Biodistribution and dosimetry of [99mTc]Tc-N4-CXCR4, a novel ligand to the C-X-C motif chemokine receptor 4

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Abstract

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Introduction: Due to its important role in the context of tumor cell growth and the process of metastasis, the C-X-C motif chemokine receptor 4 (CXCR4) has generated significant interest in medicine. CXCR4 expression is generally high in hematologic malignancies including non-Hodgkin's lymphoma, multiple myeloma, or acute myeloid leukemia. There is already broad experience with CXCR4-targeted PET imaging in patients with such diseases. Now, a CXCR4 ligand that allows labeling with Tc-99m ([99mTc]Tc-N4-CXCR4) and thus imaging on widely used gamma cameras has been developed. The aim of this retrospective study was to evaluate the whole-body distribution and radiation dosimetry of this probe.

Methods: Four patients with a history of hematologic malignancy were injected intravenously with a mean activity of 502 ± 95 MBq of [99mTc]Tc-N4-CXCR4. Planar whole-body imaging was performed at 5 and 30 min as well as at 1, 2, 3, 5, and 24 h post injection. SPECT images were acquired at 1.3, 3.5, 6, and 24 h post injection. Time-dependent changes of the injected activity per organ were determined. Mean organ-absorbed (± SD) and effective doses were calculated using Olinda/EXM 1.0.

Results: Rapid blood clearance and fast excretion of the tracer by the kidneys into the bladder was observed. Injection of a standard activity of 500 MBq of [99mTc]Tc-N4-CXCR4 resulted in a mean effective dose of 1.6 ± 0.3 mSv (1.3 - 1.9 mSv). The spleen absorbed the highest dose of 15.4 ± 3.0 µGy/MBq (range, 13.3 - 19.8); other organ doses were 8.6 µGy/MBq (range, 6.8 - 10.4) for the kidneys, red bone marrow 6.3 µGy/MBq (range, 4.2 - 8.3), and liver 5.5 µGy/MBq (range, 4.4 - 6.4), respectively. No drug-related pharmacological effects occurred.

Conclusions: The use of [99mTc]Tc-N4-CXCR4 resulted in a low radiation exposure comparable to other Tc-99m-based tracers and had no adverse effects in this small cohort of patients. The labeling of the ligand with Tc-99m and its longer half-life compared to Ga-68-labeled ligands could make wide-area noninvasive imaging of CXCR4 expression feasible.