Dopamine transporter (DAT) imaging with single-photon emission computed tomography (DAT-SPECT) is being evaluated to improve the differential diagnosis of parkinsonian syndromes (PS) from nonparkinsonian tremor and of dementia with Lewy bodies (DLB) from Alzheimer disease (AD). Most of the available literature is from Europe, where a ligand has been available for over a decade. In terms of technical performance, the ligand is specific for the striatal dopamine transporter, and studies indicate reliability in assessment of the images when performed by experienced readers.

For diagnosing Parkinson disease (PD) in patients with parkinsonian symptoms, studies of diagnostic accuracy report good specificity for confirming nigrostriatal degeneration, with less sensitivity for ruling out disease. These findings are dependent, however, on a reference standard (clinical diagnosis) which may be flawed, and it is unknown whether DAT-SPECT would show greater sensitivity when compared with the criterion standard of histopathologic diagnosis. Evidence on clinical utility includes a randomized controlled trial that showed more patients evaluated with DAT-SPECT have changes in diagnosis and management compared with controls without imaging; however, no improvement in quality of life was observed within the one year follow-up. In other studies, DAT-SPECT findings are consistent with about 90% of diagnoses made by specialists in movement disorders and that in a relatively small proportion of patients, the diagnosis has been altered based on DAT-SPECT.

For discriminating between DLB and AD, the sensitivity and specificity of DAT-SPECT is somewhat lower than for PS, although the comparison standard used in the available studies may be flawed. One retrospective community-based study suggests that DAT-SPECT may influence the clinical diagnosis and management of a large proportion of patients with possible DBL.

Overall, the evidence available at this time is insufficient to determine with certainty the effect of this technology on health outcomes.

Policy

Dopamine transporter imaging with single-photon emission computed tomography (DAT-SPECT) is investigational for all indications, including but not limited to, aiding in the diagnosis of patients with clinically
uncertain parkinsonian syndromes, essential tremor, or dementia with Lewy bodies, and for the monitoring of disease progression.

Background

PSs are a group of diseases that share similar cardinal signs, characterized by bradykinesia, rigidity, resting tremor and gait disturbance. PD is the most common cause of parkinsonism; however, diagnosing PD in the early stage of the disease can be difficult. In addition other etiologies such as essential tremor (ET), corticobasal degeneration, multisystem atrophy, progressive supranuclear palsy, vascular parkinsonism, and drug-induced parkinsonism can lead to a similar set of symptoms. Even in specialized movement disorders centers, up to 25% of patients may be misclassified, and some patients, such as those with ET who have been diagnosed with PD, may be erroneously treated. This has led to the development of additional tests to improve the accuracy of clinical diagnosis of PD and other PSs. One recent approach is to evaluate the integrity of dopaminergic pathways in the brain with dopamine transporter imaging with DAT-SPECT.

DAT-SPECT detects presynaptic dopaminergic deficit by measuring DAT binding. In general, striatal DAT binding is reduced in PD, genetic parkinsonism, DLB, corticobasal degeneration, progressive supranuclear palsy, and multiple system atrophy, while striatal DAT binding is in the normal range in AD, ET, dystonic tremor, orthostatic tremor, drug-induced parkinsonism, psychogenic parkinsonism, and vascular parkinsonism. It is proposed that an abnormal DAT-SPECT supports the diagnosis of PD or other neurodegenerative PS (multisystem atrophy, progressive supranuclear palsy), while a normal DAT-SPECT in a symptomatic patient increases the likelihood of a disease not affecting the nigrostriatal dopaminergic pathway.

Due to the degeneration of nigrostriatal neurons in DLB, DAT-SPECT is also proposed to differentiate DLB from AD. Some note a severe sensitivity to neuroleptics (potentially life-threatening) in patients with DLB. However, newer agents are usually well-tolerated, and patients with DLB may also respond to the cholinesterase inhibitors that are more commonly used to treat AD.

Analysis of DAT-SPECT images can be visual or semiquantitative. Since patients typically do not become symptomatic before a substantial number of striatal synapses have degenerated, visual interpretation of the scan is thought to be sufficient for clinical evaluation. A variety of methods are being tested to improve the validity and reliability of ratings, including commercially available software to define the region of interest (ROI) for semiquantitative analysis and the development of an atlas for visual interpretation. Semiquantitative interpretation may aid visual interpretation and, if performed rigorously, may increase diagnostic accuracy; however, interobserver variability tends to be high with manual ROI-based semiquantification. Semiquantitative analysis also requires normal control values and varies across imaging systems.

Dopamine transporter ligands include $^{123}$I-$\beta$-CIT, $^{123}$I-FP-CIT, and $^{99m}$Tc-TRODAT-1. $^{123}$I-$\beta$-CIT requires a delay between injection and scan of about 24 hours. $^{123}$I-FP-CIT (DaTscan) is a fluoropropyl derivate of $\beta$-CIT that can be injected three to six hours before the scan.

Regulatory Status

DaTscan™ (GE Healthcare) has been in use in Europe since 2000 with a diagnostic indication for use in parkinsonian patients and with expanded use since 2006 in patients suspected of DLB. DaTscan was approved by the U.S. Food and Drug Administration (FDA) in 2011 and is “indicated for striatal dopamine transporter visualization using single-photon emission computed tomography (SPECT) brain imaging to assist in the evaluation of adult patients with suspected parkinsonian syndromes (PS). In these patients, DaTscan may be
used to help differentiate essential tremor from tremor due to PS (idiopathic Parkinson’s disease, multiple system atrophy and progressive supranuclear palsy). DaTscan is an adjunct to other diagnostic evaluations.”

**Related Protocol**

Deep Brain Stimulation

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.

**References**

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.


