IMAGING IN DEMENTIA

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DISCLOSURES

None
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Learning Objectives

- Obtain a familiarity of Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and nuclear medicine techniques such as Positron Emission Tomography (PET) and Single-Photon Emission Computed Tomography (SPECT).

- Solidify a general knowledge of appropriate imaging evaluation of the different categories of dementia.

- Gain a basic understanding of the most common radiologic findings of the various forms of dementia on different neuroimaging modalities used in the evaluation of those with dementia.
Computed Tomography (CT)

- CT x-ray tube emits photons
- Photons go through tissue
- Detected on opposite side
- Complex mathematical algorithm
- CT reconstructed images of body
Computed Tomography (CT)

- Hyperdense- bright
  - Bones, blood, calcium
- Hypodense- dark
  - Air, fat

Appropriate for excluding acute findings or reversible causes of symptoms

A few common terms in brain imaging:
- Grey-white junction is intact
- Hypodensity of the deep cerebral white matter
- Global parenchymal volume loss
Computed Tomography (CT)
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**Advantages**
- Easily accessible
  - Acute processes
  - Trauma
- Relatively fast
- Useful for bony pathology
- Cheaper than MRI

**Disadvantages**
- Radiation
  - Methods to decrease dose
- Not as good for soft tissue characterization or bone marrow evaluation
- Large body habitus
**Magnetic Resonance Imaging (MRI)**

External Magnetic Field

Protons Align

Alignment Disrupted With Radiofrequency Energy

Protons Return To Resting State And Emit RF Energy

Frequency Information Turned Into Signal With Intensity
Hyperintense, hyperintensity- bright
Hypointense, hypointensity- dark

Appropriate to exclude mass, infarct, hemorrhage, etc that can cause symptoms

A few common terms in brain imaging:
- Scattered T2 FLAIR hyperintensities
  - Chronic white matter disease, chronic microangiopathic changes
- Global parenchymal volume loss, commensurate prominence of the sulci and ventricles
- No restricted diffusion
Magnetic Resonance Imaging (MRI)
Magnetic Resonance Imaging (MRI)
Magnetic Resonance Imaging (MRI)

Sagittal T1

Coronal T1 Post-Contrast
Magnetic Resonance Imaging (MRI)

**Advantages**
- Better soft tissue characterization and bone marrow evaluation
- No ionizing radiation
- Imaging in multiple planes
- Various sequences
- Functional imaging and white matter tract localization

**Disadvantages**
- Subject to motion and artifact
- Body habitus
- Inferior to CT for some bony injury
- Longer acquisition time
- More expensive
- Contraindications to MRI
Magnetic Resonance Imaging (MRI)

Gadolinium based IV contrast

- Mass or lesion
- Infection
- Metastatic disease
- Demyelinating process
- Cranial nerve lesions
- Hearing loss, tinnitus, IAC evaluation
- Pituitary
Fluorine 18 ($^{18}$F)-labeled glucose most common
- FDG- taken up in body and metabolized as glucose
- [$^{18}$F] FDG uptake detected when $^{18}$F decays and emits positron
  - Positron travels through tissue and collides with electron
  - Releases a photon which is detected
- PET image is a map of the distribution of the annihilations occurring, and thus metabolism
- PET images can be superimposed on CT images
Positron Emission Tomography (PET)

- Fluorine 18 ($^{18}$F) labeled glucose most common
  - FDG- tagged as glucose
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  - Positron collides with electron
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- PET images can be superimposed on CT images
Amyloid PET
- detect *in vivo* Aβ amyloid in the brain, Alzheimer’s Dz
- F-18 labeled compounds most common, carbon-11 Pittsburgh compound-B (PIB)

May be positive in cognitively normal subjects who don’t develop AD and those with other forms of non-AD dementia
- Cannot distinguish between amyloid angiopathy
- Often times positive in dementia with Lewy body

Negative amyloid PET scan likely means a low probability of AD
Positron Emission Tomography (PET)

Amyloid PET detect in vivo Aß amyloid in the brain, Alzheimer's Dz.

Carbon-11 Pittsburgh compound-B (PIB), a few newer F-18 labeled compounds also approved.

May be positive in cognitively normal subjects who don't develop AD and those with other forms of non-AD dementia.

Cannot distinguish between amyloid angiopathy.

Often times positive in dementia with Lewy body.

Negative amyloid PET scan likely means a low probability of AD.
Cognitive complaint with objectively confirmed impairment

AD as a possible diagnosis, but diagnosis is uncertain after a comprehensive evaluation by a dementia expert

When knowledge of the presence or absence of amyloid is expected to increase diagnostic certainty and alter management

- Patients with persistent or progressive unexplained MCI
- Patients satisfying core clinical criteria for AD due to any cause concomitant with an atypical course or of mixed etiology
- Patients with progressive dementia and atypically early age of onset (usually defined as 65 years or less in age)
Amyloid PET inappropriate for:

- Evaluation of non-AD types of dementias (FTD, etc)
- Patients with core clinical criteria for probable AD with typical age of onset (≥ 65 yo)
- To determine dementia severity
- Based solely on a positive family history of dementia or presence of apolipoprotein E (APOE)ε4
- Patients with a cognitive complaint that is unconfirmed on clinical examination
- Substitute for genetic testing for mutation that cause or are associated with AD
- Asymptomatic individuals
- Nonmedical use (e.g., legal, insurance coverage, or employment screening)
Single-Photon Emission Computed Tomography (SPECT)

- Tc99m-HMPAO most common
  - Most commonly used for brain imaging, evaluates CBF
- I-123 Ioflupane: imaging of the dopamine transporter
  - Defect in the nigrostriatal pathway in Parkinson disease and dementia with Lewy bodies
- Gamma emission detected by gamma camera
- Tomography enables localization of radioactivity and localization of concentration
- Poorer spatial resolution than PET
- Cheaper than PET
- Least likely to be used in evaluation for dementia
  - ACR appropriateness 2015-
    - Mostly 2 or 3 (Usually not appropriate)
Single-Photon Emission Computed Tomography (SPECT)
Categories of Dementia

- Probable Alzheimer’s Disease
- Possible Alzheimer’s Disease
- Suspected frontotemporal dementia
- Suspected Dementia with Lewy bodies
- Suspected vascular dementia
- Suspected prion disease
- Suspected normal pressure hydrocephalus
- Suspected Huntington disease
- Clinical features suggestive of neurodegeneration with brain iron accumulation
- Parkinson disease, typical clinical features; responsive to levodopa
- Parkinson disease, atypical clinical features; not responsive to levodopa
- Motor neuron disease
ACR Appropriateness Criteria - 2015

- 7, 8, 9: Usually appropriate
- 4, 5, 6: May be appropriate
- 1, 2, 3: Usually not appropriate
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Probable AD:

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- FDG-PET/CT head: 6
- CT head without and with IV contrast; CT head with IV contrast: 4
- Amyloid PET: 2
- Tc-99m HMPAO SPECT: 2
Categories of Dementia

- Probable Alzheimer’s Disease
- **Possible Alzheimer’s Disease**
  - Suspected frontotemporal dementia
  - Suspected dementia with Lewy bodies
  - Suspected vascular dementia
  - Suspected prion disease
  - Suspected normal pressure hydrocephalus
  - Suspected Huntington disease
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Possible AD:

- MRI head without IV contrast: 8
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Alzheimer's Disease

- Most common > 65 yo
- Insidious, progressive
- Impairment in memory and cognition
- Loss of functional independence in activities of daily living
- Primary goal of imaging is to exclude other significant intracranial abnormalities
Alzheimer's Disease

- **MRI/CT:**
  - Initially normal with progression of hippocampal, amygdala, and temporoparietal volume loss

- **FDG-PET:**
  - Posterior cingulate, parietal, and medial temporal hypometabolism
  - Spares motor and visual cortex

- **Amyloid PET:**
  - Positive amyloid

- **HMPAO SPECT:**
  - Hypoperfusion hippocampi and/or temporoparietal regions

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AMYLOID ANGIOPATHY

MRI:
Susceptibility weighted image (SWI)

http://www.centerforintegratedneurology.com
Categories of Dementia

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ACR Appropriateness Criteria - 2015

Suspected frontotemporal dementia

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- FDG-PET/CT head: 6
- CT head without and with IV contrast; CT head with IV contrast: 4
- Amyloid PET: 2
- Tc-99m HMPAO SPECT: 2
Frontotemporal Dementia

- 3rd most common form of dementia
- Most common form of dementia < 60 yo
- Onset rare after age 75
- Changes in personality, behavior, and/or language
- Behavioral FTD and language-predominant cognitive decline FTD (primary progressive aphasia)
**Frontotemporal Dementia**

- **MRI/CT:**
  - Atrophy and neuronal volume loss frontal and anterior temporal lobes

- **FDG-PET:**
  - Frontal and anterior temporal lobe hypometabolism; parietal lobe involved late

- **Amyloid PET:**
  - Negative

- **HMPAO SPECT:**
  - Frontal hypoperfusion

*Desai et al. Neurographics; 7(6):416–436*
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- Parkinson disease, atypical clinical features; not responsive to levodopa
- Motor neuron disease
Suspected dementia with Lewy bodies

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- FDG-PET/CT head: 6
- CT head without and with IV contrast; CT head with IV contrast: 5
- Tc-99m HMPAO or I-123 SPECT: 5
- Amyloid PET: 2
3 classic features of Dementia with Lewy bodies:
- Parkinsonism, visual hallucinations, and fluctuating cognition and level of alertness
Dementia with Lewy Bodies

- MRI/CT:
  - Initially normal with progression to diffuse atrophy in advanced disease

- FDG-PET:
  - Generalized FDG hypometabolism with involvement of visual cortex
  - Spares motor cortex

- Amyloid PET:
  - + in 2/3 patients

- I-123 Ioflupane SPECT:
  - Dopamine transporter
  - Striatal activity low in DLB and PD
Categories of Dementia

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- Suspected frontotemporal dementia
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ACR Appropriateness Criteria - 2015

Suspected vascular dementia

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- MRA head and neck; CTA head and neck; US doppler Cartoid Duplex: 6
- CT head without and with IV contrast; CT head with IV contrast: 5
- FDG-PET/CT head: 4
- Tc-99m HMPAO SPECT: 2
Some prefer the term "vascular cognitive impairment (VCI)"

Cognitive and functional impairment due to strokes or small vessel disease
- multi-infarct dementia,
- single-infarct dementia,
- and small vessel disease

Not uncommon to occur with AD
Suspected Vascular Dementia

- **MRI/CT:**
  - White matter change, lacunar infarcts, encephalomalacia
  - Subcortical microhemorrhages or superficial lobar macrohemorrhages suggest amyloid angiopathy

- **FDG-PET:**
  - Focal hypometabolism corresponding to dz on MRI

- **Amyloid PET:**
  - Negative unless amyloid angiopathy

- **HMPAO SPECT:**
  - Not helpful in differentiating between AD

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Smith E.E. Clinical Science 2017; 131 (11) 1059-1068

http://www.centerforintegratedneurology.com
Subtype of vascular dementia:
- Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarctions and Leukoencephalopathy
- Mutations of the NOTCH3 gene on chromosome 19

Clinical findings:
- Age onset 30-50 yo typical
- Recurrent ischemic strokes, migraines with aura, cognitive decline, and mood disturbances
- Variable clinical course
- Long-term prognosis is poor
- Most frequent cause of death is pneumonia, followed by sudden unexpected death and asphyxia
MRI:

- Diffuse T2/FLAIR hyperintensities in the periventricular and subcortical white matter
  - Anterior temporal lobes
- Lacunar infarctions
  - Thalamus, basal ganglia, centrum semiovale, pons
- Scattered cerebral microbleeds
  - Low intensity foci on T2*/GRE or SWI sequences
Categories of Dementia

- Probable Alzheimer’s Disease
- Possible Alzheimer’s Disease
- Suspected frontotemporal dementia
- Suspected dementia with Lewy bodies
- Suspected vascular dementia
- Suspected prion disease (Creutzfeld-Jakob, iatrogenic, or variant)
- Suspected normal pressure hydrocephalus
- Suspected Huntington disease
- Clinical features suggestive of neurodegeneration with brain iron accumulation
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Suspected prion disease (Creutzfeld-Jakob, iatrogenic, or variant)

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- CT head without and with IV contrast; CT head with IV contrast: 5
- FDG-PET/CT head: 5
- Tc-99m HMPAO SPECT: 5
Creutzfeldt Jakob Disease (Prion)

- Transmissible fatal neurodegenerative d/o caused by prions
- 4 main subtypes:
  - Sporadic, familial, iatrogenic, and variant CJD
  - Sporadic 85% of cases
  - vCJD associated with bovine spongiform encephalopathy
- Presents with rapidly progressive dementia, myoclonus, and multifocal neurologic dysfunction
Creutzfeld Jakob Disease (Prion)

- T2/FLAIR hyperintensity with restricted diffusion most commonly involving the bilateral BG and cerebral cortex +/- thalamus

Pulvinar "hockey stick sign"
Creutzfeld Jakob Disease (Prion)

- T2/FLAIR hyperintensity with restricted diffusion most commonly involving the bilateral BG and cerebral cortex +/- thalamus

“Cortical ribbon sign”
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Suspected normal pressure hydrocephalus

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 6
- CT head without and with IV contrast; CT head with IV contrast: 5
Normal Pressure Hydrocephalus

- Classic triad of dementia, gait disturbance, and urinary incontinence
CT/MRI:
- Ventricles enlarged out of proportion of parenchymal volume loss
- Exclude an obstructing mass/process
- Can be associated with chronic microvascular disease

Radiopaedia.org
Categories of Dementia

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ACR Appropriateness Criteria 2015

Suspected Huntington disease

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 5
- FDG-PET/CT head: 3
- Tc-99m HMPAO SPECT: 3
- CT head without and with IV contrast; CT head with IV contrast: 3
Huntington Disease

- Autosomal dominant
- Choreoathetosis, rigidity, dementia, and emotional disturbance
Huntington Disease

- **MRI/CT:**
  - Caudate and/or putamen atrophy
  - Signal change in striatum (caudate and lentiform nucleus)
  - Late disease with overall volume loss of brain parenchyma

- **HMPAO SPECT:**
  - May show hypometabolism of the striatum
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Clinical features suggestive of neurodegeneration with brain iron accumulation

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7
- CT head without IV contrast: 5
- CT head without and with IV contrast; CT head with IV contrast: 4
- FDG- PET/CT head: 3
- Tc-99m HMPAO SPECT: 3
Formerly known as Hallervorden-Spatz disease

Mutations in the gene encoding panthothenate kinase 2 (PANK 2)

First 2 decades of life

Progressive dystonia, oromandibular abnl, mental deterioration, pyramidal signs, retinal degeneration
MRI findings:
- Bilateral areas of hyperintensity within a hypointense zone in the medial globus pallidus on T2
- “Eye of tiger”

FDG-PET and SPECT:
- No specific findings
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ACR Appropriateness Criteria - 2015

Parkinson disease, typical clinical features; responsive to levodopa

- MRI head without IV contrast: 7, only trouble shooting
- MRI head without and with IV contrast: 7, only trouble shooting

- CT head without IV contrast: 6
- CT head without and with IV contrast; CT head with IV contrast: 5

- I-123 SPECT: 4
- Tc-99m HMPAO SPECT: 3
- FDG- PET/CT head: 3

- Amyloid PET: 2
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ACR Appropriateness Criteria—2015

Parkinson disease, atypical clinical features; not responsive to levodopa

- MRI head without IV contrast: 8
- MRI head without and with IV contrast: 7

- I-123 SPECT: 6

- CT head without IV contrast: 5
- CT head without and with IV contrast; CT head with IV contrast: 4

- Tc-99m HMPAO SPECT: 3
- FDG- PET/CT head: 3

- Amyloid PET: 2
Parkinson Disease

- Rigidity, short shuffling gait, bradykinesia, and cognitive impairment
- When clinical signs and symptoms and response to medication are typical of PD, neuroimaging is not required
- With unusual clinical features, incomplete or uncertain medication responsiveness, or clinical diagnostic uncertainty, imaging to exclude alternative pathologies may be indicated
Parkinson Disease

- MRI:
  - Occasionally see low signal in the substantia nigra on T2*/SWI

- I-123 Ioflupane SPECT:
  - Dopamine transporter
  - Striatal activity low in DLB and PD

- FDG-PET and HMPAO SPECT:
  - Not helpful
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- Motor neuron disease
Motor neuron disease

- MRI head without IV contrast: 8
- MRI spine without IV contrast: 8
- MRI head without and with IV contrast: 7
- MRI spine without and with IV contrast: 7
- CT head without IV contrast: 5
- CT head without and with IV contrast; CT head with IV contrast: 4
- Tc-99m HMPAO SPECT: 3
- FDG- PET/CT head: 3
Motor Neuron Disease

- ALS- Amyotrophic lateral sclerosis
  - Very rare
  - Usually > 50 yo
  - Degeneration of the corticospinal tract and lower motor neurons
  - Decreased motor strength and wasting of the muscles of the face, limbs, and diaphragm
    - UMN and LMN findings on clinical exam
  - Progressive loss of motor strength, with preservation of intellectual and sensory function
MRI/CT:

- Atrophy of frontal lobe in late disease
- Cortical spinal tract FLAIR hyperintensity and atrophy
- Increased deposition of iron in motor strip
  - T2 hypointensity
- Atrophy anterior and lateral spinal cord

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 4717
MRI head without IV contrast or MRI head without and with IV contrast recommended

Head CT without IV contrast used when MRI contraindicated or acute clinical changes

SPECT and PET sometimes used as a problem-solving tool, but not routinely recommended

MRA/CTA in suspected vascular dementia

Spine and brain imaging in motor neuron disease
Obtain a familiarity of Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and nuclear medicine techniques such as Positron Emission Tomography (PET) and Single-Photon Emission Computed Tomography (SPECT).

Solidify a general knowledge of appropriate imaging evaluation of the different categories of dementia.

Gain a basic understanding of the most common radiologic findings of the various forms of dementia on different neuroimaging modalities used in the evaluation of those with dementia.
References

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- Radiopaedia.org
- www.centerforintegratedneurology.com
THANK YOU!

Leslie Hartman, MD