Assessment of the 18F-labeled PET tracer LMI1195 for imaging norepinephrine handling in rat hearts.

A novel (18)F-labeled tracer, LMI1195 (N-[3-bromo-4-(3-(18)F-fluoro-propoxy)-benzyl]-guanidine), is being developed for sympathetic nerve imaging; its high specificity for neural uptake-1 mechanism has previously been demonstrated in cell associative studies and in rabbit and nonhuman primate studies assessing heart uptake. The aim of this study was to investigate the mechanisms of (18)F-LMI1195 cardiac uptake in the rat, which is known to contain norepinephrine uptake mechanisms beyond uptake-1. Tracer accumulation in the heart was studied over time after intravenous administration of (18)F-LMI1195 in healthy male Wistar rats by quantitative in vivo PET imaging. The uptake mechanism was assessed by pretreatment with the nonselective norepinephrine uptake-1 and norepinephrine uptake-2 inhibitor phenoxybenzamine (50 mg/kg intravenously; n = 4), the selective norepinephrine uptake-1 inhibitor desipramine (2 mg/kg intravenously; n = 4), or saline control (intravenously; n = 4). (18)F-LMI1195 produced high and sustained heart uptake allowing clear delineation of the left ventricular wall over 60 min after tracer administration. Pretreatment with phenoxybenzamine markedly reduced the (18)F-LMI1195 cardiac uptake when compared with controls. In contrast, there was preserved (18)F-LMI1195 uptake after desipramine pretreatment. In rats,
cardiac uptake of (18)F-LMI1195 was significantly inhibited by phenoxybenzamine but not desipramine, suggesting (18)F-LMI1195 is a substrate for the uptake-2 mechanism and is consistent with the rat heart having a dominant level of the mechanism.