Individual radiosensitivity: a key issue in radiation protection
Michel Bourguignon (ASN), N. Foray (INSERM), C. Colin (CHU Lyon-Sud), France, Ernest Pauwels (Leiden University Medical Center, Pisa University Medical School)

Individual hypersensitivity to radiation is a key cellular phenomenon at the crossroads of DNA lesions repair and signaling and cell cycle checkpoint. It is a real issue in public health since it concerns low as much as high doses of ionizing radiations and 5-15% of the population. Among these:
- thousands of patients who benefit from radiation therapy but also suffer from long term side effects. This raises the question of defining the proper dose for any given patient to cure its cancer and to avoid significant side effects;
- patients who benefit from medical exposures, especially children and young adults and women as part of breast cancer screening by mammography.

Factors of sensibility to ionizing radiations

Radiation oncologists have observed that some patients display hypersensitivity to IR and develop adverse side-effects in normal tissues after radiation therapy, although correct delivery of the dose (Twaddle and Chang-Guade, 2000). The 5 to 15% estimated rate of side-effects (Jung et al., 2001; Dors and Hends, 2001) justify to consider the impact of the individual factor in hypersensitivity to IR.

Hypersensitivity to IR is linked to genetic disorders regarding DNA lesions repair and signaling and cell cycle checkpoint control (Bourguignon et al., 2003). Radiation oncologists have been very cautious not to miss the diagnosis of homoygous patients who are very sensitive to radiations.

Patients with heterogeneous mutations for the same genes present a lower degree of radiosensitivity (Angeli et al., 2003) and account for about 10% of the population (Swift, 1981). Joubert et al. (2008) proposed a classification of individual radiosensitivity on the basis of the results obtained from cell lines of different genetic syndromes and cutaneous fibroblasts of patients. They have notably investigated DSBR with γH2AX foci and genomic instability with MRE11 foci. It represents a new insight regarding both individual radiosensitivity and side-effects following radiation therapy. Fig. 3

The phenomenon of hyper-radiosensitivity to low doses (HRS) in comparison to higher doses has been first described by Joiner et al. in 1996. Fig. 4

HRS has also been demonstrated by Slonina et al. (2009) and Kruger et al. (2010) who looked for its mechanisms.

Colin et al. (2011) irradiated human mammary epithelial from patients with low risk and high familial risk of breast cancer and quantified the number of γH2AX foci in conditions of mammography irradiation: 2 mGy mimicking one view, repetition of 2 mGy with 3 min interval mimicking a standard mammographic protocol with 2 views, and 4 mGy. They observed four statistically significant effects:
- a dose effect with an increase of the DSB yield with increasing dose,
- a supra-additive dose effect with repeated doses, i.e. more unrepaird DSB with 2×2 mGy than with 4 mGy in one single exposure,

The French Nuclear Safety Authority (ASN) recommends to the phenomenon of individual radiosensitivity in the radiation protection system in order to properly protect individuals who are sensitive to ionizing radiation. Besides fundamental research needed to better understand the mechanisms involved in radiosensitivity, a test able to predict the response to radiation is desirable to document this phenomenon on a large scale. It should be easy to perform, manage and interpret, and should produce reliable results within a short time and at a reasonable cost.