6th LOWRAD

International Conference on Low Dose Radiation Effects on Human Health and Environment

Budapest, Hungary, October 17-20, 2007

Under the auspices of the International Journal of Low Radiation, WONUC and the Hungarian Biophysical Society

Dear Colleagues,

On the behalf of the Organizing Committee, the International Journal of Low Radiation, the Hungarian Biophysical Society and WONUC, it is our great pleasure to welcome you to the 6th International Conference on Low Dose Radiation Effects on Human Health and Environment (LOWRAD2007). One of the major goals of LOWRAD2007 is to encourage international cooperation and communication in all fields of low dose radiation science. To fulfill this goal 6th LOWRAD brings together specialists from all the disciplines involved in radiation science.

This is a unique occasion to highlight the most recent knowledge's in low dose radiation research and to dialogue among scientists from different countries of the world. We anticipate the high number of participants attracted by the scientific program.

We wish you a pleasant stay in Budapest and hope that you will enjoy all aspects of the congress.

P. Závodszky
Congress President

Andre Maisseu
Co-Congress President

G. Sáfrány
Secretary General

6th LOWRAD is organized under the auspices of the Hungarian Biophysical Society, the International Journal of Low Radiation and WONUC

The conference is generously supported by

F. Joliot-Curie National Research Institute for Radiobiology and Radiohygiene, Budapest, Hungary

Atomic Power Station, Paks, Hungary

Congress venue

Hotel Budapest
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Self Publishing

Editor: G. Sáfrány

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AWARDS

Marie Curie Award
offered by the International Journal of Low Radiation

M. Tubiana

General information

Badge

Participants are requested to wear their badge at all times during the conference. The badge serves as an entrance ticket to the scientific sections, the Welcome Party and the Congress Dinner.

Insurance

The organizers do not accept liability for individual medical, travel or personal insurance and participants are strongly advised to take out their own personal insurance policies.

Language

The official language of the meeting is English. No simultaneous translations will be provided.

Poster presentations

Posters should be mounted by 9 AM on the day of presentation and should be removed by 17 PM. The poster size should be 80x110 cm.The organizers are not responsible for loss of posters.

Projection facilities

Only Power Point facilities will be provided. Slides must be presented in the lecture room 15 minutes before the start of the corresponding section.

Social events

The Welcome Reception will be organised on October 17, Wednesday at 19.00 at Hotel Budapest.

The Congress Dinner will be held on October 19, Friday at 19.15. For the location of the Congress Dinner, please watch the announcements or consult the Secretariat.

Sightseeing Tour of Budapest will start on October 20, Saturday at 9.00 and ends around 13.00 at Hotel Budapest.

The social events are open for all registered participants. Non-registered persons can buy a ticket at the Congress Secretariat.

Program Overview

Wednesday, October 17, 2007

12.00-19.00	Registration	Hotel Budapest
17.45-18.10	Opening Ceremony, Welcome Address	Room A
18.10-19.00	C. Streffer: Genomic instability and radiation effects.	Room A
19.00	Welcome Reception	Hotel Budapest

Thursday, October 18, 2007

09.00-10.20	Low dose radiation induced carcinogenesis, epidemiology	Room A
9.00-10.20	Mathematical modeling of radiation effects	Room B
10.20-10.40	*Coffee Break*	*Poster area*
10.40-12.00	Low dose radiation induced carcinogenesis, epidemiology	Room A
10.40-12.20	Mathematical modeling of radiation effects	Room B
12.20-13.20	*Lunch*	
13.20-14.20	Poster Session	Poster area

14.30-16.05	Radiation induced genomic instability, bystander effects and adaptive response	Room A
14.30-16.05	Long term radiation effects	Room B
16.05-16.30	*Coffee Break*	*Poster area*
16.30-17.50	Radiation induced genomic instability, bystander effects and adaptive response	Room A
16.30-17.40	Long term radiation effects	Room B
18.00-19.00	Low Ionising Radiation Defence Mechanisms Research Round table discussion, chaired by A. Maisseu	Room A

Friday, October 19, 2007

09.00-10.10	Radiation response modifiers	Room A
09.00-10.10	Health hazards of radiation accidents	Room B
10.10-10.30	*Coffee Break*	*Poster area*
10.30-12.00	Radiation response modifiers	Room A
10.30-12.00	Health hazards of radiation accidents	Room B
12.10-13.10	*Lunch*	
13.10-14.10	Poster Session	Poster area
14.15-15.15	Marie Curie Award Lecture: M. Tubiana	Room A

15.20-16.50	Low dose radiation effects: new aspects	Room A
15.20-16.50	Radiation-induced transcriptional and lipid profiles	Room B
16.50-17.10	*Coffee Break*	*Poster area*
17.10-18.15	Low dose radiation effects: new aspects	Room A
18.30	Closing Ceremony	Room A
19.15	Congress Dinner	

Saturday, October 20, 2007

9.00-13.00	Sightseeing tour by bus (free for registered participants)

Scientific Program

Wednesday, October 17, 2007

12.00-19.00 Registration Hotel Budapest

17.45-18.10 Opening Ceremony, Welcome Address Room A

18.10-19.00 C. Streffer: Genomic instability and radiation effects. Room A

19.00 Welcome Reception Hotel Budapest

Thursday, October 18, 2007

09.00-12.00 Low dose radiation induced carcinogenesis, epidemiology Room A

Chairpersons: I. Turai and T. Nomura

9.00-9.40 T. Nomura: Low dose and dose rate effects on radiation mutagenesis, teratogenesis and carcinogenesis

9.40-10.20 I. Turai, A. Kerekes, M. Ótos, K. Veress: A review of cancer mortality data of radiation workers of nuclear power plant, Paks, Hungary, in the light of the international radiation epidemiology study

10.20-10.40 Coffee Break Poster area

10.40-11.00 M.A. Hajnal, E. Tóth, K. Hámori, M. Minda, and Gy.J. Köteles: Correlation between radon level and confounders of cancer: a note on epidemiological inference at low doses

11.00-11.20 Y-J. Go, J-H. Shin, K-S. Jeong, D-M. Kwak, O-D. Kwon, S-H. Kim, S-Y. Ryu, T. Yang, J-S. Hae, K-R. Kim, C-M. Kang, and T-H. Kim: Studies of the biomarker available in biological dosimetry to estimate the dose with the calibration of dose-response curve of micronuclei in human lymphocytes induced by 50 MeV proton beam exposure

11.20-11.40 D. Usurelu, I. Radu, L. Gavrila, D. Timus, D. Cimponeriu, P. Apostol, E. Manaila, G. Craciun, and E. Ahmadi: Classic and molecular cytogenetic analysis regarding human reactivity to beta radiation

11.40-12.00 B. Griciene, G. Slapsyte: An influence of occupational exposure on level of chromosome aberrations in nuclear power plant workers

9.20-12.20 Mathematical modeling of radiation effects Room B

Chairpersons: B. Leonard and I. Balásházy

9.00-9.50 B. Leonard: Measurements and modeling for examination of magnitudes and thresholds and transitions of cellular radio-protective mechanisms

9.50-10.20 I. Balásházy, I. Szőke, Á. Farkas, A. Filep, Sz. Zichler, and B.G. Madas: Risk of radon progenies and the LNT hypothesis

10.20-10.40 Coffee Break Poster area

10.40-11.00 G. Kudela, I. Balásházy: Bronchial radiation burden of the up clearing deeply deposited radon progenies

11.00-11.20 J.K. Kim, V.G. Petin, and K.P. Mishra: Developing a theoretical predictive model for cellular response to combined actions of low radiation and hyperthermia

11.20-11.40 A. Shabestani Monfared, M.A. Saber, and R. Abdi: Repeat analysis program in radiology department in North of Iran. A population radiation dose point of view

11.40-12.00 A.A. Oudalova, S.A. Geras'kin, V.G. Dikarev, N.S. Dikareva, and E.V. Chernonog: Non-linearity of dose-effect relationship at low level exposure on the example of cytogenetic effects in plant cells

12.00-12.20 A.A. Sabziparvar: Comparison of various angstrom-based models for estimation of solar energy in semi-arid regions

12.20-13.20 Lunch

13.20-14.20 Poster Session **Poster area**

14.30-17.50 Radiation induced genomic instability, bystander effects and adaptive response **Room A**

Chairpersons: M. Kadhim and M. Hill

14.30-14.35 M. Kadhim: Introduction

14.35-15.05 M.A. Hill: The relevance of radiation track structure at low dose and dose rates.

15.05-15.35 M. Kadhim: The role of radiation types and dose in induced genomic instability

15.35-16.05 S. Burdak-Rothkamm, K. Rothkamm, and K.M. Prise: ATR-dependent bystander effects in non-targeted cells

16.05-16.30 Coffee Break *Poster area*

16.30-16.50 C.F. Gibbons, M. Natarajan, S. Mohan, M.A. Kadhim, and A.J. Grosovsky: TNF-α-induced genomic instability in primary vascular endothelial cells

16.50-17.05 V. Dini, B. Di Carlo, M.A. Tabocchini, O. Sapora, M. Belli, and G. Simone: HL60 human premyelocitic cell line as a model system for bystander response

17.05-17.20 E. Kis, A. Benedek, H. Hegyesi, and G. Safrany: Bystander effects of low dose ionising irradiation

17.20-17.35 R. Fedortseva, S. Aleksanin, E. Zheleznyakov, and I. Bychkovskaya: The special cell effects and somatic consequences of exposure to low-dose radiation

17.35-17.50 A.M. Dám, E.N. Bogdándi, M. Sárdy, E. Tátrai, and B. Schoket: In vitro study on the cellular effects of low dose combined exposures

14.30-17.40 Long term radiation effects **Room B**

Chairpersons: M. Streit-Bianchi and T. Koana

14.30-15.05 M. Streit-Bianchi, J.H. Hendry, J.D. Morris, and S.A. Roberts: Apoptosis in spermatogonia irradiated p53 null mice

15.05-15.35 T. Koana, M.O. Okada, and K. Ogura: Reduction of the background mutation by a low dose irradiation of Drosophila spermatocytes at a low dose-rate

15.35-16.05 S. Volovyk, D. Bazyka, K. Loganovsky, V. Bebeshko: Deciphering free-radical code of radiation effects

16.05-16.30 Coffee Break *Poster area*

16.30-16.50 B. Djurovic, V. Spasic-Jokic, and V. Selakovic: Occupational exposure to ionizing radiation as a risk factor for free-radicals mediated diseases

16.50-17.10 O. Monteiro Gil, N.G. Oliveira, A.S. Rodrigues, M. Goulart, A. Laires, T.C. Ferreira, and J. Rueff: Persistence of micronuclei in peripheral blood lymphocytes of thyroid cancer patients 24 months after treatment with ^{131}I

17.10-17.25 M.V. Shaposhnikov, A.A. Moskalev, and E.V. Turysheva: Adaptive response in Drosophila melanogaster heat shock proteins mutant strains.

17.25-17.40 A. Moskalev: Low doze γ-irradiation influence on Drosophila life span in different genetics background

18.00-19.00 Low Ionising Radiation Defence Mechanisms Research
Round table discussion, chaired by A. Maisseu **Room A**

Friday, October 19, 2007

09.00-12.00 Radiation response modifiers **Room A**

Chairpersons: K. Sree Kumar and D. Bhattacharjee

9.00-9.50 K. Sree Kumar, S.P. Ghosh, M. Berbee, Q. Fu, T-C. Kao, and M. Hauer-Jensen: Tocols as possible radioprotectants for low level radiation exposure

9.50-10.10 A. Shirazi Hosseinidokht: A radiobiological review on melatonin: a novel radioprotector

10.10-10.30 Coffee Break *Poster area*

10.30-10.50 S.M.J. Mortazavi, S. Mehdizadeh, M. Zehtabian, S. Sina, M. Owji, and S. Derakhshan: A survey on radon reduction efficiency of zeolite and bentonite in a chamber with artificially elevated radon concentration

10.50-11.10 D. Bhattacharjee, S. Endo, K. Tanaka, M. Ohtaki, A. Sakaguchi, M. Yamamoto, V.Y. Golikov, and M. Hoshi: Radionuclides detected in lime samples that consumed with tobacco and betel nuts by people of Northeast India where head and neck squamous cells cancer (HNSCC) is prevalent

11.10-11.30 H. Mozdarani: Potent radio-protective effects of vitamins E and C on radiation induced DNA damage in gametes leading to lower

frequencies of chromosomal aberrations and micronuclei in subsequent embryos

11.30-12.00 C. Seymour, C. Mothersill: Natural products as radiation response modifiers

09.00-12.00 Health hazards of radiation accidents Room B

Chairpersons: M. Iospe and and G. Macsuga

9.00-9.35 M. Iosjpe, O. Reistad, J. Brown, A. Jaworska, and I. Amundsen: Radioecological consequences of a potential accident in the Norwegian coastal waters: uncertainties and knowledge gaps in methodology

9.35-10.10 A. Durakovic , F. Klimaschewski: Health Hazards of Uranium Dust from Radioactive Battlefields of the Balkan Conflicts, Eastern Afghanistan and Iraq after the Gulf Wars - Lessons for Civil Protection in the Terrorist Scenario of Radiological Dispersion Devices

10.10-10.30 Coffee Break Poster area

10.30-11.00 V. Bebeshko, D. Bazyka, S. Volovik, K. Loganovsky, V. Sushko, J. Siedow, H. Cohen, G. Ginsburg, N. Chao, J. Chute, M. Samuhel, W. Holden, and N. Steinberg: Radiation effects on man health, environment, safety, security: global Chornobyl mapping

11.00-11.25 D. Bazyka, I. Ilyenko, S. Klymenko, T. Lubarets, and N. Belyaeva: Early progenitor cells antigens and apoptosis in patients with secondary myelodysplasia exposed to low-dose ionizing radiation after Chernobyl accident

11.25-11.45 E.B. Burlakova: On the assessment of adverse consequences of Chernobyl accident

11.45-12.00 N.L. Shevtsova, D.I. Gudkov: Genetic effects of low dose irradiation on higher aquatic plants within the Chernobyl accident exclusion zone

12.10-13.10 Lunch

13.10-14.10 Poster Session **Poster area**

14.15-15.15 Marie Curie Award Lecture: M. Tubiana **Room A**

15.20-18.15 Low dose radiation effects: new aspects **Room A**

Chairpersons: C. Mothersill and K. Lumniczky

15.20-16.00 C. Mothersill, C. Seymour: Radiation-induced stress effects following low dose exposure

16.00-16.25 A. Meunier, M. Atkinson, S. Bouffler, L. Mullenders, H. Paretzke, and L. Sabatier: Risc-rad: A European integrated approach to the problem of low doses

16.25-16.50 S. Salomaa, E.G. Wright, G. Hildebrandt, M. Kadhim, M.P. Little, K.M. Prise and O.V. Belyakov: Non-targeted effects of ionising radiation (NOTE) – a new European Integrated project, 2006-2010.

16.50-17.10 Coffee Break *Poster area*

17.10-17.35 K. Lumniczky, T. Szatmári, N. Bogdándi, and G. Sáfrány: Effects of low dose irradiation on the main immune parameters and on the antitumor immune surveillance in mice

17.35-17.55 H. Mozdarani, R.N. Moghadam: Very low dose and dose-rate X-ray induced adaptive response in human lymphocytes at various cell cycle stages against bleomycin induced chromatid aberrations

17.55-18.15 S.M.J. Mortazavi, M.R. Rahmani, A. Rahnama, A. Saeed-Pour, E. Nouri, N. Hosseini, and M.M. Aghaiee: The overall results of a study on the stimulatory effects of topical application of radioactive lantern mantle powder

15.20-16.50 Radiation-induced transcriptional profiles Room B

Chairpersons: M.A. Benotmane and H. Hegyesi

15.20-16.00 M.A. Benotmane, J. Verheyde, L. Leyns, A. Michaux, A. Janssen, M. Neefs, and L. de Saint-Georges: Transcriptomic analysis of the effect of embryonic irradiation on Cognitive functions

16.00-16.25 R. Amendola, E. Fratini, M. Piscitelli, D.E. Sallustio, M. Angelone, M. Pillon, F. Chiani, V. Licursi, and R. Negri: In vivo transcriptome modulation after low dose of high energy neutron irradiation

16.25-16.50 G. Gruel, P. Voisin, S. Roch-Lefevre, E. Gregoire, X. Gidrol, P. Voisin, and L. Roy: Gene expression variations in lymphocyte subpopulations in response to low dose of ionizing radiations

16.50-17.10 Coffee Break Poster area

18.20 Closing Ceremony Room A

19.15 Congress Dinner

Saturday, October 20, 2007

9.00-13.00 Sightseeing tour by bus (free for registered participants)

Posters

Thursday, October 18, 2007

Non DNA targeted effects of low dose radiation

1. E.B. Burlakova: Salient features of low-level radiation effects

2. E. Kis, A. Benedek, H. Hegyesi, and G. Safrany: Bystander effects of low dose ionising irradiation

3. S.I. Zaichkina, O.M. Rozanova, G.F. Aptikaeva, A.Kh. Akhmadieva, E.N. Smirnova, S.P. Romanchenko, O. Vachrucheva, S. Sorokina, and A. Dyukina: Adaptive response and genetic instability induced by a low-dose rate radiation simulating the high-altitude flight conditions on mice in vivo

4. T. Homma, M. Tsukimoto, Y. Muto, Y. Ohshima, and S. Kojima: Gamma-ray irradiation induce suppression of TNF-α production via up-regulation of mitogen-activated protein kinase phosphatase-1

5. Y-R. Choi, H-M. Choi, and G-H. Park: Detection of the proteins with different arginine methylation status induced by low dose irradiation

6. R. Georgieva, A. Acheva, E. Zaharieva, I. Rupova, and F. Lyng: Bystander effect in γ-irradiated peripheral blood

7. R. Georgieva, I. Giuleva, I. Rupova, J. Djunova, E. Zaharieva, A. Acheva, and M. Vukov: Radiation hormesis at occupational exposure

8. S. Kojima, H. Hayase, and M. Takahashi: Activation of immune functions via induction of glutathione of lymphocytes by low-dose, whole-body irradiation with gamma-rays

9. M. Tsukimoto, F. Tago, H. Nakatsukasa, and S. Kojima: Repeated 0.5 Gy gamma-ray irradiation attenuates autoimmune desease in MRL-lpr/lpr mice with up-regulation of regulatory T cells

10. S.M.J. Mortazavi, S. Mehdizadeh, E. Ganjalikhan, A. Nikfarjam, S. Darakhshan, and F. Alizadeh: Survival adaptive response in rats induced by some common radiographic procedures

11. Y. Mutou, Y. Ibuki, and S. Kojima: Immunomodulatory effects of ultraviolet B irradiation on atopic dermatitis in NC/Nga mice

12. H. Nakatsukasa, M. Tsukimoto, F. Tago, Y. Ohshima, A. Masada, and S. Kojima: Therapeutic effect of gamma-ray on collagen-induced arthritis via up-regulation of regulatory T cells

13. V.I. Vysotskii, A.A. Kornilova: The direct physico-molecular (nonenzyme) mechanism of hormesis and dose-response self-induced radioprotective effect at combined action of weak ionizing radiation and free radicals on DNA

14. V. Dini, B. Di Carlo, M.A. Tabocchini, O. Sapora, M. Belli, and G. Simone: HL60 human premyelocitic cell line as a model system for bystander response

15. Y. Ohshima, M. Tukimoto, and S. Kojima: Inhibitory mechanism of low-dose, whole-body irradiation with gamma-rays against tumor metastasis

16. S.R. Mahdavi, D. Moslemi: Long term changes of prostacyclin in radiation myelopathy

Consequences of environmental pollutions

17. K. Kant: Is exposure to over ground radon as dangerous as they say?

18. S.A. Igumnov, I.V. Grigorieva: The quality of life of the patients suffering from thyroid cancer

19. S.A. Igumnov: Mental and behavioural disorders in Belarusian persons exposed in utero to radiation following the Chernobyl accident

20. K. Kant, R.G. Sonkawade, and S.K. Chakarvarti: Radiological impact of presence of Radon, Thoron and their progeny in the environment of LPG bottling plant

21. L.S. Coretchi, and I.N. Bahnarel: Medical and biological aspects of the Chernobyl nuclear accident influence on the population of the Republic of Moldova

22. T.V. Marinenko, G.V. Gorodetski, and I.A. Kozeretskaya: Drosophila as a model object into study Chernobyl NPP after

23. A.V. Protsenko, I.A. Kozeretskaya: Natural populations of Drosophila melanogaster from radioactively contaminated territories of Ukraine

24. M. Naboka, V. Shestopalov, A. Kravez, E. Chaban, and A. Lichosherstov: Analysis of correlation between non-cancer morbidity of children and the internal dose of ^{137}Cs

Occupational radiation exposures

25. R.P. Chauhan: Low-level radiation exposure and its health effects

26. S. Aleksanin, E. Zheleznyakov, and R. Fedortseva: Analysis of the experience of providing radiation protection of population and environment within the international collaboration network

27. V.I. Vysotskii, A.B. Tashyrev, and A.A. Kornilova: Experimental observation and investigation of reactor Cs-137 isotope deactivation in biological cells

28. F. Zakeri, M. Honarjoo, M. Rajab pour, A. Zahadat, M.J. Ahmad pour, and K. Asghari: Cytogenetic and hematological studies in the workers occupationally exposed to low levels of ionizing radiation

Friday, October 19, 2007

Genetic effects of radiation

29. S. Bhattacharya, P.K. Poddar: Effect of magnetic field on the living cells and chromosomes

30. M.K. Sharma, A.S. Yadav: Increased frequency of micronucleated exfoliated cells among humans exposed in vivo to mobile telephone radiations

31. X. Wang, Y. Furusawa, M. Suzuki, R. Hirayama, Y. Matsumoto, and Y. Qin: Genomic mutation study for long-term cells induced by carbon ions

32. I.B. Mosse: Some chemical influence on genetic effects of ionizing radiation and biodosimetry problems

33. P.K. Mallick, S.K. Ghosal, and C. Chakrabotrty: Handling low radiation β rays: no grave concerned

34. H. Florou, V. Tsytsugina: Comparative radiological and conventional pollution impact recording in the aquatic environment by use of a cytogenetic tool

35. V. Balachandar, B.L. Kumar, K. Suresh, R. Sangeetha, P. Manikantan, and K. Sasikala: Chromosomal aberrations in mobile phone users in Tamilnadu, Southern India

36. V.A. Saenko, Yu. Nakazawa, T.I. Rogounovitch, K. Suzuki, N. Mitsutake, M. Matsuse, and S. Yamashita: Attenuation of radiation-induced DNA damage due to paracrine interactions between normal human epithelial and stromal cells

Modeling of radiation effects

37. S.R. Mahdavi, A. Shirazi, A. Khodadadee, M. Ghaffory, and A. Mesbahi: Monte Carlo simulation of TLD response function: scattered radiation application

38. J.K. Kim, V.G. Petin, and S.V. Belkina: Mathematical description of synergistic interaction between radon and smoking

39. S. Mehdizadeh, R. Faghihi, S. Sina, and M. Zehtabian: Evaluation of dose equivalent to the people accompanying patients in diagnostic radiology using MCNP4C Monte Carlo code

Diagnostic radiation exposures

40. S.M.J. Mortazavi, F. Aminzadeh, A. Manshouri, M. Kamali, M. Rezaiean, and R. Vazirinejad: Maternal dental radiography during pregnancy is not associated with term low birth weight

41. S.A. Rahimi: Evaluation of radiology personnel practice of Mazandaran University of Medical Sciences

42. S. Mehdizadeh, S. Vaziefehdoust: Radiation protection awareness in Dentistry students

Modification of radiation effects

43. S.J. Hosseinimehr, V. Zakaryaee, A. Ahmadi, and S. Akhlaghpoor: Radioprotective effects of chlorogenic acid against mortality induced by gamma irradiation in mice

44. R.M. Samartha: Exploration of radiomodifying effects of peppermint extract (mentha piperita linn) against gamma radiation: in vivo studies

Alterations in transcriptional and lipid profiles

45. H.M. Choi, Y-R. Choi, and G-H. Park: Identification of differentially expressed genes in normal human fibroblast irradiated with low- and high-dose γ-ray

46. L. Coretchi: DNA damage-related gene expression as biomarkers to assess low dose radiation exposure

47. A. Benedek, E. Kis, H. Hegyesi, and G. Sáfrány: Low dose radiation effects on the transcription of consensus radiation response genes in primary and immortalized human fibroblast cells

48. S.Y. Choi, and H.W. Chung: Epidemiological studies on radiation workers in Korea

49. Y-W. Jin, Y-J. Na, Y-J. Lee, S. An, M. Jung, H. Kim, S.Y. Nam, C.S. Kim, K.H. Yang, S.UP. Kim, W.K. Kim, W-Y. Park, K-Y. Yoo, C.S. Kim, and J.H. Kim: Comprehensive analysis of time and dose-dependent patterns of gene expression in a human mesenchymal stem cell line exposed to low-dose ionizing radiation

50. K-E. Moon, M-S. Jung, S-H. Sung, Y-K. Chang, I-K. Park, Y-M. Paek, S-G. Kim, T-I. Choi, and Y-W. Jin: Effects of radiation and apolipoprotein E on lipid profile among workers of nuclear power plants in Korea

Radiation effects in eukaryotes

51. B.Y. Chung, J-H. Kim, S.S. Lee, and J-S. Kim: The boosting effects of cell wall formation in Arabidopsis thaliana L. using gamma irradiation

52. B.C. An, J-S Kim, S.S. Lee, S. Barampuram, E.M. Lee, S.G. Wi, W.J. Park and B.Y. Chung: Differential modification of the pseudomonas aeruginosa PAO1 outer membrane under hydrogen peroxide and gamma ray

Increased natural background radiation

53. I.R. Ajayi: Concentration and vertical distribution of Cs-137 in the undisturbed soil of Southwestern Nigeria

54. O.S. Ajayi, T.P. Owolabi: Determination of natural radioactivity in drinking water in private dug wells in Akure, Southwestern Nigeria

55. K.S. Suh, K.C. Kim, I.Y. Chun, S.H. Jung, and C.W. Lee: Tracer experiment by using radioisotope in surface water environment

56. S.A. Mujahid: Assessment of natural radiation exposure and radon exhalation rates from the soil of Islamabad district of Pakistan

Abstracts

The abstracts are presented in alphabetical order according to the first author

CONCENTRATION AND VERTICAL DISTRIBUTION OF CS-137 IN THE UNDISTURBED SOIL OF SOUTHWESTERN NIGERIA

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The results of measurements of Cs-137 in soil profiles which were sampled in undisturbed soil in Ondo, Ekiti and Oyo states in the southwestern area of Nigeria are presented in this paper. Samples were collected from nine soil profiles. The vertical distribution of Cs-137 in the soil profiles have been determined. Caesium concentration ranged from 0.31 ± 0.10 $Bqkg^{-1}$ in the 0-2 cm depth to a maximum of 1.25 ± 0.21 $Bqkg^{-1}$ in the 6-8 cm depth at some sites and from 3.16 ± 0.16 $Bqkg^{-1}$ in 0-5 cm depth to below detection limit (BDL) at 20-25 cm at another site. The results generally show that fifteen years after the chernobyl accident and more than 40 years after the nuclear probes, Cs-137 still remains within 25 cm of upper layer of soil in the region and its penetration in the soils is a very slow process. The mean value of effective dose commitment due to the presence of caesium in soil in the entire region was found to be 10.77μSv.

DETERMINATION OF NATURAL RADIOACTIVITY IN DRINKING WATER IN PRIVATE DUG WELLS IN AKURE, SOUTHWESTERN NIGERIA.

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A gamma-ray survey and analysis of drinking water from 20 private dug wells from Akure, Southwestern Nigeria have been conducted in this work. These were done in order to quantify the activity concentrations of the gamma emitters ^{226}Ra and ^{228}Ra from ^{238}U and ^{232}Th series respectively as well as ^{40}K in these private well waters. Measurements were done using high-resolution high-purity (HPGe) vertical co-axial detectors (Canberra, GC 2018-7500 model) coupled to a Canberra Multichannel Analyzer (MCA) computer system. Activity concentrations ranged from 0.57 to 26.86Bq l^{-1}, 0.20 to 60.06Bq l^{-1} and 0.35 to 29.01Bq l^{-1} for ^{226}Ra, ^{228}Ra and ^{40}K respectively. The measured radionuclide concentrations were compared with data from other parts of the world and used to estimated annual effective dose for age groups < 1y, 2-7y and ≥ 17y. Total annual effective doses from the intake of these radionuclides in dug well drinking water ranged from 0.02 to 76.84mSv y^{-1}, 0.02 to 38.80mSv y^{-1} and 0.05 to 481.60mSv y^{-1} for age group < 1y, 2-7y and ≥ 17y respectively. The total annual effective doses were considerably higher than both the World Health Organisation (WHO) and the International Commission on Radiological Protection (ICRP) recommended limits.

ANALYSIS OF THE EXPERIENCE OF PROVIDING RADIATION PROTECTION OF POPULATION AND ENVIRONMENT WITHIN THE INTERNATIONAL COLLABORATION NETWORK

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The All-Russian Center of Emergency and Radiation Medicine (ARCERM) in St. Petersburg is a specialized radiation health institution and World Health Organization (WHO) collaborating center within the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN), which primary objectives are:

- To promote medical preparedness for radiation accidents and radio-nuclear threats among WHO Member States;
- To provide medical and public health advice, assistance and coordination of medical management at international and regional levels in the case of a nuclear accident or radiological emergency;
- To assist in follow-up studies and rehabilitation.

ARCERM serves as a national focal point for advice and possible medical care in cases of radiation injuries in humans as well as assists WHO to prepare relevant documents and guidelines, provides training in radiation medicine, distributes relevant information to the medical community and the public and carries out scientific investigations on radiation effects on humans. The Center is prepared to undertake actions on medical management of possible radiation emergencies both on national and international level as a member of REMPAN network. The assistance provided by ARCERM may also include providing radiation medicine and other appropriate specialists, scientific services and expertise, equipment and medical services for diagnosis, prognosis, medical treatment and medical follow-up of persons affected by radiation.

In case of radiation accident the Center has standard operating procedures at country level. It includes the system of warning and data collection, setting up special wards for receiving radiation victims, radioactivity control station, primary deactivation and treatment as well as providing personal protection for staff. WHO, as well as other co-operating international organizations, are notified and provided with relevant information through the International Atomic Energy Agency (IAEA). WHO helps establish a link between the country and REMPAN assisting center(s) and Regional Offices, keeping all REMPAN centers informed about the details of the accident and progress in its management.

ARCERM has all necessary capacities to perform its activities, which include 120 in-patient beds, excellent diagnostic facilities and research laboratories, psychological support team as well as qualified staff including specialists in a wide range of medical fields. The database of radiation case histories includes long-term follow-up information on 16 thousands of over-exposed persons, mostly clean-up workers of Chernobyl accident.

In November 2004 the simulation exercise was carried out with participation of ARCERM as a major player in emergency response to radiation accident. Telemedicine facilities were actively used during the exercise. In October 2006 another large-scale simulation exercise within the framework of Russia-NATO collaboration was held in Rome, Italy with the participation of ARCERM.

ARCERM regularly participates in biannual meetings between REMPAN members to promote cooperation within the network, to exchange information and experience and to maintain the network in a permanent operating state. The 10th REMPAN meeting was hosted by ARCERM in St. Petersburg in 2004.

IN VIVO TRANSCRIPTOME MODULATION AFTER LOW DOSE OF HIGH ENERGY NEUTRON IRRADIATION

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Objective: This project aims to the identification of an hypothetical transcriptome modulation of mouse peripheral blood lymphocytes and skin after exposure to high energy neutron *in vivo*. Positive candidate genes isolated from mice in *in vivo* experiments will be selected and evaluated for both radioprotection issues dealing with cosmic ray exposure, and for biomedical issues mainly for low doses and non-cancer effects.
Methods: High energy neutron irradiation is performed at the ENEA Frascati, neutron generator facilities (FNG), specifically dedicated to biological samples. FNG is a linear electrostatic accelerator that produces up to 1.0×10^{11} n/s 14 MeV neutrons via the D-T nuclear reaction. The dose-rate applied for this study is of 0.7 cGy/min. The functional genomic approach has been performed on six animals for each experimental points: un-irradiated; 20 cGy, 6 hours and 24 hours delayed time after exposure. Preliminarly, a pool of total RNA is evaluated on commercial micro-arrays containing large collections of *mus musculus* cDNAs. Statistical filtering and functional clustering of the data is carried out using dedicated software packages.
Results: Candidate genes are selected on the basis of responsiveness to 20 cGy of exposure, with a defined temporal regulation. We plan to organize a systematic screen focused on genes responding to our selection criteria, in *in vivo* mouse experiments, and correlate their differential expression to the human counterparts. A specific cross species database will be created with all the functional information available in standardized format (MIAME: minimal information about micro-arrays experiments).
Conclusions: A lack of information on *in vivo* experiments is still evident for low doses exposure, especially for neutron of cosmic interest. Individual susceptibility, extensive number of animals to be processed, lack of standardization methodologies are among problems to be solved for these studies. To this end, we pursue to define a pattern of expression related to tissues of pivotal interest for both health and biomarkers exposure.

The project is partially funded by Italian Space Agency (ASI), MOMA Contract, 2006-2009.

DIFFERENTIAL MODIFICATION OF THE *PSEUDOMONAS AERUGINOSA* PAO1 OUTER MEMBRANE UNDER HYDROGEN PEROXIDE AND GAMMA RAY

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Objective: *Pseudomonas aeruginosa* PAO1 is causes opportunistic infections in humans. Studies with animals suggest that an adaptive mechanism is important for the ability of *P. aeruginosa* PAO1. The adaptive mechanism is protective mechanism against oxidative stress. This mechanism is aimed at preventing by reactive oxygen species. Reactive oxygen species can induce and modulate a variety of biological responses including gene expression.
Materials and Methods: *Pseudomonas aeruginosa* PAO1(a wild-type strain) was grown aerobically with vigorous shaking at 30°C in LB broth (Difco). When the optical cells density at 600 nm reached 0.4 that exposed to 0.5-50 mM H_2O_2 for 30 min and 30-100 Gy Gamma irradiation (^{60}Co, ca.150 TBq of capacity, AECL) for 30 min. For the recovery, the cultures were immediately exchanged fresh media and incubation for 30 min. then, cells were prefixed with 2.5% glutaraldehyde for 30 min at 4°C. After two washes by centrifugation at 15,000 X g for 5 min each, the cells were postfixed with 1% osmium tetroxide for 16 h at 24°C. The sample was dehydrated with absolute ethanol, stained with 2% uracyl acetate, embedded in Epon resin. Thin sections were stained with lead citrate and uranyl acetate and observed with a electron microscope. Expression level of candidate genes were analyzed using real-time PCR. The amplification program was consist of one cycle at 94°C for 30 sec, followed 40 cycles of 94°C (5 sec) - 60°C (31 sec).
Results and Conclusion: In the present study, we have observed differential membrane damage to *P. aeruginosa* PAO1 cells when exposed to different oxidative stresses such as hydrogen peroxide 0.5-50 mM for 30 min and gamma radiation 30-100 Gy for 30 min using TEM. In oder to understand its behaviour, we isolated 3 genes which are related to membrane maintaining. Its transcription level was identified using Real-Time PCR. Each gene was differently expressed under various stresses.

RADIATION STERILIZATION OF HARMFUL ALGAE IN WATER

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Objective: Drinking water, water used in food production and for irrigation, water for fish farming, waste water, surface water, and recreational water have been recently recognized as a vector for the transmission of harmful micro-organisms. The human and animal harmful algae is a waterborne risk to public health and economy because the algae are ubiquitous and persistent in water and wastewater, not completely removed by physical-chemical treatment processes, and relatively resistant to chemical disinfection. Gamma and electron beam radiation technology is of growing in the water industry since it was demonstrated that gamma and electron beam radiation is very effective against harmful algae.
Materials and Methods: Harmful algae (*Scenedesmus quadricauda*(Turpin) Brebisson 1835 (AG10003), *Chlorella vulgaris* Beijerinck 1896 (AG30007) and *Chlamydomonas* sp. (AG10061)) were distributed from Korean collection for type cultures (KCTC).
Strains were cultured aerobically in Allen's medium at 25□ and 300 umol/m2s for 1 week using bioreactor. We investigated the disinfection efficiency of harmful algae irradiated with gamma (0.05 to 10 kGy for 30 min) and electron beam (1 to 19 kGy for 5 sec) rays.
Results and Conclusion: We investigated the disinfection efficiency of harmful algae irradiated with gamma and electron beam rays of 50 to 19000 Gy. We established the optimum sterilization condition which use the gamma and electron beam radiation. Gamma ray disinfected harmful algae at 400 Gy for 30 min. Also, electron beam disinfected at 1000 Gy for 5 sec. This alternative disinfection practice had powerful disinfection efficiency. Hence, the multi-barrier approach for drinking water treatment in which a combination of various disinfectants and filtration technologies are applied for removal and inactivation of different microbial pathogens will guarantee a lower risk of microbial contamination.

CHROMOSOMAL ABERRATIONS IN MOBILE PHONE USERS IN TAMILNADU, SOUTHERN INDIA.

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Radiofrequency (RF) waves have long been used for different types of information exchange via the airwaves—wireless Morse code, radio, television, and wireless telephony. Increasingly larger numbers of people rely on mobile telephone technology, and health concerns about the associated RF exposure have been raised, particularly because the mobile phone handset operates in close proximity to the human body, and also because large numbers of base station antennas are required to provide widespread availability of service to large populations. In the present study chromosomal damage investigations were carried out on the peripheral blood lymphocytes of individuals using mobile phones, being exposed to MW frequency ranging from 800 to 2000 MHz.

The aim of this study is to establish whether mobile phone use (n = 27) increases the frequency of chromosome aberrations (CA) in peripheral blood lymphocytes compared with controls (n = 27) in Tamilnadu, India. After signing a consent form, volunteers provided blood samples (5 ml) to establish cell cultures at 52 hrs. For CA analysis, 100 complete metaphase cells from each subject were evaluated.

In the present study, in mobile phone users highly significant results were obtained when compared to control groups.

These results highlight a correlation between mobile phone use (exposure to RFR) and genetic damage and require interim public health actions in the wake of widespread use of mobile telephony.

Key words: Mobile phone users, Chromosomal Aberrations, Tamilnadu

RISK OF RADON PROGENIES AND THE LNT HYPOTHESIS

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Epidemiological investigations, cell and animal irradiation experiments have demonstrated that ionizing radiation may induce cancer and the risk from exposure of comparatively high levels of ionizing radiation is proportional to dose. However, the biological response to low doses of radiation is poorly understood. In this dose range, the linear-non-threshold (LNT) dose – effect hypothesis is recommended in current radiation protection applications. Inhaled radon progenies present more than the half of the natural radiation burden. The numerical description of their deposition along the airways and the quantification of the related cellular radiation burden may provide useful information regarding the health effects of low doses and LNT hypothesis.

Histological studies of lungs of former uranium miners present strong correlation between primer deposition hot spots and neoplastic lesions. Most of these lesions were located along the carinal regions of the large bronchial airways in generations 3-5.

In the present work, computational fluid dynamics approaches have been applied to simulate the deposition distribution of inhaled radon progenies within the upper and central human airways. The geometry and epithelial lung tissue were digitally reconstructed based on anatomical and histological data available in the literature. Single and multiple hit distributions of alpha-tracks with epithelial cell nuclei and distributions of cell nucleus doses have been computed applying Monte Carlo modelling techniques. The unit track length microdosimetric approach has been integrated into the model to compute cell death and cell transformation probabilities.

Based on the results, local deposition densities, hit probabilities and other microdosimetric parameter values may be up to two-three orders of magnitude higher than the average values. Cellular radiation dose calculations revealed that some cells or cell clusters may receive high doses even at low exposure conditions. Applying the model to different radiation burdens useful relations can be received regarding the LNT hypothesis.

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EARLY PROGENITOR CELLS ANTIGENS AND APOPTOSIS IN PATIENTS WITH SECONDARY MYELODYSPLASIA EXPOSED TO LOW-DOSE IONIZING RADIATION AFTER CHERNOBYL ACCIDENT

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Background: Myelodysplastic syndromes are clonal myeloid disorder characterized by ineffective hemopoiesis associated with bone marrow dysplasia, resulting in myeloid leukemia. Increased apoptosis has been shown in MDS as a possible explanation for this paradox. Increase of apoptosis was demonstrated in healthy individuals exposed to low-dose irradiation. indicating its possible modifying role on the myelodysplasia pathway after irradiation.

Patients and Methods: A study of bone marrow (BM) and peripheral blood (PB) was performed in 49 MDS patients (refractory anemia (RA) - 25; refractory anemia with the excess of blasts (RAEB)- 16 cases; refractory anemia with the excess of blasts in transformation (RAEB-t) – 6; chronic myelomonocytic leukemia (CMML)– 2 cases). Age was between 30-77 years (mean – 55,7). In 14 patients MDS was initiated at the late period after low-dose irradiation during clean-up works at Chernobyl accident (mean dose 239.0±35.6 mSv); 15 were exposed at the radiation-contaminated territories (24.3±6.2 mSv). Control group included 20 healthy donors (mean age 51,0). Expression of CD 34, CD13, CD33, CD71, CD117, HLA-DR and bcl-2 protein was studied by flow cytometry analysis. Spontaneous and verapamil-induced apoptosis was measured by Annexin V assay and CD95 expression. Flow cytometry analysis was performed using a FACScan flow cytometer.

Results: RAEB, RAEB-t and CMML were characterized by high $CD34^+$ (68,0±7,08%), $CD71^+$, $CD117^+$ or $CD117^+34^+$ cell counts associated with poor prognosis and transformation to acute leukemia. BM CD34+ cell subset demonstrated the prevalence of the lineage committed progenitors. In RA a statistically significant increase of mean values of fluorescence intensity of CD117, CD33, CD34 and CD71 antigens was observed together with a significant decrease of SSC parameters in granulocytes population of PB and BM in MDS patients compared with healthy donors group ($p<0, 01$). Hypogranularity in granulocytic region in BM is more marked in comparison with PB.

High level of apoptosis compared with healthy donors group was observed in RA cases, whereas a switch to a low level of apoptosis was detected in the RAEB, RAEB-t and CMML blasts. Cells demonstrated an increase of verapamil-induced apoptosis in the Annexin-V/PI test as comparing with the spontaneous apoptosis levels. For granulocytes a significant increase of the verapamil-induced apoptosis was shown in vitro. Patients with MDS had significantly increased expression of CD95 antigen ($p<0, 01$). Positive correlations were found between over-expression of CD 95 and the expression of CD34-receptor in RAEB, RAEB-t, CMML groups. Levels of CD 95 and Bcl-2 expression in RAEB, RAEB-t, CMML groups show negative correlations for lymphocytic ($r = -0,72$; $p<0,03$) and granulocytic ($r = -0,90$; $p<0,001$) populations. In RA such correlations were not shown for Fas-receptor and Bcl-2 positive cell counts in lymphocytes to the contrary to granulocytes, in which the statistically significant correlation between these values ($r = -0, 84$; $p<0,005$) was detected. Radiation exposed showed the highest CD95+ and low bcl2+ cell counts.

Summary. This study demonstrated some correlations of between early progenitors and increased apoptosis in myelodysplasia patients. CD95 apoptotic cells fraction and verapamil-induced apoptosis seem to be substantially higher in radiation exposed than in other MDS cases.

RADIATION EFFECTS ON MAN HEALTH, ENVIRONMENT, SAFETY, SECURITY: GLOBAL CHORNOBYL MAPPING

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Objectives: Ionizing radiation is a primordial terrestrial and extraterrestrial background and archetypal environmental stress-factor for life origin, evolution, and existence. We all live in radiation world inevitably involving nuclear energy production, nuclear weapon, nuclear navy, radioactive waste, pertinent medical diagnostics and treatment, etc with connected certain probability of relevant accidents and terrorist attack, space and jet travels, high natural background radiation, etc - actual and potential sources of radiation exposures and effects. State-of- the art integral fundamental research on radiation effects on man health, environment, safety, and security (REMHESS) is nowadays paramount necessity and challenge.

Methods and results: In given generalized conceptual framework unique 20 years Chornobyl multidimensional research and databases for radiation effects on man's all organism systems represent invaluable original basis and resources for mapping Chornobyl data and REMHESS challenge .Granted by DOE brand new Chornobyl Research & Service Project based on "Sarcophagus-II" (Object "Shelter") workers only one in radiation history baseline cohort, corresponding biorepository prospective dynamic data, integrated conceptual database system, and "state of the art" "omics" (genomics, proteomics, metabolomics) analysis is designed specifically for coherent addressing global REMHESS problems. In this connection "Sarcophagus-II" is only one unique universal model.

Conclusions: The fundamental goals of novel strategic Project and global Chornobyl mapping are to determine specific "omics" signatures of radiation for man depending of exposure peculiarity to understand ultimate molecular mechanisms of radiation effects, gene-environment interactions, etiology of organisms systems disorders and diseases, and to develop new biomarkers and countermeasures to protect man health in the framework of global REMHESS challenge.

Acknowledgment: This study is supported by the DOE Award Number DE-FC01-06EH06028.

LOW DOSE RADIATION EFFECTS ON THE TRANSCRIPTION OF CONSENSUS RADIATION RESPONSE GENES IN PRIMARY AND IMMORTALIZED HUMAN FIBROBLAST CELLS

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OBJECTIVE: The linear non-threshold model suggests that tumors might be induced even by low radiation doses. Still, most of the conventional methods are unable to detect damages below 100 mGy. We have studied whether transcriptional responses of consensus radiation response genes can be detected after low dose radiation exposure in directly exposed or bystander primary human fibroblast cells. The short term proliferation capacity of primary fibroblast cells in culture limits their long term application. Therefore we tried to immortalize the cells by the introduction of the human telomerase gene using retroviral vectors.
METHODS: Primary human fibroblast cell lines were established from skin biopsies of cancer patients and foreskin samples of young children. To create immortalized cell lines the human telomerase gene was cloned into a retroviral vector. Primary fibroblast cells were transduced and their proliferation capacity studied. To investigate radiation induced transcriptional alterations, cells were irradiated with ^{60}Co γ-rays (0; 0.01; 0,04; 0,1; 2 and 8 Gy) and 2 hours later total cellular RNA was isolated both from directly exposed and bystander cells. Transcriptional alterations were followed in consensus radiation response genes (CDKN1, GADD45, GDF15, IER5, PLK3, TP53INP1) with quantitative real time PCR (Corbett/ SybrGreen).
RESULTS: There is an elevated expression of CDKN1, GADD45, GDF15, PLK3, TP53INP1 in the exposed cells. We see only for the PLK3 a dose-dependent increase which manifested also at low doses. It seems this gene is the most sensitive to radiation at low doses. The hTERT-immortalized cells were morphologically identical to the primary cells. the radiation-induced transcriptional profile of immortalized cells were very similar to the primary ones.
CONCLUSIONS: hTERT immortalized cells can be used to mimic alterations in primary cells. Low dose irradiation doesn't influence the expression of most of the studied genes. PLK3 might be an efficient marker to estimate individually low dose effects.

TRANSCRIPTOMIC ANALYSIS OF THE EFFECT OF EMBRYONIC IRRADIATION ON COGNITIVE FUNCTIONS

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Brain damage induced by prenatal irradiation is of major concern in radioprotection. The brain is the final result of a series of well timed consecutive or concomitant waves of cellular proliferation, migration, and differentiation. Acute irradiation during pregnancy could selectively disturb these events to result in various forms of malformation such as microcephaly, reduced cortical thickness and mental retardation. Such events were previously described in epidemiological studies of the atomic bomb survivors of Hiroshima/Nagasaki.
Using cDNA-microarrays and real-time PCR we analyzed the modulated genes upon 50 cGy X-ray irradiation in embryonic mouse brain. The main activated pathways are involved in the induction of *Trp53* dependent programmed cell death, and the intercellular signalling cascades. The strong upregulation of *Ccng1*, *Trp53inp1* and *Cdkn1a* suggested that the tumour suppressor P53 is an essential regulator of the radiation induced stress response. Although in the *Trp53* null mutant embryos, our data highlights differential expression of genes involved in cell cycle progression. Various cyclins and cyclin-dependent kinases were downregulated.
Regional analysis of the irradiated anterior brain at E15 by *in situ* hybridization *with Trp53inp1* and *Ccng1* probes, suggested that there is a specific regional dependent expression in the anterior brain. Especially *Ccng1* and the P53 downstream cell cycle regulating gene indicated that the strongest effect can be observed in the cerebral cortex.
Taken together, radiation induced cell death of astrocytes in the cerebral cortex, and reduction in neurite length in maturating neurons, may interfere with a correct patterning of the brain and could jeopardize the formation of a correct neural network, leading to cognitive deficits in the mature brain.

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RADIONUCLIDES DETECTED IN LIME SAMPLES THAT CONSUMED WITH TOBACCO AND BETEL NUTS BY PEOPLE OF NORTHEAST INDIA WHERE HEAD AND NECK SQUAMOUS CELLS CANCER (HNSCC) IS PREVALENT

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Head and neck squamous cell cancer (HNSCC) is a very predominant type of cancer amongst the population of northeastern states of India than the rest of the world. Epidemiological and other data suggest consumption of betel nuts with/without tobacco and lime or tobacco alone with lime is a probable cause of high cancer incidence. The fundamental question arises that why this particular cancer is induced more in this region while people follow the similar habits elsewhere. Here we report the results on analysis of lime samples, collected from 12 different locations spectrophotometrically by high-purity germanium detector. The calculated activity of radionuclides showed to an average of 2.68, 0.10 and 0.83 Bq/gm for ^{238}U, ^{235}U and ^{232}Th series respectively for ten samples which are about 8 times higher than the normal background level of 0.37, 0.02 and 0.02 Bq/gm for ^{238}U, ^{235}U and ^{232}Th series found in control samples, collected from outside of northeast. The results conclusively showed for the first time that the lime samples almost throughout the northeastern India contain high proportion of radionuclides of uranium, thorium and actinides series. Further, annual effective dose of gamma radiation calculations from these results of earth's crust in northeast showed that gamma rays emitted at an average dose of up to 2.5 mSv/year/consumer approximately. This dose calculation in the oral cavity is underestimated as short range radiations by decay of alpha, beta and electron-capture etc are not considered in the present study. Continuous exposure of such low dose radiations emitting from different radionuclides to the sensitive squamous cells of the oral cavity for a long twenty years or more amounting to a total minimum dose of at least 50 mSv evidently contributes towards excessive HNSCC to the people of northeast than other parts of India.

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EFFECT OF MAGNETIC FIELD ON THE LIVING CELLS AND CHROMOSOMES

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Magnetic field of $2.25X10^3$ Gauss was applied for 30 minutes, 60 minutes and 9o minutes on the living meristematic cells of *Lathyrus sativus* L., a leguminous plant and on the bone marrow cells of albino Swiss mice, *Mus musculus* L.

Mitotic indices in meristematic cells of magnetic field treated plants at different times of treatment were found increased compared to those of control sets.

Chromosomal abnormalities of magnetic field treated plants were polyteny, aneuploidy, polyploidy, clumping, chromosome erosion and anaphase bridge.

Usual aceto-ocein, root tip squash technique was followed in this endeavour.

In situ estimation of nuclear DNA in meristematic cells of magnetic field treated Lathyrus sativus plants showed enhanced DNA content compared to those of the control sets.

In case of magnetic field treated mice similar increase in mitotic indices in bone marrow cells was found compared to those of the untreated ones following the usual flame-dry technique.

Different types of chromosomal aberrations of bone marrow cells of magnetic field treated mice were

acentric fragments, clumping, ring chromosomes, chromatid breaks, pulverization, aneuploidy, micronucleus, polyploidy, centric fusion etc. compared to those of the untreated mice.

Usual C-banding technique revealed the heterochromatin content of the chromosomes of bone marrow

cells in magnetic field treated ones. Centromeric fusion was clearly revealed in this technique. Heterochromatin content was found enhanced in the magnetic field treated bone marrow cells compared to those of untreated ones.

ATR-DEPENDENT BYSTANDER EFFECTS IN NON-TARGETED CELLS

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Radiation induced non-targeted bystander effects have been reported for a range of endpoints including the induction of γH2AX foci which serve as a marker for DNA double strand breaks. We have recently reported the induction of γH2AX foci in non-targeted bystander cells up to 48 hours after irradiation and the involvement of reactive oxygen species (ROS) and TGF-beta 1 in the induction of γH2AX foci (*Oncogene* (2007) 26:993-1002). Here, we wanted to determine the role of the PI3-like kinases ATM, ATR and DNA-PK in DNA damage signalling in bystander cells.

Conditioned medium from T98G cells irradiated with 2 Gy of X-rays was transferred onto non-irradiated cells that were subsequently analysed for the induction of γH2AX, ATR and 53BP1 foci as well as clonogenic survival.

Irradiated T98G glioma cells generated signals that induced γH2AX and 53BP1 foci in cells treated with the conditioned medium from irradiated cells. These foci co-localised with ATR foci. Inhibition of ATM and DNA-PK could not suppress the induction of bystander γH2AX foci whereas the mutation of ATR in Seckel cells abrogated bystander foci induction. A restriction of bystander foci to the S-phase of the cell cycle both in T98G cells and in ATR–proficient fibroblasts was observed. These results identify ATR as a central player within the bystander signalling cascade leading to γH2AX and 53BP1 foci formation, and suggest a mechanism of DNA damage induction in non-targeted cells.
Further investigations have shown decreased clonogenic cell survival in bystander T98G and ATR wild-type fibroblasts. ATR mutated Seckel cells and also ATM-/- fibroblasts were resistant to this effect suggesting a role for both ATR and ATM in the bystander signalling cascade with regard to cell survival.

Taken together, these observations support a hypothesis of DNA damage-induced accumulation of stalled replication forks in bystander cells which are subsequently processed by cellular DNA damage checkpoint and repair mechanisms, including ATR, leading to bystander cell killing.

ON THE ASSESSMENT OF ADVERSE CONSEQUENCES OF CHERNOBYL ACCIDENT

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Since 1987 till the present time, at the Emanuel Institute of Biochemical Physics, Russian Academy of Sciences, studies on the effect of low-dose low-level irradiation on biophysical and biochemical parameters of the genetic and membrane apparatus of cells of organs of exposed animals are being carried out. We investigated the structural parameters of the genome (by the method of DNA binding to nitrocellulose filters), structural parameters of nuclear, microsomal, mitochondrial, and plasmic (synaptic and erythrocyte) membranes (by the method of spin probes localized in various layers of membranes), the composition and oxidation degree of membrane lipids, and the functional activity of cells – the activity of enzymes, relationship between isozymic forms, and regulating properties. We investigated also the effect of low-level irradiation on the sensitivity of cells, biopolymers, and animals to subsequent action of various damaging factors, including high-dose irradiation. The animals were exposed to a source of ^{137} Cs γ-radiation at the dose-rates 41.6 x 10^{-3}, 4.16 x 10^{-3}, and 0.416 x 10^{-3} mGy. The doses were varied from 6 x 10^{-4} to 1.2 Gy. As a result of the studies performed, the following conclusions were made:

1. Low radiation doses affect actively the metabolism of animals and man.
2. Over certain dose ranges, low-level irradiation is even more effective than acute high-level.
3. The dose–effect dependence of irradiation may be nonlinear, nonmonotonic, and polymodal in character.
4. Doses that cause the extreme effects depend on the irradiation dose-rate (intensity); they are lower at a lower intensity.
5. . Low-dose irradiation causes changes (mainly, enhancement) in the sensitivity to the action of other damaging factors. [1,2]

We explain the nonlinear and nonmonotonic dose–effect dependence that we obtained in our experiments with low-dose low-level irradiation by changes in the relationship between damages and reparation of the damages. With this kind of low-level irradiation, the reparative systems either are not initiated (induced), or function inadequately, or are initiated with a delay, i.e., when the exposed object has already received radiation damages. Recently, the absence of reparation at low irradiation doses was verified on the cell level, [3] and the complex character of the dose dependence was confirmed [4]. Previously, we published a similar scheme of dependence of damages on irradiation dose, which was different for different dose ranges. According to the scheme, the quantitative characteristics were similar for the doses that differed by several orders of magnitude; in a certain dose range, the effect may have an opposite sign.The results obtained and supported by numerous experiments are important because the above dose dependences made it possible to come to conclusion about a radiogenic or non-radiogenic character of changes observed in an irradiated organism. The indisputable conclusion that if the effect increases with the dose it is evidence for its radiogenic nature is by no means in favor of an opposite statement, i.e., that the absence of a direct dose–effect dependence but its nonmonotonic character is evidence for the absence of a relation of the effect to irradiation. The controversial conclusions of International and Russian organizations stem mainly from the underestimation and misunderstanding of the effects of ultra-low and low irradiation doses, reluctance to apply other criteria to assess the consequences of irradiation on human health, and conviction (groundless) that low doses cause either no damages or such minor damages that they may be neglected and disregarded. In the lecture, data that elucidate the above controversies will be presented.

SALIENT FEATURES OF LOW-LEVEL RADIATION EFFECTS

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LOW-LEVEL RADIATION EXPOSURE AND ITS HEALTH EFFECTS

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The low level exposure to alpha radiation emitted from radon and its progeny in general environment and the dwellings has received continuing attention as the radon has been found to be ubiquitous radioactive air pollutants to which all the organisms (e.g. bacteria, plants or animals including humans) are exposed everyday to varying amounts of ionizing radiation. These radiations are spontaneously emitted by naturally occurring radioactive material like ^{238}U and ^{232}Th, ever since their existence on earth. The exposure to alpha radiation emitted from radon poses health hazards not only to the workers at industrial units like thermal power plants, gas fired power plants, coal fields and oil fields but also to the dwellers in normal houses in their surroundings. Radon being an inert gas can easily disperse into the atmosphere immediately on its release. The solid alpha active decay products of radon like ^{218}Po and ^{214}Po become airborne and get themselves attached to the aerosols, dust particles and water droplets suspended in the atmosphere. When inhaled during breathe, these solid decay products along with air may get deposited in the tracho-bronchial and pulmonary region of lungs resulting in the continuous irradiation of the cells which may be the cause of lung cancer. In the present work, we report on the estimation of the radon concentration, annual exposure and annual effective doses received by the workers working in the interior environment of some industrial units like thermal power plants and different types of dwellings of North India. For these measurements we have used the alpha sensitive solid-state nuclear track detector (SSNTD). The results indicate an increase in radiation dose received by the workers in thermal power plants due combustion of coal as compared with normal dwellings.

IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN NORMAL HUMAN FIBROBLAST IRRADIATED WITH LOW- AND HIGH-DOSE γ-RAY

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Objective: To identify differentially expressed genes in normal human fibroblast response to low- and high-dose irradiation and compare the gene expression profiles.
Methods: Human fibroblast BJ cells were irradiated with 0.02, 0.2 and 2 Gy doses of γ-ray and RNA was obtained at 24 h after exposure. cDNA microarray technology was used to analyze the transcript profiles. Gene expression changes were confirmed by reverse-transcription polymerase chain reaction (RT-PCR).
Results: The microarray assay revealed a number of up- and down-regulated genes by each of 3 doses of irradiation. The common radiation-responsive genes were involved in metabolic process and development. Furthermore, the common genes responsive to the low-dose irradiation (0.02 and 0.2 Gy) showed up-regulation for cell organization and biogenesis genes and down-regulation for signal transduction and development genes. A set of 2 Gy-responsive genes included up-regulated genes involved in signal transduction and immune system process, and down-regulated genes involved in signal transduction, cell organization and biogenesis.
Conclusion: We identified differentially expressed genes in normal human fibroblast induced by low- and high-dose irradiation. The result means that irradiation led to different responses in human cells according to the doses of γ-ray. Further functional studies are necessary to validate the role of these genes in these different cellular responses that resulted from low- and high-dose irradiation.

EPIDEMIOLOGICAL STUDIES ON RADIATION WORKERS IN KOREA

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Objectives: The aim of this study is to analyze the occupational exposure for external radiation and to evaluate radiation effects on Korean radiation workers.
Methods: The National Dose Registry contains radiation exposure records for all monitored radiation workers since its creation in 1983. We are carrying out epidemiological survey for radiation workers. The items of information included personal identification, employment and dose data. The frequencies of various types of chromosome aberrations in radiation workers were compared with controls. The data were analyzed according to year, sex, age, duration of occupation, exposure dose, etc. using SPSS statistical package(version 15.0). The goodness-of-fit test for Poisson assumption and dispersion test for detecting heterogeneity for Poisson distribution were done with chromosomal aberrations among study subjects.
Results: The total number of workers registered from 1983 to 2005 was 61,610. The number of workers steadily increased and the accumulated dose somewhat increased. The collective annual dose of radiation workers was 345.823 man Sv and the mean annual dose was 1.34mSv. The frequencies of chromosome aberrations in 102 workers were compared with those in 42 controls. The frequencies of all types of chromosome aberrations in the exposed subjects were higher than those in the control group. Poisson regression analysis showed that there was significant association of chromosome aberrations with radiation dose, duration of work, age and alcohol intake. We started to survey radiation workers in order to evaluate radiation effects, collected epidemiological data for 9,157 workers at present and analyzed their lifetime radiation exposure doses. Follow-up is carrying out using the Korean Mortality Data, Cancer Registry and individual investigation. Among study patients, 11 of 38 deaths were identified with cancer.
Conclusions: The data on occupational doses shows that radiation protection in Korea is improving, even though annual doses are still higher than other countries. Nevertheless, this finding brings to light the necessity of the workers to pay more careful attention to radiation protection procedures and practices, and suggest the need for continuous effort to implement procedures. The frequencies of all types of chromosome aberrations in the exposed subjects were higher than those in the control group. We are carrying out epidemiological survey in order to evaluate radiation effects on Korean workers based on radiation dose data from 2000. The epidemiological follow-up will be performed in order to detect and measure directly the risks of cancer.

DETECTION OF THE PROTEINS WITH DIFFERENT ARGININE METHYLATION STATUS INDUCED BY LOW DOSE IRRADIATION

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Department of Biochemistry Korea University College of Medicine Seoul Korea

Objective*:* The objective of this study is to detect the noble proteins that were functionally regulated by change of arginine methylation through irradiation of the low dose. The increase of the arginine methylation which is induced by low dose gamma-ray will have meaningful
Introduction: Exposure of cells to low doses of radiation has well documented biological effect, but the underlying regulatory mechanisms are still poorly understood. Arginine methylation is a post translational modification that results in the formation of asymmetrical and symmetrical dimethylated arginines. Post-translational methylation of arginine residues of proteins involved in a growing number of cellular processes, including transcriptional regulation, cell signaling, RNA processing and DNA repair, biological influence.
Methods: Human normal cell line Chang-liver was irradiation by gamma-ray of 0.02Gy, 0.2Gy. After irradiation, cells were incubated for 4h, 8h, 24h, and then harvested to prepare protein extracts. ASYM24(anti-dimethyl-Arginine, asymetric) antibody was used to Western blot and immunoprecipitation. Proteins that show different degrees of intensity between the two samples were analyzed by Mass spectrometry.
Results: We detected increased asymmetric arginine methylation of two proteins at 24h after a dose of 0.2Gy irradiation. The mass spectrometry identified that it is 27kDa and 73kDa porteins. The 27kDa is hypothetical protein that function does not know. The 73kDa protein is Mortalin, a member of the Heat shock 70 protein family, which correlate with the radioresistance response, control of cell proliferation and act as a chaperone.
Conclusion: Low dose radiation induces the change of asymmetric arginine methylation modification of arginine residues of hypothetical protein and mortalin. We expect that increase of arginine methylation in mortarin and hypothetical protein correlates with the radioresistance, the functional study for these proteins is necessary to clarify the biological effects in radioadaptive response.

THE BOOSTING EFFECTS OF CELL WALL FORMATION IN ARABIDOPSIS THALIANA L. USING GAMMA IRRADIATION

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Objective: Low doses of gamma irradiation can induce physiological and biochemical changes, resulting in faster vegetative growth and early flowering. However, there is no report on the relationship between low dose gamma irradiation and cell wall formation. Therefore, it is necessary for investigating the effect of gamma irradiation on cell wall formation.
Materials and Methods: Dry seeds (Arabidopsis thalianaL.) were irradiated at 0-200 Gy by gamma-ray irradiator (60Co, ca.150 TBq of capacity, AECL). The plants were grown in the Chungbuk National University green house facilities. The extract free residues were performed various experiments such as germination and growth rates, lignin content, alkaline nitrobenzene oxidation (NBO), neutral sugar composition, and histochemical analyses.
Results and Conclusion: The first experiment on seeds exposed to relatively low and high doses of ionizing radiation (0-200 Gy) was performed to select optimum dose of stimulating effect. The optimum dose based on the results of germination and growth rates is 40 Gy. Nineteen days after sowing (DAS), seeds exposed to 40 and 200 Gy showed a departure from the stem height and lignin content of the control. Seeds exposed to 40 Gy were significantly higher stem height and lignin content than control. In contrast, significant decreases occurred in both stem height and lignin content at 200 Gy. These differences continued for up to 31 DAS. Interestingly, all plants return to normal in terms of stem height and lignin content from 34 DAS. These results were confirmed by analyses of lignin units. The predominant lignin units such as guaiacyl and syringyl units were very similar to the trend of stem height and lignin content. In addition, morphological changes at 40 and 200 Gy were performed by histochemical analysis. Seeds exposed to 40 Gy were well developed xylem region, while 200 Gy irradiated samples were relatively inhibited xylem from development.

DNA DAMAGE-RELATED GENE EXPRESSION AS BIOMARKERS TO ASSESS LOW DOSE RADIATION EXPOSURE

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According to the UNSCEAR, the natural rays from the Sun and the Earth transmit about 2,4 mSv to each individual every year. Human activities expose us to an additional radiation dose (1,2 mSv/year), especially the techniques used in non-invasive medical imaging (radiography, CT scanners).

Ionizing radiation can induce a large spectrum of DNA lesions, but under optimal DNA repair conditions, the principal residual lesions of importance are misrepaired double-strand breaks / 1 /. Predictive markers of intrinsic radio sensitivity in healthy individuals are needed in monitoring their occupational or environmental radiation exposure and may predict a patient's response to radiotherapy. Radiation protection requires a thorough understanding of low dose ionizing radiation. Currently extrapolation from high doses is necessary to estimate the effects of low doses. Furthermore, it is critically important to have an appreciation of the variation in individual responses to radiation among the human population / 2 /.

Present estimates of the risks from radiation exposure are based largely on the "average" individual in an exposed population. However, clinical observations of adverse reactions to radiotherapy indicate large variations in individual radio sensitivity. Quantification of risk requires the identification of new parameters taking into account these differences in radiation responses. Therefore, a detailed knowledge of the mechanisms by which radiation induces cancer is essential. It is necessary to understand the various steps involved in the multistage process of radiation-induced tumor genesis and to answer the following specific question: Is there a link between radio sensitivity of individuals (short term) and susceptibility to cancer (late after exposure)?

Appearance of mutations consist one of more prominent consequence of the radiation action. The aim of our study consisted in the restriction fragment's length polymorphism (RFLP) analysis of pERT87-8/Tag1 and *16intron/Tag1* loci with determining of presence or absence of restriction site in the group of radiologists and in control group. It was demonstrated that the pERT87-8/Tag1 allele frequency on «mutant» chromosome was 2,4 fold higher than the frequency of this allele on «normal» chromosome (45,1% in compare with 18,5%, X^2=27,7, df=1, p<0.01). Therefore, in radiologists was revealed statistically significant difference of the frequency of polymorphic site pERT87-8/Tag1 compared to healthy donors. As for *16intron/Tag1* system it have been elucidated that the without restriction allele frequency site on «normal» chromosome was 2,0 fold higher than the frequency of this allele on «mutant» chromosome (71,5% in compare with 34,8%) χ^2=78,3, df=1, p<0,01). In the conclusion it is necessary to mention that there are significant difference in the frequency of the polymorph sites pERT87-8/Tag1 and *16intron/Tag1* in the group of radiologists in compare with the control group.

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MEDICAL AND BIOLOGICAL ASPECTS OF THE CHERNOBYL NUCLEAR ACCIDENT INFLUENCE ON THE POPULATION OF THE REPUBLIC OF MOLDOVA

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Stress factors action on the population health evaluation, especially on the emergency workers remains one of the most important problems of the contemporary medicine. In this line the Chernobyl nuclear accident (CNA) that took place on the 26th April 1986 at the Chernobyl nuclear power station (NPS) is an eloquent example. Radioactive substances produced in the result of CNA fell out in a significant part of the Europe, including the Republic of Moldova territory, affecting more than 5,000,000 persons. In CNA consequences liquidation participated a lot of military staff including a great number of reservists. Lack of previous experience in the field (it was the first large-scale nuclear accident) made it impossible to prepare specially trained personnel for CNA limitation and liquidation. Consequently a lot of military staff even from the first days presented to medical authorities with a gamma of symptoms, which were henceforth characterized as somatic diseases after detailed investigations.

Ionizing radiation influence on the health status of the participants in diminishing of consequences of the Chernobyl nuclear accident (PDCCNA) evaluation is difficult enough and so calls for an ample multilateral study applying modern diagnostic techniques. Large studies were yet conducted in the Russian Federation, the Ukraine and the Republic of Belarus. Acquired data suggests the existence of noticeable deteriorating effect of ionizing radiation produced secondary to CNA with the increased incidence of health status disturbances in affected population.

Approximately 3500 inhabitants from the Republic of Moldova took part in the Chernobyl nuclear accident consequences liquidation /1/.

Study objective comprises the determination of clinical, immunological and cytogenetic features in PDCCNA from the Republic of Moldova and their descendants.

Between 1996 and 2005 period 850 patients – participants in removal of consequences of Chernobyl nuclear accident (PRCCNA) with the nervous, heart-vascular and gastric-intestinal systems morbidity and their children were investigated, the investigation including the clinical, immunological and cytogenetic analysis.

The clinical investigations indicate that the PRCCNA compared to patients from the control group, were more susceptible to infectious and non-infectious diseases, with the prevalence of large polymorphism of nervous, heart-vascular and gastric-intestinal system, accompanied by the circulatory disorder of the vegetative nervous system.

The immunological analysis elucidates alterations in the immune system of the PRCCNA expressed through the increase of the activity of humoral indices of immunity and decrease of the cell immune system expressed through the decrease of total T-lymphocytes and B-lymphocytes. The correlation and simple regression analysis demonstrated the linear negative dependence between some immunological indices and dose level, r=-0, 54.

The hyper compensatory intensity of humoral immunity and natural resistance and obvious tendency to T-cell immunity insufficiency are revealed with monoclonal antibodies to CD-19, CD-3, CD-4, CD-8, and CD-16 and rosette forming reaction.

Cytogenetic research of the lymphocyte cultures of peripheral blood of PRCCNA and their children, living in the Republic of Moldova during the 19-20 years after the accident, elucidated the deterioration of the hereditary system, being expressed through high level of genomic, chromosomal, and chromatid type aberration. At the adult populations there dominated the chromosomal type of aberrations and at children, there prevailed the chromatid type.

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IN VITRO STUDY ON THE CELLULAR EFFECTS OF LOW DOSE COMBINED EXPOSURES

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Objectives: Low dose alpha particles derived from radon, induce non-targeted effects such as bystander phenomenon, adaptive response or genomic instability, which may increase or decrease the risk of lung cancer. Our study was aimed to investigate whether the low radiation dose induced effects are involved in carcinogenesis induced by multiple environmental exposures.
Methods: The interaction of low dose (mGy) alpha particles and the environ-menttal PAHs (polycyclic aromatic hydrocarbons), cadmium, nickel and asbestos exposures were investigated on human lung cell lines (BEAS-2B and HFL1). Cells were treated separately and in combinations with alpha irradiation. PAH-DNA adduct levels were determined by ^{32}P-postlabelling. DNA strand breaks were measured by Comet-assay. Micronucleus frequency, apoptosis and proliferation were also followed.
Results: Alpha irradiation (10 mGy) prior to PAH's treatment, substantially de-creased the adduct level. Alpha irradiation significantly induced DNA strand breaks, whereas the PAHs at 0.2 μM did not have measurable effect by the Comet assay. In combination of alpha irradiation and the PAHs, only benzo[a]-pyrene had a modifying, ie. additive effect to alpha irradiation. Metal compounds (Cd and Ni-chloride;) in low concentration (0,5-1μM) reduced the cytotoxicity of alpha particles, depending on the compound, incubation time, cell line treated and also low doses of radiation (mGy-s) reduced the cytotoxic effect of metals (cross-adaptive response). Further increases in concentrations and/or doses caused additive cytotoxic responses. The rejoining of DNA breaks was more efficient when the cells were treated in combination with glass fibres and low dose radiation then after each single exposures. The radio-adaptive response in-duced by 10 mGy alpha particles was diminished by Cd (24-48 h) incubation. Cd (0,01 mM) enhanced the radiosensitivity of cells. Bystander cells found to be more sensitive to Cd, then directly irradiated ones. In the presence of Cd the re-joining of the radiation induced DNA breaks slowed down. The data on proli-feration and micronuclei induction indicated that the genetic changes were detec-ted in the progeny of irradiated and Cd-treated cells.
Conclusion: It can be concluded that low dose radiation effects must be taken into consideration in estimating the health risk from combined multiple environmental exposures.
This research was supported by NKFP-1B/047/2004 and GVOP 3.1.1.-2004-05-0432/3.0 grants

HL60 HUMAN PREMYELOCITIC CELL LINE AS A MODEL SYSTEM FOR BYSTANDER RESPONSE

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Objective: to evaluate HL60 human premyelocitic cell line as a model system to study bystander response.

Methods: Hl60 cell line, isolated from the blood of a patient affected by premyelocitic leukemia, has 45-46 chromosomes with abnormalities mainly on chromosomes 5, 8 and X and can undergo chemical-induced *in vitro* differentiation. Differentiation gives rise to granulocytes, monocytes or macrophages depending on the drug used. We define as proliferative (AP) cells those in log phase of growth with less than 10 passages from thawing and as differentiated (D) cells those treated with 10 nM TPA (phorbol ester) for 72 hours. Phorbol ester treatment induces differentiation to monocytes and macrophages. Differentiation has been evaluated through the expression of differentiation cluster membrane antigens (CD95, CD9 and CD14).

***Results*:** AP cells resulted positive for CD95 and negative for CD9 and CD14, while D cells resulted positive for CD9 and negative for CD95 and CD14. Our data on AP and D cells showed that: (i) the level of intracellular reactive oxygen and nitrogen species (ROS and RNS) is lower in D cells compared to AP cells; (ii) radiation induced DNA damage (single and double strand breaks, SSB and DSB, as measured with the comet assay technique) is lower in D cells than in AP cells. This different radiosensitivity can be related to the higher degree of compactness of nuclear structure in D cells.

Radiation induced bystander effect (BE) was analyzed with the medium transfer technique. The medium from irradiated, with 0.5 Gy of γ-rays, AP cells was collected after 0, 2, 4 and 24 hours from irradiation and added to non irradiated log phase cells. The frequency of micronuclei formation in bystander cells was measured by using the cytokinesis block technique by adding cytochalasin B to the non irradiated culture together with the irradiated medium. Preliminary data indicate about 1.4-fold increase in micronuclei formation in bystander cells at 2 h that disappears after 4 h incubation.

Conclusion: These experimental findings show that HL60 could be a valuable cellular system to compare BE in cells with different physiological status; in particular. they could be used to study the influence of factors released from irradiated AP cells on non irradiated D cells and *vice versa*.

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OCCUPATIONAL EXPOSURE TO IONIZING RADIATION AS A RISK FACTOR FOR FREE-RADICALS MEDIATED DISEASES

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It was experimentally showed, that the exposure to low doses of ionizing radiation (IR) result in over-production of oxygen derived free radicals with inverse dose-rate effect. The oxidative stress that follows, especially cell membrane damage, was considered by Petkau, as crucial step in the induction of radiation injuries. From clinical research and practice with other-unexposed patients is known that this type of cell damage can lead to an impairment of cellular function and can cause many free-radicals mediated diseases, such as atherosclerosis, damage of heart muscles, inflammatory and immuno-reactive lesions, senile dementia, cancer, etc.
The aim of this paper is to investigate if occupational exposure to low doses of IR change the redox status of exposed personnel, and if so, is it the additional risk factor for free-radicals mediated diseases.
Subjects: 77 medical workers, devided in two groups: 44 occupationally exposed to ionizing radiation (E), and 33 controls (C), matched in age, gender, habits-daitary, alcohol consumption, smoking and exposure time, were exsamined.
Methods: Radiation dose accumulated over years was calculated on the basis of individual TL-dose records. Superoxide-anion and MDA production, as well as SOD (MnSOD, CuZnSOD) and GSH activity were determined in blood samples spectrophotometrically.
Results: Signifficantlly higher incidence of cataract, and higher, but not signifficant, incidence of cardiovascular diseases was noticed in exposed. Our results also confirmed significantly higher superoxide and MDA production ($p=0.0049$, 0.000028, respectevly), as well as, increased activity of MnSOD and CuZnSOD ($p= 0.0105$, 0.001, respectevly), and decreased level of GSH ($p=0.0599$) in exposed.
Conclusions: Our results showed that low doses of IR could induce oxidative stress and for that reason could be considered as additional risk factor for free radical-mediated diseases. Further epidemiological studies are needed for final result.

HEALTH HAZARDS OF URANIUM DUST FROM RADIOACTIVE BATTLEFIELDS OF THE BALKAN CONFLICTS, EASTERN AFGHANISTAN AND IRAQ AFTER THE GULF WARS - LESSONS FOR CIVIL PROTECTION IN THE TERRORIST SCENARIO OF RADIOLOGICAL DISPERSION DEVICES

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Purpose: The purpose of this study is to identify key health hazards of uranium dust from the radioactive battlefields (Balkan, Middle East and Eastern Afghanistan conflicts) to draw lessons for civil protection in the terrorist scenario of radiological dispersion devices (RDD). Gulf War I (GW I) in 1991 resulted in 350 metric tons of depleted uranium (DU) deposited in the environment and 3 to 6 million grams of DU aerosol dust particles released into the atmosphere, by the most conservative estimates. Its possible legacy (Gulf War disease) continues after the military conflicts (Operation Enduring Freedom, OEF, in Afghanistan and Gulf War II in Iraq). The symptoms of the multiorgan incapacitating progressive disease have been as numerous as their names, including incapacitating fatigue, musculoskeletal and joint pains, headaches, neuropsychiatric disorders, affects changes, confusion, visual problems, changes of gait, loss of memory, lympadenopathies, respiratory impairment, impotence, and urinary tract morphological and functional alterations. The disease is still a matter of controversy regarding etiology and pathogenesis of the syndrome commonly named Gulf War disease. It was underestimated and subsequently evolved in its clinical description through recognition of progressive symptomatology. **Methods:** UMRC's studies of the human contamination with uranium isotopes were conducted with the exposed subjects of Jalalabad, Spin Gar, Tora Bora, and Kabul areas in Afghanistan after OEF as well as Samawah, Baghdad and Basrah in Iraq after GW II. The urine samples of the subjects were analysed by the plasma mass spectrometry. The analytical methodology involved pre-concentration of the uranium using co-precipitation and/or evaporation, oxidation of organic matter, purification of uranium with ion exchange chromatography, and mass spectrometry with a double focusing Thermo-Elemental Plasma54 multi-collector ICP-MS equipped with a Daly detector for ion counting. **Results:** The results demonstrate that contaminated subjects from Afghanistan contained total uranium concentrations over 100 times higher than the range of averages in the world. The results of the studies of uranium concentrations in the military personnel after GW II are conclusive proof of the presence of DU isotopic ratios in the contaminated veterans. In addition the results are further enhanced by the verified presence of the man made uranium ^{236}U in the urine of symptomatic veterans. The studies have identified a correlation between uranium contamination, multiorgan non-specific illnesses similar to those encountered in GWI and the Balkan conflicts. The contamination of the exposed population by the radioactive dust inhalation has been verified by the multidisciplinary scientific reports pointing to the inhalational pathway as a major route of entry in the body internal environment. The inhalation of both respirable and non-respirable radioactive particles leading to both somatic and genetic alterations warrants further investigation in the view of ever present risk of the mass casualties in the event of the terrorist use of radiation dispersion weapons. **Conclusion:** The current reality of the radiological battlefield in tactical warfare of a potential clandestine use of recently introduced radiological dispersing devices in the terrorist scenario presents a new dimension of the management of mass casualties. The sustained research of internal contamination with organotropic radio nuclides, and potential mass casualties exposed to inhalational radioactive dust necessitates further research in the mechanisms, pathogenesis and treatment of the internal contamination casualties. Only a multidisciplinary and multinational effort may contribute to better preparedness for managing the casualties in the terrorist scenario. Developing methodology of detection, radiation toxicology, pathogenesis, somatic and genetic damage have been recently enhanced by the studies of internal dosimetry, kariotype chromosomal aberration studies (sky testing) which provide a sustained improvement of the assessment and management of internal contamination with medically significant radio nuclides.

THE SPECIAL CELL EFFECTS AND SOMATIC CONSEQUENCES OF EXPOSURE TO LOW-DOSE RADIATION

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Objective: The experimental data presented in the report put some clarity into the ongoing polemics about possibility of induction of harmful non-carcinogenic effects in human body as a result of exposure to low doses of radiation. The denial of this possibility is based on the fact that traditionally studied genotoxic effects cannot be the cause of this pathology: the incidence of these effects in exposure to low doses of radiation is fairly low; the effects are not overt in critical slowly regenerating tissues, since they can only be morphologically manifested in actively growing cell populations.
Methods: Endothelium of myocardial and alveolar capillaries were studied ultra-structurally in 236 rats irradiated by a wide range of X-ray doses (0,25;0,5;2,25;4,5;9;30;48;100) and 28 intact control animals. Studies were conducted during 12-18 months. The material consisted of 2-3 portions from various parts of myocardium and lung. From each portion, sections were prepared, in which all capillary sections were analyzed and ultra-structure of all lining capillary endotheliocytes (their number most often was more than 100) was studied. In each animal the percentage of non-viable endotheliocytes with signs of generalized organoid destrution, damage of plasmalemma and nuclear structures was accounted.
Results: Irradiation of rat to low and higher doses caused significant (up to 7 times) increase number of endothelial cells with various ultra-structural damages (from relatively light ones to in the cell death). Even the lowest dose – 0,25 Gy produce an increasing degeneration, intracellular lysis and defects of mitochondria. We found unusual features of postradiational endothelium changes: dose-independence, necessity of revealing the long-term, non-mutational cellular effects, massive involvement of cells, early development of the maximum effect already after the low dose irradiation. These special somatic effects, unlike genotoxic effects, are not connected to cell division. They appear according to the principle «all or nothing» in low doses of radiation (in mammals less than 1 Gy). In slowly regenerating tissues these effects (we called them «alternative effects» result in various sub-cellular disorders (mostly cytoplasmic). An irreversible change of intracellular homeostasis and dystrophic processes occur within a few hours after exposure. This can result in morphological and functional changes in tissues (depopulation), thus providing for the development of non-carcinogenic somatic consequences of low-dose irradiation. Presumably the changes of this kind are responsible for pathogenesis of the remote somatic disorders following a moderate radiation exposure.
The alternative effects are based on special hidden non-mutational alterations. Unlike the traditionally studied alterations they involve all cells of the population and can be inherited by all off-springs (at least in F1). This substantially broadens our notion of biological and applied significance of this phenomenon.
Conclusion: The most typical manifestation of alternative effects is a persistently increasing predisposition of cells to damage and death. It is likely that other manifestations are also possible, including a non-specific increase of likelihood (due to impairment of reparation capability) of genome damage. This could give a better insight into the problem of biological risks of cancer transformation and occurrence of hereditary disorders after exposure to low-dose irradiation. It is essential that different biological organisms may develop alternative effects not only due to radiation but other kinds of exposure. This represents a substantial ecological importance of alternative effects and requires development of new methods of assessment of external factors.

COMPARATIVE RADIOLOGICAL AND CONVENTIONAL POLLUTION IMPACT RECORDING IN THE AQUATIC ENVIRONMENT BY USE OF A CYTOGENETIC TOOL

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ABSTRACT: The effects of ionizing radiation can be viewed at all levels of biological organization, ranging from the molecular to ecosystem level. Effects on organisms can be traced to molecular and cellular responses, as radiation impact does not necessarily lead to observable effects on specimens, population or ecosystem. This is because the measurable attributes of the levels differ, despite the fact that all levels are interrelated.

The cytogenetic effects of radioactive and conventional pollution as they are recorded in organisms of natural ecosystem and the apportionment of causes to each kind of pollutants is a relative new field in radioecological research. There is limited evidence on field observations in international literature; even there is a lot of evidence in concerning laboratory experiments. The study of in situ effects of ionizing radiation in the cytogenetic level is the key for determining the radiological status of the ecosystem considered, based on the relation: concentration of pollutant in abiotic components and/or bioaccumulation → dose rate → effect on organism at the cellular level.

Several field studies on the comparative effects of ionizing radiation and chemical pollution in some selected areas in the Mediterranean, the Black Sea and in inland waters combined with laboratory experiments have shown a conceptual model of response of organisms, which is unique for ionizing radiation and chemical pollution. This model is based on the effects of different pollutants on aquatic biota (Crustacea, Polychaeta, Oligochatea, Fish embryos etc), as they have been recorded at the cellular level.

The environmental assessment of an aquatic ecosystem with regards to ionizing radiation in comparison to effects of chemical pollutants is based on determining the distribution frequency of chromosomal aberrations induced in cells of natural populations. Cytogenetic methods are used in pollution research because of their high sensitivity in terms of the determination of effects of the pollutant impact. Because the impact at the cytogenetic level is not discriminated according to the primary agent, the search for the "responsibility attribution" is based on statistics i.e. the distribution pattern of the observed aberrations and the types of chromosome aberration, as well.

Key words: Radioactivity**,** Radiation impact**,** Chromosome aberration, Aquatic environment

BYSTANDER EFFECT IN γ-IRRADIATED PERIPHERAL BLOOD

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Objective: Radiation-induced bystander effects (ByEff) are still being actively researched since there are more questions than answers related to this phenomenon. There are two main approaches in studying bystander effects: transferring medium from irradiated cells to unirradiated cells and the second is by irradiation of a single cell by a microbeam. The aim of the present study is to investigate and characterize the "bystander" effect after γ-irradiation of peripheral blood from healthy donors at molecular level.
Methods: Three groups of samples: **[1]**γ-irradiated peripheral blood, **[2]**non-irradiated blood incubated with plasma from irradiated blood, and **[3]**additionally irradiated aliquots of the second group, were studied. The Comet Assay and UDS were performed for DNA-damage and repair analysis and lipid peroxidation assay for ROS production. Alamar Blue Micro-plate assay for cell viability evaluation in the presence of signal transduction pathways inhibitors, mitochondrial membrane potential **(**MMP) after rhodamine 123 accumulation, and Ca-flux measurements with Fluo 3/Fura Red were performed additionally. In these experiments immortalized human keratinocytes (HaCaT) were used as a reporter cell line.
Results: It was established that ByEffs contribute to radiation injury in the case of γ-irradiated whole blood. Significantly higher levels of DNA damage corresponding to decreases in DNA repair capacity were recorded. At a certain radiation dose DSB levels were higher than SSB levels in the second and third sample groups. Involvement of ByEffs was detected only for the JNK signal transduction pathway. In all cases there was a decrease in MMP and a slight but not significant increase in Fluo3/FuraRed ratio in individual cells treated with irradiated plasma.
Conclusion: Incubation with plasma from irradiated blood transforms sub-lethal damage in unirradiated cells into lethal damage and exerts a suppressive effect on DNA repair capacity to additional irradiation. Bystander signals produced by irradiated cells can induce an adaptive response in irradiated cells to a subsequent exposure to bystander signals. Probably, there is involvement of the MAPK signal transduction pathway in the radio-adaptive effects. ROS did not appear to be involved in bystander effects in low dose pre-treated reporter cells but rather take part in sensitizing the bystander cells to additional irradiation. The large individual differences and heterogeneity of bystander responses makes them difficult to be modulated for medical uses at present.

RADIATION HORMESIS AT OCCUPATIONAL EXPOSURE

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Objective: The idea in favour of the auspicious effect of low dose ionizing radiation in biological systems exists for years and serves as basis of the radiation hormesis hypothesis. The results in support of this phenomenon are not accepted as reliable by ICRP. The available epidemiological data could only suppose the presence of hormetic effect because of statistics limitations and relatively high spontaneous rate of the examined effects. The present work was aimed at finding appropriate biomarkers applicable in molecular epidemiological surveys of occupationally exposed individuals and/or population to prove radiation hormesis.

Methods: Blood samples were taken from more than 400 NPP workers, divided in two groups: from the "strict regimen" area (exposed) and from the administration staff (control). Two levels of evaluation were used: **[1]***molecular* - spontaneous and induced DNA repair by UDS, protein synthesis evaluated radio-metrically, DNA damage by SCGE – all of them in white blood cells, concentration of malonedialdehyde in blood serum; and **[2]***cellular* – the Ly-subsets by flow cytometry, using a FacScan analyzer and immunofluorescent stained mouse monoclonal antibodies.

Results: A significant decrease of potentially lethal damage was found in persons with "mean annual dose" lower or equal to 5 mSv/a, compared to the control group. The highest repair capacity after a challenging dose of 2,0 Gy gamma rays as well as a significant decrease in the level of oxidative stress was evaluated for persons from the same group. At doses below 200 mSv statistically different decrease of the index of *CD3+4+*, *CD4+25+, CD4+62L+* lymphocyte populations and *CD4/CD8* cell ratio was established, and increased levels of *NK cells, CD57+8+* , *CD8+28+* and *CD8+38* were recorded.

Conclusion: The present investigation showed that annual doses lower than twice the natural radiation background exert positive effects on DNA damage and repair, increase cellular resistance and decrease oxidative stress. It is possible that the positive correlation between the dose and the cells with phonotype *CD4+25+* and *CD57+8+*, as well as the negative one with *CD4+62L+, CD8+28+* and *CD8+38+*, could reflect adaptive processes and compensatory activated immune system due to low dose irradiation.

TNF-α-INDUCED GENOMIC INSTABILITY IN PRIMARY VASCULAR ENDOTHELIAL CELLS.

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Genomic instability has been demonstrated in the progeny of irradiated cells and unirradiated bystander cells. Bystander responses are thought to depend on the activation of cellular communication processes. In this study we examine one such mediator of cellular communication, the pro-inflammatory cytokine tumor necrosis factor alpha (TNF-α) TNF-α is known to increase in expression following ionizing radiation (IR) exposure. Upon binding to its cellular receptors, TNF-α initiates a signaling cascade mediated by reactive oxygen species (ROS) that can activate sequestered NF-κB, thus initiating a pro-inflammatory and anti-apoptotic pathway. NF-κB can in turn upregulate TNF-α expression, which when secreted can induce subsequent autocrine and paracrine stimulation of TNF-α and NF-κB. We speculate that this increase in TNF-α signaling and concomitant ROS generation has a mechanistic role in the initiation of genomic instability and a potential involvement in producing bystander responses.

Genomic instability is induced by IR in a non-dose-dependent manner. Previous investigation by our group using primary human vascular endothelial cells has shown that both low (0.1 Gy) and high (2 Gy) doses of IR raise levels of secreted TNF-α in a non-linear manner, that both immediate genetic damage and delayed chromosomal instability can be induced at similar levels following treatment with either 0.1-10 ng/mL TNF-α or 0.1 or 2 Gy IR, and that this immediate damage was abrogated by pre-incubation with antioxidants. The current study is therefore focused on the mechanism responsible for this TNF-α-induced instability, and whether TNF-α is a signaling mediator of bystander-induced responses. TNF-α suppressors are added to either directly irradiated or bystander cell cultures exposed to low or high doses of low-LET radiation, and the results are compared to cells pre-treated with antioxidants. Cellular damage is assessed by cell survival, the comet assay, formation of damage-induced foci, and presence of delayed chromosomal instability. Preliminary results indicate that: 1) suppressing TNF-a prevents immediate genetic damage in directly irradiated cells, similar to antioxidant treatment, 2) antioxidants but not TNF-a suppression can abrogate delayed chromosomal instability in directly irradiated cells, and 3) the suppression of either TNF-α or nitric oxide in bystander cells increases survival and protects against immediate genetic damage after exposure to medium from cells irradiated with 2 Gy.

STUDIES OF THE BIOMARKER AVAILABLE IN BIOLOGICAL DOSIMETRY TO ESTIMATE THE DOSE WITH THE CALIBRATION OF DOSE-RESPONSE CURVE OF MICRONUCLEI IN HUMAN LYMPHOCYTES INDUCED BY 50MeV PROTON BEAM EXPOSURE

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Abstract

The purpose of this paper is to establish an easy and reliable biodosimeter to evaluate the biological effect and has led to theoretical approaches to explain observation with high-linear energy transfer (LET) exposure. Human peripheral blood lymphocytes were irradiated using 50MeV proton beams(LET: 34.6 KeV μm^{-1}) up to 6Gy, and analyzed by Giemsa staining of cytokinesis-blocked(CB) MN assay.

The MNs were found at very low doses, and in increasing dose-dependent frequencies. The frequencies of MNs were found to be significantly dose-effect calibration curve after proton beam exposure.

When plotting on a linear scale against radiation dose, the line of best fit was $Y = 0.004+(1.882x10^{-2}\pm9.701x10^{-5})D+(1.43x10^{-3}\pm1.571x10^{-5})D^2$. These data show a trend towards increase of the numbers of MNs with increasing dose. The number of MN in lymphocytes that were observed in the non-irradiated group is 0.1610±0.0093/cell. The dose-response curve for proton beams induced MNs frequencies was linear-quadratic and has a significant relationship between the frequencies of MNs and dose.

Thus, we found that the number of Giemsa-stained MNs can be used for dose estimation, since the total MN number was linear-quadratic correlated with radiation dose($R^2= 0.9996$). These findings anticipate that proton beams-induced MN may be more complex than expected from cytogenetic analysis. While conventional Giemsa staining was found to be the method of choice for the triage situation, it is expected that MN analysis will add to the knowledge of underlying mechanisms for proton beams exposure associated cytogenetic damage.

Accordingly, this simple protocol will be particularly useful for helping physicians to decide medical therapy for the initial treatment of victims with rapid and precise dose estimation after radiation accidents and has potential for use as a valuable biomarker to evaluate cell sensitivity to densely ionizing radiation with implications for tumor therapy with protons.

AN INFLUENCE OF OCCUPATIONAL EXPOSURE ON LEVEL OF CHROMOSOME ABERRATIONS IN NUCLEAR POWER PLANT WORKERS

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Objective. The workers of Ignalina Nuclear Power Plant (INPP) receive the highest occupational ionising radiation doses in Lithuania. Their occupational exposure results mainly from external low LET gamma radiation. Some workers receive additional internal and neutron exposure. Though exposure doses are generally low and don't exceed the annual dose limit, the higher doses are obtained during outages. The aim of the present study was to analyse chromosome aberration frequencies in lymphocytes of INPP workers exposed to the different types of ionising radiation.

Methods. The blood sampling of 52 INPP male workers was performed in 2004-2006. For 29 workers radiation exposure resulted from the external gamma rays only. Their mean annual dose averaged over the 3-year period prior blood sampling was 11.7±8.7 mSv. The mean cumulative dose - 197.7±174.7 mSv. 15 workers had an intake of gamma radionuclides (^{60}Co, ^{137}Cs), contributing to the doses less than 0.1 mSv. Their mean cumulative dose - 278.2±191.9 mSv. The mean annual dose averaged over the 3-year period prior blood sampling was 11.8±5.3 mSv. For 8 subjects neutron doses below 0.2 mSv were recorded. Their mean annual dose averaged over the 3-year period prior blood sampling was 7.0±2.9 mSv. The mean cumulative dose was 241.8±93.0 mSv.

Heparinized venous blood samples were taken and cultures were initiated according to the standard procedures. Phytohaemagglutinin (7.8 μg/ml) stimulated cultures were incubated at 37^{0}C for 72 hours in RPMI 1640 medium supplemented with 12% heat-inactivated newborn calf serum, 40 μg/ml gentamycin. Colchicine was added to the culture during the initiation at a final concentration of 0,25 μg/ml. 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 stained with Giemsa, coded and scored blind. Generally 500 first-division cells per individual were analyzed for chromosome aberrations.

Results. Chromosome aberration analyses revealed significant increase in the total chromosome aberration frequency for the radiation workers with internal exposure (2.42±0.40 CA/100 cells, P=0.01) and for those with additional neutron exposure (2.63±0.40 CA/100 cells, P=0.01). However, no significant differences between the workers with external gamma radiation exposure and the controls (1.62±0.25 vs. 1.65±0.15 CA/100 cells, P=0.83) was observed. There was no correlation between the chromosome aberration frequency and the cumulative dose, mean annual doses averaged over the last 3-years or the last year before the blood sampling. The confounding effects of internal and neutron exposure on the frequency of chromosome aberrations was determined. The impact of other factors (smoking habits, age, duration of employment, cumulative dose) was found to be not significant.

Conclusion. Though no increase in chromosome aberration frequency was determined in workers exposed to external gamma radiation only, the demonstration of the elevated levels of chromosome aberrations in the workers with incorporated radionuclides and neutron exposure indicates their more hazardous work activities with consequential risk to health.

GENE EXPRESSION VARIATIONS IN LYMPHOCYTE SUBPOPULATIONS IN RESPONSE TO LOW DOSE OF IONIZING RADIATIONS

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Objective: Our purpose was to characterize the most responsive lymphocyte subpopulation to low dose exposure of ionizing radiation.
Methods: Using the microarray technology, we examine gene expression variations in two types of T lymphocyte subpopulations. Blood samples from 6 healthy donors were independently exposed to 0 (sham irradiation), 0.05 and 0.5 Gray of ionizing radiations. Three and 24 hours after exposure, $CD4^+$ and $CD8^+$ cells were negatively isolated with magnetic beads sort system and total RNA was extracted from each sample. After linear amplification, RNA from each condition was competitively hybridized on 26k oligonucleotide microarray against a common reference RNA. Microarray data were analyzed with R software using marray and multtest Bioconductor packages.
Results: Three kinds of gene expression modulations were observed: a time dependent one, a dose dependent one and a cell specific one. Indeed a large number of gene expression downregulation was measured specifically in $CD4^+$ cells 3 hours post-exposure. This modulation was early, independent of the received dose and specific of this lymphocyte subpopulation. Twenty four hours after exposure, inductions of known IR-responsive genes were measured only for 0.5 Gy dose in both of the tested lymphocytes subtypes. This more late modulation was independent of the T lymphocyte subpopulation but specific of the highest tested dose. In fact, no more gene expression variation was measured for 0.05 Gy exposed cells at 24 hours post-exposition.
Conclusion: $CD4^+$ lymphocyte cells appear to be highly and early sensitive to doses as low as 0.05 Gy of ionizing radiations. It means that biological mechanisms could be sensitive enough to such stress. These cells could be of interest in the detection of low dose of ionizing radiation exposure.

CORRELATION BETWEEN RADON LEVEL AND CONFOUNDERS OF CANCER: A NOTE ON EPIDEMIOLOGICAL INFERENCE AT LOW DOSES

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Objective. The aim of this study was to examine and further clarify the extent of radon and progeny induced carcinogenesis, both separated from and combined with other confounders and health risk factors. This work was financed by National Development Agency, Hungary, with GVOP-3.1.1.-2004-05-0384/3.0.
Methods. A case-control study was conducted in a Hungarian countryside region where the proportion of houses with yearly average radon level above 200 Bq.m^{-3} was estimated to be higher than 20% by our preceding regional surveys. Radon levels were measured with CR39 closed etched detectors for three seasons separately yielding yearly average by estimating the low summer level. The detectors were placed in the bedrooms, where people were expected to spend one third of a day. 520 patients with diagnosed cancers were included in these measurements, amongst which 77 developed lung or respiratory cancers. The control group consisted 6333 individuals, above 30 years of age. Lifestyle risk factors of cancers were collected by surveys including social status, pollution from indoor heating, smoking and alcohol history, nutrition, exercise and mental health index 5. Except smoking and alcohol habits, these cofactors were only available for the control group. Comparing disease occurrences the authors selected the multivariate generalised linear models. The case and control proportions along a given factor are binomially distributed, thus the logit link function was used. For radon both log and linear terms were probed for.
Results. Many known health confounders of cancers correlated with radon levels, with an estimated total net increase of 50-150 Bq m^{-3} with increased risks. For lung cancers the model with the terms radon, age, gender and smoking was found to have the lowest Akaike Information Criterion (AIC). Heavy dependency on age, gender and smoking contribute largely to observed lung cancer incidence. However log linear relationship between incidence and radon level was significant between 0-1000 Bq m^{-3}. Between 0-300 Bq m^{-3} a fit with linear radon gave odds ratios (OR) of 1.8(1.43-3.0) per 100 Bq m^{-3} increase. The relative contribution of radon to the odds of developing lung cancer is around two orders of magnitudes less than of the other model terms combined. Similar OR results were found for all other cancer types combined.
Conclusion. Lifestyle confounders largely determine cancer incidences in our sample. Milder, though strongly significant correlations were found with radon as well. More precise assessment of health risk factors of cases are necessary to conclude with more certainty. That requires better medical records than those were available for this study in the examined region of elevated radon levels.

THE RELEVANCE OF RADIATION TRACK STRUCTURE AT LOW DOSE AND DOSE RATES

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All ionising radiation interacts in the form of highly structured tracks of ionisations and excitations which vary significantly with radiation quality. Energy deposition is highly inhomogeneous and this becomes more apparent the smaller the target volume and especially at lower doses and dose rates. The spatial and temporal distribution of these events are important in determining the resultant biological response. Current risk assessments are based on acute high dose exposures, however typical human exposures are associated with much lower doses and dose rates with many individual cells unlikely to experience more than one track over long time periods of months to years, with many cells unirradiated over this period. Biological responses are not only observed in irradiated cells but also non-exposed neighbouring cells as a result of inter-cellular signalling and this potentially has important implications on the estimates of risk for low dose and low dose rate exposures. The relevance of radiation tracks structure a low dose and dose rates will be discussed along with recent experimental results, including data showing that doses as low as 2 mGy γ-rays and 0.3 mGy α-particles to a cell population were sufficient to produce an observable increase in apoptosis in unirradiated transformed cells co-cultured with the irradiated cells.

GAMMA-RAY IRRADIATION INDUCE SUPPRESSION OF TNF-α PRODUCTION VIA UP-REGULATION OF MAITOGEN-ACTIVATED PROTEIN KINASE PHOSPHATASE-1

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Ionizing irradiation induces DNA damage and activates a lot of signalling pathways, such as ATM and p53, due to repair the DNA damage. On the other hand, irradiation also induces activation of extracellular signal regulated protein kinase (ERK1/2) through trans-activation of EGF receptor. However, EGF-receptor-independent signalling pathways induced by irradiation are unclear. Here, we studied gamma-ray irradiation-induced signaling pathways focusing mitogen-activated kinase (MAPK), such as ERK1/2 and p38 MAPK in human keratinocyte HaCat cells, which express EGF receptor, and mouse macrophage RAW264.7 cells, which express EGF receptor at low level.

These cells were irradiated by gamma-ray (0.05-2.5 Gy) from ^{137}Cs source (0.96 Gy/min), and phosphorylated MAPKs were detected by immune blotting. Gamma-ray irradiation (0.1-2.5Gy) induced phosphorylation of ERK1/2 in HaCat cells. However, dephosphorylation of p38 MAPK was occurred 15 min after the irradiation, indicating activation of MAPK phosphatase (MKP). On the other hand, dephosphorylation of not only p38 MAPK but also ERK1/2 were induced 15 min after irradiation (0.5 Gy) in RAW264.7 cells. At the same time point, expression of MKP-1, which dephosphorylates ERK1/2 and p38 MAPK, was significantly increased. Up-regulation of MKP-1 and dephosphorylation of p38 MAPK were also observed in irradiated mouse peritoneal macrophage. Because phosphorylation of p38 MAPK mediates pro-inflammatory cytokines, such as TNF-α , we examined the change in production of TNF-α after irradiation. Production of TNF-α was suppressed in 0.5 Gy irradiated RAW264.7 cells.

In conclusion, our results suggest that gamma-ray irradiation induces up-regulation of MKP-1, leading to dephosphorylation of p38 MAPK and suppression of TNF-α production in RAW264.7cells, though ERK1/2 is activated through activation of EGF receptor in HaCat cells.

RADIOPROTECTIVE EFFECTS OF CHLOROGENIC ACID AGAINST MORTALITY INDUCED BY GAMMA IRRADIATION IN MICE

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The radioprotective effects of the naturally occurring compound chlorogenic acid has been investigated against mortality induced by gamma irradiation in mice. Chlorogenic acid administrated at single doses of 100, 200 and 400 mg/kg 1 and 24 h prior to lethal dose of gamma irradiation (8.5 Gy). At 30 days after treatment, the percentage of animal survival in each group was: control, 20%; 100 mg/kg, 20% and 15%; 200 mg/kg, 45% and 15%; 400 mg/kg, 25% and 35% for 1 h and 24 h treatment prior gamma irradiation, respectively. Percentage of survival increased in animal treated with this agent at 200 mg/kg at 1 h statistically compared with irradiated alone group. Other doses of chlorogenic acid have not showed any enhanced survival at 1 and 24 h before irradiation. Chlorogenic acid exhibited concentration-dependent activity on 1, 1-diphenyl 2-picrylhydrazyl free radical to show strong antioxidant activity. It appeared that chlorogenic acid with antioxidant activity reduced mortality induced by gamma irradiation.

MENTAL AND BEHAVIOURAL DISORDERS IN BELARUSIAN PERSONS EXPOSED IN UTERO TO RADIATION FOLLOWING THE CHERNOBYL ACCIDENT

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Objectives – Investigation of mental health and psychosocial development of persons from Belarus exposed *in utero* to radiation following the Chernobyl accident in 1986.
Methods – Ten year follow-up of 245 persons exposed *in utero* following the Chernobyl accident and 239 persons of the same age from non- or slightly contaminated regions. Psychiatric and psychosocial assessments were performed at the age 6–7 years, 10–12 years, and 15–16 years. Psychiatric diagnosis of the children in both groups was established by means of a semi-structured clinical interview based on the diagnostic criteria of the ICD-10, Chapter V (Mental and behavioural disorders).
Results - The persons who were exposed to the influence of radionuclides antenatally showed a relative increase in mental and behavioral disorders compared to the control group. This was mainly due to the increased prevalence of cases of specific developmental disorders of speech and language, specific developmental disorders of motor function, emotional disorders and disorders of social functioning. Phobic anxiety disorders were the most common emotional disorders in both groups (27 cases – 10.8 % in the exposed group vs 17 cases – 6.8 % in the control group. The relative risk of the development of emotional disorders was 2.67 ($P<0.001$). There was no difference between the cases and control groups in terms of the prevalence of mental retardation, specific learning disorders, hyperkinetic disorders and other mental and behavioral disorders. At adolescent age there was also no difference in the prevalence of conduct disorders between the cases and the control groups. Conduct disorders were often associated with unfavorable psychological surroundings, including unsatisfactory family relations and learning difficulties at school. Conduct disorders at adolescent age (15-16) were closely correlated with hyperkinetic disorders ($r=0.72$; $P<0.01$), disorders of scholastic skills ($r=0.72$; $P<0.01$) and borderline intellectual functioning ($r=0.56$; $P<0.05$) of the same people at age 10-12.

THE QUALITY OF LIFE OF THE PATIENTS SUFFERING FROM THYROID CANCER

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A comparative analysis is given of the results of the assessment of the quality of patients who were operated on oncological pathology of thyroid gland and obtained life-time substitute of therapy by L-thyroxin, and the sample group, which consisted of people, who didn't have any pathology of thyroid. We examined 56 patients, who were operated on oncological pathology of thyroid (operation was performed from 1 to 10 years ago). The patients took the course of radioiodine therapy and obtained life-time substitutional therapy with L-thyroxin. To assess the quality of life during the after operation period we used the Russian language version of the questionnaire SF (36 (Medical Outcomes Study Short Form) (Ware J.E., 1993). The quality of life in case of cancer of thyroid gland, as compared to the sample group, appeared to be significantly decreased in all the scales of the questionnaire SF-36. With reliability of $P<0,05$, as compared to the sample group, the following indices decreased: physical functioning (69,1±2,8 и 92,1±2,4); the role of physical problems in the restriction of vital activity (22,3±4,0 и 70,2±6,8); social functioning (42,0±1,6 и 52,8±2,3); the role of emotional problems in the restriction of vital activity (19,6±5,4 и 73,1±8,9). These data indicate to the prolonged effect of the psychotraumatic experience and the changes of subjective perception of one's social status. On this background we noticed a reliable increase of indices of perception of physical pain (65,4±2,2 и 37,6±3,6; $P<0,05$) and indices of the general perception of health (65,4±2,2 и 37,6±3,6; $P<0,05$) in the patients operated, which characterizes subjective raise of attention towards such patients. The data obtained show the significant influence of psychological aspects of the perception of the case of cancer of thyroid gland on the level of subjective assessment of vital activity and, as a result, social adaptation.

RADIOECOLOGICAL CONSEQUENCES OF POTENTIAL ACCIDENT IN THE NORWEGIAN COASTAL WATERS: UNCERTAINTIES AND KNOWLEDGE GAPS IN METHODOLOGY

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A potential accident involving the transport of spent nuclear fuel along the Norwegian coastline has been chosen for evaluation of a dose assessment methodology.

The accident scenario assumes that the release of radioactivity takes place under water and that there is free exchange of water between the spent fuel and the seal. The inventory has been calculated using the ORIGEN programme.

Radioecological consequences are provided by the NRPA compartment model which includes the processes of advection of radioactivity between compartments and water-sediment interactions. The contamination of biota is further calculated from the radionuclide concentrations in filtered seawater in the different water regions. Doses to man are calculated on the basis of assumptions about human diet. Doses to biota are calculated on the basis of radionuclide concentrations in marine organisms, water and sediment and dose conversion factors.

Collective dose-rates to man, doses to the critical group, concentration of radionuclides in biota, sea-foods and doses to marine organisms were calculated through the evaluation of radioecological consequences after accidents.

Results of calculations indicate that concentrations of radionuclides for some marine organisms can exceed guideline levels. At the same time, collective dose rates to man as well as doses to a critical group are not higher than guideline levels. Comparison of results from calculations with provisional benchmark values suggests that doses to biota are in most cases unlikely to be of concern. However doses to some marine organisms can be much higher than the screening dose of 10 μGy/h over long periods.

It is apparent that water-sediment distribution coefficients and concentration factors constitute the main sources of uncertainties in the present case. It is important to note that knowledge gaps concerning the influence of relatively low doses to populations of marine organisms over long time periods (many generations) substantially constrain the assessor's ability to evaluate, with any great certainty, statistically significant effects on such organisms.

COMPREHENSIVE ANALYSIS OF TIME AND DOSE-DEPENDENT PATTERNS OF GENE EXPRESSION IN A HUMAN MESENCHYMAL STEM CELL LINE EXPOSED TO LOW-DOSE IONIZING RADIATION

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We focus on transcriptional responses induced by low and very low doses of ionizing radiation with time effect. A few and limited studies have been done regardless of their importance. Here we have applied large-scale gene transcript profile to elucidate the genes and biological pathways. Immortalized human mesenchymal stem cells were irradiated with 0.01, 0.05, 0.2 and 1 Gy of gamma radiation and total RNA was extracted from each cell line at 1, 4, 12 and 48 hours after exposure. The essential transcriptional responses were identified according to does and time. The 6,016 genes showed altered expression patterns at more than one time points or dose levels among the investigated 10,800 genes. Genes that showed dose-dependent expression responses were involved in *signal transduction*, *regulation of transcription*, *proteolysis*, *peptidolysis* and *metabolism*. Those that showed time-dependent responses could be divided into two distinct groups: the up-and-down group was associated with 'cellular defense mechanisms' such as *apoptosis*, *cell adhesion*, *stress response* and *immune response* and the down-and-up group with 'fundamental cellular processes' such as *DNA replication*, *mitosis*, *RNA splicing*, *DNA repair* and *translation initiation*. Genes showing both dose-and-time dependent responses exhibited a mixture of both features. Highly nonlinear relationship between IR dose and transcriptional relative response are obtained from the dose dependent group. Time-dependent group also has nonlinear relationship as complex effect group does. Some of the early–reactive-phase (1 - 4 h) genes showed differential expression response to 0.01, 0.05 and 0.2 Gy but were unresponsive to 1 Gy. Some of the late-recovery-phase (12 - 48 h) genes showed differential expression to 1 Gy but were relatively unresponsive to other doses. We further characterized the gene-expression patterns that could be implicated in the molecular mechanism of the cellular responses to low and very low-dose irradiation.

THE ROLE OF RADIATION TYPES AND DOSE IN INDUCED GENOMIC INSTABILITY.

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Genomic Instability (GI) is defined as long-term alterations induced by low-dose exposure to a variety of genotoxic agents in mammalian cells that act to increase the 'apparent' spontaneous mutation frequency.GI is a hallmark of tumorigenic progression and is observed in the progeny of irradiated and bystander cells as the delayed and stochastic appearance of de novo chromosomal aberrations, gene mutations and delayed lethal mutations both in vitro and in vivo. It occurs at a frequency several orders of magnitude greater than would be expected for mutation in a single gene, implying that GI is a multigenic phenomenon.

The expression of GI can be influenced by genotype, cell type and radiation quality; however the underlying mechanisms are not fully understood. While several studies have demonstrated GI induction by high and low LET radiation, our work on human and mouse primary cell systems has shown significant differences in the capacity to induce GI and the spectrum of alterations depending on LET. These differences might be attributed to differences in radiation track structure, radiation dose and radiation exposure regime (distribution of hit and un hit cells).
In this presentation I shall review the role of radiation quality; describe the possible mechanisms underlining the observed differences between radiation type and present results of experiments demonstrating that the dose of low LET radiation might be the most significant factor in determining the role of radiation type in the induction of GI.

IS EXPOSURE TO OVER GROUND RADON AS DANGEROUS AS THEY SAY?

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Natural sources of radioactivity are all around us, and man-made radioactive materials are a vital part of medicine and industry. Exposure to some radiation, natural or man-made, is inevitable. Sixty-eight percent of our exposure to natural sources of radiation usually comes from radon, a colorless, tasteless, and odorless gas that comes from the decay of uranium found in nearly all soils. Radioactive radon gas is widely considered to be a health hazard by environmental agencies in the United States [1] and in Europe [2]. Yet despite the warnings of these agencies, thousands of people annually expose themselves to radon for therapeutic purposes, in facilities ranging from rustic old mines, to upscale spas and clinics [3-5]. Moreover, while modern biomedicine has been enormously successful in the treatment of acute illnesses, it has dealt less well with chronic illnesses. In living with radiation, we must understand the risks and benefits. In order to assess the risk at high doses, LNT hypothesis of ICRP (and consequently also of IAEA, EU, NCRP, BEIR VI, etc.) is used. Current radiation risk estimates, drawn by linear extrapolation, from high dose and dose rate of radiation from very high and complex miner's data orders of magnitude down to completely different current mining conditions, residential radon doses and dose-rates, and a multitude of other confounding factors, even very careful epidemiological studies have not demonstrated any cancerogenic radon effects up to levels around 1000 Bq/m³, or ca. 7 times the EPA limit [6-7]. This paper addresses the possibility that the LNT model may not be applicable for low doses of radon, and that low doses of radon may in fact be beneficial for certain chronic illnesses. There are growing numbers of studies indicating an inverse relationship between cancer occurrence and low dose environmental radon exposure, as well as numerous studies examining the therapeutic effects of low dose radiation. This protective or beneficial effect, called hormesis, has gained recognition by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). A large body of anecdotal evidence in support of hormesis exists, in the form of thousands of people who annually use radon spas worldwide. Moreover, there are also recent studies which indicate that not only lung cancer, but also other cancers including childhood leukemia are substantially lower in high natural background and radon than in low-dose areas [8]. Similar effects have also been recently observed in Kerala/India, Russia, etc. - usually with the explanation that it is not the radiation level, but other factors such as industrial pollution and living habits, which far outweigh any possible small detrimental radiation effects beyond statistical detection - if they should exist at all. Regarding over ground radon, it may be concluded that the radon balneology remains an important therapy against painful joint diseases, etc., with a hypothetical minor negative radiation effect certainly negligible compared to the benefits.
In the present work, a comprehensive study of the available literature, data and reports of various radiation exposure and protection studies will be presented. In summary, an analysis of all available data shows that, with a few exceptions such as early miners, the human health effects of radon are most likely to be substantially more beneficial than harmful.

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RADIOLOGICAL IMPACT OF PRESENCE OF RADON, THORON AND THEIR PROGENY IN THE ENVIRONMENT OF LPG BOTTLING PLANT

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The problem of radon, a ubiquitously present radioactive gas, is an important global problem of radiation hygiene concerning the world population. Measurement of radon, thoron and their progeny is important because the radiation dose to human population due to inhalation of radon and its progeny contribute more than 50% of the dose from all sources of radiation, both naturally occurring and man-made (UNSCEAR, 2000). The estimated level of health risk associated with average indoor radon levels is much higher than those due to other environmental carcinogen (Nazaroff and Nero, 1988). Recently, a pooled analysis of seven case control studies showed a positive correlation between residential exposure to radon and lung cancer (Krewski et al., 2005). The U.S. Environmental Protection Agency (EPA) currently recommends that all levels beneath the third floor be tested for radon (USEPA, 2005). In this light, tracking indoor radon concentration is thus fundamental from health and hygiene point of view. In the present work, the inhalation dose rates, annual effective dose and the lifetime fatality risk to the workers in the LPG bottling plant due to exposure from the mixed field of radon and thoron were measured.

The measurements have been carried out by using tracks etch technique using solid state nuclear track detectors (SSNTDs) has been used. It is one of the most widely used techniques for radon measurement.

The radon and thoron concentration and the inhalation dose were found to vary from 7.78+/-2.02 Bq/m^3 to 59.01+/-5.57 Bq/m^3, 1.16+/-0.28 Bq/m^3 to 65.08+/-5.09 Bq/m^3, and 0.23 mSv/y to 2.29 mSv/y respectively. The concentration of radon daughters was found to vary from 0.84 mWL to 6.38 mWL, the concentration of thoron daughters was found to vary from 0.03 mWL to 1.76 mWL, the annual exposure due to radon and thoron daughters, collectively, was found to vary from 0.036 WLM to 0.273 WLM, the life time fatality risk was found to vary from 0.11 $\times 10^{-4}$ to 0.82 $\times 10^{-4}$ and the annual effective dose from radon and thoron (PAEC) was found to vary from 0.14 mSv/y to 1.06 mSv/y.

The measurements indicated moderate to high levels of radon/thoron concentrations at different locations in the environment of the LPG bottling plant. At certain locations, the inhalation dose is almost 100% was more than that the Global average value (1mSv). However the dose levels observed in the environment of the LPG bottliong plasnt were marginally below the ICRP recommendations (20mSv) for workers. In the light of these findings, the LPG bottling plants may affect doses from external irradiation and the inhalation of radon decay products is significant from health point of view.

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MATHEMATICAL DESCRIPTION OF SYNERGISTIC INTERACTION BETWEEN RADON AND SMOKING

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Background: A certain level of background exposure to ionizing radiation and natural or man-made chemicals is always present in the environment. Radon and its short-lived decay products are considered as important sources of public exposure to the natural radioactivity. It is well known from epidemiological and toxicological studies that synergistic interaction between smoking and radon occurs, which is especially important for high natural background areas.

Objective: This study has been done to suggest a mathematical model to describe the synergistic interaction of radon with tobacco smoking, and to demonstrate the ability of the model to describe carcinogenic effects of the combined action.

Methods: A simple mathematical model was formulated to describe and predict the synergistic interaction of radon with smoking. The model postulates that the occurrence of synergism is to be expected as a result of additional carcinogenic damage arisen from the interaction of sublesions induced by the two factors under consideration.

Results: The predictions of the model were verified by comparison with experimental data published by other researchers. The model appears to be appropriate and the predictions are valid.

Conclusions: : The suggested mathematical model predicts the greatest level of synergistic effect and condition under which the maximum synergy is attained. The synergistic effect appeared to decline with any deviation from the optimal value of the ratio of carcinogenic effective damages produced by each agent alone.

Key words: smoking, radon, carcinogenic effect, synergistic interaction, mathematical model

DEVELOPING A THEORETICAL PREDICTIVE MODEL FOR CELLULAR RESPONSE TO COMBINED ACTIONS OF LOW RADIATION AND HYPERTHERMIA

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Background: Organisms in their living environment are not exposed to merely a single stress agent. Several factors such as radiation and heat may simultaneously exert their stressful effect to the organisms. The combined exposure to two stressors can result in an enhanced effect that would be expected from the addition of the separate exposures to individual agents.
Objective: This study has been undertaken to develop a theoretical model for assessment of combined effects of low dose radiation and mild heat for predictive cellular response assay.
Rationale: Present study was motivated from the belief that synergism may occur in terms of lethal lesions arising from the interaction of non-lethal sub-lesions induced by individual agents. The sub-lesions induced by each agent may be negligible or undetectable. But, there exists a possibility of some cross talk between sublesions produced by radiation and heat. These processes may reflect the real mechanisms for inflicting the lethal damage by otherwise ignorable or undetectable insults to exposed organisms.
Results: A theoretically developed mathematical model of the synergy was formulated which was tested for validation on the experimental data. The model predictions fairly closely corresponded with several experimental results. .The significance of synergistic effects for radiation biology has been demonstrated. A number of common peculiarities of synergistic interactions were found to play their roles. A unified biophysical concept for synergistic interaction has been suggested.
Conclusions: For a constant dose rate, synergistic interaction between radiation and hyperthermia especially at low intensity is realized only within a certain range of temperature, independently of the target object analyzed. For temperatures below the range, the synergistic effect was not observed and cell killing was mainly determined by the damage induced by ionizing radiation. On the contrary, the synergistic effect for temperature above the range was also not observed but cell killing was chiefly caused by hyperthermia. On the basis of the results obtained, it is fairly inferred that, for any constant temperature, there should be an optimal intensity of ionizing radiation which could result in the greatest synergy.

Key words: radiation, hyperthermia, combined action, theoretical model

EFFECT OF GAMMA RADIATION ON GREENING OF ETIOLATED MUNG BEAN SEEDLINGS

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Ionizing radiation causes many alterations in photosynthetic machineries. However, there is no information about effects of ionizing radiation on the development of photosynthetic machineries in plants. We investigated the greening of etiolated mung bean seedlings irradiated with gamma rays of 50 to 300 Gy. The gamma-irradiation inhibited seedling growth with great dependence on the radiation dose. In particular, growth of stems was more affected than that of hypocotyls. Irradiated leaves showed inhibition in growth, aberration in morphology, and yellowing in color depending on the radiation dose. Pigment analysis indicated that contents of chlorophylls and carotenoids were significantly decreased in the irradiated leaves. The maximal electron transport rate of photosynthesis was also decreased in the irradiated leaves except the 50-Gy samples. However, the maximal photochemical efficiency was little affected by the irradiation. These results may imply that the overall photosynthetic machineries can develop and work to some extent as a concerted system for photosynthesis after exposure to acute doses of ionizing radiation.

BYSTANDER EFFECTS OF LOW DOSE IONISING IRRADIATION

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Introduction: Many recent findings question the validity of the linear non-threshold model of stochastic radiation effects. In the low dose range the non DNA targeted effects might have high influence on radiation damages. We have investigated the consequences of low dose irradiation in directly exposed and bystander immortalized human fibroblast cells.
Methods: Immortalized human fibroblast cells were irradiated with various doses (0.01, 0.04, 0.1, 0.5 and 2 Gy) of ^{60}Co γ-radiation. To study bystander effects both the medium change and the co-culture technique was applied. Radiation induced damages were investigated by a modified micronucleus assay. Fibroblasts were seeded on cover glasses and irradiated 10-12 h later. After additional 6 hours 2 μg/ml cythochalasin B were added and 48 hours later cells were stained either with Giemsa or ethidium-bromide. The ratio of binucleated cells and the frequency of micronuclei in 1000 binucleated cells were evaluated.
Results: In directly irradiated cells the ratio of binucleated cells decreased with dose beyond 0.1 Gy. We detected a moderate hypersensitivity at 10 mGy. The frequency of micronuclei increased with dose beyond 0.1 Gy. Again, slight hypersensitivity was detected at 10 mGy. Bystander treatment had no effect on the frequency of binucleated cells. The ratio of micronuclei increased at doses higher than 0.1 Gy.
Conclusions: Our preliminary data suggest that human fibroblast cells might respond to low doses in a hypersensitive manner.

REDUCTION OF THE BACKGROUND MUTATION BY A LOW DOSE IRRADIATION OF DROSOPHILA SPERMATOCYTES AT A LOW DOSE- RATE.

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[OBJECTIVE] As the Linear Non Threshold model was first established in 1930, based on the results of a genetic study using *Drosophila*, we tried to indicate the conditions under which LNT holds.

[METHODS] A sex-linked recessive lethal mutation assay was performed in *Drosophila melanogaster*. DNA repair proficient immature spermatocytes and spermatogonia were irradiated with X-rays at a high or low dose-rate.

[RESULTS AND DISCUSSION] Mutation frequency in the sperms irradiated with a low total dose (0.2Gy) at a low dose-rate (0.05Gy/min) was significantly lower than that in the sham-irradiated group whereas irradiation with a high dose (10Gy) at the same dose-rate resulted in a significant increase in the mutation frequency. It was obvious that the dose-response relationship was not linear, but U-shaped. A low dose irradiation at a high dose-rate (0.5Gy/min) did not cause a significant reduction in mutation frequency. Mutation in the high dose, high dose-rate group was more frequent than in the high dose, low dose-rate group. A dose-rate effect was evident. When mutant male flies defective in DNA excision repair function were used instead of wild type flies, a low dose irradiation at a low dose-rate did not cause the reduction in the mutation frequency. These observations suggest that the dose-response relationship is dependent not only on the dose-rate, but also on the DNA repair function. It is inferred that error-free DNA repair functions were activated by a low dose of low dose-rate irradiation, and this repaired spontaneous DNA damage rather than the X-ray induced one, thus forming a practical threshold. As the human somatic cells are usually repair function proficient, we conclude that LNT can not estimate the human cancer risks properly.

ACTIVATION OF IMMUNE FUNCTIONS VIA INDUCTION OF GLUTATHIONE OF LYMPHOCYTES BY LOW-DOSE, WHOLE-BODY IRRADIATION WITH GAMMA-RAYS

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We have recently found that low doses of radiation, unlike higher doses, do not always cause a decrease of cellular glutathione, but they can increase it, leading to an elevation of Con A-induced proliferation of splenocytes. In this study, we first examined whether the increase of glutathione level induced by low-dose □amma-ray irradiation is involved in the appearance of enhanced natural killer (NK) activity and antibody-dependent cellular cytotoxicity (ADCC), leading to delayed tumor growth in Ehrlich solid tumor (EST)-bearing mice. NK activity in ICR mouse splenocytes was significantly increased from 4 h to 6 h after a single whole-body □amma-ray irradiation at 0.5 Gy, and thereafter decreased almost to the zero-time level by 24 h post-irradiation. ADCC was also increased significantly in a similar way. Reduced glutathione exogenously added to splenocytes obtained from normal mice enhanced both NK activity and ADCC in a dose-dependent manner. The inhibitory effect of the radiation on tumor growth was then examined in EST-bearing mice. Repeated low-dose irradiation (0.5 Gy, four times, before and within an early time after the inoculation) significantly delayed the tumor growth.

Finally, the effect of single low-dose (0.5 Gy), whole-body □amma-ray irradiation on immune balance (Th1/Th2) was examined in order to elucidate the mechanism underlying the anti-tumor immunity. Recent studies indicate that Th1/Th2 balance plays an important role in the immune responses involved in anti-tumor immunity. The activity of NK is hallmarks of cell-mediated immunity, and play key roles in anti-tumor immunity. The percentage of B cells in blood lymphocytes was selectively decreased after the radiation, concomitantly with an increase in that of helper T cell population, favoring Th1 polarization. The IFN-□amma level in splenocyte culture prepared from EST-bearing mice was significantly increased 48 h after the radiation, though the level of IL-4 was unchanged. IL-12 secretion from macrophages was also enhanced by the radiation.

In conclusion, it has been shown that the anti-tumor effect of 0.5 Gy gamma- ray irradiation is induced by the enhancement of cell-mediated immunity via Th1 polarization. From the viewpoint of others, it may be suggested that Th1-dominant polarization following irradiation is mediated by a decrease of B cell population and enhance the activities of tumoricidal effector cells, leading to a delay of tumor growth in EST-bearing mice.

BRONCHIAL RADIATION BURDEN OF THE UP CLEARING DEEPLY DEPOSITED RADON PROGENIES

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Most of the lung cancers of former uranium miners developed in the large central airways. More than 90% of the neoplastic lesions have been found in airway generations 3-5. Current computational fluid dynamics calculations indicated high primary deposition density values in this region. However, no one analysed the dose contribution of the deeply deposited up clearing radon progenies in the same region, that is, in airway generations 3-5. The surface of the airways highly increases and the deposition efficiency does not decrease remarkably with generation number, thus, it looks a reasonable supposition that the dose contribution of the up clearing, deeply deposited, radon progenies can be significant.

In the present work, the primary deposition distributions of inhaled radon progenies were computed in the whole respiratory system by the stochastic lung deposition model at different breathing conditions. In addition, a new bronchial clearance model has been elaborated to simulate the up cleared fractions of attached and unattached radon progenies in each of the bronchial airway generations. Finally, the ratio of the up cleared and primarily deposited fractions has been calculated at airway generation level at two different breathing patterns.

The main input data of the clearance model are the deposition data, the velocity of the mucus in a generation, the length of the airways and the half life of the radon progenies.

Based on the results, in the central airways, the radiation burden of the up clearing, more deeply deposited, radon progenies can be even ten times higher than the burden of the primarily deposited fraction in this airways both at resting and light physical activity breathing conditions in case of unattached and attached radon progenies. The dose contribution of the deeply deposited ^{218}Po and ^{214}Pb isotopes in the large airways are much higher than that of ^{214}Bi. The radiation burden of the more deeply deposited ^{214}Po in the central airways is practically zero because of its short half life. The results demonstrate that one of the reasons of radon induced lung cancer may be the dose contributions, in the central airways, of the up clearing, more deeply deposited, radon progenies.

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TOCOLS AS POSSIBLE RADIOPROTECTANTS FOR LOW LEVEL RADIATION EXPOSURE.

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Objective of this study is to develop non-toxic tocols as radiation protective agents against acute exposure to lethal doses of gamma radiation. In this presentation these studies will be reviewed to explore the possibility of using tocol isoforms – tocopherols and tocotrienols as radiation protective agents against exposure to low levels of radiation doses.

Methods used in these studies involve administration of selected tocols (α-and δ-tocopherol and γ-tocotrienol) to male CD2F1 mice subcutaneously before exposure to Cobalt-60 and monitoring their survival, which is used as a parameter for radioprotective efficacy. Amelioration of peripheral blood cell cytopenia was used as another parameter of radioprotective efficacy. *Ex-vivo* aorta was used to explore some of the mechanistic aspects of radiation protection related to endothelial cells.

Results and conclusions. Gamma-tocotrienol (GT3) exhibited significantly higher protection than equivalent doses of α- and δ-tocopherols (AT, DT). Gamma-tocotrienol was also protective at higher radiation doses and was effective at a low dose of 1.25 mg per mouse. Hematological studies indicated that both tocopherols and tocotrienol prevented radiation induced peripheral blood cytopenia. *Ex-vivo* studies with abdominal aorta showed that GT3 protected also from accumulation of potent reactive nitrogen species (RNS) induced by radiation exposure, which persisted for 4 days after exposure.

Low level radiation exposure can be of 3 types – acute one time exposure, exposure for protracted durations lasting for a few days to months as in the case of an attack by a radiological terror weapon like 'dirty bombs', and residual radiation exposure from a major nuclear power plant accident (example- Chernobyl) or from a major nuclear attack. An interesting aspect of protection by AT is the large window of protection from 12 to 24 hrs and very low toxicity. Therefore, a mixture of tocols - GT3 and AT could be easily administered repeatedly at low doses without any toxic side effects as a radioprotectant. GT3 can also protect from any possible accumulation of RNS with protracted or long-term exposure to low levels of radiation.

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ALTERATIONS IN SHIKONIN DERIVATIVES OF *LITHOSPERMUM ERYTHRORHZON* CELL CULTURES AFTER GAMMA-IRRADIATION

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To help mass-production of shikonin applicable to medicine, dye and cosmetic, we have studied generation of *L. erythrorhizon* callus lines with a high content of shikonin using gamma irradiation. However, other shikonin derivatives as well as shikonin have similar medicinal efficacy. In the present study, we investigated contents of shikonin derivatives in *L. erythrorhizon* cell cultures, which were irradiated with 2-Gy gamma radiation and cultivated for 23, 25, 28, 29, 32 or 36 days. HPLC analysis revealed a higher total yield of shikonin derivatives in the irradiated cultures than in the control ones which could be attributed to noticeable increase in the content of acetylshikonin. Moreover, although acetylshikonin, deoxyshikonin and hydroxyisovalerylshikonin existed as major shikonin derivatives in the control and irradiated cultures, dimethylacrylshkonin, isobutyrylshikonin, isovalerylshikonin and 2-methylacrylshikonin among shikonin derivatives were detectable only in the irradiated cultures. This data suggest that gamma irradiation may increase other shikonin derivatives, e.g. acetylshikonin, as well as shikonin in *L. erythrorhizon* cell cultures.

MEASUREMENTS AND MODELING FOR EXAMINATION OF MAGNITUDES AND THRESHOLDS AND TRANSITIONS OF CELLULAR RADIO-PROTECTIVE MECHANISMS

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Purpose: To provide results of dose and dose rate measurements, modeling and analysis for the high Radon "inverse" dose-rate effect (IDRE), adaptive response (AR) , Bystander Effects (BE), Hyper-radiosensitivity and dose induced radioresistance (HRS/IRR) and the low LET IDRE. **Methods:** Radon progeny particle diameters decrease at high Radon levels, due to increased neutralization rates. Underground miners data are used to confirm lung dose effects. An adaptive response Microdose Model formulated from the microdose concepts of Feinendegen and his cohorts, is extended to include BE and applied to IDRE, AR and BE experimental data. **Results:** Analysis of underground miners data conclusively supports a factor of 4.3 in lung dose from increased deposition in the nasel passages, negating BE as cause of the Lubin et al (1995) high Radon lung cancer IDRE. This negates support of BE as major concern at domestic Radon levels and high LET galactic radiations for manned Mars mission. AR Microdose Model use for mammography X-rays shows single Specific Energy Hits, at very low dose rates to the cell nucleus, activates AR protection against spontaneous neoplastic transformations of a factor of 2 further supporting Redpath (2007) of no deleterious cancer risk from mammography X-rays and a dose/dose-rate coupling. IRR in HRS/IRR is from increased repair capability "triggered" at a very low dose of 15 cGy. The "triggering" is shown in low LET IDRE with G2/M checkpoint arrest. The correlation suggest IRR in both HRS/IRR and low LET IDRE dose and dose rate radio-protection are from the activation of same increased repair rate protective mechanisms i.e. dose/dose-rate coupling. In examination of LDR Brachytherapy, it's plausible the high excess post-treatment complications, especially for cervix cancer, compared to HDR Brachytherapy is from a high-radiosensitivity for the decaying permanent implant sources below the IDRE threshold with a possible factor of 10 excess dose to connective tissue and organs. Finally, a method for measuring the changes in endogenic cell capabilities to carry-out increased radio-protective processes i.e. separate decreased direct damage (greater ROS scavenging) and the increased repair rates (increased damage recognition, increased damage site location, increased repair mobilization and finally increased repair of the actual damage). This method shows for low LET IDRE no decreased direct damage occurs and significant increased repair occurs. After the "triggered" threshold and transition of IDRE protection against cell killing, a larger fraction of cell damage produces viable mutations. This suggests that the cells bio-chemically conclude it is senseless to provide protection against potentially mutations in the low dose rate region if all the cells are being killed. **Conclusions:** The BE does not cause the underground miners high Radon IDRE. Single Specific Energy nucleus hits at very low dose rates activate adaptive response protection of spontaneous neoplastic transformations from mammography X-rays. A dose and dose-rate coupling is modeled. A correlation between the "triggering" of the transition of the radio-protection for the Hyper-radiosensitivity and dose induced radio-resistance effect (HRS/IRR) and the low LET "inverse" dose-rate effect (IDRE) as if they are from same radio-protective mechanisms. Possible excess connective tissue and organs damage occurs from low LET IDRE in LDR Brachytherapy treatments with permanent implants.

EFFECTS OF LOW DOSE IRRADIATION ON THE MAIN IMMUNE PARAMETERS AND ON THE ANTITUMOR IMMUNE SURVEILLANCE IN MICE

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Objectives: We investigated the effect of low dose ionizing radiation on the quantitative and qualitative changes of major immune parameters in healthy mice and studied how low doses influence the anti-tumor immune surveillance.
Methods: Mice were irradiated with different doses of gamma-radiation (0.01, 0.05, 0.1 and 2 Gy) and 24 h later a moderately immunogenic mouse glioma 261 tumor was transplanted subcutaneously into the mice and tumor growth followed. To study radiation effects on various lymphocyte subsets, mice were irradiated (0.01, 0.05, 0.1, 0.5, 1, 2 and 4 Gy), one, three or seven days later the animals were killed and lymphocytes isolated from spleen. The ratio of various lymphocyte subsets were determined by flow cytometry. The proliferative response of lymphocytes to non-specific stimuli (Concanavalin A) was also investigated.
Results: Pre-irradiation of mice before tumor transplantation seriously prohibited tumor growth. Three days after whole body irradiation, non-specific stimuli-induced lymphocyte proliferation was inhibited in a dose dependent manner; even radiation doses as low as 0.01 Gy suppressed lymphocyte proliferation. The anti-proliferative effect persisted at least for a week. Flow cytometry data show that low dose irradiation affects the main compartments of T-cell immunity, but ample differences exist in the radiosensitivity of various cellular compartments, with the Cd4+CD8+ compartment being the most radiosensitive and the CD4+CD25+ compartment being the most radioresistant. Interestingly, these lymphocyte subsets presented hypersensitivity to radiation at low doses (10, 50 and 100 mGy). The low dose hypersensitivity was most prevalent for NK cells, where 100 mGy and 1 Gy radiation doses killed nearly the same number of NK cells (about 50% survival). The time course of these alterations was followed, and the most ample changes could be seen at day 3 after irradiation.
Conclusion: The experiments suggest that even low doses of ionizing radiation might have substantial impact on various compartments of the immune system.

LONG TERM CHANGES OF PROSTACYCLIN IN RADIATION MYELOPATHY

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Objectives: Prostaglandins changes in response of radiation induced myelopathy have been reported. Long term study was proposed to determine the profile of Prostacyclin content in irradiated rat cervical cord.
Methods: Wistar rats were irradiated with doses of 2,4,6,15,25,30 and a single group of 35 Gy's of X-rays. After 13, 26 and 39 weeks post-irradiation, samples of spinal cord were prepared for evaluation of PGI2 and histopathologic changes. Prostacyclin content was determined by quantification of 6-keto-prostaglandin-F1α (prostacyclin stabilized metabolite). Irradiated segments of spinal cord were stained routinely for histological studies. Results of irradiated were compared to control groups.
Results: The 50% latent period and Effective dose were obtained 14.86±1.16 and 25.66±0.54 Gy ($p< 0.0001$), respectively. Average ratio values of 6-keto-PG-F1α for doses of 2-30 Gy were between 62.20-98.89%, 78.33-112.93% and 79.48-99.96% for 13, 26 and 39 weeks post-irradiation, respectively. Prostacyclin level after 35 Gy shows approximately 7:1 ratio in comparison to control group ($p< 0.002$). Histopathological glial and vascular changes were diagnosed by light and electron microscopes.
Conclusion: Our results were compatible with the results of other reported experimental studies. PGI2 bimodal secretory profile was observed along with histopathological changes in this study. radiation show more complex fluctuations of prostacyclin, however, they may be associated with the marked histopathological changes.
Key-words: Spinal Cord, Radiation Myelopathy, Prostaglandin, Histopathology

MONTE CARLO SIMULATION OF TLD RESPONSE FUNCTION: SCATTERED RADIATION APPLICATION

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Objectives: Thermoluminescent dosimeters (TLDs) have various applications for measuring of non-primary radiation dose. Purpose of the present study is to simulate the calibration factor quality dependence of TLD for more robust clinical use in scattered beam dosimetry.
Material/Methods: TLD material made from LiF doped with Mg and Ti in size of 3.1x3.1x1 mm^3 were used for experimental measurements as well as modeling by MCNP-4c monte-carlo simulation. TLDs were irradiated for diferent doses of beam qualities ranged from 120, 180, 200, 250 and 300 kVp x-rays generated from orthovolage machine and 1.25 MeV gamma rays from Co-60 teletherapy unit at reference depth in water phantom. The simulation was the same as experimental condition. The calibration factor, $(CF)_q$, and its quality dependence factor, $\left(F_{Co}^{X}\right)$, were defined as:

$$\left(CF\right)_q = \text{Calibration Dose/TL} \quad , \quad F_{Co}^{X} = \frac{TL(X)/D_{med}(X)}{TL(Co)/D_{med}(Co)}$$

Results: The normalized values of measured quality dependence factors for different xray beams were 1.28, 1.24, 1.16, 1.07 and 1.03 for different beam qualities, respectively. Comparatively, the MCNP simulated findings were 1.134, 1.96, 1.139, 1.052 and 1.034. The change of calibration factor with energy followed the equation:

$$CF = B_0 + B_1 E + B_2 E^2 + B_3 E^3$$

where CF and E are calibration factor and energy (keV), respectively. B_0, B_1, B_2 و B_3 are constants.
Conclusion: Our finding showed significant deviation of true dose value when TLDs are calibrated at different beam quality. The greatest deviation was $19.9 \pm 2.1\%$ in beam quality of 120 kVp. Obtaining a dose response curve may be helpful to calculate the calibration factor with more precision.
Key words: TLD response, calibration, quality dependence, MCNP

HANDLING LOW RADIATION BETA RAYS: NO GRAVE CONCERNED

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Autoradiography was done in monitoring the kinetics of spermatocytes labeled from their 'S' period with a view to estimating the duration of individual stages of meiosis and spermiogenesis in a large number of vertebrates from Fish to Mammals since 1970's during our research work in other University and the Genetics Laboratory, University of Burdwan, West Bengal. A pilot study was engineered by injecting intraperitoneally, or intratesticularly, or even directly into blood vessels in any vertebrate without any distinction of mammal or non-mammal, 05 μ Ci of ^{3}H TDR (Sp. Act. 14600 m ci/mM, BARC, Trombay).

Exclusive studies had been made using isotopes at the level of Karyotypes and individual chromosomes were identified through autoradiography, Banding and Fluorescence microscopy but no chromosomal aberration has been noticed.

DROSOPHILA AS A MODEL OBJECT IN TO STUDY CHERNOBYL NPP AFTER.

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Water extractions of soil probes, which were selected on areas with different density of radioactive pollutions near Chernobyl exclusion zone („Apple-tree garden" (Chernobyl); "Island" (the bank of the pond-cooler of the Chernobyl nuclear power plant); "Torch" (the area of revegetation near the Chernobyl nuclear power plant); "Red forest" (side of a road) and "Red forest" (edge of a forest)) were investigated. Dosimetric metering of all studied areas was conducted. γ- and β-activities of soil probes were determined by spectrometry and radiochemistry methods. The contents of trace elements in the soil probes of areas the „Apple-tree garden" and "Island" were determined. Water extractions from soil were prepared according to standard method (ratio - 1 : 2,5).

The mutagenicity of water extractions of soil was estimated using the test of frequency of the sex-linked lethal mutations of *Drosophila melanogaster*. Water extractions were directly adds to a nourishing medium instead of standard component - distilled water. The strain of wild type of *Drosophila Canton-S* and natural populations of *Drosophila* from Pyriatin and Chernobyl were used in our study. The natural populations of Chernobyl and Pyriatin were included in study for more fully estimation of influence of factor on genetic processes of *Drosophila*, because of presence of unspecific adaptations of natural populyations from radioactive polluted territories (as was shown before).

According to dosimetric analysis data radiation activity of all water extractions of soils did not exceed a natural background. The probes of soil from areas the „Red forest" and the „Torch" were marked the higher activity; total activity of them was over 110 Mbk/kg.

It is possibly that this fact was the reason of the absence of descendants in all variants of experiments conducted on medium with water extraction the „Red forest" and in a variant of experiments concerned on study of activity of water extraction from soil of area „Torch" on the strain of *Canton S.* According to analysis of water extractions of soils the statistically significant increase of frequency of the sex-linked lethal mutations was observed in population of *Drosophila* from Chernobyl breed on the medium with water extractions of soils from probe of the area „Torch" only. In other variants, namely in the study of influence water extractions of soil on a laboratory *Drosophila* line and on the individuals of population of Pyriatin we did not obtained the data. It is possibly because of high toxicness of this probe. Survival of Chernobyl population on this medium maybe reflects the adaptations to this factor. Toxic for all of studied strains or populations of *Drosophila* was the water extraction of soil collected from the area the "Red forest" (edge of a forest). The death of paternal individuals and their descendants on the stage of egg was observed in all variants of experiments.

RADIATION PROTECTION AWARENESS IN DENTISTRY STUDENTS

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Using an anonymous questionnaire, the radiation protection awareness of
Dentistry students were assessed in one of the school of dentistry in Iran.11% of responders had attended a radiation protection course. This study showed that those who have attended this course had improved knowledge of ALARA principle, assessment of the impact of digital imaging in patient dose reduction and usage of personal dosimeter systems. Course attendance made no considerable difference to knowledge of the patient dose, dosereduction techniques and annual permissible dose limits of general public and radiation workers. The results of this study revealed that the majority of students have not received adequate radiation protection teaching and even if a course has been attended, overall knowledge is still poor and formal teaching at undergraduate level should be corrected in the future.

EVALUATION OF DOSE EQUIVALENT TO THE PEOPLE ACCOMPANYING PATIENTS IN DIAGNOSTIC RADIOLOGY USING MCNP4C MONTE CARLO CODE

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Objective: X rays used in diagnostic radiology contribute a major share to population doses from man-made sources of radiation. In some branches of radiology, it is necessary that another person stay in the imaging room and immobilize the patient to carry out radiological operation. ICRP 70 recommends that this should be done by parents or accompanying nursing or ancillary personnel and not in any case by radiation workers.
Methods: Dose measurements were made previously using standard methods employing LiF TLD-100 dosimeters. A TLD card was installed on the main trunk of the body of the accompanying people where the maximum dose was probable. In this research the general purpose Monte Carlo N-particle radiation transport computer code (MCNP4C) is used to calculate the equivalent dose to the people accompanying patients exposed to radiation scattered from the patient (Without protective clothing). To do the simulations, all components of the geometry are placed within an air-filled box. Two homogeneous water phantoms are used to simulate the patient and the accompanying person. The accompanying person leans against the table at one side of the patient. Finally in case of source specification, only the focus of the X-ray tube is modelled, i.e. as a standard MCNP point source emitting a cone of photons. Photon stopping material is used as a collimator model to reduce the circular cross section of the cone to a rectangle. The X-ray spectra to be used in the MCNP simulations are generated with spectrum generator software, taking the X-ray voltage and all filtration applied in the clinic as input parameters. These calculations are done for different patient sizes and for different radiological operations.
Results: In case of TL dosimetry, for a group of 100 examinations, the dose equivalents ranged from 0.01 μsv to 0.13 msv with the average of 0.05 msv. The results are seen to be in close agreement with Monte Carlo simulations.
Conclusion: The results suggest that under correct technical conditions, the doses received by accompanying people in radiodiagnostic examinations can be limited to acceptable values and certainly can be under the limits of permissible dose to publics (1msv per year). However; if exposure are repeated frequently, exceeding the limits mentioned above will be probable.

RISC-RAD: A EUROPEAN INTEGRATED APPROACH TO THE PROBLEM OF LOW DOSES

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Funded by the European Commission in the framework of a dedicated programme supporting research in the Nuclear sector (FP6 Euratom), the project RISC-RAD[2] undertakes experimental and modelling studies ultimately to improve low dose radiation cancer risk assessment by exploring and providing evidence for the most appropriate radiation cancer risk projection and interpolation models. It started on 1st January 2004 and is running until 31st October 2008. It mobilizes a consortium of 31 partners and is coordinated by Dr. Laure Sabatier from the French atomic energy commission.

Indeed the project represents an unprecedented attempt to integrate horizontally the research on the effects of low doses of IR at the European level. A multipartner project supporting objective-driven research, RISC-RAD aims at contributing to bridge the remaining gap of scientific knowledge about effects of lows doses of ionizing radiation. It spans a large part of the research spectrum, including many topics addressed during the LOWRAD2007 conference.

This presentation intends to give an account of the integrative aspects of the project, insights on the innovative solutions found to approach a complex and controversial scientific topic like the biological effects of low doses of ionizing radiation, and links with some areas of social studies on science.The concept of “integration” implies the development of a new kind of activity in the research field, which crosses its traditional boundaries : controversies of several kinds must temporarily be overcome within the project management board in order to define and follow a common strategy. Among them, how to reconcile the creative part of fundamental research with the compliance to strict project planning rules has come up as a debate which questions the best way a significant collective and coordinated action can address the issue of the low dose cancer risk assessment on the long term. The knowledge and experience gained within RISC-RAD, and the results of the project will give the low dose community an interesting perspective on interdisciplinary research issues.

[1] the acronym stands for Radiosensitivity of Individuals and Susceptibility to Cancer induced by Ionizing Radiations.

PERSISTENCE OF MICRONUCLEI IN PERIPHERAL BLOOD LYMPHOCYTES OF THYROID CANCER PATIENTS 24 MONTHS AFTER TREATMENT WITH ^{131}I

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Objective: The persistence of DNA damage after exposure of human populations to low LET radiation is a key issue in radiobiology. The aim of this work is to present micronuclei data from a set of non-familial thyroid cancer patients that have undergone treatment with the same dose of ^{131}I (2590 MBq; 70 mCi) following surgical thyroidectomy. We have previously shown that, up to six months after ^{131}I treatment, a mild but significant and persistent increase in the frequency of micronucleated lymphocytes was observed in the 19 patients studied. The work reported here is a further step on the micronuclei analysis, by following the patients 24 months after the treatment in order to evaluate if the DNA damage was still present.

Methods: The cytokinesis-blocked micronucleus (CBMN) assay was performed with whole blood cultures. The frequency of micronucleated binucleated lymphocytes (‰ MNBN) presented 24 months after therapy was compared with the levels observed before any therapy. The number of patients involved in the present study was 11, since 8 patients from initial group were submitted to an additional ^{131}I treatment, and therefore excluded.

Results and Conclusion: At 24 months after therapy the ‰ MNBN (mean value ± SEM) increased from the pre-therapy value of 5.5 ± 1.3 to 9.6 ± 0.8 (P<0.05). This represents a near 2-fold increase of the initial levels of DNA damage presented by the patients. Furthermore, the increase herewith observed is similar to the ones observed at 1 and 6 months after treatment, reinforcing that the induction of micronuclei is a persistent effect of ^{131}I treatment.

EFFECTS OF RADIATION AND APOLIPOPROTEIN E ON LIPID PROFILE AMONG WORKERS OF NUCLEAR POWER PLANTS IN KOREA

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Several studies reported that the radiation was positively related to fatty liver, low HDL cholesterol, and hypertriglyceridemia. Genetic polymorphism affect prevalence of chronic disease by molecular epidemiology studies. Apolipoprotein E is an important genetic determinant of cardiovascular disease (CVD), namely through its influence on lipid metabolism. Thus, we investigated whether radiation and apo E polymorphism, and environmental factors contribute to the lipid profile in workers of nuclear power plants in Korea. DNA was extracted from the whole blood of 6896 study subjects (6357 males and 359 females), and apo E polymorphism was investigated using PCR. Plasma lipid profiles were measured by standardized enzymatic procedures and radiation dose was measured by the thermoluminescence dosemeter (TLD). Environmental factors such as exercise, smoking were measured from health management database of KHNP. Total of 6802 subjects (aged 20-58) were investigated and radiation exposure dose was 168.51±463.94 mSv in the recent 1-year dose and 248.24±559.21 mSv in the total accumulative dose. In addition, Apo E polymorphism was associated with significant differences in total cholesterol, HDL cholesterol, radiation dose, AI but others no significant. The multiple regression model showed that total cholesterol was positively correlated with age, SBP, BMI, AI, fasting glucose. HDL cholesterol was negatively correlated with AI. LDL cholesterol was positively correlated with age, BMI, fasting glucose. And triglyceride was significantly correlated in the BMI, AI, somking dose, vegetables but others no significant. Metabolic syndrome did not show any relation to the others; only age, SBP, DBP, BMI, fasting glucose, HOMA-IR influenced. However, there was no significant association between radiation dose and lipid profile. In conclusion, Apo E and well-known variables such as SBP, BMI were significantly associated with lipid profile level but radiation was not. These results suggest that radiation doses in the nuclear power plant workers in Korea may not cause the cardiovascular disease (CVD).

SUPPRESSION OF NON-PHOTOCHEMICAL QUENCHING IN *ARABIDOPSIS* LEAVES TO A IONIZING RADIATION

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Non-photochemical quenching (NPQ) of chlorophyll fluorescence has been known to be involved in a protection of photosystems against photoinhibition through a dissipation of excess light absorbed by photosynthetic pigments. In the present study, we aimed to elucidate the effects of a ionizing radiation on NPQ by comparing alterations in the development and release of NPQ after gamma-irradiation between the wild-type (WT) and the npq1-2 mutant of Arabidopsis. The npq1-2 mutant can't develop with a normal NPQ under excess light, since it is defective in its de-epoxidase activity for conversion of violaxanthin to zeaxanthin. Gamma-irradiation with a dose of 200 Gy inhibited the development of NPQ in both the WT and mutant but more noticeably in the latter. Moreover, Fv/Fm as an indice of the photochemical efficiency of photosystem II (PSII) was almost the same in both the WT and npq1-2 mutant throughout the post-irradiation period of 5 d. The obtained results will be also discussed with those from photoinhibition induced by non-ionizing radiations such as visible light and UV-B.

A SURVEY ON RADON REDUCTION EFFICIENCY OF ZEOLITE AND BENTONITE IN A CHAMBER WITH ARTIFICIALLY ELEVATED RADON CONCENTRATION

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Objective: Zeolite which is made of a special crystalline structure is a naturally occurring mineral group and can be used in radioactive waste management for site remediation /decontamination. There are a wide variety of naturally occurring and synthetic zeolites, each with a unique structure. The cations in zeolite are highly mobile and can be exchanged for other cationic species. On the other hand, bentonite forms from weathering of volcanic ash. This material may be used as an engineering barrier to enclose nuclear waste. In this study, radon reducing properties of zeolite and bentonite have been investigated.

Methods: Using radioactive lantern mantle, a radon prone area with radon levels reaching the EPA's action level (200 Bq/m^3) was designed. Two sets of identical chambers (cylindrical chambers, diameter 10 cm, height 16 cm) were used in this study. No zeolite/bentonite was used in the 1st set of the chambers. A thin layer of either zeolite or bentonite powder was applied to the base of the first set of chambers. An unburned radioactive lantern mantle (activity 800 Bq) was placed in all chambers (both sets) to artificially increase the radon level inside the chamber and simulate the condition of a radon prone area. Radon level monitoring was performed by using a PRASSI portable radon gas survey meter.

Results: After placing the cap on its place, the radon levels inside the 1st set of the chambers were 871.9, 770.3, 769.2 and 635.7 Bq/m^3 after 15, 30, 45 and 60 minutes respectively. Zeolite significantly decreased the radon concentration inside the chambers and radon levels were 367.9, 435.4, 399.0 and 435.4 Bq/m^3 after 15, 30, 45 and 60 minutes. The observed reduction in the radon level was statistically significant. As the radon concentrations in identical chambers with Bentonite were 550.7, 526.5, 536.2 and 479.8 Bq/m^3 after 15, 30, 45 and 60 minutes respectively, it is evident that zeolite is more efficient in reducing indoor radon levels.

Conclusions: Zeolite and bentonite significantly decrease the indoor radon level. The efficiency of zeolite in radon reduction is significantly higher than that of bentonite. As both zeolite and bentonite can be found in many parts of IR Iran, these mineral sorbents can be used in national remedial action programs.

THE OVERALL RESULTS OF A STUDY ON THE STIMULATORY EFFECTS OF TOPICAL APPLICATION OF RADIOACTIVE LANTERN MANTLE POWDER

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Background: Over the past 3 years we have studied the bio-stimulatory effects of the topical application of radioactive lantern mantle powder on rats' neck wounds. Poor educated people in some parts of Iran use burned mantles as a wound healing powder to prevent the bleeding and infections caused by injuries. Some lantern mantles contain low levels of radioactive thorium for maximizing the light output, while non-radioactive mantles contain yttrium. Although radioactive lantern mantles present a minimal radiation health hazard, it is generally believed when inhaled or ingested, thorium containing mantle powder, will be dangerous. In this paper the overall bio-stimulatory effects of burned radioactive lantern mantles on wound healing are presented.

Materials and Methods: To perform surface area measurement, twenty rats were divided randomly into two groups of 10 animals each. After inducing general anesthesia, full thickness excision wound was made on the dorsal neck in all animals. The 1st group received topical burned radioactive lantern mantle powder at 1st-3rd day after making excision wounds. The 2nd group received non-radioactive lantern mantle powder at the same days. Accurate blind surface measurement of the wounds by transparency tracing was used for assessment of the wound healing at 1st, 3rd, 7th, 10th and 15th days after making wounds. For histological study, 36 male rats randomly divided into two groups of 18 animals each. Full thickness excision wound (314±31.4 mm2) was made on the dorsal neck in all animals after inducing general anesthesia. For the first 3 days, cases received topical application of the radioactive lantern mantle powder while controls received non-radioactive lantern mantle powder. Three, seven and fourteen days after wounding, 6 rats were chosen by random in each group for wound sampling. Finally to measure the tensile strength, an incision was made on the dorsal neck of the rats. Samples were obtained at 14th, 21st and 31th days after making incisions.

Results: Surface area measurement of the wounds showed a progressive surface reduction in both groups. However, for thorium treated group, the rate of recovery was significantly enhanced compared to that of the control group. Although the wound area in the thorium group was not significantly different from that of the control group at the 3rd and 5th days after wounding, a statistically significant difference was observed between the thorium and the control groups at the day7, day10 and day 15. The mean wound surface in thorium and control groups were 150.20±15.87 and 186.37±12.68 mm2 at day7 ($P<0.001$), 92.90±15.97 and 134.12±14.19 mm2 at day 10 ($P<0.001$), 1.4±0.41 and 8.56±2.04 mm2 at day15 after wounding, respectively ($P<0.01$). On the other hand, histological study showed a significant statistically difference between cases and controls with respect to fibrinoid necrosis and exudative neutrophilic at the days 3 and 14. Considering the existence of granulation tissue, a significant difference was observed between case and control groups at days 3 and 7. No difference was observed in superficial epithelization and collagen fiber synthesis at all days. Tensile strength study showed no statistically significant difference between the cases and controls at the days 14 and 21. However, a significant difference was observed at day 31 ($P<0.001$).

Conclusion: The overall results obtained in this long-term study suggest that low-level radioactive burned mantle is capable of decreasing inflammatory reactions and accelerates wound healing in rats. However, as thorium oxide is a known human carcinogen, more research is needed to clarify if low levels of radioactive burned mantle can be utilized for accelerating the healing of human wounds. These results confirm the findings of other investigators who showed a wide variety of stimulatory effects in human and laboratory animals after exposure to low levels of ionizing radiation.

SURVIVAL ADAPTIVE RESPONSE IN RATS INDUCED BY SOME COMMON RADIOGRAPHIC PROCEDURES

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Objective: Low dose irradiation suppresses the molecular responses against a subsequent high dose irradiation. Survival adaptive response can be defined as increased survival of laboratory animals pre-exposed to a conditioning (adapting) dose after irradiation with a high (challenge) dose. In this study, the induction of survival adaptive response is investigated in rats exposed to x-rays generated by a common radiographic machine followed by a challenge irradiation.

Methods: Twenty rats (average weight of 200g) were divided randomly into four groups each consisting of 5 animals. The 1st-3rd groups were pre-exposed to 3 different common diagnostic levels of x-rays; low (0.22±0.03 mGy; mean±SD), intermediate (0.43±0.05 mGy) and high (0.93±0.10 mGy). These entrance surface doses were similar to doses received in common radiographic procedures. The 4th group was only sham exposed to x-rays. Twenty four hours after conditioning dose, a Cs-137 source was used for irradiating all animals with a sublethal challenge dose of 7 Gy.

Results: Two weeks after the irradiation with challenge dose, 2, 3, 5 and 2 animals survived in 1st to 4th groups respectively. Thirty days after irradiation with challenge dose, 2, 1, 4 and 2 animals survived in 1st to 4th group respectively. The observed differences in survival rates in either 1st or 2nd group with the 4th group were not statistically significant. Although the animals in the 3rd group (high adapting dose) had a higher survival rate compared to either 1st and 2nd groups or the 4th group, these differences were not statistically significant.

Conclusions: These findings may confirm the previous reports that indicated the existence of a narrow window of adapting doses for induction of adaptive response.

MATERNAL DENTAL RADIOGRAPHY DURING PREGNANCY IS NOT ASSOCIATED WITH TERM LOW BIRTH WEIGHT

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Objective: In a report published in JAMA in 2004, Hujoel and colleagues indicated that maternal dental radiography during pregnancy may be associated with term low birth weight. Interestingly, they concluded that dental radiographies cause measurable radiation doses to the hypothalamus-pituitary-thyroid axis and the radiation effects on this axis is the reason for term low birth weight. On the other hand, low birth weight is the second leading cause of infant death. In this paper the results obtained in a 2 year study conducted at a midwifery hospital in Rafsanjan, IR Iran are reported.

Methods: Four hundred seventy-five singleton infants with gestational periods of 37-44 wk born between 2006 and 2007 at the Niknafs Teaching Hospital affiliated with Rafsanjan University of Medical Sciences and met the inclusion criteria were enrolled in the study. Demographic data and clinical findings at birth including gestation age, sex of infant, birth order, season of birth, maternal age, and maternal education were collected from maternal and newborn hospital records and by interviews with parents. Maternal history of exposure to common sources of man-made ionizing and non-ionizing (exposure to radiations emitted by mobile phones, CRTs, cordless phones) radiation before and during pregnancy were carefully recorded.

Results: Among the 475 infants who were studied, there were only 15 cases with a history of maternal dental radiography during pregnancy. The average newborn infants' birth weight in non-exposed and exposed (maternal dental radiography during pregnancy) groups were 3166.69 ±481.31 g and 3118.67±341.42 g respectively. This difference was not statistically significant.

Conclusions: In this study, low birth weight was not associated with maternal dental radiography during pregnancy. These results are generally inconsistent with those reported by Hujoel and colleagues.

LOW DOZE Γ-IRRADIATION INFLUENCE ON *DROSOPHILA* LIFE SPAN IN DIFFERENT GENETICS BACKGROUND

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The main goal of this work was to study in Drosophila melanogaster the contribution of DNA damage sensing and repair, apoptosis and heat shock defence into life span and physical activity alteration after gamma-irradiation at low doze rate.
In our experiments, the strains were exposed to chronic gamma-irradiation from a 226Ra source (50 R/h) at doze rate 0.17 cGy/h at pre-imago development stages only. The absorbed radiation dose per generation (from embryo to imago, 12 days) was 60 cGy. Life span estimation was prepared in adult males and females separately. We compared the life span of apoptotic (p53, *DIAP-1, dApaf-1, Dcp-1, reaper, grim and hid*), heat shock defence (HSP70, HSP23, HSF), DNA damage sensing (ATR) and repair (XPF, *XPC, PCNA, DSB repair helicase homologs*) mutants after chronic irradiation with the control.
On the basis of our investigation we have concluded:

1) Low doze irradiation alter the life span depending on genetic background (mutant alleles, heterozygosity level and sex)
2) Age dynamics of physical activity positively correlates with the life span
3) Longevity potential forms at early development stages
4) DNA damage sensing, DNA repair, heat shock defence and apoptosis as aging preventing mechanisms play crucial role in radiation-induced life span hormesis.

SOME CHEMICAL INFLUENCE ON GENETIC EFFECTS OF IONIZING RADIATION AND BIODOSIMETRY PROBLEMS

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Radiation sensitivity is a quantitative character from genetic point of view and the distribution of this character values in populations is characterized by a binomial curve. So, 50% of the population have the mean values of radiosensitivity ($x \pm 0.67\sigma$), 95% of individuals have radiosensitivity values equal to $x \pm 1.96\sigma$ and 5% of the population have this characters ranged from $x \pm 1.96\sigma$ to $x \pm 3\sigma$, with division into the supersensitive fraction (2.5%) and the superresistant one (2.5%). Radiosensitivity as well as other quantitative characters is caused by the interaction of some pairs of polymeric genes determining a lot of physiological and biochemical organism features. Thus, irradiation in the same dose can induce different level of mutations or other biological effects in different humans.

Besides, radiosensitivity depends to a great degree upon environmental factors. For instance, a level of radiosensitivity depends on physical activity, nervous and psychological state, hormonal balance etc. A diet can change an individual radioresistance - food rich in vitamins, microelements, adaptogens and so on favors the increase in individual radioresistance. Many food stuffs contain radioprotectors or antimutagens. So, tea, coffee, cocoa, chocolate, mushrooms and other products have melanin, which is a very effective radioprotector not only against acute irradiation, but even against chronic one according to out data. On the contrary some substances in our food such as residual amounts of fertilizers or herbicides can be mutagenic or increase mutagenic action of radiation. In the last case we observed synergetic or antagonistic effects.

Radioadaptive response is one of the most significant factors which can be responsible for uncorrected radiation dose evaluation by biodosimetry methods. This phenomenon decreases effects of ionizing radiation approximately twice. Adaptive reaction can be induced by low radiation dose as well as by weak chemical mutagens or by many other factors and can change biodosimetry results. Some drugs, stress, virus diseases and so on can change biological effects of radiation too.

So, many factors which are not under control can change significantly biological effects of radiation and by this way can be responsible for serious mistakes of individual biodosimetry. It is necessary to take into account that these factors are averaged over a population. That's why biological methods can be used for population radiation dose estimation but not for personal one.

RADIATION-INDUCED STRESS EFFECTS FOLLOWING LOW DOSE EXPOSURE

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Recent advances in our understanding of effects of radiation on living cells suggest that fundamentally different mechanisms are operating at low doses compared with high doses. Also, acute low doses appear to involve different response mechanisms compared with chronic low doses. Both genomic instability and so called "bystander effects" show many similarities with well known cellular responses to oxidative stress. These predominate following low dose exposures and are maximally expressed at doses as low as 5mGy. At the biological level this is not surprising. Chemical toxicity has been known for many years to show these patterns of dose response. Cell signaling and coordinated stress mechanisms appear to dominate acute low dose exposure to chemicals. Adaptation to chemical exposures is also well documented although mechanisms of adaptive responses are less clear. In the radiation field adaptive responses also become important when low doses are protracted or fractionated. Recent data from our group concerning bystander effects following multiple low dose exposures suggest that adaptive responses can be induced in cells which only receive signals from irradiated neighbours. We have data showing delayed and bystander effects in humans, rodents 3 fish species and in prawns following in vitro and/or in vivo irradiation of haematopoietic tissues and, from the aquatic groups, gill and skin/fin tissue. Bystander signals induced by radiation can be communicated from fish to fish in vivo and are detectable as early as the eyed egg stage, i.e. as soon as tissue starts to develop. Using proteomic approaches we have determined that the bystander and the direct irradiation proteomes are different. The former show significant upregulation of 5 proteins with anti-oxidant, regenerative and restorative functions while the direct radiation proteome has 2 upregulated proteins both involved in proliferation. These data have implications for environmental radiation protection of human and non-human species alike and suggest a highly conserved mechanism of stress response. Simple extrapolations from high to low dose exposure may need to be re evaluated. This presentation will discuss our knowledge about these low dose radiobiological effects in both human and non-human biota.

POTENT RADIO-PROTECTIVE EFFECTS OF VITAMINS E AND C ON RADIATION INDUCED DNA DAMAGE IN GAMETES LEADING TO LOWER FREQUENCIES OF CHROMOSOMAL ABERRATIONS AND MICRONUCLEI IN SUBSEQUENT EMBRYOS

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Objective: To compare the effects of parental and maternal exposure of NMRI mice with γ-rays on gametes in the absence or presence of vitamins E and C and subsequent cytogenetic damage in pre-implantaion embryos generated from irradiated gametes.
Materials and Methods: Male and female NMRI mice were whole body irradiated in the presence of 200 IU/Kg vitamin E and 100 μg/ml vitamin C. Various mating schemes were designed for mating of irradiated mice, e.g. mating irradiated male with non-irradiated female, irradiated female with non irradiated male or both male and female irradiated. About 68 h post coitous, 4-8-cell embryos were flushed out from oviducts and fixed on slides using standard methods in order to screen for chromosome abnormalities and micronuclei.
Results: In control embryos, frequencies of abnormal metaphase and embryos with micronuclei was low and there was no significant difference between
vitamins treated samples and controls. However there was an increase in both abnormal metaphases and micronuclei frequency in embryos generated after parental or maternal irradiation or both. Vitamin E effectively reduced the frequency of aneuploidy in all irradiated groups and vitamin C was very effective in reducing the frequencies of micronuclei. DRF calculated for both vitamins indicate that vitamin C is more potent than vitamin E in reducing clastogenic effects of gamma-rays in pre-implantation embryos.
Conclusion: Data indicate that γ-irradiation affects spermatogenesis and preovulatory stage oocytes in male and female mice respectively. These effects might be due to DNA alterations in sperms and oocytes affecting meiotic segregations that may lead to chromosome abnormalities in subsequent embryos expressed as numerical chromosome abnormalities or micronuclei. Administration of vitamins E and C before irradiation effectively reduced the frequency of chromosomal abnormalities. The way these vitamins reduces genotoxic effects of radiation might be via radical scavenging mechanism or antioxidative effects. Higher DRF observed for embryos generated after vitamin C treatment might be due to water soluble nature of this vitamin or its direct involvement in DNA repair.

VERY LOW DOSE AND DOSE-RATE X-RAY INDUCED ADAPTIVE RESPONSE IN HUMAN LYMPHOCYTES AT VARIOUS CELL CYCLE STAGES AGAINST BLEOMYCIN INDUCED CHROMATID ABERRATIONS

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Objective: To study the adaptive response induced by very low doses of X-rays at very low dose rate in human lymphocytes at different cell cycle stages followed by a challenge dose of bleomycin sulphate at G2 phase.
Materials and Methods: Human peripheral blood lymphocytes before (G0) and after PHA stimulation (G1 and G2) were exposed to 1 and 5 cGy X-rays generated by a fluoroscopy unit with a dose rate of 5.56 mGy/min and challenged with 5 μg/ml bleomycin sulphate (BLM) 48 hours after culture initiation. Mitotic cells were arrested at metaphase by addition of colcemid in cultures 1.5 h before harvesting. Harvesting and slide preparation was performed using standard method. 100 well spread metaphases were analyzed for the presence of chromatid type aberrations for each sample.
Results: Results obtained indicate that there is a linear relationship between the dose of BLM and chromatid aberrations below 5 μg/ml ($R=0.93$, $p<0.0001$). The results also show that pre-treatment of lymphocytes with low dose X-rays at G0, G1 and G2 phases of the cell cycle significantly reduced the sensitivity of lymphocytes to the clastogenic effects of BLM in G2. Much lower frequencies of chromatid aberrations were observed in X-ray irradiated lymphocytes following BLM treatment ($p<0.05$). The magnitudes of adaptation induced at different phases of the cell cycle were not significantly different. Furthermore, there was no a significant difference in the magnitude of adaptive response induced by either 1 or 5 cGy X-rays.
Conclusion: These observations might indicate that resistance of pre-exposure of lymphocytes to very low doses of X-rays protects them from clastogenic effects of BLM. This effect might be due to initial DNA damage induced in these cells leading to provocation of an active DNA repair mechanism independent of cell cycle stage.

ASSESSMENT OF NATURAL RADIATION EXPOSURE AND RADON EXHALATION RATES FROM THE SOIL OF ISLAMABAD DISTRICT OF PAKISTAN

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The earth's crust is a main source of natural radionuclides in soils and rocks. The specific levels of background gamma radiation depend upon the geological composition of each lithologically separated area, and the content of the rock from which the soils originate the radioactive elements of 226Rn, 232Th and 40K. These naturally occurring radionuclides of terrestrial origin in soil can be a source of external radiation exposure through the gamma ray emission whereas internal exposure occurs through the inhalation of radon gas. The measurements of natural radioactivity and the assessment of radiological hazards in the soil samples of Islamabad district of Pakistan have been carried out using High Purity Germanium (HPGe) detector. The radon exhalation rates from these samples have also been estimated employing the "closed-can" technique of passive dosimeters. The measured activities of 226Ra, 232Th and 40K were found in the range 14 - 30, 18 - 40 and 301 – 655 Bq.kg-1. The annual effective dose was calculated in the range 0.15 – 0.31 mSv. The values of external and internal hazard indices were less than 1. The radon exhalation rates these areas were found in the range 200 - 345 mBq.m-2h-1.

IMMUNOMODULATORY EFFECTS OF ULTRAVIOLET B IRRADIATION ON ATOPIC DERMATITIS IN NC/NGA MICE

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Background: Atopic dermatitis (AD) is a common pruritic inflammatory skin disease with severe itching which occurs primarily in childhood. Overexpression of serum IgE are also a characteristic feature in many patient. Furthermore, Th2-type T cell cytokine, such as IL-4, IL-5, and Il-10, are produced in AD lesions. Recently, ultraviolet B (UVB) irradiation may increase according to depletion of the ozone layer. Furthermore, phototherapy is used to treat AD patient, but the mechanism involved is unknown. In this study, we investigated whether UVB irradiation influences atopic dermatitis in the NC/Nga mouse model.
Methods: The mice were separated into 3 groups, control, AD-control (immunized with mite antigens), and AD + UVB-irradiated (immunized with mite antigens and UVB irradiation) groups. The mice of the irradiation group were exposed to 1 kJ/m^2/day twice a week from 6 to 12 weeks of age. Animals of the control and AD-control groups were shaved, but not irradiated.
Results: In the AD + UVB-irradiated group, the atopy score, ear thickness, and total IgE were increased in comparison with the AD-control group. On day 40, the levels of IL-4, IL-5, and IL-10 in the spleen lymphocytes were significantly increased compared with the AD-control group, resulting in a marked decrease of the IFN-г/IL-4 ratio compared with the AD-control group. In addition, the levels of IL-6, TNF-α, and NO_X production by peritoneal macrophages were significantly elevated.
Conclusion: These results indicate that UVB irradiation promotes the development of AD-like symptoms in NC/Nga mice, with an increased inflammatory response owing to increases of both IgE and NO_X. In addition, systemic immune responses to local UVB were observed. It is possible that upstream proteins involved in IL-4, IL-5, IL-6, IL-10, and TNF-α, and NO_X production play roles in the UVB-induced inflammatory responses. Our results also suggest that sunlight may aggravate the pathological symptoms of AD.

ANALYSIS OF CORRELATION BETWEEN NON-CANCER MORBIDITY OF CHILDREN AND THE INTERNAL DOSE OF ^{137}CS

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Objectives: **1)** to define relationship of child morbidity of the digestive system from the internal dose, taking into account also the environmental conditions of residence and age peculiarities of children.; **2)** to select the groups of comparison of children 0-14 years old, who residents in analogical environmental and social-economic conditions for study of preferential influencing only of radiation factor; **3)**to reveal tendencies in the dynamics of IR of diseases of the digestive system (520-579 by ICD-9) for period after the Chernobyl accident for children – residents of high (>100 kBq\ m^2), middle (47 kBq\ m^2) and low (<10 kBq\ m^2) contamination levels of territories; **4)** to calculate the internal doses of ^{137}Cs for variable cohorts of supervisions with different history of dose forming (different age at the moment of start of exposure, its duration and contamination of diet).
Methods: The official indexes of child morbidity of the Zhitomir area (adjoin to Chernobyl), through 1988-2006, were used for time series analysis and their retrospective comparison, analysis of trends with the statistical support (the SAS system was used to create the regression lines), calculation of attributive risk, coefficients of correlation and statistical support of relationship between morbidity and time after Chernobyl accident, density of soil contamination and internal dose of ^{137}Cs. The environmental conditions of residence with analogical intensity of migration of 137Cs from soils in local food products were chosen by a landscape - geochemical cards. ^{137}Cs internal doses were calculated by the ecological model of estimation of radiation consequences of agrocenosis contamination (Kravets, 2003).
Results: The analysis of dynamics of risk morbidity showed the peaks in 1997-2001 for children from high contamination regions and small vibrations from low one. Increasing of IR trend line were from 1991 to 1999 statistically significant (< 0,05) . Then the trends went down in contamination regions and hesitated round the former level in low contamination regions. The morbidity peaks (1999) correlated with the level of contamination of soils (r=0,99). The children, who are born during Chernobyl accident, were reached 14 years in 1999 and they were excluded from child's group of statistical account after that year. Group was filled up by children, who are born after Chernobyl accident. Morbidity began to go down in high contamination regions as far as new born children were added to the group of statistical account and after excluding of children, who were born in the year of accident and who had accumulated the large doses. We have defined direct relationship of morbidity of the digestive system from the internal dose in children – residents of high contamination regions with predominance of sour soils, who are born during and on the eve of the Chernobyl accident.
Conclusion: Children, who are born during and on the eve of the Chernobyl accident, are the group of the promoted risk of morbidity of diseases of the digestive system.

THERAPEUTIC EFFECT OF GAMMA-RAY ON COLLAGEN-INDUCED ARTHRITIS VIA UP-REGULATION OF REGULATORY T CELLS

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We previously showed that small doses of total-body irradiation prevent type I diabetes, chemically induced hepatotoxicity and autoimmune disease in respective animal model. Here, we studied the effect of 0.5 Gy gamma-ray irradiation on collagen-induced arthritis (CIA) in DBA/1J mice. CIA is the most widely used as an arthritis model so far. Immunization of DBA/1J mice with type II collagen in complete Freund's adjuvant induces the development of arthritis. The histopathology of CIA is characterized by synovitis, pannus density, which are quite similar to human rheumatoid arthritis.

Mice were immunized with type II collagen, and exposed to gamma-rays (0.5 Gy per week for 5 weeks). We observed delayed onset and reduced severity of the pathology of arthritis in irradiated CIA mice compared to non-irradiated CIA mice. The incidence of CIA was also reduced by the irradiation. Moreover, bone degradation and increase of spleen weight were suppressed by the irradiation. Production of tumor necrosis factor-alpha, interferon-gamma, and interleukin-6, which play important roles in the onset of CIA, was suppressed by the irradiation. The level of anti-collagen II antibody, which is essential for the onset of CIA, was also lower in irradiated CIA mice. The population of plasma cells was increased in CIA mice, but irradiation blocked this increase. Since regulatory T cells, which suppress activated T cells, are involved in amelioration of autoimmune disease, the population of $CD4^+CD25^+Foxp3^+$ regulatory T cells was measured. Intriguingly, a significant increase of these regulatory T cells was found in irradiated CIA mice.

In conclusion, our data suggest that 0.5 Gy gamma-ray irradiation could ameliorate CIA by inhibiting cytokines and autoantibody production, and through induction of regulatory T cells. Furthermore, since interleukin-6 is also known to be involved in differentiation of naïve T cells into regulatory T cells, irradiation –induced suppression of interleukin-6 could contribute to up-regulation of regulatory T cells.

LOW DOSE AND DOSE RATE EFFECTS ON RADIATION MUTAGENESIS, TERATOGENESIS AND CARCINOGENESIS

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Low dose and dose rate effectiveness is one of the most important subject to study for the risk of radiations in humans. In the present study, analyses were made at various dose rates (0.04 to 1, 189 mGy/min) for our data on radiation induced cancer, malformation and mutation in mice after the germ-line, *in utero* or postnatal exposure and also for the direct effects of radiation on human thyroid tissues maintained in SCID mice.

Exposure of young adult mice to high dose γ-rays (6.8 Gy) at high dose rate induced high incidence of tumors in various organs. However, the incidences of leukaemia, skin tumors and hepatomas decreased strikingly by lowering the dose rate (DDREF; 20-45). DDREF of leukaemia was 1.8-2.5 at lower doses (0.4 and 2.0 Gy). Dose rate effects were observed in all the other tumors (DDREF; 2-4) except breast tumor. *In utero* exposure to X-rays, ^{60}Co γ-rays, ^{252}Cf neutron, and ^{3}H water resulted in the significant increase of somatic (coat color) mutations, malformations and tumors in $PTHTF_1$ mice at dose range from 0.1 to 1.0 Gy, and significant reduction of these defects was observed by low dose rate exposure (DDREF; 3-20). Furthermore, significant increases of leukemia, skin cancer and lung tumor were observed in the offspring of mice exposed to X-rays and γ-rays at spermatogonial stage at high dose rate, but there was no increase of these tumors in the offspring after low dose rate exposure, showing an apparent dose rate effect or protracted dose effect, as in the case in specific locus mutation.

In contrast, double-strand break repair deficient SCID mice showed extremely high sensitivity to both high and low dose rate γ-rays for the induction of leukemia, fetal death and malformation, and there were no dose rate effects in the incidences of these defects, while dose rate effect was apparent in wild-type mice. This indicates that double-strand break repair is a major cause of dose rate effectiveness in radiation induced fetal death, malformation and leukemia.

We have established a novel biotechnology to maintain normal human organs/tissues for a long period (3 years) in the improved SCID mice which are defective of T-cell and B-cell function and can not reject human tissues. Consecutive exposure of human thyroid tissues to X-rays and ^{137}Cs γ-rays at high dose rate resulted in significant yields of *p53* and *c-kit* mutations in the human thyroid tissues in addition to morphological and functional disorder. However, no mutations have been induced by low dose rate γ-ray exposure, showing an apparent dose rate effects, i.e., high repairing ability in the human thyroid tissue. (Supported by MEXT Japan, Mitsubishi Foundation, Princess Takamatsu Cancer Research Foundation, Research for the Future-JSPS, and Japan Space Forum)

INHIBITORY MECHANISM OF LOW-DOSE, WHOLE-BODY IRRADIATION WITH GAMMA-RAYS AGAINT TUMOR METASTASIS

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A lot of beneficial effects of low-dose irradiation are well known. Of them, an inhibitory effect of the radiation on lung metastasis is reported so far. It has been reported that low-dose whole-body irradiation with gamma rays enhanced cytotoxic immune response as one of the mechanisms. In our laboratory, it has been confirmed an enhancement of natural killer activity in mice irradiated with whole-body 0.5Gy gamma-rays. Metastasis is accomplished by multistep process, involving basement membrane destruction, local invasion, intravasation, survival in the bloodstream, extravasation into distant organs, and proliferation at the target site. Besides, a lot of growth factors and proteases are involved in these steps. As to mechanism of inhibition of tumor metastasis induced by low-dose whole-body irradiation, studies from the standpoint of tumor invasion have not been reported.

Here, inhibitory effect of 0.5Gy whole-body gamma-ray irradiation on tumor metastasis and its mechanism were examined in pulmonary metastasis model mice injected with B16 melanoma cells. Consequently, 0.5Gy whole-body gamma ray irradiation significantly suppressed colony formation in the lungs. Expression of matrix metalloproteinase- 2 (MMP-2), a proteinase related to metastasis, in lung tissues was suppressed by the radiation. Alteration of tissue inhibitor of matrix metalloproteinase (TIMP) after the gamma-ray irradiation was examined. Expression of TIMP-1 and TIMP-2 mRNA in the lungs were significantly increased.

In order to clarify the inhibitory effect obtained in the *in vivo* metastatic lung cancer model mice, we studied effects of gamma-rays on cell proliferation, alterations of mRNA and proteins related to tumor metastasis in cultured B16 melanoma cells. Proliferation of B16 melanoma cells was decreased in a dose-dependent manner. MMP-2 mRNA expression was not altered in any doses of gamma-rays. Thought expression of the protein was slightly decreased by 0.5Gy gamma-ray irradiation, there were no significant changes in the activity. Thus, it was concluded that 0.5Gy gamma irradiation had not any significant direct effects on cultured B16 cells.

As a whole, it would be suggested that TIMPs were elevated in the *in vivo* metastatic model mice by low-dose gamma-ray irradiation, resulting in lowering MMP-2 by which tumor metastasis was inhibited.

NON-LINEARITY OF DOSE-EFFECT RELATIONSHIP AT LOW LEVEL EXPOSURE ON THE EXAMPLE OF CYTOGENETIC EFFECTS IN PLANT CELLS

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There has been an increasing concern in the current scientific society and among the public about the need to protect the environment in order to maintain the ecosystem sustainability and future well-being of man. The linear non-threshold (LNT) hypothesis as the most officially acknowledged concept of biological effect of radiation fails to explain many facts on effects at low level exposures (LLE) accumulated lately. Available information on the dose-effect relationship at low doses is scarce and incomplete for non-human species despite the fact that, under conditions of increased radiation exposure, some biota species occur at a risk of higher impact than humans because of differences in ecological niches occupied.

Dose-effect relationships for cytogenetic damage in the range of LLE are studied in a series of experiments with plant (*Hordeum vulgare* L.) meristem cells. Dose-effect dependences obtained show an obvious non-linear behavior in the LLE region. A piecewise linear model (PLM) for dose-cytogenetic effect relationship that considers an existence of dose-independent part at LLE ("plateau") is developed and specified on the data obtained. An advantage of the PLM over linear model in approximating the frequency of cytogenetic disturbances is demonstrated. From an empirical probability distribution analysis, it is shown that the increase in cytogenetic damage level is tightly connected with changes in a process of absorbed energy distribution between target volumes in terms of fraction of cells experienced a radiation hit event. An appropriateness of the LNT hypothesis to the description of cytogenetic disturbances yield in plant meristem cells in the LLE region is discussed. The results support a conclusion about indirect mechanism of mutagenesis induced by low doses.

New data obtained concern a perception of fundamental mechanisms governing cell response to LLE. These findings are of general biological interest, since response to LLE is one of the manifestations of basic laws determining and ensuring the living systems resistance and their adaptation potential under varying habitat conditions. Revealing dose dependence shape and LNT hypothesis eligibility are important at development of both the general ideology of environment radiation protection and the derivation of radiation safety standards that will ensure the human population and ecosystem integrity.

NATURAL POPULATIONS OF *DROSOPHILA MELANOGASTER* FROM RADIOACTIVELY CONTAMINATED TERRITORIES OF UKRAINE

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Drosophila melanogaster has been used as a model object to study Chernobyl NPP after-effects on biological processes. We performed study of natural populations from sites contaminated with radionuclides.

Drosophila individuals were collected in autumn 2005 and 2006 in the regions with different degrees of radioactive contamination. The flies were sampled in Polesskoe with radioactive background of 50 uR/h; near cooling pond of Chernobyl NPP (2100 uR/h); Chernobyl city (60 uR/h); Kyiv (17 uR/h), Lubny (16 uR/h); Piryatin (15 uR/h); Uman (12 uR/h); Odessa (13 uR/h). Hybridological analysis was performed using drosophila laboratory lines *Canton S* (wild type strain) and *C(1)DX* (to detect lethal mutations in sex chromosome). The flies were kept on a standard medium in laboratory conditions. Occurrence of hybrid dysgenesis was monitored by gonad reduction, isolating the gonads and evaluating visually the degree of their development.

Visual mutations have not been found in all the natural populations studied. When the populations were transferred to culture breeding, an elevation of the mutation visible frequency in generations has been detected. The elevation was the highest for Chernobyl (2100 uR/h) population. All the mutations observed are typical for Ukraine.

Low frequency of gonad reduction has been detected. Since the gonad reduction is one of the traits of mobile elements activity in *drosophilids*, a conclusion has been made about the absence of mobile elements activity in all the populations, including the laboratory wild-type line *Canton S*. The results of the gonad reduction analysis indirectly confirm the low frequency of visual mutations in the populations studied.

To assess the spontaneous level of lethal sex-linked mutations, the male/female ratio was evaluated in the first generation and compared with the ratio in the strain *Canton S* (using as control) using $\chi 2$-criterion. In natural populations from Lubny and Piryatin, the level of the sex-linked lethal mutations statistically exceeded the control level during the two years monitoring. For other populations the level of the sex-linked lethal mutations was not higher than that of the control.

EVALUATION OF RADIOLOGY PERSONNEL PRACTICE OF MAZANDARAN UNIVERSITY OF MEDICAL SCIENCES

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Background and purpose:
Radiology department that provides images with proper quality plays a vital role in diagnosis of diseases. Good image is obtained by proper technical criteria and correct Positioning. Personnel practice of radiology department has a principal role on radiographs quality. This study was carried out to determine the radiology department personnel practice in university hospitals.

Method & Material:
Data collection was made using an observational check list. Its validity and reliability was determined previously. The sample size of which was thirty-nine persons. 29 items of practice related to technical and protect ional aspects at three working shifts were observed and recorded separately.

Results:
Results showed that most of the personnel were female (61.5%), over 40 years old (59%) and technicians (53.8%). On the whole, personnel's score percentages in technical field on three shifts of morning evening and night were 47.5%, 46.2%, and 45.9%, respectively which were less than them in protect ional field (60.3%, 56A% and 55.8%, respectively). Comparison of technical protection and total scores related to individual variables showed significant difference only in organizational grades ($p<0.000l$, $p<0.05$, $p<0.000l$, respectively) Le. The mean scores of radiological technologists holding BSc and associate degrees were more than those of technologists not holding university degrees.

Conclusion:
The quality of the personnel practice is not desirable; therefore continuing education programmers are needed for personnel. Protection against radiation exposure, availability of equipment and continuous evaluation of use of equipment can be effective in dose reduction in patients.

Keywords: Radiography - Radiology Department, Hospital - Personnel, Hospital Efficiency

COMPARISON OF VARIOUS ANGSTROM-BASED MODELS FOR ESTIMATION OF SOLAR ENERGY IN SEMI-ARID REGIONS

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Solar radiation data at several stations (34^{o}-35^{o} $30^{'}$ N) in the west of Iran (Hamedan Province) were used to test the applicability of 16 Angstrom-based radiation models available for computing the monthly average global radiation on a horizontal surface. Unlike the basic Angstrom model, the selected radiation models take into account for other meteorological and geographical variables such as ground albedo, altitude, latitude and longitude. To assess the model results, a 12-year (1992-2003) measured daily TSR data were applied. The model results were compared with the experimental data on the basis of statistical error tests. Results indicate that in cold semi-arid climates, the inclusion of altitude, latitude and longitude in Angstrom-based models will not significantly improve the model accuracy. It is shown that the inclusion of ground albedo in non-linear Angstrom models can improve the model results. Among the existing models, the following polynomial relationship:

$$H/H_0 = 0.16 + 0.87\,(n/N) - 0.61(n/N)^2 + 0.34\,(n/N)^3$$

performs the best monthly mean prediction for cold semi-arid mountainous regions. On the average, the amplitude of the errors for the suggested method was less than 1%. Estimating global solar radiation by the adopted approach has proved sufficiently reliable. The selected model could, thus, be used to predict mean daily radiation in areas with no measuring systems or in equipped areas where there are missing data.

Keywords: Global solar radiation; Correlation models; Angstrom-based models; Cold semi-arid climate; Hemedan (Iran)

ATTENUATION OF RADIATION-INDUCED DNA DAMAGE DUE TO PARACRINE INTERACTIONS BETWEEN NORMAL HUMAN EPITHELIAL AND STROMAL CELLS

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Objective
Developmentally, every tissue accommodates different types of cells, such as epitheliocytes and stromal cells in parenchymal organs. To better understand the complexity of radiation response, it is necessary to evaluate possible cross-talk between different tissue components. This work was set out to investigate reciprocal influence of normal human epithelial cells and fibroblasts on the extent of radiation-induced DNA damage.

Methods
Model cultures of primary human thyrocytes (PT), normal diploid fibroblasts (BJ), PT/BJ cell co-culture and conditioned medium transfer were used to examine DNA damage in terms of γ-H2AX foci number per cell or by Comet assay after exposure to different doses of γ-rays.

Results
In co-cultures, the kinetics of γ-H2AX foci number change was dose-dependent and similar to that in individual PT and BJ cultures. The number of γ-H2AX foci in co-cultures was significantly lower (~25%) in both types of cells comparing to individual cultures. Reciprocal conditioned medium transfer to individual counterpart cells prior to irradiation resulted in approximately 35% reduction in the number γ-H2AX foci at 1 Gy and lower doses in both PT and BJ demonstrating the role of paracrine soluble factors. Comet assay corroborated the results of γ-H2AX foci counting in conditioned medium transfer experiments. In contrast to medium conditioned on PT cells, conditioned medium collected from several human thyroid cancer cell lines failed to establish DNA-protected state in BJ fibroblasts. In its turn, medium conditioned on BJ cells did not change the extent of radiation-induced DNA damage in cancer cell lines tested.

Conclusion
The results imply the existence of a network of soluble factor-mediated paracrine interactions between normal epithelial and stromal cells that could be a part of natural mechanism by which cells protect DNA from genotoxic stress.

NON-TARGETED EFFECTS OF IONISING RADIATION (NOTE) – A NEW EUROPEAN INTEGRATED PROJECT, 2006-2010

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The general objectives of the NOTE project are: (1) to investigate the mechanisms of non-targeted effects, in particular, bystander effects, genomic instability and adaptive response; (2) to investigate if and how non-targeted effects modulate the cancer risk in the low dose region, and whether they relate to protective or harmful functions; (3) to investigate if ionising radiation can cause non-cancer diseases or beneficial effects at low and intermediate doses; (4) to investigate individual susceptibility and other factors modifying non-targeted responses; (5) to assess the relevance of non-targeted effects for radiation protection and to set the scientific basis for a modern, more realistic, radiation safety system; (6) to contribute to the conceptualisation of a new paradigm in radiation biology that would cover both the classical direct (DNA-targeted) and non-targeted (indirect) effects. The NOTE brings together 19 major European and Canadian groups involved in the discovery, characterisation and mechanistic investigation of non-targeted effects of ionising radiation in cellular, tissue and animal models. The NOTE research activities are organised in six work packages. Four work packages (WPs 2-5) are problem-oriented, focussing on major questions relevant for the scientific basis of the system of radiation protection: WP2 Mechanisms of non-targeted effects, WP3 Non-cancer diseases, WP4 Factors modifying non-targeted responses, WP5 Modelling of non-targeted effects. The integration activities provided by WP6 strengthen the collaboration by supporting the access to infrastructures, mobility and training. WP7 provides dissemination and exploitation activities in the form of workshops and a public website. Managerial activities (WP1) ensure the organisation and structures for decision making, monitoring of progress, knowledge management and efficient flow of information and financing. Coordinator of the NOTE project is Prof. Sisko Salomaa, STUK - Radiation and Nuclear Safety Authority, Helsinki, Finland. The project is supported by the European Commission under the Euratom specific programme for research and training on nuclear energy, 6th Framework Programme. Please visit the project website http://www.note-ip.org to obtain more information or contact us by e-mail note@stuk.fi.

EXPLORATION OF RADIOMODIFYING EFFECTS OF PEPPERMINT EXTRACT (*MENTHA PIPERITA* LINN) AGAINST GAMMA RADIATION: *IN VIVO* STUDIES

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The radiomodifying effect of peppermint extracts against sublethal and lethal doses of gamma radiation in Swiss albino mice has been explored in our several studies. Peppermint extract (1 g/kg) or peppermint oil (40 μL/animal) pretreatment decreased serum acid phosphatase and increased serum alkaline phosphatase compared with controls after irradiation, but the levels returned to normal within 5 days. Significant alterations in the intestinal mucosa of mice treated daily with 1 g/kg peppermint extract were observed within 20 days post irradiation at 8 Gy. Compared with controls, peppermint pretreatment increased villus height, total number of cells and mitotic cells, and decreased the number of goblet and dead cells. Oral administration of *M. piperita* before exposure to gamma radiation was found to be effective in protecting against the chromosomal damage in bone marrow of mice. A significant increase in percentage of chromatid breaks, chromosome breaks, centric rings, dicentrics, exchanges, acentric fragments, total aberrations and aberrations/damaged cell was observed at 12 hr post-irradiation autopsy time in control animals, whereas *M. piperita* pretreated irradiated animals showed a significant decrease in percentage of such aberrations. Pretreatment with an aqueous extract of peppermint prior to whole body gamma irradiation at 4, 6, 8 and 10 Gy significantly increased the spleen weight and the number of endogenous spleen colonies compared with irradiated mice without pretreatment. A daily oral dose of 1 g/kg administered for 3 days prior to irradiation significantly increased hematological parameters and improved the survival rate compared with irradiated control animals at 10 days post-irradiation. A regression analysis of the survival data in irradiated mice revealed that mice pretreated with peppermint were able to withstand a 1.78-fold higher dose of radiation than untreated mice. A daily oral dose of peppermint oil (40 μL/animal) administered for 3 days prior to irradiation significantly increased hematological parameters (erythrocytes, leukocytes, hemoglobin and hematocrit) compared with controls. Animals pretreated with leaf extract of *M. piperita* and exposed to 8.0 Gy gamma radiation showed a significant increases in the activities of reduced glutathione content, glutathione peroxidase, glutathione reductase, glutathione S-transferase, superoxide dismutase, and catalase. Irradiated group pretreated with leaf extract of *M. piperita* showed significant decrease in malondialdehyde formation in liver. The leaf extract of *M. piperita* showed strong radical scavenging activity in both the DPPH* and ABTS*+ assays. These results suggest the antioxidant and free radical scavenging activities of *M. piperita* constitute a likely mechanism of radiation protection.

Keywords: *Mentha piperita,* gamma radiation, Swiss albino mice, intestinal mucosa, bone marrow, hematological parameters, antioxidant and free radical scavenging activities.

NATURAL PRODUCTS AS RADIATION RESPONSE MODIFIERS

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Protection of cells and organisms against low doses of radiation is a complex issue which must be considered at the level of cells, tissues and organisms. “Protection” at one level, for example, prevention of cell death, may be adverse at another level, if it allows a damaged cell to survive and form a malignant tumour. Conversely, death of a cell carrying damage can be protective for the organism if it eliminates a damaged cell. Thus, it is important to understand the mechanisms involved in protection against radiation damage at several hierarchical levels.

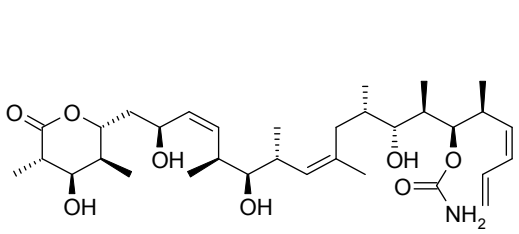
The use of natural products as radiation response modifiers is very attractive. Many of these compounds are readily available and their function and pharmacology is well understood. Some derive from venoms or natural defenses and are currently used in medicine, others include vitamins, antioxidants or cofactors, which are tried and tested nutritional supplements.

Radiation effects may be targeted or untargeted. Radiation may interact directly within a cell causing a direct DNA lesion or it may elicit a bystander response from the irradiated cell. A bystander effect is produced when the irradiated cell apparently exhibits no damage from the radiation, but passes on a biochemical signal which induces neighbouring cells to apoptose or undergo a number of other responses usually associated with irradiation such as mutation induction, transformation, induction of ROS responses etc.. Effects induced in progeny of non-targeted cells in receipt of bystander signals include genetic instability, mini and microsatellite mutations and carcinogenesis. A key characteristic of these non targeted effects is that they occur at very low acute doses (of the order of 5mGy) and saturate so that effective prevention requires an agent which can effectively shut off the mechanism. While the mechanism is not fully known, it is thought to involve signals from irradiated cells communicating via membrane receptors, to induce stress. There is evidence in vivo from bomb survivors of the persistence of these effects for 50 years. The instability consequent on the process can predispose to later carcinogenic insult. At low radiation doses (as might be predicted from a dirty bomb where widespread, disruptive low level contamination is a desired outcome) untargeted effects may predominate in terms of long-term major human health effects.

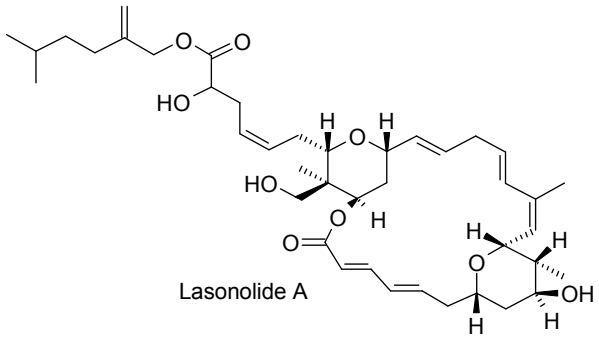
Our hypothesis is that chemicals derived from marine invertebrates will be useful in terms of modifying and negating any long term health consequences. Sessile benthic invertebrates including marine tunicates, cnidarians, and sponges in particular, have developed an array of structurally unique bioactive natural products, which have been demonstrated to afford the producing organism a competitive advantage in ecosystems such as tropical coral reefs, characterized by extreme resource limitations. In addition to limited resources, environmental pressures such as predation, fouling, competition for space and exposure to ultraviolet radiation drive the production of these chemicals. In addition to the variety of toxic compounds produced as defensive agents, organisms use highly coloured pigments to protect against the high levels of UV radiation in tropical coral reefs and pigments such as these are known radioprotectors in radioresistent bacteria .

This paper will review the literature concerning known radiation response modification by natural products, with particular reference to substances which modify low dose effects and will present new data concerning the effects of some marine substances derived from sponges which we have found to sensitise cells to radiation. Drawing together the data in this area

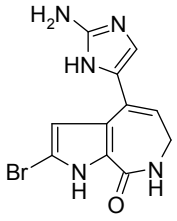
should permit some conclusions to be drawn about the mechanisms operating at low doses which can be targeted for radiation protection. We will also present new preliminary data which uses natural products derived from marine sponges. These products have been shown to have very active radiobiological activity. The structures are shown below



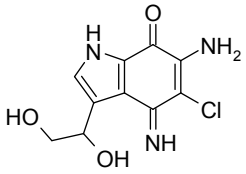
Discodermolide



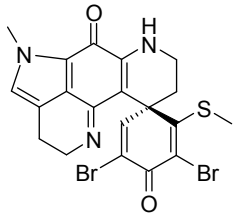
Lasonolide A



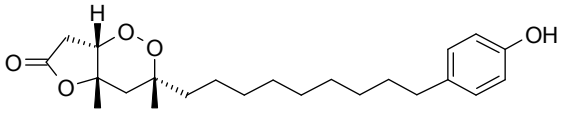
Stevensine



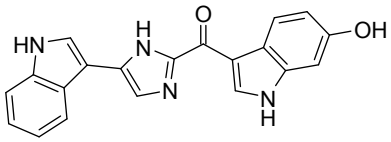
Secobatzellin A



Discorhabdin S



Plakortolide F



Topsentin

These compounds are radiation response modifiers acting via bystander mechanisms

REPEAT ANALYSIS PROGRAM IN RADIOLOGY DEPARTMENT IN NORTH OF IRAN. A POPULATION RADIATION DOSE POINT OF VIEW

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Introduction & Objectives: The analysis of rejected films gives an indication of the sources of radiographic errors. The rejected films may also be responsible for an unnecessary increase in the radiation dose to the population. The effective dose to population is a very important factor in estimation of stochastic risk in radiology. The main goal of this study was to determine the effective dose to members of the public due to discarded films in diagnostic radiology departments in the Northern Province- Mazandaran- of Iran.
Materials and Methods: A Repeat Analysis Program was set in all radiology departments in Mazandaran province (population = 2976219 person) to determine the total number and type of rejected films. All repeat and discarded films were collected and separated into types according to the etiology leading to their being discarded. Considering technical data about various radiological procedures and using the standard dosimetry tables, the annual effective dose per caput as well as annual gonadal dose per caput due to image retake was estimated.
Results: The total number of rejected radiographs in one year period was 73857 (overall reject rate ~11.15%) lead to 34.91 μSv and 37.17 μGy as annual average effective dose to member of the public and annual average gonadal dose per caput respectively. The main reason of retaking the images was improper exposure factors.
Conclusion: The reject rate was in the middle range of similar values in other studies. Whereas in the present study the main reason for rejection was improper exposure factors (67.11%), the main reason for retaking in various countries was different. Comparing to the estimated 2.4 mSv from natural background radiation, the average annual effective dose and annual average gonadal dose per caput due to repeat/retake films are negligible. However, reducing the reject films is economically rewarding. Further national studies are suggested.

ADAPTIVE RESPONSE IN *DROSOPHILA MELANOGASTER* HEAT SHOCK PROTEINS MUTANT STRAINS

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The members of the heat shock proteins (Hsp) family function as molecular chaperones and assist intracellular folding of newly synthesized proteins. Also it is possible that molecular chaperones are induced during adaptive response to oxidative stress and radiation. The aim of our research was to exam the role of heat shock proteins in adaptive response to oxidative stress after low dose rate gamma-irradiation in *Drosophila melanogaster*.

Drosophilamelanogaster strains were kindly provided by Bloomington *Drosophila* Stock Center (University of state of Indiana, Bloomington, USA). We used wild type strain (CS), heat shock protein mutant strains (Hsp22, Hsp70, Hsp83), and heat shock factor mutant strain (Hsf). Strains were chronically exposured to adaptive dose of gamma-irradiation in dose rate of 0.17 cGy/h during all stages of life history (from the embrional stage to the stage of matured imago). The rate of absorbed dose was 60 cGy. For oxidative-stress challenge two-days old flies were starved in empty vials for 6 h and then transferred to vials containing only filter paper soaked with 20 mM paraquat in 5% sucrose solution. Survival data were collected after 26 h of treatment. Dead flies were counted daily. The obtained data were subjected to survival analysis by Kaplan and Meier method and presented as survival curves. Statistical analysis was held by non-parametric methods. To test the significance of the difference between the two age distributions Kolmogorov-Smirnov test was applied. Gehan-Braslow-Wilcoxon and Cox-Mantel tests were used for estimation of median life span differences. In addition the minimal and maximal life span, time of 90 % death, and mortality rate doubling time (MRDT) were estimated.

The obtained results will be discussed in presentation.

INCREASED FREQUENCY OF MICRONUCLEATED EXFOLIATED CELLS AMONG HUMANS EXPOSED *IN VIVO* TO MOBILE TELEPHONE RADIATIONS

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The health concerns have been raised following the enormous increase in the use of wireless mobile telephones through out the world. This investigation had been taken, with the motive to find out whether mobile phone radiations cause any *in vivo* effects on the frequency of micronucleated exfoliated cells in the exposed subjects. A total of 109 subjects including 85 regular mobile phone users (exposed) and 24 non-users (controls) had participated in this study. Exfoliated cells were obtained by swabbing the buccal-mucosa from exposed as well as sex-age-matched controls. One thousand exfoliated cells were screened from each individual for nuclear anomalies including micronuclei (MN), karyolysis (KL), karyorrhexis (KH), broken egg (BE) and bi-nucleated (BN) cells. The average daily duration of exposure to mobile phone radiations is 61.26 minutes with an overall average duration of exposure in term of years is 2.35 years in exposed subjects along with the 9.84±0.745 MNC (micronucleated cells) and 10.72±0.889 TMN (total micronuclei) as compared to zero duration of exposure along with average 3.75±0.774 MNC and 4.00±0.808 TMN in controls. The means are significantly different in case MNC and TMN at 0.01% level of significance. For all other nuclear anomalies (KL, KH, BE and BN cells) the means are found statistically non-significant. A positive correlation was found in the frequency of MNC and TMN with respect to duration of exposure time.

GENETIC EFFECTS OF LOW DOSE IRRADIATION ON HIGHER AQUATIC PLANTS WITHIN THE CHERNOBYL ACCIDENT EXCLUSION ZONE

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The rate of chromosome aberrations has been studied in four species of higher aquatic plants: common reed (*Phragmites australis*), sagittaria (*Sagittaria sagittifolia*), flowering rush (*Butomus umbellatus*) and manna (*Glyceria maxima*).

The main water bodies were Glubokoye Lake and Dalekoye-1 Lake (left-bank flood lands of the Pripyat River), Azbuchin Lake and Yanovsky Crawl (right-bank flood lands of the Pripyat River), cooling pond of the Chernobyl NPP as well as Pripyat River and Uzh River. The absorbed dose rate for hydrobionts from above water bodies in decreasing sequence was: 3.4-1.6 (Glubokoye Lake) > 0.09-0.05 (Dalekoye Lake) > 0.08-0.02 (Azhbuchin Lake) > 0.05-0.01 (Yanovsky Crawl) > 0.03-0.01(cooling pond of Chernobyl NPP) > 0.004-0.002 (Pripyat River) > 0.003-0.001 Gy $year^{-1}$ (Uzh River).

The highest chromosome aberrations rate in root meristems (17.8-10.8 %) were registered in plants from lakes within the left-bank flood lands of the Pripyat River, the lowest one (4.5-2.2 %) - in plants from the Pripyat River and Uzh River. The rate of chromosome aberration in closed and slow-running water bodies of the Pripyat River flood land in 3-4 times higher than spontaneous mutagenesis level. It seems that spectrum of the main types of chromosome damages in plants of the right-bank flood land determines by the chemical mutagens (up to 69 % of single fragments). The type of chromosome damages distribution in plants of the left-bank flood land points to practically equivalent effects of radiation and chemical factors - 44-49 % of bridges, 43-50 % of fragments and 6-8 % of plural aberrations.

Partial or close to complete seed sterility (from 47 to 72 %.) are observed for common reed from investigated water bodies, except of running ones. The correlation between high level of chromosome damages and decrease of plant production has been registered.

A RADIOBIOLOGICAL REVIEW ON MELATONIN: A NOVEL RADIOPROTECTOR

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For the sake of improvement in radiation therapy, radiobiology plays a crucial role through explaining observed phenomena, and suggesting improvements to existing therapies.
Due to the damaging effects of ionizing radiation, radiobiologists have long been interested in identifying novel, nontoxic, effective, and convenient compounds to protect humans against radiation induced normal tissue injuries. Melatonin (N-acetyl-5-methoxytryptamine), the chief secretory product of the pineal gland in the brain, has been documented to ameliorate the oxidative injuries due to ionizing radiation.
This article reviews different features that make melatonin a potentially useful radioprotector. Moreover, based on radiobiological models we hypothesize that melatonin may postpone the saturation of repair enzymes which leads to repairing more induced damage by repair system and more importantly allows the use of higher doses of radiation during radiotherapy to get a better therapeutic ratio. The implications of the accumulated observations suggest by virtue of melatonin's radioprotective and anticancer effects; it is time to use it as a radioprotector both for radiation workers and patients suffering from cancer either alone for cancer inhibition or in combination with traditional radiotherapy for getting a favorable efficacy/toxicity ratio during the treatment. Although compelling evidence suggests that melatonin may be effective for a variety of disorders, the optimum dose of melatonin for human radioprotection is yet to be determined by further research. We propose that, in the future melatonin improve therapeutic ratio in radiation oncology.

Key Words: Melatonin, Ionizing Radiation, Radiobiology, Radioprotective, Radiotherapy, Repair Enzyme.

GENOMIC INSTABILITY AND RADIATION EFFECTS

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Cancer, genetic mutations and developmental abnormalities are apparently associated with an increased genomic instability. Such phenomena have been frequently shown in human cancer cells in vitro and in situ. It is also well-known that individuals with a genetic predisposition for cancer proneness, such as ataxia telangiectesia, Fanconi anaemia etc. demonstrate a general high genomic instability e.g. in peripheral lymphocytes before a cancer has developed. Analogous data have been found in mice which develop a specific congenital malformation which has a genetic background.

Under these aspects it is of high interest that ionising radiation can increase the genomic instability of mammalian cells after exposures in vitro an in vivo. This phenomenon is expressed 20 to 40 cell cycles after the exposure e.g. by de novo chromosomal aberrations. Such effects have been observed with high and low LET radiation, high LET radiation is more efficient. With low LET radiation a good dose response is observed in the dose range 0.2 to 2.0 Gy, Recently it has been reported that senescence and genomic instability was induced in human fibroblasts after 1 mGy carbon ions (1 in 18 cells are hit), apparently bystander effects also occurred under these conditions. The instability has been shown with DNA damage, chromosomal aberrations, gene mutation and cell death. It is also transferred to the next generation of mice with respect to gene mutations, chromosomal aberrations and congenital malformations.

Several mechanisms have been discussed. The involvement of telomeres has gained interest. Genomic instability seems to be induced by a general lesion to the whole genome. The transmission of one chromosome from an irradiated cell to an non-irradiated cell leads to genomic instability in the untreated cells. Genomic instability increases mutation rates in the affected cells in general. As radiation late effects (cancer, gene mutations and congenital malformations) develop by going through several mutation steps, an increase of genomic instability can have the consequence that the probability for the necessary mutation steps after the initiation processes will be enhanced and facilitated. In this connection it is of high interest that genomic instability is increased in several human populations who have developed or will develop a cancer with/or without radiation. The genomic instability was studied in peripheral lymphocytes of these patients. Such an effect has been found in patients with head and neck cancers before treatment. It has been observed in uranium miners and patients with Morbus Hodgkin who developed secondary cancers after exposures. The implications of these phenomena for low dose radiation seem to be important.

APOPTOSIS IN SPERMATOGONIA IRRADIATED P53 NULL MICE

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The exposure of germ cells to ionizing radiations is of concern both from high-dose therapeutic exposures and from low doses causing deleterious trans-generational mutations. P53 protein plays an important role in cellular damage and is expressed in the testis normally during meiosis, its expression being localised to the preleptotene and early/mid pachytene spermatocytes. P53 null mice, heterozygotes possessing a 129 Sv/C57BL6 genetic background and B6D2F1 mice have been irradiated to 1 and 2 Gy single doses. Fractionated exposures of 1+1 Gy at 4 hours interval were also carried out. Apoptosis induction, spermatogonia and spermatocytes survival were assessed by microscope analysis of histological samples at 4 to 96 hours after irradiation in time-course experiments. The same end-points were also assessed at 72 and 96 hours after irradiation to single doses in the region between 20cGy to 2Gy.

A dose dependent level of p53 expression was observed at 4 hours after irradiation to 1 and 2 Gy which returned to normal level by 24 hours. Our data support a two process mode of apoptosis with a first wave around 12 hours followed by a second wave at 2–3 days. The first wave apoptosis is substantially reduced in p53 null mice whereas the second wave is reduced in B6D2F1 mice.

The initial increase in apoptosis was delayed in some stages of the of germ cells development which were identified by the spermatids shape. Clear correlation exists between apoptosis and survival assessed in stage XI–XII Tubules 72 hours after irradiation. The data are in agreement with other data in literature indicating that irradiated spermatogonia die through apoptosis. The lack of apoptosis observed in p53 null mice results in a very high survival rate of daughter cells assessed later. Theses spermatocytes and the following progenitor cells are likely to carry mutations as most will not die in the smaller second wave of apoptosis observed 3 days after irradiation and may contribute to a greater mutational burden with respect to transgenerational effects.

Split-dose data when compared to single dose also shows for p53 null mice a very high rate of spermatogonia survival. The strain +/+ indicates a large mortality rate when the second dose is given at the time mitotic radiation induced delay is highest whereas the strain +/- shows intermediate values. In the +/+ mice efficient apoptosis activity is shown by a first and second wave appearance whereas in p53 null mice only a second wave is clearly visible. These data seems to indicate that in +/+ mice repair mechanisms in spermatogonial cell are extremely low and that poor cellular damage proofreading exists in p53 null mice. The deficiencies in apoptosis related to the p53 status contribute to the high cancer-proneness of individual with p53 deficiency in the Li-Fraumeni syndrome.

TRACER EXPERIMENT BY USING RADIOISOTOPE IN SURFACE WATER ENVIRONMENT

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1. Objective

An expansion of industrial activities and urbanization result in still increasing amount of pollutants discharged into surface water. Discharged pollutants in surface water have harmful effects on the ecology of a river system and human beings. Pollutants discharged into surface water is transported and dispersed under conditions characteristic to particular natural water receiver. Radiotracer method is a useful tool for monitoring the pollutant dispersion and description of mixing process taking place in natural streams. A tracer experiment using radioisotope was carried out to investigate the characteristics of a pollutant transport and a determination of the diffusion coefficients in a river system.

2. Methods

The upper area of the Keum river was selected for the tracer experiment, which is located in a mid west of Korea. The measurements of the velocity and bathymetry before a tracer experiment were performed to select the sampling lines for a detection of the radioisotope. The radioisotope was instantaneously injected into a flow as a point source by an underwater glass-vial crusher. The detection was made with 60 2inch NaI(Tl) scintillation detectors at 3 transverse lines at a downstream position. The multi-channel data acquisition systems were used to collect and process the signals transmitted from the detectors. Two-dimensional numerical models were used to simulate the hydraulic parameters and the concentration distributions of the radioisotope injected into the river.

3. Results and Conclusion

The calculated results such as velocity and concentrations were compared with the measured ones. The dispersion characteristics of the radioisotope were analyzed according to a variation of the flow rate, water level and diffusion coefficients. Also, the diffusion coefficients were calculated by using the measured concentrations and the coefficients obtained from the field experiment were compared with the ones obtained by the theoretical and empirical formulas. The tracer method by using radioisotope appears to be convenient tool to investigate the pollutant transport and dispersion processes in surface water. The data obtained by tracer experiment will be supplied the basis of assessment of actual state of pollution in surface water.

REPEATED 0.5 Gy GAMMA-RAY IRRADIATION ATTENUATES AUTOIMMUNE DESEASE IN MRL-*lpr/lpr* MICE WITH UP-REGULATION OF REGULATORY T CELLS

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MRL-*lpr/lpr* mice present a single gene mutation on the Fas (CD95) gene that leads to reduced signaling for apoptosis. With aging, these mice spontaneously develop autoimmune disease and are used as a model of systemic lupus erythematosus. We previously reported attenuation of autoimmune disease in MRL-*lpr/lpr* mice by repeated □-ray irradiation (0.5 Gy each time). In this study, we investigated the mechanisms of this attenuation focusing the highly activated $CD3^+CD4^-CD8^-B220^+$ T cells, which are characteristically involved in autoimmune pathology in these mice.

We measured the weight of the spleen and the population of $CD3^+CD4^-CD8^-B220^+$ T cells. Splenomegaly and increase in percentage of $CD3^+CD4^-CD8^-B220^+$ T cells, which occur with aging in non-irradiated mice, were suppressed in irradiated mice. To investigate the function of $CD3^+CD4^-CD8^-B220^+$ T cells, we isolated these cells from splenocytes by magnetic cell sorting. Isolated $CD3^+CD4^-CD8^-B220^+$ T cells were more resistant to irradiation-induced cell death than isolated $CD4^+$ T cells. Although high proliferation rate and IL-6 production were observed in isolated $CD3^+CD4^-CD8^-B220^+$ T cells, the proliferation rate and IL-6 production were lower in the cells isolated from the irradiated mice. Moreover, the production of autoantibodies (anti-collagen antibody and anti-single strand DNA antibody) was also lowered by irradiation. These results indicate that activation of $CD3^+CD4^-CD8^-B220^+$ T cells and progression of pathology would be suppressed by repeated 0.5 Gy □-ray irradiation. To uncover the mechanism of the immune suppression, we analyzed population of regulatory T cells ($CD4^+CD25^+Foxp3^+$), which suppress activated T cells and excessive autoimmune responses. Intriguingly, significant increase of the percentage of regulatory T cells was observed in irradiated mice.

In conclusion, we found that repeated 0.5 Gy □-ray irradiation suppresses proliferation rate of $CD3^+CD4^-CD8^-B220^+$ T cells and productions of IL-6 and autoantibodies, and up-regulates regulatory T cells. These results indicate that up-regulation of regulatory T cells would involve in these therapeutic effects induced by irradiation. The up-regulation of regulatory T cells induced by irradiation could be a novel and important observation in low-dose irradiation-mediated therapeutic effects.

A REVIEW OF CANCER MORTALITY DATA OF RADIATION WORKERS OF NUCLEAR POWER PLANT, PAKS, HUNGARY, IN THE LIGHT OF THE INTERNATIONAL RADIATION EPIDEMIOLOGY STUDY

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Objective:
To give a review of cancer mortality data among Hungarian radiation workers in nuclear industry in comparison with the results of the international nuclear workers' study prevailing the size of the study group of all former studies.

Methods:
Retrospective cohort study including 598,068 workers of 154 nuclear establishments in 15 countries (AUS, BEL, CAN, FIN, FRA, GER, HUN, JAP, LIT, ROK, SLK, SPA, SWE, UK, USA) coordinated by the International Agency for Research on Cancer (IARC, Lyon, France). The national study was extended for an additional 4-year period.

Results:
In the international study 407,391 persons in 13 years of average employment received 19.4 mSv mean cumulative dose, while in the national study 3322 radiation workers of Nuclear Power Plant (NPP) Paks, Hungary, in 14 years of follow-up period accumulated in average 5.13 mSv, only.
There were 5233 cancer deaths registered in the international study, associated with an estimated ERR of 0.97 per Sv. Thus, 19.4 mSv recorded cumulative dose can explain 1 to 2 % of cancer death cases.
In radiation workers of NPP, Paks, during the period of 1985-1998 there were 40 cancer deaths observed against the expected 58.8 cases. In a further four year period (1999-2002) 29 cancer death cases were identified vs. the expected 65.5 cases. The SMR for the cancer death cases registered in recent and former radiation workers of NPP, Paks in the 18-year follow-up period is 56 %. The SMR from all causes was even lower, 40 % only.

Conclusions:
Íin the international study the mean accumulated radiation dose received by nuclear workers in 13 years is below of the recent annual dose limit (20 mSv/yr of the effective dose). The average value for the whole of radiation workers in 15 countries is almost 4-times higher of that registered in Hungary. The 'healthy worker effect' in the nuclear industry, and particularly in Hungary has been proven, once again.
Nevertheless, the results suggest that an excess cancer risk exists, albeit small, even at the low doses and dose-rates typically received by nuclear industry workers. Estimates from the international study are statistically compatible with the bases for current radiation protection standards.

CLASSIC AND MOLECULAR CYTOGENETIC ANALYSIS REGARDING HUMAN REACTIVITY TO BETA RADIATION

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One of the most important mutagen agents in developing different types of cancer is the action of ionizing radiation. The main events induced by irradiation are: chromosome breakage, chromosome rearrangements and genomic instability. The chromosomal aberrations are very useful biomarkers as intermediate end points in evaluating harmful biological effects of ionizing radiation. So, the main objectives of this work were: the study of human genome reactivity to beta radiation by classic microscopy; the study of the integrity/modification of the telomeres after irradiation and the analysis of the amplification of the RNA telomerase compound by FISH technique.

Irradiations were performed at Electron Accelerators Laboratory, National Institute for Laser, Plasma and Radiation Physics, Magurele-Bucharest, Romania. The samples were irradiated using an ALIN 10 linear electron accelerator. ALIN 10 is a travelling wave type *linac* operating at 2.998 GHz, 6.5 MeV mean energy, with a 0.1 mm Al foil exit window. Improved Fricke, ferrous sulphate, cupric sulphate and sulphuric acid in triple distilled water dosimetry system has been used to perform preliminary dose measurements.

The conventional Hungerford method on short-term cultures for 72 hrs was adapted for human chromosome investigation. The peripheral blood was collected from aged 27, healthy, non-smoker donor. The doses used to irradiate human blood cultures were: 4, 6, 8 and 10 Gy. The slides for optic microscopy were prepared by air-drying and stained with a 10% Giemsa solution. For FISH technique was used Chromosome In Situ Hybridization Kit. The probes were: one satellite probe - for revealing the telomere and the second one for the RNA telomerase compound.

A large spectrum of chromosomal rearrangements was induced by beta irradiation in humans in vitro: complex chromosomal interchange involving at least two nonhomologous chromosomes, *double minutes* (DM), acentric fragments, dicentric chromosomes, monochromatidic gap and so on.

The most important targets for ionizing radiation being the telomeres, we've tested from this point of view the integrity/modification of telomeres by FISH technique. After we analyzed 100 fluorescent metaphases/irradiation doses/normal case we found the fluorescent signal in aproximativelly 98% of the normal metaphases. After the irradiation, in cases like complex chromosomal interchange or telomere to telomere translocation we did not identified the fluorescent signal at the chromosomal ends implicated in the rearrangements. This observation and the fact that we found the signal on different acentric fragments revealed that the beta irradiation generates important destruction at the chromosomal end.

In this study we've also analyzed one of the telomerase compounds – RNA compound, in normal condition and after beta irradiation by FISH technique. After the molecular cytogenetic analysis we identified the RNA telomerase compound on chromosome 3, q arm, at the two homolog chromosomes in normal probes and also in irradiated one. The fact that we did not found additional signals (more than four signal/metaphase) after irradiation with beta rays revealed the fact, that in this case, the telomerase is not amplified in order to repair the broken telomeres.

DECIPHERING FREE-RADICAL CODE OF RADIATION EFFECTS

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Objective: Ionizing radiation is fundamental environmental factor for life origin and evolution. Free radicals, primordial "sea" for life conceiving and existence, induced by cosmic and terrestrial background radiation, are evolutionally archetypal, ubiquitous, and omnipotent in physiological- pathophysiological dichotomy. Classical free-radical paradigm in radiation biology and medicine, focused in essence on oxidative damage, needs new conceptualization and generalization.

Methods: Suggested novel insights into free radicals dual immanent nature and functions in organism systems are based on original concepts of radicals dynamic charge transfer (CT) - redox ambivalence (interactional nucleo-, electro-, and ambiphilicity spectrum); pertinent chemical reactivity and selectivity delocalization model; physiological functional ambivalence and complementarity, and dynamic free-radical homeostasis.

Results: Subtle perturbations in radicals CT spatiotemporal homeodynamics, in responsive signaling / controlling networks, concomitant alterations in genes expression, transcription, and apoptosis, redox control of mitochondrial ET chain, telomere/telomerase balance, DNA CT, circadian clock, hemispheric biochemical dominance/accentuation, including alteration of nitric oxide-superoxide complementarity, membranes permeability, neurotransmission pattern, synaptic circuitry, etc under radiation exposure have more fundamental impact on organism systems (especially CNS and CVS) deterioration than simple radicals inflicted oxidative (nitrosative) damage of cellular constituents.

Conclusions: This novel conceptualization of free-radical paradigm constitutes new dimension in deciphering molecular mechanisms of radiation effects on subtle borderline norm-pathology and continuity-discontinuity dichotomy in organisms systems disorders – CT(redox)omics, which involves investigation of CT, redox, and spin states of free radicals, DNA bases, intermediates, interacting substrates and milieu, and penetrates and links genomics, proteomics, metabolomics, and chronomics, including mt-DNA domain and epi-counterparts. This can be a basis for deeper understanding molecular nature of gene-expression biomarkers, including genome dynamics, for radiation biodosimetry.

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THE DIRECT PHYSICO-MOLECULAR (NONENZYME) MECHANISM OF HORMESIS AND DOSE-RESPONSE SELF-INDUCED RADIOPROTECTIVE EFFECT AT COMBINED ACTION OF WEAK IONIZING RADIATION AND FREE RADICALS ON DNA

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The time-dependent dynamics of depolymerisation and autorepairing of DNA at separated and combined action of weak and intensive ionizing radiation (including problems of long-distant DNA damage recognition, radiation antagonism and synergism at combined irradiation, low-dose radiation effects and the phenomenon of hormesis) are discussed. Investigations have been aimed at determining the conditions under which double breakages of DNA chains (owing to detrimental irradiation action) become self-eliminable. Nonenzyme mechanism of DNA self-reparation was studied for the first time in our works [1-3]. The main result of ionizing radiation action upon biological system is the creation of double breaks of DNA macromolecules. The energy V(L) of interaction (long-distant stacking) between two end-pairs of DNA nucleotides on the opposite sites of double break are totally under the control of: a) Coloumb interaction of charges, distributed on a surfaces of these nucleotides; b) dispersion features of dielectric permeabilities of the nucleotides and intercellular salt-aqueous medium through all the range of frequencies (Van-der-Waals-like forces). It was shown that at low (natural) concentration η of hydrated electrons in intercellular liquid the energy of interaction of two end-pairs (AT-AT, CG-CG) has the anti-repair barrier $V(L) > kT$ at L=5-7 A [1]. If η is increasing the barrier is reducing. All other transversal end-pairs experience only attraction. Other results of irradiation are generation of hydrated electrons and heavy ions in intercellular medium. Formation of these electrons and ions influences the energy of interaction in two main ways - changing both the permeabilities $\varepsilon(\omega)$ and Coloumb interaction. From one hand irradiation leads to additional DNA breaks. From the other one irradiation leads to the controlled reducing of anti-repair barrier and possible double breaks autorepairing. The time-dependent dynamics of DNA depolymerization, self-repairing at separated and combined action of free radicals, weak and intensive irradiation and low-dose action are studied. Some of our main findings are that [1-3]:

1). With irradiations of short duration ("sharp" irradiation) the usual linear (additive) radiation effect take place: the number of double-strand breaks of DNA is proportional to radiation dose.

2). During irradiation with a small dose with the presence of sufficiently high barrier V(L) there is paradoxical effect – acceleration of DNA degradation at the same full doses and extension of exposure time compared with the case of short-duration irradiation. That result tells us that for the case of small doses, the highest degree of DNA degradation corresponds to long (“chronic”) but not "sharp" irradiation.

3). With chronic, low-intensity irradiation the phenomenon of “hormesis” is seen - decreasing concentrations of double-strand DNA breaks caused by free radicals action, increasing with the intensity of the ionizing radiation. The essence of the process of “hormesis” is the fact that an extremely weak ionizing radiation doesn’t cause additional DNA damage, but creates conditions for elimination of damage to DNA, caused by the effect of free radicals of non-radiation origin.

4). For the case of combined action of two different kinds of irradiation the phenomenon of radiation antagonism (self-induced radioprotective effect) take place: the number of DNA double breaks caused by one kind of intensive irradiation decreases with increasing intensity of the other kind of weak irradiation.

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EXPERIMENTAL OBSERVATION AND INVESTIGATION OF REACTOR Cs-137 ISOTOPE DEACTIVATION IN BIOLOGICAL CELLS

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The problem of natural accelerated deactivation of radioactive waste (including deactivation in environmental) is studied.

In the work the process of direct controlled deactivation of water mixture of selected different long-lived radioactive isotopes in growing microbiological cultures has been studied. The process was connected with transmutation of long-lived active nuclei to non-radioactive isotopes during growth and metabolism of special microbiological MCT ("microbial catalyst-transmutator"). The MCT is the special granules that include: concentrated biomass of metabolically active microorganisms, sources of carbon and energy, phosphorus, nitrogen, etc., and gluing substances that keep all components in the form of granules stable in water solutions for a long period of time at any external conditions.

The base of the MCT is microbe syntrophin associations of thousands different microorganism kinds that are in the state of complete symbiosis. These microorganisms appertain to different physiological groups that represent practically the whole variety of the microbe metabolism and relevantly all kinds of microbe accumulation mechanisms. The state of complete symbiosis of the syntrophin associations results on the possibility of maximal adaptation of the microorganisms' association to any external conditions change. The mechanism of nuclear transmutation in growing biological system is described in details in the book [1].

The research has been carried out on the basis of the same distilled water that contained different long-lived reactor isotopes (e.g., Eu^{154}, Eu^{155}, Cs^{137}, Am^{241}).

In our experiments 8 identical closed glass flasks with 10 ml of the same active water in each were used. The "microbial catalyst-transmutator" was placed in 7 glass flasks.

In six different flasks different pure K, Ca, Mg, Na, Fe and P salts as single admixture were added to the active water. These chemical elements are vitally necessary for any cultures. Each of these replacements completely blocks the channel of transmutation with the use of all biochemical analogs of the concrete chemical element [1]. The results obtained confirmed the importance of such replacements. Two additional flasks were used for control experiments: one flask contained the active water and MCT (but without salts) and in another one was only active water (without salts and MCT). The cultures were grown at the temperature 25^0 C. Activity of all closed flasks has been measured every 7 days by amplitude Ge detector.

The results of controlled influence on gamma-radioactivity of different isotopes in different biochemical compositions are reported. The accelerated deactivation of Cs^{137} isotope was observed!

We have observed speeded up decay of Cs^{137} isotope in all experiments with MCT and with the presence of different additional salts during more 100 days. In control experiment (flask with active water) the law of decay was "usual" and the life-time was about 30 years.

The most speeded up decay of Cs^{137} isotope with $\tau^* \approx 310$ days (accelerated by 35 times) was observed at the presence of Ca salt. At the presence of abnormal (redundant) quantity of potassium in the nutritious media the process of caesium transmutation becomes very weak and life-time of decay was about 10 years.

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GENOMIC MUTATION STUDY FOR LONG-TERM CELLS INDUCED BY CARBON IONS

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[Objective] Densely ionizing（high LET）radiation can increase the relative biological-effectiveness of cell and tissue. Astronauts in the space exploration have the potential exposure of chronic low-dose radiations in the field of low-flux galactic cosmic rays (GCR) and the subsequent biological effects have become one of the major concerns of space science. Furthermore, Heavy ions also are used new radiation therapy owing increased lethal effectiveness of high LET radiation. During radiation therapy, normal tissues also are exposed to ionizing radiation. Radiation can induce genomic mutation and instability in descendants of irradiated cells. Induction of genomic instability can represent one of the initiating steps leading to malignant transformation. Higher frequencies of mutation can be expected to provide higher rates of carcinogenicity with human exposure. Therefore, the study of radiation induced genomic mutation and instability is relevant to the estimates of the risk of secondary malignancies associated with radiation therapy and the carcinogenic effects of space environmental radiation.
The hypoxanthine-guanine phosphoribosyltransferase (hprt) locus has been the most commonly used as a target gene for mutation detection studies. In this study, we investigated the generation expression dependence of mutation induction on HPRT locus in CHO cells irradiated with carbon ions.
[Methods] Chinese hamster ovary (CHO) cells were irradiated with graded doses of carbon ions (290MeV/u, LET:13kev/um) accelerated with Heavy Ion Medical Accelerator in Chiba(HIMAC) at National Institute of Radiological Sciences(NIRS). The survival effect of cells plated immediately after irradiation was measured with cell colony formation assay. After irradiation, cells were continues reseeding and cultures for lone-term proliferation. Cell samples were collected at 6, 12, 18, 24, 30, 37 and 44days post irradiation. Mutation induction of cell samples at the HPRT locus was detected to measure 6-thioguanine-resistant colonies.
[Results] The survival fraction of the cells irradiated by carbon ions was lower than sparsely ionizing (low LET) radiation, and it was also lower in high dose rate (~1.5Gy/min) than in low dose rate (~0.008Gy/min) irradiated at the same dose. Furthermore, high dose (D10 dose) induced high mutation fraction. Low dose and low dose rate had the low mutation fractions and different dose rate induced different mutation fraction even at the same dose. Mutation fraction had lower value before 6 days, and the higher level between 12 to 24 days after irradiated, then value went down.
[Conclusion]The results suggest that high LET radiation may cause higher mutation induction dependent with irradiated dose. Different dose rate also may induce different mutation affection. The heavy ion radiation may cause the long-term genomic mutation and instability of cells. HPRT mutant detection system can be application evaluating the carcinogenic effects of space environmental radiation and heavy ion radiation therapy.

ADAPTIVE RESPONSE AND GENETIC INSTABILITY INDUCED BY A LOW-DOSE RATE RADIATION SIMULATING THE HIGH-ALTITUDE FLIGHT CONDITIONS ON MICE *IN VIVO*

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In the present work, we investigated the effect of a low-dose rate of high-LET radiation that simulates the spectral and component composition of radiation fields formed in the conditions of high-altitude flights on mice in *vivo*. The dose dependence, adaptive response, and genetic instability in generation F_1 born from males irradiated under these conditions were examined in polychromatic erythrocytes of bone marrow using the micronucleus test.
Two-month-old males of SHK white mongrel mice were used. Irradiation was performed for 24 h a day in the radiation field behind the concrete shield of the U-70 accelerator of 70 GeV protons (Serpukhov), which adequately simulates radiation field formed in the atmosphere at a height of about 10 km, to accumulate doses of 11.5, 21.5 and 31.5 cGy (1 cGy/day).
The experiments demonstrated that: 1) irradiation of mice in vivo with these doses of low-dose rate high-LET radiation leads to an increase in cytogenetic damage in polychromatic erythrocytes; 2) irradiation of mice with these doses induces no adaptive response in polychromatic erythrocytes as opposite to γ-radiation; and 3) in mice of the F_1 generation born from males irradiated with doses of 11.5, 21.5 and 31.5 cGy, an increase in sensitivity to additional irradiation with a dose of 1.5 Gy of γ-radiation and the absence of adaptive response compared with the descendants of unirradiated males occur. These data indicate a genetic instability in generation F_1 born from irradiated males.

CYTOGENETIC AND HEMATOLOGICAL STUDIES IN THE WORKERS OCCUPATIONALLY EXPOSED TO LOW LEVELS OF IONIZING RADIATION

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OBJECTIVE:
This study was aimed at detecting both the incidence of chromosomal aberrations and changes in the hematological parameters as biomarkers of possible radiation injury among workers occupationally exposed to low levels of ionizing radiation and detecting the dose-effect relationship.

METHODES:
Samples of peripheral blood were collected from 38 male industrial radiographers exposed to ionizing radiation for 1-16 years and from 24 age- and sex-matched healthy blood donors without radiation history served as control group. All radiation workers were routinely monitored with film badge. Cytogenetic analysis in peripheral blood lymphocytes assessed by the conventional chromosome aberration assay and at least 200 metaphases for each person were scored. The collected blood samples were analyzed for hematological assay using an automatic analyzer Sysmex KX-21, where 14 different parameters were computerized. Mann-Whitney U test was used to compare the frequencies of the unstable aberrations and hematological parameters between test and control groups. Dose –effect relationship and the influence of age and duration of employment was tested by regression analysis.

RESULTS AND CONCLUSION:
The mean frequencies of dicentric and acentric chromosome aberrations were significantly higher in the exposed group than in the control group ($P< 0.0005$). No correlation between chromosomal aberrations and physical dose and age was observed in the exposed group. Also there is no clear relation between chromosome damage and duration of exposure. However, the increase in chromosome aberrations in the exposed group was not followed by a corresponding hematological depression. The average values of hematological indices were within the reference levels and did not show any significant differences with control group. A tendency of decreasing the absolute lymphocyte count within the referential levels was the only hematological effect in radiation workers.
The present results point out the value of chromosome aberration analysis as an important biological indicator and sensitive predictor of the actual risk run by radiation-exposed individuals, in absence of any significant hematological changes. The general underlying principles of the damaging influence of low level radiation in respect to the hemopoiesis are rarely on the mature cells of peripheral blood. The issues of the present biomonitoring study corroborate, in addition to physical dosimetry, the importance of radiation safety programs and the use of up-to-date equipment in reducing the workers' radiation exposure.