### Variant 1: Cognitive decline. Suspected Alzheimer disease. Initial imaging.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Appropriateness Category</th>
<th>Relative Radiation Level</th>
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<tbody>
<tr>
<td>MRI head without IV contrast</td>
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<tr>
<td>CT head without IV contrast</td>
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<tr>
<td>Amyloid PET/CT brain</td>
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<tr>
<td>FDG-PET/CT brain</td>
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<td>MR spectroscopy head without IV contrast</td>
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### Variant 2: Suspected frontotemporal dementia. Initial imaging.

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<td>FDG-PET/CT brain</td>
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<td>HMPAO SPECT or SPECT/CT brain</td>
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<td>Amyloid PET/CT brain</td>
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<td>MR spectroscopy head without IV contrast</td>
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<td>MRI functional (fMRI) head without IV contrast</td>
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<td>CT head without and with IV contrast</td>
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### Variant 3: Suspected dementia with Lewy bodies. Initial imaging.

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<th>Appropriateness Category</th>
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<td>CT head without IV contrast</td>
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<td>FDG-PET/CT brain</td>
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<td>Amyloid PET/CT brain</td>
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<td>MRI functional (fMRI) head without IV contrast</td>
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### Variant 4: Suspected vascular dementia. Initial imaging.

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<td>FDG-PET/CT brain</td>
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<td>MR spectroscopy head without IV contrast</td>
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<tr>
<td>MRI functional (fMRI) head without IV contrast</td>
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### Variant 5: Suspected idiopathic normal-pressure hydrocephalus. Initial imaging.

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<td>MRI head without and with IV contrast</td>
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<td>CT head with IV contrast</td>
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<td>CT head without and with IV contrast</td>
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<td>MR spectroscopy head without IV contrast</td>
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DEMENTIA

Introduction/Background

Degenerative disease of the central nervous system is a growing public health concern. The prevalence of dementia, one of the leading degenerative conditions, is expected to quadruple by 2050 [1]. Other degenerative diseases may affect the extrapyramidal system and the motor system.

Dementia is characterized by a significant loss of function in multiple cognitive domains without affecting the general level of arousal. Several forms are now recognized, including Alzheimer disease (AD), frontotemporal dementia (FTD), Lewy bodies disease, vascular dementia (VaD), and mixed dementias [2]. Although the causes of most dementias remain elusive, genetic research has opened many frontiers to understanding the pathophysiology of heretofore enigmas such as AD [1,3]. Additionally, infectious, autoimmune, and toxic etiologies have become increasingly more appreciated as causes of cognitive decline. Trauma with brain injury may also be associated with premature dementia.

Discussion of Procedures by Variant


In 2011, the National Institute on Aging-Alzheimer’s Association [4] proposed the following terminology for individuals with dementia caused by AD: 1) probable AD, 2) possible AD, and 3) probable or possible AD with evidence of AD pathophysiological process. The first two causes are intended for use in all clinical settings and have defined core clinical criteria. The third cause is currently intended for research purposes and includes individuals who have biomarkers for AD pathology (including both cerebrospinal fluid [CSF] and imaging biomarkers).

AD dementia is part of a continuum of clinical and biological phenomena. The workgroup emphasizes that AD dementia is fundamentally a clinical diagnosis. To make a diagnosis of AD dementia with biomarker support, the core clinical diagnosis of AD dementia must first be satisfied. In these recommendations, the term mild cognitive impairment (MCI) that is due to AD is used to refer to the symptomatic predementia phase of AD [5]. Similar to AD dementia, MCI that is due to AD cannot be currently diagnosed by a laboratory test but requires the judgment of a clinician. In addition, similar to AD dementia, etiologies in addition to AD pathophysiological processes may coexist in an individual that meets the criteria for MCI that is due to AD but in whom the AD pathophysiological process is the main cause of the cognitive dysfunction.

The stage of preclinical AD precedes MCI and encompasses the spectrum of presymptomatic autosomal dominant mutation carriers, asymptomatic biomarker-positive older individuals at risk for progression to MCI that is due to AD dementia, as well as biomarker-positive individuals who have demonstrated a subtle decline from their own baseline that exceeds the expected in typical aging but would not yet meet criteria for MCI [6].
The major AD biomarkers that have been widely investigated at this time [7] can be subdivided into two classes based on the biology that is measured. Biomarkers of brain amyloid-beta (Aβ) protein deposition are low CSF Aβ42 and positive PET amyloid imaging. The second category is that of biomarkers of downstream neuronal degeneration or injury. The three major biomarkers in this category are 1) elevated CSF tau, total tau, and phosphorylated tau; 2) decreased fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) uptake on PET in temporoparietal cortex; and 3) disproportionate atrophy on structural MRI in medial, basal, and lateral temporal lobe and medial parietal cortex.

In persons who meet the core clinical criteria for probable AD dementia, biomarker evidence may increase the certainty that the basis of the clinical dementia syndrome is the AD pathophysiological process. The recommendations of the working group did not advocate the use of AD biomarker tests for routine diagnostic purposes [4]. However, this opinion was refined in the 2014 position paper from the International Working Group-2, which proposed that the diagnosis of AD required an appropriate clinical AD phenotype (typical or atypical) and a pathophysiological marker consistent with AD pathology (including increased tracer retention on amyloid PET), moving amyloid PET into the diagnostic realm. The biomarkers of downstream neuronal injury, such as volumetric MRI and FDG-PET, were considered agents to measure or monitor the course of disease but not for initial diagnosis [8].

The primary role of neuroimaging in the workup of patients with probable or possible AD has typically been to exclude other significant intracranial abnormalities. In general, the imaging findings in structural studies such as MRI are nonspecific but may suggest other forms of dementia. The American Academy of Neurology (AAN) has recommended that the routine use of structural neuroimaging, such as a noncontrast CT or MRI examination, may assist with the diagnosis of dementia [9]. Advanced methods, such as volumetric MRI, amyloid PET, and FDG-PET, are not routinely used in community or general practices for the diagnosis or differentiation of forms of dementia [10-12].

**CT Head**

Noncontrast CT head is used as a primary examination to exclude treatable lesions like a mass or subdural hematoma [9]. Although not as accurate as MRI, CT also permits detection of hippocampal atrophy in AD patients [13] but is not recommended as first-line imaging for this purpose because MRI provides higher resolution images. Contrast-enhanced CT head is not recommended because the examination is mainly used to rule out other pathologies that do not typically require contrast for detection. Similarly, dual-phase CT head is not indicated in the evaluation of AD.

**Amyloid PET/CT Brain**

PET has been used to detect in vivo Aβ protein in the brains of patients with AD. Until recently, this has been achieved using the carbon-11 Pittsburgh compound-B (PIB). This method requires an on-site cyclotron in clinical practice because of the very short half-life of this compound [14]. Carbon-11 PIB has been used to show that in patients with amnestic MCI, PIB-positive patients with abnormal amyloid deposition are significantly more likely to convert to AD [15].

Recently, three F-18–based amyloid PET agents, F-18 flurbetapir, F-18 flutemetamol, and F-18 florbetaben, have been approved for use by the FDA. These agents have been shown to be well tolerated, to distinguish patients with AD from healthy controls, and to correlate with amyloid load on pathology at autopsy [16-20]. A recent meta-analysis showed that pooled sensitivity and specificity values were, in general, high for all three tracers and had no marked differences in the diagnostic accuracy [21]. All tracers perform better when used to discriminate between patients with AD and healthy controls.

However, amyloid PET may be positive in cognitively normal subjects who do not develop AD and in patients with other forms of non-AD dementia [22]. Although a negative amyloid PET scan likely means a low probability of AD, the patient may still harbor a non-AD neurodegenerative condition.

The Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association has proposed guidelines for the use of amyloid PET [23,24]. The taskforce suggests that amyloid PET may be useful and appropriate in patients with a cognitive complaint and confirmed impairment when AD is in the differential but the diagnosis is uncertain after evaluation by a dementia expert and the knowledge of the presence or absence of amyloid deposition is felt to add to patient care (although currently no treatment can slow AD progression, and the presence of amyloid cannot be sufficiently predictive in many cases). The taskforce cites specific appropriate use criteria in which amyloid PET might be useful: persistent or progressive unexplained MCI, possible AD (unclear clinical presentation, atypical clinical course or etiologically mixed presentation, and
progressive dementia with early age of onset [≤65 years of age]). The taskforce considered amyloid PET inappropriate in patients with probable AD with typical age of onset, for judgment of dementia severity, for patients with only unconfirmed cognitive complaints, or in asymptomatic individuals (positive family history, presence of apolipoprotein E, and nonmedical use such as insurance screening).

A CMS-convened Medicare Evidence Development and Coverage Advisory Committee that met in 2013 concluded there was low to intermediate confidence that amyloid PET would significantly contribute to the care of these patients. However, in its national coverage decision, CMS concluded that amyloid PET would be covered under a coverage with evidence development program [25].

The ACR and the Alzheimer’s Association are sponsoring the “Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study” (https://clinicaltrials.gov/ct2/results?term=NCT02420756), a CMS-approved coverage with evidence development study that began accrual in early 2016 of over 18,000 patients. Interim results from the IDEAS study were reported at the 2017 Alzheimer’s Association International Conference. Changes in medical management were seen in 67.8% of MCI patients and 65.9% of dementia patients after amyloid PET. Amyloid PET scans also reduced the need for additional diagnostic testing, such as neuropsychological testing and spinal fluid testing.

According to the practice parameter for amyloid brain PET that was developed collaboratively by the ACR and the American Society for Neuroradiology (ASNR) [26], indications for amyloid PET mirror those of the amyloid imaging taskforce as above.

**FDG-PET/CT Brain**

PET imaging in dementia can be divided into metabolic PET, which uses FDG as a marker for metabolism, and amyloid PET, which uses agents that bind to amyloid deposits within the brain. FDG-PET imaging has been shown to provide greater diagnostic accuracy when compared with clinical evaluations without functional neuroimaging [27]. Hypometabolism on FDG-PET is thought to be related to decreased synaptic activity and is a biomarker of neurodegeneration or neuronal injury [12]. FDG-PET shows characteristic reductions of regional glucose metabolic rates in patients with probable and definite AD in the parietal, temporal, and posterior cingulate regions [28]. FDG-PET accurately discriminates AD patients from normal subjects with a sensitivity of 96% and specificity of 100% [28]. CMS has made FDG-PET available to Medicare recipients to assist with the diagnosis of dementia in the appropriate clinical setting (eg, to distinguish AD from FTD) in recognition of this usefulness [27].

A practice parameter for FDG-PET/CT for patients with cognitive decline has been developed collaboratively by the ACR-ASNR [26]. The qualifications and responsibilities of the personnel conducting the study and the standardized patient preparation, positioning, and protocol are also outlined in this document. An important detail to be emphasized is that the study should be performed at the request of physicians knowledgeable in clinical diagnosis and management of dementia and under circumstances in which the results of the examination are likely to impact patient care [26].

**MR Spectroscopy Head**

MR spectroscopy may permit identification of mild to moderate AD with a specificity and sensitivity that suggests the potential for clinical usefulness and may predict the conversion of MCI to dementia [29]. Studies of automated MR spectroscopy for AD diagnosis have reported high sensitivity and moderate specificity. Findings in reported studies have varied, but decreased N-acetylaspartate (NAA) and increased myoinositol (mI) with the use of the NAA:mI ratio show the greatest promise [30]. However, prospective studies are lacking to validate this method for diagnosing AD.

**MRI Functional (fMRI) Head**

Recently tested as an imaging biomarker in AD is MRI functional (fMRI) because it may provide information about functional integrity of brain networks supportive memory and other cognitive domains [31]. Both conventional task-based fMRI and resting state fMRI (particularly the default mode network) [32] show promise as diagnostic markers but have not yet been subjected to a thorough validation. Most of the fMRI studies are single-center studies with small numbers of patients and limited test, retest, and cross-scanner reproducibility, limiting its use in the diagnosis of AD.

**MRI Head**

The primary role of neuroimaging in the workup of patients with probable or possible AD has typically been to exclude other significant intracranial abnormalities. A noncontrast MRI examination will assist with the diagnosis
of dementia by excluding structural pathology like tumors or subdural hematomas [9]. Contrast-enhanced MRI is not needed in the initial imaging evaluation in dementia patients.

Volumetric MRI can be used as a second-line imaging test for aiding in the diagnosis once the patient has been seen by a specialist. Medial temporal lobe atrophy has been noted to correlate with cognitive decline and nonfunctional test accumulation and is seen in patients with MCI compared with normal patients. Atrophy measures can be a visual rating system (Scheltens score) [33], semiautomated, or automated volumetric techniques. Whole-brain and hippocampal atrophy rates are sensitive markers of progression of neurodegeneration and are increasingly used as surrogate outcomes in trials of potentially disease-modifying drugs. Volumetric MRI, along with FDG-PET and high CSF tau, is felt to be a biomarker of neurodegeneration or neuronal injury and could be able to document and follow disease severity [10,34].

In an evidence-based review of dementia diagnosis, the AAN did not recommend routine quantitative volumetry of the hippocampus or the entorhinal cortex because these techniques are labor intensive [9].

Diffusion-weighted imaging/apparent diffusion coefficient [35,36] and magnetization transfer imaging [37] are all either sensitive to early change or can add complementary information to atrophy measures but are second-line imaging tests.

**HMPAO SPECT or SPECT/CT Brain**
Regional cerebral blood flow determined using single-photon emission computed tomography (SPECT) imaging with Tc-99m hexamethylpropyleneamine oxime (HMPAO) shows bilateral temporoparietal or hippocampal hypoperfusion in patients with AD. Whether brain SPECT contributes substantially to diagnostic accuracy after a careful clinical examination using current diagnostic criteria is controversial. Although perfusion MRI is promising, SPECT remains superior in identifying pathologic perfusion [38]. An evidence-based review performed by the AAN concluded that SPECT imaging cannot be recommended for either the initial assessment or to clarify the differential diagnosis of suspected dementia because it has not demonstrated superiority to clinical criteria [9]. When compared with FDG-PET, SPECT has a lower diagnostic accuracy and is inferior in its ability to separate healthy controls from patients with true dementia [39,40].

**Multimodality Imaging for Evaluation of Cognitive Decline, Suspected AD**
Combining volumetric MRI, PET, and CSF biomarkers may improve accuracy of the diagnosis of AD [41]. Investigators with the Alzheimer’s Disease Neuroimaging Initiative [42] compared neuroimaging modalities to predict conversion from MCI to AD. Multivariate modeling found that, among individual modalities, quantitative MRI had the highest predictive accuracy (67%) that increased by 9% to 76% when combined with PIB-PET, producing the highest accuracy among any biomarker combination. Individually, PIB-PET generated the best sensitivity, and FDG-PET had the lowest. Among individual brain regions, the temporal cortex was found to be most predictive for MRI and PIB-PET. It appears that these examinations may be complementary to each other but are not front line for initial imaging of suspected AD.

**Variant 2: Suspected frontotemporal dementia. Initial imaging.**
FTD is a neurodegenerative disorder that may be mistaken for AD. Pathologically, it includes a heterogeneous group of sporadic and familial neuropsychiatric disorders. Pick disease is one of the neuropathological entities of FTD. Unlike AD, which increases in frequency with age, FTD is rare after the age of 75.

Although the diagnosis of FTD is primarily clinical, neuroimaging serves several purposes: exclusion of other structural brain abnormalities that could clinically mimic FTD, differentiation of FTD from other neurodegenerative disorders (most commonly AD), and classification of the known subtypes of FTD [43].

Multimodal imaging is a promising approach in neuroimaging of FTD. Integrated PET/MRI systems allow a combination of structural and functional imaging in one examination that can increase sensitivity and specificity of these modalities in a smaller cohort of patients and thus may represent a method of choice in FTD [44].

**CT Head**
Noncontrast CT head is used to exclude other lesions that may clinically mimic the disease. CT head with intravenous (IV) contrast or dual-phase imaging is not needed for initial evaluation.
Amyloid PET/CT Brain
Use of amyloid PET in FTD is limited to the exclusion of underlying amyloid brain pathology that can be seen in cases of AD with atypical presentation. PET tracers specific for tau protein deposits in the brain are currently being investigated, but no systematic studies on their application in FTD have been published [44].

FDG-PET/CT Brain
FDG-PET is an established tool for differentiating FTD and AD and classifying different FTD subtypes. FDG-PET has a sensitivity of 60% and a positive predictive value of 78.5% for differentiating the subtypes of FTD [44]. The CMS coverage decision for payment for FDG-PET brain, in 2004, was based on FDG brain PET being a very valuable diagnostic study to differentiate AD and FTD in patients with documented cognitive decline of at least 6 months and a recently established diagnosis of dementia [45].

MR Spectroscopy Head
MR spectroscopy metabolite changes in FTD are similar to the changes encountered in AD: lower NAA to creatine (Cr) ratio (NAA/Cr) and higher mI to Cr ratio (mI/Cr) than normal, but findings are more commonly centered on the frontal cortex in early FTD [46]. MR spectroscopy could be a helpful secondary test in patients who have clinical findings of FTD, but it is not a first-line imaging test.

MRI Functional (fMRI) Head
Brain activation has been shown to be significantly decreased in FTD in the frontal and parietal lobes compared with AD [47]. Resting state fMRI demonstrates alterations in structural and functional connectivity in presymptomatic FTD [48]. However, fMRI remains in the realm of research and is not recommended in routine evaluation of FTD.

MRI Head
MRI of the brain without IV contrast serves as a first-line imaging test to exclude secondary causes of symptoms such as subdural hematoma and tumor in patients with suspected FTD. IV contrast is not necessary for initial evaluation. Volumetric MRI has a second-level role in diagnosis and has been actively studied as a tool to assess brain atrophy patterns associated with different FTD clinical phenotypes. Studies show that volumetric MRI allows differentiation of atrophy patterns when analyzed at a group level but currently does not allow assessment on an individual patient level [44]. Several other advanced MRI techniques provide additional information about brain microstructure, and their role in diagnosis of FTD is being investigated [44]. Zhang et al [49] demonstrated that diffusion tensor imaging has significantly greater accuracy for classifying subtypes of FTD than volumetric brain MRI. The role of arterial spin labeling MRI in FTD is currently being studied. The patterns detected using arterial spin labeling MRI has been shown to be similar to FDG-PET findings, and this technique potentially could represent a future alternative to FDG-PET [44].

HMPAO SPECT or SPECT/CT Brain
Tc-99m HMPAO SPECT has been found to be useful in distinguishing FTD from AD and VaD with a pattern of bilateral anterior hypoperfusion. Tc-99m HMPAO SPECT may be used as an adjunct to clinical evaluation and CT but it is not a first-line test [50].

Variant 3: Suspected dementia with Lewy bodies. Initial imaging.
Dementia with Lewy bodies (DLB) has been recognized as the second most prevalent neurodegenerative dementia in the elderly, causing up to 15% of cases [51]. It is a synucleinopathy with accumulation of insoluble alpha-Synuclein that aggregates to form Lewy bodies, which are the major pathological feature of the disease.

To increase the accuracy of diagnosis of DLB, the latest diagnostic criteria incorporate findings from neuroimaging such as CT, MRI, SPECT, and PET [52]. Some authors have suggested a multimodality approach combining MRI and SPECT modalities as a useful and practical approach for differentiating DLB from AD [51].

CT Head
Noncontrast CT head is a good first-line examination to exclude mimics like brain tumor or subdural hematoma. Relative preservation of the medial temporal lobe structures is also a supportive imaging biomarker according to the fourth consensus report of the DLB consortium [52]. CT with IV contrast or dual-phase CT imaging is not needed for initial evaluation.
Amyloid PET/CT Brain
DLB is also accompanied by amyloid deposition like AD, but overall, there is decreased uptake compared when with AD patients on amyloid imaging. Compared to Parkinson disease, DLB patients show a higher level of amyloid deposition [53]. At this time, amyloid PET/CT has very limited usefulness for diagnosis of DLB.

FDG-PET/CT Brain
Generalized low uptake on FDG-PET/CT with occipital hypometabolism has been demonstrated and is a useful supportive imaging biomarker [54]. FDG-PET/CT head has also been shown to distinguish between AD and DLB. Relative preservation of posterior or midcingulate metabolism on FDG-PET/CT—the cingulate island sign—has been described in DLB. However, most studies are hampered by small sample size, and FDG-PET/CT is a second-level examination for the evaluation of DLB.

Ioflupane SPECT or SPECT/CT Brain
In the present guidelines, decreased dopamine transporter uptake is of the greatest importance among various neuroimaging findings and is listed as one of the suggestive features. Functional imaging of the dopamine transporter (I-123 Ioflupane) using SPECT might identify a defect in the nigrostriatal pathway that occurs in a variety of disorders including DLB and Parkinson disease. I-123 Ioflupane striatal activity tends to be normal in AD and low in DLB and Parkinson disease; however, AD and DLB can coexist in the same patient, potentially confounding results [11,51]. This is not a first-line imaging test but may be valuable after cross-sectional imaging to exclude other pathology.

MR Spectroscopy Head
There is sparse MR spectroscopy data on DLB. In one study [55], DLB patients were characterized by decreased NAA/Cr in the occipital voxel. AD patients were characterized by lower NAA/Cr in the frontal and posterior cingulate voxels. Normal NAA/Cr levels in the frontal voxel differentiated DLB patients with preserved hippocampal volumes from AD patients. MR spectroscopy abnormalities associated with loss of neuronal integrity localized to the occipital lobes in DLB, and the posterior cingulate gyri and frontal lobes in AD. The pattern of MR spectroscopy abnormalities may have a role in differential diagnosis of DLB and in distinguishing DLB patients with overlapping AD pathology. Although in the future, MR spectroscopy can provide additional useful information in the ante-mortem diagnosis of DLB; at present, its usefulness is limited.

MRI functional (fMRI) Head
Studies with fMRI show reduced activation of the occipital-temporal lobe regions during visual tasks. Resting state fMRI has demonstrated increased functional connectivity between the right posterior cingulate gyrus and other regions of the brain and reduced cortico-cortical connectivity. However, the diagnostic utility of fMRI for diagnosis of DLB has not been validated, and thus it cannot be recommended [56].

MRI Head
Routine MRI head is performed to exclude other lesions like tumor or subdural hematoma. Contrast-enhanced MRI is not needed for initial evaluation.

Volumetric MRI can be done as a secondary test to support the diagnosis. On structural MRI, patients with DLB show less atrophy of the hippocampus and other medial temporal lobe structures compared with AD. For similar levels of dementia severity, DLB appears to have greater subcortical structure atrophy (thalamus, caudate, amygdala, ventral diencephalon, substantia nigra, and midbrain) compared with AD [57]. However, on a single subject level, structural changes are not helpful in differentiating DLB from other dementias. Diffusion tensor imaging studies have described the potential importance of the precuneus in the pathogenesis of DLB as well as AD [35].

HMPAO SPECT or SPECT/CT Brain
The most important finding on brain-perfusion SPECT in DLB is occipital hypoperfusion. This hypoperfusion is listed as a supportive feature in the consensus guidelines [52], and this can be a second-line imaging test to help with the diagnosis. However, this test is less commonly used in clinical practice and has been largely replaced by other imaging modalities.

Variant 4: Suspected vascular dementia. Initial imaging.
Cerebral vascular disease, especially common in the elderly, can lead to VaD [11]. The diagnosis of VaD involves the presence of significant cerebrovascular pathology or risk factors, assessed clinically or using neuroimaging. Recently, the concept of vascular cognitive impairment has been invoked, which refers to the whole spectrum of
disorders in which there is cognitive impairment and either clinical evidence of previous stroke or imaging evidence of vascular brain injury, either in isolation (pure vascular disease) or in association with other pathologies (mixed disease) [58]. The three main causes of vascular cognitive impairment are large vessel strokes (macroangiopathy, arteriosclerosis), small vessel disease (microangiopathy, arteriolosclerosis), and microhemorrhages. Structural neuroimaging has been incorporated as an important element of the diagnosis of VaD [59].

Cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy is an autosomal-dominant hereditary small-artery vasculopathy caused by mutations in the notch3 gene on chromosome 19. Clinically, the disease is characterized by migraine with aura, strokes and progressive subcortical dementia, and mood disturbances. MRI in these patients shows focal lacunar infarcts and leukoaraiosis. Lesion load increases with age. Besides familial anamnthesis and clinical history, structural MRI changes in these patients help to suggest the diagnosis by showing characteristic hyperintense T2 or fluid-attenuated inversion recovery lesions, which predominate in the frontal, parietal, and anterior temporal cortices and in the external capsule [60]. Diagnosis is confirmed by skin biopsy or detection of a pathogenic notch3 mutation on direct sequencing.

**CT Head**
Most acute stroke patients undergo brain imaging by unenhanced CT head to evaluate for size, territory, and acuity of infarct to exclude hemorrhage and evaluate for stroke mimics (such as brain tumors). Furthermore, the presence and severity of white matter changes and brain atrophy can also be readily determined from CT head imaging. CT head with IV contrast is not needed to evaluate VaD.

**CTA Head**
CT angiography (CTA) is a sensitive modality and may be used as an alternative to MR angiography (MRA) to detect vascular occlusion or stenosis intracranially. However, vascular imaging is not needed to make a diagnosis of VaD; rather, the diagnosis relies on clinical criteria and evidence of end organ damage in the brain.

**FDG-PET/CT Brain**
FDG-PET/CT in VaD can show multiple focal cortical and subcortical metabolic defects, a pattern different from AD and may be useful in differentiating the two entities in the demented patient [61]; however, it is not a first-line imaging test.

**MR Spectroscopy Head**
MR spectroscopy shows injury to the axons by measuring the levels of NAA and Cr [62,63]. MR spectroscopy is a research tool and, to date, does not appear to clinically help establish a diagnosis of VaD or mixed VaD and AD.

**MRA Head**
Although vascular imaging is not needed for diagnosis of suspected VaD, MRA is a sensitive modality to detect vascular occlusion or stenosis intracranially.

**MRA Neck**
Vascular imaging is not needed for workup of suspected VaD.

**MRI functional (fMRI) Head**
The use of fMRI is investigational and, to date, does not appear to clinically help establish a diagnosis of VaD or mixed VaD and AD.

**MRI Head**
One of the roles of neuroimaging is to document the presence or absence of strokes. Although CT can detect the presence or absence of infarctions in patients with dementia, histopathologically verified cases of VaD with normal CT studies have been reported [28]. Thus, MRI is preferable to CT for detecting vascular lesions in patients with dementia. On MRI, evidence for vascular abnormalities includes cortical or subcortical infarcts, leukoaraiosis or white matter T2 hyperintensity, microhemorrhages, and lacunar infarct. Hippocampal atrophy has been seen in patients with vascular cognitive impairment [64], and some studies have argued that it is the best predictor of post stroke dementia [65].

The above-mentioned imaging findings on routine MRI lack specificity and correlation with degree of cognitive impairment. Diffusion tensor imaging has been shown to correlate better with cognitive deficits, but its use has been confined to research settings [66].

Differentiation of VaD from either AD with superimposed cerebrovascular disease or mixed AD and VaD is especially difficult and is best performed by amyloid PET/CT brain. On MRI, extensive infarctions (cortical or
lacunar or both) and white-matter changes (hyperintense on T2-weighted MRI) in a patient with dementia favor a contribution from VaD or mixed VaD and AD over AD. The absence or mild extent of these changes in a patient with dementia argues against a diagnosis of VaD. The abovementioned findings are optimally visualized on noncontrast MRI; IV contrast is not needed.

**HMPAO SPECT or SPECT/CT Brain**

“Patchy” cerebral blood flow changes significantly increase the odds of a patient having VaD as opposed to AD [50]. SPECT may be an ancillary test in the evaluation of VaD. However, there is no diagnostic utility in performing this procedure in patients with suspected VaD.

**US Duplex Doppler Carotid**

Atherosclerotic burden, as defined by carotid ultrasound (US), is associated with worse cognitive performance and subsequent cognitive decline [67]. However, US duplex Doppler is not needed to diagnose VaD.

**Variant 5: Suspected idiopathic normal-pressure hydrocephalus. Initial imaging.**

Normal-pressure hydrocephalus (NPH) is characterized by the clinical triad of dementia, gait disturbance, and urinary incontinence. Other diagnostic features include normal CSF pressure at lumbar puncture, communicating hydrocephalus documented on MRI or CT, and ventricular influx but no passage of isotope over the convexities on radionuclide DTPA cisternography.

The Guideline Development, Dissemination, and Implementation Subcommittee of the AAN has concluded that shunting is possibly effective in idiopathic NPH (INPH) [68]. Several clinical, laboratory, and imaging signs can improve distinction between responders and nonresponders to shunting. However, there is no test or combination of clinical findings and tests that accurately predicts response to shunting. Clinical features that favor shunt responsiveness include predominance of gait disturbance, mild to moderate degree of dementia, and rapid clinical progression of urinary incontinence. Imaging features of responders versus nonresponders are discussed below.

**CT Head**

CT head without IV contrast is an appropriate first-line imaging test to evaluate for ventriculomegaly out of proportion to sulci and to exclude other pathologies. It can also show transependymal CSF flow. CT head with IV contrast is not indicated for initial evaluation of NPH.

**MR Spectroscopy Head**

MR spectroscopy is not useful in differentiating INPH from other types of dementia nor does it help in patient selection for ventriculoperitoneal shunting [69].

**MRI Head**

MRI findings include at least moderate ventriculomegaly (with rounded frontal horns and marked enlargement of the temporal horns and third ventricle) and absence of or only mild cortical atrophy [70]. Increased CSF flow void through the cerebral aqueduct on MRI appears to correlate with a good response to shunt surgery. Cine MRI with inflow technique showing hyperdynamic aqueductal CSF can also help in identifying shunt-responsive NPH patients. Evidence-based guidelines have been developed for diagnosing INPH. In these guidelines, the patients are divided into probable INPH, possible INPH, or unlikely INPH. Brain imaging features for diagnosing probable INPH include ventricular enlargement not entirely attributable to cerebral atrophy or congenital enlargement (Evan index = maximal width of frontal horns/maximal width of inner skull >0.3); no macroscopic obstruction of CSF flow; and at least one of the following features: enlargement of the temporal horns, callosal angle of <90°, evidence of altered brain water content, and aqueductal or fourth ventricle flow void on MRI. Other MRI findings considered supportive of the diagnosis but not necessary for probable INPH designation are (a) MRI performed before onset of symptoms showing smaller ventricular size and (b) cine MRI study showing increased ventricular flow rate. The abovementioned findings are optimally visualized on a noncontrast MRI; MRI with IV contrast is not needed.

**DTPA cisternography**

Radioisotope cisternogram using In-111-diethylenetriamine pentaacetic acid (DTPA) shows delayed clearance of radiotracer over the cerebral convexities and abnormal reflux of radiotracer into the ventricles. SPECT DTPA cisternography permits more accurate localization of radionuclide activity than planar DTPA cisternography, which partially superimposes different CSF compartments. However, there is insufficient evidence to determine whether patients with suspected INPH and persistent ventricular stasis on radioisotope DTPA cisternography would respond to shunting [68].
HMPAO SPECT or SPECT/CT Brain
There is some suggestion that in patients with suspected INPH those with impaired cerebral blood flow reactivity (measured on Tc-99m HMPAO SPECT) to acetazolamide are possibly more likely to respond to shunting than those without impaired cerebral blood flow reactivity to acetazolamide [71]. This is a second-level test to stratify patients with INPH who may benefit from shunting.

Summary of Recommendations

- **Variant 1**: In patients with cognitive decline and suspected AD, MRI head without IV contrast or CT head without IV contrast is usually appropriate for the initial imaging. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care).

- **Variant 2**: In patients with suspected frontotemporal dementia, MRI head without IV contrast or CT head without IV contrast is usually appropriate as the initial imaging. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care).

- **Variant 3**: In patients with suspected DLB, MRI head without IV contrast or CT head without IV contrast is usually appropriate as the initial imaging. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care).

- **Variant 4**: In patients with suspected vascular dementia, MRI head without IV contrast or CT head without IV contrast is usually appropriate as the initial imaging. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care).

- **Variant 5**: In patients with suspected idiopathic normal-pressure hydrocephalus, MRI head without IV contrast or CT head without IV contrast is usually appropriate for the initial imaging. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient’s care).

Supporting Documents
The evidence table, literature search, and appendix for this topic are available at [https://acsearch.acr.org/list](https://acsearch.acr.org/list). The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents go to [www.acr.org/ac](http://www.acr.org/ac).
### Appropriateness Category Names and Definitions

<table>
<thead>
<tr>
<th>Appropriateness Category Name</th>
<th>Appropriateness Rating</th>
<th>Appropriateness Category Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usually Appropriate</td>
<td>7, 8, or 9</td>
<td>The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.</td>
</tr>
<tr>
<td>May Be Appropriate</td>
<td>4, 5, or 6</td>
<td>The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.</td>
</tr>
<tr>
<td>May Be Appropriate (Disagreement)</td>
<td>5</td>
<td>The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel’s recommendation. “May be appropriate” is the rating category and a rating of 5 is assigned.</td>
</tr>
<tr>
<td>Usually Not Appropriate</td>
<td>1, 2, or 3</td>
<td>The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.</td>
</tr>
</tbody>
</table>

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [72].

#### Relative Radiation Level Designations

<table>
<thead>
<tr>
<th>Relative Radiation Level*</th>
<th>Adult Effective Dose Estimate Range</th>
<th>Pediatric Effective Dose Estimate Range</th>
</tr>
</thead>
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<tr>
<td>☀</td>
<td>0 mSv</td>
<td>0 mSv</td>
</tr>
<tr>
<td>☀</td>
<td>&lt;0.1 mSv</td>
<td>&lt;0.03 mSv</td>
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<tr>
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<td>0.03-0.3 mSv</td>
</tr>
<tr>
<td>☀</td>
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<td>0.3-3 mSv</td>
</tr>
<tr>
<td>☀</td>
<td>10-30 mSv</td>
<td>3-10 mSv</td>
</tr>
<tr>
<td>☀</td>
<td>30-100 mSv</td>
<td>10-30 mSv</td>
</tr>
</tbody>
</table>

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies.”

### References

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient’s clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient’s condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.