Clinical PET of Neuroendocrine Tumors Using 64Cu-DOTATATE: First-in-Humans Study

The use of positron emitter–labeled compounds for somatostatin receptor imaging (SRI) has become attractive because of the prospect of improved spatial resolution, accelerated imaging procedures, and the ability to quantify tissue radioactivity concentrations. This paper provides results from first-in-humans use of 64Cu-DOTATATE, an avidly binding somatostatin receptor ligand linked to a radioisotope with intermediate half-life and favorable positron energy (half-life, 12.7 h; maximum positron energy, 0.653 MeV). Methods: In a prospective setup, 14 patients with a history of neuroendocrine tumors underwent both PET/CT with 64Cu-DOTATATE and SPECT/CT with our current routine imaging agent 111In-diethylenetriaminepentaacetic acid–octreotide. After intravenous injection of 193–232 MBq of 64Cu-DOTATATE, whole-body PET scans were acquired at 1 h (n = 14), 3 h (n = 12), and 24 h (n = 5) after administration. Tissue radioactivity concentrations for normal organs and lesions were quantified, and standardized uptake values were calculated for the early (1 h) and delayed (3 h) scans. Using the data for 5 patients, we assessed the radiation dose with OLINDA/EXM software. Furthermore, the clinical performance of 64Cu-DOTATATE with respect to lesion detection was compared with conventional SRI. Results: SRI with 64Cu-DOTATATE produced images of excellent quality and high spatial resolution. Images were characterized by high and stable tumor-to-background ratios over an imaging time window of at least 3 h. Compared with conventional scintigraphy, 64Cu-DOTATATE PET identified additional lesions in 6 of 14 patients (43%). In 5 patients, lesions were localized in organs and organ systems not previously known as metastatic sites, including the early-stage detection of a secondary neuroendocrine tumor in a patient with a known mutation in the multiple endocrine neoplasia type I gene. All major additional findings seen only on PET could be confirmed on the basis of a clinical follow-up interval of 18 mo. Calculated radiation dose estimates yielded an effective dose of 6.3 mSv for an injected activity of 200 MBq of 64Cu-DOTATATE, with the liver being the organ with the highest absorbed radiation dose (0.16 mGy/MBq). Conclusion: This first-in-humans study supports the clinical use of 64Cu-DOTATATE for SRI with excellent imaging quality, reduced radiation burden, and increased lesion detection rate when compared with 111In-diethylenetriaminepentaacetic acid–octreotide.

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