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Medical Policy Manual Radiology, Policy No. 44

Single Photon Emission Computed Tomography (SPECT) of the Brain

Effective: June 1, 2019

Next Review: March 2020
Last Review: April 2019

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Single photon emission computed tomography (SPECT) is a nuclear imaging technique that is used to visualize functional information about body organs, including the brain.

MEDICAL POLICY CRITERIA

Notes:

- This policy addresses only single photon emission computed tomography (SPECT) of the brain. This policy does not address the use of SPECT other than SPECT of the brain.
- This policy does not address the use of dopamine transporter (DAT)-SPECT. Please refer to the Cross References below for the health plan commercial policy on DAT-SPECT.

I. Single photon emission computed tomography (SPECT) of the brain for indications other than those listed below may be considered **medically necessary**.

II. SPECT of the brain is considered **investigational** for the following conditions:

A. Attention-deficit/hyperactivity disorder (ADHD)

B. Autism

C. Behavioral health disorders (including, but not limited to bipolar disorder, major depressive disorder, schizophrenia, and personality disorders)

D. Cerebrovascular disease (including stroke, transient ischemic attack, and subarachnoid hemorrhage)

E. Chronic fatigue syndrome

F. Dementias (including Alzheimer's, vascular dementia, frontal temporal dementia, Pick's disease and dementia with Lewy bodies)

G. Encephalopathy (including but not limited to Lyme, Wernicke's, hypoglycemia, and hypoxic-ischemic encephalopathy)

H. Motor neuron disorders [including amyotrophic lateral sclerosis (ALS), progressive bulbar palsy, primary lateral sclerosis, and progressive (spinal) muscular atrophy]

I. Multiple sclerosis

J. Parkinsonian syndromes and essential tremor

K. Substance-related disorders (including alcohol)

L. Traumatic brain injury

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Diagnosis and indication for testing

CROSS REFERENCES

1. Dopamine Transporter Single-Photon Emission Computed Tomography (DAT-SPECT), Radiology, Policy No. 57

BACKGROUND

Brain imaging requires the use of radiopharmaceuticals that cross the blood-brain barrier. The radioactive isotope decay results in emission of gamma rays that are detected by a gamma camera which allows reconstruction of cross-sectional slices.

SPECT has been used to determine dopamine and serotonin receptor availability and to study regional cerebral blood flow in the brain. Because cerebral blood flow correlates with brain metabolism, the images provide information regarding which regions of the brain are affected, which in turn aids with differential diagnosis. In addition, SPECT has been proposed as a tool to diagnose and estimate treatment response in attention deficit/hyperactivity disorder (ADHD), Alzheimer's disease /dementias, and other psychiatric conditions, such as major depression.

REGULATORY STATUS

There are a number of radiopharmaceutical agents that have been approved by the U.S. Food Drug Administration (FDA) for use with SPECT for a variety of indications. Some of these include:

- Adreview (iobenguane sulfate I-123)
- Technetium TC-99m (mebrofenin)
- I-123 isopropyliodoamphetamine (IMP, Spectamine)
- Tc-99m HMPAO (hexamethyl propylamine oxime, Ceretec)
- Tc-99m ECD (ethyl cysteinate dimer, Neurolite)
- thallium 201 diethyldithiocarbamate (T1-DDC)

EVIDENCE SUMMARY

The most rigorous evaluation of the impact of a diagnostic test on clinical outcomes is a randomized controlled trial (RCT) that evaluates health outcomes in patients who receive the new diagnostic test compared with patients who are evaluated without the new test and according to standard of care. Evidence from RCTs are necessary in order to establish how SPECT may be used in the clinical setting to either diagnose or direct treatment

A significant number of published studies have focused on investigating pathologic differences in regional cerebral perfusion, for the purpose of diagnosis of disease, in response to drug therapy or for the evaluation of brain function for a number of neurological, psychiatric, and neurodegenerative conditions. The majority of these studies are case reports or small case series/cohort studies that may limit the conclusions that can be drawn about the clinical utility of SPECT.[1-41] Furthermore, evidence regarding the use of SPECT to evaluate brain function for a number of clinical indications listed above is limited to case series and studies that utilize SPECT as a component of the study design, but do not evaluate the clinical utility of this imaging technique compared to other standard modalities.

There have been comparative studies performed for a number of indications including autism, chronic fatigue syndrome, dementia, essential tremor, and stroke that were published more than ten years ago. However, these older studies are not described here.[3,42-54]

The evidence summarized below is focused on systematic reviews, randomized controlled trials, and comparative studies that investigate the utility of SPECT compared to other imaging modalities and/or standard clinical diagnostic criteria. In addition, the evidence summary only addresses the investigational indications listed in the policy criteria.

CEREBROVASCULAR DISEASE

Nonrandomized Studies

Mutoh (2018) performed a cohort study to analyze the ability of SPECT to predict prognosis in 29 patients following aneurysmal subarachnoid hemorrhage (SAH).[55] Patients who had undergone surgery for ruptured anterior communicating artery aneurysms underwent routine measurements using technetium-99 m hexamethyl propyleneamine oxine SPECT on days four and 14 after SAH. SPECT results were analyzed by three-dimensional stereotactic surface projection (3D-SPP) and an age-matched normal database (NDB) was used as a reference. The analysis showed that cortical hypoperfusion around the surgical site in bilateral frontal lobes was evident on day four ($p<0.05$ vs NDB), and was improved significantly on day 14. The recovery was significantly less complete in patients with poor clinical grades ($p<0.05$) and patients presenting symptoms attributable to delayed cerebral ischemia ($p<0.05$). SPECT results indicating mild to moderate recovery were independently associated with poor functional outcome at three months in a multivariate analysis ($p=0.014$; odds ratio [OR], 2.5; 95% confidence interval [CI], 1.93-3.31)

Kincaid (2009) performed a retrospective analysis on 152 patients with subarachnoid hemorrhage to assess the accuracy of the routine clinical use of transcranial Doppler (TCD) ultrasonography and SPECT in predicting angiographically demonstrated cerebral vasospasm.[56] TCD was able to predict vasospasm with an OR of 27 (95% CI 3-243) in the anterior cerebral arteries (ACA), 17 (95% CI 5.4-55) in the middle cerebral arteries (MCA) and 4.4 (95% CI 0.72-27) in the basilar cerebral arteries (BA). Conversely, SPECT was able only to predict vasospasm with an OR of 0.97 (95% CI 0.36-2.6) in the ACA, 2.0 (95% CI 0.71-5.5) in the MCA, and 5.6 (95% CI 0.89-36), in the BA. Overall, the investigators concluded that the standard transcranial Doppler appeared to be more predictive of cerebral vasospasms in multiple areas of the brain compared to SPECT.

DEMENTIAS

Systematic Reviews

Archer (2015) performed a Cochrane systematic review in 2015 to assess the diagnostic accuracy of cerebral blood flow (rCBF) SPECT for diagnosing frontal temporal dementia (FTD) in populations with suspected dementia settings and the ability of SPECT to differentiate between FTD from other dementia subtypes.[57] Five cohort studies (two retrospective cohort studies and three prospective) were included to assess the diagnostic capabilities of SPECT in patients with suspected dementia.[58,59] Six case-control studies were included that assessed the ability of SPECT to differentiate between different types of dementias in participants who had a clinical diagnosis of FTD or other dementia subtype using standard clinical diagnostic criteria.[60] The review found that study design and methods varied widely between included studies, participant selection was not well described, and that the studies had either high or unclear risk of bias. The reviewers also reported that in most studies the threshold used to define a positive SPECT result was not predefined. Sensitivities and specificities for differentiating FTD from non-FTD ranged from 0.73 to 1.00 and from 0.80 to 1.00, respectively, for the three multiple-headed camera studies. However, sensitivities were significantly lower for the two single-headed camera studies; reporting sensitivities from 0.36 to 0.40. The reviewers recommended against the use of SPECT in these patients due to insufficient evidence.

In 2015, the Washington State Health Care Authority published a health technology assessment on “Functional Neuroimaging for Primary Degenerative Dementia or Mild Cognitive Impairment”.[61] This study assessed a number of neuroimaging techniques including

FDG-PET, C-DTBZ-PET, SPECT and fMRI for the diagnosis of primary degenerative dementia or mild cognitive impairment. The authority concluded that there was sufficient evidence not to cover SPECT for these indications. The reliability of HMPAO-SPECT in providing a differential diagnosis of either AD or FTD in patients with an uncertain diagnosis was determined by the inclusion of two studies. [60,62] The diagnostic accuracy of HMPAO-SPECT was determined by one study by Bonte, which found that SPECT had a sensitivity of 93% and a specificity of 85% in in differentiating between AD and non-AD dementia in post-mortem samples.[63]

Davison and O'Brien (2014) performed a systematic review in 2014 comparing FDG-PET and rCBF SPECT in the diagnosis of neurodegenerative dementias, including nine studies that directly compared the two imaging modalities (N=117 subjects with AD, 46 subjects with other dementias and 100 controls).[64] Eight of these studies involved patients with AD, four of which included vascular dementia, frontal temporal dementia, or Pick's disease. One study examined patients with Dementia with Lewy Bodies.[45,65] Published studies of SPECT sensitivities ranged from 65-85% for diagnosing Alzheimer's disease (AD) and specificities (for other neurodegenerative dementias) of 72-87%. PET sensitivities and specificities were slightly higher than SPECT, ranging from 75-99% and 71-93%, respectively. Both of these modalities are therefore just as sensitive at predicting and diagnosing AD as the current standard for clinical diagnosis, NINCDS-ADRDA, which has sensitivity ranging from 65-96%. Limitations of the included studies listed were small sample size, poorly matched control groups, and heterogeneity in study design.

Yeo (2013) performed systematic review of the diagnostic utility of HMPAO SPECT in neurodegenerative dementia, and pooled studies with a clinical diagnosis and those using 99mTc-HMPAO SPECT in a meta-analysis.[66] Forty-nine studies were included in the review; AD versus FTD (n = 13), AD versus VD (n = 18), AD versus DLB (n = 5), and AD versus NC (n = 18). However, the majority of these included studies had small sample sizes, with only five studies having more than 100 subjects. The reviewer reported sensitivity and specificity of 99mTc-HMPAO-SPECT in distinguishing clinically diagnosed AD from FTD are 79.7 and 79.9%, respectively, AD from VD are 74.5 and 72.4%, AD from DLB are 70.2 and 76.2%, and AD from NC are 76.1 and 85.4%. Limitations of this analysis include small numbers of studies for each diagnostic comparison group and high methodological heterogeneity between studies. The reviewers concluded that SPECT is valuable in differentiating Alzheimer's disease from frontotemporal dementia and normal controls, but should only be used in with clinical information and other test results.

Nonrandomized Studies

In a 2017 retrospective study, Höller compared SPECT with EEG and with a combination of SPECT and EEG in patients with diagnosed dementias.[67] Standard clinical electroencephalography (EEG) and 99mTc-hexamethyl-propylene-aminoxime (HMPAO)-SPECT were used to assess 39 patients with Alzheimer's dementia (AD), 69 patients with depressive cognitive impairment (DCI), 71 patients with amnestic mild cognitive impairment (aMCI), and 41 patients with amnestic subjective cognitive complaints (aSCC). Patient groups were classified pairwise (using a linear support vector machine) separately for each biomarker and then again for each EEG biomarker combined with SPECT. HMPAO-SPECT alone was not able to reliably identify the individual disorders, but a combination of HMPAO-SPECT with EEG outperformed EEG alone and was able to classify aSCC verus AD, aMCI versus AD, and AD versus DCI.

Brayet (2017) analyzed the ability of SPECT scans to differentiate between AD patients and healthy controls.[68] Eight aMCI subjects and 16 age-matched controls underwent SPECT scans during wakefulness and during REM sleep. A significant decrease in perfusion in the anterior cingulate cortex was reported in aMCI cases during wakefulness ($p<0.024$), and a larger decrease was reported during REM sleep ($p<0.001$).

Chiba (2016) evaluated the early differential diagnosis between Alzheimer's disease and dementia with Lewy bodies which compared (18)F-FDG PET and (123)I-IMP SPECT.[69] The study was small, with only nine patients, limiting the conclusions that can be drawn. However, the authors concluded that for the occipital regions, there was significant accuracy in a differential diagnosis for both FDG PET and IMP SPECT. FDG PET was more useful than IMP SPECT for the differential diagnosis of mild cognitive impairment Alzheimer's disease versus dementia with Lewy bodies.

O'Brien (2014) compared the diagnostic ability of perfusion SPECT with FDG-PET to differentiate between Alzheimer and Lewy body dementias.[70] Subjects clinically diagnosed with Alzheimer disease (AD; n = 38) and dementia with Lewy bodies (DLB; n = 30), and controls (n = 30) underwent FDG-PET and SPECT; and area under the curve (AUC) of receiver-operating-characteristic analysis was reported. Investigators reported that diagnosis, as determined by two clinicians, indicated that FDG-PET was superior to SPECT for both dementia vs. no-dementia (AUC = 0.93 vs. 0.72, p=0.001) and AD vs. DLB (AUC = 0.80 vs. 0.58, p=0.005). The investigators concluded that perfusion SPECT is of limited diagnostic utility for differentiating DLB from AD.

Takahashi (2014) compared the ability of perfusion SPECT with 3D arterial spin-labeled brain perfusion imaging to diagnose AD.[71] This study included 68 patients with clinically suspected AD who underwent both 3D arterial spin-labeling and SPECT. Images were assessed by two clinicians and the area under the ROC curve distinguishing AD from non-AD was 0.80-0.82 for SPECT alone and 0.69 for 3D ASL images alone. Statistical parametric mapping showed that the perisylvian and medial parieto-occipital perfusion in the arterial spin-labeled images was significantly higher than that in the SPECT images. The investigators concluded that diagnostic performance of 3D arterial spin-labeling and SPECT for Alzheimer disease was almost equivalent.

Ito (2013) performed a multicenter prospective cohort study to examine the ability of ^{123}I-N-isopropyl-4-iodoamphetamine cerebral blood flow (IMP-CBF) SPECT to diagnose AD in patients with mild cognitive impairment (MCI).[72] One hundred and thirteen patients with amnestic MCI underwent clinical and neuropsychological examinations and ^{123}I-IMP-CBF SPECT at baseline and were followed for three years and evaluated for progression to dementia. SPECT images were classified as AD/DLB (dementia with Lewy bodies) pattern and non-AD/DLB pattern by image interpretation. Ninety-nine of the 113 patients converted to AD within the observation period. Image interpretation predicted conversion to AD with 56% diagnostic accuracy (sensitivity, 76%; specificity, 39%). Multivariate logistic regression analysis identified SPECT as a predictor, which distinguished AD converters from non-converters. The ability of a positive SPECT to predict conversion to AD on its own was low (OR 2.5, but if used in combination with gender and mini-mental state examination there was an improved diagnostic accuracy (OR 20.08). Therefore, SPECT on its own was concluded to be sensitive but relatively nonspecific for prediction of clinical outcome during the 3-year follow-up.

MULTIPLE SCLEROSIS

Nonrandomized Studies

Assadi (2010) performed a small study of 16 patients with confirmed multiple sclerosis (MS) to evaluate with ability of SPECT with Tc-99m MIBI or Tc-99m ECD (ethyl cysteinate dimer) to detect brain abnormalities compared to MRI.[73] MRI was performed on 16 patients (13 women and three men, aged 16-38 years) and an average of 1-10 lesions in a number of different areas of the brain, including periventricular white matter, juxtacortical white matter, corpus callosum, cerebellar peduncles, and brainstem. Of the 16 patients, eight had SPECT with Tc-99m MIBI, and the other eight had SPECT with Tc-99m ECD. Neither type of SPECT was able to detect any abnormality, indicating that the use of SPECT is insufficient to evaluate brain lesions in multiple sclerosis.

PARKINSONIAN SYNDROMES AND ESSENTIAL TREMOR

Systematic Reviews

Sharifi (2014) performed a systematic review of the role of neuroimaging techniques in the diagnosis and evaluation of essential tremor.[74] The reviewers included two small studies using SPECT to determine rCBF at rest.[75,76] One confirmed increased bilateral cerebellar activity, whereas the other did not find any significant differences between essential tremor patients and healthy controls. One study focused on cognitive functioning and related the rCBF with cognitive performances in patients and healthy controls, and determined differences in test performances, but showed no difference in rCBF values.[76]

In a 2007 systematic review of the literature on diagnostic accuracy of SPECT in parkinsonian syndromes, Vlaar included 15 small case series that used SPECT with post-synaptic tracers, which measure dopamine receptor density.[42] When SPECT was used to differentiate between PD and essential tremor (ET), two studies were included and the pooled OR with 95% CI was 2 (0.4–5). Five studies were included in a pooled analysis to determine if SPECT could reasonably differentiate between PD and atypical parkinsonian syndromes, with a pooled OR with 95% CI of 2.0 (0.8 – 6). The reviewers concluded that the accuracy of SPECT with post-synaptic tracers to differentiate between PD and atypical parkinsonian syndrome is relatively low.

PRACTICE GUIDELINE SUMMARY

AMERICAN PSYCHIATRIC ASSOCIATION (APA)

An APA 2012 consensus report from the APA work group on neuroimaging markers of psychiatric disorders,[77] recommends the following steps for biomarker validation in psychiatric disorders:

1. There should be at least two independent studies that specify the biomarker's sensitivity, specificity, and positive and negative predictive values;
2. Sensitivity and specificity should be no less than 80%; positive predictive value should approach 90%;
3. The studies should be well powered, conducted by investigators with expertise to conduct such studies, and the results published in peer-reviewed journals;
4. The studies should specify type of control subjects, including normal subjects and those with a dementing illness but not AD; and

5. Once a marker is accepted, follow-up data should be collected and disseminated to monitor its accuracy and diagnostic value.

According to this standard, the report concludes, "...the psychiatric imaging literature currently does not support the application of a diagnostic biomarker to positively establish the presence of any primary psychiatric disorder."

AMERICAN COLLEGE OF RADIOLOGY (ACR)

The 2015 ACR Appropriateness Criteria® for evaluating head trauma[78] indicated that SPECT is usually not appropriate (rating: 1) in the following situations:

- Initial evaluation of minor, mild, moderate or severe acute closed head injury
- Short-term follow-up imaging of acute traumatic brain injury with or without neurologic deterioration, delayed recovery, or persistent unexplained deficits
- Subacute or chronic traumatic brain injury with new cognitive and/or neurologic deficit(s)
- Suspected intracranial arterial injury
- Suspected intracranial venous injury

The 2014 Appropriateness Criteria® for evaluating seizures and epilepsy[79] indicated that SPECT with perfusion agents may be appropriate (rating: 5) to provide confirmatory localization information in patients with medically refractory epilepsy. However, the ACR guidelines conclude, "Only electroencephalogram (EEG) (using either scalp electrodes or intracranial electrodes [iEEG]) and magnetoencephalography (MEG) directly measure the brain's electrical activity. As such, they could or should be the gold standard for seizure localization." In addition, the ACR guidelines state that the utility of SPECT with regards to clinical diagnosis, management, or outcomes of new-onset seizure patients has not been scientifically established.

The 2015 ACR Appropriateness Criteria® for dementia and movement disorders[80] provides guidance on the use of SPECT. A rating of 2 or 3 ("usually not appropriate") was assigned to the following conditions:

- Dementia and movement disorders (consider for problem solving)
- Probable or possible Alzheimer's disease
- Suspected frontotemporal dementia
- Suspected vascular dementia
- Suspected normal pressure hydrocephalus
- Suspected Huntington disease
- Clinical features suggestive of neurodegeneration with brain iron accumulation
- Motor neuron disease (consider for problem solving)
- Parkinson disease with typical clinical features and responsive to levodopa
- Parkinsonian syndrome with atypical clinical features not responsive to levodopa.

A rating of 4 or 5 ("may be appropriate") was assigned to the following conditions:

- Suspected prion disease (Creutzfeldt-Jakob, iatrogenic, or variant)
- Suspected dementia with Lewy bodies

- Parkinson disease with typical clinical features and responsive to levodopa.

The 2016 ACR-Society for Pediatric Radiology (SPR)[81] developed a practice parameter that states SPECT brain perfusion is clinically indicated for the following:

- Evaluating patients with suspected dementia
- Localizing epileptic foci preoperatively
- Diagnosing encephalitis
- Monitoring and assessing vascular spasm following subarachnoid hemorrhage
- Mapping of brain perfusion during interventions
- Detecting and evaluating cerebrovascular disease
- Predicting the prognosis of patients with cerebrovascular accidents
- Corroborating the clinical impression of brain death

In addition, for other indications, such as neuropsychiatric disorders and chronic fatigue syndrome, the findings of SPECT brain perfusion imaging have not been fully characterized. In human immunodeficiency virus (HIV) encephalopathy, SPECT brain perfusion imaging can detect altered brain perfusion.

SUMMARY

For some indications, there is enough research to show that single photon emission computed tomography (SPECT) of the brain improves health outcomes. Therefore, SPECT for the brain may be considered medically necessary when criteria are met.

There is not enough research to show that single photon emission computed tomography (SPECT) of the brain in the evaluation, diagnosis or treatment for a variety of indications improves health outcomes. Additional research is needed to know how SPECT may be used to guide patient management compared to other imaging techniques and standard clinical diagnostic criteria. Therefore, SPECT of the brain is considered investigational for the neurologic, psychiatric, psychological, as well as other nononcologic indications as specified in the policy criteria.

REFERENCES

1. McGough, JJ, Barkley, RA. Diagnostic controversies in adult attention deficit hyperactivity disorder. *Am J Psychiatry*. 2004 Nov;161(11):1948-56. PMID: 15514392
2. Voeller, KK. Attention-deficit hyperactivity disorder (ADHD). *J Child Neurol*. 2004 Oct;19(10):798-814. PMID: 15559895
3. Nobili, F, Frisoni, GB, Portet, F, et al. Brain SPECT in subtypes of mild cognitive impairment. Findings from the DESCRIPA multicenter study. *J Neurol*. 2008 Sep;255(9):1344-53. PMID: 18958573
4. Ruhe, HG, Booij, J, v Weert, HC, et al. Evidence why paroxetine dose escalation is not effective in major depressive disorder: a randomized controlled trial with assessment of serotonin transporter occupancy. *Neuropsychopharmacology*. 2009 Mar;34(4):999-1010. PMID: 18830236

5. Yao, WJ, Pan, HA, Wang, ST, Yang, YK, Yu, CY, Lin, HD. Frontal cerebral blood flow changes after hormone replacement therapy in depressed postmenopausal women. *J Cereb Blood Flow Metab*. 2009;29:1885-90. PMID: 19654591
6. van Heeringen, K, Van den Abbeele, D, Vervaet, M, Soenen, L, Audenaert, K. The functional neuroanatomy of mental pain in depression. *Psychiatry Res*. 2010;181:141-4. PMID: 20074915
7. Song, SH, Kwak, IS, Kim, SJ, Kim, YK, Kim, IJ. Depressive mood in pre-dialytic chronic kidney disease: Statistical parametric mapping analysis of Tc-99m ECD brain SPECT. *Psychiatry Res*. 2009;173:243-7. PMID: 19682866
8. Palhagen, SE, Ekberg, S, Walinder, J, Granerus, AK, Granerus, G. HMPAO SPECT in Parkinson's disease (PD) with major depression (MD) before and after antidepressant treatment. *J Neurol*. 2009 Sep;256(9):1510-8. PMID: 19430931
9. Kume, K, Hanyu, H, Murakami, M, et al. Frontal Assessment Battery and brain perfusion images in amnestic mild cognitive impairment. *Geriatr Gerontol Int*. 2011;11:77-82. PMID: 20807243
10. Kim, BN, Kim, JW, Kang, H, et al. Regional differences in cerebral perfusion associated with the alpha-2A-adrenergic receptor genotypes in attention deficit hyperactivity disorder. *J Psychiatry Neurosci*. 2010;35:330-6. PMID: 20731965
11. Kataoka, K, Hashimoto, H, Kawabe, J, et al. Frontal hypoperfusion in depressed patients with dementia of Alzheimer type demonstrated on 3DSRT. *Psychiatry Clin Neurosci*. 2010;64:293-8. PMID: 20602729
12. Joensuu, M, Lehto, SM, Tolmunen, T, et al. Serotonin-transporter-linked promoter region polymorphism and serotonin transporter binding in drug-naive patients with major depression. *Psychiatry Clin Neurosci*. 2010;64:387-93. PMID: 20653909
13. Imamura, K, Okayasu, N, Nagatsu, T. The relationship between depression and regional cerebral blood flow in Parkinson's disease and the effect of selegiline treatment. *Acta neurologica Scandinavica*. 2011 Jul;124(1):28-39. PMID: 20880269
14. Ho, PS, Shih, MC, Ma, KH, et al. Availability of the serotonin transporter in patients with alcohol dependence. *The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry*. 2011 Mar;12(2):134-42. PMID: 20642399
15. Giovacchini, G, Mosca, M, Manca, G, et al. Cerebral blood flow in depressed patients with systemic lupus erythematosus. *J Rheumatol*. 2010;37:1844-51. PMID: 20595265
16. Chou, YH, Wang, SJ, Lin, CL, Mao, WC, Lee, SM, Liao, MH. Decreased brain serotonin transporter binding in the euthymic state of bipolar I but not bipolar II disorder: a SPECT study. *Bipolar Disord*. 2010;12:312-8. PMID: 20565438
17. Brugnolo, A, Morbelli, S, Dessi, B, et al. The reversed clock drawing test phenomenon in Alzheimer's disease: A perfusion SPECT study. *Dement Geriatr Cogn Disord*. 2010;29:1-10. PMID: 20093833
18. Brockmann, H, Zobel, A, Joe, A, et al. The value of HMPAO SPECT in predicting treatment response to citalopram in patients with major depression. *Psychiatry Res*. 2009;173:107-12. PMID: 19540732
19. Bhardwaj, R, Chakrabarti, S, Mittal, BR, Sharan, P. A single photon emission computerized tomography (SPECT) study of regional cerebral blood flow in bipolar disorder. *The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry*. 2010 Mar;11(2 Pt 2):334-43. PMID: 20218796

20. Azuma, H, Segawa, K, Nakaaki, S, et al. Neural correlates of memory in depression measured by brain perfusion SPECT at rest. *Psychiatry Clin Neurosci*. 2009;63:685-92. PMID: 19788630
21. Amen, DG, Prunella, JR, Fallon, JH, Amen, B, Hanks, C. A comparative analysis of completed suicide using high resolution brain SPECT imaging. *J Neuropsychiatry Clin Neurosci*. 2009;21:430-9. PMID: 19996252
22. Knopman, DS, DeKosky, ST, Cummings, JL, et al. Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001 May 8;56(9):1143-53. PMID: 11342678
23. Habert, MO, Horn, JF, Sarazin, M, et al. Brain perfusion SPECT with an automated quantitative tool can identify prodromal Alzheimer's disease among patients with mild cognitive impairment. *Neurobiol Aging*. 2011;32:15-23. PMID: 19250707
24. Siepel, FJ, Rongve, A, Buter, TC, et al. (123I)FP-CIT SPECT in suspected dementia with Lewy bodies: a longitudinal case study. *BMJ open*. 2013;3(4). PMID: 23572198
25. Varrone, A, Dickson, JC, Tossici-Bolt, L, et al. European multicentre database of healthy controls for [123I]FP-CIT SPECT (ENC-DAT): age-related effects, gender differences and evaluation of different methods of analysis. *European journal of nuclear medicine and molecular imaging*. 2013 Jan;40(2):213-27. PMID: 23160999
26. Sakakibara, R, Uchida, Y, Ishii, K, et al. Correlation of right frontal hypoperfusion and urinary dysfunction in iNPH: a SPECT study. *Neurourology and urodynamics*. 2012 Jan;31(1):50-5. PMID: 22038765
27. Yeh, CB, Huang, WS, Lo, MC, Chang, CJ, Ma, KH, Shyu, JF. The rCBF brain mapping in adolescent ADHD comorbid developmental coordination disorder and its changes after MPH challenging. *European journal of paediatric neurology : EJPN : official journal of the European Paediatric Neurology Society*. 2012 Nov;16(6):613-8. PMID: 22417719
28. Park, MH, Kim, JW, Yang, YH, et al. Regional brain perfusion before and after treatment with methylphenidate may be associated with the G1287A polymorphism of the norepinephrine transporter gene in children with attention-deficit/hyperactivity disorder. *Neuroscience letters*. 2012 Apr 18;514(2):159-63. PMID: 22405810
29. Yilmaz, Z, Zai, CC, Hwang, R, et al. Antipsychotics, dopamine D(2) receptor occupancy and clinical improvement in schizophrenia: a meta-analysis. *Schizophrenia research*. 2012 Sep;140(1-3):214-20. PMID: 22795368
30. Pavese, N, Simpson, BS, Metta, V, Ramlackhansingh, A, Chaudhuri, KR, Brooks, DJ. [(1)(8)F]FDOPA uptake in the raphe nuclei complex reflects serotonin transporter availability. A combined [(1)(8)F]FDOPA and [(1)(1)C]DASB PET study in Parkinson's disease. *NeuroImage*. 2012 Jan 16;59(2):1080-4. PMID: 21963917
31. Song, IU, Park, JW, Chung, SW, Chung, YA. Brain SPECT can differentiate between essential tremor and early-stage tremor-dominant Parkinson's disease. *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia*. 2014 Sep;21(9):1533-7. PMID: 24814853
32. O'Brien, JT, Firbank, MJ, Davison, C, et al. 18F-FDG PET and perfusion SPECT in the diagnosis of Alzheimer and Lewy body dementias. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 2014 Dec;55(12):1959-65. PMID: 25453043
33. Hazouard, E, Bergemer-Fouquet, AM, Hommet, C, et al. [Amyotrophic lateral sclerosis manifesting as cognitive disorders. Value of brain perfusion scintigraphic tomography in intensive care]. *Presse Med*. 2000 Feb 19;29(6):299-302. PMID: 10719444

34. Guedj, E, Le Ber, I, Lacomblez, L, et al. Brain spect perfusion of frontotemporal dementia associated with motor neuron disease. *Neurology*. 2007;69:488-90. PMID: 17664410
35. Chiu, NT, Huang, CC, Chang, YC, Lin, CH, Yao, WJ, Yu, CY. Technetium-99m-HMPAO brain SPECT in neonates with hypoglycemic encephalopathy. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 1998 Oct;39(10):1711-3. PMID: 9776274
36. Tajima, Y, Isonishi, K, Kashiwaba, T, Tashiro, K. Two similar cases of encephalopathy, possibly a reversible posterior leukoencephalopathy syndrome: serial findings of magnetic resonance imaging, SPECT and angiography. *Intern Med*. 1999 Jan;38(1):54-8. PMID: 10052744
37. Christensson, B, Ljungberg, B, Ryding, E, Svenson, G, Rosen, I. SPECT with 99mTc-HMPAO in subjects with HIV infection: cognitive dysfunction correlates with high uptake. *Scandinavian journal of infectious diseases*. 1999;31(4):349-54. PMID: 10528871
38. Shah, S, Fernandez, AR, Chirla, D. Role of brain SPECT in neonates with hypoxic ischemic encephalopathy and its correlation with neurodevelopmental outcome. *Indian pediatrics*. 2001 Jul;38(7):705-13. PMID: 11463957
39. Celik, Y, Kaya, M. Brain SPECT findings in Wernicke's encephalopathy. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*. 2004 Apr;25(1):23-6. PMID: 15060813
40. Logigian, EL, Kaplan, RF, Steere, AC. Successful treatment of Lyme encephalopathy with intravenous ceftriaxone. *J Infect Dis*. 1999;180:377-83. PMID: 10395852
41. Logigian, EL, Johnson, KA, Kijewski, MF, et al. Reversible cerebral hypoperfusion in Lyme encephalopathy. *Neurology*. 1997 Dec;49(6):1661-70. PMID: 9409364
42. Vlaar, AM, van Kroonenburgh, MJ, Kessels, AG, Weber, WE. Meta-analysis of the literature on diagnostic accuracy of SPECT in parkinsonian syndromes. *BMC Neurol*. 2007;7:27. PMID: 17764571
43. Saur, D, Buchert, R, Knab, R, Weiller, C, Rother, J. Iomazenil-single-photon emission computed tomography reveals selective neuronal loss in magnetic resonance-defined mismatch areas. *Stroke*. 2006;37:2713-9. PMID: 17023671
44. Trott, CM, El Fakhri, G. Sequential and simultaneous dual-isotope brain SPECT: comparison with PET for estimation and discrimination tasks in early Parkinson disease. *Medical physics*. 2008 Jul;35(7):3343-53. PMID: 18697558
45. Nihashi, T, Yatsuya, H, Hayasaka, K, et al. Direct comparison study between FDG-PET and IMP-SPECT for diagnosing Alzheimer's disease using 3D-SSP analysis in the same patients. *Radiation medicine*. 2007 Jul;25(6):255-62. PMID: 17634878
46. Weih, M, Krinninger, M, Zimmermann, R, et al. [Sensitivity of neurochemical dementia diagnostics in CSF compared to 99mTc-SPECT in Alzheimer's dementia]. *Fortschritte der Neurologie-Psychiatrie*. 2009 Jul;77(7):407-11. PMID: 19582652
47. Morinaga, A, Ono, K, Ikeda, T, et al. A comparison of the diagnostic sensitivity of MRI, CBF-SPECT, FDG-PET and cerebrospinal fluid biomarkers for detecting Alzheimer's disease in a memory clinic. *Dement Geriatr Cogn Disord*. 2010;30:285-92. PMID: 20861634
48. Schmidt, D, Zimmermann, R, Lewczuk, P, et al. Confirmation rate of blinded (99m)Tc-SPECT compared to neurochemical dementia biomarkers in CSF in patients with Alzheimer disease. *J Neural Transm (Vienna)*. 2010 Sep;117(9):1111-4. PMID: 20694486
49. Galuska, L, Szakall, S, Jr., Emri, M, et al. [PET and SPECT scans in autistic children]. *Orvosi hetilap*. 2002 May 26;143(21 Suppl 3):1302-4. PMID: 12077922

50. Ryu, YH, Lee, JD, Yoon, PH, Kim, DI, Lee, HB, Shin, YJ. Perfusion impairments in infantile autism on technetium-99m ethyl cysteinate dimer brain single-photon emission tomography: comparison with findings on magnetic resonance imaging. *European journal of nuclear medicine*. 1999 Mar;26(3):253-9. PMID: 10079316
51. Schmaling, KB, Lewis, DH, Fiedelak, JI, Mahurin, R, Buchwald, DS. Single-photon emission computerized tomography and neurocognitive function in patients with chronic fatigue syndrome. *Psychosomatic medicine*. 2003 Jan-Feb;65(1):129-36. PMID: 12554824
52. Abu-Judeh, HH, Levine, S, Kumar, M, et al. Comparison of SPET brain perfusion and 18F-FDG brain metabolism in patients with chronic fatigue syndrome. *Nuclear medicine communications*. 1998 Nov;19(11):1065-71. PMID: 9861623
53. Schwartz, RB, Garada, BM, Komaroff, AL, et al. Detection of intracranial abnormalities in patients with chronic fatigue syndrome: comparison of MR imaging and SPECT. *AJR American journal of roentgenology*. 1994 Apr;162(4):935-41. PMID: 8141020
54. Schwartz, RB, Komaroff, AL, Garada, BM, et al. SPECT imaging of the brain: comparison of findings in patients with chronic fatigue syndrome, AIDS dementia complex, and major unipolar depression. *AJR American journal of roentgenology*. 1994 Apr;162(4):943-51. PMID: 8141022
55. Mutoh, T, Totsune, T, Takenaka, S, et al. Reduced CBF recovery detected by longitudinal 3D-SSP SPECT analyses predicts outcome of postoperative patients after subarachnoid haemorrhage. *Clinical and experimental pharmacology & physiology*. 2018 Feb;45(2):127-32. PMID: 28981977
56. Kincaid, MS, Souter, MJ, Treggiari, MM, Yanez, ND, Moore, A, Lam, AM. Accuracy of transcranial Doppler ultrasonography and single-photon emission computed tomography in the diagnosis of angiographically demonstrated cerebral vasospasm. *Journal of neurosurgery*. 2009 Jan;110(1):67-72. PMID: 18821830
57. Archer, HA, Smailagic, N, John, C, et al. Regional cerebral blood flow single photon emission computed tomography for detection of Frontotemporal dementia in people with suspected dementia. *The Cochrane database of systematic reviews*. 2015;6:CD010896. PMID: 26102272
58. Boutoleau-Bretonniere, C, Lebouvier, T, Delaroche, O, et al. Value of neuropsychological testing, imaging, and CSF biomarkers for the differential diagnosis and prognosis of clinically ambiguous dementia. *J Alzheimers Dis*. 2012;28:323-36. PMID: 22008265
59. Rollin-Sillaire, A, Bombois, S, Deramecourt, V, et al. Contribution of single photon emission computed tomography to the differential diagnosis of dementia in a memory clinic. *J Alzheimers Dis*. 2012;30:833-45. PMID: 22460325
60. McNeill, R, Sare, GM, Manoharan, M, et al. Accuracy of single-photon emission computed tomography in differentiating frontotemporal dementia from Alzheimer's disease. *J Neurol Neurosurg Psychiatry*. 2007;78:350-5. PMID: 17158559
61. Technology Assessment: Functional Neuroimaging for Primary Degenerative Dementia or Mild Cognitive Impairment. Issue date: 12/04/14. Available at: https://www.hca.wa.gov/assets/program/neuro_final_report_120513[1].pdf. Accessed on 4/17/2019.
62. Doran, M, Vinjamuri, S, Collins, J, Parker, D, Larner, AJ. Single-photon emission computed tomography perfusion imaging in the differential diagnosis of dementia: a retrospective regional audit. *Int J Clin Pract*. 2005;59:496-500. PMID: 15853870

63. Bonte, FJ, Hynan, L, Harris, TS, White, CL, 3rd. TC-99m HMPAO Brain Blood Flow Imaging in the Dementias with Histopathologic Correlation in 73 Patients. *International journal of molecular imaging*. 2011;2011:409101. PMID: 21490729
64. Davison, CM, O'Brien, JT. A comparison of FDG-PET and blood flow SPECT in the diagnosis of neurodegenerative dementias: a systematic review. *International journal of geriatric psychiatry*. 2014 Jun;29(6):551-61. PMID: 24123413
65. Dobert, N, Pantel, J, Frolich, L, Hamscho, N, Menzel, C, Grunwald, F. Diagnostic value of FDG-PET and HMPAO-SPET in patients with mild dementia and mild cognitive impairment: metabolic index and perfusion index. *Dement Geriatr Cogn Disord*. 2005;20:63-70. PMID: 15908747
66. Yeo, JM, Lim, X, Khan, Z, Pal, S. Systematic review of the diagnostic utility of SPECT imaging in dementia. *European archives of psychiatry and clinical neuroscience*. 2013 Oct;263(7):539-52. PMID: 23917803
67. Höller, Y, Bathke, AC, Uhl, A, et al. Combining SPECT and Quantitative EEG Analysis for the Automated Differential Diagnosis of Disorders with Amnestic Symptoms. *Frontiers in Aging Neuroscience*. 2017;9:290. PMID: PMC5594223
68. Brayet, P, Petit, D, Baril, AA, et al. Brain perfusion during rapid-eye-movement sleep successfully identifies amnestic mild cognitive impairment. *Sleep medicine*. 2017 Jun;34:134-40. PMID: 28522082
69. Chiba, Y, Iseki, E, Fujishiro, H, et al. Early differential diagnosis between Alzheimer's disease and dementia with Lewy bodies: Comparison between (18)F-FDG PET and (123)I-IMP SPECT. *Psychiatry Res*. 2016 Mar 30;249:105-12. PMID: 26857415
70. O'Brien, JT, Firbank, MJ, Davison, C, et al. 18F-FDG PET and perfusion SPECT in the diagnosis of Alzheimer and Lewy body dementias. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 2014;55:1959-65. PMID: 25453043
71. Takahashi, H, Ishii, K, Hosokawa, C, et al. Clinical application of 3D arterial spin-labeled brain perfusion imaging for Alzheimer disease: comparison with brain perfusion SPECT. *AJNR Am J Neuroradiol*. 2014;35:906-11. PMID: 24263694
72. Ito, K, Mori, E, Fukuyama, H, et al. Prediction of outcomes in MCI with (123)I-IMP-CBF SPECT: a multicenter prospective cohort study. *Annals of nuclear medicine*. 2013 Dec;27(10):898-906. PMID: 24061691
73. Assadi, M, Salimipour, H, Seyedabadi, M, et al. Brain single photon emission computed tomography with Tc-99m MIBI or Tc-99m ECD in comparison to MRI in multiple sclerosis. *Clin Nucl Med*. 2010;35:682-6. PMID: 20706041
74. Sharifi, S, Nederveen, AJ, Booij, J, van Rootselaar, AF. Neuroimaging essentials in essential tremor: a systematic review. *Neuroimage Clin*. 2014;5:217-31. PMID: 25068111
75. Czarnecki, K, Jones, DT, Burnett, MS, Mullan, B, Matsumoto, JY. SPECT perfusion patterns distinguish psychogenic from essential tremor. *Parkinsonism Relat Disord*. 2011;17:328-32. PMID: 21317018
76. Sahin, HA, Terzi, M, Ucak, S, Yapici, O, Basoglu, T, Onar, M. Frontal functions in young patients with essential tremor: a case comparison study. *J Neuropsychiatry Clin Neurosci*. 2006;18:64-72. PMID: 16525072
77. American Psychiatric Association. Consensus Report of the APA Work Group on Neuroimaging Markers of Psychiatric Disorders: Resource Document. [cited 4/17/2019]; Available from: https://www.psychiatry.org/File%20Library/Psychiatrists/Directories/Library-and-Archive/resource_documents/rd2012_Neuroimaging.pdf

78. Shetty, VS, Reis, MN, Aulino, JM, et al. ACR Appropriateness Criteria Head Trauma. *Journal of the American College of Radiology : JACR*. 2016 Jun;13(6):668-79. PMID: 27262056
79. ACR Appropriateness Criteria® seizures and epilepsy. [cited 4/17/2019]; Available from: https://acsearch.acr.org/docs/69479/Narrative/
80. American College of Radiology. ACR Appropriateness Criteria(R) Dementia and Movement Disorders. Reviewed 2015. . [cited 4/17/2019]; Available from: https://acsearch.acr.org/docs/69360/Narrative/
81. ACR–SPR Practice Parameter for the Performance of Single Photon Emission Computed Tomography (SPECT) Brain Perfusion Imaging, Including Brain Death Examinations. . [cited 4/17/2019]; Available from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/brainperf-spect.pdf?la=en

CODES

Codes	Number	Description
CPT	78607	Brain imaging, tomographic (SPECT)
HCPCS	None	

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