TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

Macroarea di Scienze MM. FF. NN.
Dipartimento di Fisica

INFN

AVVISO DI SEMINARIO INFN
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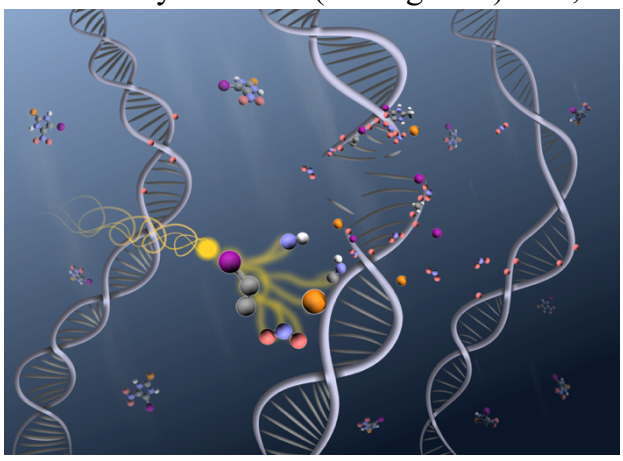
Enhanching Radiotherapy with High-Z doped Nitroimidazoles

Radiosensitisers (RSs) are compounds that make cancer cells more sensitive to radiotherapy. For the sensitising effect to take place, these compounds need to be activated by radiation (see Figure 1). Yet, the atomic and molecular level mechanisms of this activation are poorly understood, resulting in a lack of comprehension as to why some RSs are better than others.



We have studied nitroimidazole-based RSs, which utilise doping of high-Z element iodine as the photoabsorption antenna, using a combined experimental/theoretical approach [1,2]. The nitroimidazoles are known to accumulate in oxygen-deficient (hypoxic) regions, which is often the case for many tumours of a larger size [3]. There, the nitroimidazole can, via the release of the nitro group, affect the repair mechanisms in the cancer cell [4]. Using synchrotron light tuned to the K- and L-edges of the samples, and thereby isolating the dominating ionisation site, we have studied fragmentation mechanisms and the production of harmful secondary species from the dissociation of these imidazoles. To complement the experiments, we have employed Born-Oppenheimer-based molecular dynamics simulations to investigate the integrity of the intramolecular bonds and follow fragmentation pathways from the site-specific ionisation. These studies have so far been performed while the RS have been in the gas phase and isolated from nearby molecules, and only recently, we can show new results on radiation damage of this molecular bioagent during monosolvation.

1. Svensson PHW, et al. Heavy element incorporation in nitroimidazole radiosensitizers: molecular-level insights into fragmentation dynamics. Physical Chemistry Chemical Physics. 2024;26(2):770-9.
2. Pihlava L and Svensson PHW, et al. Shell-dependent photofragmentation dynamics of a heavy-atom-containing bifunctional nitroimidazole radiosensitizer. Physical Chemistry Chemical Physics. 2024;26(11):8879-90.
3. Masaki Y, et al. Imaging mass spectrometry revealed the accumulation characteristics of the 2-nitroimidazole-based agent “pimonidazole” in hypoxia. PLoS One. 2016 Aug 31;11(8):e0161639.
4. Oronsky BT, Knox SJ, Scicinski JJ. Is nitric oxide (NO) the last word in radiosensitization? A review. Translational Oncology. 2012 Apr 1;5(2):66-71.