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CYTOGENETIC EFFECTS OF LOW IONISING RADIATION DOSES AND BIOLOGICAL DOSIMETRY

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VILNIAUS UNIVERSITETAS

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MAŽŲ JONIZUOJANČIOSIOS SPINDULIUOTĖS APŠVITOS DOZIŲ POVEIKIO CITOGENETINIAI TYRIMAI IR BIOLOGINĖ DOZIMETRIJA

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1. INTRODUCTION

Relevance of the study

The intensive use of ionising radiation (IR) sources and development of IR technology is related to increased exposure and adverse health risk to workers and public. The importance of detecting risk of low doses in radiation protection is well recognised; the IR doses are measured and regulated. Although the occupational exposure doses are generally low and reduced consistently, the exposure makes a potential hazard to induce various types of cytogenetic damage. Recent studies have confirmed chromosome aberration assay as a reliable indicator of future cancer risk and an applicable method to assess the biological effects of IR. The significant increase of all types of cancer has been shown in the subjects with high frequency of chromosomal aberrations. Number of studies reported the presence of elevated chromosome damage frequencies in the exposed workers compared to those in the general population.

Despite of the large amount of literature, effects induced by low doses of IR are not sufficiently investigated, the results are contradictory (UNSCEAR, 2000). Results sometimes are quite inconsistent, particularly about the dependence of chromosome aberration frequency on duration of work with the sources of IR and the received dose. Therefore, it remains important to continue cytogenetic studies of new critical groups to determine the potential genotoxic risk exposure to low ionising radiation doses.

The staff of the Ignalina Nuclear Power Plant (NPP) constitutes the largest group of occupationally exposed workers in Lithuania. Though exposure doses are generally low and don't exceed the annual effective dose limit (20 mSv), somewhat higher doses were obtained during the planned maintenance outages. The additional occupational exposure, most likely, will be also received during the decommissioning activities at the Ignalina NPP: performing the shutdown of the reactor unit, dismantling of equipment and decontamination. That is why this occupational group was chosen for the cytogenetic studies.

The use of IR sources is related to radiation accident risk and also remains the threat of a terrorist act using radioactive or nuclear materials. In case of radiation accident, more people could be exposed, thus it is important to estimate the absorbed doses in order to determine whether the medical intervention is needed and to plan appropriate medical treatment. The dicentric assay in peripheral blood lymphocytes is most reliable, sensitive and most frequently used biological dosimetry method for assessing radiation dose. The absorbed dose to an individual can be estimated by comparing the individual aberration yield to an appropriate dose-response curve generated *in vitro,* since *in vitro* and *in vivo* irradiation of lymphocytes induces similar yields of chromosome damage per dose unit (IAEA, 2001). Dose assessment using a calibration curve produced by other laboratories may have significant uncertainties. Therefore it is important for biological dosimetry laboratory to produce its own curve. According to international practice the gamma calibration curve is the most important for dealing with large scale accidents or a terrorist event because the overexposure doses are most frequently received from gamma or X-ray sources. Therefore in our study we aimed to establish gamma (^{60}Co) radiation dose-response curves for unstable chromosome aberrations. The Lithuanian Committee of Bioethics has approved the study.

Objectives of the study

1. To assess chromosome aberration frequencies in peripheral blood lymphocytes from radiation workers exposed to low levels of ionising radiation and to estimate the potential occupational exposure risk.
2. To produce gamma radiation (^{60}Co) dose-response calibration curves for unstable chromosome aberrations in human peripheral blood lymphocytes *in vitro* and estimate biological doses of cytogenetically investigated people.

The main tasks of the study

The following tasks were set to achieve the objectives:

1. To analyse occupational exposure doses of Ignalina NPP radiation workers in order to select the study groups properly.
2. To assess the unstable chromosome aberration (CA) frequencies in the peripheral blood lymphocytes of radiation workers.
3. To compare CA frequencies between groups of workers receiving external gamma, neutron and internal exposure radiation.
4. To estimate the impact of different factors (IR exposure type, measured exposure dose, duration of work with IR, age and smoking) to the CA frequencies.
5. To perform the CA analysis for study subjects with the highest CA frequencies determined repeatedly.
6. To estimate the stable CAs in the study subjects group using FISH method.
7. To establish the gamma radiation (^{60}Co) dose-response curves for dicentrics and acentrics in human peripheral blood lymphocytes *in vitro*.
8. To perform the biological dosimetry for cytogenetically examined radiation workers using the produced dose-response curve; to compare the estimated (using biological dosimetry methods) doses to those measured (using the physical dosimetry methods).

The novelty and practical relevance of the research

Cytogenetic analysis of the nuclear energy workers in Lithuania was carried out in the present study for the first time. Previously, the Chernobyl NPP accident liquidators, medical radiation workers and patients after X-ray diagnostic procedures had been investigated. During this study the assessment of chromosome of aberration frequencies in peripheral blood lymphocytes from radiation workers exposed to low levels chronic ionising radiation exposure was carried out. For the study a group of the Ignalina NPP workers, who received significantly higher doses than the doses received by previously investigated groups, was selected. The results of this cytogenetic study showed quantitative and qualitative dependence of CAs on the occupational activities of donors. The assessment of impact of IR type and exposure type and work activities for CA frequency in the study group subjects was done. Such data in the scientific papers are limited. The risks were found to differ with the type of activities, type of exposure and IR. The activity of radioactive waste processors at the Decontamination Department and metal workers at the Reactor Department, can be considered to be more dangerous as compared to other activities at the Ignalina NPP. The estimation of the impact of IR type and exposure type has shown the statistically significant impact of internal and neutron exposure to the frequency of chromosome type aberrations ($p<0.05$). Activities related to internal and neutron exposure risk may be regarded as potentially more dangerous when

compared to other activities related with external gamma exposure doses only. The relationship between CA frequencies and radiation doses recorded as total cumulative dose, cumulative dose over the last three-year, one-year dose prior blood sampling and corrected doses, taking into account the lymphocyte life span and their elimination from the blood circulation was estimated.

The gamma radiation (^{60}Co) dose-response curves *in vitro* for unstable CAs in biological dose assessment was established for the first time in Lithuania. Application of the established dose-response curves enables to perform the biological dosimetry in this country, to assess the doses of the first responders and people accidentally exposed to IR. These curves can be used to assess the measured increased IR exposure dose for radiation workers, to confirm or reject the IR doses measured above the annual dose limit. The calibration gamma radiation (^{60}Co) dose-response curve established during this study for dicentric chromosomes was used to assess the biological doses received by the study subjects. This curve also was used for the investigation of a suspected overdose of occupational exposure by a radiation worker. After the biological dose assessment was done, the measured physical dose to occupational exposure was not found to exceed the limit, thus, the worker was allowed to continue his work with IR sources.

The determined CA frequencies in the radiation workers involved in different type activities from different departments will provide additional information to ensure and optimise the radiation protection of the Ignalina NPP workers. The results of this study show that CA analysis can be used for IR exposure risk assessment for different occupational groups of radiation workers and may provide additional information to ensure and optimise the radiation protection of radiation workers.

Defended statements:

1. The low ionising radiation doses being lower than annual dose limits can induce CAs in lymphocytes of people occupationally exposed to ionising radiation.
2. The CA frequency observed in peripheral blood lymphocytes of radiation workers depends on the ionising radiation type and exposure type.
3. The established gamma radiation dose-response curve for dicentrics fits to the linear-quadratic dose-response model and can be used for biological dosimetry.

Validation of the results (scientific approval and publications)

The results of this research have been presented at 9 international and 5 national conferences (8 oral presentations and 6 posters). The subject of the dissertation has been covered in 12 publications, including 2 scientific papers in the journals listed by *ISI Master Journal List*, 4 scientific papers in Lithuanian and foreign scientific journals, and 6 publications in the proceedings of the conferences.

Structure of the dissertation

The dissertation manuscript is written in Lithuanian and composed of the following chapters: Introduction, Literature review, Material and Methods, Results, Discussion of Results, Conclusions, References and the List of author's Publications. The work volume makes 134 pages, 20 pictures and 21 table, as well as the annexes with 1 picture and 8 tables. The list of references contains 181 sources.

2. LITERATURE REVIEW

This chapter contains a brief review of the properties of IR and the main dosimetric units, biological effects of low IR exposure doses, IR-caused carcinogenic effects, a review of epidemiological findings of the studies of different study groups: the survivors of the atomic bombings in Hiroshima and Nagasaki (Japan), the population groups exposed to increased natural IR exposure doses, the radiation workers affected by occupational exposure, the patients affected by medical IR exposure doses. The application of CA analysis in the studies on IR impact, the use of CAs as biomarker of cancer risk assessment and CA analysis in biological dosimetry are also reviewed.

3. RESEARCH OBJECTS AND METHODS

Study subjects

The study group comprised 84 male radiation workers of the Ignalina NPP. The mean age of the radiation workers during the blood sampling was 46.1±1.0 years and mean duration of work at nuclear power plant was 14,4 ± 0,6 years. The study group comprised 24% of Ignalina NPP radiation workers who received annual IR doses above minimal registered level (1mSv). The analysis of the occupational exposure doses of Ignalina NPP workers showed that the highest doses were received by workers employed at the Reactor, Centralised Repair, Metal and Technical Control departments. Therefore the study group was formed mainly from the departments listed above. The blood sampling was performed at the end of the outages in 2004-2006. A questionnaire on personal data and life style (health status, occupational and medical history, involvement in radio-diagnostic procedures and smoking habits) was obtained from all subjects. In order to estimate the impact of IR type and exposure type to CA frequency the study group subjects were divided into three subgroups according the IR and exposure type: group A – workers whose exposure resulted from the external gamma rays only, group B – those with additional internal exposure, group – those with external gamma and neutron exposure and internal exposure.

The controls comprised 82 healthy male donors who were not exposed to the IR. None of the radiation workers and the control subjects received the radiotherapy, chemotherapy or medical drugs. A summarised information on age and smoking habits of the study groups is provided in Table 1.

Table 1. Summarised information on age and smoking habits of study groups and control group

Study group	Number of donors	Age, years ± SEM	Smoke,Y/N*
Total study group	84	46.1 ± 1.0	52/32
Group A - with external gamma exposure	29	45.1 ± 1.9	27/17
Group B - with external gamma and internal exposure	44	46.5 ± 1.1	17/12
Group C - with external gamma and neutron and internal exposure	11	47.3 ± 2.6	8/3
Control group	82	35.4 ± 1.4	28/54

*- Y, smoke; N, does not smoke.

Cytogenetic analysis

Peripheral blood samples were obtained from each donor by venipuncture and collected into heparinised "BD Vacuteiner" tubes. For cultivation of lymphocytes, the standard technique was used. In brief, phytohaemagglutinin (7.8 μg/ml) stimulated cultures were incubated at 37^0C for 72 hours in RPMI 1640 medium supplemented with 12% heat-inactivated newborn calf serum, 40 μg/ml gentamycin, 0.25 μg/ml colchicine. All reagents were purchased from Sigma (St. Louis, MO, USA). The harvested lymphocytes were treated with hypotonic KCl (0.075 M) and then fixed in methanol-glacial acetic acid (3:1). Flame-dried slides were prepared and stained using the conventional Giemsa staining procedure. All slides were coded and scored blind. Generally 500 cells per subject were analysed. The examples of normal lymphocyte cell metaphase and metaphase cells with CAs are given in Figs. 1-4.

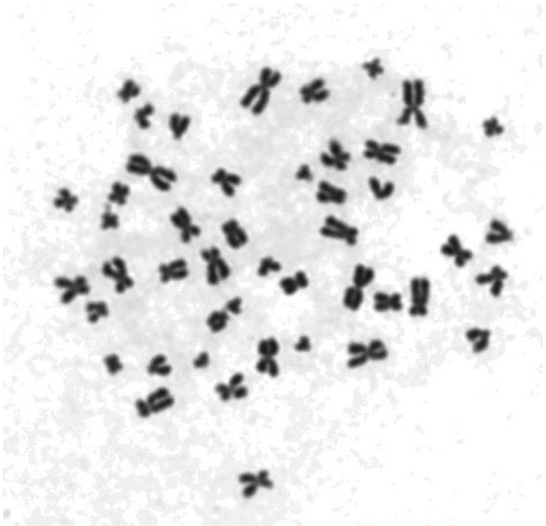

Fig. 1. Normal human lymphocyte metaphase containing 46 normal chromosomes (Giemsa staining)

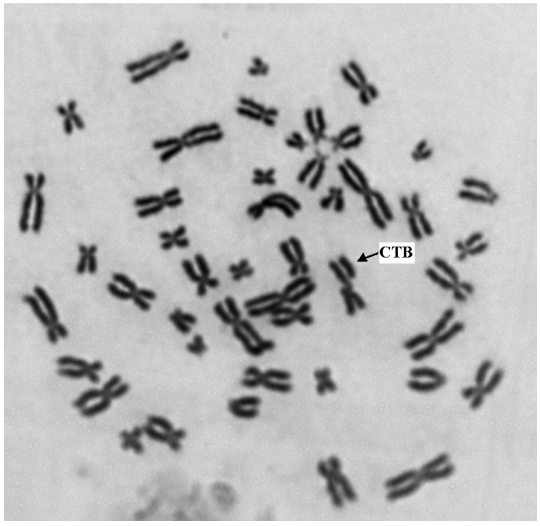

Fig. 2. Abnormal metaphase containing chromatid-type aberrations

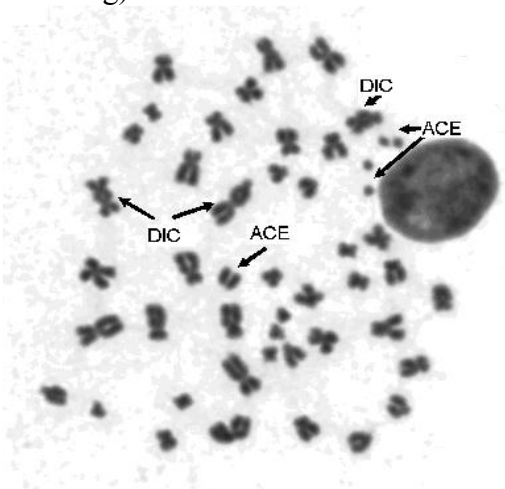

Fig. 3. Abnormal metaphase cell containing dicentric chromosomes (DIC) and acentric fragments (ACE)

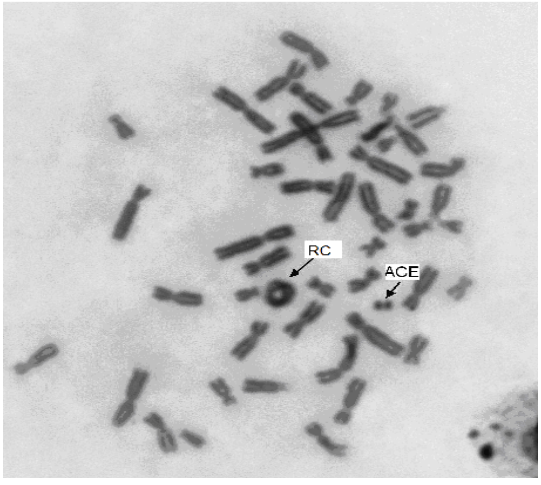

Fig. 4. Abnormal metaphase cell containing ring chromosome (RC) and acentric fragment (ACE)

The CAs for statistical analysis were grouped as chromosome-type (dicentrics, centric rings, excess acentrics, i.e., fragments, acentric rings, minutes) and chromatid-type (chromatid breaks, chromatid exchanges, i.e., quadri- and tri-radials) aberrations. Gaps were not included into the analysis.

Translocation analysis using fluorescent *in situ* hybridisation (FISH) method

The preparation of metaphase chromosomes from peripheral blood cells was carried out as described earlier in cytogenetic analysis methodology with exception that lymphocytes were fixed in methanol-glacial acetic acid (4:1) and slides were dried in air. The prepared lymphocytes were painted using FISH technique. The FISH analysis was carried out following the chromosome painting protocol of the Department of Toxicogenetics Leiden University Medical Centre. Whole chromosome painting probes (Cambio, UK) for chromosome 1 (Biotin labelled, red) and chromosome 4 (FITC – labelled, green) were used with pancentromeric probe (FITC labelled, green). The metaphase cells for different types of translocations, namely terminal, reciprocal and interstitial were scored with fluorescent microscope Zeiss Axioplan using DAPI, FITC, BIO filters. The typical human metaphase visualised with different filters is presented in Fig. 5. Classification of aberrations was carried out using PAINT CA nomenclature system (Tucker et al., 1994). Metaphase spreads were scored for unstable aberrations (dicentrics, acentric fragments, etc.) using DAPI filter also. The genomic translocation frequency (F_G) was calculated by using the formula for the painted fractions of the genome (Lucas et al., 1992) as follows:

$$F_G = Fp/2.05fp(1 - fp)$$

where the translocation frequency detected by FISH is Fp, and fp is the fraction of genome hybridised taking into account the sex of the subjects.

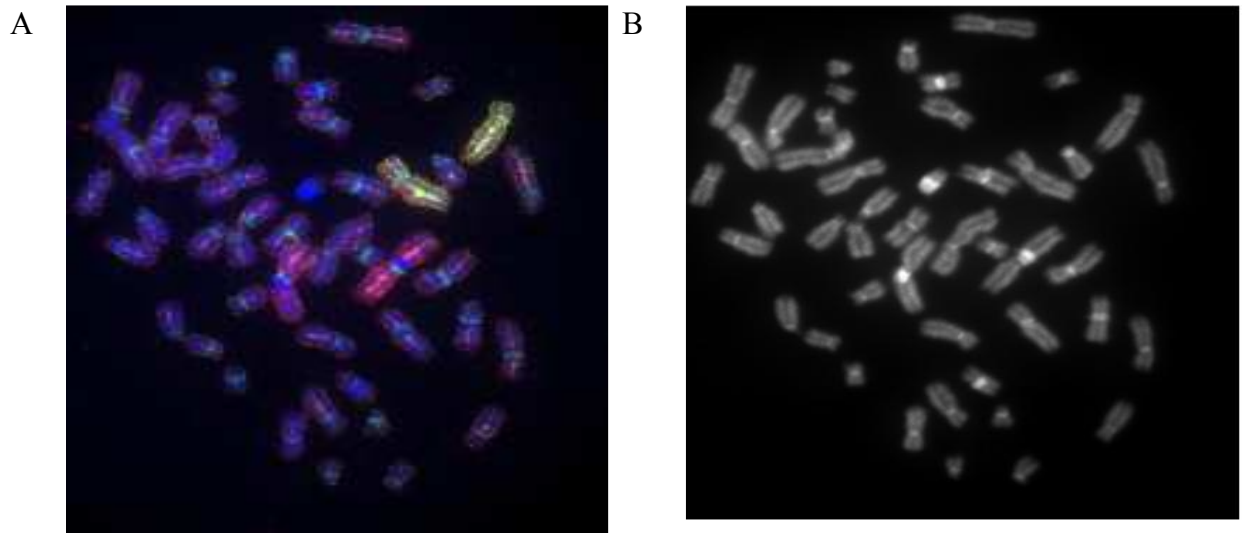

Fig. 5. Human metaphase with dual coloured chromosome #1 (biotin labelled, red) and chromosome #4 (FITC – labelled, green), centromeres painted with pan-centromeric probe FITC (green) and contrastained with DAPI. A – metaphase using FITC and BIO filters; B – metaphase using DAPI filter.

Production of gamma radiation dose-response curve in peripheral blood lymphocytes *in vitro*

Heparinised blood samples were taken from healthy female (age 48 year) and male (age 28 year) donors with no drug and radiation exposure at least one year prior to sampling. Irradiation and preparation of blood samples was carried out following the International Atomic Energy Agency (IAEA) recommendations (2001). Blood samples from donors were exposed to gamma rays from ^{60}Co gamma-therapy AGAT-S unit located at Institute of Oncology, Vilnius University. Samples were irradiated in a water bath at +37ºC with 9 doses ranging from 0.1 to 4.0 Gy at a dose rate of 0.256 Gy min^{-1}. Samples were cultured according to the same procedure, which was used for cytogenetic studies of radiation workers. 400-2000 first cycle metaphases were scored for the presence of unstable CAs for each radiation dose per donor after the standard metaphase preparation and staining of the slides. The pooled observed dose calibration data were fitted to a linear quadratic model using software program CABAS (*Chromosomal ABerration cAlculation Software*) (Deperas et al., 2007). The software uses maximum likelihood method to fit calibration data to a linear quadratic dose response curve. The standard *u*-test was used to test the yield of CAs with dose for Poisson probabilities. The method is also based on the concept that for Poisson distribution, the ratio of variance ($\sigma 2$) to mean (y) is equal to 1. If the value of u is greater than ± 1.96, the under- or over-dispersion of CA yield is significant at 95% confidence interval. The calibration curve parameters were compared with results from other studies.

Statistical analysis of data

Statistical evaluation of cytogenetic analysis data was performed using GraphPad InsStat v. 2:02 and SPSS/w 12.0 (Statistical Package for Social Sciences, SPSS Inc., USA) programs and Microsoft Office Excel. One-way analysis of variance (ANOVA), post-hoc LSD test, Poisson regression analyses, Pearson correlation test were applied for detection of differences between the groups and correlations among the variables. $P < 0.05$ was considered as the level of significance.

4. RESULTS AND DISCUSSION

4.1. Analysis of the occupational exposure doses

Gamma radionuclide measurements and internal exposure dose assessment

We have performed gamma radionuclide activity measurements at the Radiation Protection Centre (RPC) for 9 study subjects and compared our data with the results obtained in Ignalina NPP Individual Dosimetry Control Laboratory (IDCL). This study has shown that the recorded activities of radionuclides (^{60}Co, ^{137}Cs, ^{59}Fe, ^{54}Mn) are comparable and the internal exposure measurements performed in IDCL are reliable. The results of the intercomparison measurement are given in Table 2.

Four case scenarios have been developed by author to simulate routine or accidental realistic cases for internal exposure dose assessment. According to these case scenarios we calculated an intake and committed effective doses and compared our results with those obtained in IDCL. The internal exposure committed effective doses

were calculated according to the requirements of Lithuanian Hygiene Standard HN:112:2001 (2001) and the ICRP recommendations (1998).

Table 2. Comparison of gamma radionuclide activity measurements of Ignalina NPP workers made in RPC and IDCL

Institution	RPC	IDCL	RPC	IDCL	RPC	IDCL
Person code	Co-60, Bq		Cs-137, Bq		Mn-54, Bq	
1	532±111	567±128	n.*	n.	n.	n.
2	941±143	677±146	n.	n.	n.	n.
3	476±103	446±150	n.	n.	n.	n.
4	624±117	389±97	n.	n.	n.	n.
5	733±125	230±67	139±85	122±59	n.	n.
6	780±129	765±162	240±103	233±89	n.	n.
7	201±74	290±80	n.	n.	n.	n.
8	394±95	343±91	n.	n.	203±90	356±122
9	152±68	243±69	n.	n.	n.	n.

*- n. – not determined.

The committed effective doses were estimated by using computer software IMBA Professional (*Integrated Modules for Bioassay Analysis*) which operates the latest ICRP biokinetic models and dose coefficients (Birchall et al., 2003; Birchall et al., 2007). The results of the internal exposure assessment intercomparison were in good agreement. In conclusion we can say, that comparison study showed that the gamma radionuclide activities measured at the Ignalina NPP are similar with the radionuclide activities measured at RPC and that the internal exposure doses calculated at Ignalina NPP are similar with those calculated by us.

Occupational exposure dose analysis of study subjects

Occupational exposure doses of the study subjects were evaluated in the IDCL at Ignalina NPP. The subjects were routinely monitored with "Rados" thermoluminescent dosimeters consisting of 3 $Li_2B_4O_7$ pellets covered with 1-mm Al filter in a standard holder. The background radiation was subtracted from the accumulated dose. Monitoring periods varied from one day to one month depending on the type of the work performed. Doses that resulted from neutron exposure were estimated assuming that they are equal to the gamma doses measured by thermoluminescent dosimeter during the work period at neutron exposure. The whole body counter with HPGe and NaI(Tl) detectors enabling to detect radionuclides with gamma energies from 50 keV to 3 MeV were used for direct measurements of the internal exposure. The main estimated radionuclides were ^{60}Co and ^{137}Cs. The received neutron doses were estimated assuming that neutron dose is equal to the gamma dose measured with personal dosimeter during work period under conditions where neutron exposure was possible. The analysis of occupational exposure doses of Ignalina NPP workers showed that the highest doses were received by workers employed in the Reactor, Centralized Repair, Metal and Technical Control departments (2-4 times higher than the average doses of all workers).

The summarised results of the analysis on occupational exposure doses for the study subjects are presented in Table 3. The investigated 84 radiation workers of the Ignalina NPP received cumulative doses of 1–632 mSv (mean 227.9 ± 20.0 mSv) during employment periods of 1–25 years. For 29 subjects studied, the IR exposure resulted

from the external gamma rays only. Their mean dose over the 3-year period prior blood sampling was 23.8±3.7 mSv. The mean total cumulative dose was 135.0 ± 25.0 mSv. For 44 investigated subjects, the intake of gamma radionuclides (^{60}Co, ^{137}Cs) was contributing to the total dose up to several mSv. Their mean total cumulative dose was 289.8 ± 29.6 mSv. The mean dose over the 3-year period prior blood sampling was 31.3 ± 2.4 mSv. For 11 subjects, additionally to external gamma and internal exposure doses, the neutron doses below 1 mSv (≤0.1 mSv) were recorded. Their mean dose over the 3-year period prior blood sampling was 25.4 ± 2.9 mSv. The mean total cumulative dose was 224.9 ± 35.4 mSv.

Table 3. The employment duration (years) and occupational exposure doses (mSv) of study groups

		Study groups			
		Total study group	Group A With external gamma exposure	Group B With external gamma and internal exposure	Group C With external gamma, neutron and internal exposure
Number of donors		84	29	44	11
Years of employment, mean ± SEM		14.4 ± 0.6	13.3 ± 1.2	15.0 ± 0.9	15.1 ± 1.3
Exposure, mSv ± SEM	Dose over last 3 years period	28.0 ± 1.9	23.8 ± 3.7	31.3 ± 2.4	25.4 ± 2.9
	Dose over last year prior blood sampling	7.9 ± 0.7	7.0 ± 1.2	8.6 ± 0.9	7.2 ± 1.0
	Total dose	227.9 ± 20.0	135.0 ± 25.0	289.8 ± 29.6	224.9 ± 35.4

4.2. Chromosome aberration analysis in radiation-exposed workers and controls

The analysis of CA frequencies for Ignalina NPP radiation workers was done by using the conventional cytogenetic analysis method. An estimated CA frequency in the total radiation-exposed group (N=84) was 2.27 ± 0.17 CA / 100 cells, while the individual CA frequency ranged from 0.16 to 9.00 CA / 100 cells. CA frequency of the study group ($p=0.018$) differed significantly from that determined in the control group (1.76 ± 0.13 CA / 100 cells). Significant differences in frequencies of acentric fragments (0.89 ± 0.09 vs. 0.6 ± 0.08 CA / 100 cells, $p=0.014$), dicentrics (0.2 ± 0.04 vs. 0.07 ± 0.02 CA / 100 cells, $p=0.004$) and chromosome type (1.11 ± 0.10 vs. 0.70 ± 0.08 CA / 100 cells, $p=0.002$) aberrations were found in the study group as compared to those in the control group. However the differences for chromatid type (1.16 ± 0.10 vs. 1.06 ± 0.10 CA / 100 cells, $p=0.52$) aberrations were not significant. Chromosome-type aberrations are typical indicators of IR exposure. Significant increase in the frequency of acentric fragments ($p < 0.05$) and dicentric chromosomes ($p < 0.01$) was found in the study group as compared to that for the controls. Our data are in agreement with the findings of other authors who reported a more pronounced increase in acentric fragments as compared to dicentrics in workers exposed to low doses (Balasem et al., 1992;

Barquinero et al., 1993). Barquinero et al. (1993) consider acentric fragments to be the best indicators of irradiation for doses below 50 mSv. As compared to the controls, a significant increase in the frequency of dicentric chromosomes was determined in the radiation exposed groups. The background level for the total dicentrics determined in our controls (0.07 ± 0.02 per 100 cells) is in accordance with the findings of other authors who reported the mean frequency of dicentrics to be between 0.035 and 0.15 per 100 cells (Bonasi et al., 1997; Rozgaj et al., 1999; Jha, Sharma, 1991). The spontaneous yield of excess acentrics is usually higher than that of dicentrics. The range of aberration frequencies for acentric fragments varies from 0.3 to 0.7 per 100 cells. Though acentrics are more variable and cannot serve as a dosimeter for radiation exposure alone, the presence of high frequency of acentrics along with dicentrics supports radiation exposure to a low dose rate at a low LET exposure.

The data of investigations on the dependence of CA frequency upon the exposure and IR type are limited. In order to investigate the impact of IR and exposure type for CA frequency the study group subjects were divided into three subgroups according the IR and exposure type: group A – workers whose exposure resulted from the external gamma rays only, group B – those with additional internal exposure, group C – those with external gamma and neutron exposure and internal exposure. The results of the cytogenetic analysis are presented in Table 4.

Table 4. Frequencies of chromosome aberrations in radiation-exposed and control individuals (number / 100 cells± SEM)

Group	Group A	Group B	Group C	Total study group	Control group
Number of subjects	29	44	11	84	82
Chromosome-type aberrations					
Acentric fragments	0.67±0.11	0.93±0.13*	1.29±0.23^{**,2}	0.89±0.09*****	0.59±0.08
Dicentrics	0.10±0.03	0.24±0.06**	0.30±0.09^{2}	0.20±0.04**	0.07±0.02
Translocations	0,03±0.01	0.01±0.01	0.03±0.02	0.02±0.01	0.03±0.01
Total	**0.79±0.12**	**1.18±0.16****	**1.63±0.23**^{***,2}	**1.11±0.10****	**0.70±0.08**
Chromatid-type aberrations					
Chromatid breaks	0.77±0.14	1.25±0.12^{2}	1.23 ±0.25	1.08±0.09	0.99±0.10
Chromatid exchanges	0.04±0.02	0.11±0.03	0.09±0.03	0.08±0.02	0.07±0.04
Total	**1.81±0.15**	**1.36±0.13^{2}**	1.32±0.25	**1.16±0.10**	**1.06±0.10**
Total	**1.60±0.21**	**2.54±0.25**^{**,2}	**2.95±0.34**^{**,2}	**2.27±0.17***	**1.76±0.13**

* P<0.05, **P<0.01, ***P<0.001 as compared with controls;
^{1}P<0.05, ^{2}P<0.01, ^{3}P<0.001 as compared with group A (with external gamma exposure).

CA analyses revealed no significant differences between the group A and the control group (1.60 ± 0.21 vs. 1.76 ± 0.13 CA / 100 cells, $p = 0.50$). However, significant increase in total CA frequency was observed in group B (2.54 ± 0.25 CA / 100 cells, $p = 0.002$). Besides, significant increase in chromosome type aberrations ($p = 0.003$), excess acentrics ($p = 0.002$) and dicentrics ($p = 0.001$) was estimated for the workers with additional internal exposure as compared to the controls. Significant increase in total CA frequency was observed in group C (2.95 ± 0.34 CA / 100, $p = 0.002$) as compared to the controls.

Also differences were significant between these groups for chromosome type aberrations ($p = 0.0001$), dicentrics ($p = 0.001$) and excess acentrics ($p = 0.004$). The group A was observed to have significantly lower CA frequency if compared to CA values in group B ($p = 0.002$) and Group C ($p = 0.009$). Significantly higher frequencies in chromosome type aberrations ($p=0.001$), excess acentrics ($p=0.01$) and dicentrics ($p = 0.01$) were estimated in group C if compared to those in group A. Significant differences in chromatid-type aberration frequencies ($p = 0.008$) were found between group B and group A. However, no significant difference in chromosome aberration frequencies between group B and group C was found.

The analysis of CA frequency distribution in the study subjects showed that one-two CA/100 cells was the prevalent CA frequency in lymphocytes of the studied persons (for 33 from 84 persons). CA frequency less than 3 CA / 100 cells were found for 61 study subjects (72.6%) and for 70 control subjects (85.4%). Assuming that the background frequency of CAs is 0–3 CA / 100 cells, we can confirm that increased CA frequency was found in 27.4% investigated workers and 14.6% subjects of the control group.

During the study the correlation, dispersion and regression analyses were used to investigate the impact of different factors, which can influence the CA frequency: the duration of work with IR sources, type of IR exposure, total occupational exposure dose, dose over the last three-year or one-year periods prior blood sampling, age and smoking. Tests on the between-subject effects revealed the confounding impact of the internal exposure ($p < 0.001$) on the total CA frequency, chromosome-type aberration frequency ($p < 0.05$) and chromatid type aberration frequency ($p < 0.05$). The confounding impact of neutron exposure ($p < 0.05$) on the frequency of chromosome-type aberrations was also determined.

No significant trend of increased aberration frequency as a function of duration of employment was found in the total study group, however correlation was significant ($r = 0.44$, $p < 0.001$) between CA frequency and duration of employment in the study group with internal exposure.

No significant trend of increased aberration frequency as a function of the total occupational exposure dose (Fig. 6.), dose over the last three-year or one-year periods prior blood sampling was determined. This observation is in agreement with other cytogenetic studies among radiation workers (Littlefield et al., 1998, Balakrishnan, Rao, 1999; Lindholm et al., 2001; Ballardin et al., 2007). However, it should be noted that the results of numerous studies on the effect of cumulative dose and/or exposure duration on CA yield are quite inconsistent. Since the qualities and quantities of IR are different and poorly described, sometimes it is difficult to compare the results obtained in different studies. The absence of correlation between aberration frequency and radiation dose may be attributed to several factors. According to most authors, the main reason is thought to be the limited life span of lymphocytes and the slow disappearance of cells with aberrations from the circulation (Jha, Sharma, 1991; Ramalho et al., 1995). Variable half-lives in the range of 130–1600 days were reported in circulating lymphocytes (Ballardin et al., 2007).

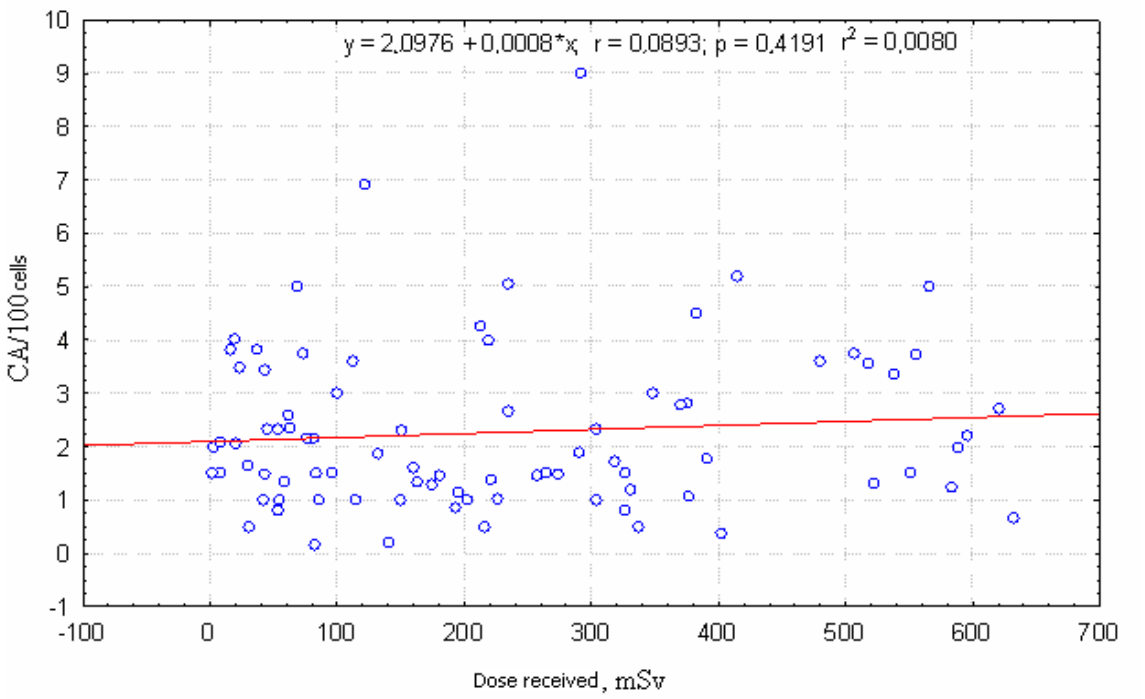

Fig. 6. Cumulative doses (mSv) and CA frequencies (CA/100 cells) for the Ignalina NNP workers

Peripheral lymphocytes are eliminated from circulation with time, thus the measured physical doses were corrected taking into account the mean life of lymphocytes and the exponential loss of those with unstable aberrations. The corrected physical doses were calculated by weighting annual recorded doses for mean-life of lymphocytes m = 4.3 years (half-life $T_{1/2}$ = 3 years) or m = 10 years (half-life $T_{1/2}$ = 7 years) (Balakrishnan, Rao, 1999). The formula was used:

$$\sum \text{Annual dose} \times \exp - (0.693 \times t / T_{1/2})$$

where t is the elapsed time in years for each annual dose, $T_{1/2}$ is lymphocyte half-life.

The corrected physical doses ranged from 0.5 mSv to 243 mSv for $T_{1/2}$ being 7 years and from 0.2 mSv to 103 mSv for $T_{1/2}$ being 3 years. The relationship between corrected cumulative doses and CA frequencies was found not significant. However a significant correlation was found between CA frequencies and corrected doses (T½ = 7 year) in the study group with internal and neutron exposure ($p < 0.05$). It is interesting to note, that Balakrishnan and Rao (1999), Braselmann et al. (1994) found a good agreement between the biological dose and the corrected physical dose based on a half-life of 6.9 years for lymphocytes. The dose-response relationship may also be influenced by inter-individual differences in the proliferation rate of PHA-responsive lymphocytes (Crossen et al., 1977), the variability of individual radiosensitivity and adaptive response to a very low level of IR (Aka et al., 2004).

The data of investigations on the dependence of CA frequency upon the exposure type and work type of NPP employees are limited. An attempt to assess the impact of different working conditions on the frequencies of CAs was made in the present study. The comparison of CA frequencies for study subjects employed at different departments was done. The lowest CAs frequency was found in group of persons occupied at

Chemical Protection Department (1.38 ± 0.19 / 100 cells), and it was the highest in the study group from the Decontamination Shop (2.88 ± 0.48 / 100 cells) and the Reactor Department (2.80 ± 0.37 / 100 cells) (Fig. 7.). The dispersion analysis showed the significant impact of the department the study subjects worked on total CA frequency $p < 0.01$), chromosome type aberration frequency ($p < 0.05$) and chromatid-type aberration frequency ($p < 0.05$). The impact of different occupation type on frequencies of CAs was also assessed. The highest CA frequencies – 3.16 CA/100 cells and 3.14 CA / 100 cells – were established for such staff positions as radioactive waste processors and metalworkers, correspondingly. Among other profession groups, the difference in CAs frequency was found to be insignificant. Therefore we suppose that the higher risk of having an occupational activity at the Ignalina NPP can be considered for workers dealing with the radioactive waste processing at the Decontamination Shop and metalworkers employed in Reactor Department if compared to other employees at the Ignalina NPP.

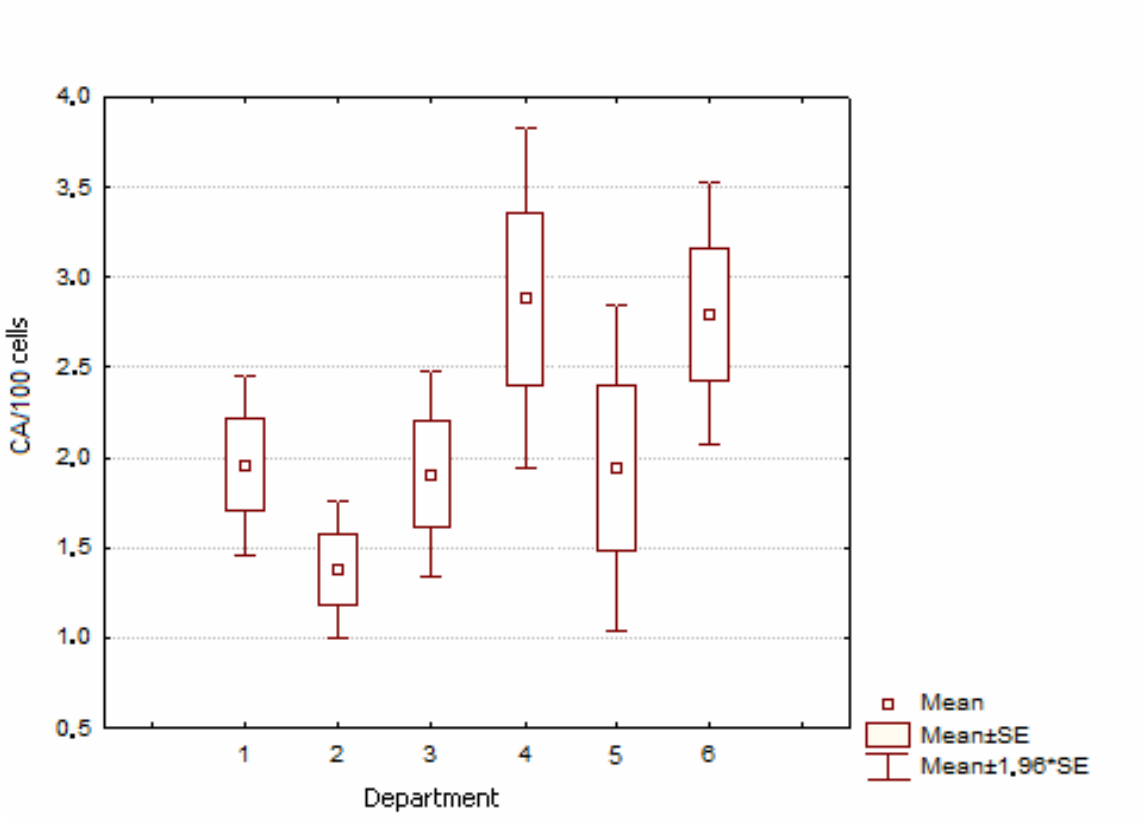

Fig. 7. Average frequencies of chromosome aberration in the study groups from different Departments of Ignalina NPP: 1 – Centralised Repair Dept, 2 – Chemical Protection Dept, 3 – Work Security Dept, 4 – Decontamination Shop, 5 – Metal and Technical Control Dept, 6 – Reactor Dept

The impact of other factors – smoking and age – on CA frequency for the study subjects was also assessed. There is no doubt regarding tobacco smoke as carcinogen, and a number of studies had been conducted to assess the impact of smoking on CA frequency in peripheral blood lymphocytes. The present study showed that CA frequency in the group of smokers ($N = 80$) did not differ significantly from that observed in non-smokers ($N = 86$) group ($p > 0.05$). No reliable difference in frequency of chromosomal aberrations was found ($p > 0.05$) in comparing smokers of Ignalina NPP

workers to the non-smoking group. No significant difference between smokers and non smokers in the control group subjects ($p = 0.05$) was also observed. The Poisson regression analysis showed that smoking has no significant association with the yield of different types of CAs. The data concerning the impact of smoking to CA frequency are controversial. There are number of studies, the authors of which found no impact of smoking on chromosomal damages (Carpenter et al. 1989, Peterson et al. 1990, Kubelka et al. 1992, Chung et al. 1996; Rozgaj et al.. 2002) However, there are studies, which showed higher frequency of CAs for smoking radiation workers compared to non-smokers (Gribbin et al. 1993, Ramsey et al. 1995, Murata et al. 2002; Maffei , 2004, Au et al. 2005). The impact of age on the frequency of CAs was found to be insignificant. Some authors state that the age is not an important factor in the frequency of CAs (Bauchinger et al. 1980; Rozgaj et al.. 2002). On the other hand, other authors determined the relationship between the chromosomal aberrations, in particular the stable ones, and the age (Anderson et al. 1993; Znaor et al. 2003).

Other studies indicate that IR at doses far below annual dose limits can increase the CA frequencies in lymphocytes of occupationally exposed workers (Maffei et al., 2001; Cardoso et al., 2001). We did not observe any increase of chromosome damage in the Ignalina NPP workers exposed to the external gamma rays only, but determined significantly higher aberration frequencies in the workers with incorporated radionuclides and additional neutron exposure. Thus, despite very low neutron and internal exposure doses, the present results suggest that radiation exposure type seems to be quite relevant in determining the radiation-induced chromosome damage.

To conclude, the present study showed no dose-related increase in the CA frequency for the Ignalina NPP workers. However, no increase in the CA frequency was determined only for the workers exposed to external gamma radiation, while the demonstration of the elevated levels of CAs for the workers with incorporated radionuclides and neutron exposure indicates their more hazardous work activities with consequential risk to health.

4.3. Translocation analysis using fluorescent *in situ* hybridisation (FISH) method

This chapter deals with the results of translocation analysis done for 4 study subjects using fluorescent *in situ* hybridisation (FISH) method. The analysis was done during the IAEA fellowship at the Department of Toxicogenetics of Leiden University Medical Centre. The frequencies of translocations were determined in Ignalina NPP workers occupationally exposed to doses of 163–326 mSv. Overall, 4156 metaphase spreads were scored and 10 stable translocations, (8 from them full reciprocal translocations) were determined. The translocation frequency measured by FISH was extrapolated to whole genome translocation frequency for each person. It was found that the mean genomic translocation frequency (0.00865) of studied group is slightly higher than the background frequency of population for the same age group (0.00732) (Whitehouse et al., 2005). The results of cytogenetic analysis of translocations and dicentric results are presented in Table 5. The spontaneous translocation frequency in the of 45–59 year population group is one translocation per 500 metaphases (Whitehouse et al., 2005). In our study we found a higher genome translocation frequency (0.03194) in one person. However the total frequency of unstable chromosome aberrations

(0.46/100 cell) and dicentric chromosomes (0.0/100 cell) determined in this person was not increased. The measured total occupational exposure dose (192 mSv) during his work at the Ignalina NPP should not lead to increased translocation frequency; it could be resulted due to received IR exposure prior work at NPP.

Table 5. The determined numbers of translocations, genome translocation frequencies, total unstable chromosome aberration (CA) and dicentric (DIC) frequencies for a group of Ignalina NPP workers

Code of donor	Number of translocations	Total of scored cells	Genome translocation frequency	CA/100 cells	DIC/100 cells
AE 80	5	563	0.03194	0.46	0
AE 92	3	1810	0.00596	0.66	0.13
AE 77	1	510	0.00705	0.8	0
AE 89	1	1273	0.00282	1.33	0.11

4.4. A repetitive study of persons with the highest frequencies of chromosomal aberrations

Repetitive cytogenetic analysis of unstable CAs was carried out in 2008 for a selected group (N=7) of persons, for whom in 2006 year the highest frequencies of CAs were determined. The summarised results of this study are presented in Table 6. Comparing the first and the second analyses of the study group, it was found that the CA frequencies did not differ significantly (5.37 ± 0.74 vs 4.38 ± 0.62, p = 0.173). However, the determined statistically significant decrease in chromatid-type aberrations (1.70 ± 0.23 vs 2.75 ± 0.40, p = 0.024) and chromatid breaks (1.53 ± 0.20 vs 2.48 ± 0.31, p = 0.015) in the second sampling were found. The decrease in chromatid type aberrations can be attributed to the fact that chemical exposure at the workplace of the study subjects was reduced.

Table 6. Frequencies of CAs (number/100 cells ± SEM) in lymphocytes of individuals, for whom cytogenetic analysis was done in 2006 and 2008 year

Chromosome aberrations	Year of donors blood sampling	
	2006 year	2008 year
Chromosome type aberrations/100 cells ± SEM		
Acentric fragments	2.19 ± 0.52	1.97 ± 0.21
Dicentric chromosomes	0.42 ± 0.19	0.60 ± 0.27
Translocations	0.00 ± 0.00	0.11 ± 0.07
Total	**2.61 ± 0.43**	**2.68 ± 0.44**
Chromatid-type aberrations/100 cells ± SEM		
Chromatid breaks	2.48 ± 0.31	1.53 ± 0.20*
Chromatid exchanges	0.27 ± 0.12	0.16 ± 0.08
Total	**2.75 ± 0.40**	**1.70 ± 0.23***
Total chromosome aberrations	**5.37 ± 0.74**	**4.38 ± 0.62**
**p < 0,05; Student t-test for dependent samples*		

4.5. The production of gamma radiation (^{60}Co) dose-response curves for dicentrics and acentrics in the human peripheral blood lymphocytes *in vitro*

In total, 14700 metaphase cells of irradiated peripheral blood samples were scored, and 1636 dicentrics and 76 centric rings and 960 access accentrics were registered. The summarised results of the analysis of dicentrics and centric rings are presented in Table 7. The yield of dicentrics at 0.0 Gy dose, which corresponds to the spontaneous dicentric aberration yield, was $0.46 \pm 0.49/1000$ cells. A similar yield was reported by other authors (Top et al., 2000; Senthamizhchelvan et al., 2007). The intercellular distribution of the observed dicentric chromosome and centric ring chromosomes is given in Table 8.

Table 7. The yields of dicentrics and centric rings in peripheral blood lymphocytes after acute *in vitro* irradiation with various doses of ^{60}Co gamma rays

Dose, Gy	Cells scored	Number of chromosome aberrations		
		Dicentrics (DIC)	Centric rings (CR)	(DIC+CR)/100 cells ± SEM
0.0	1800	1	0	0.06 ± 0.06
0.1	2000	9	1	0.50 ± 0.16
0.2	2000	34	0	1.70 ± 0.29
0.3	2000	42	6	2.40 ± 0.34
0.5	2000	77	2	3.95 ± 0.43
0.75	2000	156	6	8.10 ± 0.61
1	1500	209	5	14.27 ± 0.90
2	600	251	7	43.00 ± 2.02
3	400	376	20	99.00 ± 0.51
4	400	481	29	127.50 ±2.96

Table 8. Distribution of dicentric chromosomes (DIC) observed in peripheral blood lymphocytes after acute *in vitro* irradiation with ^{60}Co gamma rays at various doses

Dose, Gy	Cells scored	DIC	Distribution of DIC						σ^2/Y^*	u^{**}
			0	1	2	3	4	6		
0	1800	1	1799	1	0	0	0	0	1.00	0.00
0.1	2000	9	1991	9	0	0	0	0	0.996	–0.134
0.2	2000	34	1967	32	1	0	0	0	1.042	1.359
0.3	2000	42	1958	42	0	0	0	0	0.980	–0.656
0.5	2000	77	1523	75	1	0	0	0	0.988	–0.383
0.75	2000	156	1847	150	3	0	0	0	0.961	–1.239
1	1500	209	1300	191	9	0	0	0	0.947	–1.443
2	600	251	381	191	24	4	0	0	0.869	–2.265
3	400	376	134	185	59	17	4	1	0.848	–2.147
4	400	481	87	185	86	32	7	0	0.722	–3.921

*σ^2/Y- dispersion index, ***u* – *unit normal deviate.*

In order to test the homogenenity of irradiation, the dispersion index (σ^2/Y) and the magnitude of statistical test quantity *u* were calculated (Table 8). The *U*-test analysis showed that the data fitted in Poisson distribution as values ranged between –1.96 and +1.96 in the range of irradiation doses of 0.1–1 Gy. The dicentric data show overdispersion after 1 Gy.

The relationship between CAs and IR was expressed by the linear quadratic model:

$$Y = c + \alpha D + \beta D^2,$$

where Y is the frequency of dicentrics and central rings, D is the dose, c is the background frequency, α - represents the linear component, where CAs are result of single-track events and it is mostly responsible for aberrations at low doses, β - represents the quadratic component, where CAs are the result of two-track events, and it is mostly responsible for aberrations at high doses.

Yields of dicentrics, centric rings and excess acentrics following different radiation doses were used to establish dose-response curves. The pooled observed dose calibration data were fitted to a linear quadratic model using software program CABAS (*Chromosomal ABerration cAlculation Software*) (Deperas et al., 2007). The dose-response curve for dicentric and centric rings yield is:

$$\text{Yield} = (0.00046 \pm 0.00049) + (0.055 \pm 0.006)D + (0.076 \pm 0.004)D^2.$$

An appropriate dose-response curve with the 95% confidence intervals of the yield of dicentric chromosome and centric rings as a function of radiation dose is shown in Fig. 8.

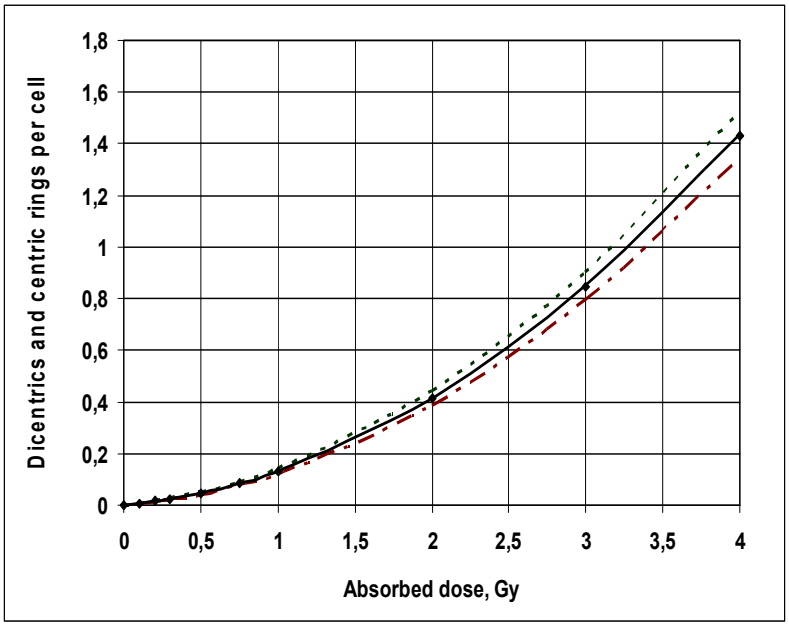

Fig. 8. Dose-response curve for induction of dicentrics and centric rings in human lymphocytes following *in vitro* irradiation with ^{60}Co gamma rays. The 95% confidence intervals are represented in dashes.

The parameters of calibration curve were compared to results from other studies. The β value was somewhat higher than the other reported studies. Besides the inter-laboratory variations in the established dose-response curve coefficients, in comparison of our dose-response curve with similar published studies shows general good agreement (Lloyd et al., 1986; Lindholm et al., 1998; Top et al., 2000; Venkatachalam et al., 2001).

Biological dose is estimated when the frequency of dicentric chromosome is greater than the background, and the biological dose estimate may be regarded as a

measurement of the 95% lower confidence limit greater than zero (Lloyd et al. 2000). The minimum estimated absorbed dose depends on background frequency of dicentrics, amount of cells analysed, the number of data used for fitting the dose-response curve. In this study, according the established dose-response curve the minimum estimated dose in case of analysis 500 metaphase cells is 90 mGy with the confidence interval 14–234 mGy. According to literature data, the unstable CAs method reliably enable to estimate 100 mGy, and higher doses (IAEA, 2001, Voisin et al. 2004). Increasing the number of scored cells leads to the decreasing of the minimum estimated dose and the range of confidence intervals.

Acentric fragments associated with dicentrics, tricentrics, tetracentrics or rings were not included in the number of excess acentrics. At high doses of radiation, higher numbers of acentrics in cells were observed. The background level of excess acentrics was 0.0066± 0.0016. The observed dose-response data for acentrics were fitted to a linear quadratic model. The α and values β with their standard errors were respectively 0.0768 ± 0.0067 and 0.0099 ± 0.0028). The dose-response curve for acentrics yield is:

$$\text{Yield} = (0.0066 \pm 0.0016) + (0.0768 \pm 0.0067)D + (0.0099 \pm 0.0028)D^2.$$

An appropriate dose-response curve with the 95% confidence intervals of the yield of acentrics as a function of radiation dose is shown in Fig. 9.

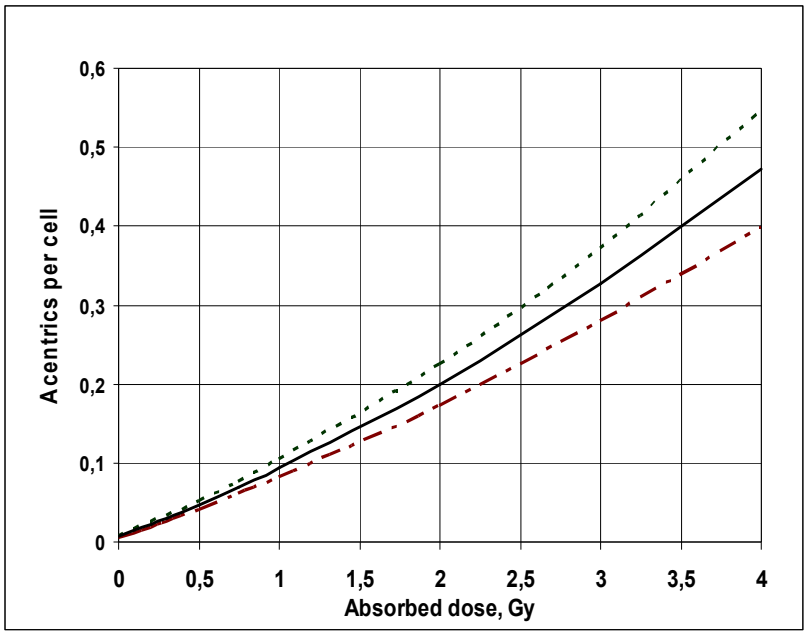

Fig. 9. Dose-response curve for induction of acentrics in human lymphocytes following *in vitro* irradiation with ^{60}Co gamma rays. The 95% confidence intervals are represented in dashes.

The determined value of α was higher, while β value was lower than in the other reported studies (Top et al., 2000; Senthamizhchelvan et al., 2007). Formation of excess acentrics is not specific to IR since they may occur as a result of exposure to other clastogenic agents. Therefore, these aberrations for biological dose assessment alone are not used. However the established dose-response curve for acentrics can be used for biological dose assessment as additional method, when there is no sufficient data only on dicentrics.

4.6. Application of the established dose-response curve for biological dosimetry

The biological dose assessment of radiation worker occupational exposure dose

During this study the established calibration gamma radiation (^{60}Co) dose-response curve for dicentric chromosomes was used for the investigation of suspected overexposure of radiation worker. The external exposure dose (138 mSv) above the annual dose limit was measured with individual dosimeter for industrial radiography worker. It was estimated that in order to statistically evaluate the resulting dose of 138 mSv, a minimum number of cells analysed should be 220 cells. After scoring of 500 peripheral blood lymphocytes metaphase cells the biological dose assessment was done using dicentric and ring chromosome findings and CABAS software program. The calculated absorbed dose is 65 mSv (8-201 mSv, with 95% confidence interval). Fixed odds ratio (OR=6.12) indicates that the probability of the fact that the investigated person did not receive dosimeter measured exposure dose (138 mSv) is 6.12 times higher than the fact that has received. The estimated biological dose was close to the total dose (51 mSv) recorded during the work with IR. Based on these results the measured dose was not assigned to the occupational exposure, and this worker was allowed to continue work with IR sources.

The biological dose assessment for study subjects

The established dose-response curve *in vitro* has been used for biological dose assessment for 34 study subjects, for whom dicentric chromosomes were determined (Table 9). The resulting exposure doses were calculated using dicentric and ring chromosome findings and CABAS program. The absorbed dose assessment was based on α component (α=0.055) of the dose-response curve. The β component was ignored since only chronic low level exposure was suspected. The absorbed doses were estimated and ranged from 18 to 225 mSv. The maximum estimated dose – 225 mSv – was close to the corrected dose measured by physical methods (197 mSv). In this group there were 10 subjects, for whom doses with lower confidence interval above 0 mSv were estimated. The average biological dose of this study group was 132 ± 7 mSv, the measured corrected dose was $53 \pm 5{,}6$ mSv, assuming the lymphocyte half life $T_{1/2} = 3$ years, and 116 ± 13 mSv, assuming $T_{1/2} = 7$ years. The average biologically estimated dose was in good agreement with that measured by physical methods and corrected dose taking into account lymphocyte half life T½ = 7 years.

Application of the established dose-response curves presents an opportunity to perform the biological dosimetry in Lithuania, to investigate the measured dose above the annual limit for a radiation worker, to assess the doses of first responders and people accidentally exposed to IR. In case of radiation accident the information about the received doses will help to develop the treatment strategy of an IR-exposed person.

Table 9. The results of study group (N=34) cytogenetic analysis, doses measured by physical dosimetry, doses estimated by biological dosimetry

Code of person	Results of cytogenetic analysis		Doses measured by physical dosimetry methods			Doses estimated by biological dosimetry methods		
	Amount of analysed cells	DIC+ŽC amount	Total effective dose, mSv	Corrected dose ($T_{1/2}$ = 3 y)	Corrected dose ($T_{1/2}$ = 7 y)	Effective dose, mSv	LCC* 95%	UCL** 95%
9	435	5	234.8	85.4	142.3	163.4	55.2	329.2
12	400	1	550.7	84.0	201.4	35.3	0.0	193.1
13	558	1	376.6	92.0	184.7	23.4	0.0	144.2
14	975	2	81.0	54.6	67.5	27.8	0.0	109.6
23	645	1	19.2	1.6	6.5	19.3	0.0	126.4
26	600	2	7.6	0.6	2.4	48.9	0.0	170.2
34	580	2	43.4	24.9	33.7	50.7	0.0	175.3
35	660	1	29.6	15.3	21.8	18.7	0.0	123.8
37	680	1	212.3	51.2	102.8	17.9	0.0	120.4
38	480	1	72.7	32.4	50.7	28.4	0.0	164.9
42	676	2	273.6	67.2	138.1	42.8	0.0	153.2
43	303	1	522.1	86.0	207.4	48.3	0.0	243.6
47	500	1	414.0	76.3	170.3	27.0	0.0	159.0
48	270	2	43.3	32.7	38.2	109.5	7.9	328.6
49	400	3	506.2	87.9	204.1	110.8	19.2	280.8
52	340	1	15.8	0.7	3.4	42.5	0.0	221.5
53	300	1	58.9	17.1	29.7	48.9	0.0	245.6
55	680	6	121.4	16.2	41.6	128.9	47.3	252.4
58	470	1	36.5	25.8	31.4	29.1	0.0	167.9
60	200	1	22.8	8.8	14.4	74.7	0.0	339.0
69	303	2	150.5	18.0	53.8	98.2	6.1	300.2
70	400	1	96.0	38.6	63.2	35.3	0.0	193.1
76	307	1	174.0	43.5	87.6	47.6	0.0	241.0
83	461	2	317.9	38.4	117.3	64.6	0.0	213.4
86	500	2	159.7	44.1	85.4	59.4	0.0	199.2
87	100	1	219.1	64.1	122.1	144.4	0.0	564.4
89	900	1	162.6	55.3	93.8	11.7	0.0	92.3
91	150	1	234.0	72.2	130.8	99.1	0.0	421.3
92	770	2	226.5	76.2	131.5	36.9	0.0	136.3
94	333	2	8.0	4.7	5.7	89.6	4.8	278.5
96	699	5	554.8	76.8	190.7	106.0	32.4	224.9
99	659	11	565.8	89.8	196.8	224.9	122.3	357.6
101	357	4	537.3	65.7	165.0	159.8	44.4	346.7
102	400	3	381.9	54.3	124.8	110.8	19.2	280.8

*- LCL- CI lowel level, **- UCL - CI upper level

CONCLUSIONS

1. Significantly higher frequencies of total chromosome aberrations (2,27 *vs* 1,76), chromosome type aberrations (1,11 *vs* 0,70), acentric fragments (0,89 *vs* 0,59) and dicentric chromosomes (0,20 *vs* 0,07) ($p<0.05$) were determined in the whole nuclear energy workers group, if compared to the control.

2. The observed chromosome aberration frequency in peripheral blood lymphocytes of radiation workers depends on IR type and exposure type. Chromosome aberration analyses revealed no significant differences in chromosome aberration frequency between the study group with external exposure doses and the control group (1.60 *vs* 1.76 $p > 0.05$). A reliable increase in chromosome aberration frequencies was determined in both study groups – with additional internal exposure doses (2.54 *vs* 1.76 CA/100 cells, $p < 0.01$) and with additional internal and neutron exposure doses (2.95 *vs* 1.76 CA/100 cells, $p < 0.01$).

3. The activities of radioactive waste processing workers in Decontamination Shop and metal workers in the Reactor Department are at the highest risk in the Ignalina NPP. The highest chromosome aberration frequencies of 3.16 CA/100 cells and 3.14 CA/100 cells were determined for radioactive waste processing group and metal workers, correspondingly.

4. For a study group, exposed to low level chronic exposure doses, the cytogenetic analysis of which was performed repeatedly, there were no significant differences in total chromosome aberration frequency between the first and second analyses done in a two-year span (4.38 *vs* 5.37, $p > 0.05$). However, significant decrease in chromatid-type aberrations (1.70 *vs* 2.75, $p < 0.05$) was determined during the second analysis.

5. There was no statistically significant correlation among occupational exposure doses, corrected doses taking into account lymphocyte lifespan and elimination from blood circulation and chromosome aberrations frequencies ($p > 0.05$).

7. Dispersion analysis of cytogenetic results showed statistically significant confounding impact of internal exposure factor to the total chromosome aberration frequency and chromosome type aberration frequency and confounding impact of neutron exposure factor to the chromosome type aberration frequency ($p < 0.05$). The impact of smoking and age for chromosome aberration frequency was found to be insignificant.

8. The gamma radiation dose-response curves were established *in vitro* for dicentric and centric rings and acentrics in human peripheral blood lymphocytes, as described by equations:

$$Yield_{DIC} = (0.00046 \pm 0.00049) + (0.055 \pm 0.006)D + (0.076 \pm 0.004)D^2.$$

$$Yield_{ACE} = (0.0066 \pm 0.0016) + (0.0768 \pm 0.0067)D + (0.0099 \pm 0.0028)D^2.$$

9. Using gamma radiation dose-response curve for dicentrics and centric rings, the study group average dose (estimated by biological dosimetry methods as 132 ± 7 mSv) was found to be close to that measured by physical methods and corrected taking into account lymphocyte half life T½ = 7 year (116 ± 13 mSv).

Recommendations

Summarising the obtained results the following recommendations are given:

1. To use the established gamma radiation dose-response curve *in vitro* for dicentric and ring chromosomes in the following cases:

(a) for determination and approval of occupational exposure dose, above the annual limit (50 mSv) measured by personal dosimeter;

(b) for emergency exposure dose assessment for radiological emergency rescue workers, people involved in emergency work, and population.

2. To perform cytogenetic monitoring by analysing chromosome aberration frequencies in human peripheral blood lymphocytes for evaluation of the occupational IR exposure risk to the separate groups of workers. In case of determined increased chromosome aberration frequency to recommend for worker to repeat the cytogenetic analysis after one year and in case if chromosome aberration frequency remains increased to recommend to change the type work activity.

3. For optimisation of radiation protection of Ignalina NPP radiation workers, whom activities related with internal and neutron exposure, we recommend to increase the internal exposure monitoring measurement frequency, to re-estimate the neutron dose calculation coefficient and in case of possibility periodically to change the nature of work activity of these workers.

List of author's publications on the dissertation subject:

The main results of the research described in this dissertation have been published in the following scientific journals and proceedings of national and international conferences:

Scientific papers in journals listed by ISI and reviewed scientific periodicals:

1. **Griciene B**, Slapsyte G, Mierauskiene J. Chromosome Aberrations in Nuclear Power Plant Workers. *In: Cebulska-Wasilewska, Osipov A. N, Darroudi F (edc): Rapid Diagnosis in Populations at Risk from Radiation and Chemicals. NATO Science for Peace and Security. Series-E: Human and Societal Dynamics*. 2010;73:115-121.
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Curriculum vitae

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SANTRAUKA

Darbo aktualumas

Jonizuojančiosios spinduliuotės šaltinių intensyvus naudojimas įvairiose medicinos, pramonės, mokslo srityse yra susijęs su juos aptarnaujančių darbuotojų ir gyventojų apšvita bei jos žalingo poveikio sveikatai rizika. Todėl didelis dėmesys yra skiriamas gyventojų ir darbuotojų radiacinei saugai, gaunamos apšvitos dozės yra matuojamos ir reglamentuojamos, atliekami JS apšvitos poveikio tyrimai. Gauti tyrimų rezultatai patvirtina prielaidą, jog net mažos apšvitos dozės gali iššaukti įvairius genetinių struktūrų pažeidimus. Citogenetinių tyrimų dėka galima nustatyti jonizuojančiosios spinduliuotės padarytą žalą. Yra žinoma, kad chromosomų struktūros pokyčiai vaidina svarbų vaidmenį aktyvinant protoonkogenus ir inaktyvinant naviką slopinamųjų genų veikimą, yra įrodytas ryšys tarp padidinto chromosomų pažaidų kiekio ir padidintos susirgimų vėžiu rizikos (Bonassi et al., 2000). Daugelio mokslininkų tyrimai rodo, kad net ir nedidelės profesinės apšvitos dozės sukelia citogenetinių pažaidų kiekio padidėjimą periferinio kraujo limfocituose (Chung et al., 1996; Cardoso et al., 2001). Tačiau tyrimų rezultatai dažnai būna nevienareikšmiai, gaunami gana prieštaringi rezultatai visų pirma vertinant pažaidų dažnio priklausomybę nuo darbo su jonizuojančiosios spinduliuotės šaltiniais trukmės ir gautos apšvitos dozės. Mažų dozių sukeliami reiškiniai yra nesibaigiančių diskusijų objektas. Nors šiuo metu tarptautinės organizacijos – Tarptautinė atominės energijos agentūra (TATENA), Tarptautinė radiacinės saugos komisija (ICRP), mažų dozių sukeliamai rizikai taiko linijinę beslenkstinę apšvitos dozės ir atsako priklausomybę (ICRP, 1990), ja remiamasi reglamentuojant galimą apšvitą, nustatant apšvitos dozės ribas, tačiau mažų jonizuojančiosios spinduliuotės dozių sukeliami reiškiniai nėra pakankamai ištirti, tyrimų rezultatai yra prieštaringi (BEIR VII, 2005; UNSCEAR, 2000). Tai rodo, kad tikslinga tęsti naujų rizikos grupių citogenetinius tyrimus, siekiant išaiškinti gaunamos apšvitos galimą riziką.

Intensyvus jonizuojančiosios spinduliuotės šaltinių naudojimas yra susijęs su radiologinių avarijų ir padidintos apšvitos rizika, kartais neišvengiama nelaimingų atsitikimų, kurių metu viršijamos leistinos dozių ribos. Pastarųjų metų įvykiai rodo, kad taip pat išlieka teroristinio akto, panaudojant radioaktyvias ar branduolines medžiagas, grėsmė. Įvykus radiacinėms ar branduolinėms avarijoms, padidintą jonizuojančiosios spinduliuotės dozę gali gauti daugiau asmenų. Siekiant efektyviai suteikti medicininę pagalbą, labai svarbu greitai įvertinti gautą apšvitos dozę (IAEA, 1989). Nukentėję asmenys dažniausiai neturi dozimetrų, ir fizikiniai dozių vertinimo metodai yra negalimi. Šiais atvejais biologinė dozimetrija yra geriausias gautos apšvitos dozės įvertinimo būdas (IAEA, 1986; IAEA, 2001). Antra vertus, žinoma, jog skirtingi žmonės pasižymi skirtingu radiojautrumu - įvairių žmonių apšvitinimas vienoda doze gali sukelti skirtingus biologinius padarinius (Bender et al., 1988). Nors fizikinės dozimetrijos metodai ir yra tikslesni, ne visada galima pasakyti, kokio dydžio biologiniai pakitimai gali būti sukelti apšvitinto žmogaus organizme.

Citogenetiniais tyrimais įrodyta, kad vienoda apšvitos dozė indukuoja panašų chromosomų pažaidų kiekį tiek *in vivo,* tiek *in vitro*. Turint *in vitro* sąlygomis sudarytą kalibracinę dozės-atsako kreivę, avarinę apšvitos dozę galima įvertinti nustačius chromosomų pažaidų kiekį ją gavusių žmonių limfocituose (IAEA, 1986; IAEA, 2001; Voisin et al., 2002). Biologinė dozimetrija, paremta chromosomų pažaidų analize, kartu

su klinikiniais simptomais bei fizikine dozimetrija jau yra neatsiejama avarinių apšvitos dozių įvertinimo dalis (Bender et al., 1988; Voisin et al., 2002). Iš biologinėje dozimetrijoje naudojamų citogenetinių metodų (mikrobranduolių, išankstinės chromosomų kondensacijos, translokacijų tyrimo fluorescencinės *in situ* hibridizacijos metodu ir kt.), nestabilių chromosomų aberacijų, dažniausiai dicentrinių chromosomų, analizė yra tinkamiausias ir dažniausiai naudojamas apšvitos dozių nustatymo būdas (IAEA, 1986, 2001).

Biologinis dozės įvertinimas, panaudojant kitose laboratorijose sudarytas dozės-atsako kreives, gali sąlygoti žymias paklaidas. TATENA (2001) rekomenduoja, kad kiekviena laboratorija, numatanti atlikti biologinę dozimetriją, sudarytų savo kalibracinę dozės-atsako kreivę. Kadangi Lietuvoje kaip ir kitose šalyse gama ir rentgeno spinduliuotės avarinės apšvitos tikimybė yra didžiausia, vienas iš šio darbo tikslų yra sudaryti kalibracinę gama spinduliuotės dozės-atsako kreivę naudojant nestabilių chromosomų aberacijų analizės žmogaus periferinio kraujo limfocituose *in vitro* metodą.

Biomedicininiams tyrimams atlikti yra gautas Lietuvos Bioetikos Komiteto leidimas (2004.06.14, No. 49, tyrimo pavadinimas "Profesinės/medicininės apšvitos poveikio citogenetinis įvertinimas"). Dalį tyrimų parėmė Lietuvos valstybinis mokslo ir studijų fondas (Nr. T33/06).

Darbo tikslai

- Atlikti chromosomų pažaidų analizę jonizuojančiosios spinduliuotės aplinkoje dirbančių asmenų periferinio kraujo limfocituose ir įvertinti galimą gautos profesinės apšvitos riziką.
- Sudaryti kalibracines gama spinduliuote indukuotų nestabilių chromosomų aberacijų dozės-atsako kreives ir atlikti citogenetiškai ištirtų asmenų biologinį dozių įvertinimą.

Pagrindiniai darbo uždaviniai

1. Atlikti Ignalinos AE darbuotojų gaunamų apšvitos dozių analizę siekiant tinkamai atrinkti tiriamųjų asmenų grupes.
2. Įvertinti nestabilių chromosomų aberacijų dažnius jonizuojančiosios spinduliuotės aplinkoje dirbančių asmenų kraujo limfocituose.
3. Palyginti chromosomų aberacijų dažnį darbuotojų, gaunančių jonizuojančiosios spinduliuotės išorinę, vidinę bei neutronų apšvitą, grupėse.
4. Įvertinti skirtingų veiksnių (apšvitos tipo, gautos apšvitos dozės, darbo jonizuojančiosios spinduliuotės aplinkoje trukmės, amžiaus, rūkymo) įtaką chromosomų pažaidų dažniui.
5. Pakartotinai atlikti chromosomų aberacijų analizę asmenims, kuriems buvo nustatyti didžiausi chromosomų aberacijų dažniai.
6. Įvertinti stabilių chromosomų pažaidų dažnius FISH metodu grupėje tiriamųjų asmenų.
7. Sudaryti gama spinduliuote (^{60}Co) žmogaus periferinio kraujo limfocituose *in vitro* indukuotų dicentrinių chromosomų ir acentrinių fragmentų dozės-atsako kreives.
8. Naudojant parengtą gama spinduliuote indukuotų dicentrinių chromosomų dozės-atsako kreivę atlikti tirtų asmenų biologinį dozių įvertinimą ir palyginti su fizikinės dozimetrijos būdu nustatytomis dozėmis.

Darbo naujumas ir praktinė reikšmė

Šio darbo metu pirmą kartą buvo atlikti Lietuvos branduolinės energetikos darbuotojų citogenetiniai tyrimai, nustatyti chromosomų pažaidų dažniai didžiausias apšvitos dozes gaunančių darbuotojų periferinio kraujo limfocituose. Anksčiau Lietuvoje buvo tirti Černobylio AE avarijos likvidavimo darbuose dalyvavę asmenys, padidintos JS aplinkoje dirbantys medicinos darbuotojai bei pacientai po rentgenodiagnostinių procedūrų. Šio darbo metu atlikti mažų JS dozių lėtinės apšvitos poveikio tyrimai asmenims, ilgą laiką dirbantiems su JS ar jos aplinkoje. Tyrimams atrinkti Ignalinos AE darbuotojai gavo žymiai didesnes apšvitos dozes, palyginti su anksčiau tirtomis grupėmis. Gauti citogenetinių tyrimų rezultatai parodė kiekybinę ir kokybinę chromosomų aberacijų priklausomybę nuo donorų profesinės veiklos pobūdžio, nustatyta skirtinga atliekamų darbų bei skirtingų profesinės apšvitos tipų rizika. Pirmą kartą nustatyta, kad didesnę riziką turinčia veikla gali būti laikoma radioaktyviųjų atliekų perdirbėjų, dirbančių Dezaktyvacijos ceche, ir šaltkalvių, dirbančių Reaktorių ceche, profesinė veikla, palyginti su kita veikla. Skirtingų veiksnių įtakos analizė parodė patikimą vidinės apšvitos ir neutronų apšvitos įtaką chromosominio tipo aberacijų dažniui ($p < 0,05$). Įvertinta priklausomybė tarp chromosomų aberacijų dažnio ir išmatuotų fizikinių bei koreguotų, atsižvelgiant į limfocitų gyvavimo trukmę ir jų eliminaciją iš kraujo apytakos, dozių.

Šio darbo metu sudarytos gama spinduliuote indukuotų nestabilių chromosomų aberacijų dozės-atsako kreivės, skirtos biologiniam jonizuojančiosios spinduliuotės dozių įvertinimui. Gautos kreivės atitinka tiesinį-kvadratinį dozės ir atsako modelį, o nustatyti koeficientai artimi kitų autorių nustatytoms reikšmėms. Ši kreivė panaudota tiriamųjų asmenų gautų JS dozių biologiniam įvertinimui. Taikant sudarytą dozės-atsako kreivę atliktas biologinis dozės įvertinimas asmeniui, kuriam individualiuoju dozimetru išmatuota išorinės apšvitos dozė, didesnė už metinę ribinę. Atlikus biologinį dozės įvertinimą padidinta profesinė apšvita buvo atmesta.

Šio darbo metu sudarytas dozės-atsako kreives bus galima naudoti atliekant biologinę dozimetriją. Šios kreivės skirtos naudoti atliekant darbuotojų gautos JS padidintos apšvitos įvertinimą, patvirtinant arba atmetant individualiaisiais dozimetrais išmatuotą išorinės apšvitos dozę, viršijančią metinę ribinę dozę, taip pat, įvertinti JS avarinę apšvitą gavusių radiacinės avarijos gelbėtojų ir kitų asmenų dalyvaujančių avarijos likvidavimo darbuose gautas dozes bei gyventojų, gavusių JS avarinės apšvitos dozes. Radiacinės avarijos atveju bus galima nustatyti nukentėjusius asmenis, gavusius dideles JS apšvitos dozes ir kuriems būtina skubi medicininė pagalba ir tai leis tinkamai parinkti gydymo metodus.

Nustatyti chromosomų aberacijų dažniai Ignalinos AE atskirų cechų ir pareigų bei pareigybių grupėse suteiks papildomos informacijos užtikrinant ir optimizuojant AE darbuotojų radiacinę saugą. Gauti tyrimų rezultatai rodo, kad chromosomų pažaidų analizė gali būti taikoma atskirų darbuotojų grupių JS apšvitos rizikos vertinimui.

Ginamieji teiginiai

1. Mažos jonizuojančiosios spinduliuotės dozės, neviršijančios metinių dozių ribų, gali iššaukti chromosomų aberacijas profesinę apšvitą gavusių asmenų limfocituose.
2. Jonizuojančiosios spinduliuotės aplinkoje dirbančių asmenų limfocituose stebimas chromosomų aberacijų dažnis priklauso nuo jonizuojančiosios spinduliuotės rūšies ir apšvitos tipo.
3. Sudaryta gama spinduliuote indukuotų dicentrinių chromosomų dozės-atsako kreivė atitinka tiesinį-kvadratinį dozės ir atsako modelį ir gali būti naudojama biologinėje dozimetrijoje.

Darbo aprobavimas

Darbo rezultatai buvo pristatyti 9-iose tarptautinėse ir 5-iose šalies konferencijose (8 žodiniai pranešimai ir 6 stendiniai pranešimai). Disertacijos tema paskelbti 6 straipsniai (2 – recenzuojamuose užsienio periodiniuose leidiniuose, įtrauktuose į Mokslinės informacijos instituto duomenų bazės pagrindinį sąrašą (angl. *ISI Master Journal List*), 4 publikacijos – recenzuojamuose mokslo žurnaluose ir tęstiniuose mokslo leidiniuose) ir 6 publikacijos konferencijų medžiagoje.

Apimtis ir struktūra

Disertaciją sudaro šie skyriai: įvadas, literatūros apžvalga, tyrimų objektas ir metodai, tyrimų rezultatai ir jų aptarimas, darbo išvados, cituojamos literatūros sąrašas, (181 šaltinis), 12 publikacijų darbo tema sąrašas ir priedai. Darbo apimtis – 134 puslapiai, darbe pateikiama 20 paveikslų, 21 lentelė o prieduose yra 1 paveikslas ir 8 lentelės. Įvade trumpai pagrindžiamas darbo temų aktualumas pateiktas darbo tikslas ir uždaviniai, mokslinis naujumas ir praktinė reikšmė, ginamieji teiginiai, autorės publikacijų sąrašas. Antrame skyriuje pateikta literatūros apžvalga. Trumpai apžvelgiamos jonizuojančiosios spinduliuotės (JS) savybės ir pagrindiniai dozimetriniai vienetai, JS biologinis poveikis, mažų jonizuojančiosios spinduliuotės dozių sukelti reiškiniai, JS kancerogeninis poveikis, atominius bombardavimus išgyvenusių Hirosimos ir Nagasakio gyventojų epidemiologiniai tyrimai, padidintos gamtinės apšvitos vietovėse gyvenančių asmenų epidemiologiniai tyrimai, profesinę apšvitą gavusių asmenų epidemiologiai tyrimai, medicininę apšvitą gavusių asmenų epidemiologiniai tyrimai. Aptariamas chromosomų pažaidų analizės taikymas jonizuojančiosios spinduliuotės poveikio tyrimuose, chromosomų pažaidų taikymas kaip biožymuo vėžio rizikos įvertinimui, chromosomų pažaidų analizė biologinėje dozimetrijoje. Trečiame skyriuje pateikiami tiriamieji asmenys ir taikyti tyrimo metodai. Ketvirtame skyriuje pateikiami tyrimų rezultatai: gama radionuklidų aktyvumų palyginamųjų matavimų ir vidinės apšvitos dozių įvertinimo rezultatai, nestabilių chromosomų aberacijų analizės tiriamųjų asmenų limfocituose rezultatai, veiksnių, galinčių turėti įtakos nestabilių chromosomų pažaidų dažniui, analizės rezultatai, translokacijų analizės taikant fluorescencinės in situ hibridizacijos (FISH) metodą rezultatai, asmenų, kuriems nustatyti didžiausi chromosomų aberacijų dažniai, palyginamojo tyrimo rezultatai, gama spinduliuotės sukeltų chromosomų aberacijų *in vitro* dozės-atsako kreivių sudarymo rezultatai, sudarytos gama spiduliuotės dozės-atsako kreivės taikymo rezultatai: darbuotojui išmatuotos padidintos profesinės apšvitos dozės įvertinimui ir tiriamųjų asmenų gautos biologiniam dozės nustatymui. Rezultatų aptarime ir išvadose pateiktas rezultatų aptarimas ir bendrosios išvados.

IŠVADOS

1. Visoje tirtų branduolinės energetikos darbuotojų grupėje nustatytas patikimai didesnis, palyginti su kontroline grupe, bendras chromosomų aberacijų dažnis (2,27 *vs* 1,76 CA/100 ląst.), chromosominio tipo aberacijų (1,11 *vs* 0,70), acentrinių fragmentų (0,89 *vs* 0,59) ir dicentrinių chromosomų (0,20 *vs* 0,07) dažnis ($p < 0,05$).

2. Nustatyta chromosomų aberacijų dažnio priklausomybė nuo jonizuojančiosios spinduliuotės rūšies ir apšvitos tipo. Asmenų grupėje, kurioje buvo registruota tik išorinė gama apšvita, chromosomų aberacijų dažnis patikimai nesiskyrė nuo dažnio, stebėto kontrolinių asmenų grupėje (1,60 *vs* 1,76 CA/100 ląst., $p > 0,05$). Patikimas chromosomų aberacijų kiekio padidėjimas nustatytas grupėse tiriamųjų asmenų, kuriems be išorinės gama spinduliuotės buvo registruotos papildomos vidinės (2,54 *vs* 1,76 CA/100 ląst., $p < 0,01$) ir vidinės bei neutronų (2,95 *vs* 1,76 CA/100 ląst., $p < 0,01$) apšvitos dozės.

3. Didžiausią riziką turinčia profesine veikla Ignalinos AE galime laikyti radioaktyviųjų atliekų perdirbėjų, dirbančių Dezaktyvacijos ceche, ir šaltkalvių, dirbančių Reaktorių ceche, veiklą. Šių pareigybių darbuotojams buvo nustatyti didžiausi chromosomų aberacijų dažniai: 3,16 CA/100 ląst. radioaktyviųjų atliekų perdirbėjų ir 3,14 CA/100 ląst. šaltkalvių grupėje.

4. Asmenų, gavusių mažų dozių lėtinę apšvitą ir kuriems pakartotinis citogenetinis tyrimas atliktas po dviejų metų, chromosomų aberacijų dažnis nesiskyrė nuo nustatyto pirmojo tyrimo metu (4,38 *vs* 5,37 CA/100 ląst., $p > 0,05$), tačiau buvo stebimas patikimai mažesnis chromatidinio tipo aberacijų (1,70 *vs* 2,75, $p < 0,05$) dažnis.

5. Patikimos koreliacijos tarp chromosomų aberacijų dažnio ir išmatuotų bei koreguotų (atsižvelgiant į limfocitų gyvavimo trukmę ir jų eliminaciją iš kraujo apytakos) dozių dydžio nenustatyta ($p > 0,05$).

6. Rezultatų dispersinė analizė įrodė patikimą vidinės apšvitos veiksnio įtaką bendro chromosomų aberacijų ir chromosominio tipo aberacijų ($p < 0,05$) dažniui ir patikimą neutronų apšvitos veiksnio įtaką chromosominio tipo aberacijų dažniui ($p < 0,05$). Rūkymo ir amžiaus įtaka chromosomų aberacijų dažniui nenustatyta.

7. Sudarytos kalibracinės *in vitro* gama spinduliuote (^{60}Co) indukuotų dicentrinių ir žiedinių chromosomų bei acentrinių fragmentų dozės-atsako kreivės, kurias aprašo lygtys:

$$Y_{DIC+ŽC} = (0,00046 \pm 0,00049) + (0,055 \pm 0,006)D + (0,076 \pm 0,004)D^2.$$

$$Y_{ACE} = (0,0066 \pm 0,0016) + (0,0768 \pm 0,0067)D + (0,0099 \pm 0,0028)D^2.$$

8. Panaudojant sudarytą gama spinduliuote (^{60}Co) indukuotų dicentrinių ir žiedinių chromosomų dozės-atsako kreivę, apskaičiuota tiriamųjų asmenų grupės vidutinė efektinė dozė (132 ± 7 mSv) yra artima koreguotai, fizikiniais metodais išmatuotai, dozei (116 ± 13 mSv) laikant, kad limfocitų gyvavimo pusėjimo trukmė T½ yra 7 metai.

Rekomendacijos

Apibendrinus gautų tyrimų rezultatus teikiamos šios praktinės rekomendacijos:

1. Sudarytą kalibracinę gama spinduliuote (^{60}Co) indukuotų dicentrinių ir žiedinių chromosomų dozės-atsako kreivę rekomenduojame taikyti:

a) dozės nustatymui ir patvirtinimui, kai darbuotojui individualiuoju dozimetru išmatuota dozė yra didesnė už metinę ribinę (50 mSv);

b) asmenų, dalyvaujančių radiacinės avarijos likvidavimo darbuose, bei gyventojų avarinės apšvitos dozių nustatymui.

2. Citogenetinį monitoringą, tiriant chromosomų aberacijų dažnį darbuotojų periferinio kraujo limfocituose, rekomenduojame taikyti jonizuojančiosios spinduliuotės apšvitos profesinės rizikos vertinimui. Nustačius padidintą chromosomų aberacijų (dicentrinių chromosomų) dažnį, rekomenduoti darbuotojui po vienerių metų atlikti pakartotinį tyrimą ir jei chromosomų aberacijų (dicentrinių chromosomų) dažnis išlieka padidintas, siūlyti darbuotojui pakeisti darbo veiklos pobūdį.

3. Optimizuojant Ignalinos AE darbuotojų, vykdančių veiklą, kurios metu yra galima neutronų ir vidinė apšvita, radiacinę saugą, rekomenduojame padidinti vidinės apšvitos monitoringo matavimų dažnį, peržiūrėti neutronų apšvitos dozių skaičiavimo koeficientą ir, esant galimybei, periodiškai keisti šių darbuotojų darbų veiklos pobūdį.

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Birutė Gricienė gimė 1972 m. kovo 12 d. Panevėžyje. 1990 m. baigė vidurinę mokyklą Nemunėlio Radviliškyje, Biržų raj. 1997 m. Vilniaus Universitete įgijo biologijos (ekologijos) mokslų magistro laipsnį. 1998 m. baigė tarptautines studijas ir Londono Universitete įgijo radiacinės biologijos magistro laipsnį. 2003-2010 m. Vilniaus Universiteto doktorantė. Dirba Radiacinės saugos centre Individualiosios dozimetrijos skyriaus vedėja. Skaito paskaitas radiacinės biologijos, radiacinės saugos ir dozimetrijos temomis. Stažavosi Leideno Universitete, Čekijos, Graikijos radiacinės saugos institutuose. Mokslinių tyrimų kryptis – Jonizuojančiosios spinduliuotės poveikio žmogui citogenetiniai tyrimai, profesinės, ir gamtinės apšvitos dozių tyrimai, jų fizikinis ir biologinis vertinimas. Kartu su bendraautoriais yra paskelbusi 16 mokslinių straipsnių, 12 straipsnių konferencijų pranešimų medžiagoje, su pranešimais dalyvavo 17 konferencijų. Vadovėlio “Radiacija: sauga, sveikata, ekologija“ (2005) bendraautorė. Knygos „ Radonas ir gamtinė apšvita“ (2009) bendraautorė. Lietuvos radiacinės saugos draugijos valdybos narė.

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CYTOGENETIC EFFECTS OF LOW IONISING RADIATION DOSES AND BIOLOGICAL DOSIMETRY

Summary of Doctoral Dissertation
Biomedical Sciences, Biology (01 B)

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MAŽŲ JONIZUOJANČIOSIOS SPINDULIUOTĖS APŠVITOS DOZIŲ POVEIKIO CITOGENETINIAI TYRIMAI IR BIOLOGINĖ DOZIMETRIJA

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