva et al., 2015), therefore, much larger data samples are required to record statistically significant differences.

On the contrary, the intensification of reproductive process (increase in the proportion of females and their fertility) of Alexandromys oeconomus from natural populations, lived for 100 generations under conditions of chronic low-intensity exposure of radionuclides on the territory near settlement Vodny, was revealed that is also one of the types of adaptation to stressful conditions (Ermakova et al., 2020). The relationship between reproductive function of earthworms A. caliginosaand population density under radioactive and chemical contamination of soil was shown in our study. The population density of earthworms was significantly ($p< 0.05$) lower in soil of contaminated site than in reference site with suppressed reproductive function of A. caliginosa earthworms. The same changes in populations density was shown in invertebrates populations inhabiting territories affected by an underground nuclear explosion in the Northern Urals, and areas with increased natural radioactivity (Kolesnikova, Taskaeva, 2005; Kolesnikova et al., 2015).It should be remembered that not only technogenic but also natural factors affect the natural populations of living organisms. Natural factors often play animportant role enhancing the effect of anthropogenic factors. We have shown that soil radioactive contamination and pH value has a negative influence on population density of Lumbricidae family. As an example, the study of impact of copper smelters emissions in the Sverdlovsk region on population density of earthworms showed that there was the effect of “Lumbricidae desert” on the plots near smelters - complete absence of earthworms. The author explains this result by the synergistic effect of increased concentrations of heavy metals (Cu, Cd, Pb) and reduced soil acidity (pH 4.7–5.2) (Vorobeichik, 1998).

The survival is less sensitive biomarker of technogenic exposure in invertebrates than reproduction. It is confirmed by the fact that the values of effective doses (ED_{10} and ED_{50}) are tens to hundreds times lower than the half-lethal doses (LD_{50}). After acute γ-irradiation LD_{50} was 825 Gy for E. fetida earthworms, but effective doses to reduce reproduction were much lower LD_{50} (ED_{10} = 3.3 Gy, ED_{50} = 11.1 Gy) (Nakamori et al., 2009). Generally, the half-lethal doses of ionizing radiation for different species of Lumbricidae family vary from 20 to 1600 Gy and depend on their stage of ontogenesis (cocoons, juveniles, adults) (Table 1). The most sensitive stage of ontogenesis is a stage of cocoon. The half-lethal doses of irradiation for cocoons and juveniles can be 10% of LD_{50} for adults (Krivolutskii, 1988). For instance, LD_{50} for cocoons of Dendrobaena octaedra was 20 Gy (Table 1).

The analysis of survival of A. caliginosa adult earthworms after acute γ-irradiation did not allow confirming the results of preliminary laboratory experiments that the dose ~ 2000 Gy is $LD_{50/30}$, that is, the causing mortality of 50% of individuals during 30 days. However, it should be mentionedthat dose 2270 Gy is half-lethal for A. caliginosa earthworms from reference site after 6 days of exposure, for invertebrates from polluted site – 10 days (Fig. 2A, Table 1). A. caliginosa earthworms from contaminated site showed neither statistically significant increased sensitivity nor resistance for this indicator after additional γ-irradiation. However, we observe a tendency to greater survival after additional acute exposure in invertebrates previously lived in conditions of chronic radiation exposure (Fig. 2A).

CONCLUTION

Finally, soil radioactive and chemical contamination induces the biological effects in earthworms of family Lumbricidae such as reduction of reproduction of individuals and associated population density, but also can lead to higher survival rate of A. caliginosa after additional acute γ-irradiation with dose of 2270 Gy. This dose was $LD_{50/10}$ for earthworms from contaminated by radionuclides and heavy metals site and $LD_{50/6}$ – from reference site. This may be sign of adaptation for higher doses of ionizing radiation invertebrates that previously lived under soil contamination with radionuclides and heavy metals.

This study was performed within the frameworks of thebudget federal program of the Russian Federation (the state task number is AAAA-A18-118011190102-7).

Table 1 – LD$_{50}$ for earthworms after irradiation

Species	LD$_{50}$, Gy	Time of survival	Publications
Eisenia fetida	20	30 days	Viktorov, 1999
	600	30 days	
	650	4 weeks	Suzuki, Egami, 1983
	825	2 weeks	Nakamorietal., 2009
Lumbricus rubellus	100	30 days	Viktorov, 1999
	<600	30 days	
	>1024 (β)	30 days	
Lumbricus terrestris	1000	35 days	Hancock, 1962
	678	30 days	Reichle et al., 1972
	600	5 days	Viktorov, 1989
Aporrectodea caliginosa			
Kursk population	1120 ± 30	30 days	Viktorov, 1989
Ural population	1340 ± 60		
Aporrectodea rosea	570 ± 60	30 days	Viktorov, 1989
Dendrobaena octaedra (cocoons)	20	30 days	Viktorov, 1989
Earthworms*	600–1600	30 days	Krivolutskii, 1988; Krivolutsky, 1994
Earthworms *	~1000	–	Krivolutskii, 1988
Aporrectodea caliginosa			
Reference site	2270	6 days	our study
Contaminated site		10 days	

* – the species were not identified.

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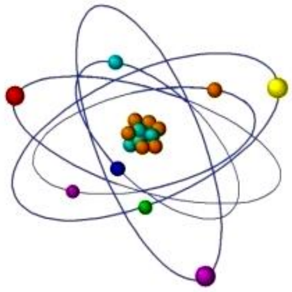
RESEARCH OR RADIONUCLIDES ACCUMULATION REGULARITY BY GEORGIAN POPULAR CULINARY HERBS FOR THE DETERMINATION OF HEALTH-CONNECTED RISKS



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ABSTRACT**:** *In all neighboring countries of Georgia, programs for the construction and operation of nuclear power plants of various capacities are being actively developed, which does not exclude the problems of radionuclide emissions and migration during technogenic accidents. A special place in this regard is occupied by the study and forecasting of possible food contamination mechanisms by taking into account the specifics of the food ration of the local population for each region. The present paper discusses the peculiarities of the accumulation of radionuclides by culinary herbs typical for Georgia. They are one of the main ingredients for Georgian national cuisine. Based on the experimental data obtained, calculations have been made on the possible risks to the health of the population in the event of extreme contamination of territories with anthropogenic radionuclides. By comparing the accumulation coefficients of radionuclides (radiocesium) in the tissues of culinary herbs with the level of the average consumption of these ingredients, additional parameters of dose load at the level of various organs of the human body have been determined. Based on the use of software modeling methods, the possible risks of radiobiological effects dangerous to health, on the example of radiation cancer development, during radionuclide contamination of culinary herbs in Georgia, through their long-term consumption for food, were identified.*

Key words: radionuclides accumulation, culinary herbs, cancer risk

INTRODUCTION

The main factors for population defense and strengthening are population nutrition conditions, raw nutrient materials, and product quality and safety [1]. During the last few years, important attention is paid to healthy nutrition, which includes food products biological, chemical and radiation safety [2,3,4,5].

The safety of food products proposes the non-existence of unacceptable risks connected to the harmful impacts on humans. Harmful impacts have resulted from the presence of pollutant substances in food, such as radionuclides that pose important dangers to human life and health.

The last decades showed that large-scale radionuclide pollution is created by technogenic problems at atomic energy facilities and the radiation industry [6,7,8,9]. On the example of the Chernobyl disaster, Georgian past years experience showed the dangers of food products radiation pollution. Despite the significant distance, due to the atmospheric migration from the catastrophic site, most of the country was polluted by short-lived, as well as, long-lived radionuclides [10].

Based on scientific research, it is determined that such pollution of different qualities has been kept during the decades [11]. At the same time, nowadays, practically in every neighboring country of Georgia, the process of construction and exploitation of nuclear power plants with different capacities is developed, which does not exclude radionuclides dispersion and migration problems. In this direction, an important role relies on the research of possible nutrient pollution mechanisms and forecasting considering local population nutrition ration specificity for each region of Georgia.

Culinary herbs represent one of the main ingredients of Georgian national cuisine. Because of this, they are not only utilized in dry and raw forms, but are also used as an additional component during the cooking in practically every region's nutrition rations. Accordingly, research of radionuclide accumulation specificity by different culinary herbs has significant scientific and practical importance for determining the level of risks during the possible pollution by technogenic radionuclides of different territories.

RESEARCH OBJECT AND METHODS

The research object was represented by popular culinary herbs for Georgian population’s nutrition ration: Coriander (*Coriandrum sativum*), Dill (*Anethum graveolens*), Parsley (*Petroselinum crispum*), Salad (*Lactúca satíva*), Savory garden (*Satureja hortensis*), Cress (*Lepidium sativum*), Baselik (*Ocimum basilicum*). Soil contaminated with radiocesium was used as the radioactive substrate. Plants grown on contaminated soil and intended for radiometry were subjected to drying and shredding on an electric homogenizer until a powdery mass was obtained. The content of radionuclides was determined by gamma-spectrometry (Gamma-Beta Spectrometer, Atomtex-MKC-AT-1315 and Gamma-Spectrometer CANBERRA with liquid nitrogen cooled germanium detector).

The accumulation coefficient in different organs of the plant was calculated with the content of ^{137}Cs in the soil and plant tissues. Additionally, estimation of different parameters (Table 3-4) were performed by processed software product FRAMES (Framework for Risk Analysis in Multimedia Environmental Systems – Version 1.7), by Pacific Northwest National Laboratory (PNNL).

RESULTS AND DISCUSSION

Radiation safety issues of food products are characterized by global, alongside with national, specificities. First of all, the importance of this idea relies on the consumption of different food products, which has significant regional and national specificity. The undeniable importance of the aforementioned work is a determination of plant species and varieties specificities in terms of radionuclide accumulation which can lead to the calculation of the dose-load in a single organism of the specific population. For the research, we chose popular Georgian culinary herbs. Conducted radiometric analysis showed significant differences in radioactive cesium accumulation levels. For example, if in *Petroselinum crispum* tissues isotope accumulation level was only 920 Bq/kg, in *Lepidium sativum* and *Satureja hortensis* variants the same indicators were 4890 Bq/kg and 6081 Bq/kg, accordingly. Relatively intermediate accumulation levels in research objects had the following species: Coriander, Dill, Cress, and Basilic.

Table 1 - Activity of ^{137}Cs in culinary herb tissues, cultivated on radionuclide polluted soil.

#	**Expermental Plant**	**Radioactivity of plant tissues (Bq/kg, calculated from dry weight)**
1	Coriander (*Coriandrum sativum*)	1125±65
2	Dill (*Anethum graveolens*)	3955±79
3	Parsley (*Petroselinum crispum*)	920±81
4	Salad (*Lactúca satíva*)	2640±84
5	Savory garden (*Satureja hortensis*)	6081±71
6	Cress (*Lepidium sativum*)	4890±91
7	Basilic (*Ocimum basilicum*)	1210±63
	Activity of radiocesium polluted soil	12200±39

It is acknowledged that the radionuclide accumulation issue, mainly, depends on the soil contamination levels, as well as specific plant cultivation conditions. To standardize and make a relative analysis of the obtained results, we used an accumulation coefficient indicator. As it is seen from figure 1, individual varieties of experimental plants are characterized by specific indicators of radiocesium accumulation level.

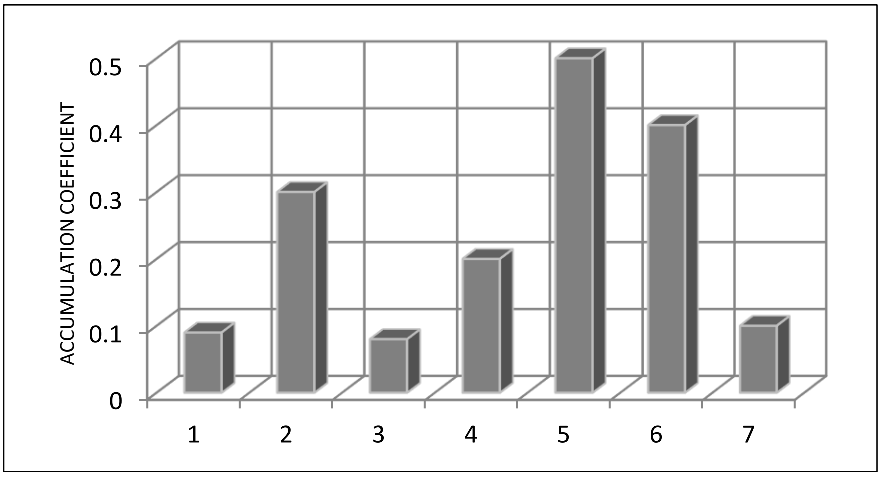

Fig. 1 -^{137}Cs accumulation coefficient in plant tissues, cultivated on radionuclide polluted soil. 1 - Coriander (*Coriandrum sativum*), 2 - Dill (*Anethum graveolens*), 3 - Parsley (*Petroselinum crispum*), 4 - Salad (*Lactúca satíva*), 5 - Savory garden (*Satureja hortensis*), 6 - Cress (*Lepidium sativum*), 7 - Baselik (*Ocimum basilicum*).

As it is known, every radionuclide, natural or anthropogenic origins, is characterized by common radiological signs as far as they can enter the organism through consumption of food and water, as well as through breathing, where radionuclides can be mixed up with the air particles. However, some forms of human activity, such as industrial, medical, or agricultural, can increase radiation exposure at the expense of those radionuclides which exist naturally in the environment [12]. Additionally, the exclusive danger is created by long-lived anthropogenic radionuclides [13,14]. ^{137}Cs is an example of such radionuclide. Alongside the other dangerous features for human health, this isotope is characterized by cumulative properties [15]. For the latter reason, when using radionuclide-contaminated culinary herbs in food, to investigate possible risks, it is necessary to determine characteristics such as indicator of daily consumption of such plant ingredients, calculation of further extrapolation of this data for longer periods, and radionuclide absorption as a result of their use.

To obtain these indicators, we determined the average rate of daily consumption of culinary herbs' 75 families, cultivated in different parts of Georgia. Furthermore, calculations were performed for each type of culinary herb consumption, and the level of equivalent radioactive cesium content was determined. As it is seen from Table 2, all presented plant species are distinguished with species peculiarities in terms of radioisotope contents, as well as their quantitative consumption level. Thereby, the total dose of radiocesium daily penetration in the organism during the consumption of food with different culinary herbs was formed into the grams quantitative ratio (for standardization, which was represented by dry weight calculation) of the daily consumption mass to the total activity of ^{137}Cs in each variant.

Table 2. Average daily consumption norm of culinary herbs contaminated by radiocesium and its absorption indicator

#	Experimental Plant	Average daily consumption norm (g/dry weight calculation)	Activity of ^{137}Cs, taken with food (Bq/kg)
1	Coriander (*Coriandrum sativum*)	9	10,1
2	Dill (*Anethum graveolens*)	2	7,9
3	Parsley (*Petroselinum crispum*)	6	5,7
4	Salad (*Lactúca satíva*)	5	13,2
5	Savory garden (*Satureja hortensis*)	0,5	3
6	Cress (*Lepidium sativum*)	3	14,7
7	Basilic (*Ocimum basilicum*)	4	4,8
	Total Indicator	**29,5**	**59,4**

Based on the experimental results we gained, in case of extreme contamination of different territories by anthropogenic radionuclides, calculations were done on the possible risks of population health and cultivation of different species of culinary herbs used for consumption.

It is established that in terms of organism's different responses to the exposure of radiation, issues of the radial carcinogenesis process become very important. They represent a constant attention area for numerous scientific centers (ICRP, UNSCEAR). Such particular interest is conditioned form the fact that radiation-caused carcinogenesis materials create the radiation impact risk assessment basis. Data on the carcinogenic effects of radionuclides are fundamental to understanding the general patterns of pathogenesis and tumor growth, to developing methods for the prevention and therapy of malignant neoplasm, and to determining the dose load of radionuclides induced in the body. During the radionuclide absorption into the organism, depending on the exposure dose, early, as well as distant, effects can be developed. It is assumed that early effects have a threshold nature. The damages occur only after the exposure dose exceeds the threshold dose. These effects can be formed during accidental situations when a significant amount of radionuclides enter the organism. However, in practice, the massive radionuclide penetration in the organism is conditioned by the consumption of food products. Because of this, one of the main and especially dangerous distant effects of incorporated radiation is the development of various types of cancer. To study the specific case of the penetration of radionuclides into the body through the use of culinary herbs for food, we used the methods of calculating the possible risks related to the differential radiation load on individual human organs, as well as the consumption of culinary herbs popular in Georgia. Namely, the equivalent dose and effective dose were evaluated (Tab.3) for each ingestion exposure pathway using the ingestion dose coefficients (Federal Guidance Report 13, ICRP 60) [16] assessed as follows:

$$\mathbf{IH_{cigT}}\ (\mathbf{t}) = \mathrm{I_{cig}}\ (\mathbf{t})\ \mathbf{HC_{igcT}}$$

where $\mathbf{IH_{cigT}(t)}$ = equivalent dose to organ **T** from ingestion intake of radionuclide **i** in food crop **c** for an individual in age group **g** for exposure over time period **t** (Sv), $\mathbf{I_{cig}(t)}$ **-** ingestion intake of radionuclide **I** in food crop **c** for individuals in age group **g** for exposure over time period **t (Bq)**

$\mathbf{HC_{igcT}}$ = equivalent dose coefficient to organ **T** for ingestion intake of radionuclide **i** of class **c** for an individual in age group **g (Sv/Bq).**

Additionally, the evaluation of the food crop (leafy vegetables) intake parameter was performed as follows:

$$\mathbf{I_{cig}(t) = C_{ci}\ (t)\ U_{cg}T_{cg}\ ED_{\ cg}}$$

Where $\mathbf{I_{cig}(t)}$= total intake radionuclide i in food crop **c** over the period **t** from ingestion for individuals in age group **g** (Bq),

$\mathbf{C_{csi}(t)}$ = average concentration in food crop **c** at agricultural location **s** for radionuclide

I (Bq/kg),

Ucg = ingestion rate of food crop c by an individual in age group **g**(kg/d)

$\mathbf{T_{cg}}$= annual intake factor giving the days per year that food crop **c** is eaten by individuals in age group **g** (d/y),

$\mathbf{ED_{cg}}$= exposure duration for consumption of food crop **c** for individuals in age group **g** (y).

Tab.3 Distribution of radiocesium to Organs, absorbed from the food intake (Based on computational model)

Duration of chronic exposure	Year
Constituent	**^{137}Cs**
Dataset	**usr2:Soil**
Pathway	**Leafy vegetables**
Route	**Ingestion**
Measure	**dose (μSv)**
Dose Organ	Ages 0 to 70
Adrenals	305
Bld Wall	314
B Surface	299
Brain	256
Breasts	243
Esophagus	284
St Wall	291
SI Wall	304
ULI Wall	313
LLI Wall	363
Kidneys	293
Liver	295
Lungs	275
Muscle	272
Ovaries	311
Pancreas	313
R Marrow	285
Skin	233
Spleen	293
Testes	273
Thymus	284
Thyroid	284
Uterus	314
Total	**6697**

Tab.4 Carcinogenesis risk indicator, as a result of long-term consumption of radiocesium contaminated culinary herbs

Duration of chronic exposure	Year
Constituent	**^{137}Cs**
Dataset	**usr2:Soil**
Pathway	**Leafy vegetables**
Route	**Ingestion**
Measure	**risk (cancer incidence)**
Cancer Organ	Ages 0 to 70
Esophagus	3.36E-07
Stomach	1.2E-06
Colon	5.47E-06
Liver	4.73E-07
Lung	2.34E-06
Bone	3.91E-08
Skin	2.1E-08
Breast	1.79E-06
Ovary	5.32E-07
Bladder	1.56E-06
Kidneys	2.37E-07
Thyroid	7.38E-07
Leukemia	1.57E-06
Residual	5.58E-06
Total	**2.19E-05**

For estimation processed software product FRAMES (Framework for Risk Analysis in Multimedia Environmental Systems) Version 1.7, by Pacific Northwest National Laboratory (PNNL) was used.

During the regular consumption of radionuclide polluted nutrient herbs, on the basis of individual human organ dose load data, in the form of distant effects, development of different types of cancer risk was determined through the following method: for performing the assessment of health impacts, calculation was done using organ-dependent health effect conversion factors (Federal Guidance Report No.13) [17,18]. The risk from ingestion of food crops (leafy vegetables) is evaluated (Tab.4) as follows:

$$\mathbf{RH_{cigT}\ (t) = I_{csig}\ (t)\ RC_{igocT}}$$

where $\mathbf{RH_{cigT}(t)}$ - risk to organ **T** from ingestion intake of radionuclide **i** in food crop **c**

for an individual in age group **g** for exposure over time period **t** (risk)

$\mathbf{I_{cig}(t)}$- ingestion intake of radionuclide i in food crop **c** for individuals in age group **g** for exposure over time period **t(Bq**)

$\mathbf{RC_{igocT}}$ - risk coefficient to organ **T** for food ingestion intake of radionuclide **I** of class

c for an individual in age group **g** (1/Bq).

CONCLUSION

In general, based on the conducted studies, the forms of realization of radiation pollution of food products were determined during possible technical problems at the nuclear facilities located in the neighboring countries of Georgia. Significant data are currently available on the specifics of the migration of radionuclides in the food chain under different ecological conditions, although the universality of this data varies greatly depending on the vegetation structure of a particular region and the nature of the food at the national level. Our studies have shown particular level of accumulation of radionuclides in culinary herbs widespread in Georgia. It is clear that in the ration of the Georgian population, similarly to the diet of European population, plant products are significantly used, although the active consumption of culinary herbs in Georgia creates an additional level of dose load. By comparing the accumulation coefficients of radionuclides (for example radiocesium) in the tissues of culinary herbs with the level of average consumption of these ingredients, additional parameters of dose loading at the level of various organs of the human body were determined. Based on the use of software modeling methods, the possible risks of radiobiological effects dangerous to health, on the example of radiation cancer development, during radionuclide contamination of culinary herbs in Georgia, trough their long-term consumption for food, were identified.

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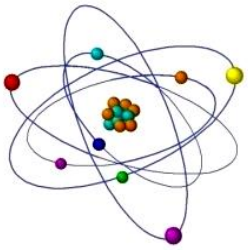
CONNECTION OF SUM LIGHT AEROIONS CONCENTRATION WITH NATURAL GAMMA RADIATION AND AIR TEMPERATURE IN WESTERN GEORGIA



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ABSTRACT: *Results of investigation of connection of sum light aeroions concentration (N) with environmental gamma radiation (Г) and air temperature (T) in western Georgia are presented.Simultaneous measurements of N, Г and T were madeat 166 different points by using portable aeroions, gamma and temperature survey meters.The terrain height (H) varied from 6 to 1928 m above sea level.The statistical characteristics of the values ofN, Г and Thave been studied. In particular, the following results were obtained. Range of changes of investigation parameters is following:N – 450÷3100 sm*$^{-3}$*, Г - 40÷180 nSv/h, T - 10÷34 ˚C. Mean values: N – 1898 sm*$^{-3}$*, Г - 80 nSv/h, T – 24.6 ˚C.Coefficient of linear correlation (R) of individual values of N with Г, T and H accordingly are: 0.08 (level of signification α=0.25), 0.30 (α<0.005) and 0.12 (α=0.10). It is absent correlation between Г and T.A multiple linear regression equation N with Г, T and H is obtained.In particular, the variability of the individual N values with the variability of other studied parameters within the variation range is as follows (166 different pointsof measurements): Г–6.9 %, T – 61.0 % and H – 47.1 %. Thus, the main factor in the variability of the content of light air ions in this case is not the ionizing effect of gamma radiation from the soil, but the air temperature (variability of radon emanation from the soil) and the height of the terrain (variability of cosmic radiation). Connection of the averaged values of N on the Г has the form of a linear function: N = 2.9228·Г + 1671.2 (R = 0.96, α<0.005).*

Key words: environmental gamma-radiation, natural radioactivity, light Ions

INTRODUCTION

The light ions concentration in the atmosphere in many respects defines the ecological state of medium both itself and being the indicator of the purity of air in the aspect of aerosol pollution [1-5].

The content of light ions in the atmosphere plays the significant role in molding of the physiological state of people [6-9]. Under the "good weather" condition, the minimally necessary level of the sum light ions content for the favorable influence on the health of people is ≈1000 cm^{-3} and more. If the sum light ions concentration is ≈600 cm^{-3} and less, the following negative physiological action on the human organism are observed: fatigue, weakening attention, retarding of reactions, worsening in the memory, headache, the disturbance of the regime of blood pressure, etc. Air, saturated by the high content of ions (4500 cm^{-3} and more), possesses therapeutic properties - optimization of blood pressure, positive influence on the course of the diseases of respiratory organs, bronchial asthma, antiseptic action, etc. The very high concentrations of light ions (100000 cm^{-3} and more) negative affect the health of people [1, 10, 11].

The formation of light ions in the ground layer of the atmosphere occurs due to the alpha radiation of radon and short-lived products of its decay (40 %), gamma-radiation of soil (40 %) and cosmic rays (20 %). The disappearance of ions occurs due to their recombination and attachment to the aerosols. Usually the concentration of light ions always directly depends on the intensity of the ionizing radiation [12].

Atmospheric aerosol is the mixture of the usual particles of the natural and anthropogenic origin (mineral aerosol, sea aerosol, the solid ejections of industrial enterprises and transport, etc.) and the so-called secondary aerosol. Secondary aerosol is formed in the presence of the chemical and photochemical reactions according to the scheme of gas→ particle. However, it turned out that radioactive (including gamma radiation) and cosmic radiation contributes to the acceleration of the processes of the secondary aerosol formation [1,2 4,5, 13-16].

Therefore, in highly polluted areas, instead of direct the feedbacks between ionizing radiation and the content of light ions in the air may appear. For example, in Tbilisi city according to the data of the complex monitoring of small ions concentration, radon, aerosol, cosmic rays and gamma-radiation the effect of feedback of intensity of ionizing radiation with the small ions content in atmosphere is discovered. One of the reasons for this effect just may be catalyzation of the processes of formation secondary aerosols in atmosphere according to the scheme of gas→ particle by the ionizing radiation, which occur more intensive than the ions formation [1,2, 4, 5].

In particular, a comparison of the influence of gamma radiation on the content of light ions in twenty points of Tbilisi city and an ecologically cleaner atmosphere in western Georgia (111 points, height range from 100 to 500 m above sea level) showed that the correlation between Γ and N in Tbilisi is inverse, and in western Georgia, as it should be, is direct correlation [1, 2].

In addition to the above-mentioned ionized radiation and aerosol air pollution, the content of light ions is influenced by many other factors: weather conditions, terrain, places with waterfalls, fountains, national parks, nature reserves, forests, alpine regions, mountain gorges, river and sea coasts, tectonic faults (increased concentration of radon), karst caves, etc. [1, 6, 8, 9, 17, 18].

So in [18] the data about the content of aeroions in Tbilisi and some locations of Western Georgia with different types of landscape are represented. In particular, it is shown that even in the limits of the strongly contaminated city the landscape has vital importance for creating the medium ecologically favorable for human health (Tbilisi National Botanical Garden, territory of Tbilisi Sea, etc.). Therefore, variations in the content of light ions in the air often depend more on some listed factors (weather conditions, landscape, hydroionization, phytoionization, etc.) than on direct alpha, beta, gamma and cosmic radiation.

This work is a continuation of the study [2].Results of investigation of connection of sum light aeroions concentration with environmental gamma radiation and air temperaturein western Georgia are presented below.

STUDY AREA, MATERIALS AND METHODS

Study area – western Georgia. Measurement of values of gamma radiation was made on ~ 20 cm above the ground surface, sum aeroions concentration and air temperature measured on ~ 1.0 m above the ground surface.The portable survey meters were using [1-5,18,19].Simultaneous measurements of investigation parametersin 2007-2008 at 166 different pointswere made (fig. 1).The terrain height varied from 6 to 1928 m above sea level.

In the proposed work the analysis of data is carried out with the use of the standard statistical analysis methods of random events [20].

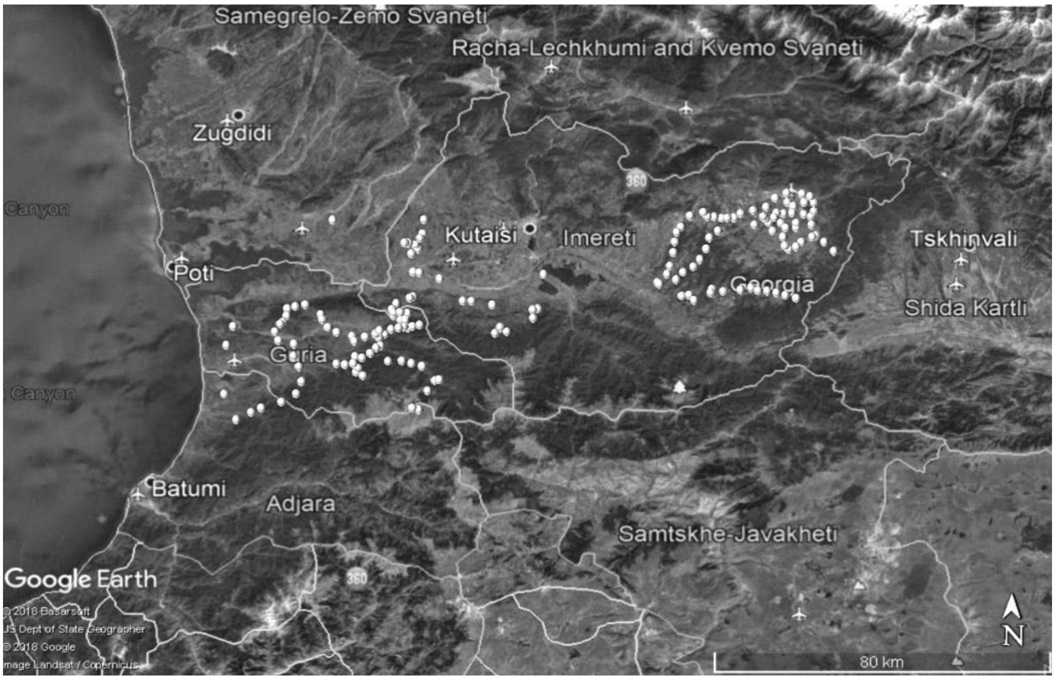

Fig. 1. Location of measurement points in western Georgia.

The following designations will be used below: Mean – average values; Min – minimal values; Max - maximal values; Range – Max-Min; St Dev - standard deviation; C_V = 100·St Dev/Mean – coefficient of variation, %; R^2– coefficient of determination;R – coefficient of linear correlation;α - the level of significance; N – sumaeroions concentration, cm^{-3}; Γ- value of gamma radiation,nSv/h; T - air temperature, ˚C; H - terrain heightabove sea level, meter.

RESULTS

The results in table and fig. 2 are presented.

In table the statistical characteristics of Γ, T, H and N in western Georgia are presented.

Table. Statistical characteristics of Γ, T, H and N in western Georgia.

Variable	Γ, nSv/h	T, C^o	H, m	N, cm^{-3}
Mean	80	24.6	341	1898
Max	180	34	1928	3100
Min	40	10	6	450
Range	140	24	1922	2650
St Dev	25.3	4.46		547
Cv,%	31.8	18.1		28.8
	Correlation Matrix			
Γ, nSv/h	1	-0.004	0.44	0.08
T, C^o	-0.004	1	-0.35	0.30
H, m	0.44	-0.35	1	0.12
N, cm^{-3}	0.08	0.30	0.12	1

As follows from table range of changes of investigation parameters is following: N – 450÷3100 sm^{-3}, Γ - 40÷180 nSv/h, T - 10÷34 ˚C. Mean values: N – 1898 sm^{-3}, Γ - 80 nSv/h, T – 24.6 ˚C. The largest variations are noted for the values of Γ(Cv=31.8%), the smallest - for T(Cv=18.1%). Coefficient of linear correlationof individual values of N with Γ, T and H accordingly are: 0.08 ($\alpha=0.25$), 0.30 ($\alpha<0.005$) and 0.12 ($\alpha=0.10$). It is absent correlation between Γ and T.

It should be noted that for an altitude range of 100-500 m above sea level (111 measurement points) the linear correlation between Γ and N is higher (R=0.27, $\alpha<0.005$) [2] than in this case (an altitude range from6 to 1928 m, 166 measurement points). Nevertheless, a positive correlation between these parameters remains.

A multiple linear regression equation N with Γ, T and H is presented below:

$$N = -0.939\cdot\Gamma + 48.244\cdot T + 0.465\cdot H + 627.86 (R^2 = 0.147, \alpha<0.005)$$

The variability of the individual N values with the variability of other studied parameters within the variation range is as follows (166 different points of measurements): Γ – 6.9 %, T – 61.0 % and H – 47.1 %.

Thus, the main factor in the variability of the content of light air ions in this case is not the ionizing effect of gamma radiation from the soil, but the air temperature (variability of radon emanation from the soil) and the height of the terrain (variability of cosmic radiation).

In fig. 2 linear correlation and regression between averaging values of N and Γ is presented.

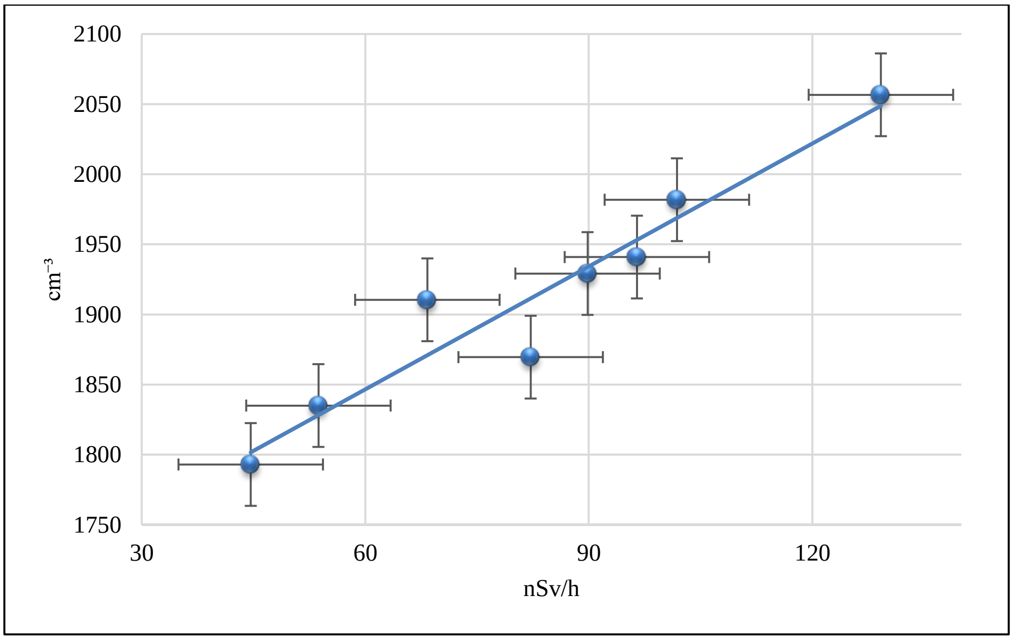

Fig. 2. Linear correlation and regression between averaging values of N and Γ.

In this case connection of the values ofN on the Γ connection is very close:

$$N = 2.9228\cdot\Gamma + 1671.2 (R = 0.96, \alpha<0.005).$$

Thus, when averaging the data, the relationship between Γ and N is revealed more clearly (fig. 2) than in the case of correlating their individual values (table). Apparently, in this case, the effects of temperature and altitude in the variability of the concentration of light ions are leveled.

CONCLUSION

In the future, we plan conduct more detailed studies in this direction for different regions of Georgia.

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INFLUENCE OF METAL IONS AFTER ONE YEAR REPEATED IRRADIATION OF SPIRULINA PLATENSIS

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ABSTRACT: *Combined effects of Cs*^{137}*gamma irradiation and heavy metal ions Ni(II), Zn(II), Cu(II), Mg(II), Mn(II), Cr(III), Cr(VI), Co(II),Pb(II),Cd(II) on Spirulina platensis cells using UV-VIS spectrometryafter one year again repeated cultivation, irradiation and recultivation were discussed.*

It was shown, that possible use of gamma irradiation together with Ni(II),Cr(III), Cu(II),Pb(II), Cd(II),Co(II) and Zn(II) ions does not change nature of interaction of these metal ions on Spirulinaplatensis.In the case combined effects of ionizing radiation and Mg(II) ions for Spirulina platensis exhibit synergetic effects for all components of Spirulina platensis as a stimulatory agent to raise the contents of it. This trend is seen to continue for all constituents of Spirulina platensis when these metal ions were added in vitro after one year irradiation and recultivation. Chromium (VI) does not contribute to a decrease in absorption intensity unlike Cr(III) and Cu(II). Influence of these metal ions on the constituent (Chl a, Phycocyanin, soret band of Chl a) of cyanobacterium Spirulina platensis differs from its effectiveness.

Key words: Spirulina platensis, metal ions, gamma irradiation

INTRODUCTION

All biological material has affinity for metals and radionuclides, some biomolecules function specifically to bind metals. The bioaccumulative properties of marine organisms towards radionuclides may be very useful for potential application in monitoring and assessment procedures of the marine environment as such and especially in monitoring nuclear facility waste sites. Radionuclides can be used as radiotracers in studies of heavy metal and organic pollutant behaviour in marine flora [1,2]. Because heavy metals can have different influences on marine algae, it is important to recognize bioaccumulation as a means of assessing the potential risk arising from the presence of heavy metals in the environment. Once in the environment, metals may undergo transformation, either into various mobile forms in an environmental. Biological activity accounts for a large number of the environmental for heavy and toxic metals whether derived from natural or anthropogenic sources. Metal ions can be accumulated by microorganisms by non-specific physico-chemical interactionsas well as specific mechanisms of sequestration or transport [3].

Spirulina is one of multicellular unbranched non-heterocystous filamentous microalgae which are recognizable by the unique open left-handed helix along the entire length of the filament. Compared to other foods, Spirulina shows extraordinary nutritional value as it provides high levels of many essential nutrients and minerals. Spirulina is the most highly consumed microalga [4], which has been widely used as human healthy food centuries ago and it is currently produced commercially as healthy food and valued additives in a hugely profitable business. In our works [5,6] influence of 7.2 kGy Cs^{137} gamma irradiation have been studied with optical and differential scanning microcalorimetry (DSC) methods for cyanobacterium Spirulina platensis intact cells in the suspension, wet mass, and dry mass samples and also simultaneous effects of Cd(II), Pb(II) ions and γ-irradiation on stability of Spirulinaplatensisintact cells after 7.2 kGy Cs^{137} gamma irradiation and without irradiation.

In this paper, discussed combined effects of Cs^{137} gamma irradiation and heavy metal ions same concentrations on Spirulina platensis cells using UV-VIS spectrometry ,when after one year the same Spirulina platensis (which was irradiated with 7.2 kGy one year ahead) again irradiated and recultivated 2-times with 10kGy gamma irradiation.

MATERIALS AND METHODS

Spirulina platensis IPPAS B–256 strain was cultivated in a standard Zarrouk [7] alkaline water–salt medium at 34ºC, illumination ~5000lux, at constant mixing in batch cultures [8]. The cultivation of the Spirulinaplatensiscells was conducted for 14 days. The growth was measured by optical density by monitoring of changes in absorption at wave length 560nm using the UV–Visible spectrometer Cintra 10e. The intact cells suspension of Spirulina platensisat pH 9.1 in the nutrition medium was used for scanning the absorption spectra from 400 to 800nm.

The concentration of Spirulinaplatensis was determined by the instrumental data [9,10]. In this work Spirulina platensiswhich was irradiated with 7.2 kGy, then recultivated and re-irradiated with the same dose as studied by us in the papers [5,6]. After one year this irradiated and cultivated Spirulina platensis stood up for re-cultivation. 100 ml of this was added to 100 ml a standard Zarrouk medium. After 2 weeks of incubation the reseived mass was irradiated again.Spirulinaplatensissuspension after 14 days of cultivation have been irradiated with 10kGy gamma radiation for 14 days using Cs^{137} as a gamma radiation source at the Applied Research Center, E. Andronikashvili Institute of Physics.

Dose rate - 0.017Gy/sec. In this case after 2-times repeited irradiation and recultivation were studied effect of metal ions on Spirulina platensis. The dry weight and the concentration of different compounds were estimated at late exponential phase.

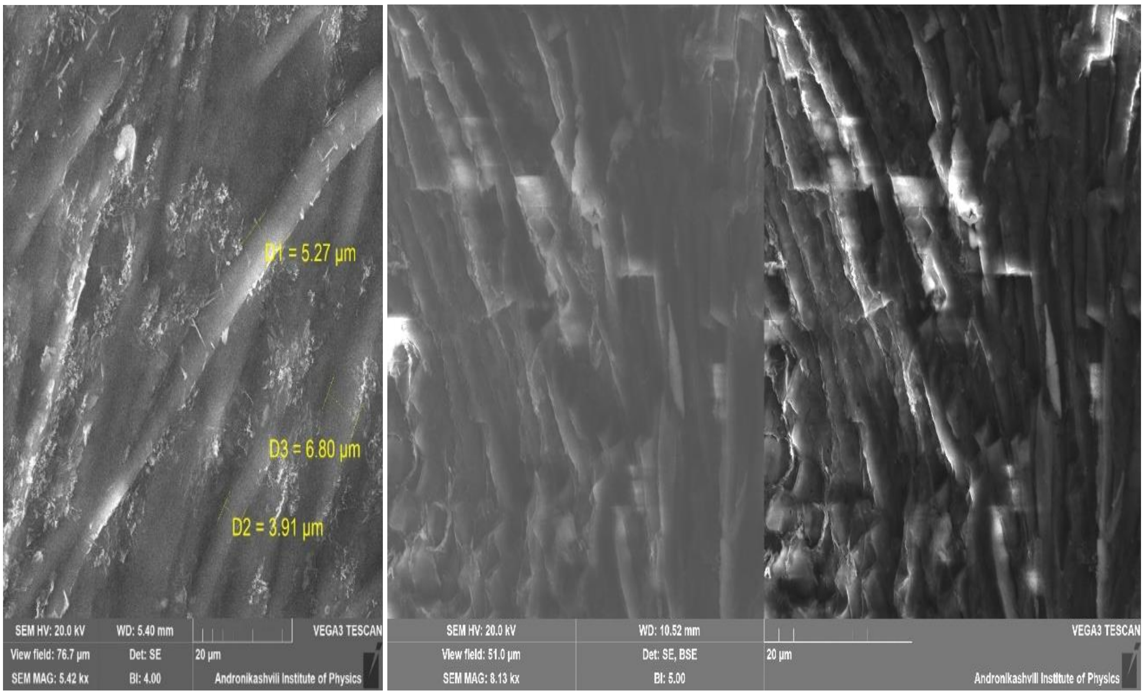
In addition, Spirulina platensis image was taken under an electron microscope after 1 year the first incubation and 10 kGy after irradiation and recultivation. Reagents: $CuCl_2 \cdot 6H_2O$, $Pb(NO_3)_2$, $CdS0_4$, $MgCl_2 \cdot 6H_2O$, K_2CrO_4, $CrCl_3$,$MnCl_2 \cdot 4H_20$, ZnSO4, $CoCl_2$, $NiCl_2$, $AgNO_3$ were of analytical grade.

RESULTS AND DISCUSSIONS

In fig.1 are presented electron microscope images of intact cells of Spirulina platensis and cells after irradiation. It is clear, that in the case after radiation the structure of cells of Spirulina platensis is ,,broken”.

Fig.2 shows the absorption spectra of after two times irradiation (every case irradiation dose 10 kGy) and recultivation of Spirulina platensis. The peak at 681 nm is due to the absorption of Chl a peak. At 621 nm is due to the absorption of phycocyanin (PC). A peak at 440 nm is due to soret band of Chl a [11].

Absorbance peaks of all components (Chl a peak, PC, soret band of Chl a) of Spirulina platensis are observed in the same wavelengths, as in the case intact cells of Spirulina platensis. In fig.3 also are shown effect of Cu(II), Mg(II) ions same concentrations on the absorption of the intact cells after irradiation and recultivation of Spirulina platensis. For illustration only some absorption spectra of metal ions are shown on Fig.3 (as an example Mg(II) and Cu(II))), for disregard pictures rebooting .It is seen from figures, that with increasing metal concentrations absorption intensity decreased for Cu(II) metal ions and increased for Mg(II) ions.



1 **2** **3**

Fig.1. Images of intact cells of Spirulina platensis (1) and cells after irradiation (2,3) using electron microscope

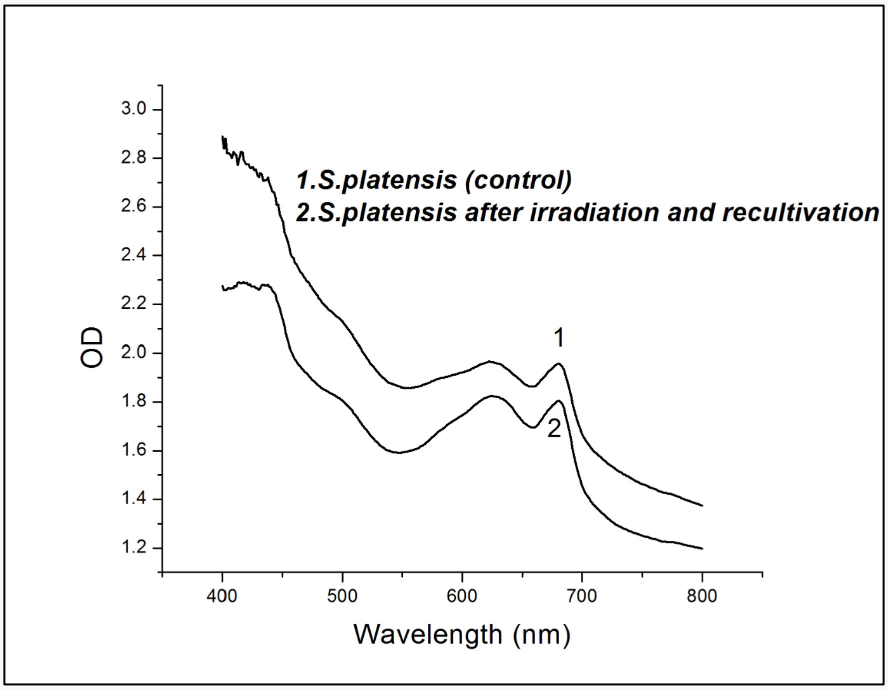


Fig.2. The absorption spectra of the cells of Spirulina platensis recorded after cultivation

1 – Control after incubation 7 days

2 – Suspension after 2- times with 10 kGy gamma-irradiation and after incubation for 14 days

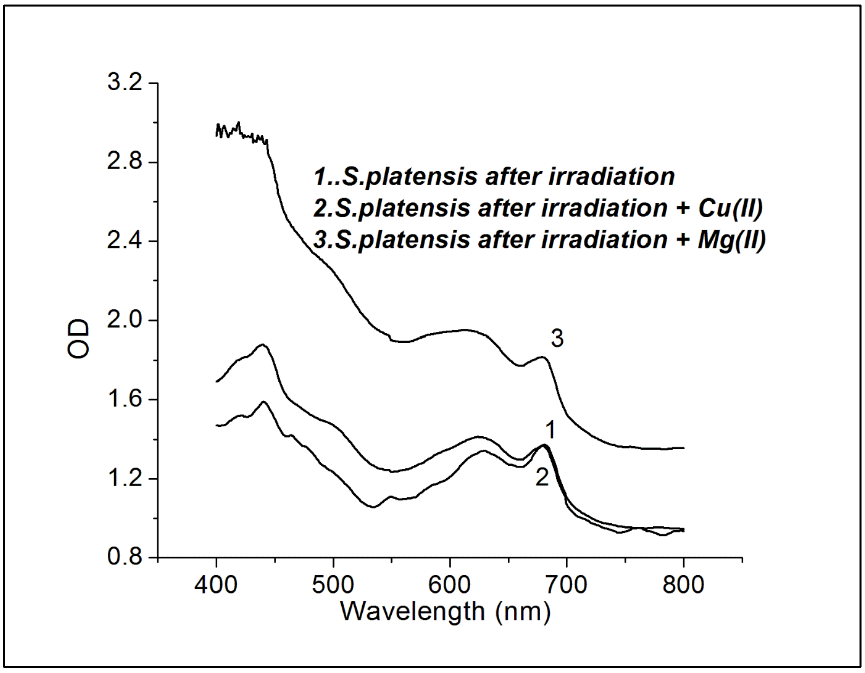


Fig.3. Effect of Mg(II) and Cu(II) ions on the absorption of irradiated suspension of Spirulina platensisafter 2- times irradiation and recultivation

By us influence of the same metal ions on the same cellular components of Spirulina platensis the same irradiation dose was also investigated. Effect of metal ions on the absorption intensity maximums for wavelengths 440nm, 621 nm and 681nm are shown in fig.4. It is evident, that effect of metal ions to components of Spirulina platensis (Chl a, Phycocyanin, soret band of Chl a) strongly depend upon the metal and influence is arranged in the descending order as follows:

1.For soret band of Chl a →440 nm : Co(II) > Ni(II) > Zn(II)>Pb(II) > Cu(II) > Cr(III)>Cd(II) >Mn(II)
2. For Phycocyanin→621 nm : Co (II)> Zn(II)>Cr(III) >Ni(II) > Cd(II) > Cu(II) > Pb(II) >Mn(II).
3. For Chl a →681 nm: Ni(II)> Cd(II)> Cr(III) > Zn(II)> Cu(II)>Co(II)>Pb(II)>Mn(II).

It is clear, that the efficiency for different metal ions is arranged in not the same sequence for soret band of Chl a , for phycocyanin and for Chl a. In particular, in the case of soret band of Chl a more effective isfor Co(II) and not effective Mn(II). For phycocyanin Co(II) and Mn(II), for Chl a Ni(II) and Mn(II) respectively. Though the efficiency Co(II) and Mn(II) ions in the case soret band of Chl a and phycocyanin are in good agreement , but efficiency for other metal ions are difference. This study show that possible use of gamma irradiation together with Co(II) and Zn(II) ions does not change nature of interaction of these metal ions on Spirulina platensis after irradiation, because without irradiation effect was the same[13]. In the case combined effects of ionizing radiation and other stressor such is Mg(II) ions for Spirulina platensis exhibit synergetic effects for all components of Spirulina platensis as a stimulatory agent to raise the contents of it. It is known that the standard Zarrouk medium contains Mg(II) ions since they contribute to the growth of Spirulina. This trend is seen to continue for all constituents of Spirulina platensis when these metal ions were added in vitro after irradiation and recultivation.

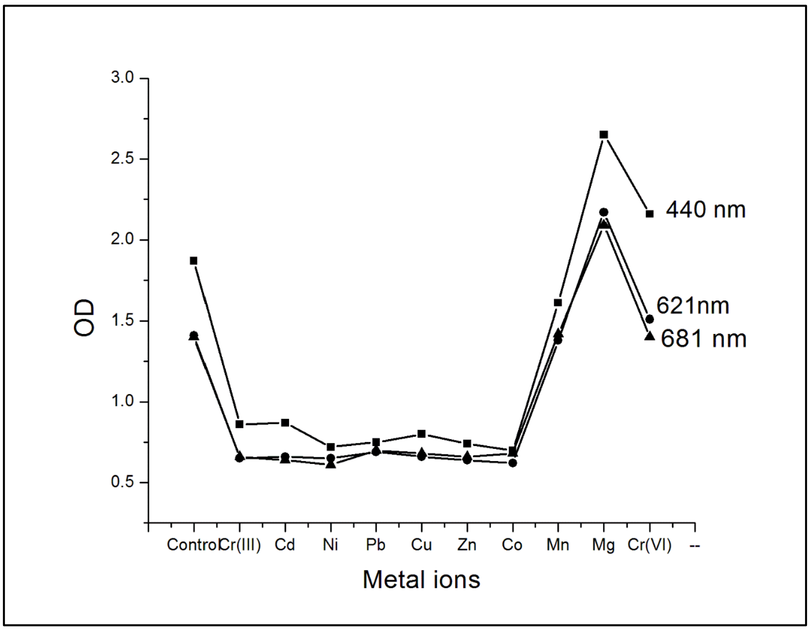


Fig.4 Changes in the absorption of components (soret band of Chl a→ 440 nm, C-phycocyanin→621 nm, Chl a →681 nm) of Spirulina platensis under various metal ions after 2-times irradiation

The absorption intensity of intact cells of Spirulina platensisdecreases, when Cr (III), Cr (VI), Cu (II) ions are added [14]. Significant difference between the absorption intensity for Cu (II) – Spirulina platensisand Cr (VI), Cr (III) Spirulina platensis were observed. Cu (II) was more effectively adsorbed by cyanobacterium than Cr (VI) and Cr (III) [14]. As shown in Figure 4, those ratios are destroyed after irradiation in this case, chromium (VI) leads in a completely different way, namely chromium (VI) does not contribute to a decrease in intensity unlike Cr (III) and Cu (II). Due to the repulsive electrostatic interactions, Cr (VI) anion species are generally poorly adsorbed by the negatively charged soil particles and can move freely in the aqueous environments. In contrast, Cr (III) species normally carry positive electric charges and therefore can be easily adsorbed on the negatively charged soil particles [15]. Apparently this difference is more noticeable after irradiation.

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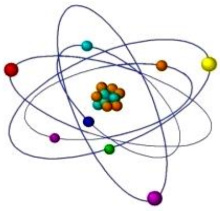
SOME OF THE SIMILARITIES BETWEEN MULTIORGAN DAMAGES CAUSED BY COVID-19 AND HIGH DOSES OF RADIATION



(Brief Review)

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ABSTRACT: *The modern world has a number of challenges. Climate change, rising radiation backgrounds, cancer, cardiovascular diseases, infections threaten the sustainable development of humanity. Today, as never before, it is time for scientists to work together to overcome these challenges. The spread of SARS-COV-2 virus has completely changed the biomedical research agenda. Multi-organ lesions caused by the virus require the analysis of knowledge and experience accumulated in various fields. One of the most serious factors causing multi-organ injuries is radiation. As studies show, pathologies obtained with covid-19 and high-dose radiation are very similar to each other. Determining the advantages of many years of experience and methods of radiation disease management for treatment of similar disorders caused by the SARS-COV-2 virus creates an excellent prospect for rescuing patients with moderate to severe symptoms.*

Inflammation is a major common player in COVID-19 and ARS (Acute Radiation Syndrome) and causes multiple systemic damage. Both cause cytokine storms, the number of pro-inflammatory cytokines increases, and the number of anti-inflammatory cytokines decreases. Both COVID-19 and radiation exposure result in systemic damage of the vascular system, lungs, heart, kidneys, liver, intestines, eyes, and brain. Regardless of the target organ, the management of immunogenic pathway hyperactivity is a major target for overcoming COVID-19and acute radiation exposure.

The goal of presented review is to underline some ofthe similarities of multisystem damages caused by Covid-19 infection and ARS. A long-term and diversified study of ARS has identified the main targets of radiation exposure and developed ARS medical management strategies that can be successfully adapted to manage systemic lesions in patients with COVID-19.

Key words: acute radiation disease, covid-19, inflammation, cytokine storm

INTRODUCTION

Acute Radiation Syndrome (ARS), the same radiation sickness develops in people whoselarge part of the body is exposed to high doses in a short period. The result is damage to the hematopoiesis, gastrointestinal tract, skin, neurovascular systems, and immune dysfunction as part of the damage to the hematopoietic system [1,10,28].

COVID-19 affects virtually every organ. It causes inflammation, endotheliitis, vasoconstriction, hypercoagulation and edema. Lymphocytopenia, elevated D-dimer, elevated fibrin degradation products, and widespread intravascular coagulation have been reported. Regardless of which organ or system is damaged, hyperactivity of the immune system is an acute reaction to withstand to both SARS-CoV-2 and acute radiation exposure [18, 29].

Physiological and pathological processes in different tissues can initiate production of Cytokines by eg. macrophages, mast cells, endothelial cells, and Schwann cells [8, 45]. Under normal conditions, cytokines have a short half-life and act as mediators. A complex communication network gives a healthy immune system the proper signals to respond in a proportionate response against an infectious agent or inflammatory stimulus [38]. A dramatic increase in cytokine levels triggers a cytokine storm, to which the body responds with acute systemic inflammation [39, 46]. The cytokine storm is common effect of SARS-CoV-2 infection and radiation exposure [37]; the result in both cases is the systemic inflammation that injures numerous tissues and organs [24, 27, 31]. Further, inthe review we will discuss some of pathologies resulting from Covid-19 and RAS diseases.

HEMATOPOIETIC DISORDERS

Hematology studies were found to be a valuable tool for assessing the status of COVID-19 patients. Assessment of neutrophils, lymphocytes, and platelets reveals a strong correlation between neutrophil-lymphocyte-platelet (NLP) and progression of COVID-19 disease [22]. Moreover, lymphocyte depletion is associated with COVID-19 severity. In addition, the number of T cells, eosinophils and platelets is significantly reduced in particularly critical and fatal patients [48]. Studies have shown that an increase in the neutrophil-lymphocyte ratio (NLR) is an early warning sign for severe COVID-19 [16, 19]. Lymphopenia and thrombocytopenia are commonly observed in hospitalized COVID-19 patients, and low platelet counts are associated with higher mortality [4, 44]. SARS-CoV-2 is thought to damage both bone marrow cells and platelets via the CD13 receptor, leading to cell growth inhibition and apoptosis. Another cause of thrombocytopenia is platelet activation, aggregation, and thrombus formation at the site of lung injury [9, 33].

As in COVID-19 patients, radiation exposure also causes profound hematologic disorders in humans characterized by granulocytopenia, lymphopenia, and thrombocytopenia [14, 25].

Unlike COVID-19, in addition to other cytopenias, a significant decrease in neutrophils is a hallmark of ARS [6]. The kinetics of lymphocyte decline is directly related to the dose of absorbed radiation from 0.5 to 10 Gy. In additions, a change in the ratio of neutrophils to lymphocytes was used to determine radiation dose exposure [32]. Thrombocytopenia is directly related to radiation dose [14].

VASCULAR DYSFUNCTION

Histological analysis of COVID-19 showed that SARS-CoV-2 infection causes endothelitis throughout the human body, leading to systemic macro- and microcirculatory dysfunction. VEGF-D (vascular endothelial growth factor –D involved in formation of lymphatic vasculature around lung bronchioles) is used as a procoagulant biomarker of COVID-19 progression [23], and angiopoietin-2 (marker of endothelial activation) is a marker of microvascular dysfunction. Disorders such as vascular thickening are also characteristic of COVID-19 disease [20].

Vascular dysfunction due to radiation exposure is also known. The main target of vascular radiation damage is the endothelial cell. The acute phase of the lesion occurs from the moment of irradiation to several weeks and is characterized by endothelial edema, decreased vascular permeability, lymphocyte adhesion and infiltration, and apoptosis [11].

Interestingly, many of the symptoms as well as the underlying pathogenesis in multi-organ damage caused by SARS-CoV-2 are similar to the multifaceted damage caused by exposure to acute ionizing radiation. In a nuclear incident, the entire human body can be damaged by large doses of ionizing radiation, and SARS-CoV-2 can cause multiorgan damage by interacting with cells whose membranes express angiotensin-converting enzyme 2- ACE2 and Type 2 transmembrane serine protease TMPRSS2 [3, 5]. Viruses reach cells as soon as viral spike protein binds to the ACE2. The virus uses endocytosis or fusion with the membrane to enter cells [17]. In both cases, it is necessary to cleave the ACE2-associated Spike protein with specific proteases in order for the Spike fusion domains to act. In endosomes, the spike is cleaved by cathepsin L, and then the viral membrane fuses with the endocytic membrane [21, 43]. On the cell surface, to ensure fusion of the virus and the host cell membrane, the spike digs into other proteases, mainly

TMPRSS2, after fusion, SARS-CoV-2 is transferred to the cytosol and the virus begins a replication cycle [40].

These proteins are expressed to varying degrees in airway and alveolar epithelial cells, pulmonary macrophages and vascular endothelial cells, ileum and large intestinal enterocytes. Systemic inflammation and coagulopathy, intravascular coagulation (DIC) and extracellular neutrophil counts are both signs of COVID-19 and signs of acute radiation damage. Injuries found in both COVID-19 and ARS can cause similar distant side effects in many organ systems [35].

OTHER COMPLICATIONS

Acute respiratory syndrome is the most common complication of COVID-19 and is the most common cause of death, while in irradiated patients it is a late effect, which often progresses to pulmonary fibrosis [7, 12, 15].Although pulmonary symptoms are most common in COVID-19 patients, GI symptoms are also common [2, 47]. Nausea, vomiting and diarrhea are all common symptoms for both COVID-19 and irradiated patients [30, 36].

Another organ of concern is the heart. Although coagulopathy, seen in both COVID-19 and ARS, may contribute to cardiomyopathy and circulatory failure, direct remodeling of heart tissue is also seen in both disease processes [10, 42]. Cardiac ischemia, inflammation, fibrosis, and wall thickening have been reported in COVID-19 patients [41] and after irradiation, although dose-dependent and post-irradiation time. SARS-CoV-2 infection and radiation both increase myocardial infarction and most likely have long-term effects.

Central nervous system damage has been reported in patients with COVID-19 and ARS. Headache, disorientation, cognitive dysfunction, ataxia, seizures, unconsciousness, as well as other symptoms have been reported in patients receiving high-dose lethal radiation and in adult and juvenile COVID-19 patients [13].

In addition, there is some evidence that radiation exposure can cause long-term psychological problems [26] and given that, there are similarities between radiation and COVID-19-induced central nervous system inflammation and coagulopathy, SARC-2 may cause long-term neurological and psychological effects [34]. Comparison of systemic damages caused by Covid-19 and acute radiation exposure Fig. 1 and Fig. 2.

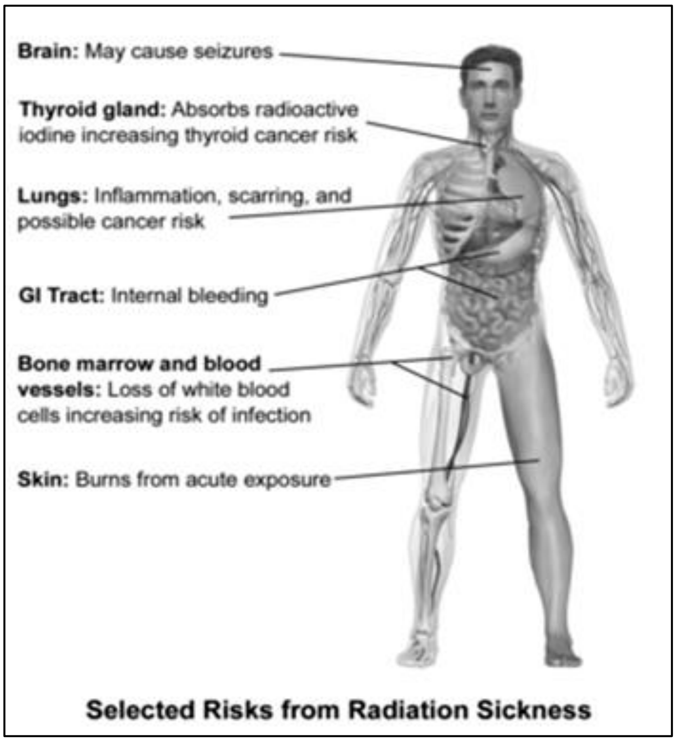

Fig. 1. Organs targeted by radiation: brain, thyroid gland, lungs, GI tract, bone marrow, blood vessels, skin. https://commons.wikimedia.org/wiki/File: Radiation_Sickness.png

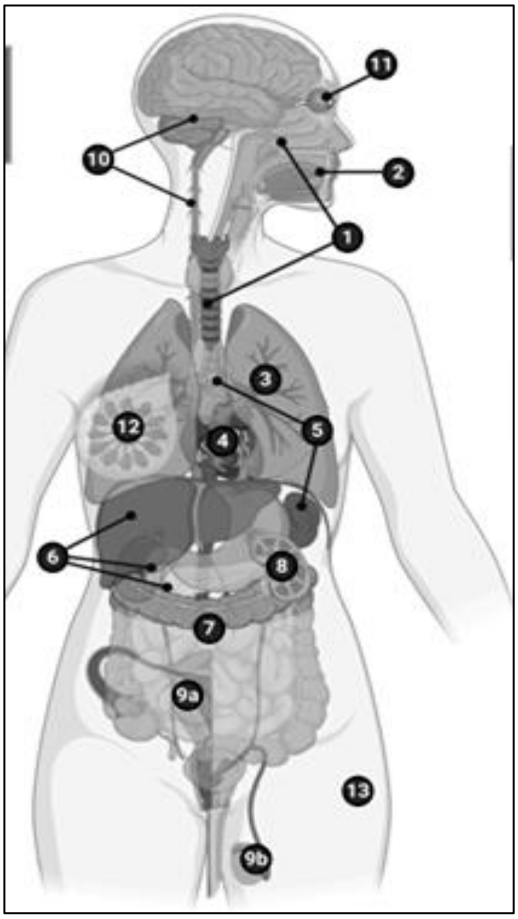

Fig 2. Organs targeted by of SARS-CoV-2: brain, thyroid gland, lungs, cardiovascular system, immune system, bone marrow etc. This figure was created with
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1-Upper airways, Mucus, Nasopharynx, Trachea ciliated epithelial cells; 2-Mouth, Sputum, Oropharynx; 3-Lungs, Bronchoalveolar lavage, Ciliated and secretory epithelial cells, Type I and II pneumocytes, Alveolar macrophages; 4-Cardiovascular system, Heart interstitial fibroblasts, Vessel endothelial cells; 5-Immune system, Blood, Lymph nodes, spleen; 6-Liver, gallbladder, Pancreas; 7-Gastrointestinal tract (GI), Stool, Stomach, Enterocytes; 8-Urinary system, Urine, Kidney tubular epithelial cells, podocytes; 9-9a. Female reproductive tract; 9b. Male reproductive tract, Testicular spermatogenic, Sertoli and Leyding cells; 10-Nervous system, Brain, Cerebrospinal fluid; 11-Eye, Tears, Conjunctiva; 12-Mammary glands, Breast milk; 13-Skin and adipose tissue

CONCLUSION

Presented review underlined some of the similarities of multisystem damages caused by Covid-19 infection and ARS. Mechanisms of immune dysregulation, disease progression, and organ damage during COVID-19 are similar to the biological reactions to high doses of ionizing radiation. A long-term and diversified study of ARS has identified the main targets of radiation exposure and developed ARS medical management strategies that can be successfully adapted to manage systemic lesions in patients with COVID-19.There is extensive experience in radiation biology for treatment of inflammation, pulmonary fibrosis, and vascular damage, and due to the symptomatic similarity between the two diseases (Covid-19 and RAS) the use of same methods for treatment may be appropriate. Moreover, versus, new treatment achievements considered for COVID-19 infections may be used for anti-radiation therapy.

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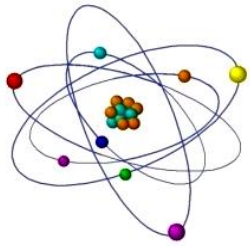
GENERAL PRINCIPLES OF THE ORGANISATION OF THE MECHANISMS OF BIOLOGICAL ADAPTATION



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ABSTRACT**:** *The existence of a hierarchy of mechanisms of their functioning and a hierarchy of mechanisms of the response to stressors is substantiated. That is based on the fact of the existence of a hierarchical organization of biological systems. It was shown that the adaptive response had been based on the hormesis action of the factor, and the study of the mechanism of adaptive action can be reduced to the study of the mechanism of hormesis effects caused by hypercompensatory processes in objects exposed to a certain stress factor. There is constitutive and inducible/stimulated phenotypic hyperadaptation (PHA). It occurs at the certain stage of positive readjustment of the initial state of the biological object in response to the action of above-threshold levels of factors of any nature. PHA is a process and it is the result of the functioning of constitutive or inducible/stimulated mechanisms of recovery. The whole hierarchy of recovery mechanisms, of which there are as many as there are recovery mechanisms (levels), can provide PHA at a particular level of the organization. PHA has a transitive and transient nature. There is a possibility of consolidating the state of hyperadaptation, when post-factor (post-stress) conditions contribute to its manifestation. At the base of PHA there are the processes of modification (in particular, degradation), the result of which is the emergence of appropriate signals that determine the final implementation of the mechanisms of hyperadaptation.*

Key words: system approach, radiohormesis, adaptation.

INTRODUCTION

One of the areas of modern biology is the study of resistance of biological objects to extreme factors - low and high temperatures, drought, anoxic conditions, heavy metals, ionising radiation, etc. [Baraboy, 2006, Cordyum et al., 2003, Calabrese, 2000]. Along with the development and application of measures which aim is usual protecting or protecting biological objects, including humans, from the effects of stressors, the study of means to increase the initial (current, constitutive, "control") resistance to their action is not less important. At the same time, well-studied phenomenology and developed practice of hardening and training of biological objects to the action of inhibitory factors [Henkel, 1982, Kaplan, Tsyrenzhapova, 1990] created an empirical basis for basic research focused on revealing the actual mechanisms of stability and theoretical justification of methods of its modification and, in particular, increasing the initial level of stability, i.e. adaptability.

In its theoretical and experimental components, the problem of adaptation, from our point of view, with its significance (scale) is in the same range with such archival important medical and biological problems as the mechanism of aging, cancer transformation, morphogenesis, evolution, principles of the human brain and more. What are the difficulties along the way? Firstly, subjective, i.e. "human":

– lack of skills to develop and use meta-knowledge (philosophical, systemic, etc.) or general disregard for the need and possibility of their application;

– inability to form full-fledged cognitive information blocks that could be used to construct a general theory;

– inability to use heuristics or their complete ignorance;

– logical categoricalness and one-sidedness of statements;

– unclear understanding of the concept of "mechanism" and, as a result, the dominance of vulgar reductionism, when there is a reduction of multilevel mechanisms only to the molecular-biological;

– abuse of "native" terminology and unwillingness to unify it;

– subjective orientation to create "finished" theories and "adjust" the existing facts to them;

– vague awareness of the need to distinguish between the adaptation of systems organized on stochastic and structural principles.

The objective difficulties should include, first of all,:

– complex dynamic and spatial nature of biological processes and phenomena, their multilevel, multistage, large length of time, for instance, large time intervals in which adaptation processes can unfold;

– lack of adequate and unified language for formulating problems and describing the phenomena themselves;

– insufficient development of the theory of dosimetry of stressors (for example, dosimetry of antioxidants);

– incomplete phenomenology of adaptive processes;

– undeveloped metascientific (for instance, the same systemological) approaches, non-usage of methods and techniques of related sciences;

– the difficulty of determining the contribution of genetic and epigenetic components of the adaptation mechanism.

Without any doubt, this is not a full list of difficulties in studying adaptation, but it still gives the idea of the complexity of this problem, which is almost equivalent to the problem of determining the essence of life.

Phenomenology of adaptive answer (answer to the question "What?")

It should be noted that almost all the problems of resistance of biological objects to extreme influences of the factors of different nature are centered around the nature and the mechanism of stress in general, as well as its varieties - eustress and distress (Selye, 1972; 1982). The greatest difficulties in solving this problem arise in relation to plant objects, as indicated by the paradoxical situation in the sphere of plant physiology. Its essence is that with the widespread use of the term "stress", introduced into scientific usage by Hans Selye, in the literature on the biology of stress in plants (plant stress biology) almost does not pay attention to the impossibility of direct (practical) usage of traditional definitions of stress to describe this phenomenon in plants. This is due, on the one hand, to a very high degree of generalization of the proposed definition, and, on the other hand, the presence of specific signs of plant reactions to extreme actions. In addition, mutual understanding among scientists studying the reactions of plants to prolonged or chronic exposure to extreme factors is complicated by the ambiguity of their use of the term "stress". Thus, in some cases, stress is understood as an extreme factor of the external environment that acts on the body [Kostyuk, Ostaplyuk, Levenko, 1994]. Most often, the interpretation of this concept is based on the understanding of stress as an altered state of biological objects, which arose as the result of the action of environmental factors on it [Baraboy, 2006; Veselova, Veselovsky, Chernavsky, 1993; Urmantsev, Gudskov, 1986]. However, despite the difficulties above , this definition of stress by G. Selye due to the same high degree of its abstraction causes a high level of its heuristics, which allows to identify the universal elements in the response to the mechanisms of biological objects of any level of integration to extreme factors. in different doses, including those that are actually adaptive, i.e. those that increase the initial level of stability. In particular, there is an opportunity and necessity to study the features of the multi-stage process of response of biological objects to the entire range of doses and capacities of possible extreme effects (distressors). There is also an obvious need to study multilevel mechanisms of adaptation as opposed to attempts to reduce them only to intracellular mechanisms. Indeed, it is difficult to assume that the change in resilience, for example, of any level of integration of the ecological system (population, group, etc.) is due solely to molecular, in particular, reparation mechanisms. There is no doubt that other recovery systems are involved in this process - cell-repopulation, regeneration, repopulation processes at the population level, and so on**.**

All the above determines the relevance and necessity of studying the peculiarities of the manifestation of the effects of adaptation of biological objects at different levels of their integration. Note that from the point of view of this relevance, the results of the study of actual hormesis (positively stimulating) effects are also of interest for this topic, as our results proved the connection of adaptation processes with hormesis and, in particular, radiohormesis processes (Mikheev, 2018).

Given the complex dynamics of the response of biological objects to the stressful effects of factors of different nature, from a purely phenomenological (observational, descriptive) standpoint, all reactions of biological objects at certain levels of their organization, depending on the direction of change (modification) of the initial level of stability can be divided into three types: 1) reactions without a final change (even a temporary excess during the observation) of the initial level of adaptability; 2) reactions with an increase (at least temporarily during the observation) of the initial level of adaptability - hyperadaptive (hyperbiotic); 3) reactions with a constant (irreversible) decrease in the level of initial adaptability - hypoadaptive (hypobiotic). Note that in the literature, the concept of "hyperadaptation" corresponds to the concept of "adaptive response" (Volkert, 1988). Of course, each type of reaction corresponds to a certain dose / concentration / power range of the active factor, i.e. any factor with certain quantitative characteristics of the effect can be neutral, hypoadapting or hyperadapting. For instance, based on these positions, we can assume that at certain concentrations, antioxidants will act as carcinogens (eg, aminophenols), and carcinogens will have antitumor effects.

The result of modification of the initial level of stability of a biological object under the influence of alternating (modifying) action of a factor of any nature to the action of a stressor (stress factor) of any nature, only potentially occurs to either adapt (hyperadapt) or maladapt (hypoadapt) object. The sign (direction) and the magnitude of the influence of the modifying factor can be detected only with the subsequent application of the so-called "test factor", also called "damaging factor", which, in our opinion, adequately reflects the interaction of factor and object. to establish the level of organization of the object, where there is rebuilding (in particular, destructive) changes under the influence of stress. If such a factor increases the initial level of stability of the object, it is called "hormesis" or "adaptive factor".

Since the scheme of studying modifying effects involves the use of two doses (alternating and testing), in the case of observational response (hyperadaptation), it is significant to emphasize that there is a paradoxical nature of such effects, when the negative impact of one stress factor is more pronounced than the combined effect adaptive (hormesis) factor and the same test factor.

This refers, in fact, to the possible preventive action of the factor-modifying the initial stability of the object, when its action precedes the action of the test factor. But the therapeutic (post-stress, "therapeutic") effect of the modifying factor is also possible. We have called this phenomenon "reverse adaptation", the mechanism of which is probably the ability to activate the recovery system in the post-stress period, i.e. to find (unfortunately, purely empirically) the balance between damage and recovery. In other words, there is a relative symmetry of the joint action of the two factors, i.e. the order of their action may not be significant, which, in relation to hyperadaptive response, means the possibility of hyperadapting effect after testing as a therapeutic, not just prophylactic (Mikheev, Shilina, Ovsyannikva, 2008).

Note that we consider only the phenotypic manifestation of the hyperadaptive response - phenotypic hyperadaptation - PHA, which has a transitive (transient), i.e. transient in nature, relativity by parameters and a certain nonspecificity to subsequent effects. The duration of PHA is determined by the duration of the phases of positive re-regulation of the transition period (process), For example, the transient increase in the level of ROS under the action of stressors (Kolupaev, Karpets, 2019) can be considered as the primary mechanism of PHA.

Given the fact of the existence of endogenous rhythm of the values of structural and functional parameters of a biological object, we can assume the existence of constitutive (synonyms: spontaneous, initial, "control", endogenous, background) along with inducible / stimulated (synonyms: induced, induced) (epigenetic) hyperadaptation (PHA).

From a practical point of view, it is important to point out the possibility of consolidating the state of hyperadaptation, when post-factor (post-stress) conditions contribute to its manifestation. Thus, the hormesis effect (PHA condition) of plants obtained from seeds irradiated in a potentially hormesis dose depends on the conditions of their post-factor cultivation. Thus, in the field, when irradiated seeds are often sown in insufficiently moist soil, stimulated by irradiation seedlings with longer roots are found to be better supplied with water and nutrients. And the longer the period of arid conditions, the greater the growth stimulation and the greater will be (positive towards plants from irradiated seeds) differences in the phases of development and yield (Churyukin, Geraskin, 2013).

To create a consistent concept of adaptive response, it is necessary to study the structure of transients induced by extreme influences and establish their relationship with the types of adaptive response (actually adaptation or maladaptation), as well as show the role of multilevel mechanisms in adaptive response. PHA occurs at a certain stage of positive overregulation (overrecovery) of the initial state of the biological object in response to the action of the transboundary level of a factor of any nature (Mikheev, 2015).

Manifestation of PHA of biological objects is possible at any level of their structural and functional organization. The higher this level is, the higher is the dose of stressor to which it can be induced hyperadaptive response, and the higher the hyperadaptive dose. In other words, if the dose / power of the stress factor exceeds the threshold of the object's response for a specific level of its integration, it induces / stimulates the transition process, the presence of a hypercompensatory phase in terms of parameters that positively characterize its viability (for example, growth rate), is a necessary condition for obtaining a hyperadaptive response. In general, the higher the level of absorbed doses / capacities / concentrations of the active factor is, the higher the structural-functional level induces / stimulates the transition process.

Mechanisms of PHA (answer to the question "How?")

Given the multilevel structural and functional organization of biological systems, we can assume that there is a whole hierarchy of mechanisms of their functioning in general and a hierarchy of mechanisms of response (perception, transduction, recovery, etc.) to the action of stressors. What meaning do we put into the concept of "mechanism", the interpretation or definition of which most researchers do not consider necessary and use only an intuitive perception of its content? In our judgment, to reveal the mechanism of a phenomenon means to describe a phenomenon established for any system by describing the behavior and interaction of the elements of this system. For instance, if the phenomenon of radiation inhibition of root growth activity is described with the involvement of data on the reaction of its tissue components (rest center, meristem, differentiation zone, etc.), then this is exactly the description of the direct mechanism of this phenomenon. It is obvious that the contribution of individual tissue elements in this situation will be well defined for a given inhibitory dose, and some tissues are likely to be critical in terms of their determinant contribution to the reaction mechanism. In a different dose range, the "weight" of the tissues may change and, consequently, there may be a different mechanism with other critical structures in the main "roles".

Due to the hierarchical organization of biological systems, the description of the mechanism of the phenomenon of higher structural and functional level will be both a phenomenon for a lower level of organization. In the example above, if the determining role of the meristem in the mechanism of inhibition of root growth is clarified, the reaction of the meristem itself to radiation will already act as a phenomenon that requires its procedure to determine the contribution of its (meristem) components.

Thus, PHA is a process and result of the functioning of constitutive or inducible / stimulated mechanisms for the restoration of such changes. PHA at a specific structural and functional level can be provided by the whole hierarchy of its recovery mechanisms, starting with reparation and ending, for example, repopulation. There are as many mechanisms (levels) of hyperadaptation as there are mechanisms (levels) of recovery, which, among other things, work in the normal conditions of existence of a biological object. In other words, there is a need for recovery mechanisms to function regardless of the presence or absence of a stressor. It is these mechanisms that ensure the dynamic stability (homeostasis) of biological systems and they also determine a certain rhythm of the level of stress resistance (endogenous rhythm of stability). The latter means that organisms are able to go spontaneously into a state of increased or decreased level of stability.

Another paradox of PHA is that it is based on the processes of degradation (destruction, change, modification in the broadest sense), the result of which is the emergence of appropriate signals that ultimately lead to the implementation of hyperadaptation mechanisms. It should be noted that just as there are endogenous recovery processes, there are endogenous degradation processes (for instance, apoptosis), which are only enhanced (stimulated) by stressors in high doses.

The above-mentioned concept of "destructive changes" or the concept of "degradation processes" allows for a fairly broad interpretation, covering all possible ways of transforming the system-object (CO). The basis for this statement is the results obtained in the framework of the general theory of systems (ZTS), developed by Yu.A.Urmantsev (1974). According to the basic law of this theory, a particular system-object is able to pass (a) either into itself - by identical transformations, (b) or into other CO - by means of one of seven, and only seven different transformations of elements, and namely changes: (1) quantity, (2) quality, (3) relations, (4) quantity and quality, (5) quantity and relations, (6) quality and relations, (7) quantity, quality, and relations of all or part elements of CO. Obviously, with any type of transformation of CO changes the rest of all the characteristics of its elements, i.e. in its pure form, each of the rearrangements does not exist, but dominant in a certain period of time or place may be one or another type. In addition, it is important to emphasize that these types of transformations can act as a signal that can trigger a cascade of recovery mechanisms.

The classification of types of transformation of systems is considered, we took as a basis and with its help the classification of primary types of adaptive transformations (mechanisms) of biological CO in case of action on it of system-factor (SF): 1) proliferative (caused by modification) numbers of pre-existing CO elements; 2) functional (associated with changes in the quality of functioning of CO elements); structural (due to changes in the relationship between the primary elements of CO).

One of the theoretical bases of our proposed approach to the description of PHA mechanisms is to substantiate the position that adaptive (adaptive) reactions are primarily due to inertia (imperfection, inaccuracy) of recovery systems and, in particular, the phenomenon of overregulation of certain structural and functional parameters. The reason for this idea is the fact that the course of reactions of objects in response to extreme factors is characterized by phase, which, in turn, causes a change in the resistance of the biological object to repeated influences. It is with the phase of overrecovery (one of the types of overregulation) and associated adaptive response, i.e. this type of reaction, when the initial level of adaptability increases. From these positions all responses of an organism or any other biological system to action of above-threshold doses of stressors are considered from the point of view of modification of their adaptive ability (potential) which is shown at the subsequent influences of the same or other by the nature factor.

Another fundamental aspect of the problem of stress state of biological objects is related to the need to take into account the multilevel structure of their structural and functional organization, which suggests the existence of a multilevel inducible / stimulated system that provides both multilevel reactions of biological objects and multilevel mechanisms adaptive reactions. The need for such an approach is due to numerous and not always successful attempts to reduce all the variety of mechanisms of adaptive responses only to mechanisms that function at the intracellular level, for example, this trend is observed in attempts to reduce various mechanisms of responses to radiation only to the mechanism of induction / stimulation repairing DNA enzymes or heat shock proteins in the case of elevated temperatures (Fippovich, 1991; Schwartz, 1998). This often does not take into account the presence and possibilities of hierarchical organization of the biological object, each structural and functional level of which (cell, tissue, organ, organ system, etc.) is capable under appropriate conditions, dose and power of the influencing factor, type of reaction, registered, the state of the biological object, etc.) to provide conditions for the adaptive response of the whole system. For example, the well-known processes of modifying the values of the parameters of cell proliferation, growth activity and reproduction of individuals at the population-organism level, etc., under certain conditions, the stage of recovery (hypercompensation), indicate the fundamental possibility of occurring with the participation of almost all levels of structural and functional organization of the biological object (Nefedov et al., 1991, Lekevicius, 1997).

If with respect to the induced / stimulated repair process (in particular, due to the higher power of the enzymatic repair system) it is clear how increased resistance to repeated stress is provided, then due to which mechanisms can increase resistance when increasing (at the stage of hypercompensation), for example, speed cell proliferation? It is clear that the increased rate of cell proliferation may be a factor in reducing the tolerance of cells to the re-action of the stressor, which is clearly indicated by the law of Bergonier-Tribondo. However, if our assumption is correct, then due to the higher rate of proliferation of modified adaptive cells can form a sufficiently large critical cell mass, which will provide a more complete and effective recovery of critical plant tissues. This assumption was confirmed in our studies of the role of proliferative activity of meristematic cells in ensuring the radioadaptive response of plants (Mikheev et al., 1998). Obviously, the enzymatic reparation system should be considered as the most fundamental (actually biological) system, the stimulation of the activity of which can directly increase the initial level of resistance (in particular, radioresistance). The stressor (stress factor) that induces the transition process in CO, in addition to stimulating the repair system, can provide at some point (phase, stage) of the transition process increased proliferative activity, for example, by irreversible damage (apoptotic or necrotic type) of cells, the degradation products of which are probably a "repopulation signal", the nature of which has not yet been fully elucidated. However, it is important to emphasize that the stressor can not only directly affect the reparation system, but also indirectly modify it through higher levels of structural and functional integration. Enhanced activity of genes encoding enzymes of the repair system can be provided not only by enhancing protein synthesis in a single cell, but also by increasing the proportion of cells synthesizing the desired complex of proteins. In addition, the total genetic activity is able to increase by increasing the number of relevant individuals, i.e. to be provided at the population level. In favor of this assumption, in particular, the results of research VN Afanasyeva and NP Motilevich (1989), who found that a significant contribution to the process of restoring the rate of DNA synthesis in a population of irradiated cells on the background of recovery in each cell is a change in the structure of the cell population under the influence of ionizing radiation. Thus, the population of HeLa cells in the logarithmic growth phase consists of 60% of cells in the G1 (G0) phase, 23% in the DNA synthesis stage (S-phase) and 17% in the G2 + M stage. In the first hour after irradiation at a dose of 10 Gy, the distribution of cells by phase of the cycle differed little from the control, due to the delay in the progress of cells in the cycle. Further, because the cells irradiated in the S- and G2-phases stop for a longer time, there is a decrease in the number of cells in the G1 phase (G0) and an increase in the number of cells in the S-phase against the background of virtually unchanged number of cells in the G2 + M phases. Subsequently, the accumulation of cells in the G2 + M phases was noted. As it can be seen, some time, after irradiation in the cell population there is an increase in the proportion of DNA-synthesizing cells, which inevitably affects the process of restoring DNA synthesis and, as a result, the hyperadaptive response. The above authors speak of "true recovery in each cell", probably referring to the "falseness" of recovery at the population level. To our mind, the position of the authors is a consequence of explicit or implicit application of the principle of endocytocentrism, according to which an attempt is made to explain everything only on the basis of intracellular mechanisms. It is clear that cellular mechanisms provide the most fundamental mechanism of biological objects' responses to extreme factors, but the hierarchy of biosystems may not be limited to the cellular level and the "gene dose" can be increased by structures of higher integration than the cell.

Thus, the biological system has a kind of structural and functional memory of previous actions of exogenous and / or endogenous factors and this memory largely determines the nature of subsequent reactions to the action of "new" stressors. It is this memory that allows the biological system, which is, in particular, in a state of hypercompensation (in this example - in a state of increased rate of cell proliferation), to provide increased resistance to further influences of stress factors, which is not so much due to reparation mechanisms, how much due to the mechanisms of restoration of higher levels of integration, which also participate in the "memorization" of traces of stress factors.

An important challenge for stress biology is to elucidate the nature of the stress signal, which exerts an epigenetic effect and thus triggers an adaptive response. Thus, it is believed that the most universal system of this kind is a system of redox regulation (Kolupaev, Karpets, 2019), which triggers the mechanism of signal transduction. We believe that such a mechanism would be more accurate to call the most common, because biological objects are most often exposed to such factors that directly cause an increase in the content of reactive oxygen species (ROS) in tissues. The importance of ROS is also indicated by the possibility of amplification of the primary ROS signal due to the increased activity of ROS-generating enzymes (Mitter et al., 2011).

From our point of view, any biological structure can perceive the action of a stressor (i.e. act as a primary target). Depending on the characteristics of the stress factor (power, dose, concentration, quality), such target structures may be unique or multiple structures. For example, in the case of ionizing radiation, depending on the dose, the target may be a unique structure such as a nucleus, or a multiple structure in the form of membrane structures. The target of the temperature factor, in fact, is the whole organism, because its (i.e. temperature factor) level depends on the functioning of all body systems. In other words, there are non-specific and specific targets. In addition, specific targets may respond nonspecifically when the factor parameters go beyond the "working" area of the target (sensor).

What is the meaning of biological adaptation (hyperadaptation, PHA), if its price is destructive processes, the recovery of which requires the consumption of certain energy and substrate resources?

Actually, in this question there is an answer to it. Biological systems would not need to use stress mechanisms if stressors did not change. However, the biological system, as an open system, is constantly exposed to exogenous and / or endogenous factors that throw it out of balance and, thus, translates it into a state that needs to be restored to its original state.

CONCLUSIONS

We consider that it necessary to make some generalized conclusions and assumptions that may become the basis for the future theory of biological adaptation, namely: all reactions of biological objects to extreme influences can be divided into three types: a) reactions without changing the initial level of adaptability; b) reactions with increasing the initial level of adaptability - hyperadaptive; c) reactions with a decrease in the level of initial adaptability - hypoadaptive.

Manifestation of PHA of biological objects is possible at any level of their structural and functional organization. The higher this level is, the higher the dose of stressor to which it can be induced hyperadaptive response is, and the higher the hyperadaptive dose too.

Constitutive and inducible / stimulated phenotypic (epigenetic) hyperadaptation (PHA) is possible. PHA is a process and the result of the functioning of constitutive or inducible / stimulated mechanisms for the restoration of such changes. PHA at a specific structural and functional level can be provided by the whole hierarchy of its recovery mechanisms (starting with reparation and ending, for example, repopulation). There are as many mechanisms (levels) of hyperadaptation as there are mechanisms (levels) of recovery. The mechanism of PHA is based on the processes of modification (in particular, degradation) of the initial state of the system, the result of which is the emergence of appropriate signals, which ultimately determine the implementation of hyperadaptation mechanisms.

PHA happens at a certain stage of positive or negative overregulation (overrecovery) of the initial state of the biological object in response to the action of above-threshold levels of factors of any nature. PHA has a transitive, transient nature and relativity in parameters, i.e. a certain nonspecificity to the following effects; the duration of PHA is determined by the duration of the phases of re-regulation of the transition period.

There is a possibility of consolidating the state of hyperadaptation, when post-factor (post-stress) conditions contribute to its manifestation.

Exogenous and endogenous factors reach the hyperadapting level only when their quantitative characteristics (dose and power) approach the characteristics of a complex endogenous factor, which determines the constitutive (spontaneous) level of changes (in some cases, damage) in the system.

There is a relative symmetry of the joint action of the two factors, i.e. the order of their action may not be important, which in relation to the hyperadaptive response means the possibility of applying the hyperadaptive effect after testing as a therapeutic, not only prophylactic.

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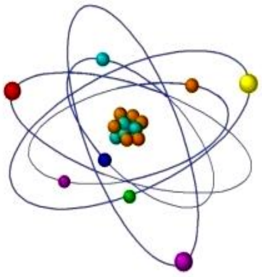
ELECTRON PARAMAGNETIC RESONANCE METHOD FOR DATING OF ARCHEOLOGICAL SITES IN GEORGIA



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ABSTRACT**:** *In Georgia there are many sites which have archeological value and interest on the side of cultural heritage but none of these sites is used as the experimental basis for modern scientific technologies. For this aim it was created a research group, including specialists in archeology, physics and radiology for development of new physical methods for dating of archeological materials found in Georgian. The first interesting results have already been by Electron Paramagnetic Resonance (EPR) method which we shortly present in this article.*

Key words: gamma-irradiation, EPR, archeological dating

For archaeological dating of human tissues and bones in range of millions of years very many physical methods were used.

One of such used method is the radiocarbon dating method of biological remains and materials of biological origin by the way of the radioactive isotope ^{14}C content establishment in the archaeological material as compared with the stable carbon isotope content. It is known that ^{14}C isotope is constantly formed in the atmosphere under the radiation effect. The ratio of the radioactive and stable carbon isotope contents in atmosphere and biosphere in the same time and place is identical because living organisms constantly participate in the carbon exchange and receive carbon from surrounding medium because isotopes due to their chemical identity participate in biochemical processes practically in the similar way. With the organism death carbon exchange ceases and after this as the radioactive isotope ^{14}C experiences the beta-decay its content in remains gradually diminishes while the stable isotope is preserved. But the method of radiocarbon analysis gives a wide data scattering and, in addition, it always exists the danger of sample contamination by alien organics.

There are also other dosimetric methods of dating such as electron paramagnetic resonance (EPR) and thermoluminescence (TL) [1-3]. For EPR and TL datings it is used unpaired electrons emerging in result of radioactive damage what causes their similarity. The EPR has some advantages as compared with TL caused by the fact that this is a non-destructive technique when signal doesn’t change during experiment and a sample could be investigated in different experimental conditions.

But EPR is less sensitive than TL in some cases, as example, in the case of ceramic item dating.

The EPR dating technique is based on the measurement of density of electrons captured by traps which were accumulated in bones and organics at irradiation after the burial of materials. It is defined the natural radioactivity of material and also the sources of radioactivity such as uranium and thorium. Then the remains are subjected to the standard dose of irradiation. The intensities of natural and laboratory EPR signals are compared and using the established dependence of EPR signals on the irradiation dose and the assessments of annual natural irradiation dose of a sample one could easily evaluate its age [4].

In the last two years for the first time in Georgia it was created a complex research group including specialists in archeology, physics and radiology from Ivane Javakhishvili Tbilisi State University and Institute of Radiology for development of new physical methods for dating of archeological materials found in Georgia. In the first turn it was started investigations using the electron paramagnetic resonance (EPR) method. The first interesting results have already been obtained by EPR method which we shortly present in this article.

On the first stage of EPR application for dating aims the tooth enamel was chosen as the object because the radiation defects created in it under natural irradiation influence are conserved during long time (~ 10^7 years) due to a large durability and stability of teeth enamel to the influence of surrounding medium. One of the important problems is also the cleaning of samples from impurities. After the carrying out the cleaning procedure of a sample the EPR spectrum is recorded and then the sample is irradiated by different doses of radiation what is accompanied by the growth of EPR signal which is proportional to dose amount until a definite value after which linearity of dependence is broken. For this reason only linear part of dependence is used for extrapolation (see graph and Fig. 1).

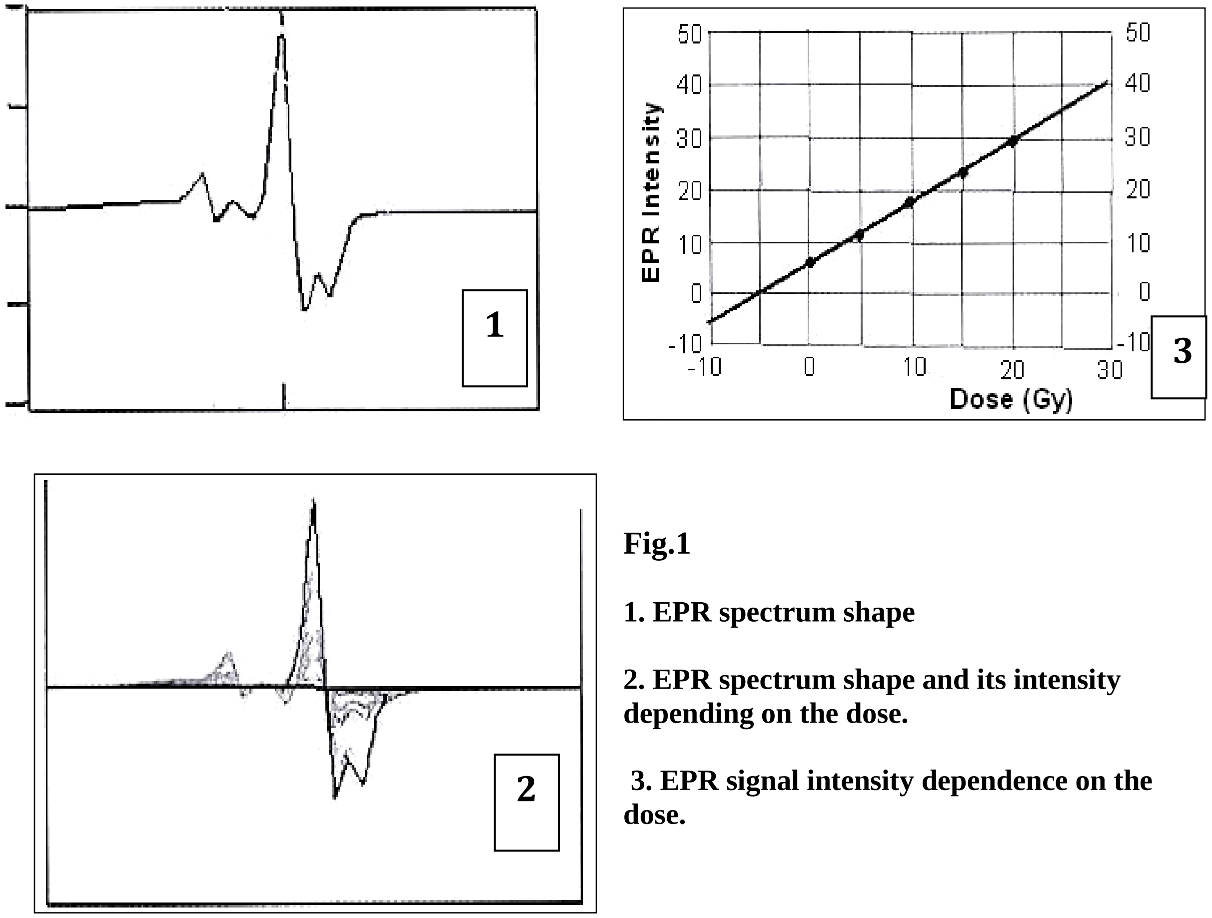


Fig.1

1. EPR spectrum shape

2. EPR spectrum shape and its intensity depending on the dose.

3. EPR signal intensity dependence on the dose.

The important advantage of this method is its non-destructive nature when it is not necessary to destruct a sample what guarantees the reproducibility of results.

For measurements it was used the tooth enamel samples taken from different archaeological sites with approximately known dating. The enamel was mechanically separated from teeth for further measurements.

The following samples were used

a) Unknown sample N 9

b) XIII-th century A.D. (found 16.12.2009), Atskuri Virgin Temple, sample N2.

c) IV-V centuries A.D. (found in April of 2010), Urbnisi, 8th burial site, sample N 5.

d) the end of IV-th century B.C., sample N 3.

e) XVII-XVI centuries B.C. (formed 18.09.09). Aspindza district, burial site N 1, sample N8.

So it is seen that all samples have definite dating.

These samples were mechanically and chemically treated to clear them off minerals. On the first stage the EPR spectra of samples were taken without their irradiation (see corresponding spectra in Fig. 2).

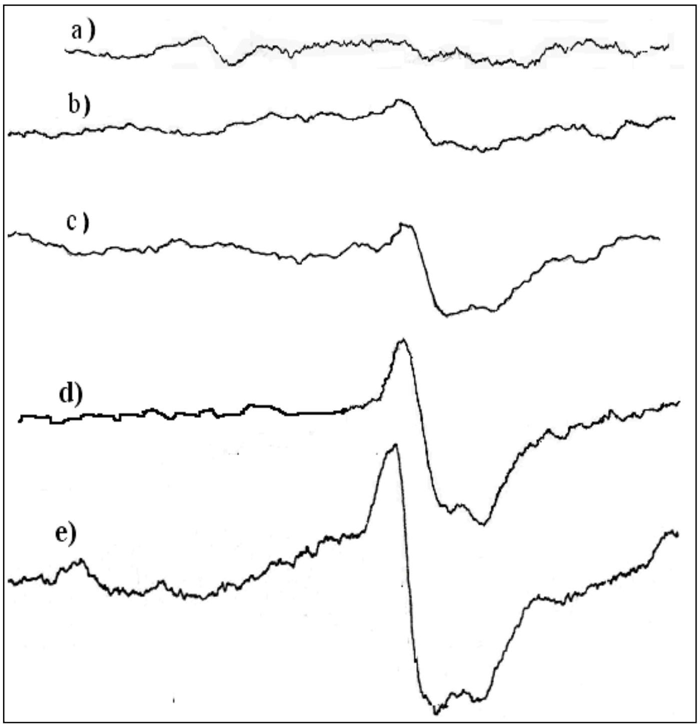


Fig. 2.

The obtained results were used to define the EPR signal integral intensity dependence on time of sample’s dating. As it is seen from spectra the older the sample the more irradiation dose was accumulated by its tooth enamel and, correspondingly, its EPR signal intensity is larger.

This dependence was obtained by us for the first time and shown in Fig. 3. The result as it is seen from figure is sufficiently interesting. Concluding from this if one has on the first stage the calibrated EPR signal intensities then it is possible with a good accuracy to predict its dating (all EPR intensities are measured in similar calibrated conditions.

On the next stage the samples were gamma-irradiated by radiation source ^{60}Co. Firstly, for measurements it was taken the Atskuri sample dated by V-IV century B.C. (d) – sample (conditionally this sample was adopted as the standard sample). At conducting experiments we encountered difficulty related with the fact that for the precision measurements it was necessary to have thoroughly calibrated radiation source. On the first stage it was chosen the same dose for the irradiation of all samples. It turned out that the EPR signal intensities quickly reached the saturation (the non-linear interval of dependence was not used – namely spectra 5 and 6 from the sequence of EPR spectra, Fig. 4).

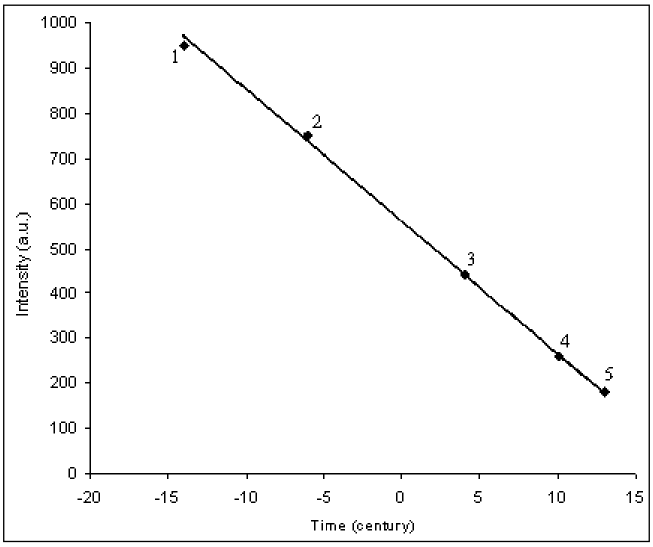


Fig.3.

Besides this, there were taken completely unknown samples with the aim of their dating which were irradiated simultaneously with the standard sample. The appearance of spectra and their shape in dependence on the dose value for the standard and other unknown samples is shown in Figs. 4-6.

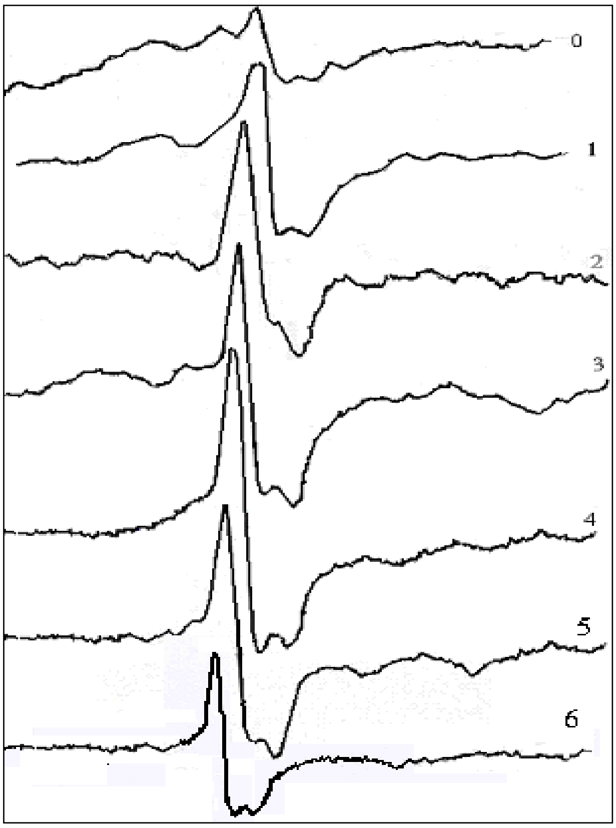


Fig.4.The end of IV-th century B.C. sequence of EPR spectra for the Atskuri tooth enamel sample-(d):

(0) – without irradiation; (1) – gamma–irradiated with dose 3.96 Gy;
(2) – 5.85 Gy; (3) – 7.8 Gy; (4) – 9.76 Gy; (5) 11.7 Gy; (6) – 15.6 Gy.

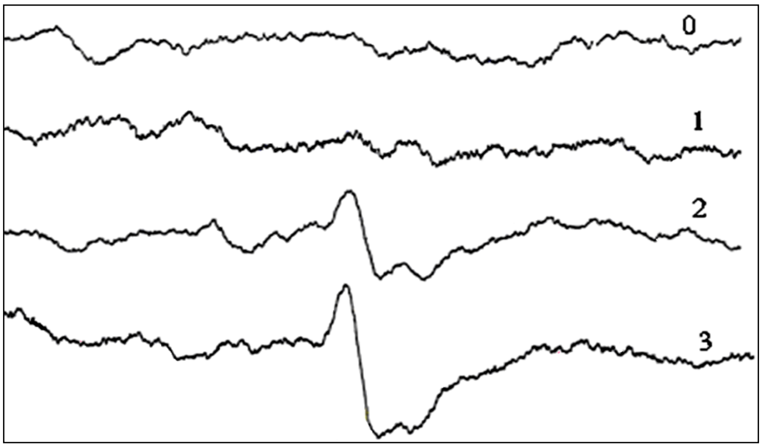


Fig.5. Sample (a): (0) – without irradiation;
(1) – irradiated by 1.95 Gy; (2) – 7.8 Gy; (3) – 11.7 Gy.

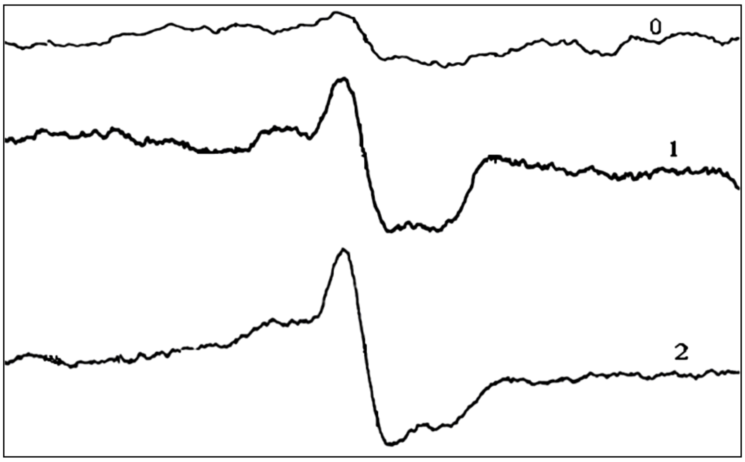
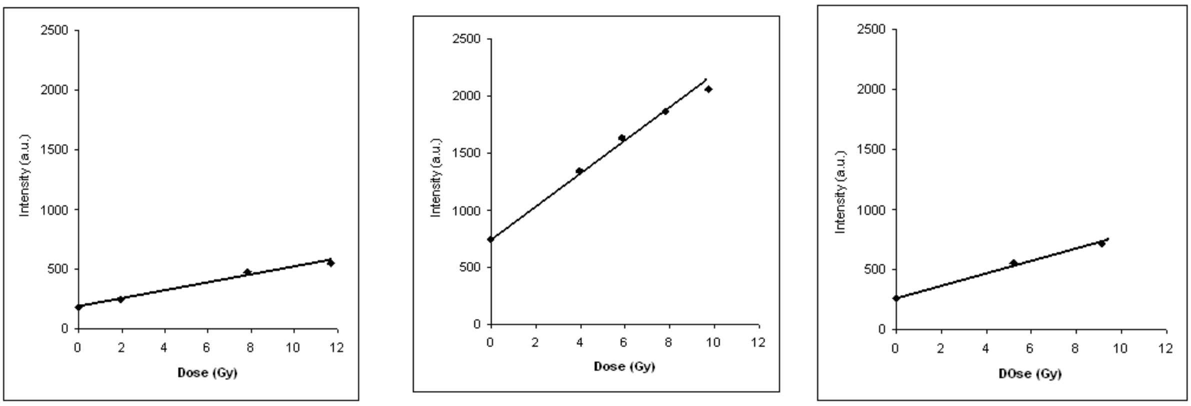


Fig.6. Sample (b): (0) – without irradiation;
(1) 5.2 Gy; (2) 9.1 Gy.

The irradiation and EPR measurements carried out on these three samples were completely identical. As it is seen from Fig. 7 for all samples EPR spectra intensities depend linearly on dose in complete agreement with work [4].



Sample (a) Sample (d) Sample (b)

Fig.7. EPR spectra intensity dependence on the gamma-irradiation dose

For obtaining dating results in accordance with works [4] it is necessary to measure annual irradiation on-site dose and know inclination angles of experimentally established straight lines (in Fig.7) of EPR spectra intensity dependence on the dose. It is also necessary to know starting intensity of EPR spectra of a sample. After establishing on-site annual irradiation dose the exact dating will be easily done what will be made on next stage of this work.

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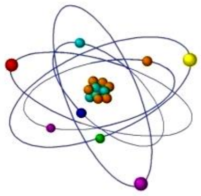
ALTERATION OF PATIENTS’ BLOOD TOTAL ANTIOXIDANT ACTIVITY DURING RADIOTHERAPY



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ABSTRACT: *This article presents the results of studies that examined the general antiradical status (TAA) of the body as a potential biomarker of the effects of radiation exposure. Thirty patients (60-70 years old) with squamous cell carcinoma of the larynx participated in the study. Every patient underwent fractional radiation therapy. Irradiation was performed on a linear accelerator in 2 gray/fraction mode, with a total dose of 70 gray given by a radical program. The examination of blood TAA was performed before the treatment (I) in the middle of treatment where the patient had received half of the total acceptable treatment dose (II) and after the radiation (III). In our study it was found that the TAA of blood increases linearly within the error, which indicates the activation of the body's antioxidant defense systems with the aim to neutralize the radicals generated by ionizing radiation.*

The results of our investigation support the fact that the non-enzymatic antiradical system plays an important role in the prevention of radiation damage during ionizing radiation exposure.

Key words: antioxidant activity, blood, irradiation

INTRODUCTION

Major advances in medical and radiation therapy have contributed to a growing population of cancer survivors. However, survivors have experienced adverse effects of radiotherapy [1,2], ICRP recommends the search for new highly effective, and inexpensive biomarkers of the individual risk for tissue reactions and strategies to prevent/mitigate tissue effects after exposure [3], which is considered to be a modern priority in radiation biomedicine [4]. Modern approaches to the search for absorbed dose (dose marker), radio-induced shifting effect, and marker of susceptibility in the conditions of the fractional partial body irradiation are concentrated on complex - genetic, cytogenetic, metabolic characteristics [5,6]. Among biodosimetry markers of radiation exposure, special attention is paid to redox status imbalance biomarkers [7, 8].

Ionizing radiation's hazardous impacts on living tissue are mediated by the generation production of reactive oxygen species (ROS) and oxidative stress mechanisms. ROS (hydroxyl radical, superoxide anion, and hydroperoxyl radicals) are generated after the irradiation, in the process of radiolysis of water [7, 8], followed by a chronic inflammatory response [9], accumulation of free radicals, and ROS, shift the redox equilibrium of the cell towards the oxidized state and development of an imbalance between pro-oxidative and antioxidative reactions, depletion of antioxidant activity together with an occurrence of negative consequences in metabolism [10].

Specialized enzymatic and non-enzymatic antioxidant systems participate in preventing the high production of free radicals in the eukaryotic organisms’ cells. An especially important role in these mechanisms plays a nonenzymatic antioxidant system (total low molecular weight antioxidants (ascorbic acid, bilirubin, estrogens, biogenic amines (dopamine, histamine, serotonin, melatonin and amino acid, tryptophan), etc.)), known as a total antioxidant activity (TAA) of the blood plasma.

This article presents the results of studies that examined the general antiradical status (TAA) of the body as a potential biomarker of the effects of radiation exposure.

MATERIAL AND METHODS

Thirty patients (60-70 years old) with squamous cell carcinoma of the larynx participated in the study. Every patient underwent fractional radiation therapy. Irradiation was performed on a linear accelerator in 2 gray/fraction mode, with a total dose of 70 gray given by a radical program. Patients were irradiated on the basis of the Live Hospital-Radiation Center with the device "Electra Synergy Platform". The study protocol was prooved by the Ethical Committee of Tbilisi State Medical University. Patients were informed about their participation in the study and signed written consent.

Postoperative patients were mostly irradiated with 66 grays in 33 fractions with a daily dose of 2 grays. Nonoperative patients were mostly irradiated with 70 grays in 35 fractions - with a daily dose of 2 grays. The examination TAA of blood was performed before the treatment (I) in the middle of treatment where the patient had received half of the total acceptable treatment dose (II) and after the radiation (III).

TAA was determined in deproteinized blood plasma by using the 2.2-diphenyl-1-picrylhidrazyl (DPPH)-scavenging assay, which was adapted from a study conducted by Chrzczanowicz et al. [11]. Briefly, plasma samples (1 mL) were deproteinized by adding 3 mL of acetonitrile and centrifuging then for 10 min (4°C, 9500 ×g). A supernatant was immediately collected and 1 ml was transferred to a tube. Subsequently, 3 mL of DPPH was added, and the resultant absorbance was read at 515 nm. A calibration curve was built with the use of gallic acid, wherein the absorbance values were interpolated and the results were expressed as equivalents of gallic acid.

Statistical analysis

Each data point represents mean standard error on the mean (SEM) of at least six pacient per group. $P < 0.05$ was considered to represent a statistically significant difference.

RESULTS

Figure 1 shows the values of the blood TAA of healthy individuals (controls) and oncological patients before radiotherapy (I), after receiving half-dose (II), and after irradiation (III). According to the results of the study, the blood TAA of patients with laryngeal cancer was no different from the blood TAA of the same age (60-70 years old) healthy individuals. After receiving a half dose of radiotherapy, the TAA of the irradiated patients; blood increased almost 2 times compared to the initial values, and after the completion of the whole course, the level of the blood TAA increased by 5 times in comparison to initial values.

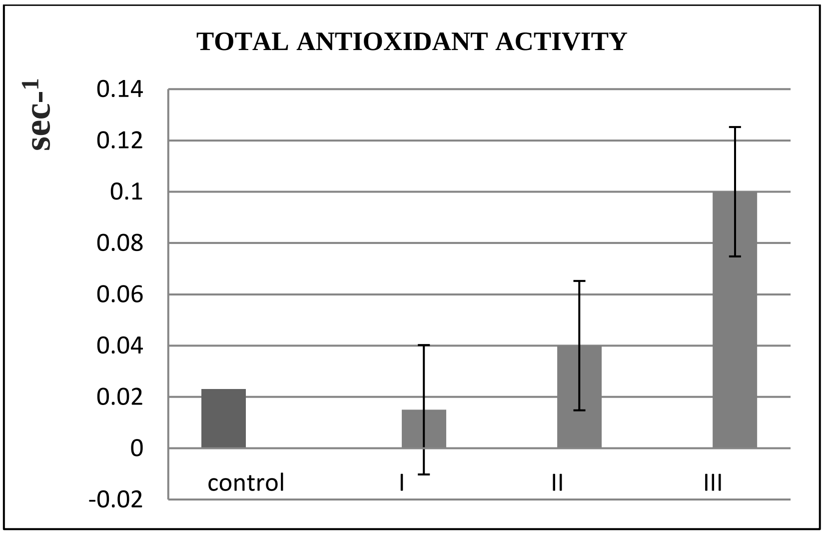

Figure 1. The blood TAA of healthy individuals (controls) and oncological patients before radiotherapy (I), after receiving half-dose (II), and after irradiation (III).

DISCUSSION

In response to the direct effect of ionizing radiation on cellular targets, in the result of radiolysis of water, as well as due to the compensatory response of the body to primary damage (increased activity of mitochondrial and microsomal electron transport systems) in tissues produced a huge amount of ROS, capable of damaging the cells and tissues of a living organism and leading it to death. The ability of cells in a living organism to prevent specific and non-specific oxidative damage is a key survival mechanism. Against the increased formation of ROS in the body, the enzymatic and the non-enzymatic antioxidant system, ensure the neutralization of free radicals [12, 13]. As shown by numerous studies, the antioxidant enzymatic system is rapidly depleted and cannot suppress an excess amount of ROSs formed during irradiation. In response to irradiation compensatory released high concentrations of low molecular weight antioxidants (ascorbic acid, biogenic amines, thiols, etc.) suppress oxidative stress [14, 15].

In our study it was found that the TAAof blood increases linearly within the error, which indicates the activation of the body's antioxidant defense systems with the aim to neutralize the radicals generated by ionizing radiation.

Small ROS-scavenging molecules present a metabolic route of tightly coordinated physiological processes ensuring the protection of cellular structures and macromolecules from ionizing radiation. The compensatory alterations of the TAA are a key mechanism of body resistance to ionizing radiation in radiated animals.

CONCLUSION

The results of our investigation support the fact that the non-enzymatic antiradical system plays an important role in the prevention of radiation damage during ionizing radiation exposure.

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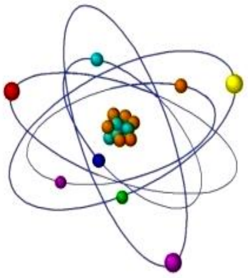
EVALUATION OF RADIOACTIVITY OF THE ROCKS IN THE FOOTHILLS OF THE MAIN CAUCASIAN RANGE IN THE TERRITORY OF KAKHETI REGION (East Georgia-Country)



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ABSTRACT: *This study investigates distribution of natural and technogenic radionuclides in rock samples in the eastern part of Kakheti region. The radioactivity of rocks in this region has not been investigated. 20 samples of rocks of various types – igneous, sedimentary and metamorphic were investigated with the gamma-spectroscopic method applied. Up to 21 naturally occurring radionuclides and 1 technogenic radionuclide have been identified in samples. Average activity concentration of Th-232 family radionuclides varied from 0.61 to 98.6 Bq/kg, U-238 family - from 9.1 to 77.0 Bq/kg, U-235 family - from 0.10 to 3.5 Bq/kg. The highest activity concentration was observed for K-40 (maximal value of 1475 Bq/kg). Activity of technogenic radionuclide Cs-137 varied from 0.10 to 1.2 Bq/kg. There are some marked features in radionuclides distribution depending, in particular, on rock type, tectonic zone. Some radionuclide activity ratios have been considered, in particular, U-238/U-235, U-238/Th-232, Ra-226/U-238 and Pb-210/Ra-226. These ratios allow to estimate condition of system (closed or opened) and to receive a certain notion about character of relevant geochemical processes. Comparison was carried out with existing data in the literature.*

Key words: radionuclides, rocks, radioactivity, activity ratios, East Georgia

INTRODUCTION

The ionizing radiation from the rocks is one of the main natural sources of the radioactivity. Geological bodies with the raised content of naturally occurring radioactive materials (NORM) concern a category of natural geological objects which define ecological conditions of the territory. As is known, natural radioactivity in the environment is caused by radionuclides of three families - Th-232, U-238 and U-235, and also K-40 which are so-called alpha-, beta- or gamma-emitters. Long-lived radionuclide Cs-137 (as well as Sr-90) is most widespread among technogenic radionuclides. Researches of radioactivity of rocks are a subject of numerous studies.

Previous work [1] has focused on rock samples selected in İkizdere and Kaptanpaşa Valley, Turkey. As a result of this work it was determined that, the activity concentrations of rock samples range from 26.12±3.24 to 44.39±4.41 Bq/kg for Th-232, 13.80±1.91 to 29.25±5.04 Bq/kg for U-238 and from 307.54±36.10 to 539.15±22.54 Bq/kg for K-40. The overall mean activity levels for Th-232, U-238 and K-40 are 35.06±3.85, 19.71±2.15 and 386.16±27.38 Bq/kg, respectively. In a different study [2] samples of igneous rocks (dolerite, granite, and granitic gneisses), sedimentary rocks (shale, limestone, sandstone) and metamorphic rocks (black shale, slate, graphite, marble, quartz mica, calcareous schist, and quartz) selected in the state of Azad Kashmir, Pakistan were studied. As a result of this work it was determined that, in samples of metamorphic rocks in particular activity concentration of Ra-226 varied from 5.4 to 100 Bq/kg; concentration of Th-232 varied from ≤1.8 to 111 Bq/kg; and K-40 varied from 9.6 to 1055 Bq/kg. An estimation of radiation hazard was made; in particular the value of the radium equivalent activity of all tested samples varied in the range from 20.6 to 294 Bq/kg, which is sufficiently lower than the recommended limit of 370 Bq/kg [3, 4].

In the work [5] there were studied samples of tuff deposits from four separate occurrences in the Dinaric Karst of Croatia. It was founded that activity concentration of Th-232 varied in the diapason 1.0-12.9 Bq/kg with average value of 4.5 Bq/kg; average value of U-238 concentration was sufficiently greater and made 7.5 Bq/kg (diapason 1.3-14.6 Bq/kg); comparable with U-238 results was obtained for Ra-226 – average value of 7.3 Bq/kg, diapason – from 2.9 to 13.0 Bq/kg. In investigated samples it was also detected technogenic radionuclide Cs-137 which activity varied within the interval 3.9-77.8 Bq/kg with average value of 24.6 Bq/kg; authors explain it as 137Cs impurity originating from rainwater; outdated tuff is not a closed system and sampling was performed after the accident in 1986, followed by heavy rain in this region. Also activities ratios was calculated which values for U-238/Th-232 varied in the diapason 0.81-5.30 with average value of 2.41, and for Ra-226/U-238 – in the diapason 0.59-2.22 with average value of 1.10.

A study in the Modane-Aussois region (Western Alps, France) [6] studied radionuclides content of various characteristic rocks, in particular, sedimentary (carbonaceous breccia, limestone dolomite, dolomite) and metamorphic (calcschist, marble, quartzite) rocks. The activity concentrations of K-40 varied from 18 Bq/kg (limestone dolomite) to 572 Bq/kg (quartzite). The activity concentration of Th-232 varied from < 1 Bq/kg (limestone dolomite) to 18 Bq/kg (calcschist). The highest concentration of U-238 was 29 Bq/kg (dolomite) and the lowest was 9.5 Bq/kg (quartzite).

Researches of various environmental objects radioactivity in Georgia were carried out in the past and, basically, were stimulated by the breakdown which took place on the Chernobyl atomic power station in 1986. The raised concentration of various technogenic radionuclides were observed (up to several thousands of Bq/kg), especially in soil of the West Georgia coastal part [7]. Some results for last period are given in the works [8, 9].

This study represents results of the investigations of the radioactivity of rocks samples selected in the foothills of the Main Caucasian Range in the territory of the region of Kakheti (East Georgia).

MATERIALS AND METHODS

Study area. The region of Kakheti is located in a southeast part of Georgia. The region is characterized sufficiently complex geotectonic structure. The territory were samples of rocks have been selected is located in the foothills of the Main Caucasian Range in the east part of Kakheti. The investigated area includes two tectonic zones (see Figure 1), in particular:

- Kazbek-Lagodekhi zone (folded-flaky) (I_2);
- Mestia-Tianeti zone (fold-napped) (I_3).

Twenty rock samples (Table 1) were collected in the investigated area (located in the canyon of the river Stori along the way from the settlement Pshaveli to the settlement Omalo, and also near settlements Lopota (Lp), Eniseli (En), Tsitskanaantseri (Tf), Mtisdziri (Mz), Lapniani (Ln), Baisubani (Bs), and cities of Kvareli (Kr) and Akhmeta (Ah)), in particular:

- in zone I_2: thirteen samples;
- in zone I_3: seven samples.

The types of samples collected were as following:

- igneous, two samples including:
  - effusive – two samples:
    - diabase – one sample (105);
    - basalt – one sample (111);
- sedimentary, eight samples including:
  - sandstone – six samples (109, 119, 122, 127, 132, 135);

    - argillite – two samples (133, 137);
- metamorphic, ten samples including:
    - sedimentary, six samples including:
        - clay-shale – six samples (102, 103, 106, 108, 113, 129);
    - volcanic, four samples, including:
        - shale – three samples (98, 99, 101);
        - marble – one sample (116).

All selected samples are of the Jurassic period.

Figure 1 shows layout of locations, and Figure 2 and Figure 3 show locations Pv-8 and Kr-3, respectively.

Table 1 List of locations (L), sample numbers (SN), types (ST) of investigated samples

#	Tc	L	SN	Lt(N); Ln(E)	ST
1	I_2	Pv-1	98	42.22982; 45.48529	Shale (chlorite-sericite, greyish) [Sl (Chl,Sr,Gr)]
2	-“-	Pv-2	99	42.22980; 45.48534	Shale (chlorite-sericite, greyish) [Sl (Chl,Sr,Gr)]
3	-“-	Pv-4	101	42.22892; 45.48372	Shale (quartz-sericite) [Sl (Q-Sr)]
4	-“-	Pv-5	102	42.22855; 45.48335	Clay-shale (rust with quartz veins) [Cl-Sl (Q,Rt)]
5	-“-	Pv-7	104	42.22732; 45.48134	Clay-shale (quartz-chlorite-sericite, rust) [Cl-Sl (Q,Chl,Sr,Rt)]
6	-“-	Pv-8	105	42.22668; 45.48226	Diabase (with pyrite flecks) [Db (Pyr)]
7	-“-	Pv-9	106	42.20423; 45.46114	Clay-shale (greyish) [Cl-Sl (Gr)]
8	-“-	Pv-11	108	42.19192; 45.45644	Clay-shale (rust with quartz veins) [Cl-Sl (Q,Rt)]
9	-“-	Pv-12	109	42.19067; 45.44211	Sandstone (silt quartzose) [Ss (Slt,Q)]
10	-“-	Pv-14	111	42.18785; 45.44946	Basalt (greyish) [Bs (Gr)]
11	-“-	Pv-16	113	42.15329; 45.42042	Clay-shale (greyish) [Cl-Sl (Gr)]
12	-“-	Lp-5	119	42.06280; 45.53373	Sandstone (carbonate silt) [Ss (Cr, Slt)]
13	-“-	Lp-2	116	42.07293; 45.60978	Marble (white) [Mrb (W)]
14	I_3	Ah-2	122	42.05140; 45.24077	Sandstone marly with argillite [Ss (Mr,Ar)]
15	-“-	En-2	127	42.00269; 45.66016	Sandstone (carbonate) [Ss (Cr)]
16	-“-	Kr-3	129	41.99424; 45.84642	Clay-shale (argillaceous) [Cl-Sl (Ar)]
17	-“-	Tf-1	132	41.90741; 45.89193	Sandstone (silt, carbonate) [Ss (Slt, Cr)]
18	-“-	Mz-2	133	41.85249; 46.04052	Argillite (carbonate) [Ar (Cr)]
19	-“-	Ln-2	135	41.83746; 46.09737	Sandstone (silt) [Ss (Slt)]
20	-“-	Bs-2	137	41.82818; 46.18119	Argillite (black) [Ar (Bk)]

Notes: Tct – tectonic zone; Lt(N) – latitude (north); Ln(E) – longitude (east).

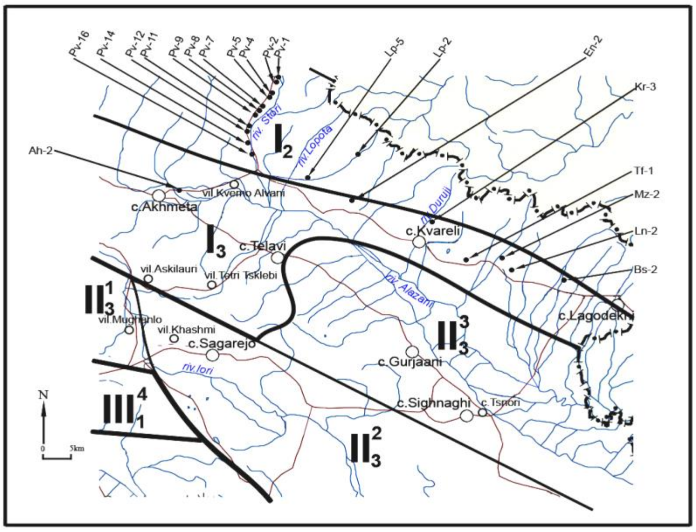

Figure 1. Layout of locations.

Figure 2. Location Pv-8.

Figure 3. Location Kr-3.

Sampling and analysis

Sampling Samples were selected from the outcropped rocks and put in plastic containers (volume up to 2.0 L). After drying in the laboratory, samples were broken into pieces < 40 mm and were then crushed using a special crusher (jaw crusher Retsch) to a size of approximately 1 mm. Then samples were dried at 105 - 110°C to constant weight and their bulk density was then determined. These values were used for the description of sample geometry. The samples were sealed in Marinelli beaker and stored for more than four weeks to achieve secular equilibrium between Ra-226 and Rn-222.

Measurement of gamma radiation activit

Measurements were carried out using a gamma spectrometer Canberra GC2020 with a semi-conductor germanium detector with relative efficiency of 24%. Gamma spectra acquisition time was 72 hour. Genie-2000 S500 software with additional modules was used for the analysis, in particular, S506 Interactive Fit Program. By means of this program, for all spectra a "decomposition" of the interference peak in the area of 186 keV was carried out (program identifies one peak in this area that is growing out of an interference of two closely spaced peaks of U-235 (185.715 keV) and Ra-226 (186.211 keV)). The program S506C processes the spectral curve mathematically; therefore, in this area two peaks are created with energies corresponding to U-235 and Ra-226. During the program identification of peaks and calculation of activity concentration a tolerance value was established in such a manner that low-energy peak was compared only with U-235 and high-energy peak only with Ra-226. Results show that, in particular, determination uncertainty of the activity concentration of Ra-226 was within 11 and 40%. Its activity was compared with the activity of its daughters, Pb-214 and

Bi-214, which had a determination uncertainty between 2 and 4%. Values of Ra-226, Pb-214 and Bi-214 activity did not differ sufficiently. Thus, it is possible to consider that similar determination uncertainty of Ra-226 concentration is satisfactory; thus, this method was also used for the determination of U-235 activity concentration by the 185.715 keV line. Received values of U-235 activity were compared to values of U-238 activity (which were determined by the line 63.3 keV line of Th-234, with an uncertainty range of 6.6-8.7%). The value of their activities ratio U-238/U-235, which is considered as constant (21.7) for natural objects [10], was used as a criterion. On occasion, in low-activity samples, Ra-226 activity was specified by the average activity of Pb-214 and Bi-214 and obtained value was considered a definitive estimation of U-235 activity. For Th-232 activity determination average values for Ac-228, Ra-224, Pb-212, Bi-212, and Tl-208 were used, which had determination uncertainties limits between 2.1 and 11.7% (except for the sample 116 for whom value of determination uncertainty for radionuclide Bi-212 has made 81.3%). Activities ratios were also determined U-238/Th-232 (which is accepted as being equal 0.81 for the closed systems [11, 12], Ra-226/U-238 and Pb-210/Ra-226 (equilibrium value 1.00), which are used to estimate the mechanism of various geochemical processes.

Taking into account the influence of matrix composition, the chemical composition of samples was determined on the basis of literary data [13, 14], which were then used in the special software (LabSOCS) for efficiency calibration of the activity concentration calculation. System LabSOCS allows to create calibrations by laboratory quality efficiency without application of radioactive calibrate sources. For radionuclides identification a special library was used that contains lines of 41 radionuclides and other specific sources (in total 351 lines). Database NuDat [15] was used for library compiling. For activity (A) calculation, the background radiation was subtracted.

The assessment of values of radium equivalent activity Ra_{eq} (Bq/kg) was carried out using the formula [16]:

$$Ra_{eq} = A_U + 1.43 A_{Th} + 0.07 A_K$$

where A_U, A_{Th}, and A_K are the activity concentrations (Bq/kg) of U-238, Th-232 and K-40, respectively.

For samples characterization by radioactivity degree, taking into account accepted limit value of Ra_{eq} (370 Bk/kg; equivalent to the annual γ-radiations dose of 1.5 mSv/y) [17]) some groups were established according to their value of equivalent activity, in particular:

1st group: nonradioactive samples (activity is low and did not exceed 30 Bq/kg);
2nd group: samples with low radioactivity (activity is in the range of 30 to 100 Bq/kg);
3rd group: samples with average radioactivity (activity is in the range of 100 to 300 Bq/kg);
4th group: samples with high radioactivity (activity is in the range of 300 to 1000 Bq/kg).

The technique is described in more detail in works [8, 9].

RESULTS

Up to 22 radionuclides were identified from the results of analysis of the gamma spectra of rock samples: the Th-232 family (Ac-228, Th-228, Ra-224, Pb-212, Bi-212, Tl-208); the U-238 family (Th-234, Pa-234, Th-230, Ra-226, Pb-214, Bi-214, Pb-210); the U-235 family (U-235, Th-231, Th-227, Ra-223, Rn-219, Pb-211); the natural radionuclides Be-7, K-40, the technogenic radionuclide Cs-137 (several specific lines were also identified that were incipient, as a result of the interaction of cosmic rays with the material of the detector or the sample).

The average activity of identified families of radionuclides varied widely, from 0.10 Bq/kg (for the U-235 family) to 98.6 Bq/kg (for the Th-232 family). Of the individual radionuclides, K-40 had the highest activity (up to 1475 Bq/kg). In some samples, the activity of radionuclides was lower than the Minimal Detectable Activity (MDA). The activity concentrations of the main radionuclides of the investigated samples, the equivalent activity, the activity ratios and their averages (av), the minimal (mn) and maximal (mx) values, among other data, are given in Tables 2 to 6. Figure 2 shows the statistically significant correlation between the U-238 and Th-232 activity concentration.

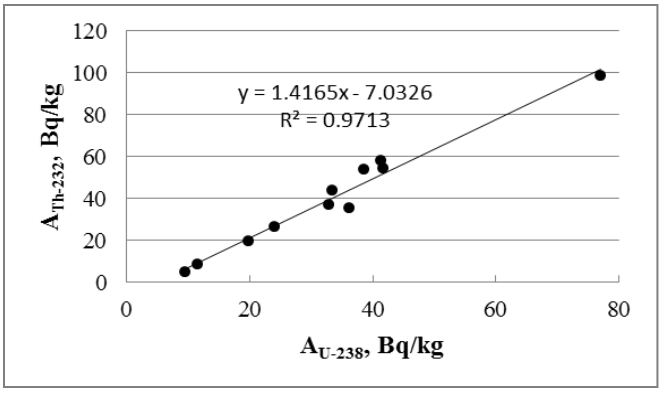

Figure 4. Correlation between U-238 and Th-232.

Table 2

The activity concentrations (A, Bq/kg) of the radionuclides of families Th-232, U-238 (Th-234), U-235, Ra-226, Pb-214, Bi-214, Pb-210, radionuclides Be-7, K-40 and Cs-137, the equivalent activity (Ra_{eq}, Bq/kg), the activity ratios U-238/U-235; U-238/Th-232, Ra-226/U-238 and Pb-210/Ra-226,

#	L	SN	A, Bq/.kg										Ra_{eq}	U-238/	U-238/	Ra-226/	Pb-210/
			Th-232	U-238	Ra-226	Pb-214	Bi-214	Pb-210	U-235	Be-7	K-40	Cs-137	Bq/kg	U-235	Th-232	U-238	Ra-226
1	Pv-1	98	5.2	9.6	8.3	9.0	8.0	23.0	0.45	<M	318	0.21	39.3	21.3	1.85	0.86	2.77
2	Pv-2	99	19.9	19.8	18.3	18.9	18.0	27.4	0.95	<M	557	0.42	87.2	20.8	0.99	0.92	1.50
3	Pv-4	101	26.3	24.0	27.4	24.2	23.6	19.6	1.09	—	490	0.61	95.9	22.0	0.91	1.14	0.72
4	Pv-5	102	98.6	77.0	82.3	78.8	75.4	62.5	3.53	—	1475	0.63	321	21.8	0.78	1.07	0.76
5	Pv-7	104	37.0	32.9	31.9	33.5	31.2	<M	1.52	—	1124	—	165	21.6	0.89	0.97	—
6	Pv-8	105	35.4	36.2	37.0	36.5	34.5	49.9	1.65	—	1172	0.70	169	21.9	1.02	1.02	1.35
7	Pv-9	106	54.1	38.6	44.0	39.3	38.7	38.2	1.72	—	802	—	172	22.4	0.71	1.14	0.87
8	Pv-11	108	43.8	33.4	33.6	32.2	31.3	26.3	1.51	—	156	—	107	22.1	0.76	1.01	0.78
9	Pv-12	109	54.5	41.8	33.6	37.0	36.2	60.4	2.00	<M	827	—	178	20.9	0.77	0.80	1.80
10	Pv-14	111	1.11	<M	4.2	2.5	2.6	19.0	0.10	—	21	—	-	—	—	—	4.52
11	Pv-16	113	58.0	41.4	41.5	40.7	39.4	—	1.90	—	766	<M	178	21.8	0.71	1.00	—
12	Lp-5	119	8.7	11.6	13.3	11.7	11.0	17.3	0.53	<M	95	0.22	30.7	21.9	1.33	1.15	1.30
13	Lp-2	116	0.61	<M	3.0	2.5	2.3	13.0	0.14	—	4.5	—	—	—	—	—	4.33
14	Ah-2	122	9.7	11.2	15.4	12.0	11.8	12.9	0.53	—	173	0.20	37.2	21.1	1.15	1.38	0.84
15	En-2	127	4.7	9.1	12.0	10.2	9.9	18.5	0.42	<M	52	0.51	19.5	21.7	1.94	1.32	1.54
16	Kr-3	129	52.8	39.8	33.7	35.5	34.3	35.0	1.90	—	710	1.2	165	20.9	0.75	0.85	1.04
17	Tf-1	132	41.0	29.5	26.9	26.8	26.3	39.8	1.38	—	709	0.32	138	21.4	0.72	0.91	1.48
18	Mz-2	133	18.7	18.5	12.5	15.1	14.4	16.4	0.90	—	319	<M	67.6	20.6	0.99	0.68	1.31
19	Ln-2	135	30.3	25.5	24.3	25.0	24.0	30.1	1.17	—	376	0.10	95.1	21.8	0.84	0.95	1.24
20	Bs-2	137	50.5	33.3	40.7	36.0	35.1	48.3	1.53	—	778	—	160	21.8	0.66	1.22	1.19
		av	*32.5*	*29.6*	*27.1*	*26.4*	*25.4*	*31.0*	*1.21*	—	*546*	*0.47*	*124*	*21.6*	0.99	1.02	1.63
		mn	*0.61*	*9.1*	*3.0*	*2.5*	*2.3*	*12.9*	*0.10*	—	*4.5*	*0.10*	*19.5*	*20.6*	0.66	0.68	0.72
		mx	*98.6*	*77.0*	*82.3*	*78.8*	*75.4*	*62.5*	*3.5*	—	*1475*	*1.2*	*321*	*22.4*	1.94	1.38	4.52

Table 3

Generalized data – the activity concentration of radionuclides (A, Bq/kg) of families (Th-232, U-238, U-235) and radionuclide K-40, the equivalent activity (Ra_{eq}, Bq/kg) depending on sample type (G)

G	**GR**	**A, Bq/kg**					Ra_{eq},	**U-238/**	**Ra-226/**	**Pb-210/**
		Th-232	**U-238**	**Ra-226**	**U-235**	**K-40**	**Bq/kg**	**Th-232**	**U-238**	**Ra-226**
Ig	*Ef*	18.3	36.2	20.6	0.88	597	169	1.02	1.02	2.94
Sd		29.7	23.7	23.8	1.11	460	98.4	0.97	1.02	1.31
	Ss	24.8	21.5	20.9	1.01	372	83.0	1.13	1.08	1.37
	Ar	34.6	25.9	26.6	1.22	549	114	0.82	0.95	1.25
Mt		35.2	30.8	29.4	1.34	591	129	1.01	0.99	1.60
	Sd	57.4	43.9	44.5	2.01	839	185	0.77	1.01	0.86
	Vc	13.0	17.8	14.3	0.66	342	74.2	1.25	0.98	2.33

Note. GR – group of rocks.

Table 4

Distribution of the average values $Ra_{eq\text{-}av}$ of the equivalent activity Ra_{eq} by the activity level group (GA), their quantity (N_s) and percentage (r, %).

#	**GA**	Ra_{eq}, **Bq/kg**	$Ra_{eq\text{-}av}$, **Bq/kg**	N_s	**r, %**
1	I	<30	19.5	1	5.6
2	II	30-100	64.7	7	38.8
3	III	100-300	159	9	50.0
4	IV	300-1000	321	1	5.6

Table 5

Generalized data – the activity concentration of radionuclides (A, Bq/kg) of families (Th-232, U-238, U-235) and radionuclide K-40, the equivalent activity (Ra_{eq}, Bq/kg) depending on the type of tectonic zone (Tct)

Tct	A, Bq/kg					Ra_{eq},	U-238/	Ra-226/	Pb-210/
	Th-232	U-238	Ra-226	U-235	K-40	Bq/kg	Th-232	U-238	Ra-210
I_2	34.1	33.3	29.1	1.31	601	140	0.98	1.01	1.88
I_3	29.7	23.8	23.6	1.11	445	97.4	1.01	1.04	1.23

General characteristics

The activity of the families of radionuclides varied in the samples by more than two orders of magnitude (Table 2); in particular, the activity of Th-232 varied from 0.61 to 98.6 Bq/kg (average value of 32.5 Bq kg-1), U-238 – from 9.1 Bq/kg to 77.0 Bq/kg (average value of 29.6 Bq/kg); and U-235 – from 0.10 to 3.5 Bq/kg (average value of 1.21 Bq/kg). The activity of K-40 varied by more than two orders of magnitude, from 4.5 to 1475 Bq/kg (average value of 546 Bq/kg). Be-7 was found in trace amounts in some samples. The technogenic radionuclide Cs-137 was measured in eleven samples in small amounts (0.10–1.2 Bq/kg), and was found in some samples in trace amounts. For the activity ratio of U-238/U-235, all the obtained values correspond (within ±10%) to a value of 21.7 (accepted for natural objects). The activity ratio of U-238/Th-232 showed marked deviation (more than ±10%) from the average value of 0.81 (for closed systems); an increase was observed in nine samples (ranging from 0.89 to 1.94), and a decrease in four samples (0.66–0.72). The value of the ratio Ra-226/U-238 differs (by more than ±10%) from the equilibrium value; in six samples, it is greater than equilibrium (1.14–1.38), and in four samples it is less (0.68–0.86). The ratio Pb-210/Ra-226 also differs from the equilibrium value (by more than ±20%[1]) in some samples; in eleven samples, it is greater than equilibrium (1.24–4.52) and in three samples it is less (0.72–0.78). (Note: activity ratios were not determined for all samples, because in some samples the activities of the corresponding radionuclides were below the MDA or were not measured). Within the Th-232 – Tl-208 chain, equilibrium was basically observed (except for Th-228, for which the determination of uncertainty was appreciable more than for other radionuclides). The majority of samples (88.8 %) by the level of the radium equivalent activity have low and average radioactivity, and the smallest quantity of samples (5.6%) applies to the group of nonradioactive samples as well as to the group with high radioactivity – 321 Bq/kg (see Table 6).

Dependence on the Type

The average activity of naturally occurring radionuclides in igneous rocks (was calculated only for one type – diabase) is greater (Table 3) than in metamorphic and sedimentary rocks (the average activity 169, 129, and 98.4 Bq/kg, respectively). The highest activity was found for the group of clay-shale (185 Bq/kg) that is connected with rather high content of radionuclide K-40 (the maximum value among all investigated samples - 1475 Bq/kg), and also Th-232 (57.4 Bq/kg) and U-238 (43.9 Bq/kg).

The calculated values of the ratios U-238/Th-232 for samples of sedimentary and metamorphic rocks are about of the same level – from 0.66 to 1.94 (the average value of 0.97) and from 0.71 to 1.85 (the average value of 1.01), at the same time the greatest diapason was observed for sandstones (0.72-1.94), and least – for the group of clay-shales (0.71-0.89). The ratio Ra-226/U-238 for samples of sedimentary rocks varied within a wide range (from 0.68 to 1.38) in comparison of metamorphic rocks (0.85-1.14) at the same time the greatest diapason was observed for argillites (0.68-1.22), and the least for clay-shales (0.85-1.14).

Dependence on the tectonic zones.

The average equivalent activity of the studied samples selected in the zone $\mathbf{I_3}$ (97.4 Bq/kg) is rather smaller than in the zone $\mathbf{I_2}$ (140 Bq/kg), however activity of several samples (clay-shale, sample 129) reach higher values (165 Bq/kg). Values of activity ratios for two zones are comparable among themselves (Table 5).

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[1] The range of limits is expanded, because determination uncertainty of Pb-210 reached up to 20%.

DISCUSSION

The concentration of radioactive elements in rocks and soils is formed by the radioactivity of original structures and the whole set of subsequent processes of rock and soil formation. The content and concentration of NORM identified in the investigated samples generally correspond to those observed [18] for various rocks and soils. For the study region, this is the first time such analysis has been carried out. All these radionuclides, except Cs-137, are of natural origin. They are also characteristic for the region of Georgia [8, 9].

Rock samples were selected in a geological area characterized by a sufficiently complex geotectonic structure. Basically, types of the selected samples corresponded to sedimentary and metamorphic groups (besides there were selected two igneous samples). Each of these groups has specific mineralogical and chemical composition as well as rock-forming mechanism, which is connected to the wide range of radioactivity concentration values, taking place practically for all identified radionuclides, and also for activities ratios of some radionuclides.

As it has been noted above, the greatest radioactivity among the investigated samples have the clay-shales concerning to metamorphic sedimentary rocks. It is necessary to notice, that sedimentary rocks, including metamorphic rocks of sedimentary origin, inherit a radioactivity of rocks from which they are formed. According to literary data, the highest and rather constant radioactivity among sedimentary rocks have clay-shales (and clays too). Relatively high radioactivity of clay-shales is explained by both the raised sorption of uranium, radium, thorium, and potassium from the natural fluids on the clay particles and relatively high potassium content in these rocks (up to 6.5 %).

In all samples the U-238/U-235 ratios observed correspond, within error, to the natural value, that, besides methodological aspect, allows making the conclusion about absence of pollution by anthropogenous U-235. The results show a deviation of the ratio U-238/Th-232 from the average value, which may be a consequence of the fact that the given system was essentially closed. The raised values of the ratio Ra-226/U-238 noted also for much samples, apparently, are connected with prevalence of dissolution processes of U-238 (that leads to decrease of its concentration), and lowered values are connected with prevalence of leaching processes of Ra-226 from surface strata (where samples were selected). The deviation of ratio Pb-210/Ra-226 from the average value is not characteristic for rocks in connection with insignificant migration of radon in relative solid rocks and insignificant effect of accumulation of atmospheric Pb-210 on a surface of rocks (because of washing off by atmospheric precipitates).

In some samples an insignificant concentration of naturally occurring radionuclide Be-7 (a so-called cosmogeneous radionuclide that is formed as a result of nuclear reactions in an upper atmosphere) are observed as a result of precipitation and in some cases can be identified in gamma-spectra.

The technogenic radionuclide Cs-137 also gets into the samples as a result of atmospheric precipitation. Usually, the presence of Cs-137 in natural objects (for example, in soil) is linked to the Chernobyl disaster. After that it decreased in quantity as a result of decay and migration. In several samples an insignificant concentration (in comparison with soils where its concentration is considerably higher) was observed that, apparently, is connected with intensive process of washing from a sample surface.

Table 6 shows some reference data in other regions of the world. Apparently, the values received in the present work, on the average, are comparable with data of other regions.

Table 6

Comparison of radioactivity of rock samples with other areas of the world.

Country	**A, Bq/kg**			**Ref.**
	U-238	**Th-232**	**K-40**	
Brazil	31	73	1648	[19]
Cyprus	1-588	1-906	50-1606	[20]
Albania	8-27	13-40	266-675	[21]
India	0.44-50.83	0.21-293.67	233.49-2091.70	[22]
Turkey	13.80-29.25	26.12-44.39	307.54-539.14	[1]
Italy	42-70	31-37	410-475	[23]
Greece	29-110	19-88	152-1593	[24]
Algeria	11-25	6-32	56-607	[25]
Georgia	9.1-77.0	0.61-98.6	4.5-1475	This study

In conclusion it is necessary to notice, that the received results represent doubtless scientific and applied interest for investigated region that confirms an urgency of such researches and necessity of their systematic character.

CONCLUSION

1. It was established that in rock samples there are up to 22 detected radionuclides, in particulat, the radionuclides of families Th-232, U-238, U-235, other naturally occurring radionuclides – Be-7**,** K-40, and the technogenic radionuclide Cs-137.
2. The main features and regularities of samples radioactivity were established, in particular:
   - activity of families radionuclides and the radionuclide K-40 varied in various samples by more than two orders of magnitude – from 0.61 to 1475 Bq/kg; the U-238/U-235 activity ratio corresponds to the value of 21.7 (accepted for natural objects); U-238/Th-232 ratio deviations (more than ±10%) from the average value of 0.81 (for closed systems) were observed as both increases and decreases; deviations of ratios Ra-226/U-238 and Pb-210/Ra-226 from the equilibrium value (1.0) were insignificant;
   - radionuclide Be-7 was measured in some samples at trace amounts;
   - the technogenic radionuclide Cs-137 was measured in some samples (activity concentration from 0.10 to 1.2 Bq/kg).
3. Some features of activity distribution were determined depending on sample type and depending on geotectonic zones.
4. Analysis of obtained results and some of their features was carried out, as well as comparison with literary data.

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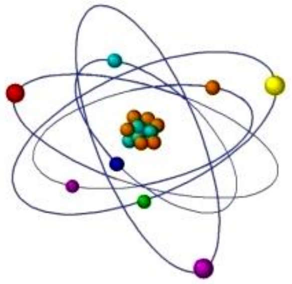
PHYTO THERAPEUTIC TREATMENT OF RADIATION-INDUCED TYPICAL MORPHOLOGICAL CHANGES OF SMALL INTESTINE



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ABSTRACT: *This study aims to identify the morphological changes in the small intestine after exposure to gamma irradiation (5Gy) and reduce the negative impact of irradiation with. Radiation-induced morphological changes of jejunum are thickening and shortening of intestinal microvilli and epithelial shedding. The villi are broken or dissolved to varying degrees, with a loose arrangement between the intestinal villus.The duckweed -Lemna minor has anti-inflammatory and antibacterial activity that reduces the negative impact of gamma irradiation on small intestines.Intake of Lemnan in the early post-irradiation period has a great significanceintheregenerative process of small intestine mucosa and increased survival rate of irradiated animals. Phytotherapeutic substance - Lemna minor. The active component of the duckweed is pectin polysaccharide - Lemnan, which increases the barrier-immune function of the small intestineThe results of the study indicate that Phytotherapeutic treatment on early post-radiation period reduces acutedelayed irradiation effects resulting in increased survival rate of irradiated animals.*

Key words: gamma- radiation, small intestine, pectin polysacarydes, *Lemna minor L.*

INTRODUCTION

Acute Radiation Syndrome is one of the most challenging aspects of human irradiation injury. Organs, tissues and cells are exposed to gamma irradiation causing three main acute radiation syndromes: Hematopoietic syndrome, Gastrointestinal syndrome, Cardiovascular central nervous system syndrome. The gastrointestinal tract is among the most radiosensitive organ systems in the body. According to radiosensitivity they are arranged in the following order: small intestine, salivary glands, stomach, rectum, colon, pancreas andliver [1].

Early radiation enteropathy is aresult of epithelial barrier dysfunction and mucosal inflammation. Delayed radiation enteropathy symptoms occur 3 months or more after irradiation and are characterized by mucosal atrophy, vascular sclerosis, and progressive intestinal wall fibrosis. These symptoms are progressive and mainly characterized by malabsorption of nutrients and abnormal intestinal peristalsis [2]. Cell damage can occur by direct or indirect action of ionizing radiation (IR). The direct effect of IR is the breaking of macromolecules. The indirect effect of IR is revealed in the production of highly reactive free radicals from the radiolysis of water and disfunctionof mitochondria. Under normal conditions, the mitochondria participate in the regulation of the physiological reactive oxygen species that are involved in the essential signaling pathways involved in cellular differentiation and proliferation process. Reactive oxygen and nitrogen species (ROS/RNS) produced after IR interact with biological targets causing damage of DNA, proteins, and lipids. Activation of the transcription factors results in the secretion of proinflammatory cytokines (tumor necrosis factor-α, interleukin-1β, and IL-6), chemokines (IL-8 and monocyte chemoattractant protein), cell adhesion molecules, stress response genes, and cell surface receptors. The target of the inflammatory factors is intestinal mucosa and submucosa; they not only induce tissue injury but also amplify the initial damage caused by gamma irradiation [8,9,10]. The outcome of this process is the development of fibrosis. Increased expression of Interleukin 1 alpha (IL-1α), Transforming growth factor-beta 1 (TGF-β1), and Platelet derived growth factor-AA (PDGF-AA) is in correlation with fibrosis and inflammatory cell infiltrates in the irradiated intestine. The sustained increase in expression of these cytokines from 24 h to 26 weeks after irradiation suggests an ongoing process that is initiated at the time of irradiation [3]. Ionizing Radiation promotes the induction of apoptosis and clonogenic cell death, which leads to mucosal breakdown. It is known that exposure to IR leads to inflammation and injury of the tissues [8,9]. The process of inflammation is amplified by the production of proinflammatory cytokines, chemokines, and growth factors decreasing the immune-barrier function of the intestinal epithelial cells. Translocation of the intestinal microflora in the basement membrane leads to bacterial infection, development of toxicosis, and sepsis [4,5,6,10].

Moreover, vascular injury is one of the most common effects of radiotherapy on normal tissues. Irradiated endothelial cells acquire a proinflammatory, procoagulant, and prothrombotic phenotype. It is suggested that the endothelial lesion occurs before crypt stem cell damage in the evolution of the GI syndrome [7].

MATERIALS AND METHODS

The experimental protocol was in accordance with the guidelines for care and use of laboratory animals as adopted by the Ethics Committee of the Tbilisi State Medical University (TSMU).

Animal care and maintenance

Three month old male mice (Mus musculus), were obtained from Vivarium of Tbilisi State Medical University. They were housed in animal cages, with room temperature maintained at 20^0-220C, relative humidity of 50-70% and an airflow rate of 15 exchange/h. Also, a time-controlled system provided 08:00-20:00 h light and 20:00-08:00 h dark cycles. All mice were given standard rodent chow diet and water from sanitized bottle fitted with stopper and sipper tubes.

After acclimatization for a week to laboratory conditions, the mice were divided into three different groups. The first control group of three months old mice not irradiated, second group - experimental group of three months old irradiated mice, third group- irradiatedmice receiving lemnan with food. Mice whole-body irradiation with ^{137}Cs was performed at a dose rate of 1,1Gy/min for the total dose of 5 Gy with a “Gamma-capsula-2” (group 2 and 3). The duckweed - Lemna minor L. was used asa herbal supplement.Cultivation of Lemna was performed onsynthetic leachate under controlled conditions using standard methods. After Cultivation biomass was dried at room temperatureand after mechanical fragmentation extracted powder was used in experiment [11,12,13].

Jejunum sections obtained from three groups of mice were fixed in 10% formalin for 48 h and embedded in paraffin blocks. Eight-micrometerthick slides were sectioned using a rotarymicrotome, andstained with hematoxylin and eosin (H&E). Images were captured with digital camera at 4x14 magnifications.

RESULTS AND DISCUSSION

In this study, we used acute gamma irradiation causing the gastrointestinal syndrome. Acute symptoms are developed after radiation exposure resulting in the morphological changes of the intestinal villus. Experimental analysis revealed that compared to bone marrow degenerative and regenerative phases are shorter in small intestines. In the case of damage, the integrity of the epithelial layer must be rapidly restored in order to prevent infections. In mice, this period varies from 24 to 55 hours. Consequently, the aim of our study was to determine morphological changes in the acute post-radiation period (48 hours) and reducing these changes using Lemnan.Morphological changes in jejunum were analyzed using H&E staining. The intestinal villi were arranged clearly and regularly in the control group (Fig.1)

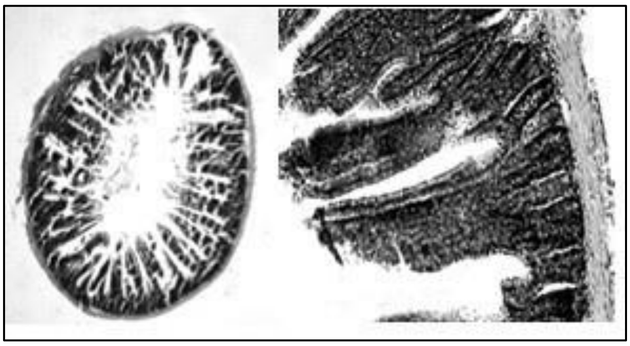
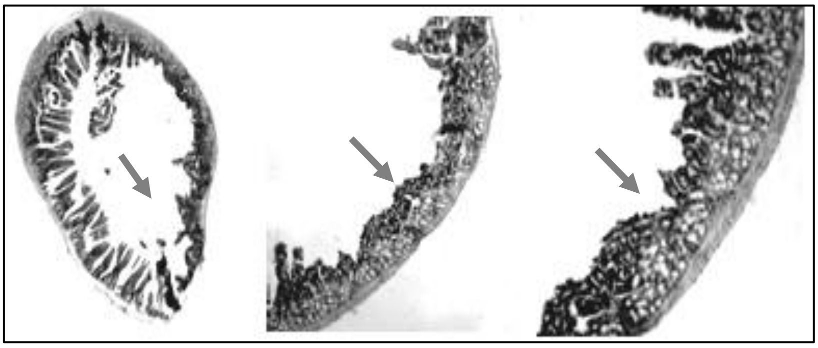


Fig.1 Histological sections of the small intestines of mice (H&E ×14x4)

The microvilli were arranged compactly, and the size of cells was approximately the same, forming an integral tight junction. Meanwhile, after irradiation (5 Gy) a thickening and shortening of intestinal microvilli and villi occurred, as well as a disruption of the tight junction structure. Furthermore, the villi were broken or dissolved to varying degrees, with a loose arrangement between the intestinal villus (Fig2). Epithelial shedding of the villi and disintegration was observed (Fig.3). The third experimental group eating lemnan showed regenerative process in small intestine mucosa after irradiation (Fig.4)

Fig.2 Shortened and irregular villi and breaking, dissolved epithelial cells (arrow**)** H&E-stained tissue sections of jejunum



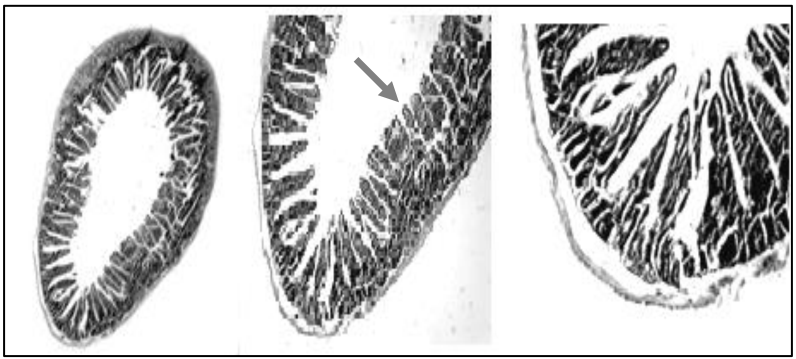


Fig.3 epithelial shedding of the villi and disintegration. H&E-stained tissue sections of jejunum.

Fig. 4 Phytotherapeutic impact on the postradiation regenerative process of tissue
H&E-stained tissue sections of jejunum. (*Arrow, indicates on the regenerative area of mucosa*)

Obtained result of the intestinal regenerative process is determined by the nature of Pectin. The physicochemical properties of pectins give them several advantages in the wound healing process, their hydrophilicity permits removal of exudates, maintenance of an acid pH, which is expected to act as a barrier against bacteria or fungi. Furthermore, pectins have the potential to bind active molecules and protect them from degradation [15,16]. Pectin reduces the secretion of pro-inflammatory factors and immunoglobulins during radiation enteritis [17].

Post-radiation recovery is a multi-component process. The universal parameter of the recovery process is reducing the mortality of irradiated mice. According to the specificity of gastro-intestinal radiation syndrome for evaluation of the positive impact of herbal supplements dose-dependent survival rate of mice was established [Fig.5].

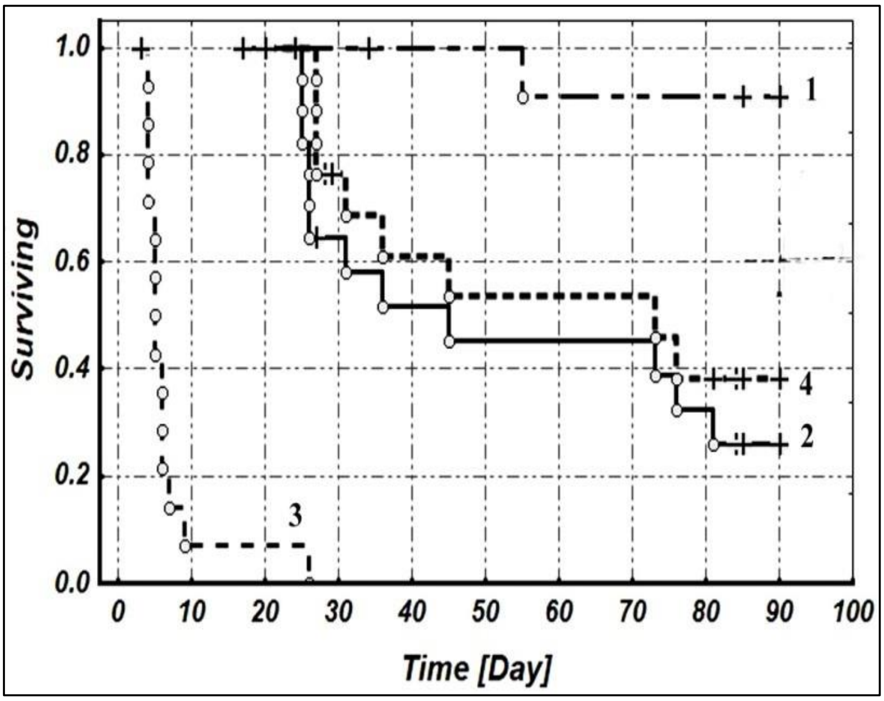


Fig. 5 Impact of Phytotherapeutic treatment on the survival rate of irradiated white mice.

5-Irradiation 3,5Gy, 2-5,0 Gy, 3-6,5, 4-Irradiation+Lemna,
0 -Complete, + - CensoredAcute ionizing radiation
X –Lifespan of the mice Y –Survival rate.Cumulative proportion surviving (Kaplan-Meier)

Threedifferent doses were used for mice irradiation: 3,5 Gy (minimal injury); 5 Gy (medium rate of injury); 6,5 Gy (acute injury). As Fig.5 shows high survival rate after 3,5 Gy irradiation (Fig.5-1). Opposite results are obtained after 6,5 Gy irradiation. Experimental animals mortality. All animals die in 2-3 weeks. (Fig.# 5-3). Consequently, for our using herbal supplement was selected 5 Gy irradiation causing medium rate of injury (Fig.#5-2). Survival rate of third experimental group (IR+Lemna) increased compared to second experimental group of irradiated mice. Survival rate increased with 15±5%(Fig.5-4).

CONCLUSION

Anti-inflammatory and antibacterial properties of Lemna minor reduces typical morphological injury developed after exposure of ionizing radiation. Radiation induced tissue-injury and post-radiation recovery is characterized by diversity of process, it can be considered that activation of recovery process and increasing survival rate of irradiated animals is related to recovery of small intestine barrier-immune function.The results of the study indicate that Phyto therapeutic treatment on early post-radiation period reduces acute delayed irradiation effects resulting in increased survival rate of irradiated animals.

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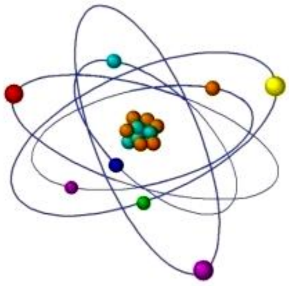
HYGIENIC ASSESSMENT OF THE WORKING ENVIRONMENT OF EMPLOYEES IN INTERVENTIONAL MEDICINE



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ABSTRACT: The study aimed to identify the peculiarities of the working conditions of the medical staff employed in specialized procedures in the cardiac catheterization laboratories of the specialized clinics.The study found that the catheterization laboratory: 25% of cases did not meet the standard requirements, the internal area was on average 41-43 m^2, instead of the minimum 47 m^2; the average height of the ceiling was 2.7 m, instead of 3 m; the walls and floor of the catheterization laboratory were not treated with X-ray-resistant material (in 7% of the clinics); 30% of the research facilities didn't have adequate lead sealing of the Procedure Room door; 7-8% of the surveyed facilities did not have a well-functioning ventilation system; In 17% of the surveyed cases the autonomous power source system of the coronary angiography was located so close to the laboratory that the noise level in the Control Room (in the remote control room) exceeded the maximum permissible noise level, which created discomfort during the operations.A study of the use of personal protective equipment (to reduce the dose of radiation) by medical personnel revealed that: the staff did't use protective glasses (98%); 7-8% did't use thyroid protection collar during the procedure;) 92% did't use small pelvic and gonad protective lead aprons; 67% did't attach the dosimeter to the body during the procedure; 98% of the staff did't use a special shield to reduce radiation in the procedure; 1-2% of the medical staff taking part in the procedure is in the usual medical uniform.

Conclusion: the profession of interventionists belongs to the group of tense and stressful work, but radiation safety requirements are not fully implemented in the workplace.

Key words: working environment, occupational hazard, hygienic essesment, catheterization laboratory

Noncommunicable diseases (NCDs) remain the number one challenge for world medical professionals. For years, diseases of the cardiovascular system have been at the top of the list of noncommunicable diseases in terms of frequency of development. Cardiovascular pathologies are one of the leading causes of lethal outcomes in all the countries of the world [2,4].

In a document developed by the World Health Organization WHO [3,5], premature (30-69 years) age-standardized mortality rates from cardiovascular diseases appear to have a leading position among other non-communicable diseases. According to WHO experts, ischemic and cerebrovascular diseases will be among the top ten causes of the disease burden in the world by 2030 [1], which will further increase the number of people involved in the management of this pathology and the number of people employed in this field. The latter in itself implies the identification of the working conditions of the employees and the management of the labor process and the importance of revealing possible health effects urgently. The share of circulatory system pathology in Georgia is 15.5% of all diseases registered in the country, and that of the new cases equals 8.6%. Hypertensive, ischemic, and cerebrovascular pathologies are characterized by high morbidity and mortality in this disease group. In 2000-2015, there is an increasing trend in the prevalence of circulatory pathologies (Diagram 1) [7].

Continuous development and modern advancementof medicine can significantly reduce the likelihood of developing diseases of the cardiovascular system, it is only necessary to detect the first signs of changes in time. According to statistics, 80% of surgeries performed due to pathologies of the cardiovascular system fall on men, and 20% - on women.

In recent years, interventional cardio therapy has achieved special development in the treatment of cardiovascular pathologies. The main achievement of interventional cardiotherapy is considered to be the reduction of the postoperative rehabilitation period and the maximum avoidance of postoperative discomfort, pain, and scar development. Interventional cardiotherapy is the "gold standard" for the treatment of acute myocardial pathology.

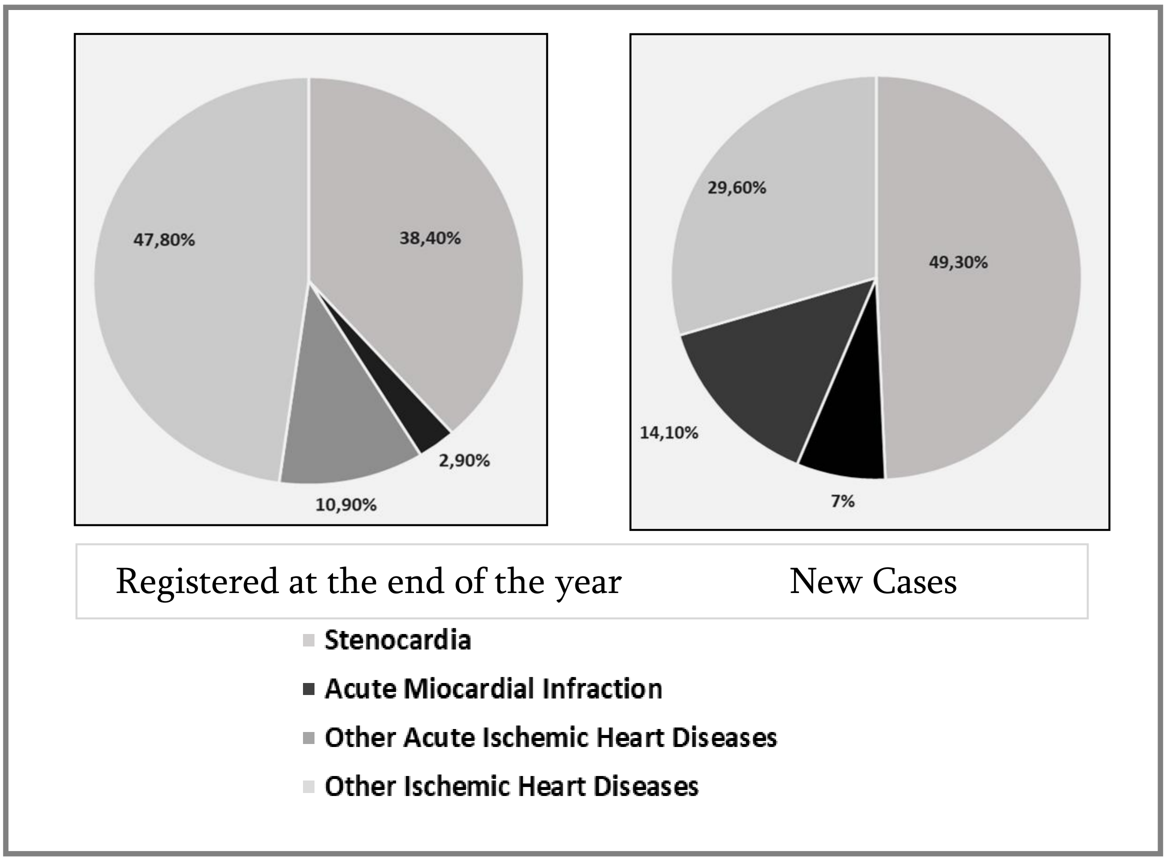


Diagram 1. Statistics of Ischemic Heart Diseases, Georgia 2013

According to the recommendation of the World Health Organization, coronary artery angiography is recommended in patients with coronary heart disease (CHD) to prevent myocardial infarction and lethal outcome of ischemic heart disease and to reduce their number.

With the refinement of cardiac catheterization techniques (better radiographic equipment, less adverse effectsof contrast agents) and the introduction of effective methods of treating coronary artery diseases (stenting, aortocoronary shunting), diagnostic coronary angiography has become one of the most important components of cardiac catheterization.

An appropriate working environment and special equipment are required for the implementation of this procedure.

In a modern catheterization laboratory (Figure 1) there is an X-ray machine that allows different angulation of the X-ray beam and directs this beam at different angles to the patient. The patient lies on a special table (4) that allows the x-ray beam to go through smoothly. The table can be moved up and down, as well as to the right and left. Under the table is placed the source of X-ray radiation and, consequently, above the table - the image receiving device.

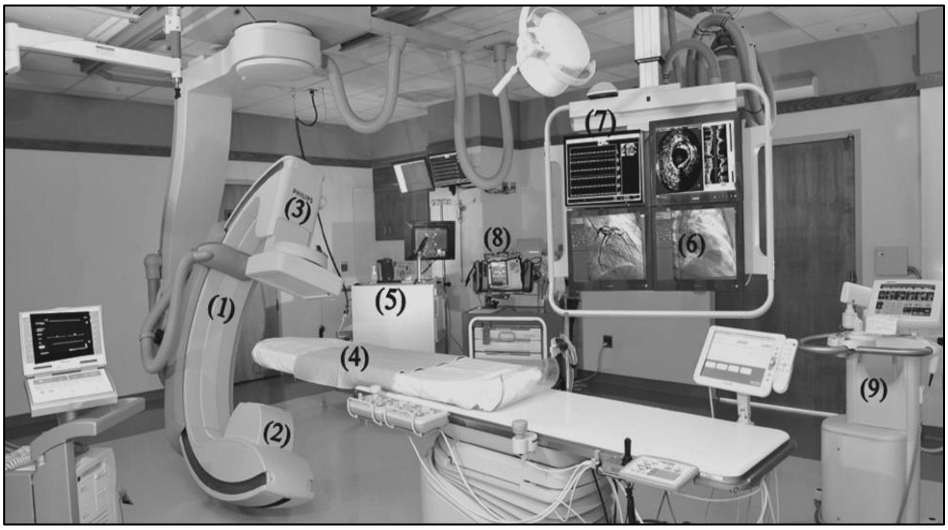


Figure 1.Catheterization laboratory

In a catheterization laboratory, there are the following items: 1. a mechanical part of an x-ray machine that hangs from the ceiling. At its lower end is an X-ray source (2), and at the top is an imaging device,an image detection system (3). X-rays fall on it, which pass through the patient, it converts these rays into a television signal and transmits them to monitors (6). The mechanical part of the X-ray machine (1) allows the X-ray source (2) and the image receiving device (3) to be positioned at different angles in different directions. Two monitors, which also hang from the ceiling, are designed to visualize angiographic images. The left monitor shows the situation in real-time, while the bottom right shows special monitors (7) that are used during the electrophysiological examination. The catheterization laboratory is equipped with a defibrillator (8), an artificial ventilator; a high-pressure input device, the so-called, contrast injector. A clinic has two catheterization laboratories to continue the procedure through the second equipment in case of failure of one. It is also necessary to have an autonomous power supply. If a clinic has one catheterization laboratory, a second portable device is necessary (5). The described system is a typical single-plane system [8]. There are also dual-plane devices (Figure 2). A dual-plane X-ray device is an integrated X-ray machine with two independent radiation sources and an independent television system - one on the floor and the other on the ceiling. Using this device, less contrast agent is expended, since two different planes are recorded with a single input of contrast substance.

Figure 2. Biplane angiography

The classic imaging procedure chain looks like this:
Generator - Cineangiography Pulse System - Imaging Receiver - Optical Distributor - TV Camera - Digital Recorder - Monitor. In this chain of images, it is possible to receive and view a direct real-time fluoroscopy image.

According to modern standards, the area of the catheterization laboratory is at least 47 m2. Ceiling height in the room - 3 m. The interior- walls, ceiling, and floor are treated with X-ray-resistant material, and the doors are hermetically sealed with lead material. The catheterization room and the remote control unit should be connected in such a way that verbal communicationamong the staff members is easily possible.

The generator of the equipment converts three-phase 480 volts to 70-120 volts and 300-800 milliamperes. The device required for cardiological purposes should have an alternating current output combined with a cineangiography pulse system that emits 4-6 ms long impulses. The voltage of the X-ray tube should be 80-100 kV. The image receiving device (so-called intensifier) should preferably be 5.7 and 9 inches in diameter. An X-ray tube should be able to emit 25-30 pulses per minute to obtain high-quality cineangiographic images. Images are taken as short films and stored digitally. They are exchanged between clinics by recording in DICOM (Digital Imaging Communications in Medicine) mode.

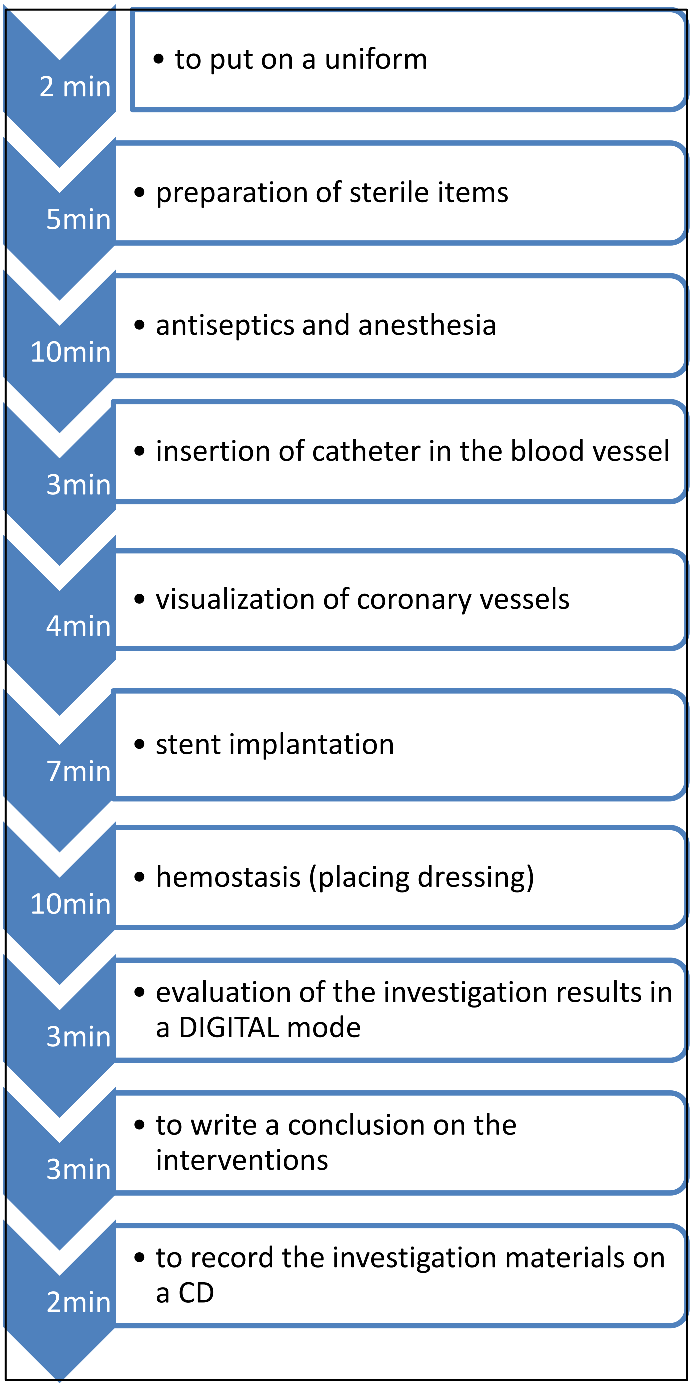
To protect against radiation, personnel are required to wear special protective clothing and neck protection shield to protect the neck and thyroid and X-ray goggles to protect the eyes. During coronary angiography and angioplasty, laboratory medical staff should have a personal dosimeter. If the dosimeter reading is close to the upper limit, a special X-ray shield should be used to reduce the radiation dose.

The studyaimed to identify the peculiarities of the working conditions of the medical staff employed in specialized procedures (in interventional cardiologyfor Coronary Artery Disease), for which the working conditions of the medical staff in the cardiac catheterization laboratories of the specialized clinics were studied. Adequate selection of medical centers was carried out at the initial stage. Criteria for inclusion of clinics in the study were: Existence of the Department of Interventional Cardiology for Coronary Diseases, smooth operation of the above-mentioned departments for the last 3 years, involvement in the Universal Healthcare (UHC) program with the component of emergency inpatient services.

Based on the listed criteria, 14 medical centers were selected for the study (9 of them were multi-profile and 5 were mono-profile), where the sanitary technical and sanitation and hygiene indicators were evaluated, which were compared to the relevant normative acts.

Survey Results: The entrance to the inpatient catheterization laboratory of the medical facility was connected to the intensive care unit via a corridor. There were isolated spaces in the catheterization block: - the entrance to the cath lab room, where the patients underwent the procedure; - the preparation space for the catheterization laboratory staff to prepare for the procedure; - the space for autonomous power supply of the catheterization laboratory equipment; - the operating room, where invasive manipulations were performed to the patients; - the Control Room (a remote control room), where additional observation took place on the course of the procedure.

The study found that the catheterization laboratory:



1) 25% of cases did not meet the standard requirements, the internal area was on average 41-43 m^2, instead of the minimum 47 m^2;

2) the average height of the ceiling was 2.7 m, instead of 3 m;

3) In 7% of the clinics, the walls and floor of the catheterization laboratory were not treated with X-ray-resistant material;

4) 30% of the research facilities didn't have adequate lead sealing of the Procedure Room door;

5) 7-8% of the surveyed facilities did not have a well-functioning ventilation system;

6) In 17% of the surveyed cases the autonomous power source system of the coronary angiography was located so close to the laboratory that the noise level in the ControlRoom (in the remote control room) exceeded the maximum permissible noise level, which created discomfort during the operations.

Timeline of Cardiovascular Interventionist Activities:

The activities of the medical staff included the following stages: Based on the timeline of the cardiovascularinterventionist activities, it was revealed that one cycle of the intervention lasted 45 min. The maximum 10 min ofeach surgical operation was spent on antiseptics and anesthesia, as well as treating hemostasis, which accounted for 22.2-22.2% of the total work cycle.

The mean duration of coronary angiography was 20 min and that of stenting was 30 min (the duration of the procedure depended on the anatomical features of the patient's coronary arteries and the number of stents required for implantation). On average, 7 procedures were performed during a day: 4 coronary angiographies and 3 stentings. Implantation of a pacemaker and cardioverter-defibrillator (ICD) took 2 hours, and the average number of procedures per month was 3-5 (often the patients refrained from such interference due to economic problems).

Cases ofcalling an interventionist for the procedure at night were 5-6 times during the month.

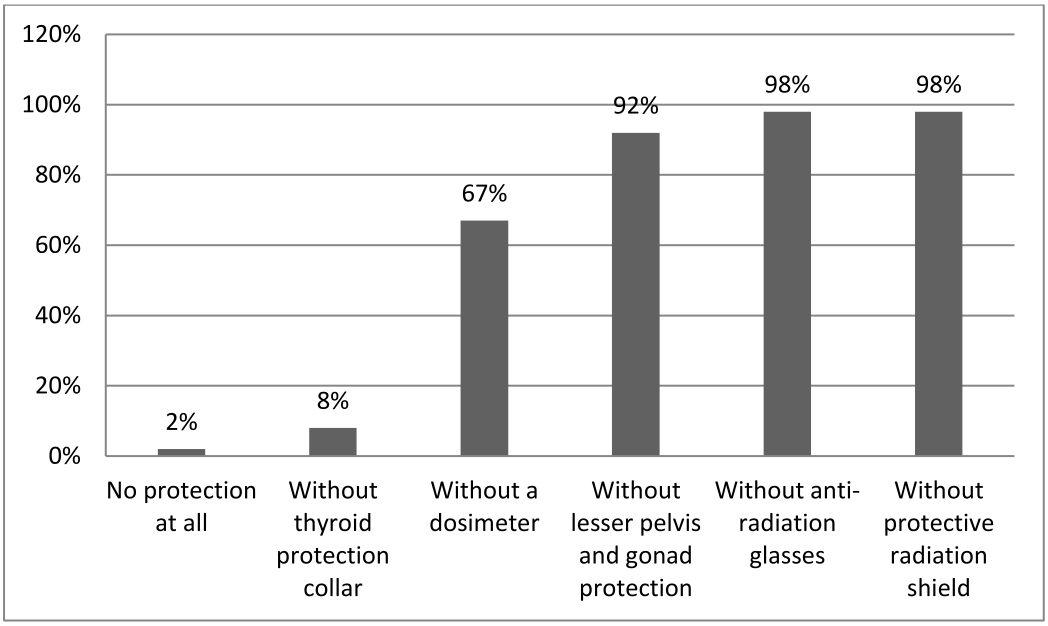


Diagram 2. Data about non-usage of the means of personal protection during the procedures

A study of the use of personal protective equipment (to reduce the dose of radiation) by medical personnel revealed that:
1) 98% of the staff of the catheterization laboratory do not use protective glasses;
2) 7-8% of the staff do not use thyroid protection collar during the procedure;
3) 92% do not use small pelvic and gonad protective lead aprons;
4) 67% of medical staff do not attach the dosimeter to the body during the procedure;
5) In most cases, it is not possible to determine if the environment meets the upper permissible limit of radiation during the day and, consequently, 98% of the staff does not use a special shield to reduce radiation in the procedure;
6) 1-2% of the medical staff taking part in the procedure is without mandatory protective equipment for the catheterization laboratory.

In 75% of the clinics surveyed, the use of a dosimeter has a formal use. At the end of the working day, the medical staff does not check what radiation dose each of them had received. Due to this situation, it became impossible to obtain a record of radiation doses for the interventionist and medical support staff, although, at the end of each procedure, an angiographer writes down the patient's radiation dose, which is written in the relevant medicalrecords book of the clinic. A review of the records book data found that the duration of the procedures was standardized for all patients and therefore the radiation rate was always the same and within the norm (meaning that no patients have been found to have relatively complex coronary anatomy for the last 2 years).

During investigating the timeline, it has been found that coronary angiography takes 20-40 minutes, while stenting takes 40-50 minutes. But the duration of the procedures is recordedwith a reduced period in the relevant protocols. This means that incorrect data on irradiation and the duration of the procedure are recorded in the medical records book.

It is known that medical personnel (unprotected parts of the body) are exposed to 0.05% of a patient's radiation dose when he or she is wearing a protective uniform. The dosimeter, inside the lead coat, identifies an additional 0.05% to 10%. The interventionist assistant and medical support staff receive 30% of the amount of the operator's radiation [9].

According to the radiation doses of the patient, the radiation rate of the medical staff was calculated: according to the official data of the clinic, during the coronary angiographic examination, which lasts 20 minutes, the patient is irradiated for 4 minutes - 800 mGy, and the operator - 800 mGy - 0.05% = 0.4 mGy. In fact, during a coronary angiography lasting 30 minutes, the patient is irradiated for 6 minutes - 1200 mGy, and the operator - (1200 mGy - 0.05%) = 0.6 mGy. Angioplasty with implantation of 1 stent lasts for 30 minutes and the patient is irradiated for 13 minutes - 2700 mGy, and the operator - (2700 mGy - 0.05%) = 1.35 mGy. In fact, angioplasty with implantation of 1 stent lasts for 40 minutes and the patient is irradiated in 17.3 minutes - 3593 mGy, and the operator (3593 mGy - 0.05%) = 1.8 mGy. Angioplasty with implantation of 2 drug-coated stents lasts for 35 minutes and the patient is irradiated for 16 minutes - 3050 mGy, and the operator (3050 mGy - 0.05%) = 1.52 mGy. Angioplasty with implantation of a drug-coated stent takes 42 minutes and the patient is irradiated for 19.2 minutes with 3660 mGy, and the operator (3660 mGy for 0.05%) = 1.83 mGy.

The annual dose of staff irradiation was calculated according to the patient's irradiation dose per procedure and the average monthly number of procedures:

During the year, on average, the catheterization laboratory emits 2348 mGy of radiation, 41% of the medical staff's body area is covered with protective clothing. Accordingly, the exposed parts of the operator's body radiate 962.68 mGy. Covered 59% - with 1385.32 mGy; 10% of the radiation penetrates the lead coat, i.e. 138.53 mGy. Accordingly, during the year the interventionist is irradiated with 1101.21 mGy, and the support staff of the catheterization laboratory, since theyare irradiated with 30% of the radiation dose of the interventionist, are irradiated with 330.3 mGy.

Based on the results of the research, we can conclude that the profession of interventionists belongs to the group of tense and stressful work, but radiation safety requirements are not implemented in the workplace: there is no special recording book in the workplace, which would describe radiation rates at the end of each working day.

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