THE AUGER ELECTRON EFFECT IN RADIATION DOSIMETRY - A REVIEW

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ABSTRACT

Radionuclides that emit Auger electrons are widely used in nuclear medicine and biomedical research. The Auger emitting radionuclides give off a cascade of low energy electrons, the total energy of which is deposited within some nanometers; the local dose is therefore very high. If the radionuclide is part of a chemical compund which forms a DNA base analogue or which preferentially enters the cell nucleus, the biological effects of the Auger electrons to the DNA or the nucleus can be as severe as from high-LET alpha particles. Neither the recommendations of the International Commission on Radiological Protection (ICRP) in Publication No. 60, nor the International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources provide any guidance on calculating the equivalent dose for these radionuclides. For the radiation weighting factor of electrons (value 1) they recommend excluding the Auger electrons emitted from nuclei bound to DNA. However, recently a Task Group of the American Association of Physicists in Medicine (AAPM) has proposed that the component of dose from the Auger electrons for radionuclides bound to DNA be given a preliminary radiation weighting factor of of 10 for deterministic effects and 20 for stochastic effects. The dose equivalent calculated with these weighting factors must be modulated by experimentally determined subcellular distributions.

INTRODUCTION

Radionuclides that emit a high proportion of Auger electrons are widely used in nuclear medicine (e.g. ^{99m}Tc, ^{123}I, ^{201}Tl) and biomedical research (e.g. ^{51}Cr, ^{125}I). Natural radioactive isotopes exist with Auger electron emissions (e.g. ^{40}K). In nuclear weapon debris exists inter alia the isotope ^{55}Fe and in the nuclear energy cycle the isotope ^{65}Zn. The dosimetry of Auger electrons and other low energy radiations has been discussed in ICRU Report 32 (1). Recent reviews of the Auger electron effect are found in two articles are by Persson (2,3).

ICRP discussed the Auger electron effect in its Publication No. 60 (4). On page 6, paragraph 26 they state: "Auger electrons emitted from nuclei bound to DNA present a special problem because it is not realistic to average the absorbed dose over the whole mass on DNA as would be required by the present definition of equivalent dose. The effects of Auger electrons have to be assessed using the techniques of microdosimetry". In the International Basic Safety Standards for Protection against Ionizing Radiation and for the Safety of Radiation Sources (5), it is stated that Auger electrons emitted from nuclei to DNA are excluded from the radiation weighting factor of value 1 for electrons of all energies with the remark that special microdosimetric considerations apply.

MEDICAL APPLICATIONS

There appears to be two important issues for Auger electron emitters in medicine. At the root of both is that characteristic of the Auger electron decay: the highly localized irradiation of the surrounding volume. Considerable exposure is delivered to the part of a cell or a macromolecule which is in the vicinity of the decaying nuclide. This on the one hand brings about a problem in risk estimation for nuclear medicine and on the other hand promises of a selective attack on cancer cells: "molecular surgery".

The following isotopes (normally bonded in a chemical compound) are of special interest in nuclear medicine as Auger electron emitters: ^{51}Cr, ^{55}Fe, ^{67}Ga, ^{75}Se, ^{77}Br, ^{80m}Br, ^{99m}Tc, ^{110}In, ^{111}In, ^{114m}In, ^{123}I, ^{125}I, ^{145}Sm, ^{193m}Pt, ^{195m}Pt, and ^{201}Tl. Some of these radionuclides may also have a role in cancer treatment.

EXPERIMENTS WITH LIVING CELLS

Rao et al. (6) have studied the radiotoxicity of ^{125}I-iododeoxyuridine (IUdR) by the determination of the survival of spermatogonial cells of mice. Narra et al. (7) studied the same issue by investigating the survival of pre-implantation mouse embryos. Iododeoxyuridine is a thymidine analogue and incorporates into the DNA of proliferating cells. ^{125}I incorporated into DNA was as effective as densely ionizing 5.3 MeV α-particles from

^{210}Po in reducing the sperm head population in mice. The embryo survival curves show that the dose at 37% survival is only about 0.15 Gy for ^{125}IUdR, whereas for 662 keV gamma rays from ^{137}Cs, it is 1.75 Gy. These results are consistent with the observations in mouse testis and cultured cells and point to the need for assessing the radiation risk from incorporated Auger electron emitting radionuclides based on their sub-cellular distribution. Also ^{125}I-labelled DNA binding agents other than ^{125}IUdR have been shown to cause severe damage to the DNA molecule, as discussed by Ludwikow et al. (8).

EQUIVALENT DOSE FOR AUGER ELECTRON EMITTERS

Howell et al. (9) stated: "Depending on the subcellular distribution of the radionuclide, the biological effects caused by tissue-incorporated Auger emitters can be as severe as those from high-LET alpha-particles. However, the recently adopted recommendations of the International Commission on Radiological Protection (4) provide no guidance with regard to calculating the equivalent dose for these radionuclides. The present work, using spermatogenesis in mouse testis as the experimental model, shows that the lethality of the prolific Auger emitter ^{125}I is linearly dependent on the fraction of the radioactivity in the organ that is bound to DNA. This suggests that the equivalent dose for Auger emitters may have a similar linear dependence. Accordingly, a formalism for calculating the equivalent dose for Auger emitters is advanced within the ICRP framework".

The equivalent dose in an organ or tissue T is defined as $H_T = w_R \cdot D_{T,R}$, where w_R is the radiation weighing factor, and $D_{T,R}$ is the absorbed dose in the tissue from radiation R. For a mixed radiation field, such as those generated by many radionuclides including Auger emitters,

$$H_T = \sum_R w_R \cdot D_{T,R} . \qquad (1)$$

Howell et al. (9) propose that the equivalent dose specifically for the Auger electrons may be expressed as:

$$H_{T,R(Auger)} = (1 + f_o(w_{R(Auger)} - 1)) \sum_{R(Auger)} D_{T,R} . \qquad (2)$$

where f_o is the fraction of the radioactivity in the organ bound to DNA. This equation limits appropriately at $f_o = 0$ and $f_o = 1$. Although this equation is fundamentally sound, separation of the biological effects of the Auger electrons from those of other radiations emitted by the radionuclide is not possible experimentally because the observed RBE values are for the composite spectrum of emissions. Therefore, it is difficult to assign a value to w_{Auger} that corresponds directly to measured RBE values.

In Report no. 3 of American Association of Physicists in Medicine - AAPM - Nuclear Medicine Task Group no. 6 methods of Auger electron dosimetry at the DNA, cellular, multicellular, and organ level are discussed (10). This Task Group recommends a preliminary value of 10 be used for $w_{R(Auger)}$ in equation (2) to obtain the deterministic equivalent dose H_T for prediction of therapeutic outcome and a value of 20 for stochastic effects. The dose equivalent calculated with these radiation factors must be modulated by experimentally determined subcellular distributions. It should be noted that equation (2) is based on experiments where ^{125}I is covalently bound to DNA in the cell nucleus. When the Auger emitter is localized in the nucleus but not covalently bound to DNA, somewhat lower RBE values may be expected. The equivalent dose from the Auger electrons may then be a factor of 2 lower.

Calculations of equivalent dose for Auger electron emitting radionuclides distribution in humans organs have recently been performed (11). These calculations show an increase in the mean equivalent dose for Auger electron emitters when a significant fraction of the organ activity localizes in the DNA.

CONCLUSIONS

The AAPM Task Group (10) recommends use of radiation weighting factors for cellular and organ dosimetry in conjunction with equivalent dose formalism that takes the subcellular distribution distribution of the Auger emitter into account. Based on the currently available radiobiological data which show that the effects caused by the Auger emitters are similar to those of incorporated alpha emitters, a preliminary radiation weighting factor of 10 is recommended for deterministic effects (i.e., cell survival) and a value of 20 is recommended for stochastic effects (i.e., risk assessment for cancer induction). The dose equivalent calculated with these weighting factors must be modulated by experimentally determined subcellular distributions.

There are good reasons to consider the Auger electron effect not only in medical radiation protection of patients but also in the context of annual limits of intake for workers and the public. It may also be prudent to review the current equivalent dose estimates for radiopharmaceuticals labeled with Auger electrons.

Further experimental and theoretical, radiobiological research in the field is advocated by the author. Inter alia studies of survival rates, chromosome aberrations, micronuclei formations, and cell tranformations, performing animal carcinogenic experiments and mathematical modeling are important tools for a deeper understanding of the subcellular structures and also for the processes involved in the interaction of radiation with biological materia. The scientific basis for radiation protection, especially against the Auger emitting isotopes, will then also improve.

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