STUDY ON THE RADIOTOXICITY OF THE AUGER ELECTRON EMITTER TECHNETIUM-99M IN FUNCTIONAL RAT THYROID CELLS

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Introduction: Because of its favorable half-life (6.02 hours) and distinct characteristic gamma-ray line, Technetium-99m (Tc-99m) is the most widespread radionuclide in nuclear medicine. Additionally, this nuclide emits low energetic, short-range Auger electrons which can deposit large amounts of energy in a rather small volume in the immediate vicinity of the decay site. When located in close proximity to the DNA, the biological effects caused by Auger emitters are severe and comparable to high-LET radiation. This poses the question towards an increased relative biological effectiveness (RBE) of the Auger electron emitter Tc-99m. To assess the potential impact of Tc-99m-Pertechnetate on cellular level, DNA double-strand breaks (gammaH2AX assay) and cell killing (colony forming assay) was investigated after extracellular and intracellular localization of Tc-99m in the functional rat thyroid cell line, FRTL-5 and effects were compared to high dose-rate external uniform γ-irradiation (Cs-137; 0.7 Gy/min).

Material and methods: FRTL-5 cells were exposed to 25, 50 and 75 MBq Tc-99m pertechnetate. Extracellular localization of Tc-99m was achieved by inhibiting the Sodium-Iodide Symporter (NIS) with sodium perchlorate (SP). Standard Colony Forming Assay was employed. GammaH2AX staining was achieved using a mouse anti-phospho H2AX antibody (Clone JBW301, Invitrogen). External high dose-rate γ-irradiation was performed with a Cs-137 source (GammaCell 40). Cell number and Tc-99m uptake was determined in each individual experiment (CASY® Schärfe System; Gamma Counter, Wallace 3" PerkinElmer). Dosimetry at cellular level was based on cell size and point kernel calculations using electron spectra provided and published by Pomplun et al. 2006 [1].

Results: A rapid cellular uptake of Tc-99m in FRTL-5 cells was observed. Inhibtion of NIS restricted the uptake efficiently. However, no complete inhibition of uptake was observed. GammaH2AX-foci induction was somewhat higher per dose unit when Tc-99m was located intracellular. Tc-99m induced more prominent cell killing when located intracellular as compared to extracellular localization per decay. However, per dose unit no significant differences were observed (Figure 1). Compared to high dose rate external γ-irradiation GammaH2AX-foci induction as well as cell killing was much weaker after Tc-99m-exposure as already published for cell killing and micronucleus induction in SCL-II cells by Kriehuber et al., 2004 [2]. SP treatment itself had no influence on cytotoxic damage.

Conclusions: No significant effect on cell killing due to the localization (intra- vs extracellular) of Tc-99m was observed per unit dose ruling out any Auger electron-associated enhanced cytotoxicity for Tc-99m pertechnetate. The cytotoxic effect of Tc-99m and GammaH2AX-foci induction is much weaker when compared to external high dose rate γ-exposure, which is most likely explained by the low dose rate of the Tc-99m exposure.

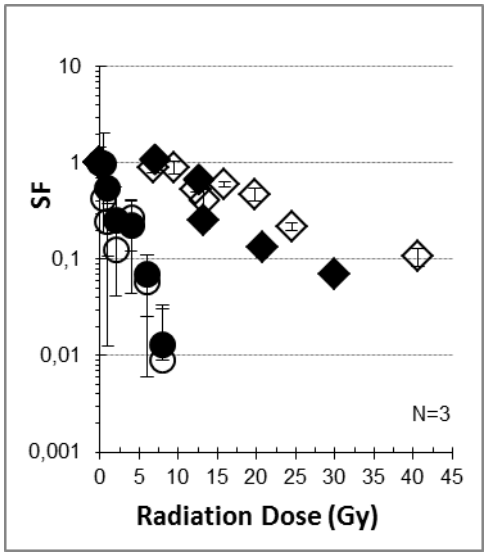

Figure 1. Cell survival of FRTL-5 cells as measured in the colony forming assay. Survival fraction (SF) as a function of cellular radiation dose revealed no significant differences in cell survival between cells with (filled diamonds) and without (open diamonds) Tc-99m uptake. External homogenous high dose-rate γ-irradiation (Cs-137 exposure, dose rate 0.7 Gy/min, circles) was 4 to 7 times more efficient in cell killing when compared to Tc-99m exposed cells (diamonds).

References:

1. Estimation of a radiation weighting factor for 99mTc (E. Pomplun et al.), *Radiat. Prot. Dosimetry* **122**, 80-81 (2006)

2. Study on cell survial, induction of apoptosis and micronucleus formation in SCL-II cells after exposure to the Auger electron emitter (99m)Tc (R. Kriehuber et al.), *Int. J Radiat. Biol.* **80**, 875-880 (2004)