Radionuclide therapy using radiolabelled peptide analogues: future perspectives

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On their plasma membranes, cells express receptor proteins with high affinity for regulatory peptides, such as somatostatin. Changes in the density of these receptors during disease, e.g. overexpression in many tumours, provide the basis for new imaging methods. The peptide analogues most successfully applied for visualisation of receptor-positive tumours are radiolabelled somatostatin analogues. A new promising application of radiolabeled somatostatin analogs is peptide receptor-targeted radionuclide therapy (PRRT) of somatostatin receptor-expressing tumors. Suitable radionuclides are ^{90}Y, a pure, high energy beta-emitter (2.27 MeV), and ^{177}Lu, a medium energy beta-emitter (0.5 MeV) with a low abundance gamma. We investigated in Lewis rats, each bearing both a small (around 0.5 cm^2) and a large (7-9 cm^2) somatostatin receptor-positive rat pancreatic CA20948 tumor in their flanks the radiotherapeutic effects of [^{90}Y-DOTA,Tyr^3]octreotide, [^{90}Y-DOTA,Tyr^3]octreotate, [^{177}Lu-DOTA,Tyr^3]octreotate and the combination of ^{90}Y- and ^{177}Lu-labeled analogs at the same tumor radiation dose. Most promising radiotherapeutic effects of the ^{90}Y-and ^{177}Lu-labeled analogs were found in this rat tumor model. In animals bearing tumors of various size the anti-tumor effects of the combination of 50% ^{177}Lu- plus 50% ^{90}Y-analogs were superior to those in animals treated with either ^{90}Y- or ^{177}Lu-analog. In smaller tumors the ^{90}Y-radiation energy will not completely be absorbed in the tumor, whereas on the other hand in larger tumors the increased number of clonogenic tumor cells may explain the failure of ^{177}Lu alone to reach cure.
The combination of different therapy modalities holds interest as a means of improving the clinical therapeutic effects of radiolabelled peptides.

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