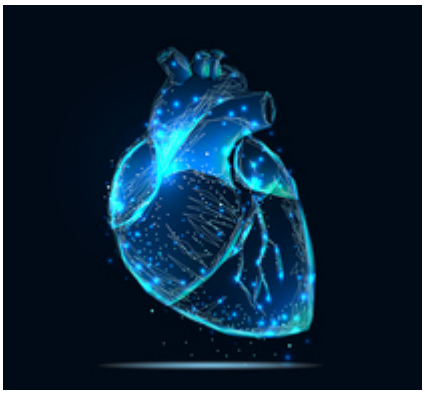
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Methods of Preparing Fluorine-18-Labeled Phenethylguanidines

TECHNOLOGY NUMBER: 5311



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Chemical Processes and Synthesis
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OVERVIEW

Preparation of 4-[18F]-MHPG isotope for PET scanning of the heart or adrenergic tumors

- Provides favorable evaluation of myocardial kinetic endpoints such as left ventricle uptake
- Preferential uptake in sympathetic neurons with a long retention time

BACKGROUND

Coronary heart disease (CAD) affects over 80 million adults and is the leading cause of death in the United States. A variety of diagnostic imaging procedures are used to evaluate for heart disease, including those which visualize blood flow patterns to the heart walls to diagnose disease as well as ones which evaluate functioning in the setting of known CAD. Cardiac nuclear medicine studies such as positron emission tomography (PET) scanning use radiolabeled agents to diagnose CAD, assess muscle damage after an MI, and to predict the benefit of a given intervention. PET scanning is considered biomedical imaging since it quantifies biological processes at the subcellular level and can therefore detect abnormalities before manifestation of gross anatomical features or physiological consequences. Though a variety of radiolabeled agents may be used in cardiac PET scanning, a need exists for new approaches that utilize lower concentrations of isotopes and that exhibit strong and temporally durable delineation of the heart compared to non-targeted organs.

INNOVATION

Researchers have developed two methods for preparation of fluorine-18 labeled phenethylguanidines for use as positron emission tomography (PET) contrast agent to both

evaluate cardiac kinetics and to assess tumors of the sympathetic nervous system. Both methods employ a 18F-labeling step followed by one or two simple steps to yield high quantities of the final radiolabeled product, specifically 4-[18F] fluoro-meta-hydroxy phenethylguanidine (4-[18F]-MHPG). The inventors analyzed the myocardial kinetics of 4-[18F]-MHPG using the established Patlak graphical analysis which utilizes metabolite-corrected plasma input functions.

The scientists established in a rat heart model that 4-[18F]-MHPG is taken up by sympathetic neurons and shows a long retention time that improves kinetic modeling of myocardial kinetics compared to existing agents. A series of microPET imaging studies performed in rhesus macaque monkeys revealed uptake consistent with uniform innervation of the left ventricle with correspondingly low uptake in the lungs and liver. Imaging analysis of the monkey following administration of a blocking dose of a norepinephrine transporter inhibitor confirmed that presynaptic sympathetic nerve terminals are the main locus of retention for 4-[18F]-MHPG in the heart.

The researchers also examined the uptake of 4-[18F]-MHPG by the adrenal gland and were able to measure kinetics that proved to be very similar to those seen in the heart, suggesting that this agent can be used for oncology applications in the clinic. This novel methodology therefore provides improved imaging through the use of 4-[18F]-MHPG in both the cardiac and oncologic clinical settings.