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Radiosensitization of cancer cells using nanoparticles in X-ray and ion beam therapy

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- Corresponding author and speaker, email: sihver@chalmers.se Abstract: Many different tumor-targeted strategies have been developed worldwide to limit the side effects and improve the effectiveness of cancer therapies, such as chemotherapy, intensity modulated radiation therapy, biology-driven personalized radiotherapy, ion beam radiotherapy, target-alpha-therapy, high intensity focused ultrasound therapy, etc. Recent advances in nanotechnology have also given rise to trials with various types of metal nanoparticles (NPs). Different metal-based NPs, e.g. gold, gadolinium, titanium, silver, hafnium and bismuth have been evaluated to enhance the radiosensitization of the cancer cells while reducing or maintaining the normal tissue complication probability during radiation therapy. When X-rays or a charged particle hit a metal, there are multiple possibilities of eventual outcome. Among the several emissions that occur, the most relevant to cancer radiotherapy are scattered X-rays/photons, photoelectrons, Compton electrons, Auger electrons and fluorescence photons. The energy of the X-rays is important, since the photoelectric effect is decided by (Z/E)3, where E is the energy of the incoming photon and Z is the atomic number of the molecule being targeted. The photoelectric effect is therefore dominant at lower energies and is prevailing until the photon energy reaches a medium energy (e.g., around 500 keV for gold (Z = 79)) with a cross section varying with Z4 or Z5, depending on the material. When using X-rays, mainly the inner electron shells are ionized, which creates cascades of both low and high energy Auger electrons. The use of higher Z NPs (e.g., gold or platinum) along with X-rays, leads to enhanced photoelectric and Compton effects, making these NPs more radio-sensitizing than others with lower Z. Gold is a promising radio-sensitizer in this regard due to its high atomic number and higher mass energy absorption coefficient in relation to soft tissue. In addition to that it, it is very inert and it is highly biocompatible. When using high LET particles, e.g., carbon ions for therapy, mainly the outer shells are ionized, which produce electrons with lower energies compared to X-rays. However, the amount of the produced low energy electrons is higher when exposing NPs to ions than when exposing them to X-rays. Since ions traverse the material along tracks, and therefor give rise to a much more inhomogeneous dose distributions than X-rays, there might be a need to introduce a higher amount of NPs when using ions compared to when using X-rays to create enough primary and secondary electrons to get the desired dose escalations. This raises the questions of toxicity. Though, even below the ionization threshold, electrons can induce molecular damage via Dissociative Electron Attachment (DEA) and production of highly reactive oxygen species, such as OH•, H•, O2-, H2O+ from the surrounding water molecules via radiolysis or DEA. The same effects apply to both Auger and photo electrons. This paper will discuss the need for systematic studies of the behavior of NPs, when exposed to different kinds of ionizing radiation, depending on the Z, surface treatment, sizes, ionizing radiation, etc.

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