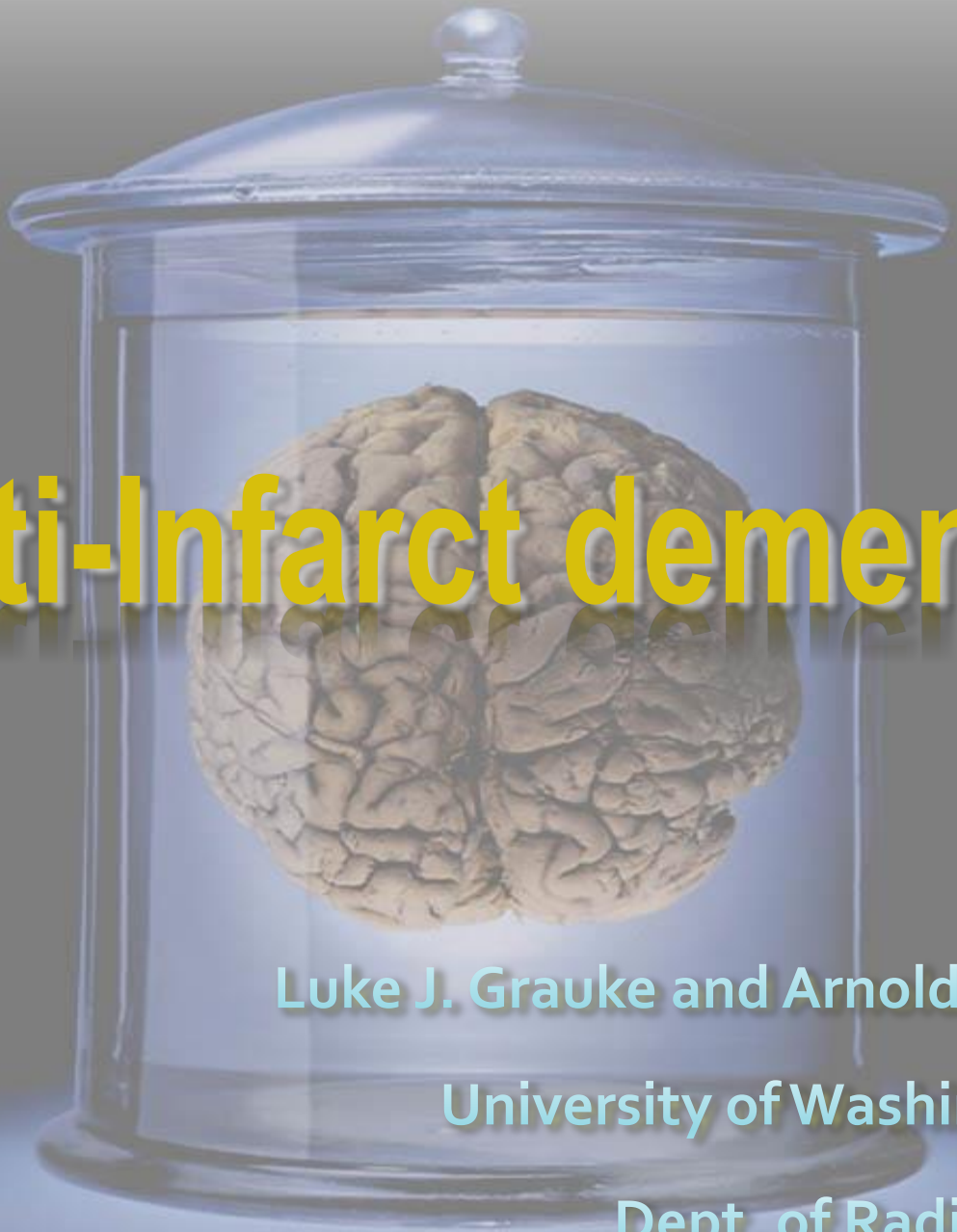
Multi-Infarct dementia



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Recommended reading:

- Advances in PET Imaging of Degenerative, Cerebrovascular, and Traumatic Causes of Dementia LB. Eisenmenger. Seminars in Nuclear Medicine, 2016-01-01, Volume 46, Issue 1, Pages 57-87.

- PET and SPECT in neurology. A. Otte, E Vries, R O Dierckx, A van Waarde

Historical Perspective

"I have observed in many, that when, the Brain being first indisposed, they have been distempered with a dullness of mind, and forgetfulness, and afterwards with a stupidity and foolishness, after that, have fallen into a palsie, which I often did predict."

--Thomas Willis (of Circle fame), 1684

Historical Perspective

- Otto Binswanger (1894) proposed the concept of “arteriosclerotic brain degeneration.”

- Alois Alzheimer first to separate another common dementia, dementia paralytica (neurosyphilis) from this “arteriosclerotic brain degeneration” and called it Binswanger’s disease.

Historical Perspective

- DSM –II (1968): The term "arteriosclerotic brain degeneration" was modified to "psychosis with cerebral arteriosclerosis."
- Hachinski (1974) proposed the term "Multi-Infarct dementia" and the first criteria for diagnosis of vascular dementia, the Hachinski Ischemic Score (HIS).

The Hachinski Ischaemic Score

Feature	Score
Sudden onset	2
Stepwise progression/deterioration	1
Fluctuating course	2
Nocturnal confusion	1
Relative preservation of personality	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
History of hypertension	1
History of strokes	2
Evidence of atherosclerosis	1
Focal neurological symptoms	2
Focal neurological signs	2

Vascular Dementia (VaD) Classifications

- Multiple current classifications with varying sensitivity and specificity (evolved from the Hachinski Ischemic Scale)
  - Diagnostic and Statistical Manual of Mental Disorders, DSM-IV
  - National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences, NINDS-AIREN
  - International Statistical Classification of Diseases, ICD-10
  - California Alzeimer's Disease Diagnostic and Treatment Centers, CAD-DTC
- Diagnostic Criteria rely on neuroimaging by CT/MRI for confirmation of cerebrovascular lesions.
  - Both large and small vessel ischemia.
- False positives are usually related to AD in combination with VaD.

VaD Morphology

- Large-vessel injuries:
  - Multiple cortical/subcortical infarcts
  - Single, strategically placed infarcts in areas crucial for cognition/behavior.
    - Angular gyrus
    - Basal forebrain
    - Thalamus
    - Ant or Post cerebral artery strokes
- Small vessel injuries:
  - Multiple basal ganglia and white matter lacunae
  - Extensive white matter lesions
- Patients can present with either large or small vessel injuries, or both.

Clinical Features in VaD

- Cognitive loss, often subcortical; memory impairment may be mild or spared.
- Executive dysfunction is common
- Clinical presentation can vary with location of infarcts
- Vascular brain lesions on neuroimaging
- A temporal link between lesions and clinical dementia
- Exclusion of other causes

Roman GC. J Am Geriatr Soc. 2003 May; 51(Suppl): S296-304.

Risk Factors

- Age
- Male sex
- HTN
- Hyperlipidemia
- MI
- Diabetes
- Generalized atherosclerosis
- CAD
- Smoking
- Prior stroke
- Pre stroke cognitive decline
- E4 allele of APOE
- Vascular disorders

Prevalence and Epidemiology

- Lack of clear and validated diagnostic criteria
- Complex brain pathologies, geographic and ethnic variations
- Considerable methodological differences

Therefore, highly variable prevalence numbers.

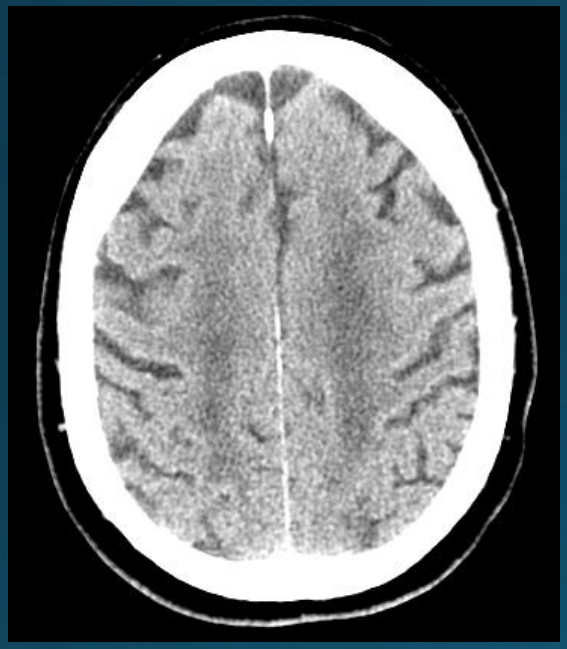
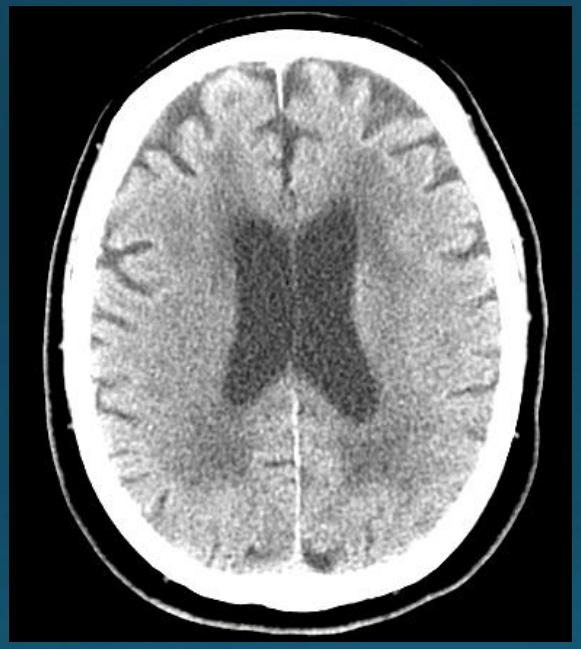
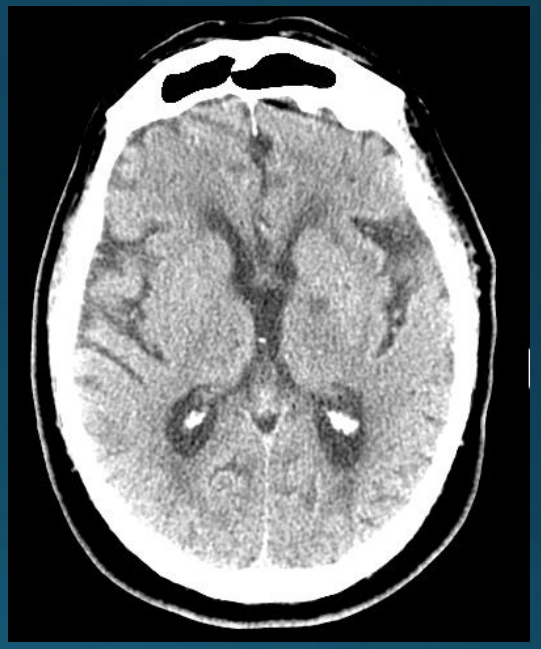
- Clinical studies: 4.5 - 39%
- Pathological studies: 0.03 - 35%
- Recent autopsy series: 23.6 – 35%.

Jellinger et al 2008

Pathogenesis in VaD

- Regional cerebral blood flow is reduced
- Oxidative stresses including free radicals
- Endothelial cell damage
- Chronic hypoperfusion
- Leukoaroiosis
- Changes in the small penetrating arteries and arterioles in the white matter

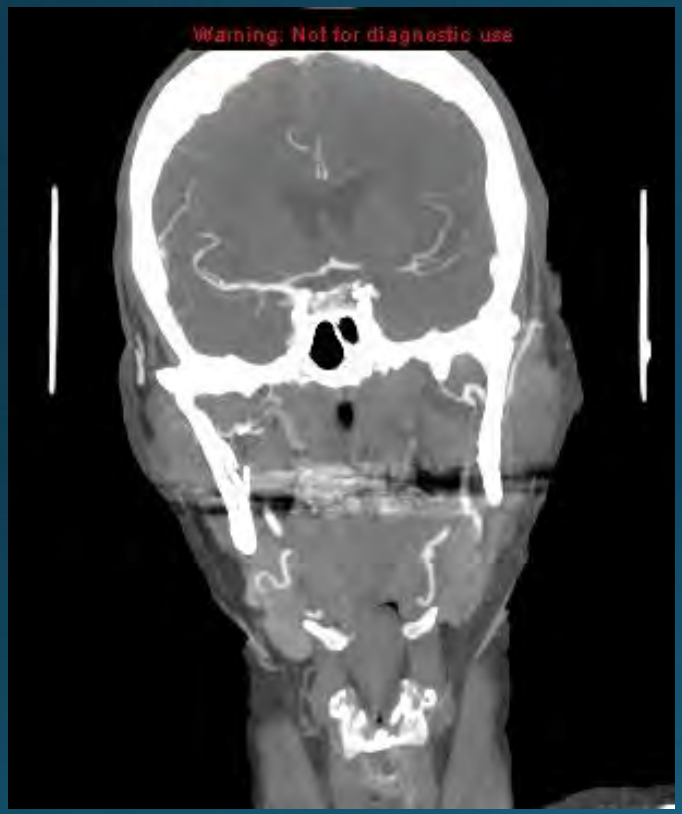
Neuroimaging
CT in VaD

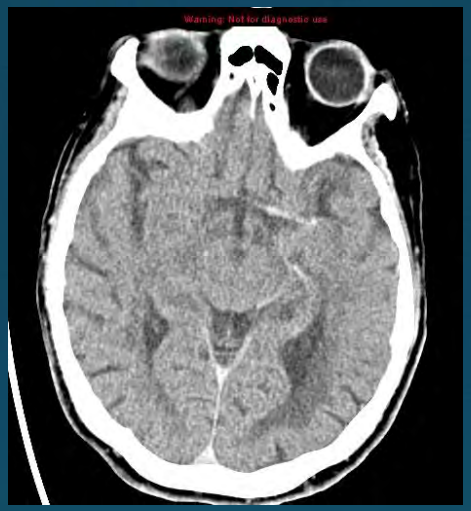




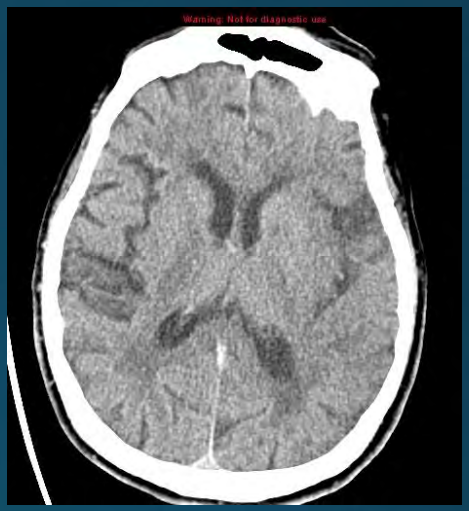
Small vessel injury

- Periventricular & subcortical white matter hypodensities
- Cerebral volume loss
- Lacunar infarcts

Neuroimaging
CT in VaD



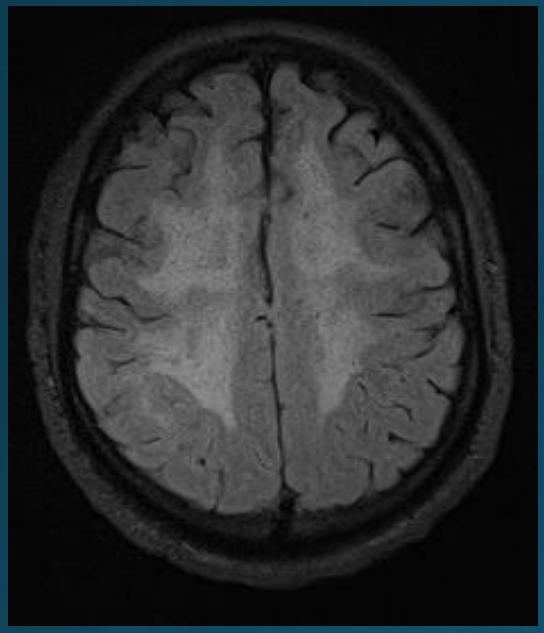
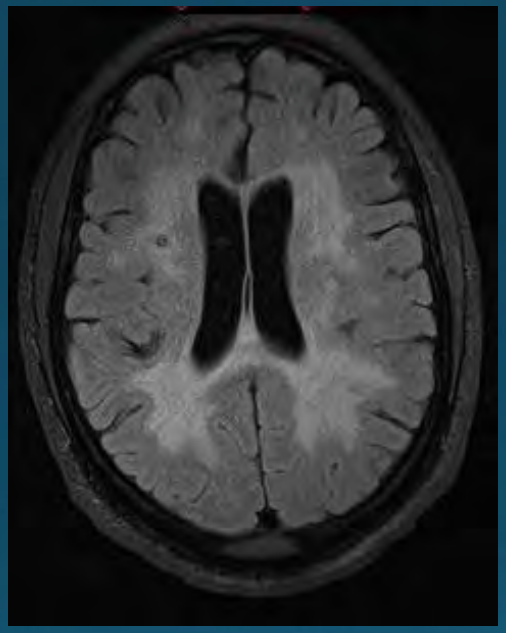
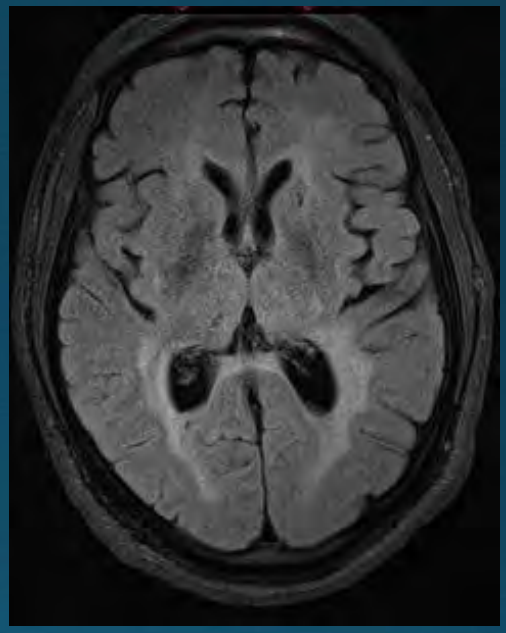




Large vessel occlusion

- Hyperdense MCA sign - Left MCA (M1) occlusion
- Loss of left insular ribbon, basal ganglia
- Loss of GW differentiation, L temporal lobe

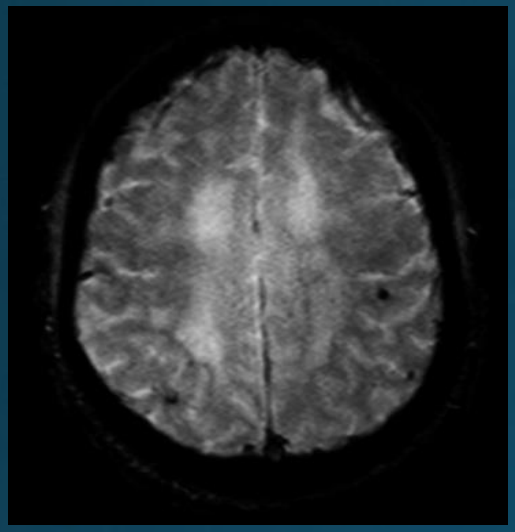
Neuroimaging
MRI in VaD

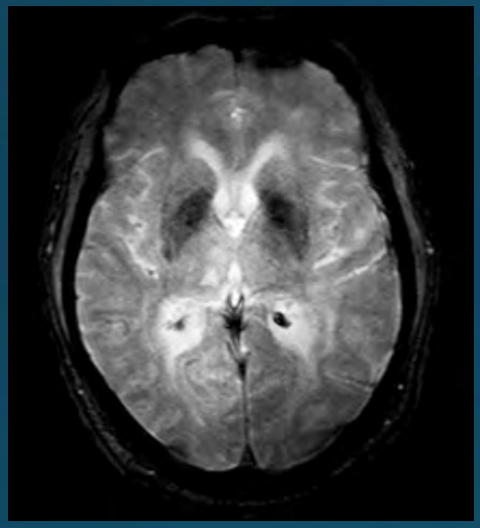




- Leukaraiosis: Confluent high periventricular white matter T2/FLAIR signal
  - Demyelinization, enlargement of perivascular spaces, gliosis, and axonal loss

Neuroimaging
MRI in VaD

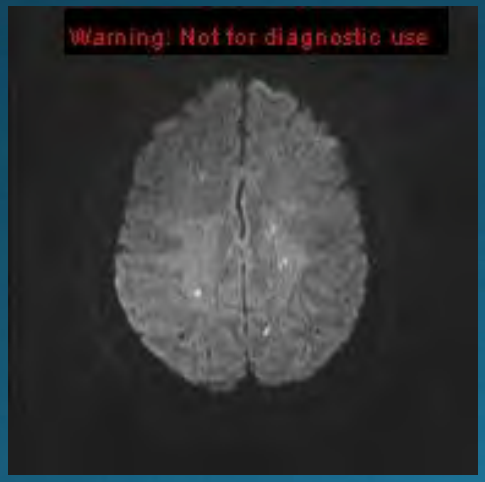
GRE

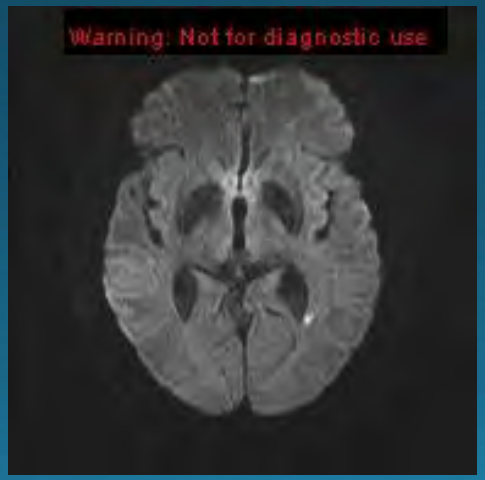




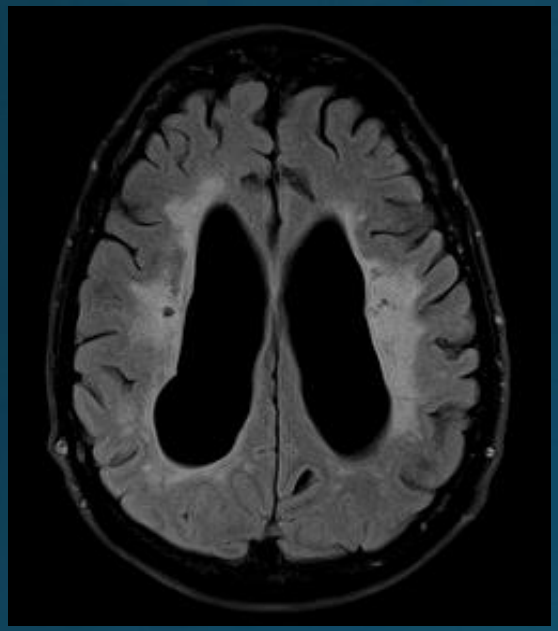
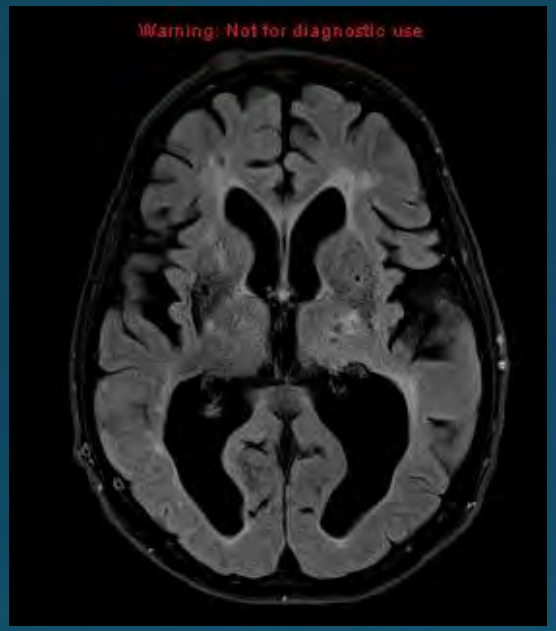
- Micro-hemorrhages – 'blooming' on GRE. Can be 2/2 long standing HTN
- Scattered foci of restricted diffusion – small infarcts.

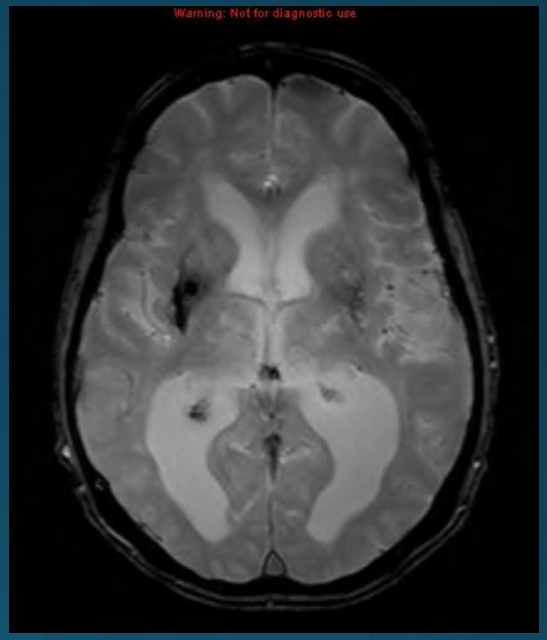
DWI





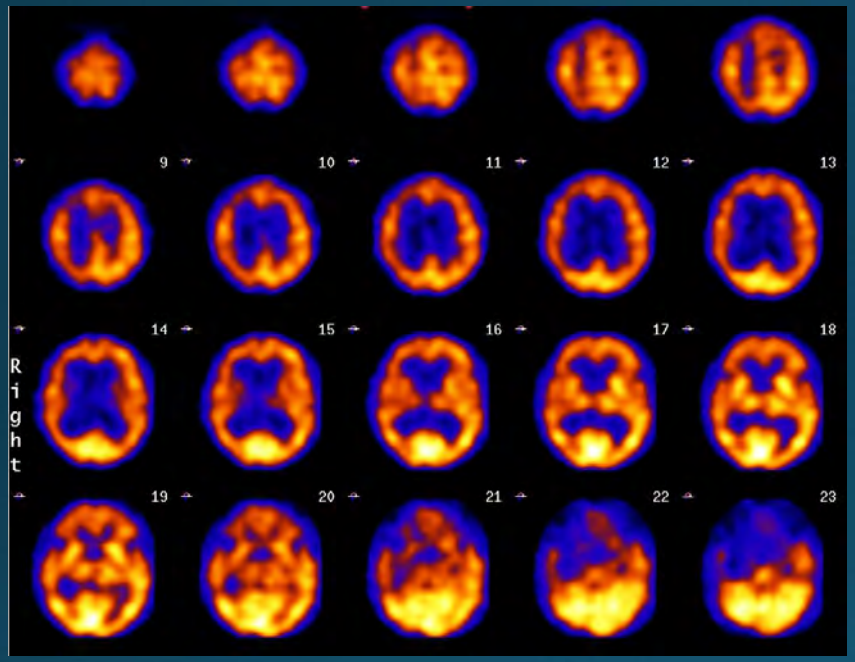
Neuroimaging
MRI in VaD

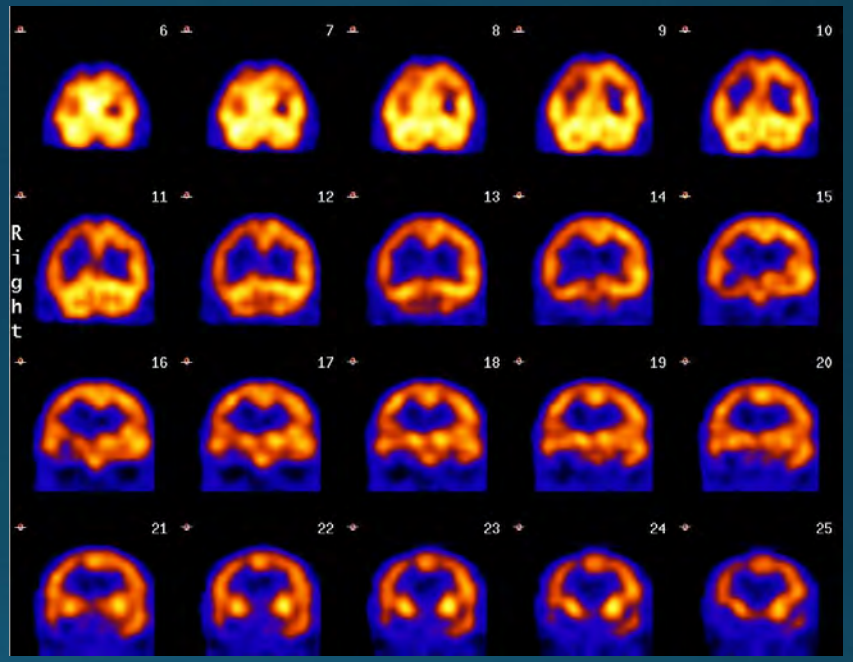



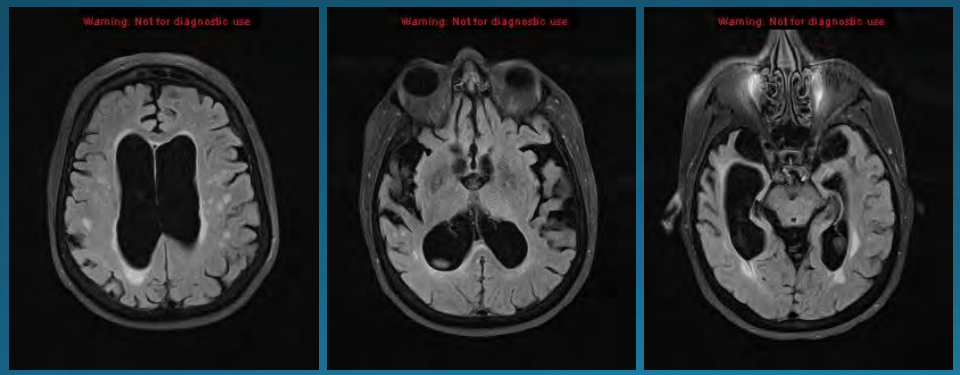


- Diffuse cerebral volume loss
- Ex vacuo dilation of ventricles
- Lacunar infarcts in basal ganglia
- Hemorrhage on GRE
- WM abnormality c/w chronic small vessel ischemic disease

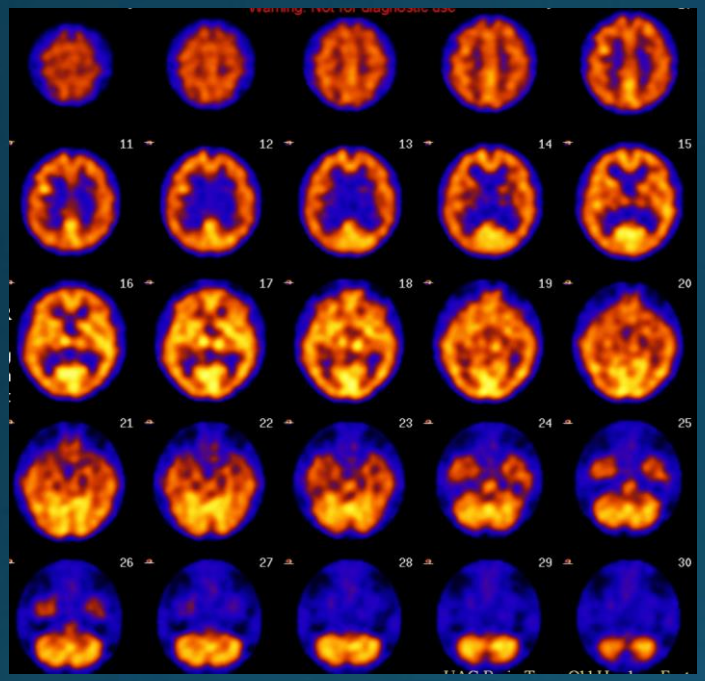
Neuroimaging
SPECT in VaD

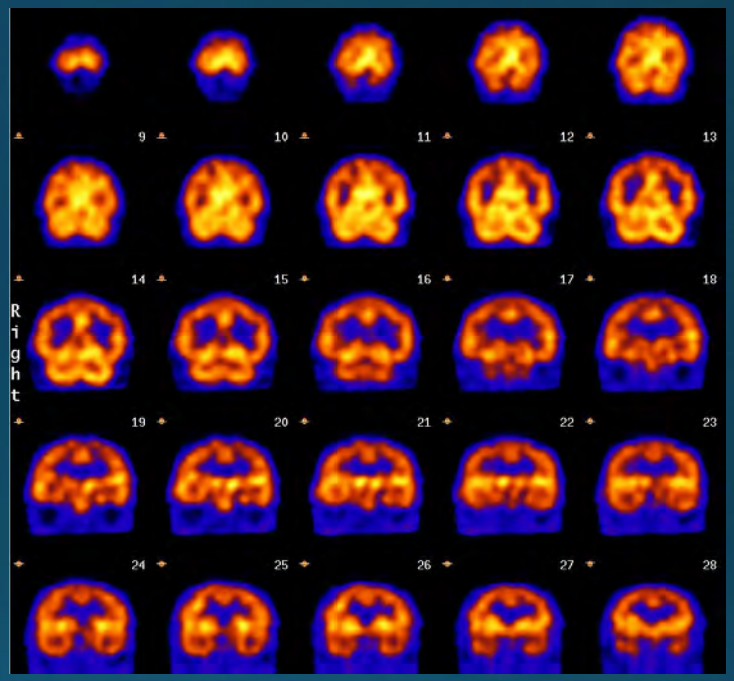


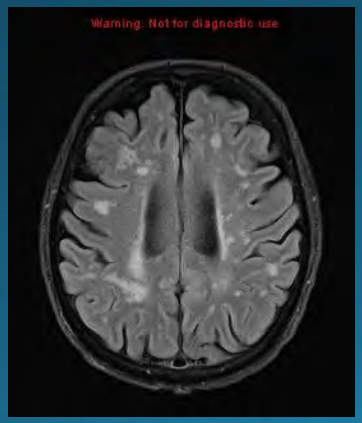


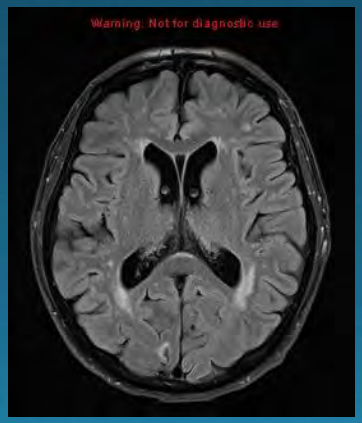


Neuroimaging
SPECT in VaD

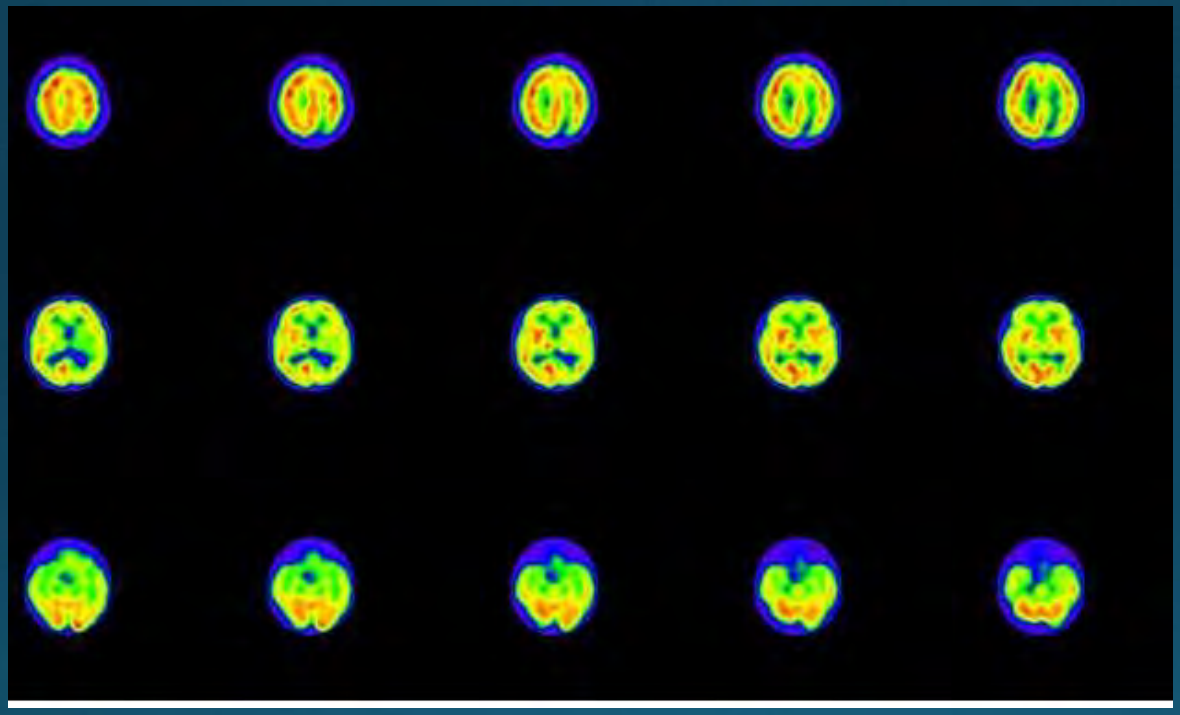






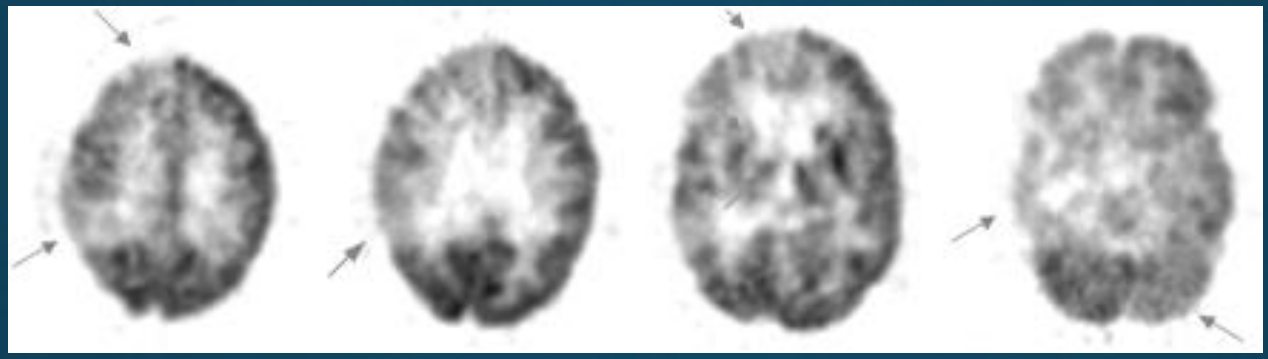


Neuroimaging
SPECT in VaD



- Left parieto-occipital perfusion defect c/w infarct

PET in VaD



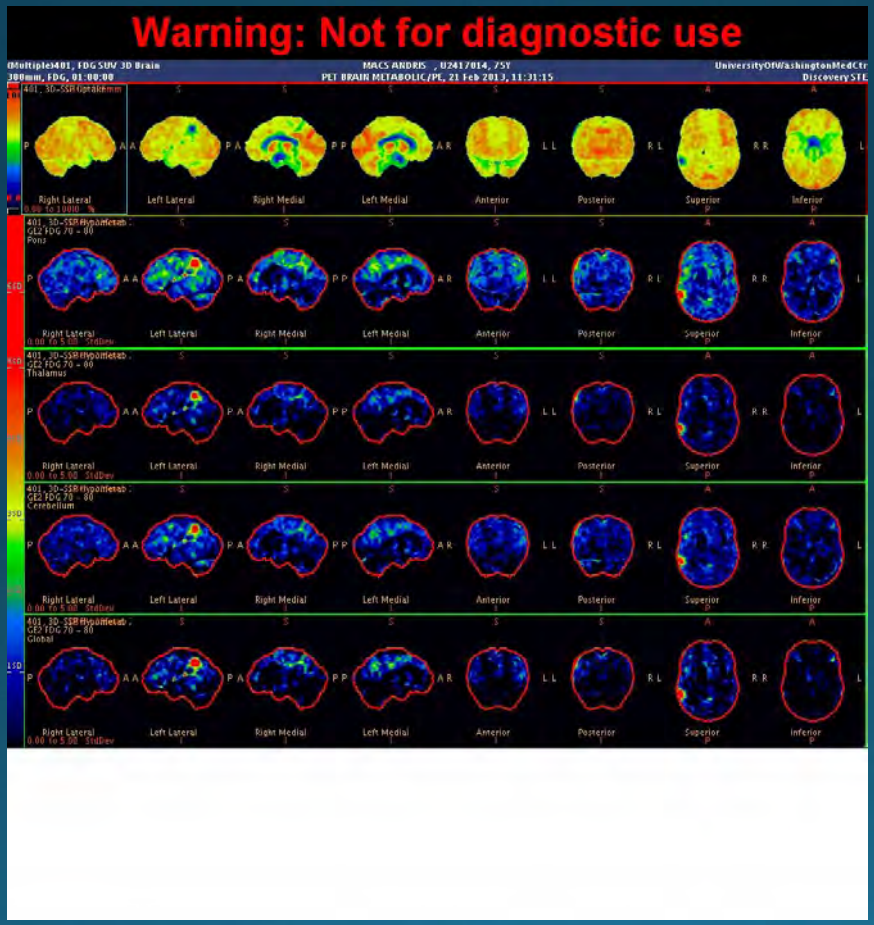
- 18F-FDG PET images in vascular dementia
- Hypometabolism affecting cortical, subcortical, and cerebellar areas is often seen
- The hypometabolism of the left cerebellum (far right) is characteristic of cross-cerebellar diaschisis, caused by diminished afferent input from the contralateral cortex.
- Typically better spatial resolution than SPECT
- Proposed 15-20% increase in diagnostic accuracy of PET relative to SPECT

Silverman, D. J Nucl Med April 1, 2004 vol. 45 no. 4 594-607

Another example

- 75 year old man
- Neurocognitive exam revealed problems with verbal memory, recognition memory and executive function.
- No previous documented history of stroke

3D SSP images



Other findings on SPECT

- Look for crossed cerebellar diaschisis
  - Occurs mostly in large cortical strokes but also in capsular strokes
- Caused by injury to the glutamatergic crossed corticopontocerebellar descending pathway (CPCP),

Tc99m-HMPAO

- HMPAO is a lipophilic compound which is chemically unstable in-vitro (it undergoes oxidation).
- It has a first pass extraction of about 80%.
- The distribution of the tracer is proportional to the regional cerebral blood flow
- The ratio of gray to white matter activity is about 2.5:1 compared to the 4:1 with Tc99m-ECD.

Tc99m-ECD

- Stable in-vitro (4 to 6 hours after reconstitution, as compared to less than 30 minutes for Tc99m-HMPAO)
- Higher gray-to-white matter ratio
- Tc99m-ECD is considered to be a perfusion marker of viable brain tissue

Normal distribution

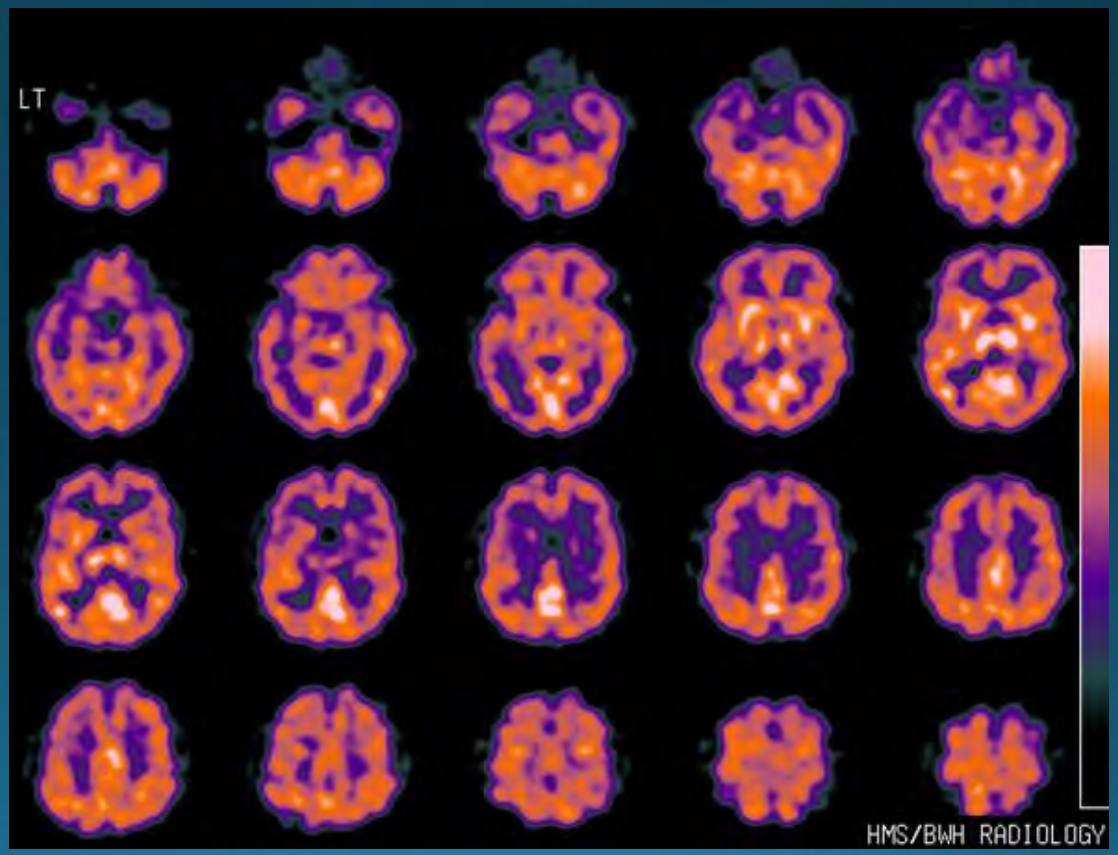
- Normally the frontal lobes, thalamus and cerebellum accumulates more radiotracer . Midline structures including the basal ganglia and thalami should be clearly evident and relatively symmetric. Eyes open

  or closed may increase

  or decrease, respectively,

  the visual cortex activity

  by 30%



Diamox brain SPECT

- Assess the circulation at rest and after a vasodilatory stimulus (stress) to access flow reserve
- Areas of decreased flow reserve should not manifest an increase in vascular flow to the same extent as regions of normal vascular supply
- Evaluation of rest along with stress images, increase the specificity for the detection of cerebral vascular disease of rest-stress imaging over rest alone

Indication of the test

Assessment of vascular reserve in patients with

1. Carotid stenosis
2. TIA
3. Cerebrovascular disease
4. Diabetes
5. Prior ECD-ICD bypass
6. Moya-Moya disease
7. Complementary method in determining selective carotid shunting during CEA

Conclusion

- Vascular dementia is 2nd most common cause of dementia in the Western world
- Brain perfusion imaging with Tc99m agents and SPECT are valuable tools to distinguish vascular dementia from Alzeihmers
- Diamox brain perfusion SPECT also has a role if considering treatment

References

- Dietmar Rudolf Thal, **Lea Tenenholz Grinberg, Johannes Attems**. Vascular dementia: Different forms of vessel disorders contribute to the development of dementia in the elderly brain. Experimental Gerontology 47 (2012) 816**–824**
- David H. Lewis, Lauren K. Toney, and Jean-Claude Baron. Nuclear Medicine in Cerebrovascular Disease. Semin Nucl Med 42:387-405

Management

Primary prevention

Secondary prevention

1. Early diagnosis and Rx of acute stroke
2. Prevention of stroke recurrence
3. Slowing of progression (Rx of risk factors)

Aim of treatment

1. Slow progression
2. Symptomatic
3. Rx of neuropsychiatric symptoms

Conclusion

- Vascular dementia: continuously evolving
- Significant impact given high prevalence of risk factors
- Variety of imaging appearances – Not specific, often overlap with AD
- Several accepted classification schemes
- No cure
  - Preventative and symptomatic treatment