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CELLULAR AND MOLECULAR EFFECTS INDUCED BY 45 MeV C-IONS AND GAMMA RAYS IN NORMAL HUMAN PRIMARY FIBROBLASTS.

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Investigation of the mechanisms underlying the biological effects induced by densely ionizing radiation has relevant implications in both radiation protection and therapy. In particular, the possible advantages of hadrontherapy with respect to conventional radiotherapy in terms of high conformal tumor treatment and sparing of healthy tissues are well known. Further improvements are limited by lack of radiobiological knowledge, particularly about the specific cellular response to the damage induced by particles of potential interest for tumor treatment.

This study investigates early and late effects induced in AG01522 normal human primary fibroblasts by C-ions or γ-rays. The C-ion beam from the Superconducting Cyclotron facility at the INFN-Laboratori Nazionali del Sud (LNS, Catania, Italy) was used, with E ~ 45 MeV/u at the cell entrance, corresponding to LET (in water) ~ 49 keV/μm; γ-rays from the Cs-137 irradiator of the ISS were used as reference.

Different end points have been investigated, namely: cell killing and lethal mutation, evaluated as early and delayed reproductive cell death, respectively; chromosome damage, as measured by micronuclei induction (MN) and DNA damage, in terms of H2AX phosphorylation/dephosphorylation kinetics.

Linear dose-response relationships were found for cell killing and for induction of lethal mutations, with RBEs of about 1.4 for the former and of about 1.6 for the latter, indicating the presence of genomic instability that is greater in the progeny of C-ions irradiated cells.

H2AX phosphorylation/dephosphorylation kinetics have shown a maximum foci number at 30 min after irradiation, higher for γ-rays than for C-ions. However, in the first 12 h the fraction of residual gamma-H2AX foci is higher for C-ions irradiated cells, indicating a lower removal rate possibly related to multiple/more complex damage along the particle track. MN induction, observed after 72 h from irradiation, was also greater for C-ions.

Overall, these data indicate a more severe DNA damage induced by 45 MeV/u C-ions with respect to γ-rays, likely responsible of an increased cellular misrepair, leading to the greater observed levels of chromosome damage and, eventually, genomic instability; they give strong support to the idea that higher damage severity at molecular level, determined by the typical deposition pattern of densely ionizing radiation, is the earliest relevant factor for the more severe late effects at cellular level.

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