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IRPA 12

Concluding Plenary Session I

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Epistemology of radiation protection

- TS I.2.1 : effects on molecules, organelles and cells = 38 abstracts
- TS I.2.2 : effects on tissues and organs = 27 abstracts
- TS I.2.3 : radiopathology = 11 abstracts
- TS I.2.4 : radio-epidemiology = 45 abstracts

⇨ Focus on main issues

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DNA lesions (1)

- DNA DSBs induce the phosphorylation of histone γH2AX are detected and evaluated with fluorescent antibodies
  - After doses as low as 100mGy in human bladder cancer EJ cells (Tian, Beijing, China)
  - To evaluate the response of mouse melanoma cells irradiated with high LET charged particles (p or Li) which have the capability to kill low LET radioresistant cells (Ibanez, San Martin, Argentina)

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DNA lesions (2)

- Cytogenetic effects (FISH) of low energy X-ray of mammography (30 kV) are 1.5 greater than effects with 120 kV photons due to the different energy deposition pattern after photoelectric interaction / Compton (Barquinero, Spain)

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DNA lesions (3)

Mitochondrial DNA

- Description of new mitochondrial deletions induced by IR and analysis of several known mitochondrial deletions in human lymphoblastoid cells exposed to 10 Gy Co60 gamma rays (Liu, Beijing, China)

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Non targeted effects (1)

European integrated project NOTE (20 countries)

- To investigate the mechanisms of bystander, genomic instability and adaptive response
- To investigate if they modulate cancer risk in the low dose region (protection or harmful effect ?)
- To investigate their role in non cancer diseases
- To assess their relevance in radioprotection
- To eventually contribute to new radiation biology paradigms

(Salomaa, Finland)

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Non targeted effects (2)

- Bystander mostly observed mostly at low dose, low dose rate is an important issue in RP . It raises the issue of supra linearity since more cells than directly hit cells are concerned. On the opposite, low dose γ-rays reduce the spontaneous neoplastic transformation (KL Azzam, USA).
- Recommandations not to look at one single mechanism alone but to have a broad view (KL Mueller, Germany)

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Non targeted effects (3)

- Bystander effect has been observed with 2 Gy 4MV photons from a linear accelerator in human breast carcinoma cell line MCF-7 by using the technique of irradiated conditioned medium where culture medium from irradiated cells is used for unexposed cells. Serious genotoxic effects are observed with a clonogenic assay pointing out that standard radiotherapy may induce bystander effect (Zubiria et al, Argentina)

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Non targeted effects (4)

- Bystander effect in 3D artificial tissue system can help understand its role which is still unknown (Belyakov, Finland)

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Non targeted effects (5)

Genomic instability

- Techa riverside population exposed from 1949 on exhibits genomic instability at late time after chronic exposure (Veremeyeva, Chelyabinsk, Russia)

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Effects of low doses of IR (1)

- A regional medicodosimetric register of the Siberian Group of Chemical Entreprises (SGCE) exposed to long term occupational radiation in low dose range (Takhauov, Russia)
  - Hemoblastosis increase incidence (Takhauov, Russia)
  - Increase myocardial infarction but causality not established (Karpov, Russia)
- Effects of chronic contamination by Cs127 in rats : slight modifications of physiological systems without apparent development of pathologies (Voisin, France)

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Effects of low doses of IR (2)

- Attributability of health effects at low radiation doses, a key issue for radiation protection carefully analyzed by Gonzales (Argentina) :
  - Their existence is highly plausible
  - They are improvable at individual level
  - Their individual causation is counterfactual
  - Their occurence is not individually attestable

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Radiation sensitivity (1)

- The on-going RISC-RAD European project on individual radiosensitivity reviewed and highlighted (Paretzke et al, Germany)
- Gene influence on radiosensitivity
  - STAT3 and Erb2 siRNA inhibit growth of U251 astrocytoma cell line. Effect increased in combination with 2Gy radiotherapy (Chen et al, Biejing, China)
  - Major mitotic delay in cultured lymphocytes of $BRCA^{+/-}$ women after 0.5 Gy of γ-rays when compared to $BRCA^{+/+}$ women (Febrer et al, Barcelona, Spain)

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Radiation sensitivity (2)

- IRM2 imbred strain mouse exhibits a resistance to radiation due to a stronger hematoimmune system in comparison to parents strain (Deguan et al, Tianjin, China)
- ATF3, a transcription factor of the ATF/CREB family, is induced in mammalian cells by ionising radiations with a time and dose dependence (Fan et al, China)

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Radiation sensitivity (3)

- Histamine, a growth factor for many neoplasms:
  - modify the radiosensitivity of human malignant mammary cells
  - does not affect the radiosensitivity of human pancreatic adenocarcinoma cells (PANC-1) (Mohamad et al, Buenos Aires, Argentina)
  - protects bone marrow (reduction of aplasia) against cellular damages induced by ionising radiations 10 Gy γ-rays Cs137 (Medina et al, Argentina)

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Radiation sensitivity (4)

- Role of receptors. Adenosine membrane receptors A1 & A3 have different pharmacological effects on myelosuppression induced by IR (Hofer, Czech Republic)
- Radiotherapy and chemotherapy. The synergy of interaction of radiotherapy and anticancer drugs needs to be properly managed in cancer patients. In mice, the highest synergistic effects are observed when the 2 treatments are simultaneous (Rupova, Sofia, Bulgaria)

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Radiation sensitivity (5)

- The interaction of radon exposure and cigarette smoking on immortalized human bronchial epithelial cells is synergistic and is impacted by the order of exposure :
  - only α+smoke cells showed malignant transformation characteristics
  - α+smoke cells showed a higher survival fraction than smoke+α cells. (Zhu et al, Beijing, China)

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Radiosensitivity tests in patients : Micronucleus and alkaline single-cell microgel electrophoresis=comet assay

- Dynamic cytogenetic studies in time (0-120 minutes) have good predictive potential for the detection of patients with a greater risk of side effects after radiotherapy (Di Giorgio, Argentina)
- The ratio of comet tail length before and after diagnostic exposure in children correlates with the dose (Milkovic, Zagreb, Croatia)

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Protective effects (1)

Many compounds have been succesfully tested as protective agents against IR

- Selenium in lipoperoxidation with the thiobarbituric acid reactive substance method / γ-rays of Co60 up to 4 Gy (Ramos de Andrade et al, Brazil)
- Carboxyfullerene C3 in human lymphoblastoid cells / 1-8 γ-rays of Co60 (Shan et al, China)
- Dimethyl sulfoxide (DMSO) in human bronchial epithelial cells / depleted uranium (Zhu et al, China)
- Cu (II) chelates of Schiff bases in animals / X-ray exposure (Malakyan et al, Armenia)

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Protective effects (2)

Many compounds have been succesfully tested as protective agents against IR

- Ethinyl estradiol derivative on the hematopoietic system of mice / 1 Gy whole body irradiation (Wang, China)
- *Mentha piperita* (Linn) in testis of Swiss albino mice / 8 Gy gamma irradiation (Samarth, India)
- Polysaccharides from *Tremella falciformis* on hematopoietic function in mice / 7 Gy γ-rays Cs137 (Xu Wenquing, China)
- Micronized clinopltilolite (as a nutriment) in human lymphocyte of medical workers (Joksic, Serbia)

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Protective effects (3)

- Heat shock proteins (stress induced proteins) HSPs 27, 70 & 90 have different radioprotective effects : HSP27 via reduced apoptosis, HSP70 in the p53-mediated DNA damage response and HSP90 in the post irradiation repair of DNA. But they may contribute to tumour cell resistance to radiotherapy (Kabakov et al, Obninsk, Russia)

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Radioepidemiology

- Review of the role, advantages and limits of epidemiology in radiation research and radiation protection (KL Cardis, Spain) :
  - Evidence of a small risk at low dose LET radiations ?
  - More information to come from cohorts with aging of the people
  - Wish for closer work with radiation biologists

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Protection of workers (1)

- Meta-analysis of more than 40 articles and reports published since 1999 on cancer risk associated with alpha emitters of radon in miners (Laurier et al, France) :
  - Excess of lung cancers, compatible with LNT
  - Radon lung cancer risk persists after taking into account smoking
  - Decrease of magnitude of the association with time since exposure
  - No inverse exposure-late effect at low levels of dose
  - Excess of leukemias but causality not demonstrated
- Similar results in a 3 case control european studies (France, Germany, Czech R) (Leuraud et al)

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Protection of workers (2)

- Overview of research with Canadian national dose registry of 600,000 radiation workers 1951-2007. First analysis of 200,000 workers reports on cancer incidence and risk evaluation (Zielinski, Canada)

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Protection of workers (3)

- Chromosomal instability evidenced as premature centromere division during prometaphase or metaphase has been observed in interventional cardiology personels in comparison to a normal group (Noditi et al, Timisoara, Romania)
- Biological indicators of occupational radiation exposure were searched by looking for differences of response of lymphocytes of workers to complementary irradiation. Subsets of clusters of differentiation (CD24+25+, CD57+8+, CD4+62L+, CD8+28+ and CD8+38+) may be useful indicators (Georgevia, Sofia, Bulgaria)

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Protection of workers (4)

- At Mayak, the first 12309 workers (1948-58) present an excess risk of leukemia, lung, bone and liver cancers (Koshumikova, Russia – Azizova, Russia).
- French workers of Areva and EDF have a lower mortality than the French national population due to a healthy worker effect (Metz-Flamant, France – Rogel, France)
- Depleted uranium :
  - Hematological effects in cleanup workers in Serbia and Montenegro (Milacic, Serbia)
  - A variety of effects in offsprings of military personels to be followed up (Atlagic, Serbia)

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Protection of medical workers (1)

- Medical workers in Canada present a 1.74 excess risk of thyroid cancer : study of 67562 workers between 1951 to 1987 (Zielinski, Canada)
- Chinese medical workers present a 1.2 overall excess risk of cancers (skin, oesophagus and leukemia in males, breast in females) : study of 27011 workers between 1950 to 1995 compared to controls (Wang, China)
- Changes in homeostatic balance parameters as an indicator of prolonged exposure of medical workers in low dose range (Karpov, Russia – Popescu, Romania)

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Protection of medical workers (2)

- Occupational exposure to ionising radiations in medical field do not induce any adaptive response as evaluated by micronucleus test, superoxide production, lipid peroxidation index, SOD and glutathione activity on lymphocytes irradiated by 2 Gy Co60 gamma rays (Djurovic, Belgrade, Serbia)

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Protection of patients

- Cardiovascular disease mortality following cancer during childhood : long term risk after radiotherapy if heart and brain doses > 5Gy or after anthracycline/alkylating chemotherapy (Tukenova, France)

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Post Tchernobyl (1)

- In Belarus state registry includes 276,000 population. Cohorts of people living in the evacuation zone and of people participating to liquidation are identified and form the base for further prospective research (Rozhko et al). Dose distribution regarding thyroid disease indicate that 26% of collective dose was received by 7% of the population in the most contaminated territories.
- Creation of a uniform Chernobyl register of Russia and Belarus on the basis of medical and dosimetry data banks for further research on subregisters of uniform population groups or diseases, e.g., thyroid cancers (Sosnouskaya et al)

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Post Tchernobyl (2)

- In Moldova, a follow up study of 850 patients among 3500 Chernobyl liquidators indicates some impairment of the immune system, i.e., a decrease of total B and T lymphocytes (Bahnarel et al, Chisinau, Moldova)
- Environmental results. Serious cytogenetical effects in embryo tissue of gastropod snails and in root meristem of higher aquatic plants in lakes nearby Chernobyl are reported. The corresponding doses are up to 3.4 Gy/y (Gudkov et al, Kiev, Ukraine).

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Thyroid (1)

- Thyroid dose estimates being improved for 2994 subjects exposed to nuclear tests fallout in Kazakstan at Semipalatinsk 1949-1962 (Drozdovitch, USA)
- Thyroid doses of 126,000 Belarussian exposed after Chernobyl revisited and found to be reasonably consistent (Shinkarev, Russia)
- Validation that thyroid mass, one parameter of dose evaluation, is correlated with body surface area : 12000 controls performed with ultrasound measurements (Skryabin, Belarus)

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Thyroid (2)

- Re-evaluation risk of thyroid cancer among Chernobyl liquidators (Evrard, France)
- Re-evaluation of thyroid dose estimates in 12,000 Belarussian who were children in 1986 (Minenko, Belarus)
- On going meta-analysis of 6 studies regarding the risk of thyroid cancer following exposure to I131 in early life (Kesminiene, France)
- Thyroid cancer morbidity in 65575 children of Gomel and Bryansk post Chernobyl : excess risk of 4.5 (Sosnouskaya, Belarus)

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Radiation injuries on tissues and organs

- Classical description of stochastic effects on cells and deterministic effects on tissues. Not so clear today because threshold values are lowered
- Cataract : threshold lower by a factor10
- Cardiovascular : from 500 mGy, much lower dose than initially said from HN data
- Teratogenesis : different thresholds in embryo
- Mental retardation : no change in paradigm
- Hereditary risk: decrease in WT from 0.25 to 0.04 (ICRP)

(KL Mueller, Germany)

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Treatment of radiation burns

- New paradigm in the treatment of radiation burns as a breakthrough in this domain (KL Benderitter, France) :
  - Early treatment
  - Dose evaluation : MRI + modelisation
  - Surgical removal of tissue > 20 Gy
  - Skin grafting and plastic surgery
  - Mesenchymal stem cells (MSC) grafting
  - Spectacular results in Chile and Senegal workers : early disparition of pain and excellent follow-up after 2-3 years
- Clinical trials for treatment by MSC of hematopoietic disorders after irradiation about to start at the Oural research center for radiation medicine (Dimov, Russia)

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Irradiation protocols and dosimetry

- A clever experimental system has been developed to give reproducible and controllable conditions for low dose and low dose rate beta irradiation in vivo (P32, Y90, I 131 and Lu177).The effectiveness of the system has been validated by measuring the production of ROS in normal human fibroblasts (Michelin et al, Argentina)
- A dosimeter to evaluate the radiosensitivity of irradiated pharmaceuticals has been developped. It uses sultamicillin tosylate. Validation has been made with Electron spin resonance for a range of doses from 1 to 15 kGy (Tepe Cam, Ankara, Turkey)

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Modelisations

- The concept of “breaking barrier cell (antioxidant defense, repair & apoptosis) mechanisms” can be used to build a stochastic model to simulate studies of irradiations and predict carcinogenetic effects, e.g., leukemias (Akushevich et al, Durham, USA)
- A dose rate model has been applied to human fibroblasts and leukemia cells and predicts that in the low dose range, biological response depends on dose rate rather than total dose (Magae et al, Tokyo, Japan)

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My apologies to all of you who were not cited in these highlights and for the eventual lack of precision on cited works