

## A Tale of Two Tracers: New Myocardial Perfusion Agents and Monitoring Gene Therapy for Parkinson's Disease

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### **Long Abstract:**

Coronary artery disease (CAD) is the greatest cause of morbidity and mortality in the USA and the greatest health care cost. Currently, myocardial perfusion scintigraphy (MPS) is the most widely applied noninvasive imaging method for the diagnosis, localization and risk stratification of patients with known or suspected CAD.

Rotenone is a natural product that binds to complex I of the mitochondrial electron transport chain. Iodine and fluorine containing rotenone analogs have been produced and labeled with iodine-125 and iodine-123 or fluorine-18. Initial rat distribution studies demonstrated a rapid and high uptake (4-7% injected dose) in the heart tissue with favorable heart/lung (8.5-9.6) and heart/liver ratios (2.2-2.4). Isolated perfused rabbit heart studies confirmed that these labeled analogs are deposited myocardial flow tracers with improved extraction and retention characteristics relative to <sup>99m</sup>Tc-sestamibi. Further evaluation of these agent towards clinical use is ongoing.

Parkinson's Disease (PD) is a neurodegenerative disorder with limited treatment options. As the disease progresses the dopamine production capability in substantia nigra is lost. L-DOPA therapy effectively replenishes the dopamine supply in early stages of the disease. However, the progressive nature of the disease coupled with the side effects of prolonged and increased use of L-DOPA diminishes the efficacy of this treatment. An adeno-associated virus has been used to insert the gene for DOPA decarboxylase into striatal neurons of MPTP-treated primates, a model of PD. The expression of the gene allows for the conversion of low dose L-DOPA to dopamine. Fluorine-18 labeled fluoro-meta-tyrosine (FMT), a substrate for DOPA decarboxylase, has been used as a PET reporter probe to establish the extent and longevity of gene expression in the primates. The application of imaging in this therapeutic development paradigm is the only way to monitor the gene expression in vivo. Clinically, these primates have demonstrated dramatic improvement in behavior due to the restoration of brain dopamine levels and phase I trials incorporating FMT imaging to monitor gene expression are planned.