SPECT Radiopharmaceuticals: In-111-Exendin, an Example from Preclinical to Clinical Studies

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A reliable method for in vivo quantification of pancreatic beta cell mass (BCM) could lead to further insight into the pathophysiology of diabetes. The glucagon-like peptide (GLP) -1 receptor, abundantly expressed on beta cells, may be a suitable target for imaging.

Preclinical studies. The potential of GLP-1 receptor targeting has been investigated using the parent GLP-1 peptide radiolabeled with I-125. Initial results indicated the the GLP-1 peptide was instable in vivo and that the radioiodine label was less suited[1]. In follow up studies it appeared that the GLP-1 analogs exendin-3 and exendin-4 were better suited, but the radiolabel was still cleared rapidly from the target. Therefore, exendin-3 was conjugated with the chelator DTPA and radiolabeled with In-111, resulting in excellent in vivo SPECT targeting properties[2,3]. In addition, it was shown that the peptide uptake correlated with the BCM[4,5].

Clinical studies. We investigated the potential of radiotracer imaging with In-111-exendin-3 for determination of BCM in patients with type 1 diabetes and healthy individuals[6]. To allow for clinical application, the peptide was synthesized according to good manufacturing practice (GMP) and the radiolabeling procedure was validated. Since exendin-3 is biologically active, the specific activity of the radiolabeled peptide is important, to allow for a very low injected peptide dose, with a sufficient amount of In-111. SPECT imaging studies demonstrated uptake of the radiolabeled peptide in the pancreas, which was higher in healthy volunteers than in patients with diabetes type 1[6].

Conclusion. Developing a radiolabeled peptide from preclinical in vitro studies to clinical studies demonstrated the importance of peptide structure, the radionuclide and labeling conditions as well as the injected dose. Clinical studies indicated that In-111-labeled exendin-3 may be suitable for non-invasive quantification of BCM.

References

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