Prior Authorization Review
Panel MCO Policy Submission

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Type of Submission – Check all that apply:
- [ ] New Policy
- [x] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

CPB 376 Single Photon Emission Computed Tomography (SPECT)

06/14/2018 - This CPB has been revised to state that SPECT is considered experimental and investigational for the following: (i) evaluation of carotid stenosis, (ii) as an imaging marker of prediagnostic Parkinson's disease, and (iii) work-up of individuals undergoing non-cardiac surgery.
08/01/2018 - This CPB is revised to state that SPECT is considered medically necessary for the diagnosis of coronary artery disease and for the assessment of prognosis in persons with coronary artery disease except as outlined in exclusion criteria.

Name of Authorized Individual (Please type or print):  Dr. Bernard Lewin, M.D.
Signature of Authorized Individual:  [Signature]

www.aetnabetterhealth.com/pennsylvania  Revised 08/01/2018
Single Photon Emission Computed Tomography (SPECT)

Policy

I. Non-Cardiac Indications: Aetna considers single photon emission computed tomography (SPECT) medically necessary for any of the following indications:

   A. Assessment of osteomyelitis, to distinguish bone from soft tissue infection; or
   B. Detection of spondylolysis and stress fractures not visible from x-ray; or
   C. Diagnosing and assessing hemangiomas of the liver; or
   D. Diagnosing pulmonary embolism (by means of SPECT ventilation/perfusion scintigraphy); or
   E. Differentiation of necrotic tissue from tumor of the brain; or
   F. Distinguishing Parkinson's disease from essential tremor (e.g., DaTSCAN (Ioflupane I-123 injection); or
   G. Imaging of parathyroids in parathyroid disease; or
   H. Localization of abscess, for suspected or known localized infection or inflammatory process; or
   I. Lymphoma, to distinguish tumor from necrosis; or
   J. Neuroendocrine tumors, diagnosis and staging; or

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*
K. Pre-surgical ictal detection of seizure focus in members with epilepsy (in place of positron emission tomography (PET)).

II. Aetna considers SPECT experimental and investigational for all other non-cardiac indications, including any of the following, because its diagnostic value has not been established in the peer-reviewed medical literature in these situations:

A. As an imaging marker of pre-diagnostic Parkinson's disease; or
B. Detection of air leak/pneumothorax; or
C. Diagnosis or assessment of members with attention deficit/hyperactivity disorder (CPB_0426 - Attention Deficit/Hyperactivity Disorder (../400_499/0426.html)); or
D. Diagnosis or assessment of members with autism (CPB_0648 - Autism Spectrum Disorders (../600_699/0648.html)); or
E. Diagnosis or assessment of members with personality disorders (e.g., aggressive and violent behaviors, anti-social personality disorder including psychopathy, schizotypal personality disorder, as well as borderline personality disorder); or
F. Diagnosis or assessment of members with schizophrenia; or
G. Diagnosis or assessment of stroke members; or
H. Differential diagnosis of Parkinson's disease from other Parkinsonian syndromes; or
I. Differentiating malignant from benign lung lesions; or
J. Evaluation of carotid stenosis; or
K. Evaluation of members with endoleak; or
L. Evaluation of members with generalized pain or insomnia; or
M. Evaluation of members with head trauma; or
N. Initial or differential diagnosis of members with suspected dementia (e.g., Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, and vascular dementia); or
O. Multiple sclerosis; or
P. Pre-surgical evaluation of members undergoing lung volume reduction surgery; or
Q. Prosthetic graft infection; or
R. Scanning of internal carotid artery during temporary balloon occlusion; or
S. Vasculitis; or
T. Work-up of individuals undergoing non-cardiac surgery.

III. Cardiac Indications: Aetna considers SPECT medically necessary for the
diagnosis of coronary artery disease and for the assessment of prognosis in
persons with coronary artery disease except as outlined in "exclusion
criteria" below.

IV. Aetna considers SPECT experimental and investigational for all other cardiac
indications because its effectiveness for indications other than the ones
listed above has not been established.

Exclusion criteria: Aetna considers SPECT myocardial perfusion imaging
experimental and investigational for the following indications for which the
study is considered “inappropriate” according to appropriateness
criteria from the American College of Cardiology (ACC):

A. As a routine screening evaluation after a percutaneous transluminal
coronary angioplasty (PTCA) with or without stenting or coronary artery
bypass surgery (CABG) prior to discharge from the acute care setting; or

B. As a routine screening evaluation after a re-vascularization procedure
(PTCA with stenting or CABG) at an interval of less than 2 years from the
procedure if there is no worsening in the members symptomatology and if
the member had symptoms prior to the intervention, and there is no history
of congestive heart failure. **Note:** If there is a history of congestive heart
failure and the member is status post re-vascularization, repeat nuclear
imaging as frequently as annually may be medically necessary; or

C. Assessment of vulnerable plaque; or

D. Evaluation of a member with an acute coronary event and hemodynamic
instability, shock, or mechanical complications of the event; or
E. In the setting of acute chest pain or equivalent symptoms with a high likelihood of being acute coronary syndrome, when there has been a diagnosis of acute myocardial infarction, in the immediate post-thrombolytic period, or when there is a high pre-test likelihood of significant coronary disease as demonstrated by marked ST segment elevation on the ECG; or

F. Prior to high-risk+ surgery when the member is asymptomatic and there was a normal cardiac catheterization, coronary intervention (PTCA, stenting, CABG), or normal nuclear stress test less than 1 year before the surgical date; or

G. Prior to intermediate-risk+ non-cardiac surgery if the member is capable of, and has no contraindication to standard stress testing; or

H. Prior to low-risk+ non-cardiac surgery for risk assessment; or

I. Re-evaluation of members without chest pain or equivalent symptoms, without known coronary disease, at high-risk for coronary disease (based upon the Framingham score greater than 10), who have an initial negative radionuclear imaging study, when it has been less than 2 years since the last radionuclear study; or

J. Re-evaluation of members without chest pain or equivalent symptoms or with stable symptoms, with known coronary disease as determined by prior abnormal catheterization or SPECT cardiac study (but without prior infarction), when it has been less than 1 year since the last radionuclear study. Note: if the member has worsening symptoms or if the member had silent ischemia, more frequent imaging or other diagnostic testing or interventions may be medically necessary; or

K. Screening of members with chest pain or chest pain equivalent symptoms when there is a low probability of coronary disease (Framingham score less than 10), no history of diabetes, and there are no impediments or contraindications to non-nuclear stress testing; or

L. Screening of members without chest pain or equivalent symptoms when there is a low probability of coronary disease (Framingham score less than 10) and no history of diabetes; or
A tool for calculating Framingham score is available from the National Heart Lung and Blood Institute at the following website:

Framingham Score from National Heart Lung and Blood Institute (http://cvdrisk.nhlbi.nih.gov/)

According to ACC guidelines, the following are impediments or contraindications to non-nuclear stress testing:

A. A history of physical impairments that would preclude physically performing the exercise portion of a stress test; or
B. A history of prior proven ischemic cardiac events; or
C. Proven CAD by past SPECT or coronary catheterization; or
D. The member's ECG would prevent interpretation of a standard stress testing by being “uninterpretable” during the test, i.e., left bundle branch block (LBBB), paced rhythm, Wolf Parkinson White syndrome, left ventricular hypertrophy (LVH) with ST segment depression, or digoxin use.

Surgical risk categories.

- High-risk surgery (risk of cardiac death or myocardial infarction (MI) greater than 5 %): emergent major operations (particularly in the elderly), aortic and peripheral vascular surgery, prolonged surgical procedures associated with large fluid shifts and/or blood loss.
- Intermediate-risk surgery (risk of cardiac death or MI 1 % to 5 %): carotid endarterectomy, head and neck surgery, surgery of the chest or abdomen, orthopedic surgery, prostate surgery.
- Low-risk surgery (cardiac death or MI less than 1 %): endoscopic procedures, superficial procedures, cataract surgery, breast surgery.

V. Aetna considers myocardial sympathetic innervation imaging, with or without SPECT, experimental and investigational because its effectiveness has not been established.
VI. Aetna considers SPECT-CT fusion medically necessary for parathyroid imaging in persons with an enlarged parathyroid gland, parathyroid hyperplasia or suspected parathyroid adenoma or carcinoma, and laboratory evidence of hyperparathyroidism (parathyroid hormone greater than 55 pg/ml and serum calcium greater than 10.2 mg/dL).

Aetna considers SPECT-CT fusion imaging as experimental and investigational for other indications because of insufficient evidence of its effectiveness.

VII. Aetna considers freehand SPECT/ultrasonography (US) fusion imaging in persons with thyroid disease experimental and investigational because of insufficient evidence of its effectiveness.

**Background**

Single photon emission computed tomography (SPECT) is a nuclear medicine technique that uses radiopharmaceuticals, a rotating camera (single or multiple-head), and a computer to produce images representing slices through the body in different planes. Single photon emission computed tomography images are functional in nature rather than being purely anatomical such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI).

**SPECT for Myocardial Perfusion Imaging**

Single photon emission computed tomography has been applied to the heart for myocardial perfusion imaging. It is an effective non-invasive diagnostic technology when evaluating patients for clinically significant coronary artery disease (CAD) in the following circumstances: for diagnosing CAD in patients with an abnormal resting electrocardiogram (ECG) and restricted exercise tolerance; or assessing myocardial viability before referral for myocardial re-vascularization.

Single photon emission computed tomography has a far greater sensitivity for detecting silent ischemia than stress ECG. Pooled data of exercise SPECT studies in over 1,000 patients revealed a 90% overall sensitivity for detecting CAD. In assessing myocardial viability, studies indicate that, even in patients with severe
irreversible thallium defects on standard exercise-redistribution imaging, thallium re-injection provides information regarding myocardial viability that is comparable to that provided by positron emission tomography (PET).

**SPECT for Detection of Neurological Diseases**

Single photon emission computed tomography examines cerebral function by documenting regional blood flow and metabolism; SPECT of the brain is a useful alternative to PET for the pre-surgical ictal detection of seizure focus. Effective surgical treatment of patients with intractable epilepsy is dependent on accurate localization of the epileptic focus and precise delineation of the epileptogenic region. It is generally agreed that this requires EEG recording with electrocorticography. This testing is designed to identify the source or sources of the seizures, as well as an assessment of brain function. The search for non-invasive and cost-effective means of seizure localization has been an important area of research.

Seizures are associated with dramatic increases in blood flow, localized in partial seizures and global during generalized seizures. Ictal SPECT uses the physiologic increase in regional cerebral blood flow during seizures to potentially localize the epileptogenic region. Ictal studies, although more difficult logistically, are reported to have a sensitivity of 81 to 93%. (Interictal SPECT demonstrates hypo-perfusion and is reported to have a sensitivity ranging from 40 to 75%).

Other imaging modalities help in localizing abnormal epileptogenic tissue. Quantitative MRI has a sensitivity of 80 to 90% for the lateralization of temporal lobe epilepsy. However, there are instances where ictal SPECT has identified lesions not detected by MRI. Depth electrocorticography and intra-operative electrocorticography, though accurate in many forms of epilepsy, are both highly invasive. In cortical developmental disorders, these EEG techniques often fail to localize the epileptogenic area. Single photon emission computed tomography imaging may offer a safe and accurate alternative.

Ictal SPECT testing requires that seizure activity be provoked through reduction of anti-epileptic medications. Video EEG monitoring may also be performed. Due to the nature of ictal SPECT, it should be performed in a hospital setting.
Studies of SPECT in the inter-ictal or post-ictal detection of seizure focus, determination of seizure subtypes and monitoring of drug therapy for epilepsy have not established its efficacy for these indications.

Clinical studies indicate that SPECT is more accurate at detecting acute ischemia than CT scan. By 8 hours after infarction, about 20% of CT scans will be positive but nearly 90% of SPECT scans will be. Beyond 72 hours, the sensitivities of CT and SPECT are nearly identical. In addition, the defects noted on SPECT are frequently larger than those noted on CT studies.

Among the treatments of acute ischemic stroke, the use of tissue plasminogen activator (t-PA) has been shown to reduce neurologic impairment if administered within 3 hours of onset. This is administered when CT is negative for hemorrhage. Single photon emission computed tomography can not detect hemorrhage in order to rule out use of thrombolysis. Therefore, while SPECT is more sensitive than CT in detecting ischemia, it has not been shown to be useful in detecting ischemia early enough to play a role in the use of thrombolysis. Studies using SPECT in the presence of cerebro-vascular accident (CVA) have timed its performance at less than 6 hours to less than 14 days from the time of onset.

Studies have also reported on SPECT’s value with regard to the assessment of prognosis after stroke, determination of stroke type, monitoring therapies used post-stroke, diagnosis of vasospasm following subarachnoid hemorrhage and in the diagnosis/prognosis regarding transient ischemic attacks (TIAs). Single photon emission computed tomography may prove to be helpful in these applications in the future.

Single photon emission computed tomography has proven useful in distinguishing recurrent brain tumor from radiation necrosis. Radiation necrosis needs to be distinguished from recurrent brain tumor to determine whether chemotherapy is necessary. Radiation necrosis is more common in brain tumor patients receiving local boost irradiation. Radiation necrosis and brain tumor may have similar clinical signs and symptoms, and are not reliably distinguished clinically.

Single photon emission computed tomography has been studied in the diagnosis of patients with Alzheimer's disease (AD). At present, the definitive diagnosis of AD can only be made on pathologic examination of brain tissue. Alzheimer's disease is largely a diagnosis of exclusion. The diagnostic evaluation of the demented patient
is therefore aimed largely at identifying other potentially treatable causes of cognitive impairment. A technology assessment of SPECT for dementia and AD prepared by the Institute for Clinical Effectiveness and Health Policy (Ferrante, 2004) concluded: "SPECT has not clearly demonstrated its usefulness in assessing patients with dementia, and it has no precise indications for diagnosis, evaluation of prognosis or monitoring response to treatment."

In AD, SPECT shows decreased perfusion in the association cortex of the parietal lobe and the posterior temporal regions. Frontal association cortex is predominantly affected in some cases, but usually is not involved until late in the course of the disease. The occipital lobes are less involved and the paracental cortex is spared. Although SPECT studies have been reported in over 500 patients with AD, in most cases the diagnosis was made clinically and only in 53 patients it was confirmed by autopsy. Controlled studies of SPECT in AD have shown a sensitivity of this procedure to vary from 50 % to 95 %. The best results have been reported in the more recent studies, using higher resolution equipment. In the 2001 practice parameter on the diagnosis of dementia, the American Academy of Neurology does not recommend SPECT for routine use in either initial or differential diagnosis of dementia (Knopman et al, 2001).

Neuroimaging markers are increasingly important in the early diagnosis of the dementias, not only to detect the rare tumor, but also to differentiate the various types of neurodegenerative dementias. The potential of MRI and PET as surrogates for disease progression for therapeutic trials is being examined in a large multi-center trial. However, SPECT has been reported to show specific findings in both fronto-temporal dementia (FTD) and AD and is much more available and less expensive than PET. McNeil et al (2007) evaluated the diagnostic accuracy of technetium-99–labeled hexamethyl propylene amine oxime SPECT images obtained at initial evaluation in 25 pathologically confirmed cases of FTD and 31 pathologically confirmed cases of AD. A nuclear medicine physician, blinded to the clinical findings, rated the images. Except in the case of 1 FTD patient, for whom neuropsychological data were unavailable, the clinical and neuropsychological evaluation was more accurate than SPECT alone in predicting the histological diagnosis.

In a longitudinal, prospective study, Devanand and colleagues (2010) examined the utility of SPECT to predict conversion from mild cognitive impairment (MCI) to AD. A total of 127 patients with MCI and 59 healthy comparison subjects followed-up for
1 to 9 years were included in this study. Diagnostic evaluation, neuropsychological tests, social/cognitive function, olfactory identification, apolipoprotein E genotype, MRI, and brain Tc hexamethyl-propylene-aminoxime SPECT scan with visual ratings, and region of interest (ROI) analyses were done. Visual ratings of SPECT temporal and parietal blood flow did not distinguish eventual MCI converters to AD (n = 31) from non-converters (n = 96), but the global rating predicted conversion (41.9 % sensitivity and 82.3 % specificity, Fisher's exact test p = 0.013). Blood flow in each ROI was not predictive, but when dichotomized at the median value of the patients with MCI, low flow increased the hazard of conversion to AD for parietal (hazard ratio [HR]: 2.96, 95 % confidence interval [CI]: 1.16 to 7.53, p = 0.023) and medial temporal regions (HR: 3.12, 95 % CI: 1.14 to 8.56, p = 0.027). In the 3-year follow-up sample, low parietal (p < 0.05) and medial temporal (p < 0.01) flow predicted conversion to AD, with or without controlling for age, Mini-Mental State Examination, and apolipoprotein E ε4 genotype. These measures lost significance when other strong predictors were included in logistic regression analyses: verbal memory, social/cognitive functioning, olfactory identification deficits, hippocampal, and entorhinal cortex volumes. The authors concluded that SPECT visual ratings showed limited utility in predicting MCI conversion to AD. The modest predictive utility of quantified low parietal and medial temporal flow using SPECT may decrease when other stronger predictors are available.

Single photon emission computed tomography has also been reported to be used in neoplasms (grading of gliomas), HIV encephalopathy, head trauma, Huntington's chorea, persistent vegetative states and in diagnosing brain death. Based upon the current evidence, SPECT has not proven to be established in any of these clinical situations. More study is needed in these areas.

The Food and Drug Administration (FDA) has approved 4 radiopharmaceuticals for imaging of the brain: I-123 isopropyliodoamphetamine (IMP, Spectamine); Tc-99m HMPAO (hexamethyl propylamine oxime, Ceretec); Tc-99m ECD (ethyl cysteinate dimer, Neurolite), and thallium 201 diethylthiocarbamate (T1-DDC).

**SPECT for the Liver**

Hemangiomas are the most common benign lesion of the liver. It is important to differentiate these lesions from others that may be malignant. Because of the risk of hemorrhage inherent in a percutaneous biopsy of liver hemangiomas, non-invasive modalities have been used for differentiation. Hepatic hemangiomas are
so vascular that their blood pool is easily differentiated from other solid hepatic masses by nuclear scanning with labeled red blood cells (RBCs). The labeled RBCs are injected intravenously and resolution is markedly improved with SPECT. Review articles and published studies support SPECT as an appropriate diagnostic modality to differentiate hepatic lesions as hemangiomas.

**SPECT for Neuroendocrine Tumors**

Carcinoids and other neuroendocrine tumors have somatostatin receptors; therefore, they can be imaged with somatostatin analogs (octreotide, pentetreotide) tagged with an appropriate radioisotope (Khan and Jones, 2005). Single photon emission computed tomography and subtraction techniques improve detection. An assessment from the Australian Medical Services Advisory Committee stated that SPECT is often performed in conjunction with antibody imaging (Octreoscan) of neuroendocrine tumors, usually at 24 and occasionally at 48 hours after the injection. The assessment explained that SPECT is able to differentiate more easily between areas of pathological uptake and physiological uptake in the abdomen. The assessment explained that SPECT can also help to discriminate between mesenteric and bone lesions. The assessment noted that extra-planar images may be obtained from areas of specific interest, using longer exposure time for more easily interpreted imaging.

**SPECT for Spondylolysis and Stress Fractures**

The role of SPECT of the spine has changed in recent years with the wide availability of MRI and especially contrast-enhanced MRI. Bone scanning with SPECT of the spine may allow for visualization of lesions related to stress fractures or stress reactions in the spine such as spondylolysis. Single photon emission computed tomography has been accepted as extremely sensitive in detecting incipient spondylolysis and stress/insufficiency fractures (Manaster et al, 2005). Single photon emission computed tomography shows stress fractures days to weeks earlier than radiographs in many instances, and differentiate between osseous and soft tissue injury as well. However, in most cases bone scans lack specificity and supplemental imaging may be necessary for conclusive diagnosis or to avoid false positives. Single photon emission computed tomography continues to be used in back pain, especially in children and adolescents, to detect incipient spondylolysis that may not be detected by conventional imaging. Because of the
sensitivity of SPECT scans, 80% of all fractures show an abnormality 24 hours post injury and 95% at 72 hours. A normal scan generally excludes the diagnosis of stress/insufficiency fracture, and the patient may return to normal activity.

**SPECT for the Internal Carotid Artery**

Internal carotid artery temporary balloon occlusion (TBO) test is a well-established part of the preoperative evaluation of patients with aneurysm or tumor involving the neck or skull base in whom arterial sacrifice or prolonged temporary occlusion is considered a possible part of the surgical or endovascular therapy. Temporary balloon occlusion is performed in conjunction with cerebral blood flow analysis to identify those patients who will not tolerate permanent carotid occlusion. Traditionally, xenon-enhanced CT has been used during TBO to detect signs of ischemia; however, SPECT has recently been reported as a method to detect focal hypo-perfusion during test occlusion. Several small studies in the published literature report preliminary results that SPECT scanning during TBO is a safe and effective method to assess cerebral blood flow. However, it is premature to recommend SPECT over the conventional xenon-enhanced CT.

**SPECT for the Diagnosis/Assessment of Attention Deficit/Hyperactivity Disorder**

Functional neuroimaging such as PET and SPECT has been used to study patients with attention deficit/hyperactivity disorder (ADHD). Although some studies have shown differences in brain structure or function comparing children with and without ADHD, these findings do not differentiate reliably between children with and without this disorder (i.e., although group means may differ significantly, the overlap in findings among children with and without ADHD results in high rates of false-positives and false-negatives). As a result, SPECT should not be used as a screening or diagnostic tool for children with ADHD. The American Academy of Pediatrics' Practice Guideline on "Diagnosis and Evaluation of the Child with Attention-Deficit/Hyperactivity Disorder" does not recommend neuroimaging studies in the diagnosis of ADHD. An evidence review by McGough and Barkley (2004) stated that there are insufficient scientific data to justify use of laboratory assessment measures, including neuropsychological tests and brain imaging, in diagnosing adult ADHD.

**SPECT for the Diagnosis/Assessment of Autism**
The American Academy of Neurology (2000) stated that there is no evidence to support a role of neuroimaging modalities such as SPECT in the clinical diagnosis of autism.

**SPECT for the Diagnosis of Pulmonary Embolism**

In a prospective, observational study, Miles and colleagues (2009) compared SPECT ventilation/perfusion (V/P) scintigraphy with multi-slice CT pulmonary angiography (CTPA) in the diagnosis of pulmonary embolism (PE). A total of 100 patients who were 50 years of age or older were recruited; 79 underwent both diagnostic 16-detector CTPA, and planar and SPECT V/P scintigraphy. The agreement between the CTPA and the SPECT V/P scintigraphy for the diagnosis of PE was calculated. The sensitivity and specificity of blinded SPECT scintigraphy reporting was calculated against a reference diagnosis made by a panel of respiratory physicians that was provided with CTPA and planar V/P scintigraphy reports, clinical information, and 3-month follow-up data. The observed percentage of agreement between SPECT V/P scintigraphy and CTPA data for the diagnosis of PE was 95 %. When calculated against the respiratory physicians' reference diagnosis, SPECT V/P scintigraphy had a sensitivity of 83 % and a specificity of 98 %. The authors concluded that these findings indicated that SPECT V/P scintigraphy is a viable alternative to CTPA for the diagnosis of PE and has potential advantages in that it was feasible in more patients and had fewer contraindications; lower radiation dose; and, arguably, fewer non-diagnostic findings than CTPA.

Gutte et al (2010) evaluated the diagnostic performance of 3-dimensional V/P SPECT in comparison with planar V/P scintigraphy. Consecutive patients suspected of acute PE were referred to a V/P SPECT, as the first-line imaging procedure. Patients with positive D-dimer (greater than 0.5 mg/L) or after clinical assessment with a Wells score of more than 2 were included and had a V/P SPECT, low-dose CT, planar V/P scintigraphy, and pulmonary multi-detector CTPA performed the same day. Ventilation studies were performed using Krypton (Kr). Patient follow-up was at least 6 months. A total of 36 patient studies were available for analysis, of which 11 (31 %) had PE. V/P SPECT had a sensitivity of 100 % and a specificity of 87 %. Planar V/P scintigraphy had a sensitivity of 64 % and a specificity of 72 %. The authors concluded that V/P SPECT has a superior diagnostic performance compared with planar V/P scintigraphy and should be preferred when diagnosing PE.
The European Association of Nuclear Medicine (EANM)'s practice guidelines on ventilation/perfusion scintigraphy (Bajc et al, 2009a) stated that PE can only be diagnosed with imaging techniques, which in practice is performed using V/P scintigraphy or multi-detector computed tomography of the pulmonary arteries (MDCT). The basic principle for the diagnosis of PE based upon V/P scintigraphy is to recognize lung segments or subsegments without perfusion but preserved ventilation, i.e., mismatch. Ventilation studies are in general performed after inhalation of Kr-labelled or technetium-labelled aerosol of diethylene triamine pentaacetic acid (DTPA) or Technegas. Perfusion studies are performed after intravenous injection of macro-aggregated human albumin. Radiation exposure using documented isotope doses is 1.2 to 2 mSv. Planar and tomographic techniques (Planar V/P and SPECT V/P) are analyzed. Single photon emission computed tomography V/P has higher sensitivity and specificity than Planar V/P. The interpretation of either Planar V/P or SPECT V/P should follow holistic principles rather than obsolete probabilistic rules. Pulmonary embolism should be reported when mis-match of more than 1 subsegment is found. For the diagnosis of chronic PE, V/P scintigraphy is of value. The additional diagnostic yield from V/P scintigraphy includes chronic obstructive lung disease (COPD), heart failure and pneumonia. Single photon emission computed tomography V/P is strongly preferred to Planar V/P as the former permits the accurate diagnosis of PE even in the presence of co-morbid diseases such as COPD and pneumonia.

The EANM's practice guidelines on VP scintigraphy also noted that to reduce the costs, the risks associated with false-negative and false-positive diagnoses, and unnecessary radiation exposure, pre-imaging assessment of clinical probability is recommended. Diagnostic accuracy is approximately equal for MDCT and Planar V/P and better for SPECT V/P, which is feasible in about 99 % of patients, while MDCT is often contraindicated. As MDCT is more readily available, access to both techniques is vital for the diagnosis of PE. Single photon emission computed tomography V/P gives an effective radiation dose of 1.2 to 2 mSv. For SPECT V/P, the effective dose is about 35 % to 40 % and the absorbed dose to the female breast 4 % of the dose from MDCT performed with a dose-saving protocol. Thus, SPECT V/P is recommended as a first-line procedure in patients with suspected PE. It is particularly favored in young patients, especially females, during pregnancy, and for follow-up and research (Bajc et al, 2009b).

Other Indications
Single photon emission computed tomography has proven useful in distinguishing lymphoma from necrosis in the chest and abdomen. It is also useful in localizing abscesses, and distinguishing abscess from other infectious or inflammatory processes. Single photon emission computed tomography is also useful in osteomyelitis in distinguishing inflammation of soft tissue from bone.

Guidelines on parathyroid scintigraphy from the Society of Nuclear Medicine (Greenspan et al, 2004) state that there is a developing consensus that SPECT imaging is useful, because, when used in conjunction with planar imaging, SPECT provides increased sensitivity and more precise anatomic localization. They note that this is particularly true in detecting both primary and recurrent hyperparathyroidism resulting from ectopic adenomas. In the mediastinum, accurate localization may assist in directing the surgical approach, such as median sternotomy versus left or right thoracotomy. The Parathyroid Task Group of the EANM (Hindie et al, 2009) stated that the use of SPECT/CT has a major role for obtaining anatomical details on ectopic foci. However, its use as a routine procedure before target surgery is still investigational. Preliminary data suggest that SPECT/CT has lower sensitivity in the neck area compared to pinhole imaging.

In a review on neuroimaging in psychopathy (including anti-social personality disorder and violent behavior), Pridmore et al (2005) noted that functional neuroimaging strongly suggests dysfunction of particular frontal and temporal lobe structures in subjects with psychopathy. However, there are difficulties in selecting homogeneous index cases and appropriate control groups. These investigators stated that further studies are needed.

An assessment of SPECT for schizophrenia by the Institute for Clinical Effectiveness and Health Policy (Pichon Riviere et al, 2004) found that SPECT has identified increases in dopaminergic activity in the striated body and other areas of the brain during the episodes of schizophrenia exacerbation. Single photon emission computed tomography has also been able to identify decreases in frontal cortex uptake that are associated with negative symptoms of schizophrenia. The investigators, however, were unable to find substantial evidence for the role of SPECT scans in therapeutic decision-making in schizophrenia. They concluded that the use of SPECT scan in schizophrenia remains investigational.
In the recent practice parameter on the diagnosis and prognosis of new onset Parkinson's disease (PD) (an evidence-based review) by the American Academy of Neurology (AAN), Suchowersky et al (2006) stated that SPECT scanning may not be useful in differentiating PD from other parkinsonian syndromes.

In a meta-analysis of the literature on diagnostic accuracy of SPECT in parkinsonian syndromes, Vlaar and colleagues (2007) concluded that SPECT with pre-synaptic radiotracers is relatively accurate to differentiate patients with PD in an early phase from normalcy, patients with PD from those with essential tremor, and PD from vascular parkinsonism. The accuracy of SPECT with both pre-synaptic and post-synaptic tracers to differentiate between PD and atypical parkinsonian syndrome is relatively low.

The American College of Radiology's " Appropriateness Criteria® dementia and movement disorders" (Wippold et al, 2010) stated that "a diminution of the width of the pars compacta on MRI has been described in PD patients compared to controls, with overlap between groups. This diminished width probably reflects selective neuronal loss of the pars compacta. Other authors have found a normal appearance of the substantia nigra on T2-weighted images in a majority of PD patients. More recently, PET and SPECT tracer studies exploring the presynaptic nigrostriatal terminal function and the postsynaptic dopamine receptors have attempted to classify the various Parkinson syndromes although much of this work remains investigational".

van der Vaart et al (2008) described the current applications of PET and SPECT as a diagnostic tool for vascular disease as relevant to vascular surgeons. These researchers noted that PET and SPECT may be used to assess plaque vulnerability, biology of aneurysm progression, prosthetic graft infection, and vasculitis. Moreover, the authors stated that considerable further information will be needed to define whether and where PET or SPECT will fit in a clinical strategy. The necessary validation studies represent an exciting challenge for the future but also may require the development of inter-disciplinary imaging groups to integrate expertise and optimize nuclear diagnostic potential.

A report by the New Zealand Health Services Assessment Collaboration (Smartt & Campbell-Page, 2009) of combined CT and SPECT (SPECT-CT) scanning in oncology concluded that SPECT-CT imaging in oncology requires further assessment. The report stated that SPECT-CT imaging is being explored in a wide
range of cancers for a variety of purposes, and, that there is some evidence of an evolving role in specific areas such as lymph node assessment and mapping and the identification of bone metastases. There is also a growing body of literature comparing the effectiveness and roles of SPECT-CT and PET-CT imaging in oncology which may be expected to mature in the next few years. "However, the quality of the evolving evidence and the cost-effectiveness of combined CT and nuclear imaging systems have yet to be fully assessed." The report stated that there are a number of outstanding questions relating to the clinical and cost-effectiveness of SPECT-CT in oncology. In particular there is a need to compare the clinical utility of hybrid scanners using low performance X-ray scanners with the newer multislice machines to assess the additional benefits of the new generation scanners in clinical practice. The report stated that there is also a need to assess the impact of SPECT-CT on patients’ outcomes and management in specific indications where SPECT imaging/ planar scintigraphy are standard practice e.g. functional imaging of bone (bone scans). Other research needs identified in the report include: 1) research on the cost-effectiveness of SPECT-CT imaging for specific purposes such as lymph-node mapping and sentinel node identification; 2) research to assess the impact of SPECT-CT on patients’ outcomes and management in specific indications where SPECT imaging/ planar scintigraphy are standard practice, e.g. functional imaging of bone (bone scans).

The American College of Radiology’s clinical guideline on “Head trauma” (ACR, 2012) stated that “Advanced imaging techniques (perfusion CT, perfusion MRI, SPECT, and PET) have utility in better understanding selected head-injured patients but are not considered routine clinical practice at this time”.

Jamadar et al (1999) stated that ventilation/perfusion scans with single-photon emission computed tomography (SPECT) were reviewed to determine their usefulness in the evaluation of lung volume reduction surgery (LVRS) candidates, and as a predictor of outcome after surgery. A total of 50 consecutive planar ventilation (99mTc-DTPA aerosol) and perfusion (99mTc-MAA) scans with perfusion SPET of patients evaluated for LVRS were retrospectively reviewed. Technical quality and the severity and extent of radiotracer defects in the upper and lower halves of the lungs were scored from visual inspection of planar scans and SPET data separately. An emphysema index (EI) (extent x severity) for the upper and lower halves of the lung, and an EI ratio for upper to lower lung were calculated for both planar and SPET scans. The ratios were compared with post-LVRS outcomes, 3, 6 and 12 months after surgery. All perfusion and SPET images were
technically adequate. Forty-six percent of ventilation scans were not technically adequate due to central airway tracer deposition. Severity, extent, EI scores and EI ratios between perfusion and SPET were in good agreement ($r = 0.52$ to $0.68$). The mean perfusion EI ratio was significantly different between the 30 patients undergoing bi-apical LVRS and the 17 patients excluded from LVRS (3.3 +/- 1.8 versus 1.2 +/- 0.7; $p < 0.0001$), in keeping with the anatomic distribution of emphysema by which patients were selected for surgery by computed tomography (CT). The perfusion EI ratio correlated moderately with the change in FEV1 at 3 months ($r = 0.37$, $p = 0.04$), 6 months ($r = 0.36$, $p = 0.05$), and 12 months ($r = 0.42$, $p = 0.03$), and the transition dyspnea index at 6 months ($r = 0.48$, $p = 0.014$) after LVRS. The authors concluded that patients selected to undergo LVRS have more severe and extensive apical perfusion deficits than patients not selected for LVRS, based on CT determination. Moreover, they stated that SPECT after aerosol V/Q imaging does not add significantly to planar perfusion scans. Aerosol DTPA ventilation scans are not consistently useful. Perfusion lung scanning may be useful in selecting patients with successful outcomes after LVRS.

Inmai and colleagues (2000) noted that 99mTc-Technegas (Tcgas) SPECT is useful for evaluating the patency of the airway and highly sensitive in detecting regional pulmonary function in pulmonary emphysema. The aim of this study was to evaluate regional ventilation impairment by this method pre- and post-thoracoscopic LVRS in patients with pulmonary emphysema. There were 11 patients with pulmonary emphysema. The mean age of patients was 64.1 years. All patients were males. LVRS was performed bilaterally in 8 patients and unilaterally in 3 patients. Post-inhalation of Tcgas in the sitting position, the subjects were placed in the supine position and SPECT was performed. Distribution of Tcgas on axial images was classified into 4 types: (i) homogeneous (ii) inhomogeneous (iii) hot spot, and (iv) defect. Three slices of axial SPECT images, the upper, middle and lower fields were selected, and changes in deposition patterns post LVRS were scored (Tcgas score). Post-LVRS, dyspnea on exertion and pulmonary function tests were improved. Pre-LVRS, inhomogeneous distribution, hot spots and defects were observed in all patients. Post-LVRS, improvement in distribution was obtained not only in the surgical field and other fields, but also in the contralateral lung of unilaterally operated patients. In 5 patients some fields showed deterioration. The Tcgas score correlated with improvements in FEV1.0, FEV1.0 % and % FEV1.0. The authors concluded that Tcgas SPECT is useful for evaluating changes in regional pulmonary function post-LVRS.
Also, an UpToDate review on “Lung volume reduction surgery in COPD” (Martinez, 2014) does not mention the use of SPECT for pre-surgical evaluation.

Nakai et al (2014) reported the case of an 84-year old woman who presented with persistent type II endoleak with sac expansion from 57 mm to 75 mm during 4-year follow-up after endovascular abdominal aortic aneurysm repair. The patient underwent trans-abdominal embolization with coils and N-butyl cyanoacrylate/ethiodized oil mixture (2.5 ml). Because of the anticipated embolization artifacts on follow-up computed tomography (CT), technetium-99m-labeled human serum albumin diethylenetriamine pentaacetic acid single-photon emission computed tomography ((99m)Tc-HSAD SPECT) was performed before and after the intervention. Peri-graft accumulation on (99m)Tc-HSAD SPECT corresponding to the endoleak disappeared after embolization. The authors noted that CT scan performed 12 months after embolization showed no signs of sac expansion; and they stated that (99m)Tc-HSAD SPECT may be useful for evaluating therapeutic effect after embolization for endoleak.

The American College of Radiology Appropriateness Criteria on “Dementia and movement disorders” (ACR, 2014) stated that “An evidence-based review performed by the AAN concluded that SPECT imaging cannot be recommended for either the initial or the differential diagnosis of suspected dementia because it has not demonstrated superiority to clinical criteria. Also, compared with PET, SPECT has a lower diagnostic accuracy and is inferior in its ability to separate healthy controls from patients with true dementia”.

Freesmeyer et al (2014) reported an initial experience regarding the feasibility and applicability of quasi-integrated freehand SPECT/ultrasonography (US) fusion imaging in patients with thyroid disease. Local ethics committee approval was obtained, and 34 patients were examined after giving written informed consent. After intravenous application of 75 MBq of technetium 99m pertechnetate, freehand 3-D SPECT was performed. Data were reconstructed and transferred to a US system. The combination of 2 independent positioning systems enabled real-time fusion of metabolic and morphologic information during US examination. Quality of automatic co-registration was evaluated visually, and deviation was determined by measuring the distance between the center of tracer distribution and the center of the US correlate. All examinations were technically successful. For 18 of 34 examinations, the automatic co-registration and image fusion exhibited very good agreement, with no deviation. Only minor limitations in fusion offset occurred in 16
patients (mean offset ± standard deviation, 0.67 cm ± 0.3; range of 0.2 to 1.0 cm). SPECT artifacts occurred even in situations of clear thyroid findings (e.g., unifocal autonomy). The authors concluded that the freehand SPECT/US fusion concept proved feasible and applicable; however, technical improvements are needed.

Ryken et al (2014) determined which imaging techniques most accurately differentiate true tumor progression from pseudo-progression or treatment-related changes in patients with previously diagnosed glioblastoma. The authors stated that the following recommendations apply to adults with previously diagnosed glioblastoma who are suspected of experiencing progression of the neoplastic process:

- Recommendation Level II: Magnetic resonance imaging (MRI) with and without gadolinium enhancement is recommended as the imaging surveillance method to detect the progression of previously diagnosed glioblastoma.
- Recommendation Level II: Magnetic resonance spectroscopy (MRS) is recommended as a diagnostic method to differentiate true tumor progression from treatment-related imaging changes or pseudo-progression in patients with suspected progressive glioblastoma.
- Recommendation Level III: The routine use of positron emission tomography (PET) to identify progression of glioblastoma is not recommended.
- Recommendation Level III: Single-photon emission computed tomography (SPECT) imaging is recommended as a diagnostic method to differentiate true tumor progression from treatment-related imaging changes or pseudo-progression in patients with suspected progressive glioblastoma.

The National Comprehensive Cancer Network’s clinical practice guideline on “Central nervous system cancers” (Version 2.2014) does not mention SPECT as a management tool. Furthermore, an UpToDate review on “Management of recurrent high-grade gliomas” (Batchelor et al, 2015) does not mention SPECT as a management tool.

Detection of Fronto-Temporal Dementia

In a Cochrane review, Archer et al (2015) determined the diagnostic accuracy of regional cerebral blood flow (rCBF) SPECT for diagnosing FTD in populations with
suspected dementia in secondary/tertiary healthcare settings and in the differential diagnosis of FTD from other dementia subtypes. The search strategy used 2 concepts: (i) the index test and (ii) the condition of interest. These investigators searched citation databases, including MEDLINE (Ovid SP), EMBASE (Ovid SP), BIOSIS (Ovid SP), Web of Science Core Collection (ISI Web of Science), PsycINFO (Ovid SP), CINAHL (EBSCOhost) and LILACS (Bireme), using structured search strategies appropriate for each database. In addition they searched specialized sources of diagnostic test accuracy studies and reviews including: MEDION (Universities of Maastricht and Leuven), DARE (Database of Abstracts of Reviews of Effects) and HTA (Health Technology Assessment) database. These researchers requested a search of the Cochrane Register of Diagnostic Test Accuracy Studies and used the related articles feature in PubMed to search for additional studies. They tracked key studies in citation databases such as Science Citation Index and Scopus to ascertain any further relevant studies. They identified “grey” literature, mainly in the form of conference abstracts, through the Web of Science Core Collection, including Conference Proceedings Citation Index and Embase. The most recent search for this review was run on the June 1, 2013. Following title and abstract screening of the search results, full-text papers were obtained for each potentially eligible study. These papers were then independently evaluated for inclusion or exclusion. The authors included both case-control and cohort (delayed verification of diagnosis) studies. Where studies used a case-control design, these researchers included all participants who had a clinical diagnosis of FTD or other dementia subtype using standard clinical diagnostic criteria. For cohort studies, they included studies where all participants with suspected dementia were administered rCBF SPECT at baseline. The authors excluded studies of participants from selected populations (e.g., post-stroke) and studies of participants with a secondary cause of cognitive impairment. Two review authors extracted information on study characteristics and data for the assessment of methodological quality and the investigation of heterogeneity. They assessed the methodological quality of each study using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool. They produced a narrative summary describing numbers of studies that were found to have high/low/unclear risk of bias as well as concerns regarding applicability. To produce 2 x 2 tables, these investigators dichotomized the rCBF SPECT results (scan positive or negative for FTD) and cross-tabulated them against the results for the reference standard. These tables were then used to calculate the sensitivity and specificity of the index test. Meta-analysis was not performed due to the considerable between-study variation in clinical and methodological characteristics.
A total of 11 studies (1,117 participants) met inclusion criteria. These consisted of 6 case-control studies, 2 retrospective cohort studies and 3 prospective cohort studies; 3 studies used single-headed camera SPECT while the remaining 8 used multiple-headed camera SPECT. Study design and methods varied widely. Overall, participant selection was not well-described and the studies were judged as having either high or unclear risk of bias. Often the threshold used to define a positive SPECT result was not pre-defined and the results were reported with knowledge of the reference standard. Concerns regarding applicability of the studies to the review question were generally low across all 3 domains (participant selection, index test and reference standard). 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 3 multiple-headed camera studies. Sensitivities were lower for the 2 single-headed camera studies; 1 reported a sensitivity and specificity of 0.40 (95% CI: 0.05 to 0.85) and 0.95 (95% CI: 0.90 to 0.98), respectively, and the other a sensitivity and specificity of 0.36 (95% CI: 0.24 to 0.50) and 0.92 (95% CI: 0.88 to 0.95), respectively. Eight of the 11 studies which used SPECT to differentiate FTD from Alzheimer's disease used multiple-headed camera SPECT. Of these studies, 5 used a case-control design and reported sensitivities of between 0.52 and 1.00, and specificities of between 0.41 and 0.86. The remaining 3 studies used a cohort design and reported sensitivities of between 0.73 and 1.00, and specificities of between 0.94 and 1.00. The 3 studies that used single-headed camera SPECT reported sensitivities of between 0.40 and 0.80, and specificities of between 0.61 and 0.97. The authors concluded that they would not recommend the routine use of rCBF SPECT in clinical practice because there is insufficient evidence from the available literature to support this. They stated that further research into the use of rCBF SPECT for differentiating FTD from other dementias is needed. In particular, protocols should be standardized, study populations should be well-described, the threshold for “abnormal” scans pre-defined and clear details given on how scans are analyzed. The authors stated that more prospective cohort studies that verify the presence or absence of FTD during a period of follow-up should be undertaken.

Detection of Air Leak/Pneumothorax

Ceulemans et al (2012) reported on the case of a 61-year old man with severe chronic obstructive pulmonary disease presented to the authors' hospital with recurrence of a right-sided spontaneous secondary pneumothorax. Thoracoscopic abrasion of the parietal pleura was performed, but an important air leak persisted.
Presumed to originate from a bulla in the right upper lobe, bullectomy and pleural
decortication were performed, but leakage remained. Lobectomy was considered,
and quantitative ventilation/perfusion SPECT was performed to predict the
functional outcome. Fused high-resolution CT/Tc Technegas images localized
leakage not only to a bleb in the right upper lobe but also to the subcutaneous
emphysema in the thoracic wall. The air leak resolved after conservative treatment.

An UpToDate review of “Imaging of pneumothorax” (Stark, 2016) mentions chest
X-ray, CT, and ultrasound for imaging pneumothorax; it does not mention SPECT
scan.

Diagnosis of Lung Cancer

In a meta-analysis, Zhang and Liu (2016) examined the value of technetium-99m
methoxy isobutyl isonitrile (Tc-MIBI) SPECT in differentiating malignant from benign
lung lesions. The PubMed and Embase databases were comprehensively
searched for relevant articles that evaluated lung lesions suspicious for malignancy.
Two reviewers independently extracted the data on study characteristics and
examination results, and assessed the quality of each selected study. The data
extracted from the eligible studies were assessed by heterogeneity and threshold
effect tests. Pooled sensitivity, specificity, diagnostic odds ratio (DOR), and areas
under the summary receiver-operating characteristic curves (SROC) were also
calculated. A total of 14 studies were included in this meta-analysis. The pooled
sensitivity, specificity, positive and negative likelihood ratio, and DOR of Tc-MIBI
scan in detecting malignant lung lesions were 0.84 (95% CI: 0.81 to 0.87), 0.83 (95%
CI: 0.77 to 0.88), 4.22 (95% CI: 2.53 to 7.04), 0.20 (95% CI: 0.12 to 0.31), and
25.71 (95% CI: 10.67 to 61.96), respectively. The area under the SROC was
0.9062. Meta-regression analysis showed that the accuracy estimates were
significantly influenced by ethnic groups (p<0.01), but not by image analysis
methods, mean lesion size, or year of publication. Deek funnel plot asymmetry test
for the overall analysis did not raise suspicion of publication bias (p=0.50). The
authors concluded that these findings indicated that Tc-MIBI scan is a promising
diagnostic modality in predicting the malignancy of lung lesions.

This meta-analysis had several drawbacks: (i) the studies varied in year of
publication, sample size, continuity of patients enrolled, and ethnic groups as
well as lesion size. In addition, 99mTc-MIBI SPECT images were performed
under variable conditions, including tracer dose, image analysis methods, the
interval time between tracer injection and scanning (ii) it is impossible for these researchers to identify all studies of 99mTc-MIBI SPECT for lung cancer diagnosis, especially unpublished studies. Since articles reporting significant results are more likely to be published than those reporting non-significant results, publication bias is a major concern in meta-analysis. However, the Deek funnel plot asymmetry test for the overall analysis did not raise suspicion of publication bias. In addition, the authors adopted rigid inclusion criteria and they selected only articles that included at least 10 patients who performed MIBI imaging for lung lesions, which may bring about selection bias, and (iii) it was not clear whether SPECT or PET is superior in differentiating malignant from benign lesions. Two recent published meta-analyses were performed to evaluate the diagnostic accuracy of FDG-PET for detecting lung cancer with a sensitivity of 94 % to 96 % and specificity of 78 % to 86 %. However, a direct comparison between PET and SPECT is absent. Only 2 of the studies comparing SPECT with PET were included in this meta-analysis, but the results were generally inconclusive. According to Santini et al, 99mTc-MIBI SPECT was similar to FDG-PET in the detection of lung malignancies and represents an alternative if PET was not available.


Evaluation of Carotid Stenosis:

Sato and Matsumoto (2017) stated that multi-phase arterial spin labeling (ASL), which obtains the imaged slices with various post-labeling delays, allows for the non-invasive assessment of cerebral hemodynamics that cannot be adequately acquired by SPECT imaging. These investigators described the clinical usefulness of multi-phase ASL in a patient with symptomatic carotid stenosis by comparison with SPECT at rest using iodo-amphetamine. A 75-year old man was referred to the authors’ hospital with severe stenosis of the left internal carotid artery (ICA). While SPECT showed no significant laterality of CBF, multi-phase ASL demonstrated relatively delayed perfusion in the left ICA territory. The patient underwent stent placement for the left ICA stenosis. Post-operatively, while SPECT demonstrated no significant laterality of CBF, multi-phase ASL revealed improved perfusion in the left ICA territory. The authors concluded that this case showed that multi-phase ASL could accurately evaluate the cerebral hemodynamic status that could not be detected using pre- and post-operative SPECT.
Imaging Marker of Pre-Diagnostic Parkinson's Disease:

Noyce and colleagues (2018) examined if pre-diagnostic features of PD were associated with changes in dopamine re-uptake transporter-SPECT and transcranial sonography. Pre-diagnostic features of PD (risk estimates, University of Pennsylvania Smell Identification Test, Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire, and finger-tapping scores) were assessed in a large cohort of older U.K. residents. A total of 46 participants were included in analyses of pre-diagnostic features and MDS-UPDRS scores with the striatal binding ratio on dopamine reuptake transporter-SPECT and nigral hyper-echogenicity on transcranial sonography. The striatal binding ratio was associated with PD risk estimates ($p = 0.040$), University of Pennsylvania Smell Identification Test ($p = 0.002$), Rapid Eye Movement Sleep Behavior Disorder Screening Questionnaire scores ($p = 0.024$), tapping speed ($p = 0.024$), and MDS-UPDRS motor scores ($p = 0.009$). Remotely collected assessments explained $26\%$ of variation in the striatal binding ratio. The inclusion of MDS-UPDRS motor scores did not explain additional variance. The size of the nigral echogenic area on transcranial sonography was associated with risk estimates ($p < 0.001$) and MDS-UPDRS scores ($p = 0.03$) only. The authors concluded that the dopamine re-uptake transporter-SPECT results correlated with motor and non-motor features of pre-diagnostic PD, supporting its potential use as a marker in the prodromal phase of PD; transcranial sonography results also correlated with risk scores and motor signs.

Work-Up of Individuals Undergoing Non-Cardiac Surgery:

Al-Oweidi and colleagues (2017) noted that the prevalence and predictors of myocardial ischemia before non-cardiac surgery are unknown. In addition to the predictive value of myocardial perfusion SPECT before non-cardiac in individual patients is uncertain. In a retrospective study, these researchers evaluated the prevalence and predictors of myocardial ischemia before non-cardiac surgery, and determined the post-operative cardiac outcome based on results of myocardial perfusion SPECT. These investigators reviewed the records of adult patients diagnosed with myocardial ischemia by myocardial perfusion SPECT who were undergoing non-cardiac surgery. Myocardial perfusion SPECT had been performed within 4 weeks prior to non-cardiac surgery requiring general anesthesia. Main outcome measures included prevalence of abnormal myocardial perfusion SPECT results on pre-operative evaluation; abnormal myocardial
Single Photon Emission Computed Tomography (SPECT) results as a predictor for post-operative cardiac events such as cardiac death, non-fatal MI, and unstable angina. Of 131 patients who underwent non-cardiac surgery from February 2015 to April 2016, 84 (64 %) patients were women and the mean (SD) age was 64.1 (13.6) years. The prevalence of abnormal myocardial perfusion SPECT was 18 % (24 of 131). Normal myocardial perfusion SPECT was highly predictive (up to 100 %), but a positive myocardial perfusion SPECT had low positive predictive value (PPV; 4 %). Variables associated with an abnormal myocardial perfusion SPECT included ischemic heart disease, congestive heart failure, American Society of Anesthesiology physical status classification score of 3 or more, limited exercise capacity (less than 4 metabolic equivalents [METs]), male sex, hypercholesterolemia, hypertension, smoking, and abnormal ECG. In a multi-variable analysis, history of ischemic heart disease and history of smoking were significant predictors of abnormal myocardial perfusion SPECT (p = 0.001, and 0.029, respectively). The authors concluded that because of the low PPV of myocardial perfusion SPECT, utilization of the technique in the work-up of cardiac patients undergoing non-cardiac surgery has been inappropriate. They stated that myocardial perfusion SPECT should be restricted to only clearly defined appropriate use criteria.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td></td>
<td>Noncardiac indications:</td>
</tr>
<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td>78071</td>
<td>Parathyroid planar imaging (including subtraction, when performed); with tomographic (SPECT)</td>
</tr>
<tr>
<td>78072</td>
<td>Parathyroid planar imaging (including subtraction, when performed); with tomographic (SPECT), and concurrently acquired computed tomography (CT) for anatomical localization</td>
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<td>78205</td>
<td>Liver imaging(SPECT)</td>
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<td>78206</td>
<td>with vascular flow</td>
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<td>78320</td>
<td>Bone and/or joint imaging; tomographic (SPECT)</td>
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<td>78607</td>
<td>Brain imaging, complete study; tomographic (SPECT)</td>
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<tr>
<td>78647</td>
<td>Cerebrospinal fluid flow, imaging (not including introduction of material); tomographic (SPECT)</td>
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<tr>
<td>Code</td>
<td>Code Description</td>
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<tr>
<td>78803</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); tomographic (SPECT)</td>
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<tr>
<td>78807</td>
<td>Radiopharmaceutical localization of inflammatory process; tomographic (SPECT)</td>
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</table>

Other CPT codes related to the CPB:

- 78608 - 78609 Brain imaging, positron emission tomography (PET)

HCPCS codes covered if selection criteria are met:

- A9584 Iodine I-123 Ioflupane, diagnostic, per study dose, up to 5 millicuries

Other HCPCS codes related to the CPB:

- A9500 Technetium tc-99m sestamibi, diagnostic, per study dose

ICD-10 codes covered if selection criteria are met:

- C16.0 - C16.9 Malignant neoplasm of stomach [carcinoid or neuroendocrine tumors]
- C25.0 - C25.9 Malignant neoplasm of pancreas [VIPoma, Islet cell tumors]
- C33 Malignant neoplasm of trachea
- C70.0 - C70.9 Malignant neoplasm of cerebral meninges [meningioma]
- C71.0 - C71.9 Malignant neoplasm of brain [differentiation of necrotic tissue from tumor]
- C74.00 - C74.92 Malignant neoplasm of adrenal gland [paragangliomas, pheochromocytomas]
- C75.0 - C75.2 Malignant neoplasm of parathyroid gland, pituitary gland and craniopharyngeal duct
- C75.5 Malignant neoplasm of aortic body and other paraganglia
- C7A.00 - C7B.8 Malignant neuroendocrine tumors
- C79.31, C79.49 Secondary malignant neoplasm of brain and nervous system [differentiation of necrotic tissue from tumor of the brain]
- C81.00 - C88.9 Lymphoma [to distinguish tumor from necrosis]
- D13.7 Benign neoplasm of endocrine pancreas [gastrinomas, glucagonomas, Islet cell tumors]
- D18.03 Hemangioma of intra-abdominal structures [liver]
- D32.0 - D32.9 Benign neoplasm of meninges [meningioma]
- D33.0 - D33.2 Benign neoplasm of brain [differentiation of necrotic tissue from tumor]
<table>
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<td>D35.00 - D35.02</td>
<td>Benign neoplasm of adrenal gland [paragangliomas, pheochromocytomas]</td>
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<td>D35.1 - D35.3</td>
<td>Benign neoplasm of parathyroid gland, pituitary gland and craniopharyngeal duct (pouch)</td>
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<td>Benign neoplasm of aortic body and other paraganglia</td>
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<td>D37.8 - D37.9</td>
<td>Neoplasm of uncertain behavior of other and unspecified digestive organs</td>
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<td>D38.1</td>
<td>Neoplasm of uncertain behavior of trachea, bronchus, and lung</td>
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<td>D42.0 - D42.9</td>
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<td>M90.80 - M90.89</td>
<td>Osteopathy in diseases classified elsewhere</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Q76.2</td>
<td>Congenital spondylolisthesis</td>
</tr>
<tr>
<td>R56.1</td>
<td>Post traumatic seizures [presurgical ictal detection of seizure focus in place of PET]</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

- E00.0 - E07.9 Disorders of thyroid gland
- F01.50 - F01.51 Vascular dementia
- F02.80 - F02.81 Dementia in other diseases classified elsewhere with or without behavioral disturbance
- F06.0 - F06.8 Other mental disorders due to known physiological condition
- F10.282, F10.982 Alcohol use with alcohol-induced sleep disorder
- F20.0 - F21 Schizophrenia
- F51.0 - F51.9 Sleep disorders not due to a substance or known physiological condition
- F60.0 - F69 Disorders of adult personality and behavior
- F84.0 - F89 Pervasive developmental disorders
- F90.0 - F90.9 Attention-deficit hyperactivity disorder
- G30.0 - G30.9 Alzheimer's disease
- G31.01 - G31.09 Frontotemporal dementia
<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>G31.83</td>
<td>Dementia with Lewy bodies</td>
</tr>
<tr>
<td>G35</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>G47.0 - G47.9</td>
<td>Sleep disorders</td>
</tr>
<tr>
<td>I63.011 - I66.9</td>
<td>Occlusion and stenosis of precerebral arteries, occlusion of cerebral arteries, and transient cerebral ischemia</td>
</tr>
<tr>
<td>I77.3</td>
<td>Arterial fibromuscular dysplasia</td>
</tr>
<tr>
<td>I77.6</td>
<td>Arteritis, unspecified</td>
</tr>
<tr>
<td>I77.89</td>
<td>Other specified disorders of arteries and arterioles</td>
</tr>
<tr>
<td>J93.0 - J93.9</td>
<td>Pneumothorax and air leak</td>
</tr>
<tr>
<td>M30.1</td>
<td>Polyarteritis with lung involvement [Churg-Strauss]</td>
</tr>
<tr>
<td>M31.0 - M31.9</td>
<td>Other necrotizing vasculopathies</td>
</tr>
<tr>
<td>R52</td>
<td>Pain, unspecified</td>
</tr>
<tr>
<td>R91.8</td>
<td>Other nonspecific abnormal finding of lung field</td>
</tr>
<tr>
<td>S02.0XX+ - S02.42X+</td>
<td>Fracture of skull and facial bones</td>
</tr>
<tr>
<td>S02.600+ - S02.92X+</td>
<td></td>
</tr>
<tr>
<td>S06.0x0+ - S06.0x9+</td>
<td>Concussion</td>
</tr>
<tr>
<td>S06.310+ - S06.339+</td>
<td>Contusion and laceration of cerebrum</td>
</tr>
<tr>
<td>S06.340+ - S06.369+</td>
<td>Traumatic hemorrhage of cerebrum</td>
</tr>
<tr>
<td>S06.4X0+ - S06.6X9+</td>
<td>Epidural and traumatic subdural hemorrhage</td>
</tr>
<tr>
<td>S06.890+ - S06.9X9+</td>
<td>Other and unspecified intracranial injury</td>
</tr>
<tr>
<td>S09.8XX+ - S09.90X+</td>
<td>Specified and unspecified head injury</td>
</tr>
<tr>
<td>T82.898+</td>
<td>Other specified complication of vascular prosthetic devices, implants and grafts, initial encounter [endoleak]</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>T82.6xx+</td>
<td>Infection and inflammatory reaction due to internal prosthetic device, implant, and graft</td>
</tr>
<tr>
<td>T82.7xx+</td>
<td></td>
</tr>
<tr>
<td>T83.51x+</td>
<td></td>
</tr>
<tr>
<td>T83.69x+</td>
<td></td>
</tr>
<tr>
<td>T84.50x+</td>
<td></td>
</tr>
<tr>
<td>T84.60x+</td>
<td></td>
</tr>
<tr>
<td>T84.63x+</td>
<td></td>
</tr>
<tr>
<td>T84.7xx+</td>
<td></td>
</tr>
<tr>
<td>T85.71x+</td>
<td></td>
</tr>
<tr>
<td>T85.79x+</td>
<td></td>
</tr>
<tr>
<td>Z01.818</td>
<td>Encounter for other preprocedural examination</td>
</tr>
</tbody>
</table>

Cardiac Indications:

CPT codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>78451</td>
<td>Myocardial perfusion imaging, tomographic (SPECT) (including attenuation correction, qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); single study, at rest or stress (exercise or pharmacologic)</td>
</tr>
<tr>
<td>78452</td>
<td>multiple studies, at rest and/or stress (exercise or pharmacologic) and/or redistribution and/or rest reinjection</td>
</tr>
<tr>
<td>78453</td>
<td>Myocardial perfusion imaging, planar (including qualitative or quantitative wall motion, ejection fraction by first pass or gated technique, additional quantification, when performed); single study, at rest or stress (exercise or pharmacologic)</td>
</tr>
<tr>
<td>78454</td>
<td>multiple studies, at rest and/or stress (exercise or pharmacologic) and/or redistribution and/or rest reinjection</td>
</tr>
<tr>
<td>78469</td>
<td>Myocardial imaging, infarct avid, planar; tomographic SPECT with or without quantification</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0331T</td>
<td>Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment</td>
</tr>
<tr>
<td>0332T</td>
<td>Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment; with tomographic SPECT</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>33140 - 33141</td>
<td>Transmyocardial revascularization</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I25.10 - I25.9</td>
<td>Atherosclerotic heart disease of antive coronary artery</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I21.01 - I24.1</td>
<td>ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction</td>
</tr>
<tr>
<td>R57.0 - R57.9</td>
<td>Shock, not elsewhere classified</td>
</tr>
<tr>
<td>Z13.6</td>
<td>Encounter for screening for cardiovascular disorders</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


http://qawww.aetna.com/cpb/medical/data/300_399/0376_draft.html 09/03/2018
Buenos Aires, Argentina: Institute for Clinical Effectiveness and Health Policy (IECS); 2004.


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tomography for evaluation of lung volume reduction surgery candidates:  
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Amendment to
Aetna Clinical Policy Bulletin Number:
0376 Single Photon Emission Computed Tomography (SPECT)

There are no amendments for Medicaid.