

Purpose: To quantify the kinetics of the cellular response to low, CT-relevant doses of ionizing radiation (IR) in U87MG human glioblastoma multiforme cancer cells in vitro.

Method and Materials: U87MG cells were irradiated with 0Gy (controls), 20mGy (in typical CT range), or 2Gy (exceeding CT dose range) using an X-ray cabinet irradiator at 150kVp. The cellular kinetics of DNA damage and response were quantified by flow cytometric quantitation of γ -H2AX foci at two time points (1hr and 6hrs post-IR); using flow cytometry allows a much higher throughput than conventional methods. An auto-fluorescence control was performed for each sample. Collected flow cytometry data, corrected for debris and dead cells using side and forward scatter gating, were analyzed with CellQuest Pro Software. Fluorescence histograms were generated for each sample and the respective auto-fluorescence histogram was subtracted from each. The percentage of gated cells staining positive for γ -H2AX (beyond an a priori threshold based on the IgG negative control) was determined.

Results: In cells exposed to 2Gy, γ -H2AX substantially increased within 1h and returned to control levels 6h post-irradiation. In contrast, although cells exposed to 20mGy showed a measureable increase in γ -H2AX formation within 1h, there was no significant decrease 6h later.

Conclusion: Our results suggest DNA damage induced by low, CT-relevant doses is repaired at a slower rate than damage induced by higher doses. This altered kinetic response could have marked biological effects for current radio-diagnostic procedures. Our study, therefore, underscores the importance of understanding the different repair mechanisms at different dose regions in order to accurately assess risk estimates and biological dose. Future work will investigate longer observation times to assess DNA repair in more detail in the current cell model as well as in normal lymphocyte cell lines.

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