Transient anion states of potential radiosensitizers

Márcio T. do N. Varella

Instituto de Física, Universidade de São Paulo

Radiosensitizers are intended to enhance tumor cells damage for a given radiation dose, ideally with much less effect on healthy tissues. As pointed out by Wardman [1], radiotherapy is free radical therapy, which means the primary interaction of high-energy radiation (or heavy particles) with the biological environment is not the main mechanism for cell killing. In fact, the secondary species produced by that interaction, such as OH radicals and free electrons, play a central role [2]. At the molecular level, the interactions of the secondary species with DNA and other biomolecules pose challenges to Physics and Chemistry, as the description of the reaction mechanisms involve thermodynamic and quantum mechanical aspects [3,4]. The present talk will address basic electron-induced damage mechanisms with particular interest on the formation of transient negative ions, often referred to as resonances. These ions are formed by electron attachment to isolated molecules or DNA sites, often inducing dissociation reactions that produce reactive species, e.g., $AB + e^- \rightarrow A^- + B^\bullet$, where A^- is typically a closed-shell anion fragment and $B^\bullet$ is a free radical. Substituted uracils and electron-affinic molecules, such as nitro-imidazoles, have been either used or suggested as radiosensitizers [1,5]. The interaction of these molecules with free electrons suggest that electron-induced dissociation could, at least partly, underlie their radiosensitizing activity. Free radical production from electron attachment would also provide a "universal" mechanism, since it can in principle take place with molecules in solution, complexed with DNA repair enzymes, or even incorporated into the gene sequence.

References

[1]. P. Wardman, Clinical Oncology **19**, 397 (2007).

[2]. S. Lehnert, *Biomolecular Action of Ionizing Radiation*, Taylor & Francis Group: New York, 2008; Chapter 6.

[3]. I. Baccarelli, I. Bald, F. A. Gianturco, E. Illenberger, J. Kopyra, Physics Reports **508**, 1 (2011).

[4]. E. Alizadeh, T. M. Orlando, L. Sanche, Annual Reviews of Physical Chemistry **66**, 379 (2015).

[5]. J. Overgaard, Radiotherapy and Oncology **100**, 22 (2011).