Preclinical Evaluation of 18F-LMI1195 for In Vivo Imaging of Pheochromocytoma in the MENX Tumor Model.

Abstract:
We evaluated (18)F-LMI1195 (1-(3-bromo-4-(3-(18)F-fluoro-propoxy)benzyl)guanidine), a metaiodobenzylguanidine (MIBG) analog, for the detection of pheochromocytoma in a preclinical in vivo model of endogenous neuroendocrine tumors (multiple endocrine neoplasia [MENX]). Adrenal uptake kinetics of (18)F-LMI1195 were evaluated in healthy Wistar rats (n = 6) by dynamic PET imaging. Distribution of (18)F-LMI1195 was evaluated in tumor-bearing MENX mut/mut rats (n = 10) and control MENX wild-type rats (n = 4) by biodistribution studies and PET imaging. Biodistribution of (18)F-LMI1195 was compared with (123)I-MIBG in MENX mut/mut rats (n = 6) and correlated with histological tumor volume and norepinephrine transporter (NET) expression. Uptake specificity was evaluated by in vivo inhibition of the NET by desipramine (n = 6). Intraadrenal distribution of (18)F-LMI1195 was evaluated by autoradiography. (18)F-LMI1195 showed rapid tracer accumulation in adrenal glands 1 min after tracer injection. Adrenal glands of MENX mut/mut animals showed significantly higher standardized uptake value than MENX wild-type controls (maximum SUV, 10.3 ± 2.3 vs. 6.1 ± 0.9, P < 0.01). Adrenal uptake in MENX mut/mut rats could be inhibited by desipramine, shown by biodistribution studies (0.06 ± 0.01 vs. 0.16 ± 0.05).
percentage injected dose, P< 0.01), PET imaging (maximum SUV, 3.8 ± 0.8 vs. 10.3 ± 2.3, P< 0.01), and autoradiography. Adrenal uptake of (18)F-LMI1195 correlated with (123)I-MIBG uptake (r = 0.91), histological tumor volume (r = 0.68), and NET expression (r = 0.50). (18)F-LMI1195 showed an overall favorable distribution for tumor imaging. (18)F-LMI1195 shows high and specific accumulation in pheochromocytomas. Its favorable biodistribution makes it a promising PET tracer for tumor imaging. Further studies are warranted to evaluate its clinical value in oncologic indications.