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DNA damage assay in blood lymphocytes in peptide receptor radionuclide therapy patients with personalised high activities

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Objectives

Radiation induces DNA double strand breaks (DSBs) that can be visualized and enumerated as microscopic γ-H2AX and 53BP1 foci. This study analysed the dose- and time-dependency of the DNA damage in blood lymphocytes in patients after a personalised high-activity ^{177}Lu-DOTATATE treatment.

Methods

We investigated multiple blood samples of three patients up to 96 h after personalised high-activity peptide receptor radionuclide therapy (PRRT) (14.4GBq-19.3GBq). Background focus rates were determined in pre-therapeutic samples. Lymphocytes were isolated by density centrifugation and fixed in 70% ethanol. After two-color immunofluorescent staining co-localizing γ-H2AX + 53BP1 foci were counted manually using a red/green double-band-pass filter. The results were compared to a previous patient study (1) and an in-vitro calibration-curve (2)

Results

Blood samples of three patients receiving a personalised high activity therapy were evaluated for γ-H2AX + 53BP1 DSB-indicating foci. Compared to the standard therapy (7.7GBq) the absorbed dose to the blood after 48 h was higher (mean: 78 mGy vs 186 mGy, resp.). In the first 4 h after administration of the radiopharmaceutical there was a strong increase of the number of radiation-induced foci/cell (RIFPC) with the average RIFPC values being in accordance with our in-vitro calibration curve. Maximum foci numbers ranged from 0.8 – 1.1 RIFPC. At t = 4 h in standard therapy the mean RIFPC values normalised to the blood dose (0.019 RIFPC/mGy) were higher than those of the high-activity patients (0.012 RIFPC/mGy). The patient with the highest activity administered and highest absorbed dose to the blood had persisting RIFPC levels after 72 h, while for the two other high activity patients RIFPC levels decreased similar to patients receiving standard therapy.

Conclusions

This study provides a first analysis of DSB induction in lymphocytes of Lu-DOTATATE patients receiving personalised high-activity Lu-DOTATATE therapy. With the exception of a late time-point in one patient our findings align well with our previous results.

References

1. Eberlein U, Novak C, Bluemel C, Buck A K, Werner R A, Lassmann M, Scherthan H. DNA Damage in Blood Lymphocytes in Patients after 177Lu Peptide Receptor Radionuclide Therapy. Eur J Nucl Med Mol Imaging. 2015;42:1739–1749.
2. Eberlein U, Peper M, Fernández M, Lassmann M, Scherthan H. Calibration of the gamma-H2AX DNA double strand break focus assay for internal radiation exposure of blood lymphocytes. PLoS ONE. 2015;10:e0123174.

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