THE CONSULT
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Appropriate Use of Advanced Imaging in Patients with a Suspected Neurocognitive Disorder

INTRODUCTION

Neurocognitive disorder (previously known as dementia) has a global presence of 24 million and is estimated to double every 20 years. Not only is it a clinically relevant condition, but there are significant socioeconomic implications associated with the diagnosis.

Mild cognitive impairment (MCI) is the condition in which individuals demonstrate cognitive impairment with minimal impact on daily living. When cognitive impairment significantly interferes with daily function, then a patient is diagnosed with neurocognitive disorder.

Despite the prevalence of MCI and neurocognitive disorder, this remains a diagnostic challenge for clinicians. Imaging clearly has an important role in the evaluation of patients with neurocognitive disorder; however, it is not the only tool for making the diagnosis.

There are many types of neurocognitive disorders. The most common include Alzheimer's disease (most common primary cause), cerebrovascular disease (most common secondary cause), frontotemporal dementia, and dementia with Lewy bodies.

Imaging is used in evaluating patients with MCI or suspected neurocognitive disorder. Imaging is also commonly used to help exclude treatable causes of neurocognitive disorder, such as normal pressure hydrocephalus, or other primary intracranial pathology such as infection, hemorrhage, or tumor.

MRI without contrast is typically the most appropriate imaging study in evaluating patients with suspected neurocognitive disorder. Compared to CT, MRI is more sensitive to subtle vascular changes and to changes that may indicate specific conditions.

CT imaging, MRI with contrast, and less common diagnostic tests such as amyloid PET scan can be beneficial in evaluating patients with suspected neurocognitive disorder. However, these are usually reserved for more specific clinical scenarios.

INSIDE THIS ISSUE

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This material summarizes key elements of Appropriate Use Criteria (AUC) developed by the CDI Quality Institute's Provider Led Entity (PLE). The CDI Quality Institute PLE has been qualified by the Centers for Medicare and Medicaid Services to develop AUC to guide the ordering of advanced imaging studies. The entire AUC library is available at myCDI.com/PLE.

This edition of *The Consult* summarizes criteria developed by Dr. Hostetter and a panel of experts:

- Mohit Agarwal, MD; Assistant Professor of Radiology, Medical College of Wisconsin
- Lawrence Cowsill, DO, internist; McLaren Healthcare, MI
- Malgorzata Franczak, MD; Professor of Neurology, Medical College of Wisconsin
- Thomas Gilbert, MD, MPP; CDI Chief Clinical Officer and PLE Chair, MN
- Susan Minette, DO; neurologist; Noran Neurological Clinic, MN

Clinical decision support (CDS) is not intended to replace clinician judgment, but rather to provide information to assist care team members in managing the complex and expanding volume of biomedical and person-specific data needed to make timely, informed, and higher-quality decisions based on current clinical science (National Academy of Medicine, 2017).

CLINICAL SCENARIOS

The strength of recommendations for imaging is indicated as follows:

- Green = indicated
- Yellow = indicated in specific scenarios
- Orange = probably not indicated, with limited exceptions
- Red = not indicated

SCENARIO #1: IMAGING INDICATIONS

Mild Cognitive Impairment:	
Green	MRI brain without contrast
Yellow	CT head without contrast
Yellow	Amyloid PET or FDG-PET in atypical cases or when an Alzheimer dementia subtype is suspected, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
Yellow	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
Orange	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
Red	Functional MRI; MR spectroscopy; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

SCENARIO #1: CLINICAL NOTES

- Mild cognitive impairment (MCI) is a condition in which individuals demonstrate cognitive impairment with minimal impairment of instrumental activities of daily living (IADL) (Petersen et. al. [AAN] 2018).
- This change can occur in a variety of cognitive domains, including memory, executive function, attention, language and visuospatial skills. An impairment in episodic memory is seen most commonly in MCI patients who subsequently progress to AD dementia (Albert et. al [NIA-AA] 2011).
- The key criteria that distinguish MCI from dementia are preservation of independence in functional abilities (ADLs and IADLs) and lack of significant impairment in social or occupational functioning (Langa & Levine 2014).
- Very rapid cognitive decline (weeks to months) is not typical of MCI due to Alzheimer's disease and should raise concerns for other causes such as neoplasm, metabolic disorders, or prion disease (Langa & Levine 2014).
- Structural brain MRI may rule out other potential causes for cognitive decline, such as subdural hematoma, stroke, normal pressure hydrocephalus, or tumor, and should be considered if the history, physical, or laboratory studies suggest one of these causes (Ries et. al. 2008).
- 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 (Moonis et. al. [ACR] 2019).
- Amyloid PET and FDG-PET imaging may be useful in the evaluation of patients with amnestic MCI. If positive, these patients can be monitored closely for any progression/conversion to Alzheimer's disease (PLE expert panel consensus opinion).
- Normal FDG-PET scan findings, in the presence of the suspicion of dementia, make a neurodegenerative diagnosis less likely (Filippi et. al. [EFNS] 2012, class II/level A recommendation).
- AD-like metabolic patterns in patients with MCI are predictive of conversion to AD within several years (Filippi et. al. [EFNS] 2012, class II/level A recommendation).

SCENARIO #2: IMAGING INDICATIONS

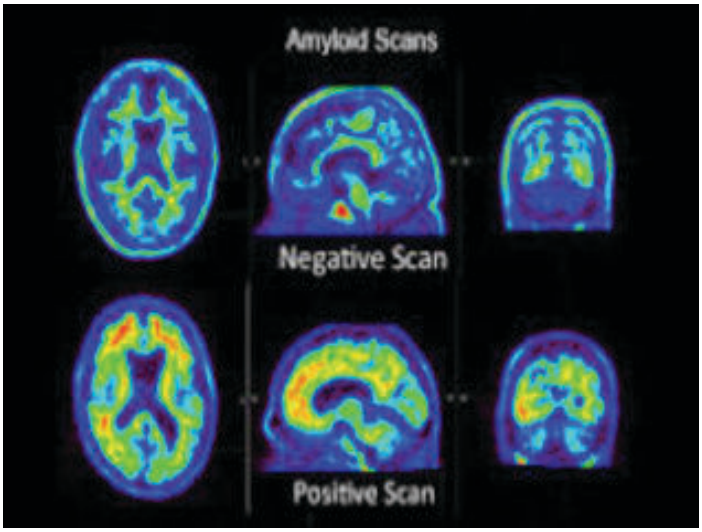
Possible Alzheimer's disease (AD):*	
Green	MRI brain without contrast
Yellow	CT head without contrast
Yellow	Amyloid PET or FDG-PET in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
Yellow	Perfusion SPECT in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
Yellow	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
Orange	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
Red	Functional MRI; MR spectroscopy; Dopaminergic SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

* A diagnosis of possible Alzheimer's disease is made in either of the following circumstances (McKhann et. al. 2011):

A. Atypical course – meets core clinical criteria in terms of nature of cognitive deficits for AD dementia, but either with sudden onset or demonstrates insufficient historical detail or objective cognitive documentation of progressive decline.

B. Etiologically mixed presentation – meets all core clinical criteria for AD dementia but has evidence of another concomitant neurological disease, medical comorbidity, or medication use that could have substantial effect on cognition.

Scenario #2: Possible Alzheimer's Disease



Amyloid PET scan (only utilized in specific clinical situations at specialist request) demonstrates amyloid plaque uptake depicted by areas of red/orange characteristic of Alzheimer's disease. Hypometabolism of the medial temporal lobes depicted by areas of blue/green corresponding to hippocampal atrophy.

SCENARIO #2: CLINICAL NOTES

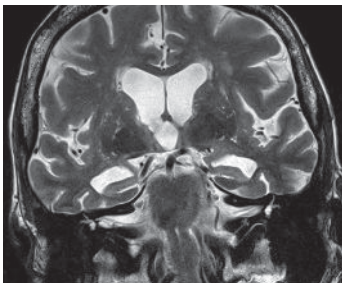
- AD pathology can manifest itself with clinically atypical presentations; memory is not the primary deficit, but visuospatial and visuoperceptual and/or language disturbances are prominent symptoms (Filippi et. al. [EFNS] 2012). Atypical presentations are more often seen in early-onset AD patients (Filippi et. al. [EFNS] 2012).
- The primary role of neuroimaging in the workup of patients with possible AD has typically been to exclude other significant intracranial abnormalities (Moonis et. al. [ACR] 2019).
- T1-weighted images should be carefully evaluated to assess specific patterns of focal atrophy, especially in the MTL, biparietal regions and posterior cingulate cortex (as seen in AD), temporal pole and/or frontal lobes (as seen in FTD), parietal/occipital lobe (as seen in posterior cortical atrophy), putamen, and midbrain and/or frontal lobe (as seen in progressive supranuclear palsy) (Fillippi et. al [EFNS] 2012).
- Combining MTL measures with other potentially informative markers, such as posterior cingulate cortex and precuneus volumetric measures, are likely to improve diagnostic confidence in AD patients, mainly in younger cases (Filippi et. al. [EFNS] 2012).
- In cases of atypical AD presentations, the involvement of the MTL is reported less consistently than that of lateral temporal and medial parietal regions (Filippi et. al. [EFNS] 2012).
- Early-onset AD patients (i.e., < 65 years) show less prominent MTL atrophy and greater involvement of the parietal, lateral temporal, and frontal regions compared to late-onset cases (Filippi et. al. [EFNS] 2012).
- Volumetric MRI can be used as a second-line imaging test for aiding in the diagnosis [of atypical AD] once the patient has been seen by a specialist (Moonis et. al. [ACR] 2019).
- Do not rule out Alzheimer's disease based solely on the results of CT or MRI scans (NICE 2018).

SCENARIO #3: IMAGING INDICATIONS

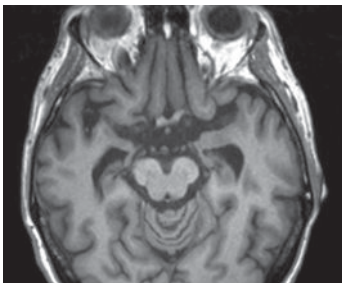
Probable Alzheimer's disease (AD):*	
🟢	MRI brain without contrast
🟡	CT head without contrast
🟡	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
🟠	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
🟠	Amyloid PET, except in cases with atypical presentations at specialist request when all other tests are inconclusive and the results will change management
🔴	Functional MRI; MR spectroscopy; FDG-PET; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

* Probable Alzheimer's disease is generally defined as dementia with insidious onset, a clear history of cognitive worsening, cognitive deficits (amnestic or nonamnestic) evidence on history and examination, and no evidence of another concurrent active neurological disease, medical comorbidity, or use of medication (McKhann et. al. 2011).

Scenario #3: Probable Alzheimer's Disease



Coronal T1 weighted MR image demonstrates typical hippocampal atrophy along the medial temporal lobe with corresponding dilatation of the temporal horn of the lateral ventricles.



Corresponding Axial T1 weighted MR image confirms the hippocampal atrophy with the dilated temporal horn of the lateral ventricles.

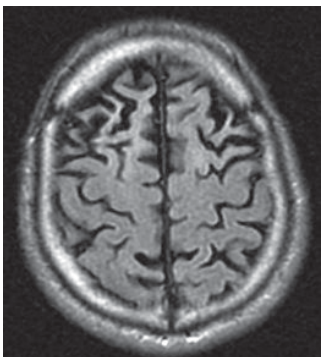
SCENARIO #3: CLINICAL NOTES

- Typical late-onset AD is radiologically characterized by global atrophy, especially in the medial temporal lobe (hippocampus and entorhinal cortex) (Health Quality Ontario 2014; Filippi et. al. [EFNS] 2012).
- The presence of temporoparietal atrophy is highly associated with AD (Filippi et. al. [EFNS] 2012).
- The primary role of neuroimaging in the workup of patients with probable AD has typically been to exclude other significant intracranial abnormalities (Moonis et. al. [ACR] 2019).
- Do not rule out Alzheimer's disease based solely on the results of CT or MRI scans (NICE 2018).

SCENARIO #4: IMAGING INDICATIONS

Frontotemporal degeneration/frontotemporal dementia (FTD) spectrum disorder:	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	Amyloid PET or FDG-PET, except in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • The results will change management
●	Perfusion SPECT, except in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • The results will change management • PET imaging is not available
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; Dopaminergic SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

Scenario #4: Frontotemporal dementia (FTD)



Axial Flair MR image demonstrates bilateral frontal lobe atrophy with cortical volume loss and prominent sulci typical of frontotemporal dementia.

SCENARIO #4: CLINICAL NOTES

- Frontotemporal degeneration/frontotemporal dementia is a clinically and pathologically heterogeneous group of disorders characterized collectively by relatively selective progressive atrophy and neuronal loss of the frontal and/or temporal lobes (Health Quality Ontario 2014; Sorbi et. al. [EFNS/ENS] 2012). Frontotemporal [lobe] degeneration represents the pathologic process whereas frontotemporal dementia refers to a clinical syndrome (Filippi et. al. [EFNS] 2012).
- Behavioral variant FTD (bvFTD) represents half of all cases, and is characterized by personality changes and inappropriate social and interpersonal conduct (Health Quality Ontario 2014; Sorbi et. al. [EFNS/ENS] 2012).
- Primary progressive aphasia (PPA) involves changes in the ability to communicate–to use language to speak, read, write, and understand what others are saying. Problems with memory, reasoning, and judgment are not apparent at first but can develop over time (National Institute on Aging, 2017). There are three types of PPA: semantic variant, nonfluent/agrammatic variant, and logopenic variant.
- Two rare neurological disorders associated with FTD occur when parts of the brain that control movement are affected. These disorders may also affect thinking and language abilities (National Institute on Aging, 2017):
  - Corticobasal degeneration (CBD) is characterized by asymmetric cortical dysfunction, often affecting motor control of a limb, along with executive dysfunction, rigidity, a jerky postural tremor, myoclonus, dystonia, and a gait disorder. Speech may be disrupted owing to apraxia or non-fluent aphasia (Budson & Solomon 2016).
  - Progressive supranuclear palsy (PSP) is an uncommon atypical parkinsonian syndrome, clinically characterized by prominent postural instability and falls, vertical supranuclear gaze palsy, and frontal-subcortical dementia (Stamelou & Oertel 2017).
- T1-weighted images should be evaluated to assess specific patterns of focal atrophy, especially in the temporal pole and/or frontal lobes (as seen in FTD) (Filippi et. al. [EFNS] 2012).
- The pattern of atrophy is more useful than atrophy of single regions in the differential diagnosis of bvFTD compared with AD: knife-like, severe frontotemporal atrophy combined with dilatation of frontal horn, and an anterior greater than posterior gradient is suggestive of a diagnosis of FTD (Filippi et. al. [EFNS] 2012, class II/level A recommendation; Sorbi et. al. [EFNS/ENS] 2012).
- A normal structural MRI scan should prompt the clinician to reconsider a diagnosis of bvFTD, if clinically severe, and semantic variant PPA (Filippi et. al. [EFNS] 2012, good practice point). The PLE expert panel noted that structural MRI is not specific in the diagnosis of semantic variant PPA (PLE expert panel consensus opinion).
- 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 (Moonis et. al. [ACR] 2019).
- Although an overlap of functional abnormalities between FTD and AD has been shown to occur, the presence of posterior temporal and parietal brain hypoperfusion or hypometabolism is predictive of a pathological diagnosis of AD, whereas a disproportionate reduction in frontal perfusion/metabolism is more common in FTD cases (Filippi et. al. [EFNS] 2012).
- 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 (Moonis et. al. [ACR] 2019).
- 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 (Moonis et. al. [ACR] 2019).
- Do not rule out frontotemporal dementia based solely on the results of structural, perfusion or metabolic imaging tests (NICE 2018).

SCENARIO #5: IMAGING INDICATIONS

Suspected dementia with Lewy bodies (DLB):	
🟢	MRI brain without contrast
🟡	CT head without contrast
🟡	Dopaminergic SPECT to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic
🟡	I-MIBG cardiac scintigraphy to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or indeterminate
🟡	FDG-PET to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or non-diagnostic
🟡	Perfusion SPECT to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or non-diagnostic
🟡	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
🟠	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
🔴	Functional MRI; MR spectroscopy; amyloid PET; diffusion tensor imaging

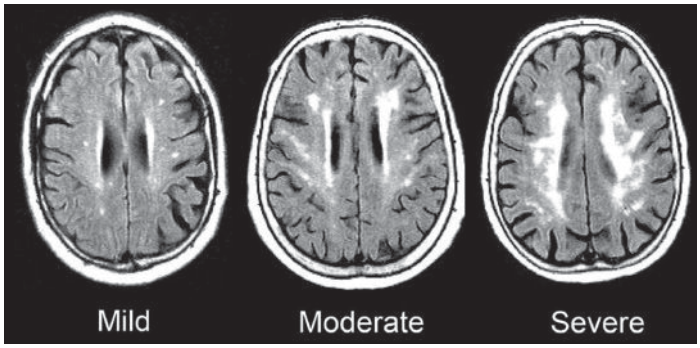
SCENARIO #5: CLINICAL NOTES

- Dementia with Lewy bodies accounts for up to 15% of cases, with classic features of Parkinsonism, visual hallucinations, and fluctuating cognition and level of alertness (Health Quality Ontario 2014; Sorbi et. al. [EFNS/ENS] 2012).
  - DLB fluctuations are typically delirium-like, occurring as spontaneous alterations in cognition, attention and arousal. They include waxing and waning episodes of behavioral inconsistency, incoherent speech, variable attention, or altered consciousness that involves staring or zoning out (McKeith et. al. 2017).
  - Recurrent, complex visual hallucinations occur in up to 80% of patients with DLB and are a frequent clinical signpost to diagnosis. Patients are typically able to report these experiences, as are observant caregivers (McKeith et. al. 2017).
  - Spontaneous parkinsonian features, not due to antidopaminergic medications or stroke, are common in DLB, eventually occurring in over 85% (McKeith et. al. 2017).
- Supportive clinical features of DLB include: severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction; hypersomnia; hyposmia; systematized delusions; apathy; anxiety; and depression (McKeith et. al. 2017).
- No established structural MRI pattern is characteristic for DLB (Filippi et. al. [EFNS] 2012, class II, level A; Sorbi et. al. [EFNS/ENS] 2012). However, the absence of MTL atrophy on CT or MRI may be suggestive of a diagnosis of DLB compared with AD (Filippi et. al. [EFNS] 2012, class II, level A).
- Similar to AD, a diffuse pattern of global grey matter atrophy including temporal, parietal, frontal, and insular cortices may occur in DLB (Filippi et. al. [EFNS] 2012).
- Volumetric MRI can be done as a secondary test to support the diagnosis of DLB (Moonis et. al. [ACR] 2019).
- Generalized low uptake on FDG-PET/CT with occipital hypometabolism has been demonstrated and is a useful supportive imaging biomarker (Moonis et. al. [ACR] 2019).
- If one or more of the following is found, associated with one or more core clinical features, probable DLB should be diagnosed (McKeith et. al. 2017):
  - Reduced DAT update in basal ganglia demonstrated by SPECT or PET imaging.
  - Reduced uptake on I-MIBG myocardial scintigraphy.
  - Polysomnography (PSG) confirmation of REM sleep without atonia.

SCENARIO #6: IMAGING INDICATIONS

Suspected vascular dementia:	
🟢	MRI brain without contrast
🟡	CT head without contrast
🟡	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
🟠	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
🔴	Functional MRI; MR spectroscopy; PET; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

Scenario #6: Cerebrovascular disease (vascular dementia)



Axial Flair MR images in 3 separate patients demonstrates varying degrees of periventricular and subcortical white matter signal hyperintensities which are typical of chronic small vessel ischemic changes.

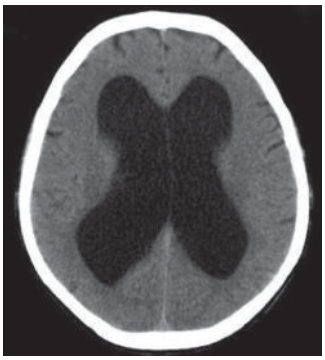
SCENARIO #6: CLINICAL NOTES

- It is particularly difficult to attribute clinical significance to evidence of cerebrovascular disease in patients with cognitive impairment. Vascular changes on CT or MRI do not preclude a diagnosis of degenerative dementia, especially in older age. A diagnosis of vascular dementia should only be made where the vascular lesion(s) can explain the cognitive deficit (Filippi et. al. [EFNS] 2012).
- Bilateral infarcts in the area of the anterior cerebral artery, infarcts in the area of the posterior cerebral artery, association areas, or watershed regions are thought to be causative of large-vessel vascular dementia (Filippi et. al. [EFNS] 2012).
- Extensive white matter lesions involving >25% of the white matter, or multiple basal ganglia, thalamic and frontal white matter lacunar infarcts, or bilateral thalamic lesions are considered relevant radiological lesions associated with small-vessel vascular dementia (Filippi et. al. [EFNS] 2012).
- DWI sequences can be useful to identify recent infarcts in patients with vascular dementia, transient global amnesia or vasculitis (Filippi et. al. [EFNS] 2012).

SCENARIO #7: IMAGING INDICATIONS

Suspected normal pressure hydrocephalus (NPH):	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	In-111 DTPA cisternography with SPECT/CT, except at specialist request when all other tests are inconclusive and the results will change management
●	Perfusion SPECT, except at specialist request when all other tests are inconclusive and the results will change management
●	Dopaminergic SPECT, except at specialist request when all other tests are inconclusive and the results will change management
●	Functional MRI; MR spectroscopy; PET; I-MIBG cardiac scintigraphy; diffusion tensor imaging

Scenario #7: Normal pressure hydrocephalus (NPH)



Axial CT scan of the brain demonstrates marked dilatation of the lateral ventricles out of proportion to cerebral atrophy with no secondary signs of acute hydrocephalus. NPH can present with the clinical triad of gait apraxia, urinary incontinence and dementia.

SCENARIO #7: CLINICAL NOTES

- Normal pressure hydrocephalus (NPH) is a syndrome which classically presents with dementia, gait disturbance and urinary incontinence, and is associated with ventricular dilation and normal cerebrospinal fluid pressure. The symptoms can be reversed by CSF shunt surgery (Mori et. al. 2012).
- NPH can be either idiopathic (iNPH) or secondary to known risk factors. iNPH constitutes the majority of cases (Isaacs et. al. 2018).
  - iNPH is primarily observed in patients age >65 years and clinically characterized by the presence of neurologic gait impairment plus additional features of cognitive impairment and urinary incontinence (Isaacs et. al. 2018).
  - Secondary NPH may result from subarachnoid hemorrhage or meningitis (Mori et. al. 2012).
- 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 (Moonis et. al. [ACR] 2019).
- The finding of tight high convexity subarachnoid spaces can differentiate iNPH from cerebral atrophy in patients with Alzheimer's disease with high sensitivity and specificity (Mori et. al. 2012).
- Cerebral atrophy may be present in some cases, but its presence does not rule out iNPH. Hippocampal atrophy and widening of the parahippocampal sulci are mild compared with Alzheimer's disease, which is useful to differentiate iNPH from Alzheimer's disease (Mori et. al. 2012).
- Perfusion of the cortices at the high convexity, and medial parietal and frontal lobes is relatively increased due to increased gray matter density and decreased CSF spaces in these regions, which are useful in differentiating iNPH from other dementia illnesses including Alzheimer's disease (Mori et. al. 2012).

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Summary: Appropriate Use of Advanced Imaging in Patients with a Suspected Neurocognitive Disorder

● = indicated, ● = indicated in specific scenarios, ● = probably not indicated, with limited exceptions, and ● = not indicated

SCENARIO #1: IMAGING INDICATIONS

Mild Cognitive Impairment:	
●	MRI brain without contrast
●	CT head without contrast
●	Amyloid PET or FDG-PET in atypical cases or when an Alzheimer dementia subtype is suspected, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

SCENARIO #2: IMAGING INDICATIONS

Possible Alzheimer's disease (AD) – atypical course or etiologically mixed presentation:	
●	MRI brain without contrast
●	CT head without contrast
●	Amyloid PET or FDG-PET in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
●	Perfusion SPECT in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • Other diagnoses have been excluded by MRI or CT • The results will change management
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; Dopaminergic SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

SCENARIO #3: IMAGING INDICATIONS

Probable Alzheimer's disease (AD):*	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Amyloid PET, except in cases with atypical presentations at specialist request when all other tests are inconclusive and the results will change management
●	Functional MRI; MR spectroscopy; FDG-PET; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

* Probable Alzheimer's disease is generally defined as dementia with insidious onset, a clear history of cognitive worsening, cognitive deficits (amnestic or nonamnestic) evidence on history and examination, and no evidence of another concurrent active neurological disease, medical comorbidity, or use of medication (McKhann et. al. 2011).

SCENARIO #4: IMAGING INDICATIONS

Frontotemporal degeneration/frontotemporal dementia (FTD) spectrum disorder:	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	Amyloid PET or FDG-PET, except in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • The results will change management
●	Perfusion SPECT, except in atypical cases or to differentiate AD from FTD, and all of the following apply: • At specialist request • All other tests (history, physical, structural imaging, lab testing) are inconclusive • The results will change management • PET imaging is not available
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; Dopaminergic SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

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Summary: Appropriate Use of Advanced Imaging in Patients with a Suspected Neurocognitive Disorder

● = indicated, ● = indicated in specific scenarios, ● = probably not indicated, with limited exceptions, and ● = not indicated

SCENARIO #5: IMAGING INDICATIONS

Suspected dementia with Lewy bodies (DLB):	
●	MRI brain without contrast
●	CT head without contrast
●	Dopaminergic SPECT to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic
●	I-MIBG cardiac scintigraphy to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or indeterminate
●	FDG-PET to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or non-diagnostic
●	Perfusion SPECT to distinguish DLB from (PCA variant) AD when clinical criteria are non-diagnostic and Dopaminergic SPECT is not available or non-diagnostic
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; amyloid PET; diffusion tensor imaging

SCENARIO #6: IMAGING INDICATIONS

Suspected vascular dementia:	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	Functional MRI; MR spectroscopy; PET; SPECT; I-MIBG cardiac scintigraphy; diffusion tensor imaging

SCENARIO #7: IMAGING INDICATIONS

Suspected normal pressure hydrocephalus (NPH):	
●	MRI brain without contrast
●	CT head without contrast
●	MRI brain with contrast to characterize abnormalities seen on initial MRI brain without contrast or CT head; OR CT head with contrast to characterize abnormalities seen on initial CT head without contrast
●	MRI brain with and without contrast or CT head with and without contrast, except when concerned for an intracranial neoplasm or infectious/inflammatory disease as an etiology in atypical cases, or when there is rapid neurological decline
●	In-111 DTPA cisternography with SPECT/CT, except at specialist request when all other tests are inconclusive and the results will change management
●	Perfusion SPECT, except at specialist request when all other tests are inconclusive and the results will change management
●	Dopaminergic SPECT, except at specialist request when all other tests are inconclusive and the results will change management
●	Functional MRI; MR spectroscopy; PET; I-MIBG cardiac scintigraphy; diffusion tensor imaging

Examples provided throughout this document are common situations. Consider consultation with your local radiologist to determine what procedure would best suit you and your patient's unique needs for diagnostic imaging assessment of the neurocognitive disorder.