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**PROFESINĖ APŠVITA IR JOS CITOGENETINIO POVEIKIO TYRIMAI
IGNALINOS AE DARBUOTOJŲ LIMFOCITUOSE**

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**Profesinė apšvita ir jos citogenetinio poveikio tyrimai
Ignalinos AE darbuotojų limfocituose**

SANTRAUKA

Lietuvoje Ignalinos AE darbuotojai sudaro didžiausią grupę asmenų, dirbančių tiesiogiai su jonizuojančiosios spinduliuotės (JS) šaltiniais ar su jų sąlygojama apšvita susijusį darbą. Profesinės apšvitos dozės paprastai neviršija leistinos 20 mSv metinės dozių ribos, tačiau daugelis tyrimų patvirtino, kad net mažos JS dozės gali reikšmingai padidinti chromosomų aberacijų (CA) dažnį periferinio kraujo limfocituose.

Šio darbo tikslas buvo ištirti CA dažnius didžiausias apšvitos dozes gaunančių Ignalinos AE darbuotojų kraujo limfocituose ir įvertinti skirtingos profesinės apšvitos tipų bei atliekamų darbų lemiamą riziką. Visoje tirtų Ignalinos AE darbuotojų grupėje nustatytas patikimai didesnis palyginus su kontroline grupe bendras CA dažnis (3,26 vs 2,18 CA/100 ląst.), chromosominio tipo aberacijų (2,18 vs 0,82), acentrinių fragmentų (1,54 vs 0,65) ir dicentrinių chromosomų (0,51 vs 0,03) dažniai ($p < 0,05$). CA dažnis Ignalinos AE darbuotojų grupėje tik su išorine apšvita patikimai nesiskyrė nuo dažnio stebėto kontrolinių asmenų grupėje (2,56 vs 2,18 CA/100 ląst., $p > 0,05$). Ignalinos AE darbuotojų grupėje, kurioje be išorinės apšvitos buvo registruota papildoma vidinė apšvita, nustatyti patikimai didesni palyginus su kontrole bendras CA dažnis (3,61 vs 2,18), chromosominio tipo aberacijų (2,37 vs 0,82), acentrinių fragmentų (1,58 vs 0,65) ir dicentrinių chromosomų (0,65 vs 0,03) dažniai ($p < 0,05$). Todėl šių asmenų darbinė veikla galėtų būti vertinama kaip potencialiai didesnės apšvitos bei rizikos sveikatai šaltinis. Citogenetinių tyrimų rezultatų dispersinė analizė parodė, kad darbas su jonizuojančiosios spinduliuotės šaltiniais Ignalinos AE gali būti siejamas su chromosominio tipo aberacijų ($F = 4,91$; $p = 0,034$) ir acentrinių fragmentų ($F = 5,90$; $p = 0,021$) dažnio padidėjimu, o vidinė apšvita turi statistiškai patikimą įtaką dicentrinių + žiedinių chromosomų dažnio padidėjimui ($F=5,37$; $p = 0,027$). Kitų veiksnių (rūkymo, amžiaus ir darbo stažo) įtaka chromosomų aberacijų dažniams nėra patikima. Taip pat nenustatyta patikimos koreliacijos tarp chromosomų aberacijų dažnių ir sukauptų fizikinių bei koreguotųjų fizikinių dozių ($p > 0,05$).

Justas Morkūnas

**Occupational radiation exposure and cytogenetic
monitoring of Ignalina Nuclear Power Plant workers**

SUMMARY

The Ignalina Nuclear Power Plant workers (INPP) represent the largest group of workers occupationally exposed to low-level doses of ionizing radiation in Lithuania. Though individual doses of the INPP workers for many years have been declining and are retained within officially accepted limits, many reports demonstrate that low-level occupational exposure to ionizing radiation can significantly increase chromosome aberration levels in blood lymphocytes. Moreover, chromosome aberrations are believed to be a possible biomarker reflecting chromosome damage in target tissues which in turn is linked to cancer development. Therefore many studies have been dedicated to investigate the cytogenetic effects of low-level radiation in blood lymphocytes, especially trying to establish dose-effect relationship and predict possible cancer risks. The objective of the current study was to analyze chromosome aberration levels in lymphocytes of the INPP workers subjected to relatively high individual doses of occupational exposure (mean accumulated doses 280.2 ± 44.9 mSv), taking into consideration different types of ionizing radiation. A total of 21 blood samples from INPP workers and 17 control samples were analyzed. Cytogenetic analysis revealed significantly increased CA levels in the whole group of INPP workers (3.26 ± 0.34 CA/100 cells) and a subgroup of workers additionally exposed to internal radiation (3.61 ± 0.45 CA/100 cells), when compared to controls (2.18 ± 0.17 , $p < 0.05$). No significant increase in CA frequency was observed for a subgroup exposed to external γ -rays only. When taking into account the yield of chromosome-type aberrations, acentric fragments and dicentric chromosomes all groups significantly differed from the control group ($p < 0.05$). Significant increase in dicentric + ring chromosomes ($0.70 \pm 0.14/100$ cells) was observed in a subgroup of workers additionally exposed to internal radiation as compared to workers with external irradiation. A comparison of two repeated samples (within period of 3 years) from 7 selected workers demonstrated a significant decrease in chromatid-type aberrations. The analysis of variance disclosed a significant input of occupational exposure to the yields of chromosome type aberrations and acentric fragments in the INPP workers. A significant influence of internal exposure was confirmed for dicentric + ring chromosome levels. No correlation between the accumulated doses and aberration yields was determined, neither was the influence of such factors as smoking, age and working time confirmed.

9 LITERATŪROS SĄRAŠAS

1. **Aitio**, A, and Commission of the European Communities.; International Agency for Research on Cancer.; International Program on Chemical Safety.; Työterveyslaitos.; World Health Organization. 1988. *Indicators for assessing exposure and biological effects of genotoxic chemicals: consensus and technical reports*. Luxembourg: Office for Official Publications of the European Communities.
2. **Астахова**, Л Н. 1996. *Щитовидная железа у детей: последствия Чернобыля*. Минск.
3. **Au**, William W, and Salama A Salama. 2005. Use of biomarkers to elucidate genetic susceptibility to cancer. *Environmental and Molecular Mutagenesis* 45, no. 2-3: 222-228.
4. **Chung**, H W, E K Ryu, Y J Kim, and S W Ha. 1996. Chromosome aberrations in workers of nuclear-power plants. *Mutation Research* 350, no. 2 (March 9): 307-314.
5. **Balaseem**, A N, A S Ali, H S Mosa, and K O Hussain. 1992. Chromosomal aberration analysis in peripheral lymphocytes of radiation workers. *Mutation Research* 271, no. 3 (June): 209-211.
6. **Ballardin**, M. 2007. Induction of chromatid-type aberrations in peripheral lymphocytes of hospital workers exposed to very low doses of radiation. *Mutat Res* 626, no. 1-2 (January 10): 61-8.
7. **Barquinero**, J F, L Barrios, M R Caballín, R Miró, M Ribas, A Subias, and J Egozcue. 1993. Cytogenetic analysis of lymphocytes from hospital workers occupationally exposed to low levels of ionizing radiation. *Mutation Research* 286, no. 2 (April): 275-9.
8. **Balakrishnan**, S, S B Rao. 1999. Cytogenetic analysis of peripheral blood lymphocytes of occupational workers exposed to low levels of ionising radiation. *Mutat Res* 442, no. 1 (June 7): 37-42.
9. **Bauchinger**, M, E Schmid, H Braselmann. 1997. Cytogenetic evaluation of occupational exposure to external gamma-rays and internal ²⁴¹Am contamination. *Mutation Research* 395, no. 2-3 (December 12): 173-8.
10. **Baverstock**, K, B Egloff, A Pinchera, C Ruchti, and D Williams. 1992. Thyroid cancer after Chernobyl. *Nature* 359, no. 6390 (September 3): 21-22.
11. **Bigatti**, P, L Lamberti, G Ardito, and F Armellino. 1988. Cytogenetic monitoring of hospital workers exposed to low-level ionizing radiation. *Mutation Research* 204, no. 2 (February): 343-7.

12. **Boffetta**, P, O Hel, H Norppa, E Fabianova, A Fucic, S Gundy, J Lazutka, et al. 2007. Chromosomal aberrations and cancer risk: results of a cohort study from Central Europe. *American Journal of Epidemiology* 165, no. 1 (January 1): 36-43.
13. **Boice**, J D, R R Monson, and M Rosenstein. 1981. Cancer mortality in women after repeated fluoroscopic examinations of the chest. *Journal of the National Cancer Institute* 66, no. 5 (May): 863-867.
14. **Bonassi**, S. 1995. Are chromosome aberrations in circulating lymphocytes predictive of future cancer onset in humans? Preliminary results of an Italian cohort study. *Cancer Genet Cytogenet* 79, no. 2 (February): 133-5.
15. **Bonassi**, S. 1999. Combining environmental exposure and genetic effect measurements in health outcome assessment. *Mutat Res* 428, no. 1-2 (July 16): 177-85.
16. **Bonassi**, S. 2000. Chromosomal Aberrations in Lymphocytes Predict Human Cancer Independently of Exposure to Carcinogens. *Cancer research* 60: 1619-1625.
17. **Bonassi**, S, H Norppa, M Ceppi, U Strömberg, R Vermeulen, A Znaor, A Cebulska-Wasilewska, et al. 2008. Chromosomal aberration frequency in lymphocytes predicts the risk of cancer: results from a pooled cohort study of 22 358 subjects in 11 countries. *Carcinogenesis* 29, no. 6 (June): 1178-83.
18. **Brasemann**, H, E Schmid, and M Bauchinger. 1994. Chromosome aberrations in nuclear power plant workers: the influence of dose accumulation and lymphocyte life-time. *Mutation Research* 306, no. 2 (April 15): 197-202.
19. **Brenner**, D J. 1999. The relative effectiveness of exposure to ¹³¹I at low doses. *Health Physics* 76, no. 2 (February): 180-185.
20. **Cardis**, E. 2005. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. *BMJ* 331, no. 7508 (July 9): 77.
21. **Cardoso**, S R, S Takahashi-Hyodo, P P Ghilardi-Neto, E T Sakamoto-Hojo. 2001. Evaluation of chromosomal aberrations, micronuclei, and sister chromatid exchanges in hospital workers chronically exposed to ionizing radiation. *Teratog Carcinog Mutagen.* 21, 431-439.
22. **Carrano**, A V. 1988. International Commission for Protection Against Environmental Mutagens and Carcinogens. ICPEMC publication no. 14. Considerations for population monitoring using cytogenetic techniques. *Mutat Res* 204, no. 3 (March): 379-406.

23. **Chen**, P D, L L Qi, B Zhou, S Z Zhang, and D J Liu. 1995. Development and molecular cytogenetic analysis of wheat-Haynaldia villosa 6VS 6AL translocation lines specifying resistance to powdery mildew. *Theoretical and applied genetics*. 91, no. 6-7: 1125.
24. **Darby**, S C. 1991. The contribution of natural ionizing radiation to cancer mortality in the United States. p. 183-190 in: *The Origins of Human Cancer* (J. Brugge et al.). Cold Spring Harbour Laboratory Press, New York.
25. **Flodin**, U. 1986. Background radiation, electrical work, and some other exposures associated with acute myeloid leukemia in a case-referent study. *Arch Environ Health* 41, no. 2 (March): 77-84.
26. **Garaj-Vrhovac**, V, N Kopjar, M Poropat. Evaluation of cytogenetic damage in nuclear medicine personnel occupationally exposed to low-level ionising radiation. 2006. *Arhiv Za Higijenu Rada I Toksikologiju* 57, no. 1 (March): 31-8.
27. **Greenpeace** International. 2006. *The Chernobyl catastrophe: consequences on human health*. Amsterdam, The Netherlands: Greenpeace.
28. **Gricienė**, B, G Slapšytė. 2007. Assessment of chromosomal aberration in workers chronically exposed to ionising radiation. *Biologija*, 57, 4, 5-10.
29. **Griciūtė**, L, D Adomavičienė. 1998. *Kancerogenezė ir vėžio biologija*. Vilnius: Leidybos centras.
30. **Hagelström**, A H, N B Gorla, I B Larripa. 1995. Chromosomal damage in workers occupationally exposed to chronic low level ionizing radiation. *Toxicology Letters* 76, no. 2 (March): 113-7.
31. **Hagmar**, L. 1994. Cancer risk in humans predicted by increased levels of chromosomal aberrations in lymphocytes: Nordic study group on the health risk of chromosome damage. *Cancer Res* 54, no. 11 (June 1): 2919-22.
32. **Hagmar**, L. 1998. Chromosomal aberrations in lymphocytes predict human cancer: a report from the European Study Group on Cytogenetic Biomarkers and Health (ESCH). *Cancer Res* 58, no. 18 (September 15): 4117-21.
33. **Hagmar**, L, U Strömberg, S Bonassi, I L Hansteen, L E Knudsen, C Lindholm, H Norppa. 2004. Impact of types of lymphocyte chromosomal aberrations on human cancer risk: results from Nordic and Italian cohorts. *Cancer Research* 64, no. 6 (March 15): 2258-2263.
34. **Holmquist**, G P. 1992. Chromosome bands, their chromatin flavors, and their functional features. *Am J Hum Genet* 51, no. 1 (July): 17-37.

35. **IAEA**. 2001. *International Atomic Energy Agency*. Vienna.
36. **IAEA**. 2008. Nuclear Power Reactors In The World. *International Atomic Energy Agency*. Vienna. ISBN 978-92-0-107708-0.
37. **ISCN**, An international system for human cytogenetic nomenclature (1978) ISCN (1978). Report of the Standing Committee on Human Cytogenetic Nomenclature. (1978). Cytogenetics and Cell Genetics. 21 (6), 309-409.
38. **Khanna**, KK. 2001. DNA double-strand breaks: signaling, repair and the cancer connection. *Nat Genet* 27, no. 3 (March): 247-54.
39. **Kubelka**, D, A Fucić, and S Milković-Kraus. 1992. The value of cytogenetic monitoring versus film dosimetry in the hot zone of a nuclear power plant. *Mutation Research* 283, no. 3 (November): 169-72.
40. **Lamberti**, L, P Bigatti, G Ardito, and F Armellino. 1989. Chromosome analysis in operating room personnel. *Mutagenesis* 4, no. 2 (March): 95-7.
41. **Lazutka**, J R, R Lekevicius, V Dedonyte, L Maciuleviciute-Gervers, J Mierauskiene, S Rudaitiene, and G Slapsyte. 1999. Chromosomal aberrations and sister-chromatid exchanges in Lithuanian populations: effects of occupational and environmental exposures. *Mutation Research* 445, no. 2 (September 30): 225-39.
42. **Leenhouts**, H P, M J Brugmans, and K H Chadwick. 2000. Analysis of thyroid cancer data from the Ukraine after 'Chernobyl' using a two-mutation carcinogenesis model. *Radiation and Environmental Biophysics* 39, no. 2 (June): 89-98.
43. **Little**, M P, H A Weiss, J D Boice, S C Darby, N E Day, and C R Muirhead. 1999. Risks of leukemia in Japanese atomic bomb survivors, in women treated for cervical cancer, and in patients treated for ankylosing spondylitis. *Radiation Research* 152, no. 3 (September): 280-292.
44. **Lloyd**, D C, R J Purrott, and E J Reeder. 1980. The incidence of unstable chromosome aberrations in peripheral blood lymphocytes from unirradiated and occupationally exposed people. *Mutation Research* 72, no. 3 (August): 523-32.
45. **Lubin**, J H, J D Boice, C Edling, R W Hornung, G R Howe, E Kunz, R A Kusiak, H I Morrison, E P Radford, and J M Samet. 1995. Lung cancer in radon-exposed miners and estimation of risk from indoor exposure. *Journal of the National Cancer Institute* 87, no. 11 (June 7): 817-827.
46. **Miller**, A B, G R Howe, G J Sherman, J P Lindsay, M J Yaffe, P J Dinner, H A Risch, and D L Preston. 1989. Mortality from breast cancer after irradiation during fluoroscopic

- examinations in patients being treated for tuberculosis. *The New England Journal of Medicine* 321, no. 19 (November 9): 1285-1289.
47. **Mitelman**, F. 2004. Fusion genes and rearranged genes as a linear function of chromosome aberrations in cancer. *Nat Genet* 36, no. 4 (April): 331-4.
48. **Moorhead**, PS. 1960. Chromosome preparations of leukocytes cultured from human peripheral blood. *Exp Cell Res* 20 (September): 613-6.
49. **Nedveckaitė** T. 2004. *Radiacinė sauga Lietuvoje*. Vilnius.
50. **Nowell**, PC. 1961. Chromosome studies in human leukemia. II. Chronic granulocytic leukemia. *J Natl Cancer Inst* 27 (November): 1013-35.
51. **OECD**. 2008. *Occupational Exposures at Nuclear Power Plants*. ISBN 978-92-64-99042-5
52. **Pierce**, D A, Y Shimizu, D L Preston, M Vaeth, and K Mabuchi. 1996. Studies of the mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950-1990. *Radiation Research* 146, no. 1 (July): 1-27.
53. **(RSC) Radiacinės saugos centas**. 2007. *Metinė ataskaita*. Vilnius.
54. **(RSC) Radiacinės saugos centas**. 2009. *Radiacinės saugos centro informacinis biuletenis* Nr. 4. Vilnius
55. **Rossner**, P. 2005. Chromosomal aberrations in lymphocytes of healthy subjects and risk of cancer. *Environ Health Perspect* 113, no. 5 (May): 517-20.
56. **Rowland**, R E. Dose-response relationships for female radium dial workers: a new look. p. 135-143 in: Kaick, Gerhard, and Commission of the European Communities. 1995. *Health effects of internally deposited radionuclides : emphasis on radium and thorium : proceedings of an international seminar held in Heidelberg, Germany, 18-21 April, 1994*. Singapore ; New Jersey: World Scientific.
57. **Slapsyte**, G, A Jankauskiene, J Mierauskiene, and J R Lazutka. 2001. Cytogenetic analysis of children under long-term antibacterial therapy with nitroheterocyclic compound furagin. *Mutation Research* 491, no. 1-2 (April 5): 25-30.
58. **Slapšytė**, G. 2007. *Antropogeninių ir gamtinių veiksnių genotoksiškumo įvertinimas*. IBSN 978-9955-33-131-5. Vilnius.
59. **Tao**, Z, Y Zha, S Akiba, Q Sun, J Zou, J Li, Y Liu, H Kato, T Sugahara, and L Wei. 2000. Cancer mortality in the high background radiation areas of Yangjiang, China during the

period between 1979 and 1995. *Journal of Radiation Research* 41 Suppl (October): 31-41.

60. **Thomas**, D C, and S Preston-Martin. 1992. Risk of leukemia caused by diagnostic x-rays. *Health Physics* 63, no. 5 (November): 576-578.
61. **UNSCEAR**, UNITED NATIONS. 2000. Sources and effects of ionizing radiation: United Nations Scientific Committee on the Effects of Atomic Radiation: UNSCEAR 2000 report to the General Assembly, with scientific annexes. UN, New York.
62. **Urbelis**, D. Adlienė, V. Atkočius, J. Augulis, B. Gricienė, K. Juškevičius, G. Klevinskas, R. Krenevičius, R. Ladygienė, R. Lekevičius, A. Mastauskas, G. Morkūnas, V. Paulavičius, P. Pipinis, R.M. Stasiūnaitienė, D. Šidiškienė, K. Zemkajus. 2005. *Jonizuojančioji spinduliuotė (radiacija): sauga, sveikata, ekologija*. Vilnius : Vilniaus universiteto leidykla.
63. **Yunis**, J J. 1983. The chromosomal basis of human neoplasia. *Science* 221, no. 4607 (July 15): 227-36.
64. **Zakeri**, F, T Hirobe. A cytogenetic approach to the effects of low levels of ionizing radiations on occupationally exposed individuals. 2008. *European Journal of Radiology* (December 1).
65. **Wang**, J. Statistical analysis of cancer mortality data of high background radiation areas in Yiangjiang. 1993. *Chin. J. Radiol. Med. Prot.* 13: 291-294 and 358.
66. **Weiss**, H A, S C Darby, T Fearn, and R Doll. 1995. Leukemia mortality after X-ray treatment for ankylosing spondylitis. *Radiation Research* 142, no. 1 (April): 1-11.

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