Introduction

- Alzheimer's disease (AD) is the most frequent cause of dementia accounting for 50%-70% of dementia cases.
- Usual considerations include Alzheimer's Disease (AD); Vascular Dementia (VD); Lewy Body Disease (LBD); Frontotemporal Dementia (FTD), and subtypes including semantic dementia and corticobasal degeneration. Parkinson's Disease, Multiple System Atrophy (MSA), and Progressive Supranuclear Palsy (PSP).
- Optimal treatment and inclusion in clinical trials requires early and precise diagnosis.
- Amnestic and cognitive complaints can be the harbinger of a devastating degenerative disease that can be difficult to manage and treat, especially when the specific diagnosis is uncertain.
- Typical diagnosis usually occurs later in the disease process and is reliant on the correlation of presenting clinical findings, and abnormalities on imaging.
- As early as 2009 it was known that MRI with hippocampal volume measurement and posterior cingulate MRI spectroscopy improved ability to identify patients with prodromal dementia compared to MRI alone.
- Multimodal imaging combines structural (MRI, CT) and molecular imaging (PET, SPECT) and can provide diagnosis using disease specific testes and treatments that allow definitive diagnosis.
- MRI alone has progressed to a point where submillimeter resolution and markedly improved tissue contrast is available in most community outpatient and hospital centers.
- Advanced MRI techniques have been developed and studied for years but have not yet been routinely utilized in clinical outpatient practice.

Objectives

- Selected patients with complex symptomatology were evaluated with Multi-Parametric MRI in a standard clinical outpatient environment. The mpMRI data was summarized at the end of the imaging report and several diagnoses were suggested to the referring clinician.
- All MRI studies were interpreted by JLS and LAJ who were blinded to the symptoms.
- All neurologic exams were performed by LAJ.
- All MRI studies were performed on GE 1.5 Tesla MRI machines.
- Multi-Parametric MRI (mpMRI) Technique:
  - Standard Sequences
    - DHN, TSE, FLAIR, SHW or GRE T2w, T1w
  - Specialized Sequences
    - SWAN/SWI extremely sensitive to microbleeds in subcortical vascular dementia and acquired amyloid angiopathy. Cerebral microbleeds are an independent predictor of cognitive impairment.
  - MRI Spectroscopy: The literature supports use of MRS in dementia since 1992, especially in the posterior cingulate gyrus for the evaluation of suspected Alzheimer’s disease.
  - ASL: Used to assess cerebral blood flow noninvasively by magnetically labeling inflowing blood, using arterial blood as a contrast agent, providing information like FSGD-PET and SHW-T1w/HMPAO SPECT. ASL has been found to separate individual with mild AD from AD-MCI using a rCBF threshold of 40%. Quantitative volumetric MRI (NeuroQuant): The technique is an outcome of the ADNI (3G)project and initially focused on mental lobes/cerebral cortex. NeuroQuant was used to demonstrate brain atrophy in association with dementia since 2009.

Conclusions

- Readily available advanced MRI techniques (especially quantitative volumetric analysis, NeuroQuant), markedly improved the usefulness of the imaging study when added to the clinical findings. MRI exam time is approximately 45 minutes and patient cost is not significantly increased. Repeat mpMRI exam is often recommended in B-12 months because it is often important to determine the rate of progression of atrophy, an important parameter used to differentiate mild cognitive insufficiency from early AD and other degenerative diseases.
- Future Directions:
  - We are beginning to incorporate the addition of diffusion tensor imaging (DTI) to our mpMRI protocol to better understand white matter connectivity and its relation to cognitive and motor function.
  - Molecular Pathology in Behavioral Variant Frontotemporal Dementia. Journal of Molecular Neuroscience, 45, 372-387.
  - Molecular Pathology in Behavioral Variant Frontotemporal Dementia. Journal of Molecular Neuroscience, 45, 372-387.

Case Series

Dementia Patterns

Alzheimer’s Dementia
- Hippocampal atrophy is the best-established MRI biomarker of AD, accompanied by variable cortical atrophy and variable diffuse cortical atrophy. Hippocampal atrophy progresses in rate in AD is over 3.5%/year per year compared to MCI (1.0%-3.0%). ASL perfusion showed reduced CBF in the posterior cingulate gyri and posterior parietal cortex. ASL can predict cognitive decline and conversion from MCI to dementia. MRI lenthicles increase in MCI in the initial stages but with AD progression these increase in volume and increased Cho. MRI changes reflect neuronal loss/degeneration and gliosis.
- Frontotemporal lobar degeneration
- Clini-Pathologically segregated into 3 subtypes: frontotemporal dementia, semantic dementia, and progressive nonfluent aphasia. Different patterns of atrophy frequently occurred in right or left temporal or in the frontal lobe. MRI in temporoparietal gray shows more reduced NAA than mOCL in the precuneus, cuneus and posterior parietal-occipital cortices. MRI shows elevated choline in normal appearing white matter. ASL cannot differentiate AD from Lewy body dementia. Blood flow is markedly reduced in the same area as in AD.

Vascular Dementia
- Excessive white matter and basal ganglia lesions for age, frequently associated with microbleeds. In the context of vascular dementia, microbleeds are most likely to result from hypertensive vasculopathy to hypertension. Hemorrhagic centrifugal atrophy without a specific pattern, however there is a less pronounced hippocampal atrophy than with AD. ASL shows generalized delayed or decreased perfusion. Posterior corticular MRI frequently shows reduced NAA with normal myoelinated and enlarged white matter relative to normal compared to normal white matter.

Early onset Alzheimer Disease
- 63 y.o. female with progressive changes in cognitive functions, memory and awareness over two years. Multimodal MRI (mpMRI) shows hippocampal atrophy and altered rate of change over two years. MRI shows typical findings of AD with reduced NAA (reflecting neuronal density) and elevated mI (increased Glx activity). ASL shows decreased parietal perfusion similar to a FDG PET scan.
- Vascular Dementia
- 76 y.o. male with progressive cognitive insufficiency and armament disorder increasing in last month.
- Vascular Imaging shows excessive white matter disease burden is 3 SD above the mean. Normal frontal, temporal, parietal and temporal lobes, normal hippocampal and cortial grey matter volume. MRI shows reduced NAA with normal Cho and mI. ASL shows normal cortical and posterior cortical perfusion for age.

Frontotemporal Dementia
- 73 y.o. male with several years of progressive cognitive difficulty, memory, speech, and reading difficulty. Defocused speech, tachypnea and dystrophy. Higher cognitive functions are not as severely effected as would be seen in AD. NeuroQuant study is very abnormal. ASL to MRI shows reduced NAA and normal Cho and mI. ASL could not be performed. Ischemic white matter burden was normal age. Initial diagnosis was Lewy Body dementia but diagnosis after multiparametric MRI is right hemispheric dominant frontotemporal dementia, previously called Pick’s Disease.

Parkerson’s Plus Syndrome (Multisystem Atrophy-PD, MSA-P)
- 64 y.o. female with diagnosis of Parkinson’s disease 5 years ago. Dyskinesia, imbalance, poor response to levodopa. Multimodal MRI shows atrophy of cortical gray matter, brainstem, thalamus, ventral diencephalon, pallium, grey matter, white matter, and basal ganglia. MRI shows reduced NAA and normal Cho and mI. ASL shows normal cortical and hemiparetic perfusion. No excess white matter.

References