Translational imaging biomarkers in rodent models of Parkinson’s: $^{123}$I-iофлуран SPECT/CT imaging of the dopamine transporter and $^{18}$F-FDG PET/CT imaging of metabolism

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Background
- Parkinson’s disease (PD) is a major health problem with unmet needs for reliable translational therapeutic response biomarkers.
- SPECT imaging of the dopamine transporter and PET imaging of brain glucose metabolism using the approved imaging agents, $^{123}$I-iофлуран ($^{123}$I-IFP) and $^{18}$F-FDG may provide PD response biomarkers.

Materials & Methods
- $^{123}$I-IFP SPECT/CT was performed in a 6-OHDA injection model of PD.
- $^{123}$I-IFP SPECT/CT and $^{18}$F-FDG PET/CT were performed in a new bacterial artificial chromosome (BAC) α-synuclein transgenic model of PD.
- For PET imaging, rats were anesthetized and injected IV with 1.3mCi FDG. A 15min emission scan was acquired after a 1h anesthetized-uptake period.
- For SPECT imaging, rats were anesthetized and injected IV with at least 0.7mCi IFP and scans acquired for 60-90min using a dual, Sphincoline collimator.
- CT scans were also acquired.
- For PET and SPECT image analysis, the striatum was segmented using a fixed volume region of interest (ROI). The cerebral cortex was also segmented for PET images over the same slices.
- Mean and maximum standardized uptake values (SUV) were calculated for all ROIs.

Conclusions
- $^{123}$I-IFP SPECT showed significantly decreased tracer uptake in the diseased vs. contralateral striatum in the 6-OHDA unilateral lesion model of Parkinson’s disease. This validates the use of $^{123}$I-IFP SPECT as a tracer for imaging dopamine transporter in this rat model in vivo.
- The BAC SYN transgenic model of Parkinson’s disease showed minor trends toward decreased $^{123}$I-IFP binding vs. wild type rats at late stage disease (13 months).
- Further evaluation of $^{123}$I-IFP SPECT as an in vivo imaging method for detection of BAC SYN disease progression is required.
- $^{18}$F-FDG uptake was significantly greater in BAC SYN rats at late stage disease.
- This is consistent with disease-associated inflammation and increased uptake in inflammatory cells in the striatum and cortex.
- Both FDG PET and IFP SPECT provide translational biomarkers that can be used in rodent models to (i) assess treatment activity in clinical candidates
- (ii) Optimize biomarker use for clinical trial translation.


Transaxial view
Coronal View

Figure 1: $^{123}$I-iофлуран SPECT imaging of the presynaptic dopamine transporter in a 6-OHDA unilateral lesion model of Parkinson’s disease. Images show low binding in the striatum of the diseased (red arrow) vs. contralateral/normal (green arrow) hemisphere.

Figure 2: $^{123}$I-iофлуран SPECT imaging of dopamine transporter activity in wild type (WT BAC) vs α-synuclein transgenic rats (BAC SYN) at late stage disease. BAC SYN rats show a minor trend toward decreased $^{123}$I-IFP in the striatum compared to WT BAC rats.

Figure 3: Glucose metabolism modulation in wild type (WT BAC) vs α-synuclein transgenic rats (BAC SYN) over time. A) Representative PET images of FDG brain uptake. Arrows indicate striatum. B) FDG PET imaging shows significantly increased metabolism in both the striatum and cortex of WT BAC rats after five months disease progression, and compared to WT BAC rats.