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Biological efficiency of different quality X-rays estimated by mFISH analysis of chromosome aberrations induced in vitro in human lymphocytes

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Structural rearrangements of chromosomes –chromosome aberrations (CA) –are the most sensitive marker of radiation exposure. The analysis of radiation induced CA in metaphase cells of peripheral blood lymphocytes is the only valuable method of human biodosimetry. It allows to estimate the dose to which an individual has been exposed occupationally, accidentally or therapeutically. The advanced method of molecular cytogenetics multicolor FISH (mFISH) based on the whole genome painting allows visualizing all chromosome rearrangements with higher precision than routine methods. CA based biodosimetry relies on accurate calibration curves obtained following exposure to reference radiation, usually γ-rays or 250 kVp X-rays. In recent decade, radionuclide γ-rays sources were replaced in research facilities worldwide with X-ray sources charaterised by lower energy, such as 130 kVp, that deliver X-ray spectrum with substantial component of soft X-rays (20-30 kV). Given multiple reports of increased relative biological efficiency (RBE) of soft X-rays, we aimed to compare CA dose response curves following exposure to X-rays from 130 and 220-250 kVp sources, as well as to X-ray spectrum for manufacturer provided settings and custom-hardened spectrum of 130 kVp X-ray source.

For the first time, we exploited multicolor FISH method to investigate the biological efficiency of different quality X-rays delivered at two LRB facilities that replaced recently deconstructed γ-60Co unit ROKUS-M: CellRad (Precision, USA) and SARRP (Xstrahl, USA) and their suitability as a reference radiation in radiobiological research. For this study, lymphocytes obtained from the blood of one healthy donor were irradiated in vitro with 130 kVp X-rays + 0.5 mm Al manufacturer-supplied filtration or 0.1 mm Cu custom-made filtration (CellRad) and with 130 kVp X-rays with 1mm Al or 220 kVp with 0.15 mm Cu filtration (SARRP) at doses 1-4 Gy. The cells were harvested after 48 h of post-irradiation culturing and CA in metaphases of the first post-irradiated cell cycle were assessed. The cytogenetic effects of X-ray radiation were compared with the results obtained previously at the γ-60Co unit (ROKUS-M, JINR) and with the results obtained earlier by one of the authors at the 250 kVp X-ray unit (Seifert, GSI, Germany) [1].

Experimental data on mean aberration number at different doses were analysed by non-linear regression using linear-quadratic model, and obtained best-fit parameters compared for different irradiation conditions. Based on the analysis we demonstrated that all X-ray regimes have the higher biological efficiency than γ-60Co. 220 kV regime of SARRP perfectly matched 250 kV Seifert machine giving the same results as previously published [1]. We found no statistically significant difference in biological efficiency of 250 kVp X-rays compared to 130 kVp + 0.1 mm Cu and ($p = 0.137$) and 220 kVp SARRP ($p = 0.143$). 130 kVp X-rays filtered with 0.5 mm Al (effective energy 25.6 keV) have the higher biological efficiency than filtered with 0.1 mm Cu (effective energy 38.8 keV) with RBE = 1.11 ± 0.04, $p = 0.006$). No statistically significant difference, however, was found between 220 kVp X-rays and and 130 kVp X-rays filtered with 1 mm Al (SARRP irradiator). The lower efficiency of SARRP 130 kVp regime, compared to 130 kVp + 0.1 mm Cu, may be explained by using the thicker Al filter (1mm compared to 0.5 mm in CellRad irradiator) which resulted in more efficient reduction of soft X-rays. In summary, our data show that X-rays from both units , 220 kVp SARRP and 130 kVp + 0.1 mm Cu Cell Rad may be used as a reference radiation in radiobiological research.

Noteworthy, the aberration spectra induced by all radiation types used were shown to be similar (~20 % simple breaks, 60% simple exchanges and 20% complex aberrations).

References:

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