Real-time radiation biology at nanometric scale

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It is commonly admitted that the early spatial distribution of energy deposition following ionizing radiation interactions with biomolecular architectures is decisive for the prediction and control of damages at cellular and tissular levels. Deeply understanding the basic mechanisms of radiation damage *in vitro* and on living cells, starting from the early radical and molecular processes to mutagenic DNA lesions, cell signaling, genomic instability, apoptosis, microenvironment and Bystander effects, radio sensitivity should have many practical consequences like the customization of radiation therapy or radioprotection protocols for instance. In this context, *spatio-temporal radiation biology* represents a newly emerging interdisciplinary field of studies driven nowadays in strong synergy with the most recent progresses of molecular biology, genomics and proteomics, detection of biomarkers, various optical methods for imaging, micro and nanodosimetries, innovating developments of synchrotron radiation sources, predictive approaches for radiation therapies [1].

One major challenge of radiation biology concerns the complete understanding of spatio-temporal events triggered by an initial energy deposition inside confined clusters of ionization and evolving over several orders of magnitude, typically from femtosecond (10^{-15} s) and sub-micrometric scales. The innovating advent of powerful laser sources and laser plasma interactions providing ultrashort relativistic particle beams (electron, proton) open exciting opportunities for a real time monitoring of high energy radiation medical physics [2]. The aims of this work were (i) to propose an original approach of discriminated spatio-temporal energy deposition in disulfide biomolecule-water system using a very high dose delivery (~10^{13} Gy s^{-1}) and an average dose profile in the range 15-17 Gy, (ii) exploration of a real-time control of early radiation effects from eigenstates of low-energy excited electrons (p-like state).

Table-top terawatt Ti:Sa laser amplifier systems combined to laser plasma interactions provide femtosecond high-energy electrons beams, typically in the 2.5 - 15 MeV range, which might conjecture the sub-picosecond observation of primary sulfur-centered radical events in nanometric aqueous radiation spurs, using near-IR probe and a 16 bit-CCD camera detection. Cystamine, the reactive centre of oxidized glutathione is used as biomolecular target for the real-time investigation of elementary radical events taking place in nascent ionisation microenvironments (spurs). For the first time it is shown that the effective reaction radius r_{eff} of aqueous cystamine molecule for a direct univalent reduction by secondary very-short lived p-like electron (lifetime less than 5×10^{-13} s) is around 10 Å. With a micromolar detection of radical events in the prethermal regime, the functional reactivity of disulfide sensor gives useful information on spatial radiation-induced early radical processes in track structure [3,4].

The femtoradical investigation of biomolecular targets opens exciting opportunities for the sensitisation of confined environments (aqueous groove of DNA, protein pockets, sub-cellular systems) to ionizing radiation, for which at a density of 1.0 g cm^{-3} target volumes of mass per area in size of about 1×10^{-6} g cm^{-2} correspond to 100 Å. In this way, high energy radiation femtochemistry (HERF) involving pulsed X-ray radiation or relativistic

particles bunches would provide guidance for advanced semi-quantum simulations on pulsed radiation damages and foreshadow the development of new applications in radiation biology (real-time nanodosimetry) or anticancer radiotherapy (highly-selective prodrug activation using quantum states of very short-lived radicals) [5].

References

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