Dopamine Transporter (DaT) SPECT Imaging

$^{123}$I-ioflupane (N-$\omega$-fluoropropyl-$\beta$-carbomethoxy-$\beta$-(4-iodophenyl) nortropane), is a single photon emission computed tomography (SPECT) molecular imaging agent for imaging the dopamine transporter (DaT) (Figure 1). It was recently approved by the U.S. Food and Drug Administration (FDA) and is available in the U.S. market. This agent was approved in Europe in 2000, and several hundred thousand patients have been scanned. It has proven to be safe, reliable and very sensitive for detection of degeneration of nigrostriatal nerve cells in the differential diagnosis of movement disorders such as Parkinson’s disease (PD) and dementia. Although clinical diagnosis is straightforward in many patients, it may be difficult in others—especially in early disease—and structural imaging with computed tomography or magnetic resonance imaging usually is of little help.

$^{123}$I-ioflupane is a cocaine analogue with high affinity and relatively good selectivity for DaT. DaT concentration is highest in striatum (putamen and caudate nucleus) where the dopamine transporters are located on the presynaptic side of dopaminergic synapses (Figure 2). They transport dopamine out of the synaptic cleft, back into presynaptic axons for either re-use or degradation.

Degeneration of these presynaptic neurons results in lower striatal DaT density. Parkinsonian symptoms typically become apparent only after at least 50 percent of nigrostriatal nerve terminals are lost. Thus, DaT imaging is excellent for early detection of nigrostriatal dopaminergic degeneration. Also, the degree of reduction in DaT binding is related to disease severity.

In PD and related parkinsonian syndromes such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP), there is presynaptic dopaminergic degeneration and therefore decreased DaT binding. Although the pattern of DaT binding tends to be somewhat different, there is a large overlap in DaT imaging findings among these syndromes, and $^{123}$I-ioflupane imaging is unable to discriminate among them. In essential tremor, psychogenic parkinsonism and neuroleptic drug-induced parkinsonism, however, there is no presynaptic dopaminergic degeneration and DaT SPECT is normal.

$^{123}$I-ioflupane SPECT can also be used to differentiate dementia with Lewy bodies (DLB) from other dementias. This can be important clinically, because DLB patients

**Indications for $^{123}$I-ioflupane imaging**

- Detection of loss of functional dopaminergic neuron terminals in the striatum of patients with clinically uncertain parkinsonian syndromes
- Differentiation of essential tremor, psychogenic parkinsonism, or neuroleptic induced parkinsonism from presynaptic parkinsonian syndromes (Parkinson’s disease, multiple-system atrophy, corticobasal degeneration, progressive supranuclear palsy)
- Early detection of Parkinson’s disease
- Assessment of disease severity and progression
- Differentiation of dementia with Lewy bodies from other dementias

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Molecular Imaging Training Course Debuts

As we all know, nuclear medicine is rapidly evolving. Molecular imaging, including non-radioactive tracers, is becoming an increasingly important part of our specialty. As a result, the Society of Nuclear Medicine (SNM) refocused its mission to incorporate the expanding role of molecular imaging in patient care and is now considering a name change to the “Society of Nuclear Medicine and Molecular Imaging.”

With this new mission, the Center for Molecular Imaging Innovation and Translation Education Task Force has examined the educational needs for current and future physicians and scientists practicing molecular imaging. Suggestions were developed for

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respond better to therapy with acetylcholinesterase inhibitors but may suffer severe side effects if given neuroleptic drugs and have worse prognosis. In DLB, DaT binding is reduced, whereas in most other dementias (with the exception of dementia associated with PD), DaT binding is normal.

Technical Aspects

Typically 185 MBq (5 mCi) of \(^{123}\)I-ioflupane is injected intravenously. To reduce exposure of the thyroid to free \(^{123}\)I, the thyroid can be blocked at least one hour before tracer injection, although even without blocking, the radiation dose to the thyroid would be low. The only contraindications are pregnancy, the inability to cooperate with SPECT brain imaging, or a known hypersensitivity to the active substance or to any of its excipients (which is rare). Iodine allergy is not a contraindication. Breastfeeding should be interrupted for at least 24 hours after injection.

Image Interpretation

Images should be reoriented to a standard plane to avoid the false appearance of asymmetry due to head tilt. Images should be checked for asymmetry and a decrease of the target to background ratio. In a normal scan, the striatum is clearly visible as right and left symmetric, comma-shaped regions, with both caudate and putamen showing a high intensity compared to background (Figure 3). With increasing age, a slight decline in target to background ratio is expected (typically some 5-8 percent per decade).

In early PD there is usually an asymmetrical pattern of reduced DaT binding starting in the dorsal putamen contralateral to the clinically most symptomatic body side, gradually progressing anteriorly and ipsilaterally as the disease becomes more severe. Activity in the caudate nucleus is relatively preserved in early disease but will also decline with advancing disease. In the atypical parkinsonian syndromes (MSA, PSP), there usually will be a more symmetrical decrease in DaT binding and relatively more involvement of the caudate nucleus; however, there is too much overlap to reliably differentiate between PD and these other conditions. In DLB, DaT binding is reduced, typically with bilateral loss of DaT binding, mainly in the putamen but also in the caudate and generally with less asymmetry than in PD.

Many specialized centers also use semiquantitative image assessment in which specific binding ratios are calculated, e.g., the ratio of striatal to occipital activity. These can be compared to values of a normal reference population. Because semiquantification is influenced by many factors (e.g., camera, scanning protocol, reconstruction algorithms, semiquantification method, etc.) there is no universal cutoff value for normal vs. abnormal. Each site needs to establish its own normal reference range. Although semiquantification may have some advantages, especially for research purposes or in case of very subtle changes, it usually is not necessary.
Conclusion
Dopamine transporter imaging with $^{123}$I-ioflupane has recently been FDA approved. It is a robust and simple technique that can sensitively detect or rule out degeneration of presynaptic striatal dopaminergic nerve cells. It can differentiate presynaptic parkinsonian syndromes (PD, MSA, PSP) from essential tremor, drug-induced parkinsonism and psychogenic parkinsonism, but it cannot differentiate between these presynaptic parkinsonian syndromes. $^{123}$I-ioflupane SPECT can also be used to differentiate dementia with Lewy bodies from other types of dementia, such as Alzheimer's disease.

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SNM Brings Molecular Imaging to the Public on Times Square Jumbotron
On December 23, SNM debuted a 15-second message on the CBS jumbotron screen in New York City's Times Square to raise public awareness of molecular imaging. The video will run once an hour for three months, including the holiday season and the New Year's Eve celebration, which alone attracted an estimated one million people.

The CBS “Super Screen” is 26 feet tall and 20 feet across and is strategically positioned at 42nd St. between 7th and 8th Avenues in the heart of the Times Square Plaza. It is estimated that 1.6 million people pass through Times Square each day.

The video focuses on how molecular imaging can provide earlier diagnosis and directs people to SNM's new patient website, discovermi.org, for more information.