Welcome to the Vizamyl™

In-person reader training workshop

This presentation contains important information to ensure accurate and reliable interpretation of PET images when using Vizamyl
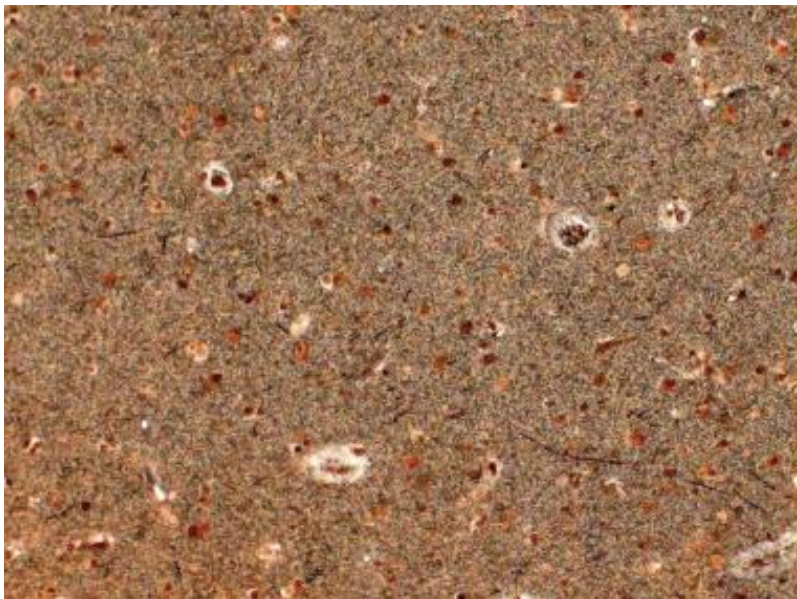
HCPs should refer to the Summary of Product Characteristics for full prescribing information

Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

Introduction to amyloid pathology

Absence of plaques

inconsistent with AD diagnosis
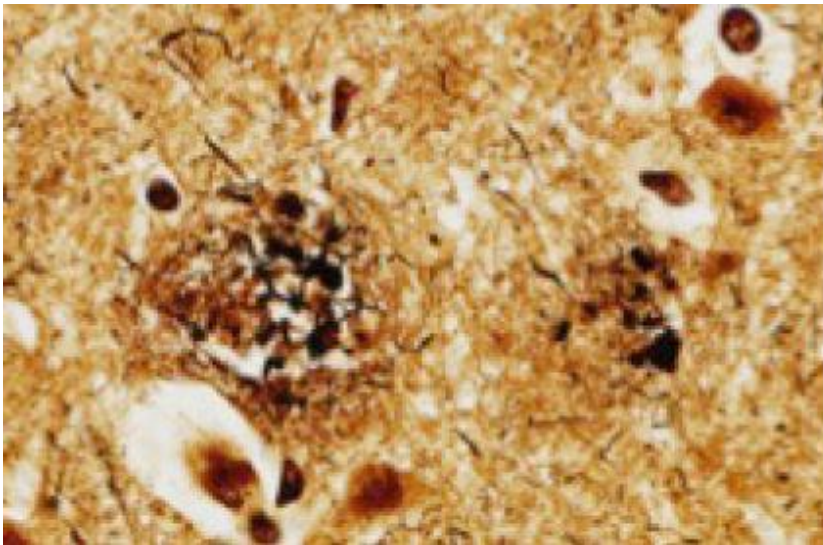
Neuritic ß-amyloid plaques

marker for AD
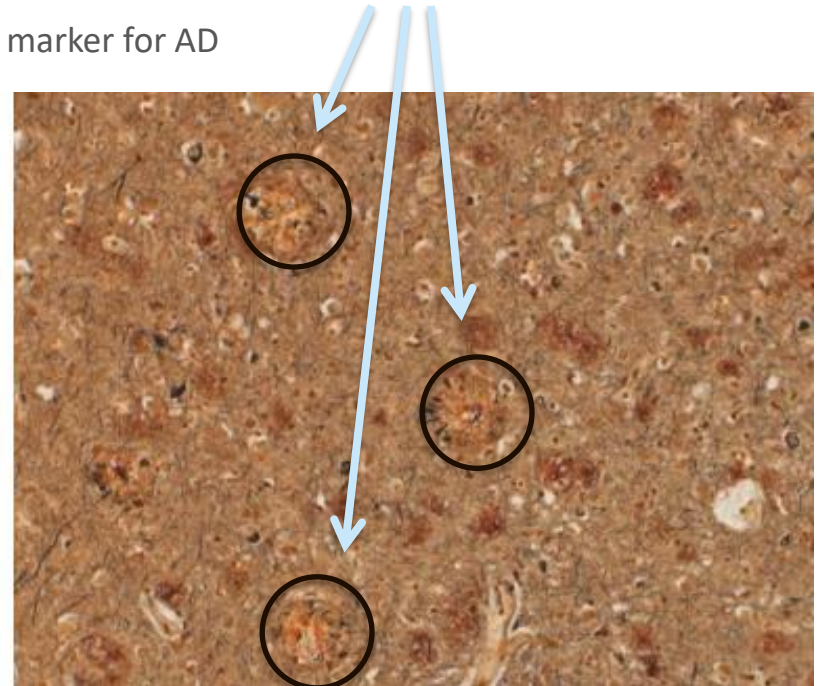
GE Healthcare. Images on file. 2014

Introduction to amyloid pathology
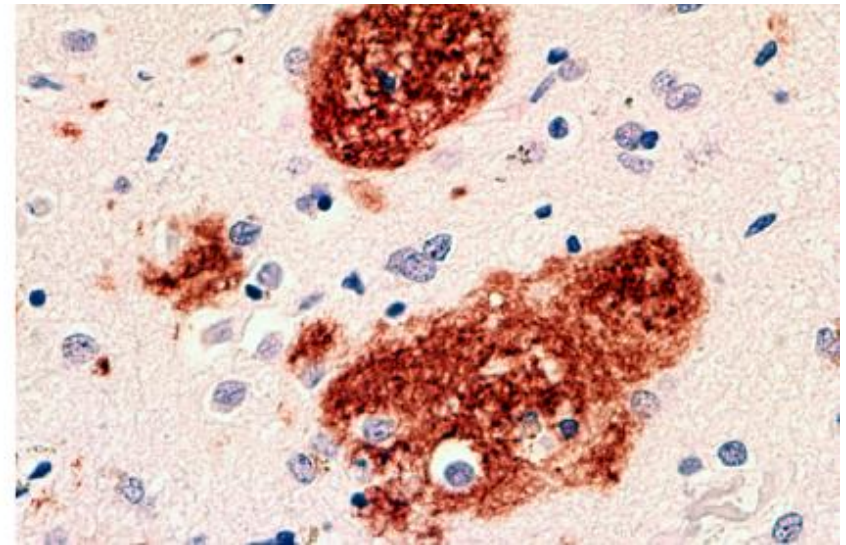

| APP | ß-amyloid | Oligomers | Fibrils | Plaque |
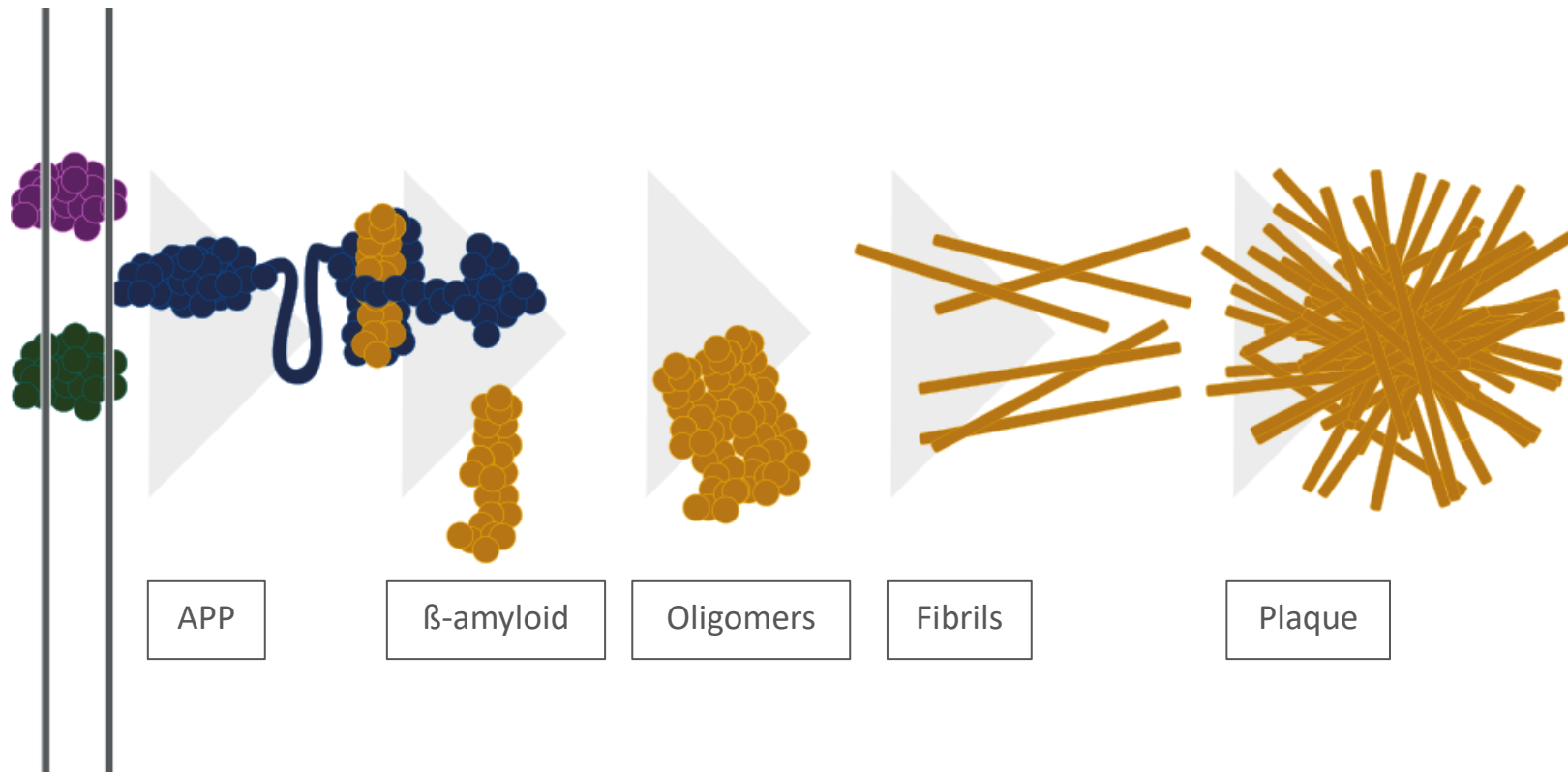
Introduction to amyloid pathology

Neuritic plaque

Bielschowsky Silver Stain

Diffuse plaque

4G8 Immunohistochemistry (IHC)

Images courtesy of Milos Ikonomovic, University of Pittsburgh

Classical Pattern of Amyloid Deposition During the Progression of AD

No accumulation

Initial deposits
basal portions
of isocortex

Midstage
progressive deposition
of isocortex

Endstage
deposits found in all
areas of isocortex

Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.

Images adapted with permission from Chris Rowe, University of Melbourne

Classical Pattern of Amyloid Deposition During the Progression of AD

No accumulation

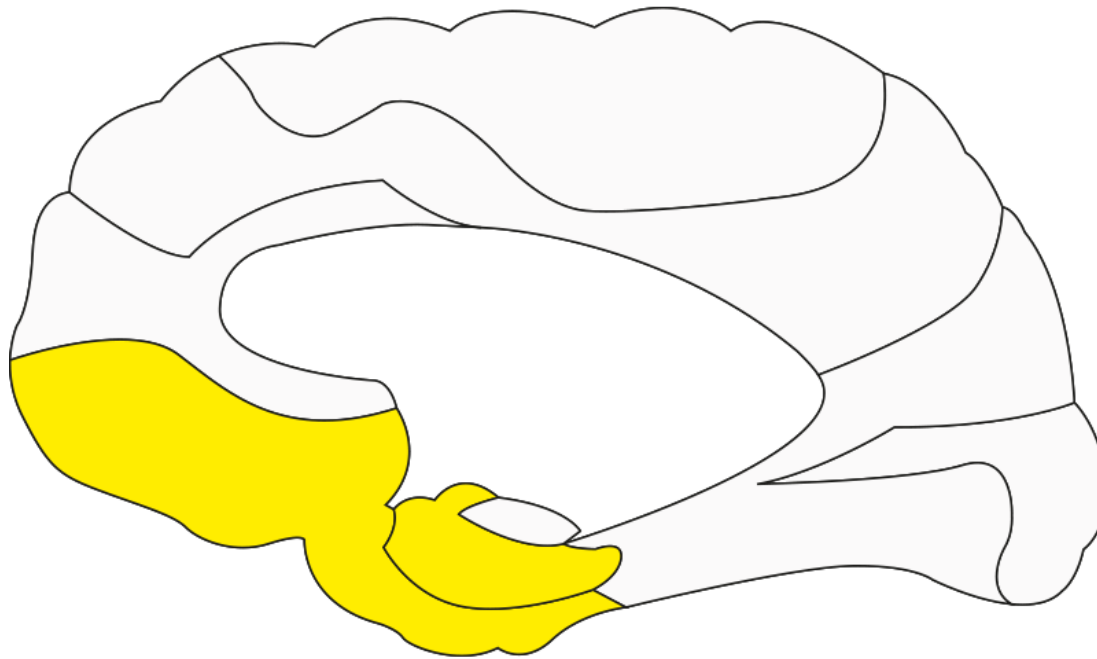**Initial deposits**
basal portions
of isocortex

Midstage
progressive deposition
of isocortex

Endstage
deposits found in all
areas of isocortex

Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.

Images adapted with permission from Chris Rowe, University of Melbourne

Classical Pattern of Amyloid Deposition During the Progression of AD

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Initial deposits
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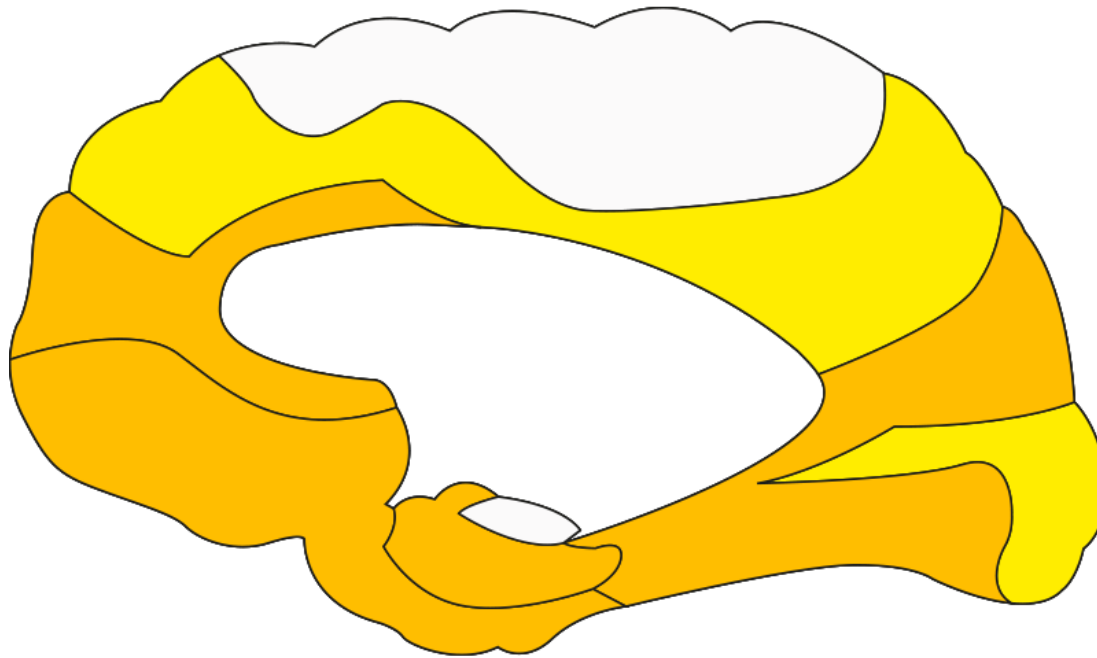Midstage
progressive deposition
of isocortex

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Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.

Images adapted with permission from Chris Rowe, University of Melbourne

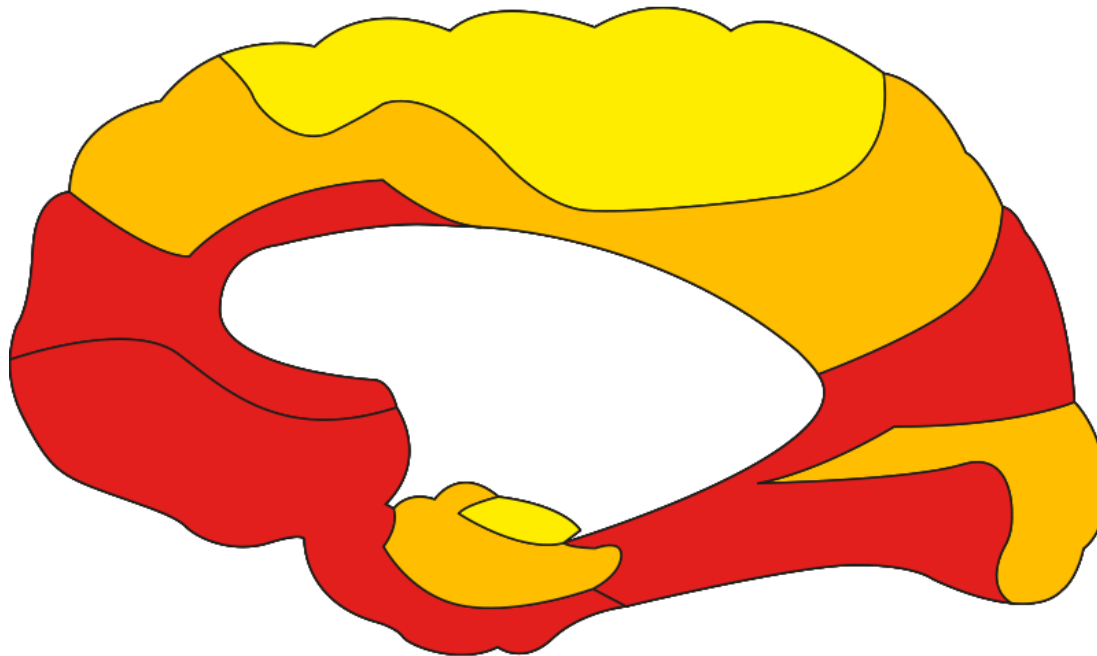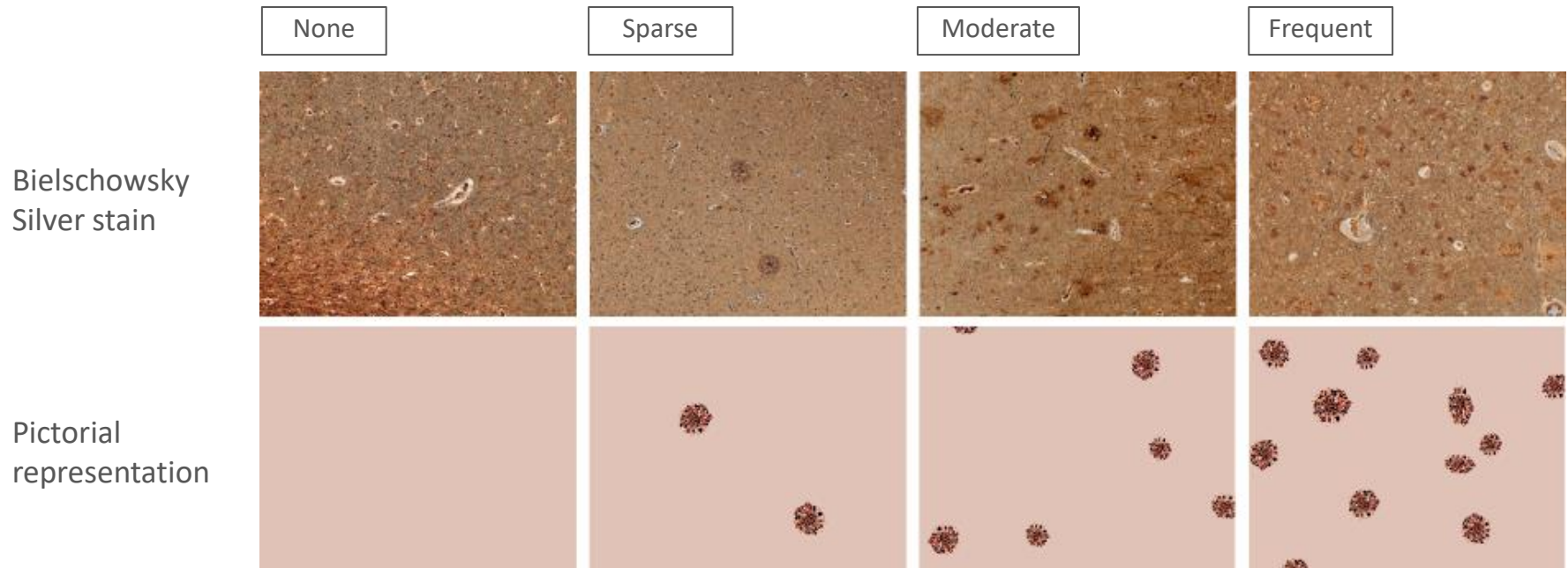# Classical Pattern of Amyloid Deposition During the Progression of AD

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deposits found in all
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Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.

Images adapted with permission from Chris Rowe, University of Melbourne

VIZAMYL™
Flutemetamol (^{18}F)
Injection

Amyloid pathology in AD

	None	Sparse	Moderate	Frequent
Bielschowsky Silver stain				
Pictorial representation				

GE Healthcare. Images on file. 2014

Mirra SS, Heyman A, McKeel D *et al*. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. Neurology 1991; 41: 479-86.

Amyloid pathology in AD diagnosis

A definitive diagnosis of AD requires the following components:

- Dementia confirmed after clinical diagnosis (via recommended criteria such as NINCDS-ADRDA (1984) or NIA-AA (2011))

- Neurofibrillary tangles

- ß-amyloid neuritic plaques
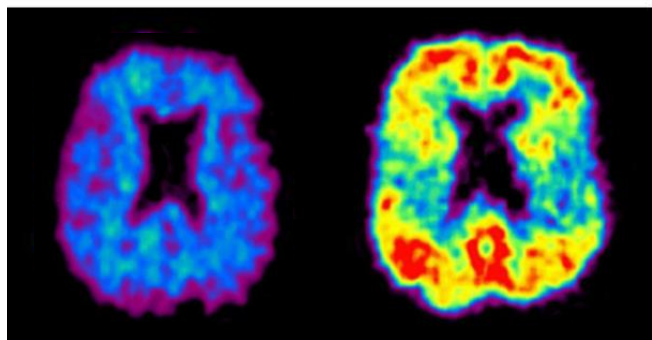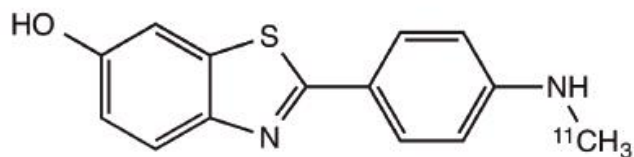
Amyloid imaging agents

Thioflavin T (ionic)

Image courtesy of Milos Ikonomovic, University of Pittsburgh
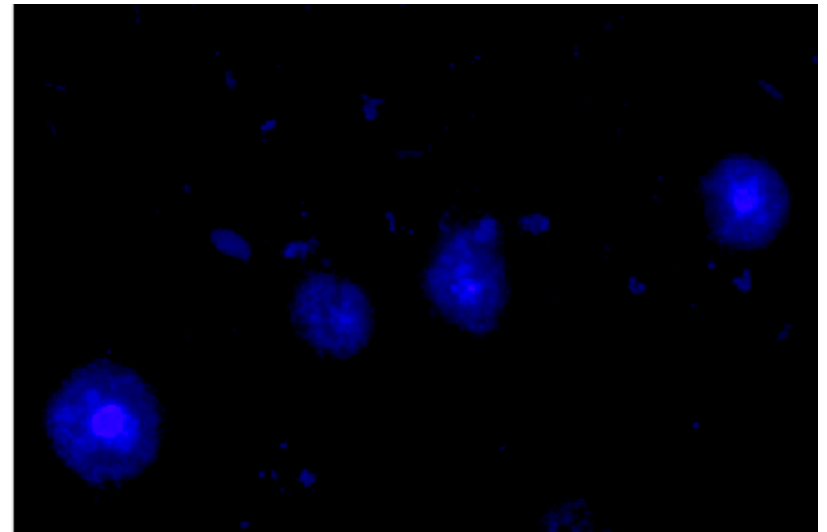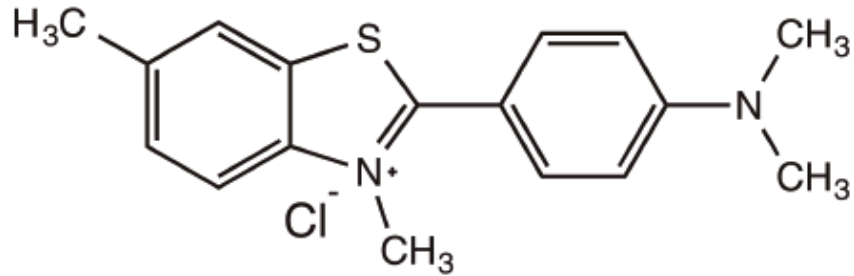
Amyloid imaging agents

^{11}C Pittsburgh compound B (PiB)

(radioactive $t_{1/2}$ ~20 min)

| Control | AD |

Flutemetamol ^{18}F – VIZAMYL

(radioactive $t_{1/2}$ ~110 min)
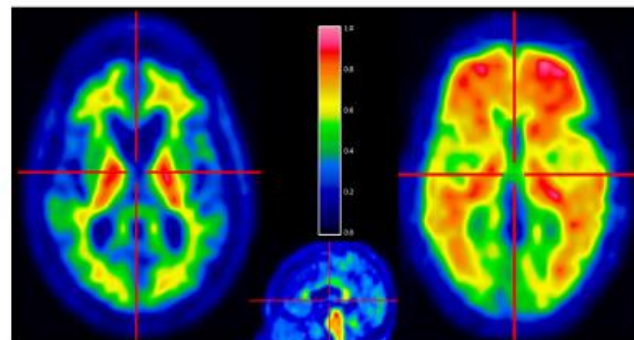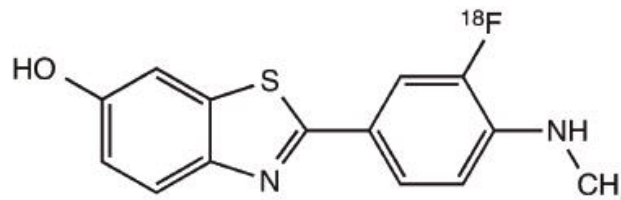
| Negative | Positive |

Vizamyl: Product description

Diagnostic radiopharmaceutical agent for PET

Imaging ß-amyloid neuritic plaques *in vivo*

Sterile solution for injection

Flutemetamol (^{18}F) 400 MBq/mL

Other ingredients: sodium chloride, ethanol anhydrous, polysorbate 80, sodium dihydrogen, phosphate dihydrate, disodium hydrogen phosphate dodecahydrate, water for injection

Available as glass vials

10 mL – containing 1-10 mL   15 mL – containing 1-15 mL

Vizamyl: Indication

Vizamyl is a radiopharmaceutical medicinal product indicated for Positron Emission Tomography imaging of ß-amyloid neuritic plaque density in the brains of adult patients with cognitive impairment who are being evaluated for Alzheimer's disease and other causes of cognitive impairment

Vizamyl should be used in conjunction with a clinical evaluation

A negative scan indicates sparse or no plaques, which is not consistent with a diagnosis of Alzheimer's disease

Vizamyl: Limitations of use

Positive scan does not independently establish Alzheimer's disease diagnosis

Patients with MCI	Prediction of AD development	Monitoring therapy response
Progression to AD cannot be estimated	Not established	Not established

Vizamyl: Limitations of use

Interpretation errors due to
Image noise
Cortical atrophy
Image blur

Posology

Recommended activity: 185 MBq

Administered intravenously as a bolus within approx. 40 sec

Injection volume: 1-10 mL

If using an intravenous line:

Follow injection with intravenous flush of 5 to 15 mL of sterile
NaCl solution 9 mg/mL (0.9%) for injection to ensure full delivery of the
dose

VIZAMYL™
Flutemetamol (^{18}F)
Injection

Posology

Vizamyl images acquired starting at 90 mins after injection

Scan duration: 20 mins

Vizamyl images should only be interpreted by readers trained in the interpretation of PET images with flutemetamol (^{18}F).
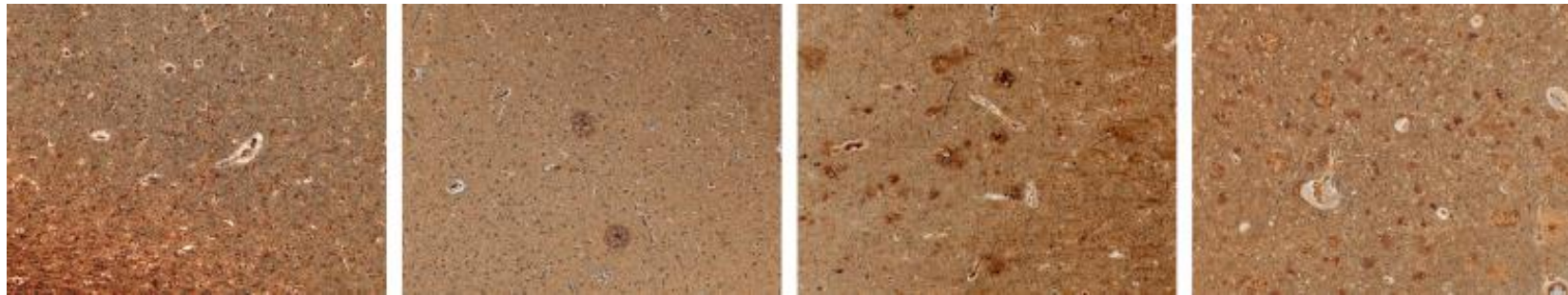
Clinical studies

Pivotal study
68 patients

Re-reading study
106 patients

VIZAMYL™
Flutemetamol (^{18}F)
Injection

Clinical studies

Bielschowsky Silver stain for neuritic plaque load

| None | Sparse | Moderate | Frequent |

Negative   **Positive**

Vizamyl image

GE Healthcare. Images on file. 2014

Mirra SS, Heyman A, McKeel D *et al*. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. Neurology 1991; 41: 479-86.
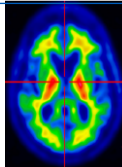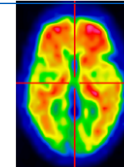
VIZAMYL™
Flutemetamol (^{18}F)
Injection

Pivotal clinical study

68 end-of-life patients

Cognitive status of the patients was not determined

Visual PET assessment

5 blinded readers

Figures based on the majority read:

Image interpretation reached independently by at least 3/5 readers

Sensitivity: 86% (95% CI: 72% to 95%)

Specificity: 92% (95% CI: 74% to 99%)

Curtis C. et al. Phase 3 Trial of Flutemetamol Labeled With Radioactive Fluorine 18 Imaging and Neuritic Plaque Density. JAMA Neurol. 2015 Mar; 72(3): 287-94.

VIZAMYL™
Flutemetamol (^{18}F)
Injection

Re-reading study

106 patients

Primary analysis – 8 neocortical regions

    Sensitivity: 91%   (95% CI: 82% to 96%)

    Specificity: 90%   (95% CI: 74% to 98%)

Secondary analysis – 3 neocortical regions (CERAD)

    Sensitivity: 92%   (95% CI: 83% to 97%)

    Specificity: 88%   (95% CI: 71% to 97%)

Figures based on the majority read

Summary of test studies

Sensitivity	Specificity
86–91%	90-92%

VIZAMYL™
Flutemetamol (^{18}F)
Injection

Safety information

761 subjects received Vizamyl

Recommended dose: 185 MBq

530/761 (70%) received 185 MBq

154/761 (20%) received 370 MBq

Safety information: Adverse reactions

Definition	Frequency	Percentage	Observed with Vizamyl
Very common	≥1/10	**over 10%**	–
Common	≥1/100 to <1/10	**in 1% – 10%**	Yes
Uncommon	≥1/1000 to <1/100	**in 0.1% – 1%**	Yes
Rare	≥1/10,000 to <1/1,000	**in 0.01% – 0.1%**	–
Very rare	<1/10,000	**less than 0.01%**	–
Not known	Cannot be estimated from the available data	–	–

Common adverse reactions

Adverse reactions	% patients
Flushing	**2**
Chest discomfort	**1**
Increased blood pressure	**1**
Nausea	**1**

Please refer to the SmPC for a full list of adverse reactions

Adverse reactions – radiation

Effective dose

5.9 mSv

Exposure to ionising radiation linked with

Cancer induction

Potential for development of hereditary defects

Reporting adverse events

Reporting suspected adverse reactions is important

Report via the national reporting system

Listed in Appendix V of the Summary of Product Characteristics

Interpretation of Vizamyl PET images

| Negative scan | Rainbow colour scale | Positive scan |
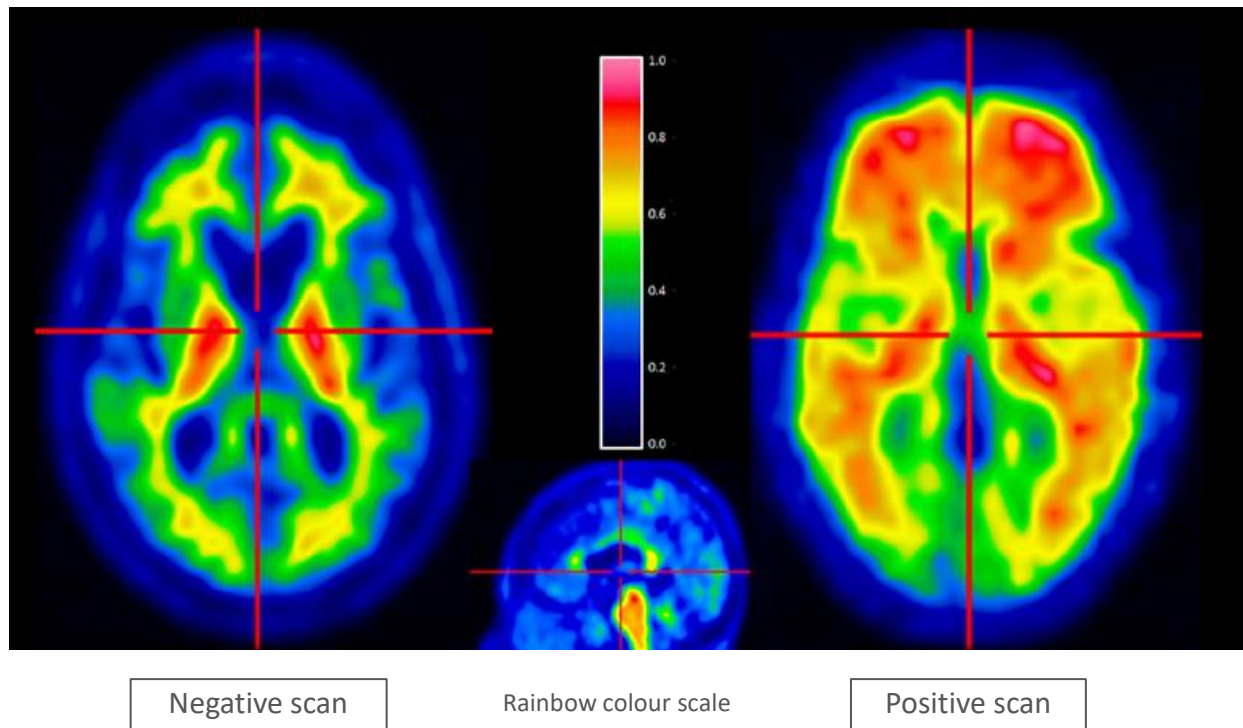
GE Healthcare. Images on file. 2014

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases observed in routine clinical practice may vary

Image review – general principles

Recommended colour scales
Sokoloff
Rainbow
Spectrum

In order to minimise the risk of inter and intra operator variability, it is imperative that the above colour scales are always used consistently in image-interpretation of Vizamyl
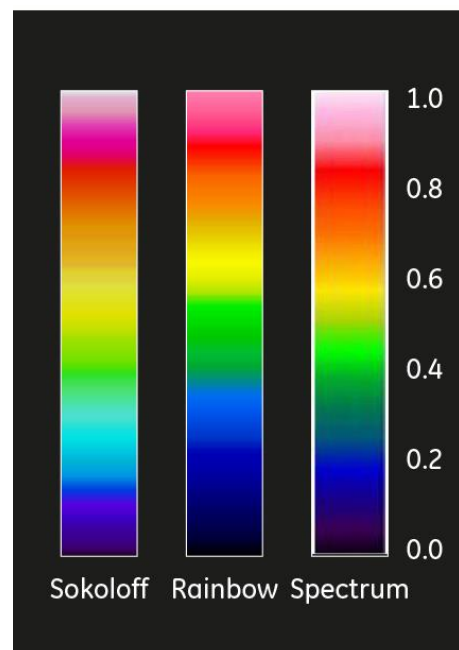
Image review – general principles
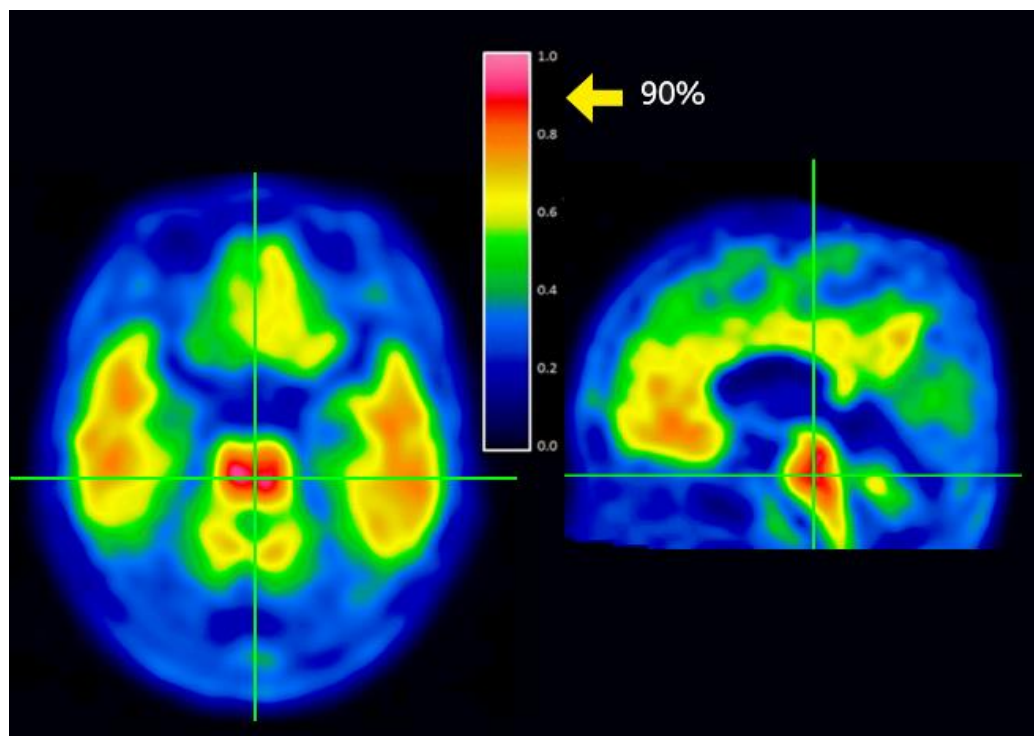
The images should be scaled such that the pons is set to 90% of the image intensity maximum

The signal intensity of the pons is set to 90% to maximise the full use of the colour scales.

Pons uptake is comparable in both negative and positive subjects and is due to non-specific partitioning by white matter
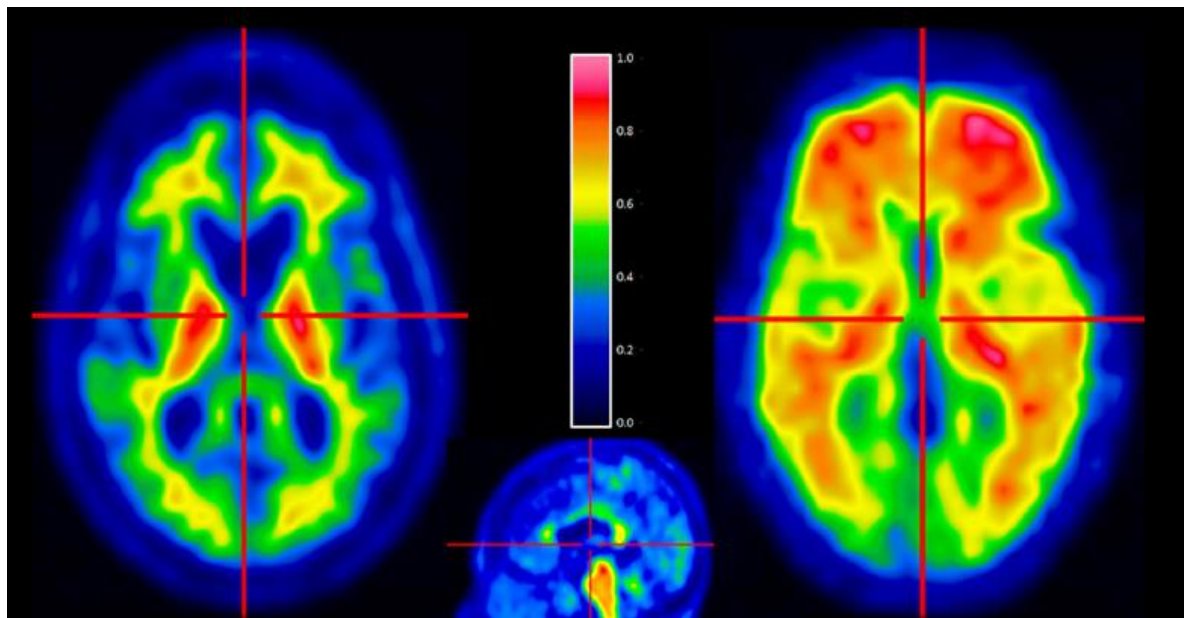
GE Healthcare. Images on file. 2014

Positive and negative Vizamyl scans

Negative scan
– white matter pattern

Positive scan
– white and grey matter pattern

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
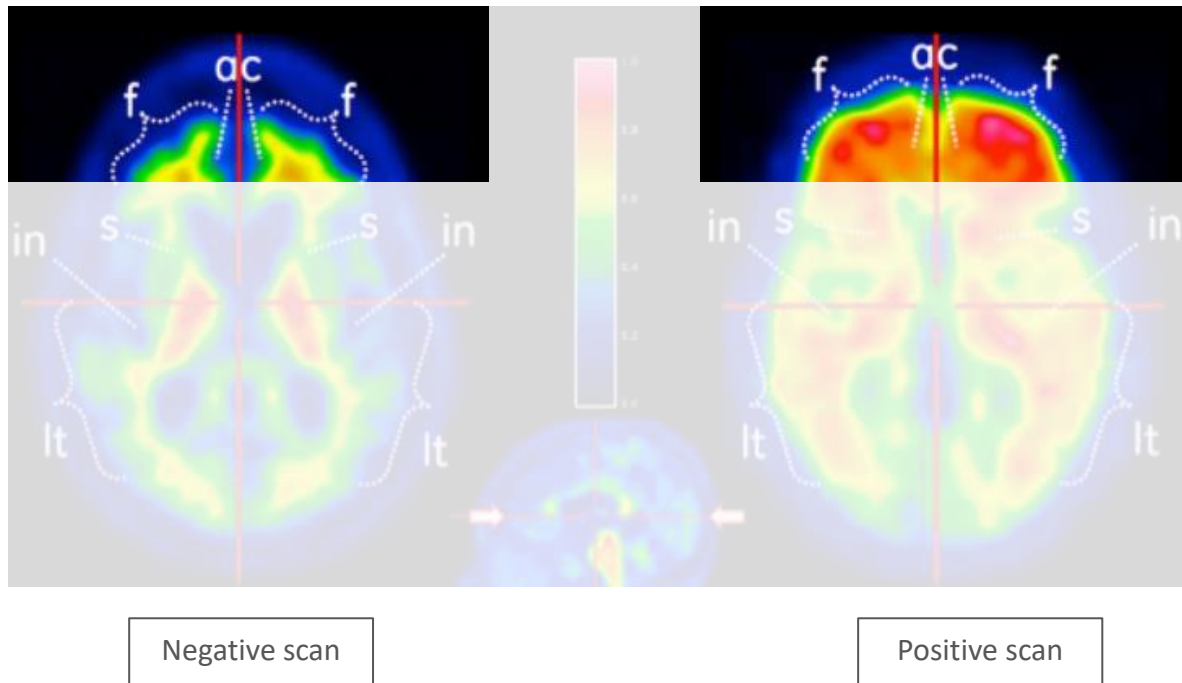Vizamyl European Summary of Product Characteristics, August 2014

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases observed in routine clinical practice may vary

Positive and negative Vizamyl scans

Negative scan
– white matter pattern

Positive scan
– white and grey matter pattern

Anatomical regions for image review

Frontal lobes and anterior cingulate
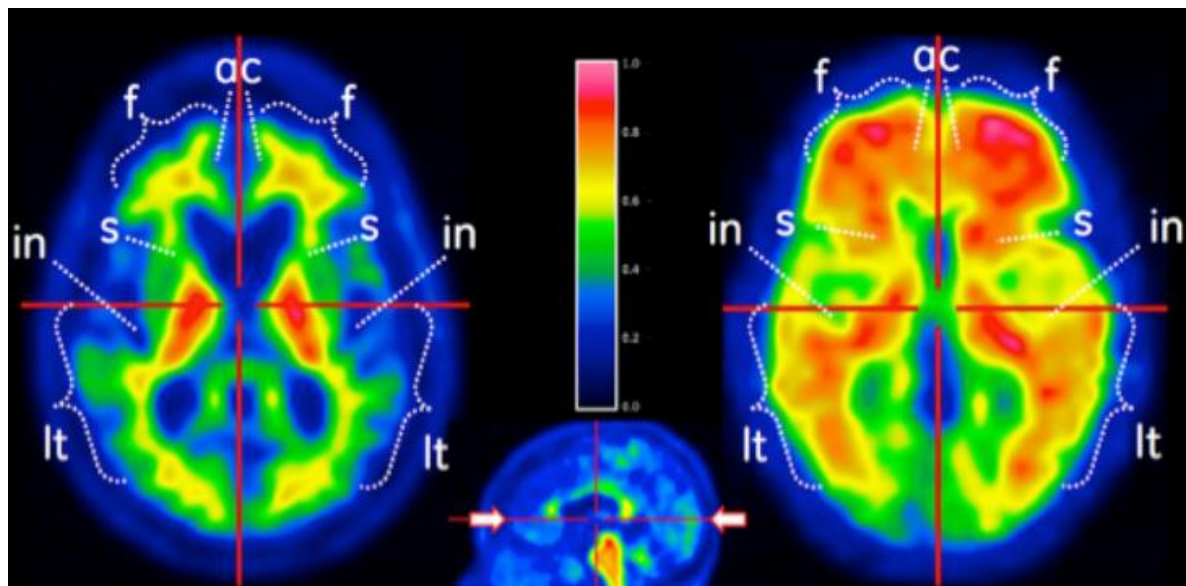
Negative scan   Positive scan

ac = anterior cingulate
f = frontal
s = striatum
in = insula
lt = lateral temporal

VIZAMYL™
Flutemetamol (^{18}F)
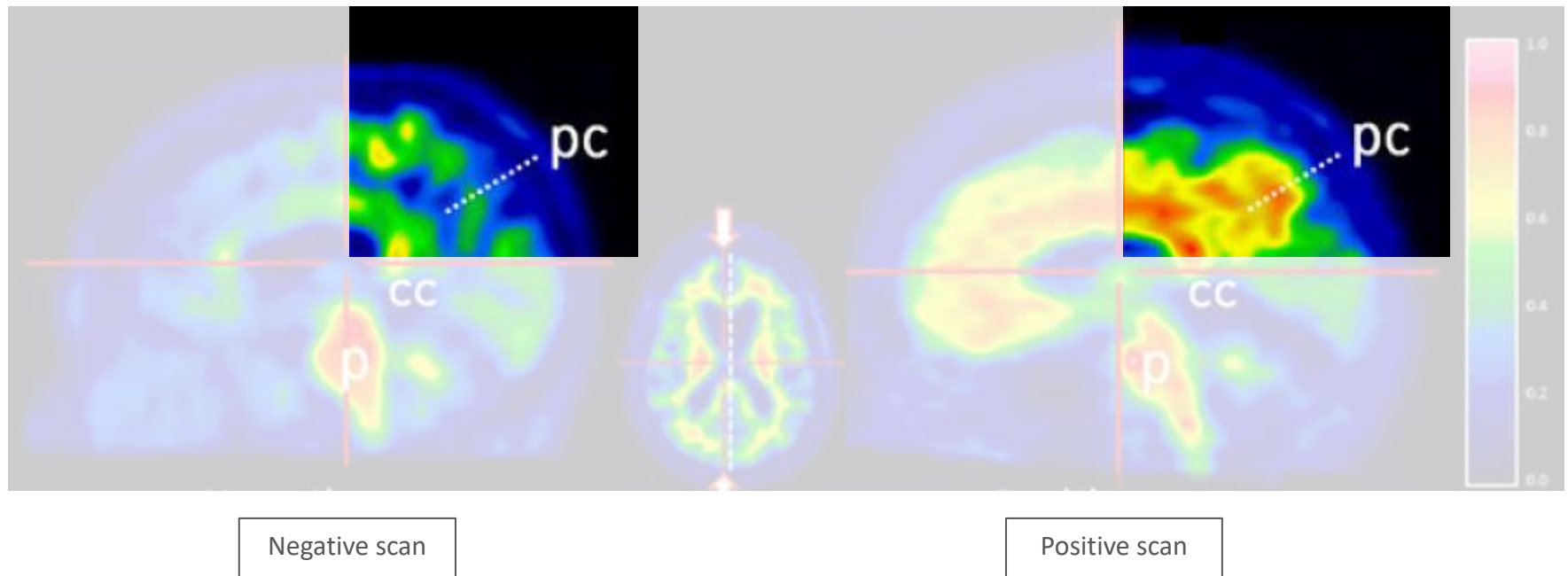Injection

Anatomical regions for image review

Frontal lobes and anterior cingulate

| Negative scan | Positive scan |

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

Anatomical regions for image review

Posterior cingulate and precuneus

Negative scan

Positive scan
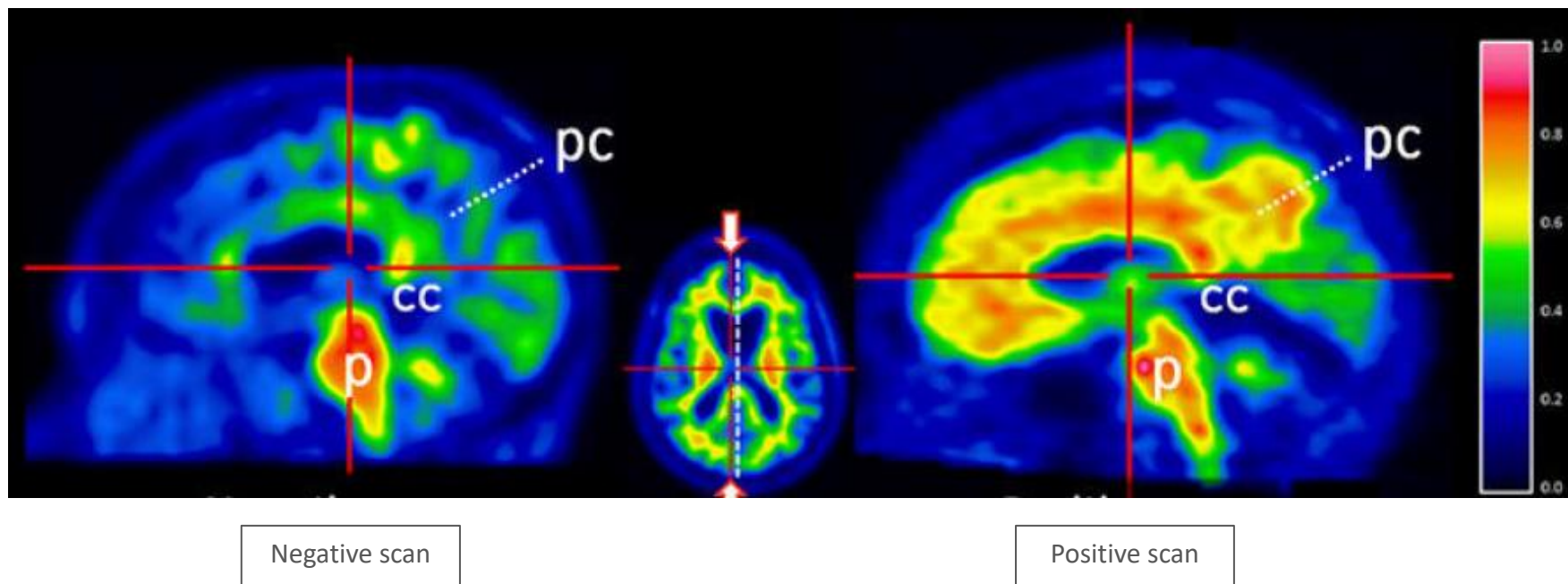
Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection

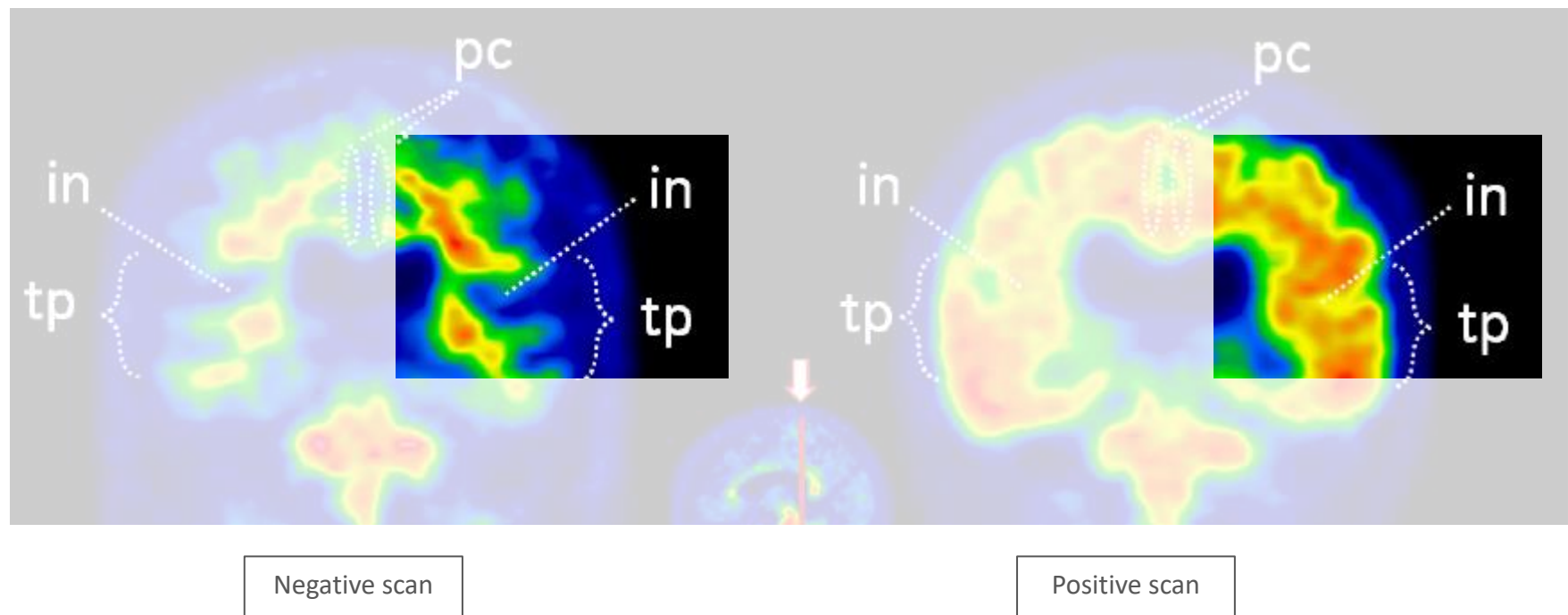Vizamyl European Summary of Product Characteristics, August 2014

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases observed in routine clinical practice may vary

pc = posterior cingulate and precuneus,
p = pons
cc= corpus callosum

Anatomical regions for image review

Posterior cingulate and precuneus

Negative scan

Positive scan

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

Anatomical regions for image review

Temporo-parietal aspects including insula

Negative scan

Positive scan
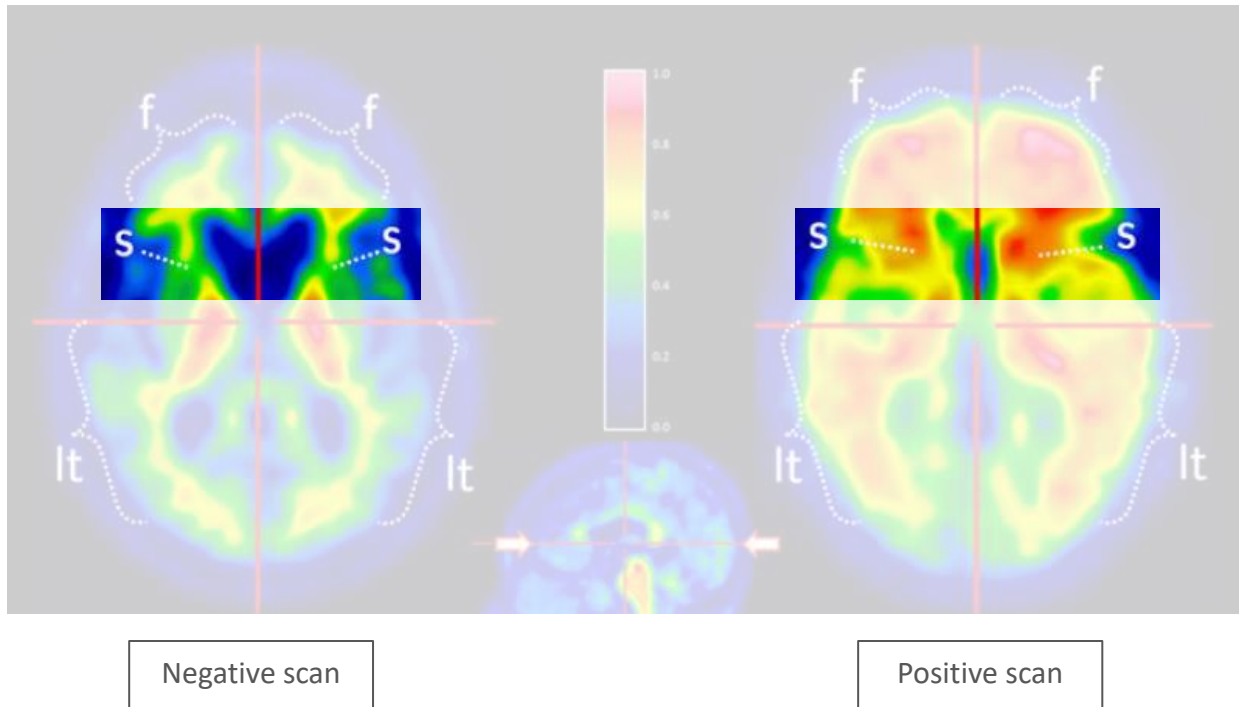
Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

pc = posterior cingulate and precuneus
in = insula
tp = temporo-parietal

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases
observed in routine clinical practice may vary

Anatomical regions for image review

Temporo-parietal aspects including insula

Negative scan

Positive scan

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

Anatomical regions for image review

Lateral temporal lobes

Negative scan

Positive scan

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases observed in routine clinical practice may vary

Anatomical regions for image review

Lateral temporal lobes

Negative scan

Positive scan

Anatomical regions for image review

Striatum

| Negative scan | Positive scan |

Vizamyl flutemetamol (^{18}F) 400 MBq/mL solution for injection
Vizamyl European Summary of Product Characteristics, August 2014

Vizamyl scans presented in the Introduction of this Educational Programme are for illustrative purposes: cases observed in routine clinical practice may vary

Anatomical regions for image review

Striatum

Negative scan

Positive scan

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Flutemetamol (^{18}F)
Injection

Potential interpretation errors

Interpretation errors are possible

Sensitivity
86%–91%

False negative rate
9%–14%

Equates to 1-sensitivity

Specificity
90%–92%

False positive rate
8%–10%

Equates to 1-specificity

False negative image reads

Atrophy can lead to a false negative PET read

CT image showing atrophy
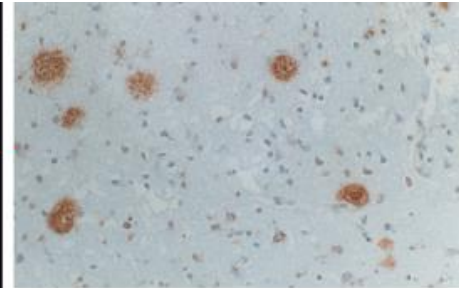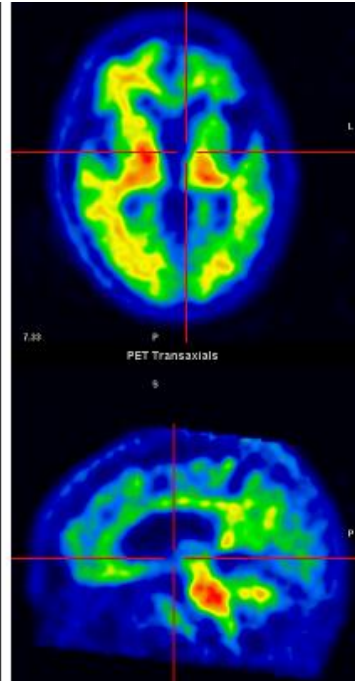
ß-amyloid immunohistochemistry

Bielschowsky Silver Stain

PET Transaxials

GE Healthcare. Images on file. 2014
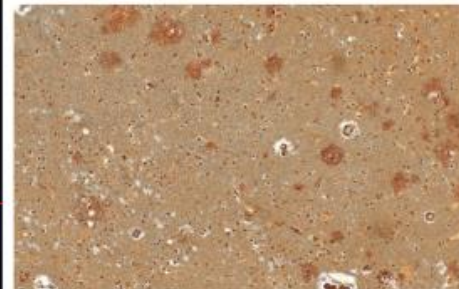
False positive image reads

An uncommon case demonstrating positive PET read with no neuritic plaque load,
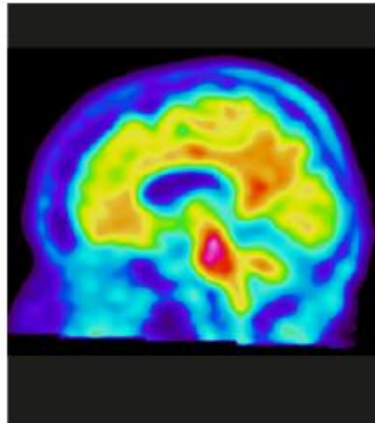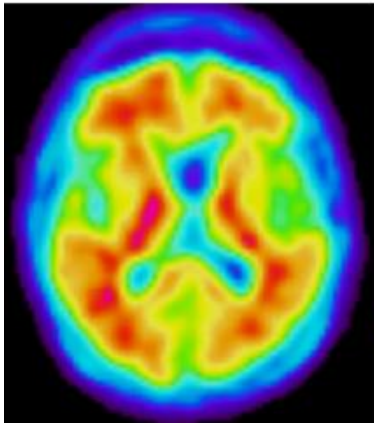but high diffuse plaque burden
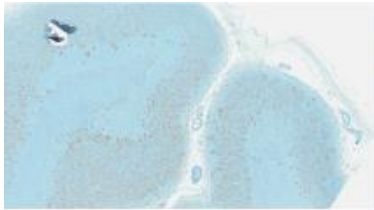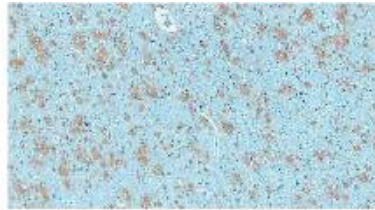
Low power   Medium power   High power   Bielschowsky Silver Stain negative
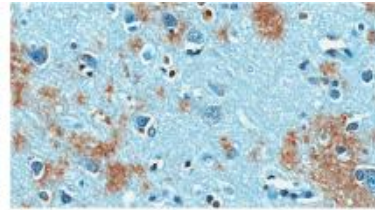
GE Healthcare. Images on file. 2014

Training programme overview

Module 1: Brain anatomy

Module 1A: Brain anatomy

Module 1B: Anatomy in PET

Module 2: Image orientation & display

Module 2A: Image orientation

Module 2B: Image display

Training programme overview

Module 3: Image interpretation

Self assessment

10 Pre-test cases

15 Test cases

References

Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.

Curtis C. et al. Phase 3 Trial of Flutemetamol Labeled With Radioactive Fluorine 18 Imaging and Neuritic Plaque Density. JAMA Neurol. 2015 Mar; 72(3): 287-94.

Hyman BT, Phelps CH, Beach TG *et al*. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimers Dement 2012; 8: 1-13.

McKhann G, Drachman D, Folstein M *et al*. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's disease. Neurology 1984; 34: 939-44.

McKhann G, Knopman D, Chertkow H *et al.* The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 2011; 7: 263-9.

Mirra SS, Heyman A, McKeel D *et al.* The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part II. Standardization of the neuropathologic assessment of Alzheimer's disease. Neurology 1991; 41: 479-86.

Vandenberghe R, Van Laere K, Ivaniou A *et al*. 18F-flutemetamol amyloid imaging in Alzheimer disease and mild cognitive impairment: a phase 2 trial. Ann Neurol 2010; 68: 319-29.

Vizamyl European Summary of Product Characteristics, August 2014.

All materials presented in this training programme have been developed by experts qualified in PET imaging and neurology

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Injection

Module 1A: Brain anatomy – Learning objectives

Welcome to Module 1A: Brain anatomy

In this module you will learn to recognise brain anatomy as it applies to amyloid imaging

- MRI anatomy and recognising structures

- Comparing MRI contrast to PET contrast in negative and positive Vizamyl scans

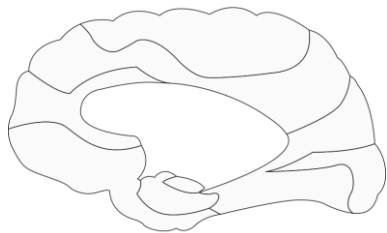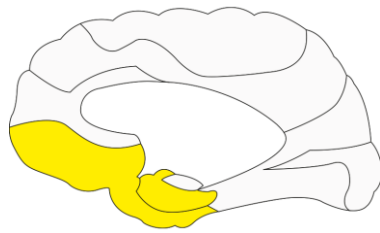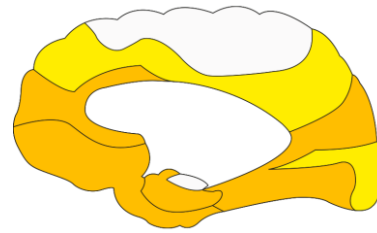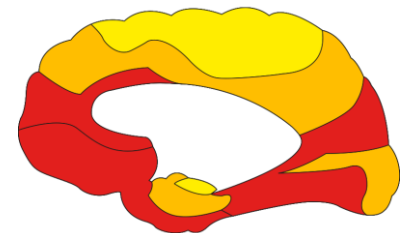- Key areas and landmarks in MRI and PET imaging

Abbreviations:
MRI: magnetic resonance imaging
PET: positron emission tomography

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Injection

Amyloid pathology in AD

No accumulation

Initial deposits
basal portions
of isocortex

Midstage
progressive deposition
of isocortex

Endstage
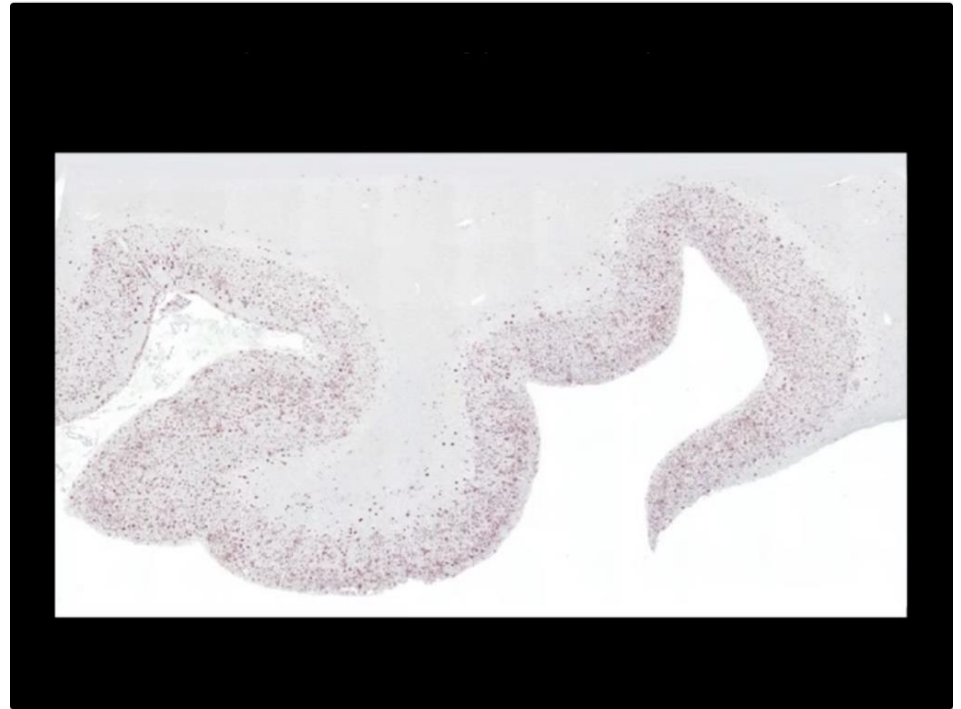deposits found in all
areas of isocortex

Images adapted with permission from Chris Rowe, University of Melbourne

Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. Acta Neuropathol 1991; 82: 239-59.
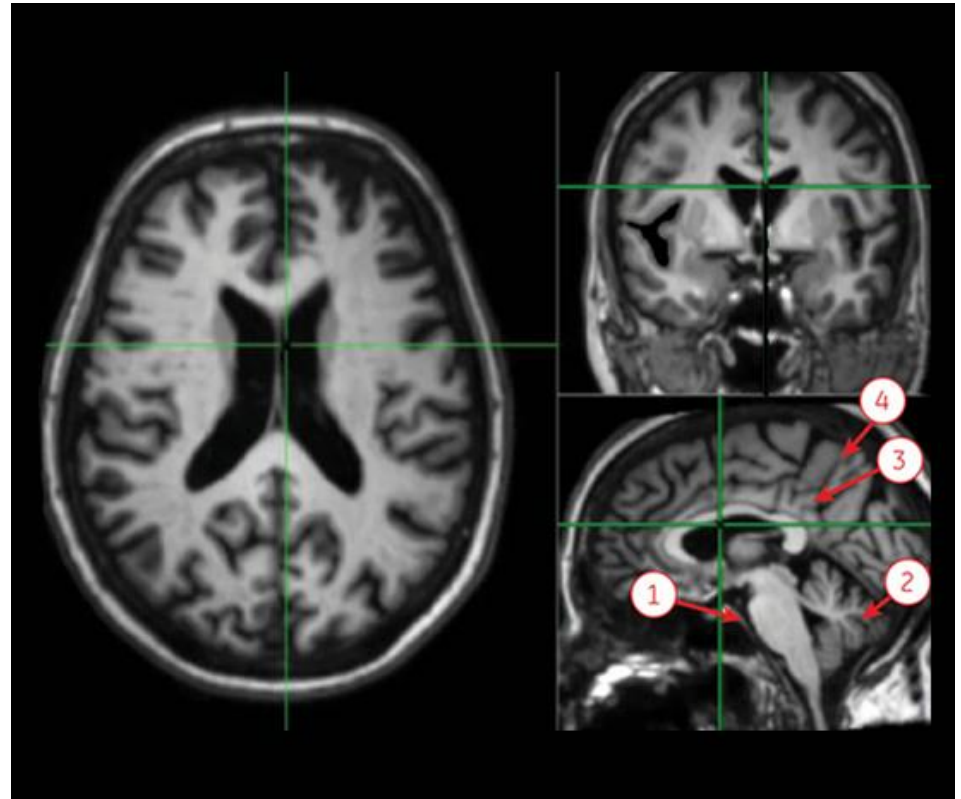
Sagittal view of human brain in MRI
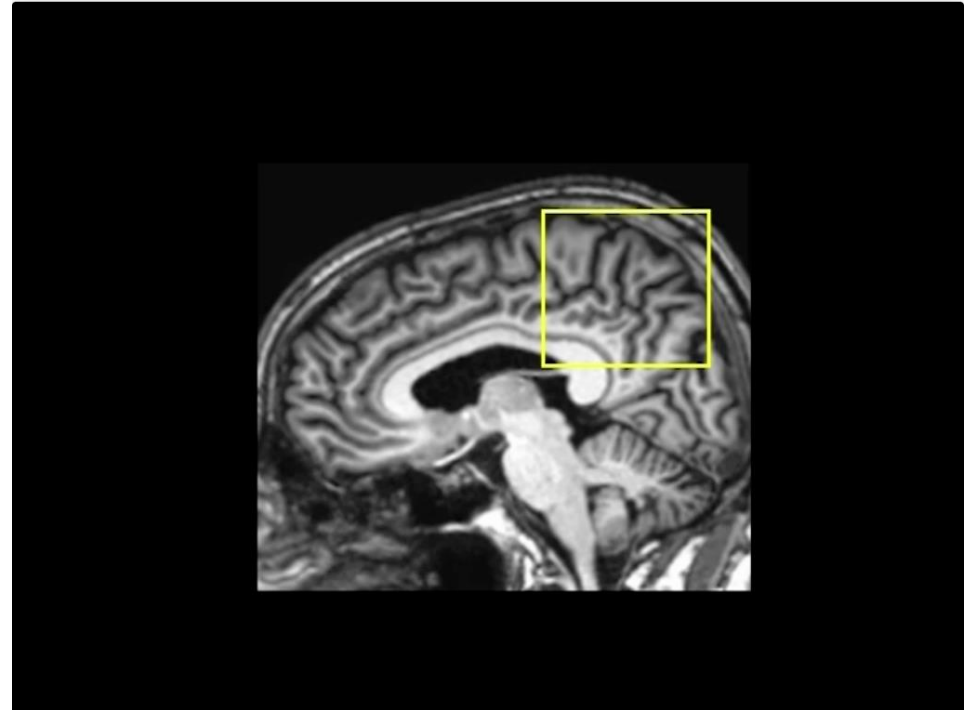
Cortical section of human brain with pathology of Alzheimer's disease

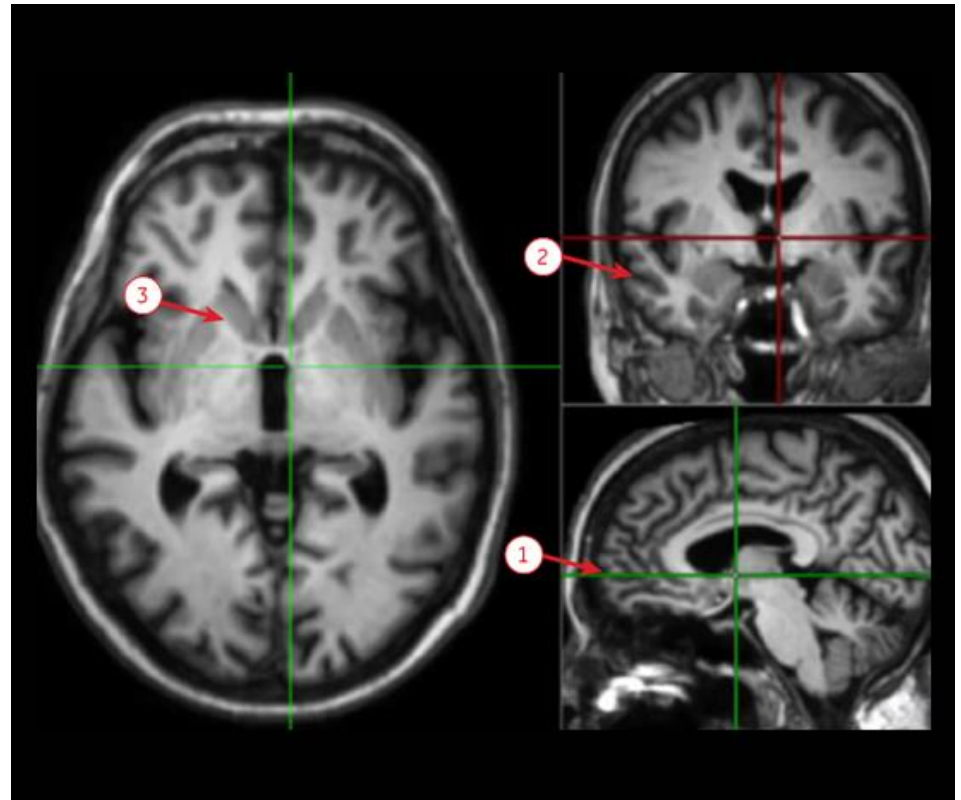Image courtesy of Milos Ikonomovic, University of Pittsburgh

Interactive Q&A session

Structural areas important to note for areas of
Vizamyl uptake

Interactive Q&A session

Structural areas important to note for areas of Vizamyl uptake
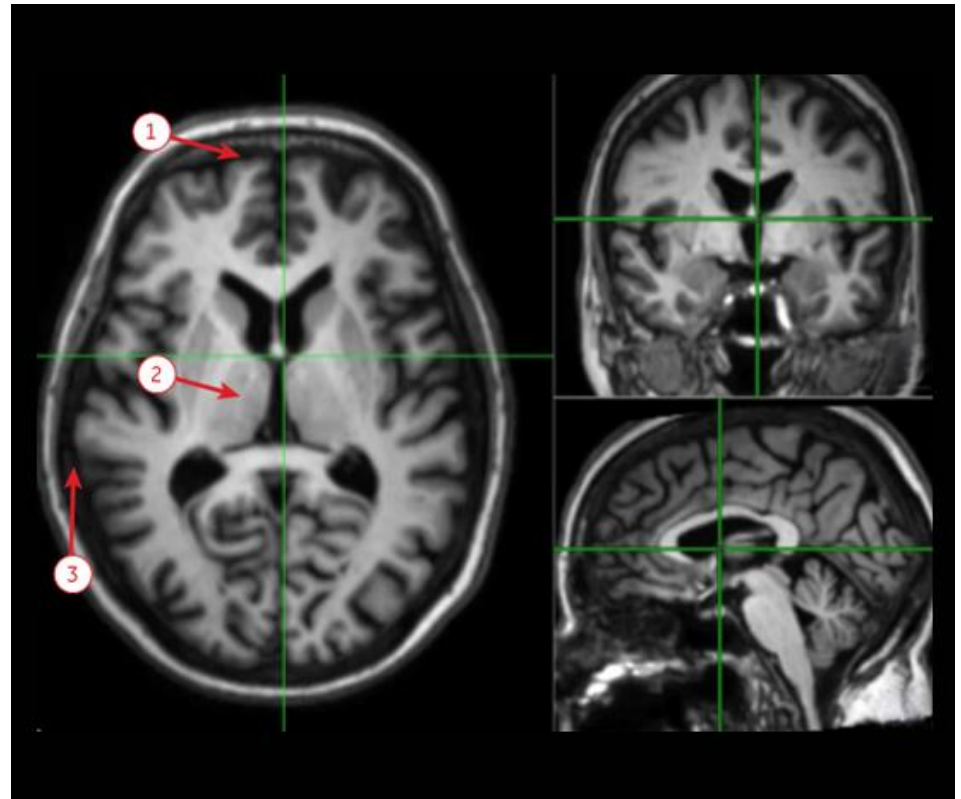
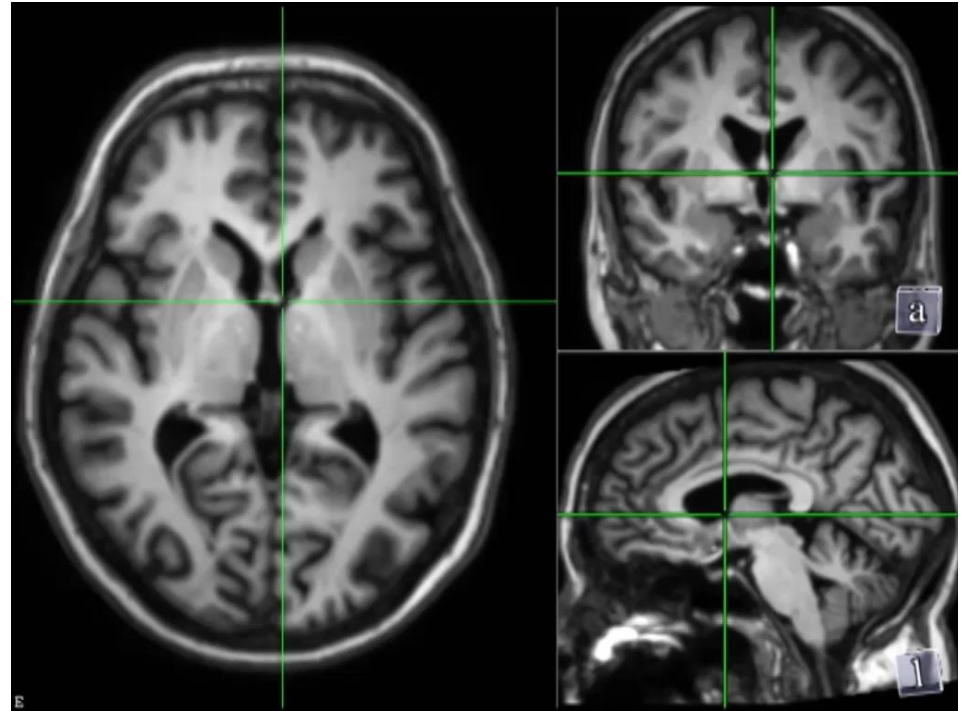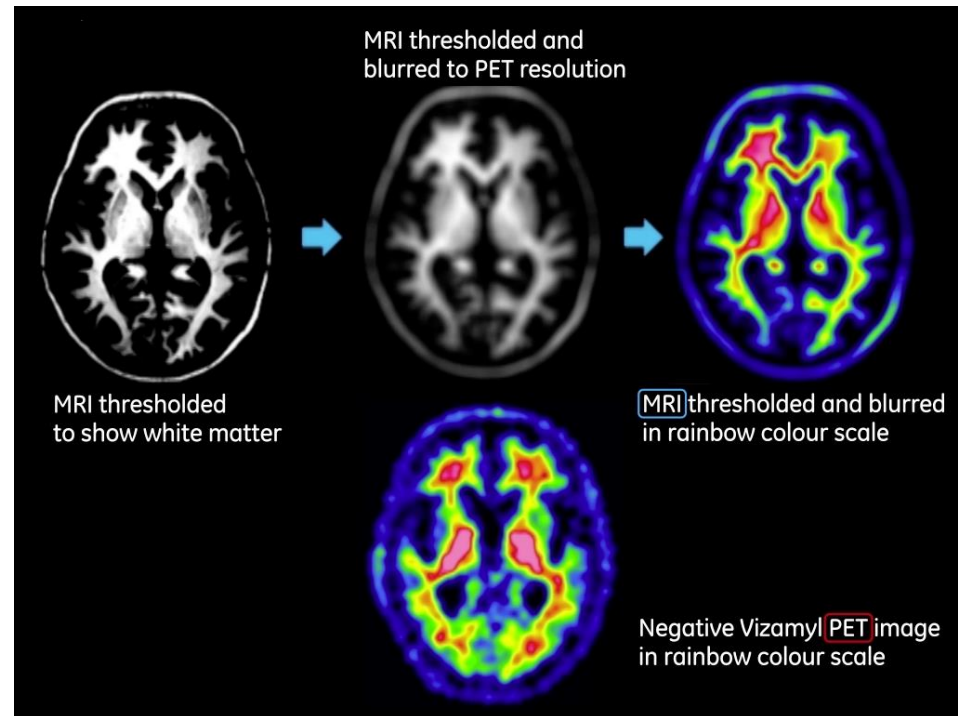## Interactive Q&A session

Structural areas important to note for areas of Vizamyl uptake

MRI anatomy and recognising structures

VIZAMYL™
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Injection

Comparing MRI contrast to PET contrast negative and positive Vizamyl scans

White matter

Comparing MRI contrast to PET contrast negative and positive Vizamyl scans

White & grey matter
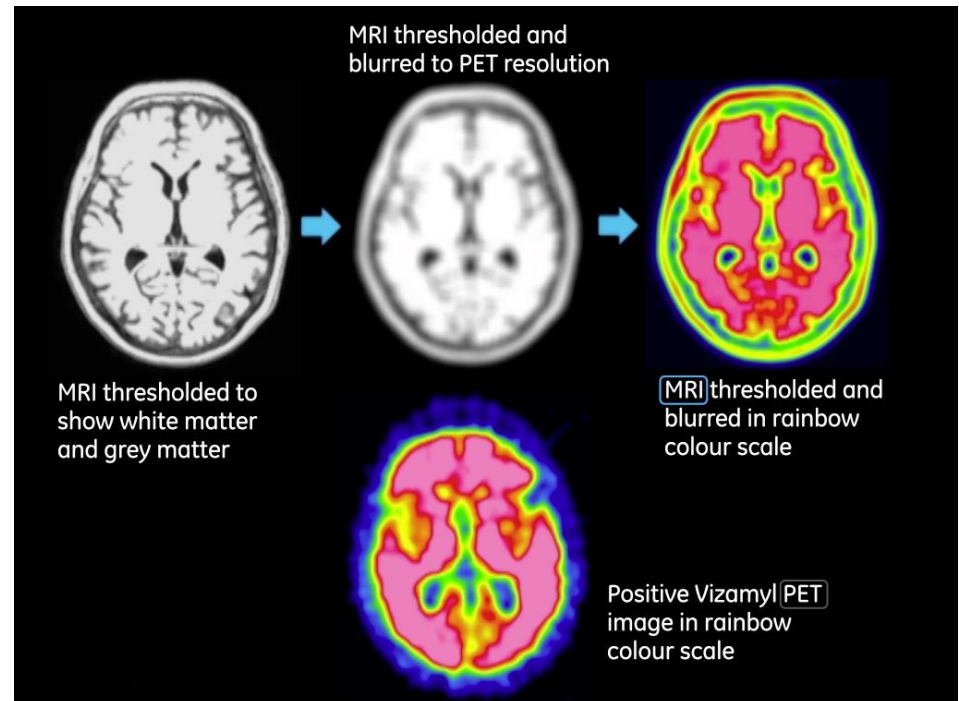
Comparing MRI contrast to PET contrast negative and positive Vizamyl scans
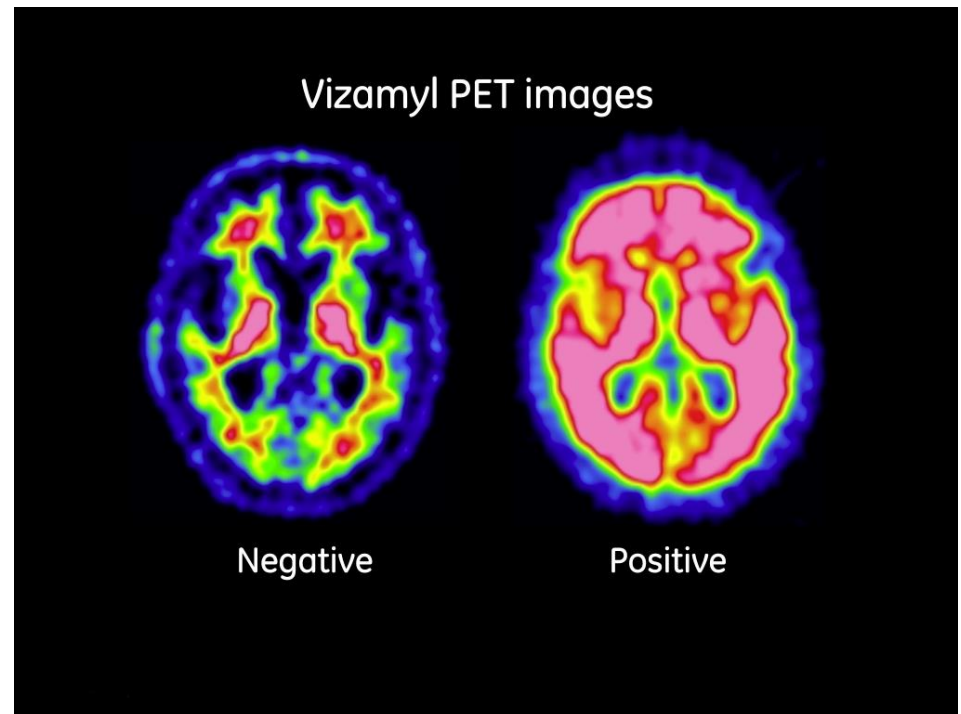
Vizamyl PET images

Negative   Positive

Abbreviations:
MRI: magnetic resonance imaging
PET: positron emission tomography

Comparing MRI contrast to PET contrast negative and positive Vizamyl scans

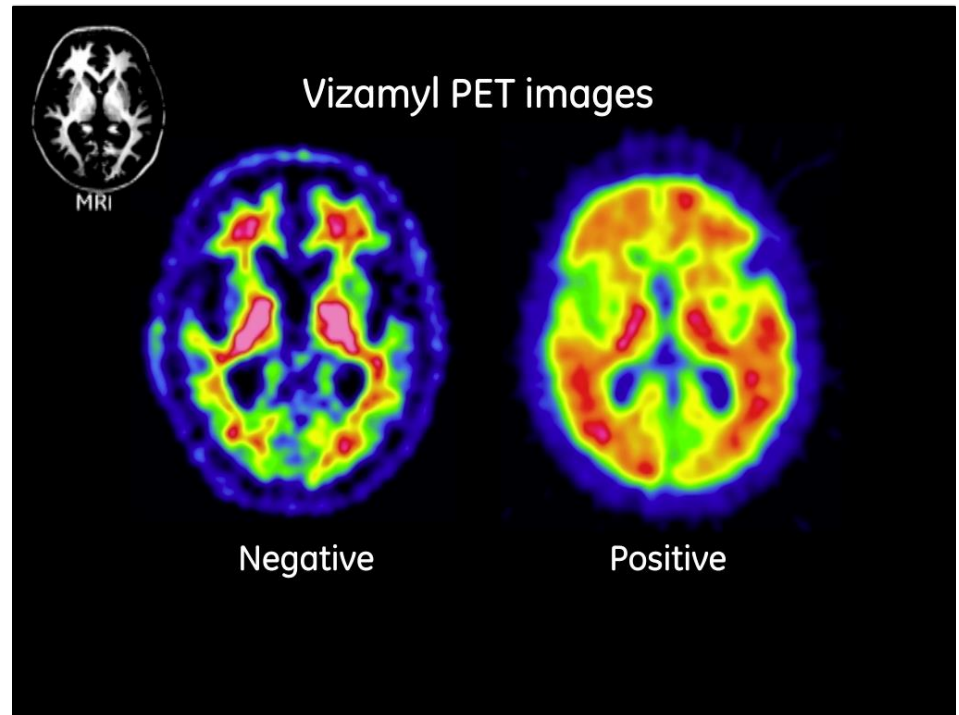Abbreviations:
MRI: magnetic resonance imaging
PET: positron emission tomography

Module 1B: Anatomy in PET – Learning objectives

Welcome to Module 1B: Anatomy in PET

In this module you will learn to recognise and navigate the key assessment areas and landmarks in PET images

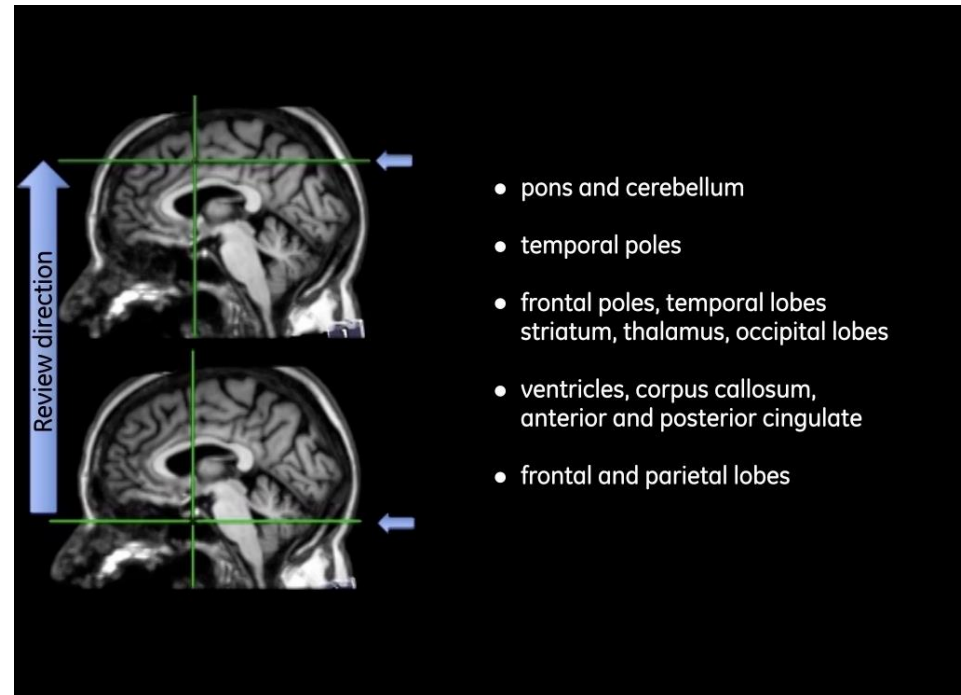- Axial display

- Sagittal display

- Coronal display

Abbreviations:
PET: positron emission tomography

Anatomy in PET – Axial display

(inferior to superior)

Review direction

- pons and cerebellum

- temporal poles

- frontal poles, temporal lobes striatum, thalamus, occipital lobes

- ventricles, corpus callosum, anterior and posterior cingulate

- frontal and parietal lobes

Abbreviations:
PET: positron emission tomography

Anatomy in PET – Axial display

Navigating key areas and landmarks
Axial review (inferior to superior)

Abbreviations:
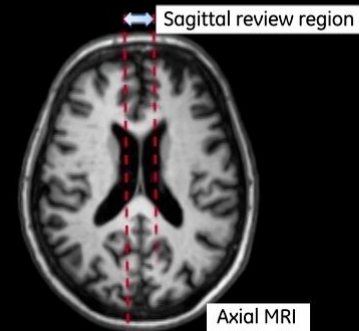PET: positron emission tomography

Anatomy in PET – Sagittal display

(medial surfaces)

- The primary purpose of the sagittal review is to assess the posterior cingulate and precuneus
- Unlike the axial review, the sagittal review is primarily confined to the region of the fissure between the two hemispheres

Sagittal review region

Axial MRI

Abbreviations:
PET: positron emission tomography
MRI: magnetic resonance imaging

Anatomy in PET – Sagittal display

Navigating key areas and landmarks
Sagittal review (medial surfaces)

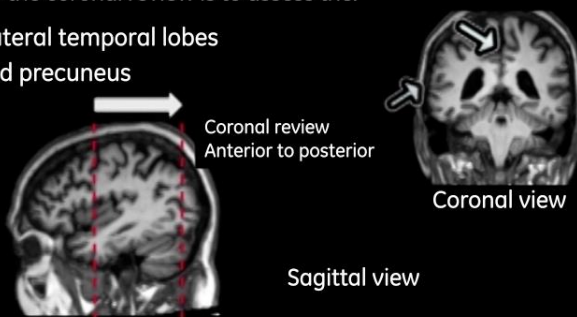Abbreviations:
PET: positron emission tomography

Anatomy in PET – Coronal display

(lateral and medial surfaces)

Anatomy in PET – Coronal display

Navigating key areas and landmarks

VIZAMYL™
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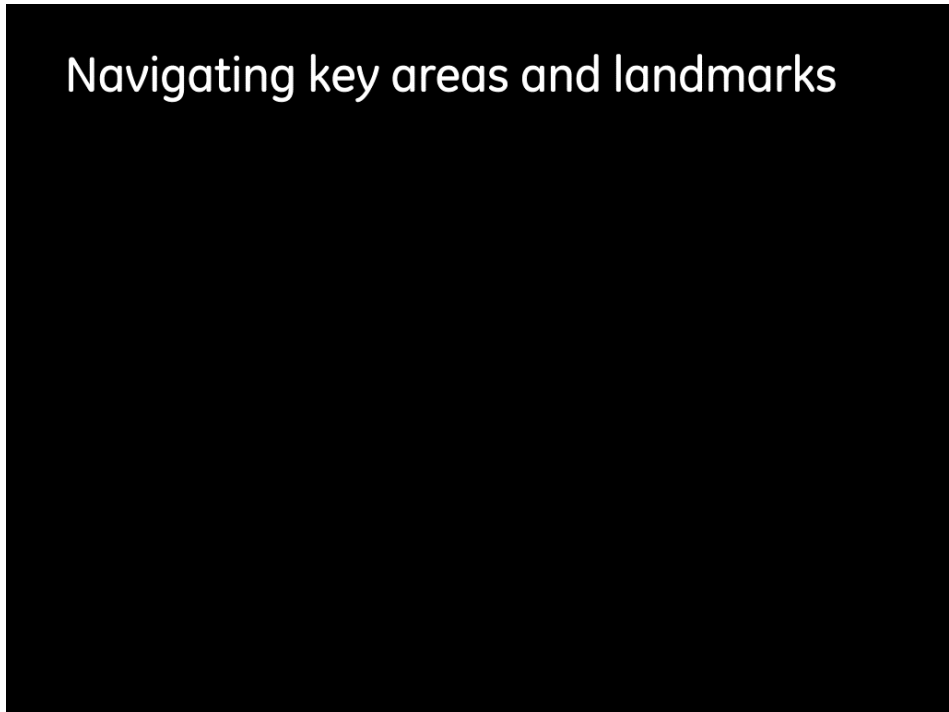
Axial review – Summary

- Scroll the image to identify any atrophy

Frontal:

- Scroll the frontal pole and look for sharp intensity gradients at the frontal edges (positive image) or gradual intensity gradients (negative)

Lateral Temporal:

- Scroll down to axial planes that intersect the temporal lobes and assess lateral aspects for absence or presence of sulcal/gyral pattern (positive or negative respectively) and assess intensity gradients as above

Striatum:

- Scroll around the position of the AC-PC plane and look for either a bridging of intensity between the thalamus and the frontal white matter (indicates a positive striatum) or a reduction of intensity between these structures – (indicates a negative striatum)

Abbreviations:
PET: positron emission tomography

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Injection

Sagittal review – Summary

Posterior cingulate & Precuneus:

- After ensuring proper alignment, touch the sagittal plane into the medial surface of one hemisphere and assess the posterior cingulate/precuneal regions for elevated signal. Do not move in to the medial surface as far as the position where the pons can be seen as being joined in intensity to the cerebella peduncle. Repeat this for the other hemisphere

Striatum:

- The striatum may be checked in sagittal view. Move the medial slice deep into one hemisphere and scroll back to the longitudinal fissure

Abbreviations:
PET: positron emission tomography

Coronal review – Summary

Inferior parietal:

- Scroll the region anterior to posterior traversing the anterior-posterior extent of the cerebellum. Observe the inferior-lateral surfaces of the parietal lobes for loss/presence of a sulcal gyral pattern and sharp or gradual intensity gradient (positive and negative parietal respectively)

Abbreviations:
PET: positron emission tomography

Module 2: Image orientation and display – Learning objectives

Welcome to Module 2: Image orientation and display

In this module you will learn procedures and recommendations for ensuring correct alignment and display of Vizamyl images:

Module 2A: Image orientation

- Axial alignment

- Coronal alignment

- Sagittal alignment

Module 2B: Image display

- Desired features of an intensity/colour scale and reference regions

- Choice of colour scale

- Image intensity levels

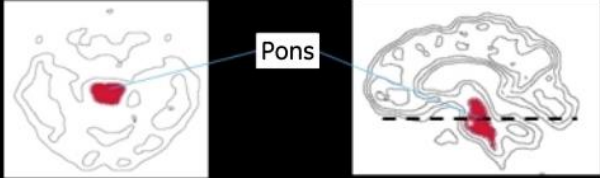## Module 2A: Image orientation – Learning objectives

Welcome to Module 2A: Image orientation

In this module you will learn procedures and recommendations for ensuring correct alignment of Vizamyl images:

- Axial alignment

- Coronal alignment

- Sagittal alignment

Setting the colour scale of Vizamyl PET Images

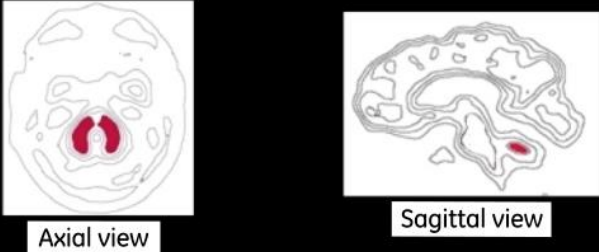First assessment: Navigate to an inferior plane passing though the bulk of the pons in axial and sagittal planes

Pons

Axial view

Sagittal view

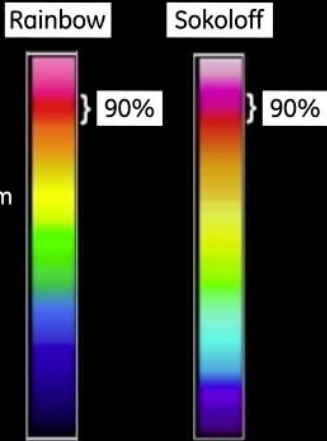Rainbow

Sokoloff

} 90%

} 90%

Inspect and ensure the average intensity in the pons is at 90% of maximum

If you must adjust the image, do so by adjusting the top level only

Second assessment: Inspect the signal saturation via the pons and cerebellar pedunculi and set to ~90% of the display maximum
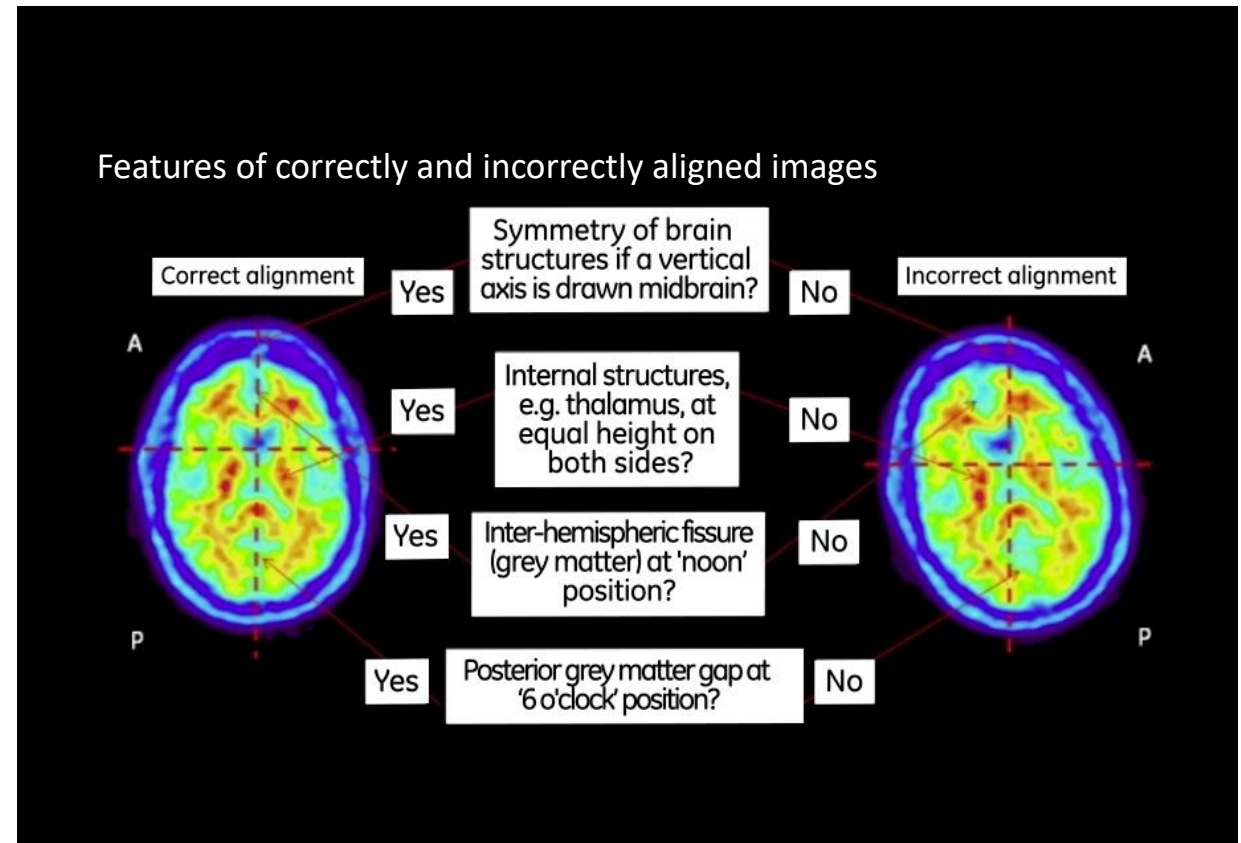
Axial view
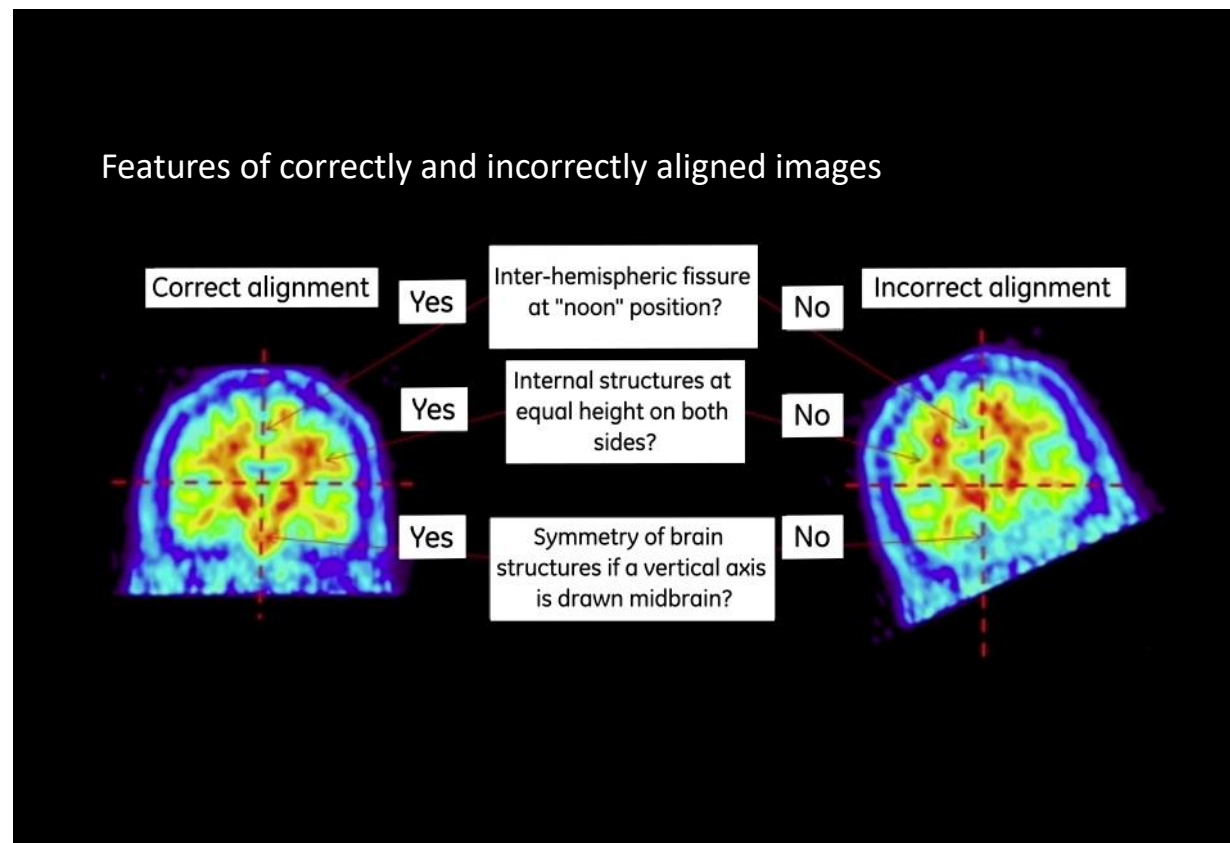
Sagittal view

Example of suitable scales

Abbreviations:
PET: positron emission tomography

Axial view alignment

Features of correctly and incorrectly aligned images

Correct alignment — Symmetry of brain structures if a vertical axis is drawn midbrain? — Yes / No — Incorrect alignment

Internal structures, e.g. thalamus, at equal height on both sides? — Yes / No

Inter-hemispheric fissure (grey matter) at 'noon' position? — Yes / No

Posterior grey matter gap at '6 o'clock' position? — Yes / No

Coronal view alignment

Sagittal view alignment
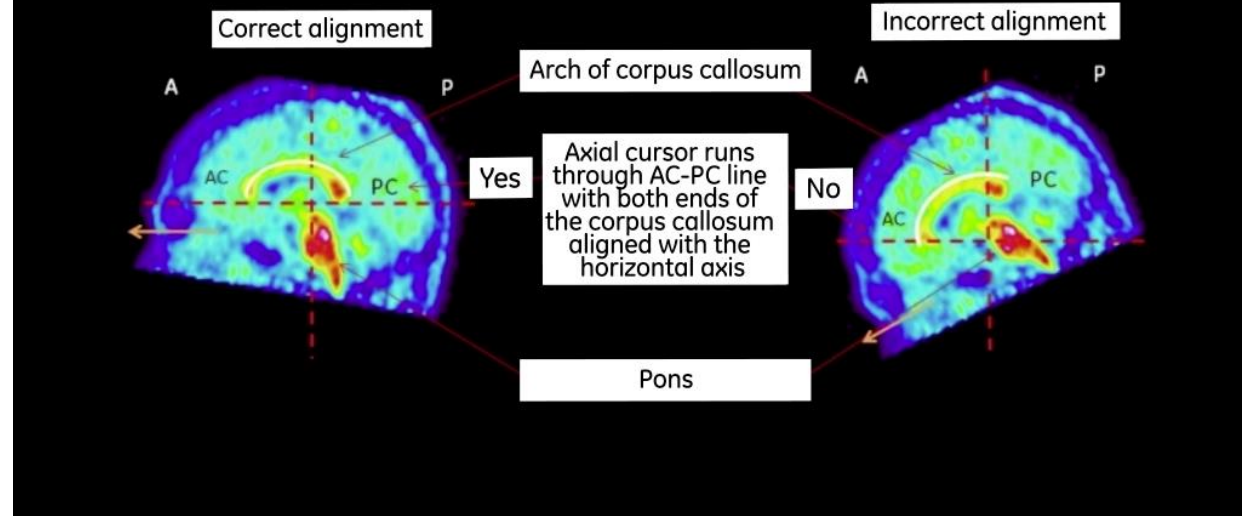
Summary

- All Vizamyl images should be assessed prior to reporting to ensure images are aligned correctly in all image planes

- Always advance to the midbrain slice in all planes before alignment is started

- **Correctly** aligned axial and coronal image: symmetry of the brain structures and they will be at equal heights bilaterally

- **Correctly** aligned sagittal image: AC PC line perpendicular to the bump of the frontal and occipital lobes

- Use outline of brain to assist in correcting head position

- Some workstations may allow all views to be displayed, and others will only allow you to view and re-orient one at a time

- Adjusting all or one of the images a number of times may be necessary to achieve optimal alignment and, therefore, anatomic symmetry

- Asymmetry of tracer uptake does not necessarily indicate asymmetry of brain structures or improper image alignment

- Ensure that all alignment changes are saved when correct alignment is achieved

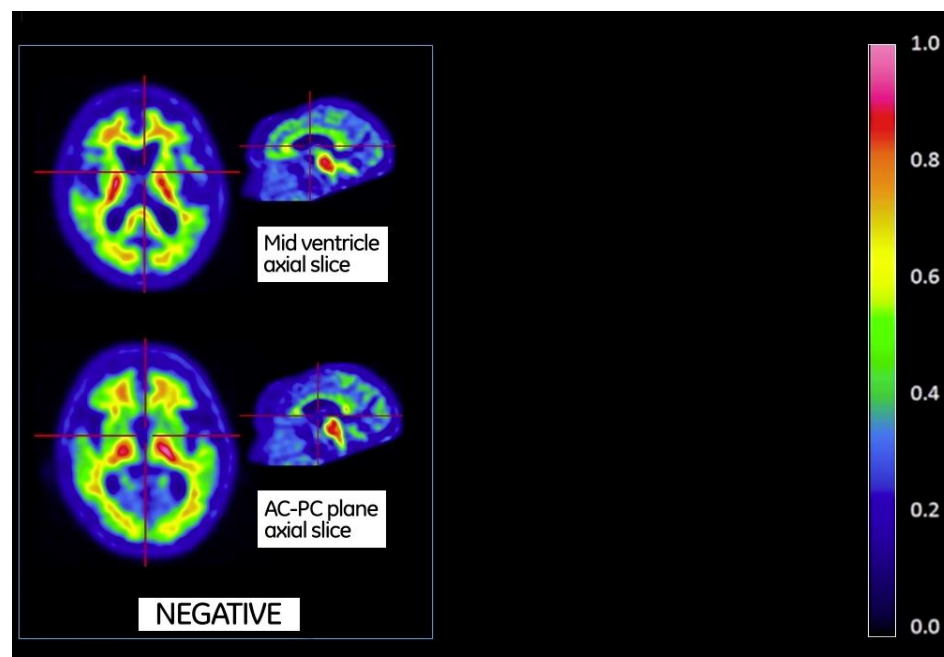## Module 2B: Image display – Learning objectives

Welcome to Module 2B: Image display

In this module you will learn procedures and recommendations for ensuring correct display of Vizamyl images:

- Desired features of an intensity/colour scale and reference regions

- Choice of colour scale

- Image intensity levels

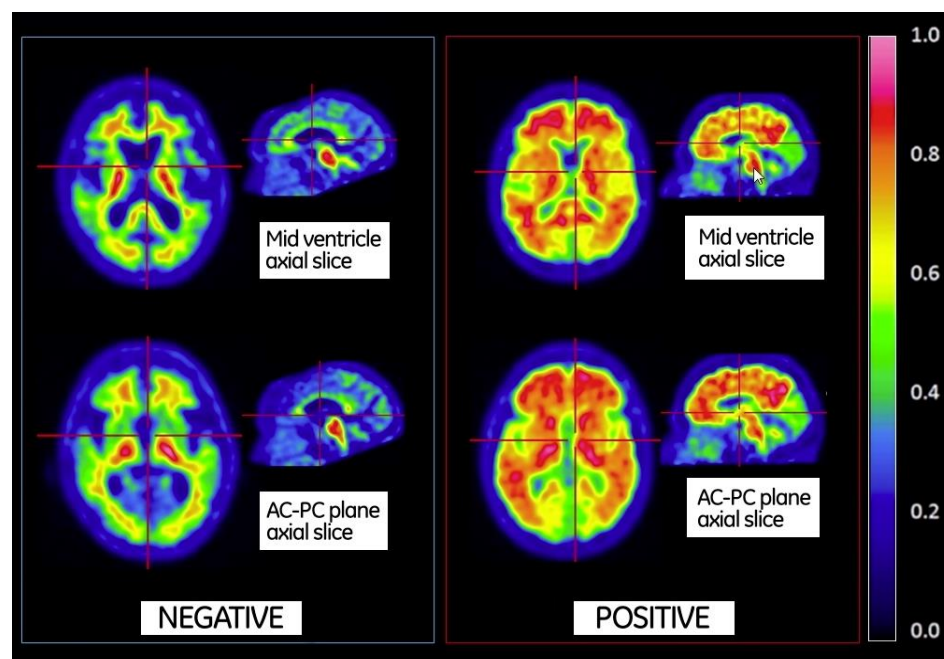# Desired features of an intensity / colour scale and reference regions

Reminder:

The images should be scaled such that the pons is set to 90% of the image intensity maximum

The signal intensity of the pons is set to 90% to maximise the full use of the colour scales

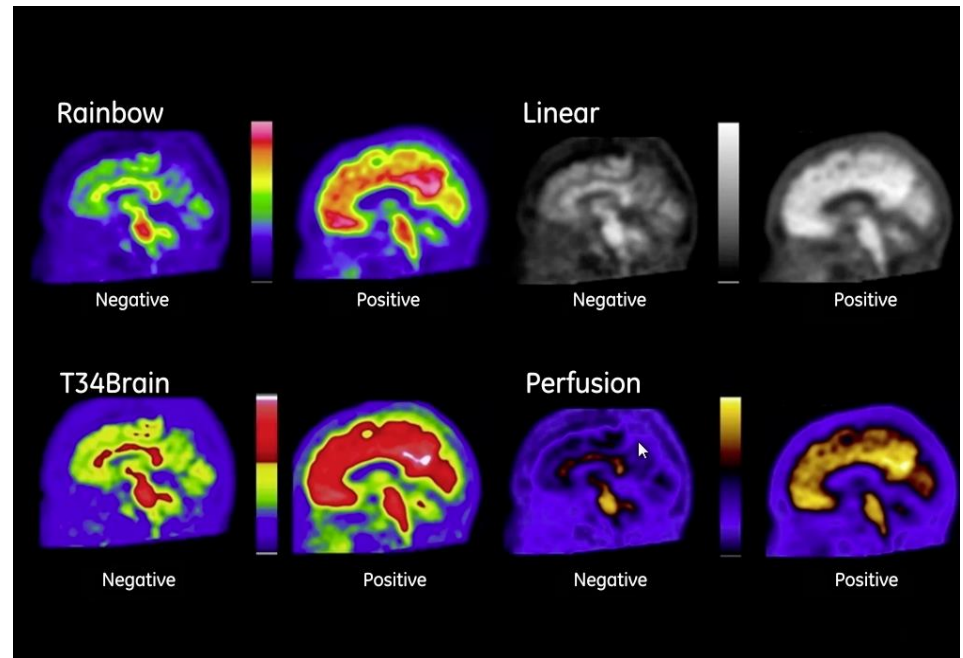# Desired features of an intensity / colour scale and reference regions

Reminder:
The images should be scaled such that the pons is set to 90% of the image intensity maximum
The signal intensity of the pons is set to 90% to maximise the full use of the colour scales

Choice of colour scale

Colour scales with gradual, rapid and abrupt changes

Choice of colour scale

Colour scales with gradual, rapid and
abrupt changes

Selection of an appropriate colour scale is a key aspect for the correct assessment of a Vizamyl scan

Choice of colour scale

Colour scales with gradual, rapid and abrupt changes

Selection of an appropriate colour scale is a key aspect for the correct assessment of a Vizamyl scan

Choice of colour scale

Colour scales with gradual, rapid and abrupt changes

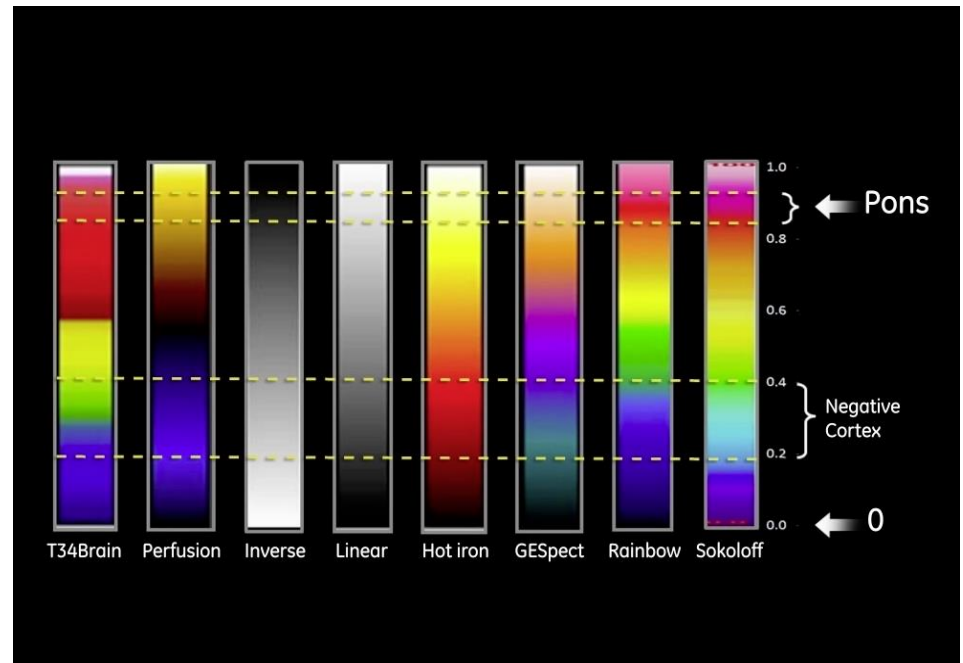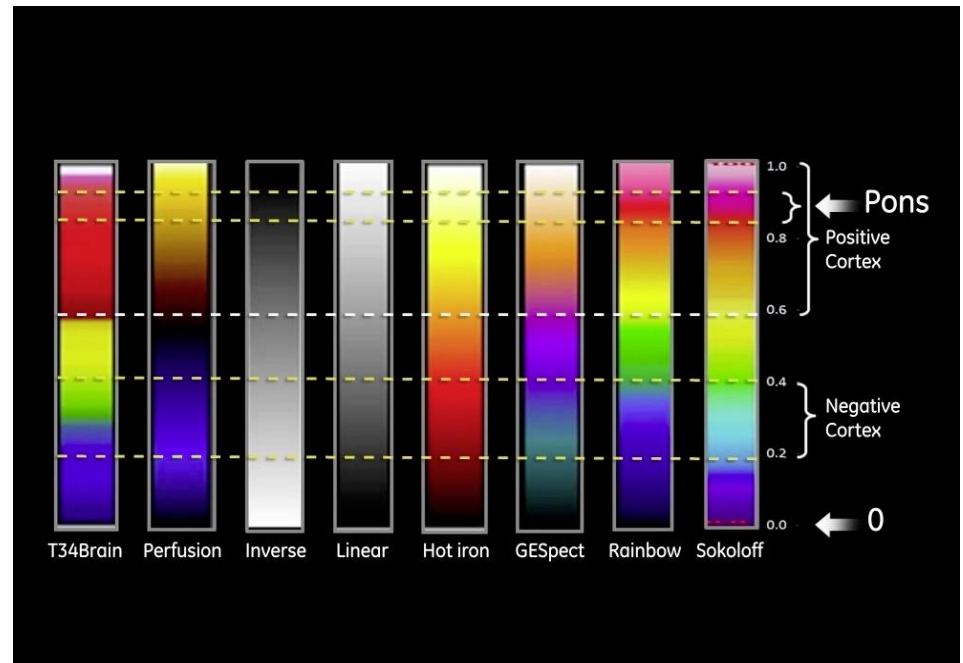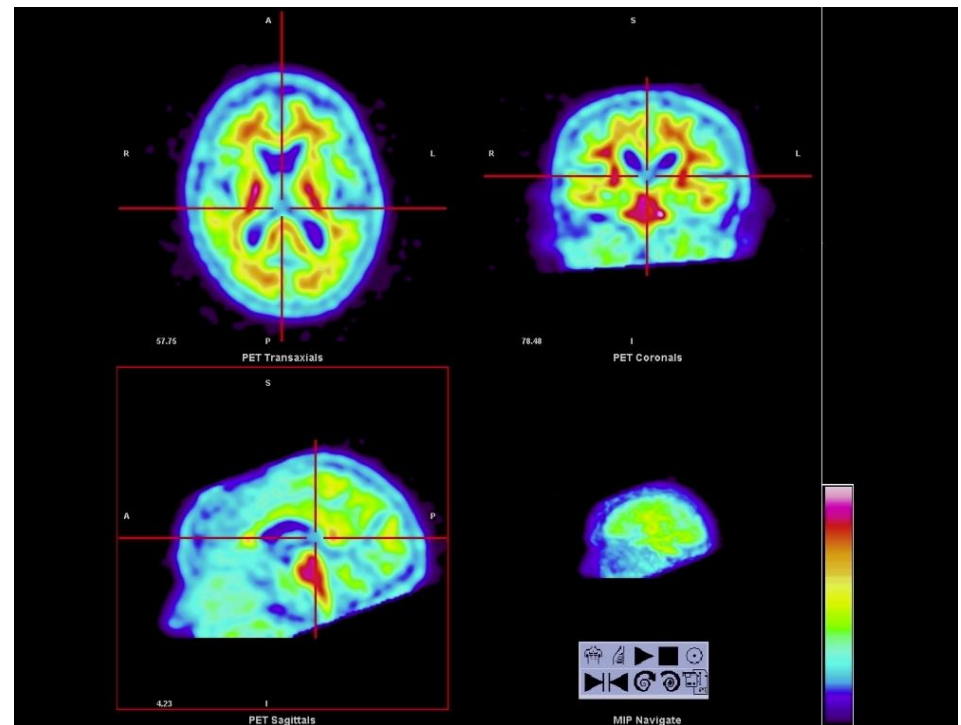
Selection of an appropriate colour scale is a key aspect for the correct assessment of a Vizamyl scan

Image intensity levels

Correctly saturated image

Image intensity levels

Undersaturated image
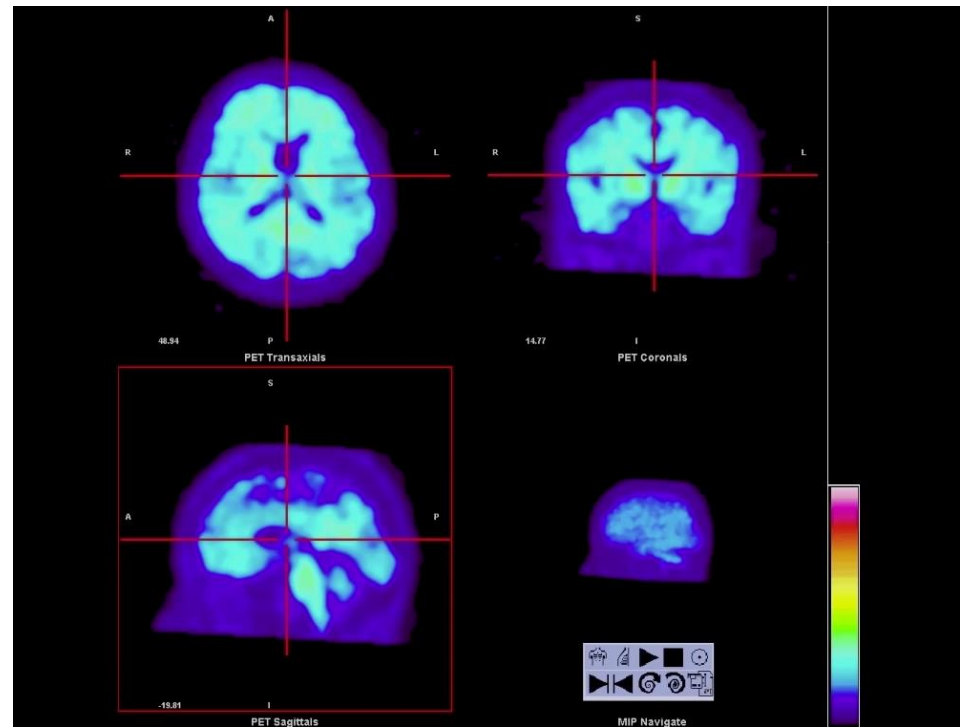
Image intensity levels

Oversaturated image
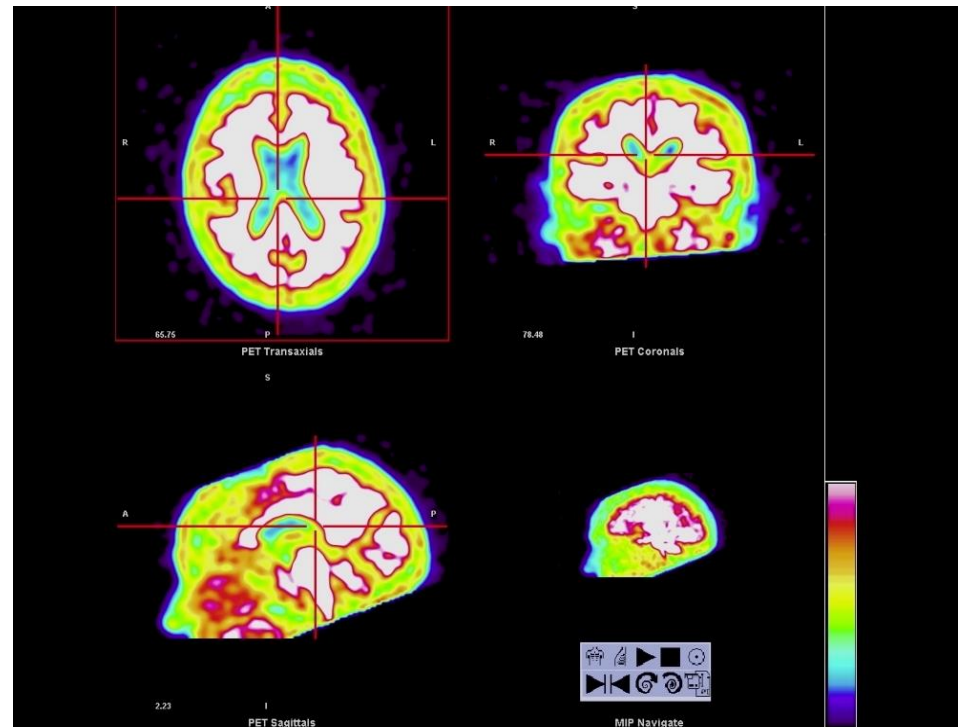
Summary

Important features of a colour scale that provide appropriate discrimination of negative and positive assessments are:

- An identifiable band of colour at 85 to 90% of the image scale to set the intensity in the pons

- A range of colours that make it easy to identify intensity levels **above** 50 to 60 % of maximum intensity which indicates abnormal grey matter intensities

- A range of colours above 60% that help differentiate levels of intensity in equivocal scans

- The Rainbow and Sokolov colour scales show all of these important features

- Grey scales are not recommended and are actively discouraged for the reading and interpretation of Vizamyl scans

Module 3: Image interpretation - Learning objectives

Welcome to Module 3: Image interpretation. In this module you will learn a systematic approach for reading Vizamyl scans

- Introduction

- Regions of interest

- Regions of interest – Frontal lobes

- Regions of interest – Posterior cingulate and precuneus

- Regions of interest – Lateral temporal lobes

- Regions of interest – Parietal lobes

- Regions of interest - Striatum

- Challenging cases

Throughout the module, surveying for atrophy and over-smoothing will be discussed

Vizamyl visual assessment

Based on differentiation of:

- Non-β-amyloid-specific tracer (white matter pattern - negative)
- Specific uptake by β-amyloid (grey matter enhanced pattern - positive)
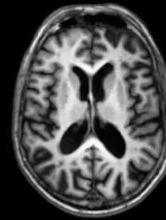
MRI

Threshold MRI white matter
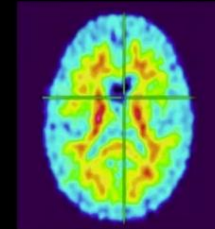
Negative Vizamyl image

Abbreviations:
MRI: magnetic resonance imaging
PET: positron emission tomography

Negative and positive examples

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Injection
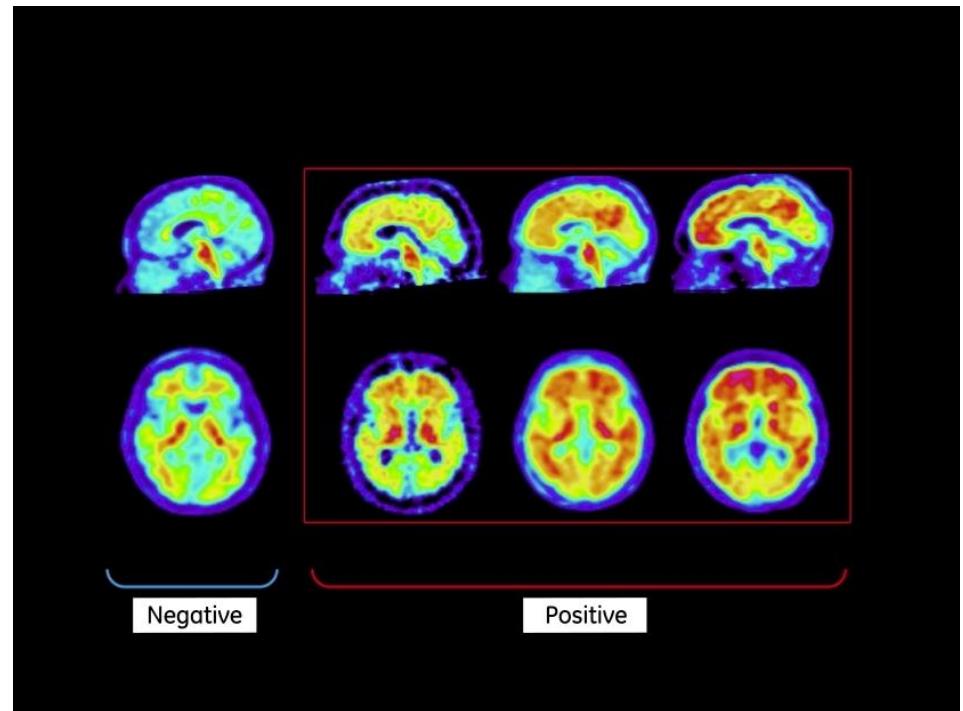
Vizamyl image evaluation

Review as standard:

- Load the image, select the colour map, make sure intensity scaling is appropriate (~90% saturation in pons)

- Survey for atrophy and over-smoothing

- Systematic review of regions of interest

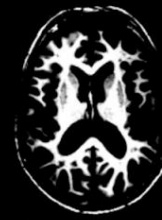| Frontal lobes	Posterior cingulate and precuneus	Lateral temporal lobes	Parietal lobes	Striatum
Axial and sagittal	Sagittal and coronal	Coronal and axial	Coronal and axial	Axial and sagittal
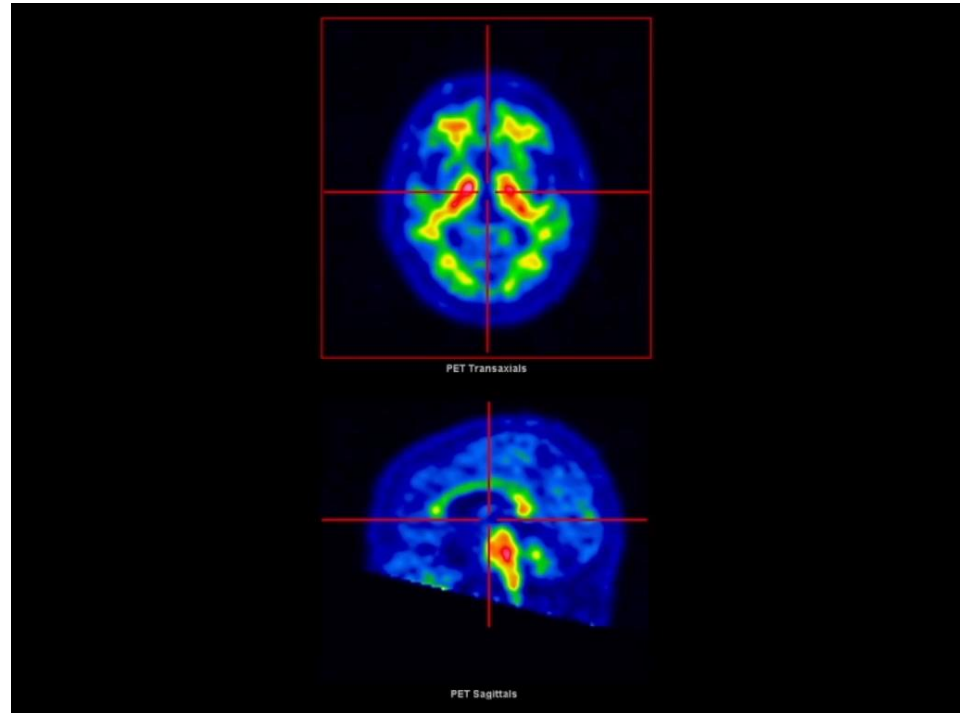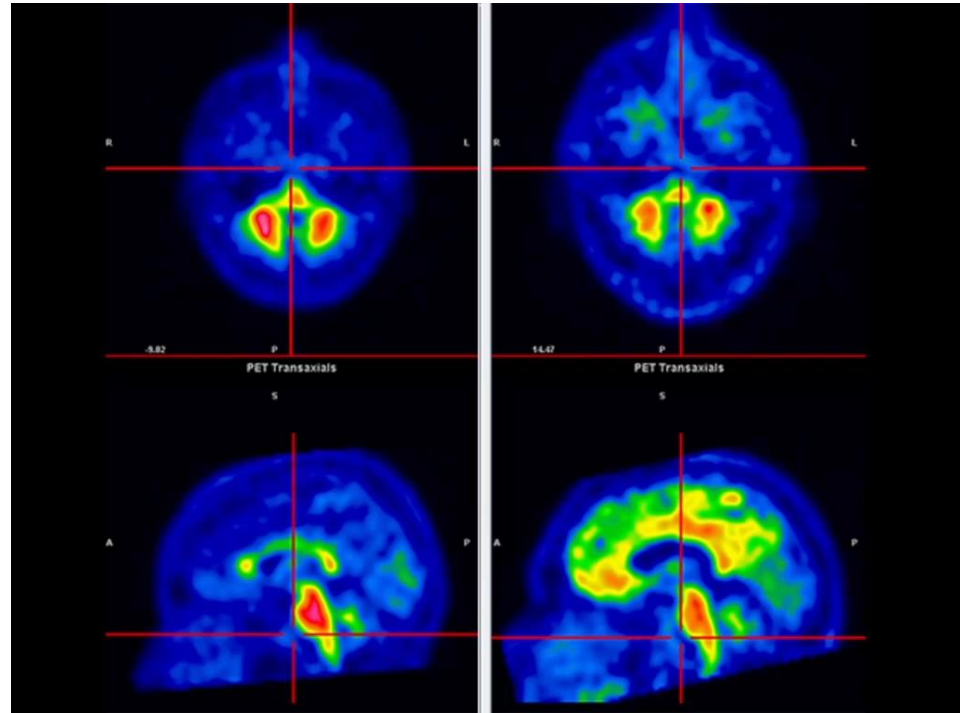
Regions of interest - Frontal lobes

Regions of interest - Frontal lobes
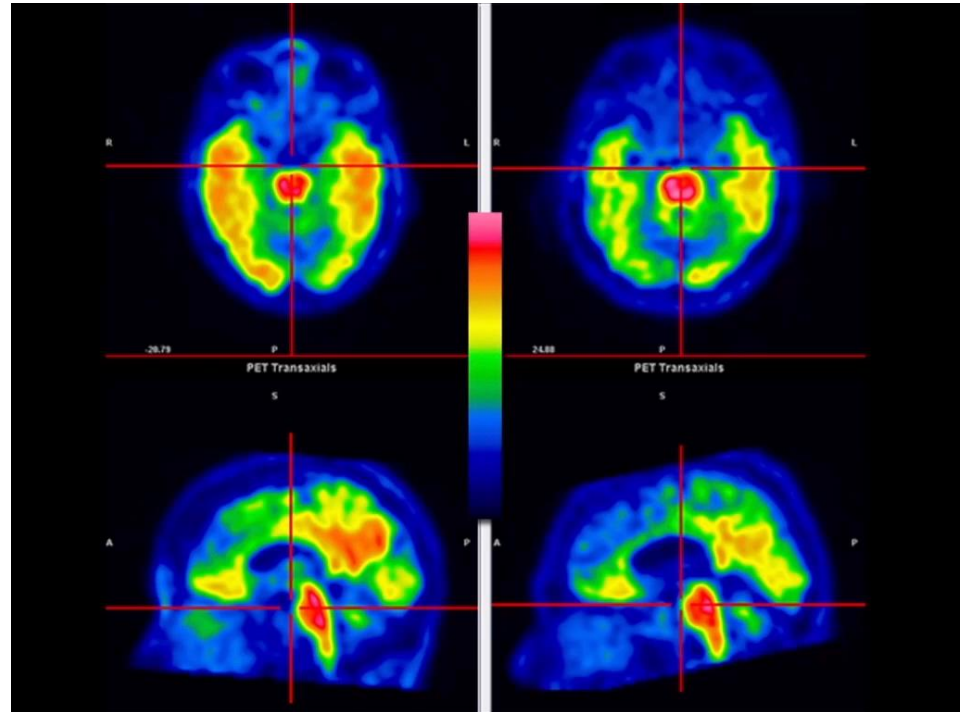
Regions of interest - Frontal lobes

Regions of interest –
Frontal lobes: Summary

Frontal review

The frontal region is generally robust for classifying images

Regions of interest - Frontal lobes: Summary
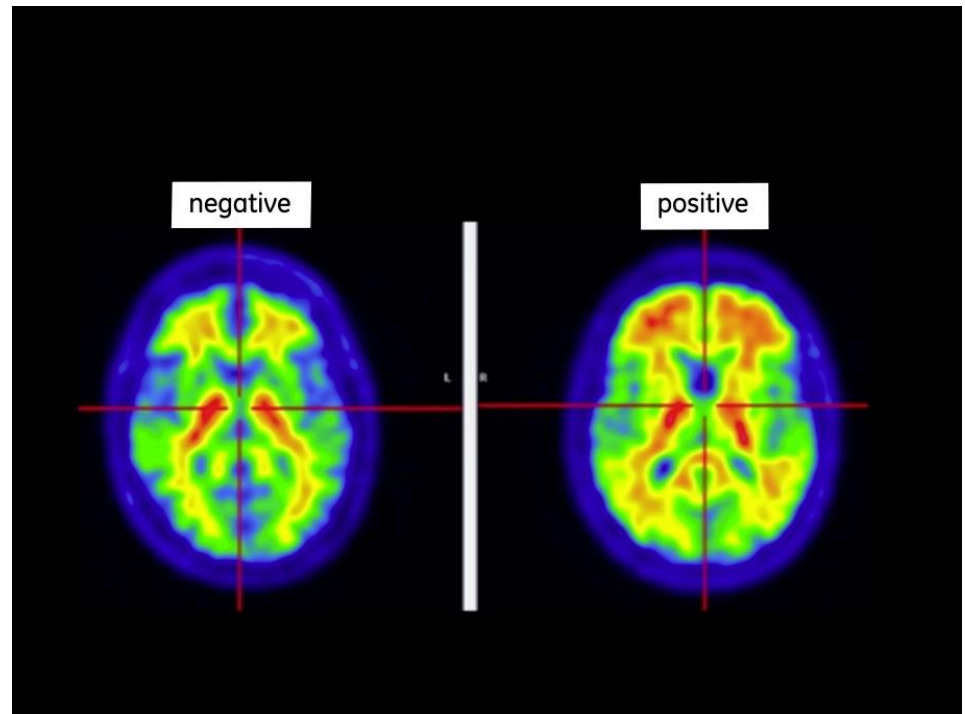
Frontal review

Frontal review:
Confounders and challenges

- Atrophy may make aspects of the frontal lobes appear negative in a positive scan

- Signs that atrophy may be present are:

  - Asymmetries to the frontal/medial surfaces seen in axial review: e.g.
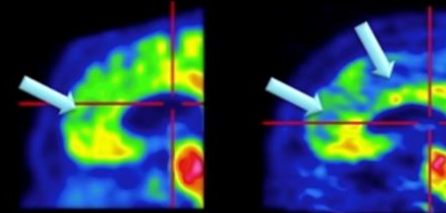
Frontal review:
Confounders and challenges

Frontal review:
Confounders and challenges

- Atrophy may make aspects of the frontal lobes appear negative in a positive scan

- Strategies to avoid the effects of atrophy:
  - Scroll the frontal pole

Frontal review: Recap

Frontal review: Recap

Regions of interest –
Posterior cingulate and precuneus

Posterior cingulate and precuneus review

- Sagittal review

- Using landmarks and features to select an appropriate review plane

- Features of negative and positive posterior cingulate & precuneus regions

- Coronal review

- The region to scroll in this review

- Confounding factors and summary
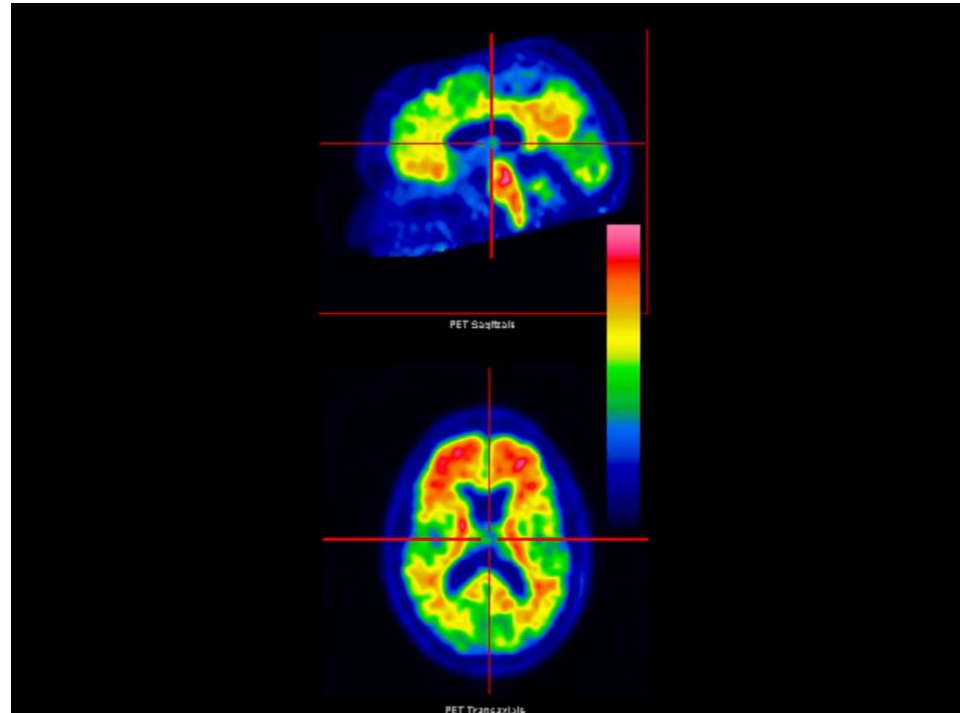
Regions of interest –
Posterior cingulate and precuneus

Regions of interest –
Posterior cingulate and precuneus

Regions of interest –
Posterior cingulate and precuneus

Regions of interest –
Posterior cingulate and precuneus
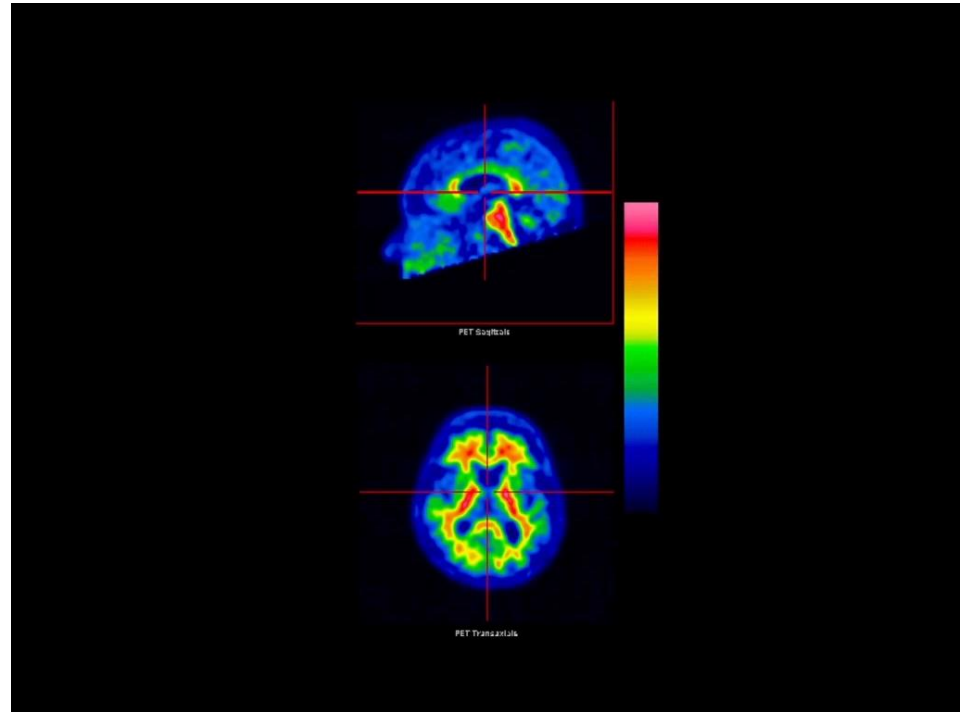
Regions of interest - Posterior cingulate and precuneus: Summary

Summary

- The sagittal review is the primary review plane

  – Avoid white matter rich regions (sagittal) by using landmarks

- This is supported by a coronal (scrolling) review

Confounders and Challenges

- Image tilt may make location of the optimal review plane difficult

  – Strategies to avoid this:

    o Survey the image to identify any tilts and take this into account in medial plane positioning

    o If the sagittal view is compromised, rely more on the coronal (scrolling) review

Regions of interest –
Lateral temporal lobes

- Axial review

  – Ascend from the base of the brain scrolling to review lateral aspects

- Coronal review

  – Scroll from the anterior aspects of the temporal poles towards the posterior

- Confounding factors and summary

Regions of interest – Lateral temporal lobes

Regions of interest –
Lateral temporal lobes

Regions of interest – Lateral temporal lobes

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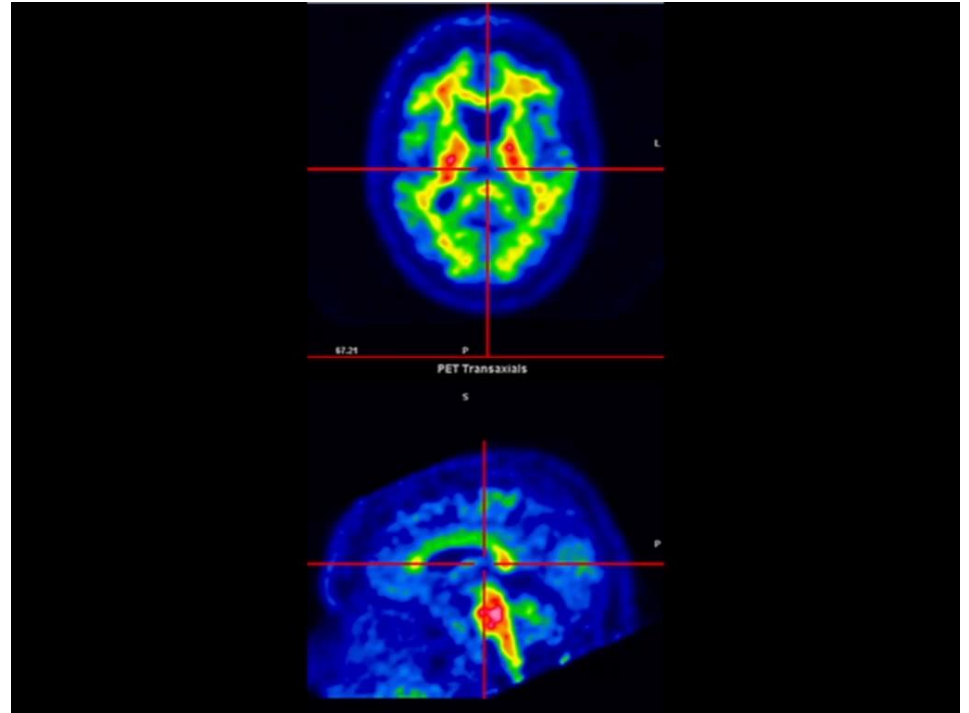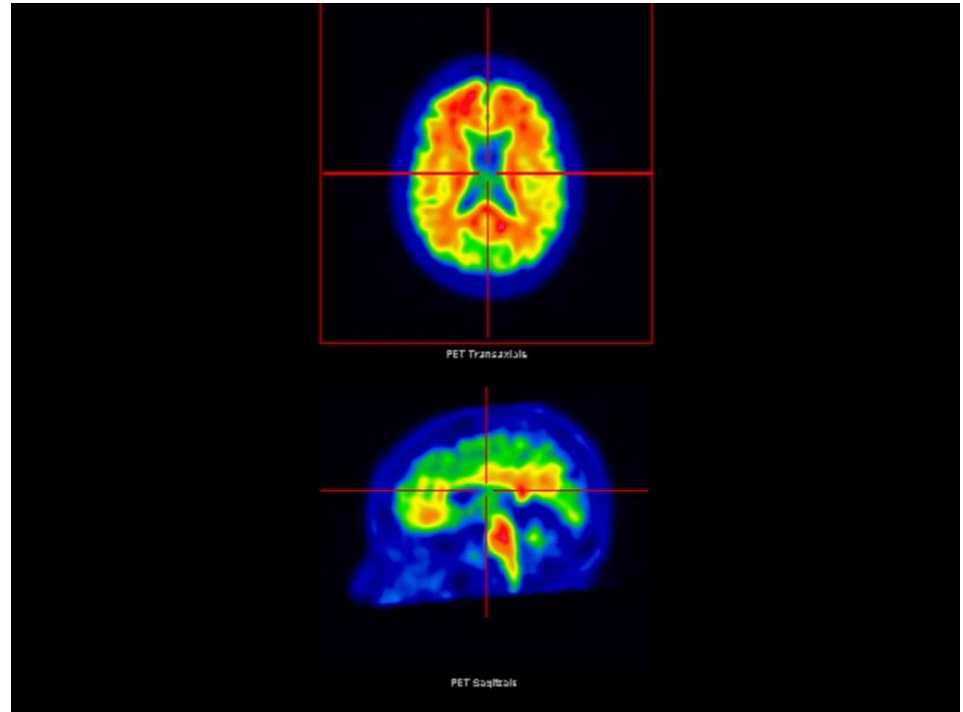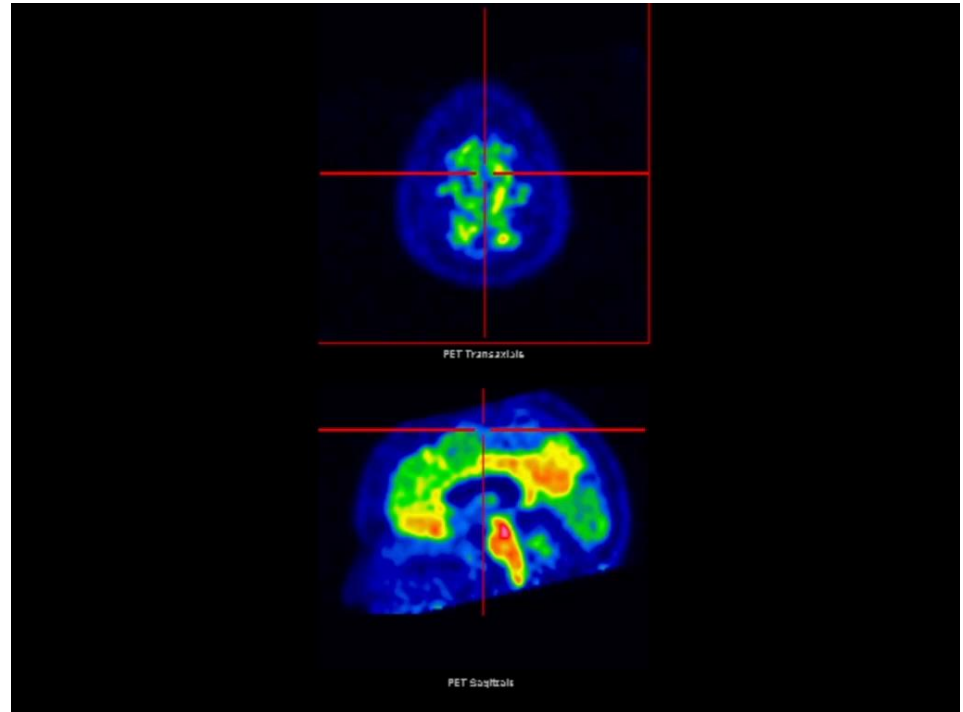
Regions of interest –
Lateral temporal lobes: Summary

Summary

- Axial review (primary review)

- Ascend from the base of the brain scrolling to review lateral aspects

- Coronal review (supporting)

- Scroll from the anterior aspects of the temporal poles towards the posterior just past the extent of the corpus callosum

Main confounding factor:

- Temporal lobes are resolved

Regions of interest –
Parietal lobes

- Axial review

- Ascend from the Sylvian fissue scrolling to review lateral aspects

- Coronal review

- Scroll from the anterior aspect of the pons towards the posterior aspect of the cerebellum

- Concentrate on the inferior aspects in coronal as superior aspects may be corrugated due to atrophy

Regions of interest –
Parietal lobes

PET Transaxials

PET Sagittals
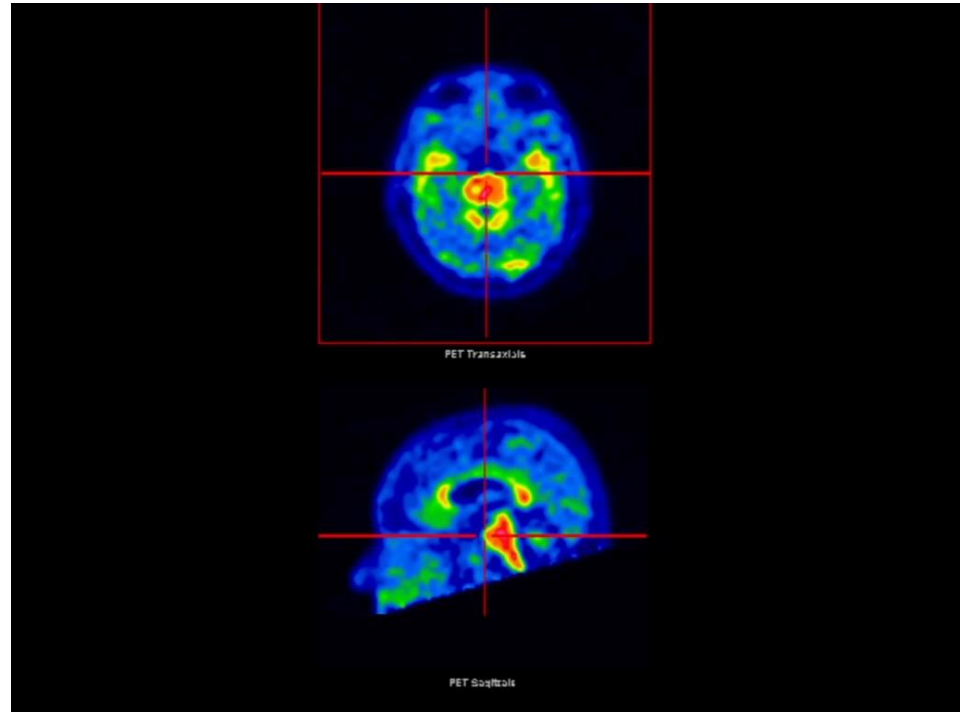
Regions of interest –
Parietal lobes
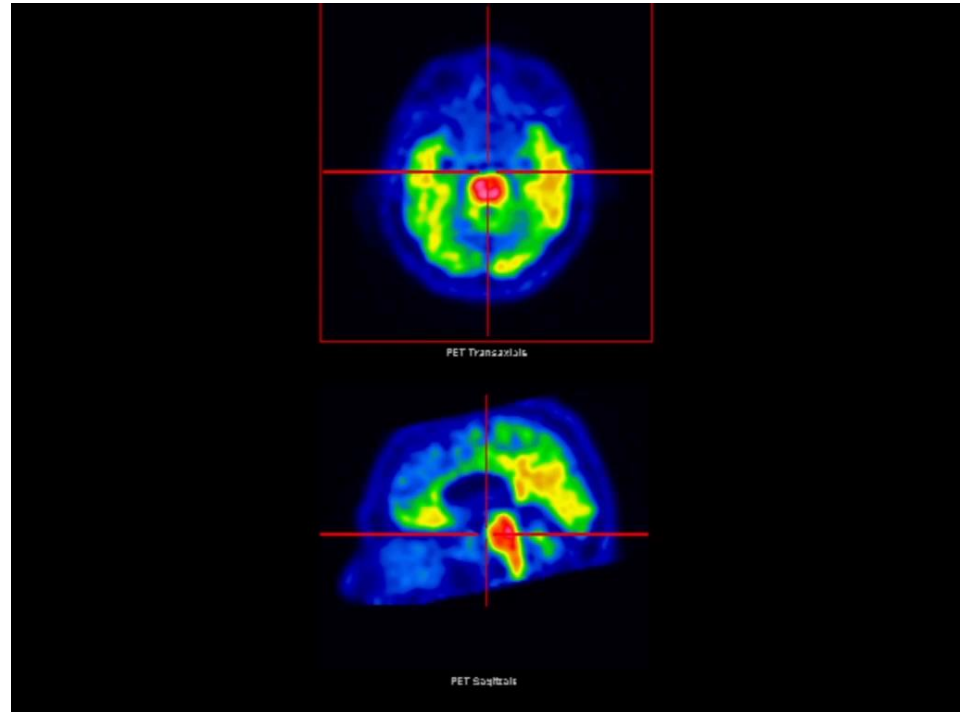
Regions of interest –
Parietal lobes: Summary

Summary

- Coronal review is the main review, and axial is supportive

- Coronal review

  – Scroll from the anterior aspect of the pons towards the posterior aspect of the cerebellum

  – Concentrate on the inferior aspects in coronal, as superior aspects may be corrugated due to atrophy

- Confounding factors

  – Subject to atrophy producing indentations

    o Particularly to the superior aspects

Regions of interest – Striatum

Axial review

- Scrolling in the region bounded by the top of the pons and the corpus callosum

- A negative striatum is characterised by a low intensity (~50% of maximum) between the thalamus and the frontal white matter

- A positive striatum has a high intensity >60% in this region, and no intensity "gap" can be seen

Sagittal review (supportive)

- Scroll deep into one hemisphere and scroll back toward the medial surface
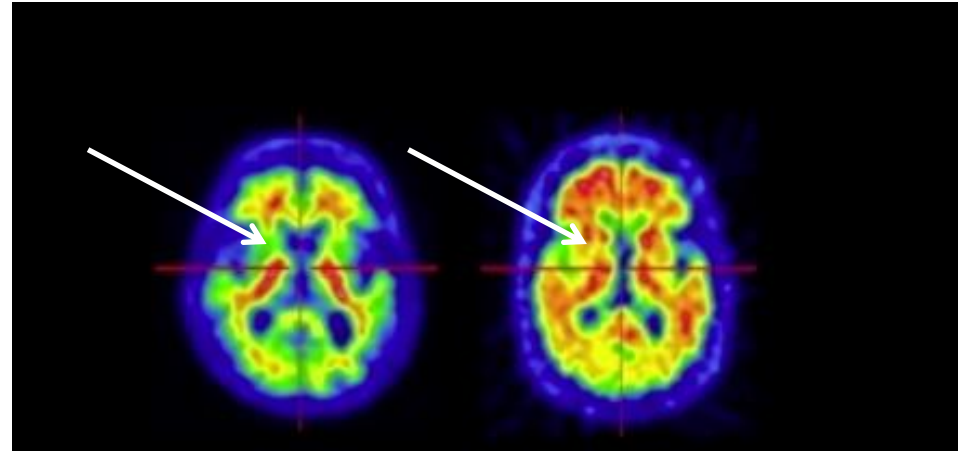
Regions of interest – Striatum

Regions of interest – Striatum

Summary

- Axial review is the main review, and sagittal is supportive

- Axial review

  - Scroll in planes bounded by the superior extent of the pons and the posterior corpus callosum

  - Look for absence or presence of bridging intensity between the thalamus and the frontal white matter

- Confounding factors

  - Involvement is quite variable; the striatum may be negative while other areas are positive

  - However, it is less influenced by atrophy than other regions

Challenging cases

Difficulty in classifying cases may arise from:

- Atrophy

  - Shrinkage of the grey matter in a positive image may make the grey matter signal less distinct

- Lesions

  - May result in diminished signal from a region or regions of the brain

- Excessive noise

  - May make the scan hard to read

- Equivocal cases

  - Result in low confidence in classification

Equivocal cases

- Most images are readily identified as either negative or positive; a small percentage of images may be equivocal

- This could mean that the cortical uptake is above 50% in some regions, but not at the higher levels of 75 to 100%

- **In order to classify such an image as positive, the image must have at least one region which is clearly positive**

Equivocal cases

Challenging cases

Equivocal cases

- Where intensity levels are equivocal, rely more on the pattern.

- Can you clearly see a sulcal pattern?

- A single case is shown in coronal (upper) and axial (lower) with linked cross hairs indicating the review location

- This case has some equivocal regions, however, lateral temporal and parietal regions have signs of positive uptake
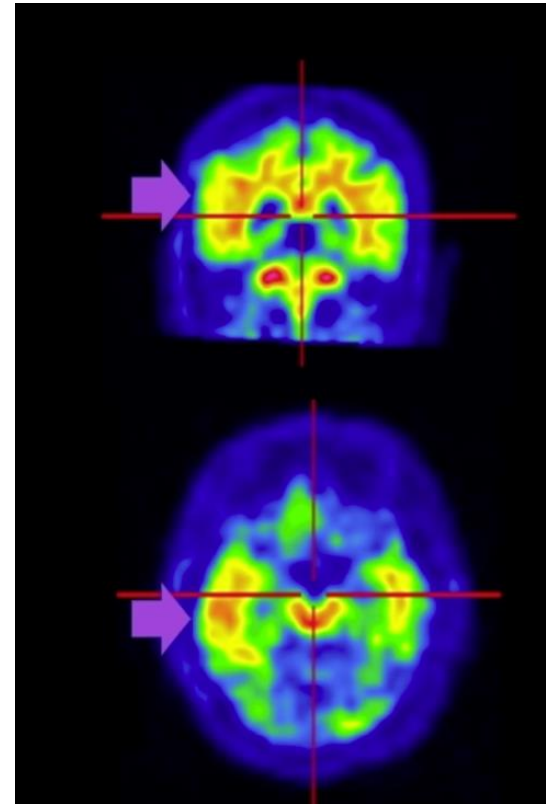
Reviewing brains that have atrophy

Atrophy precuneus/occipital

Positive Case Example

How would atrophy appear in a Vizamyl scan?

Atrophy precuneus/occipital

Positive Case Example

Atrophy precuneus/occipital

Negative Case Example

Axial assessment – Lower extent of corpus callosum

Positive Case Example

How would atrophy appear in a Vizamyl scan?

Use of CT with PET images
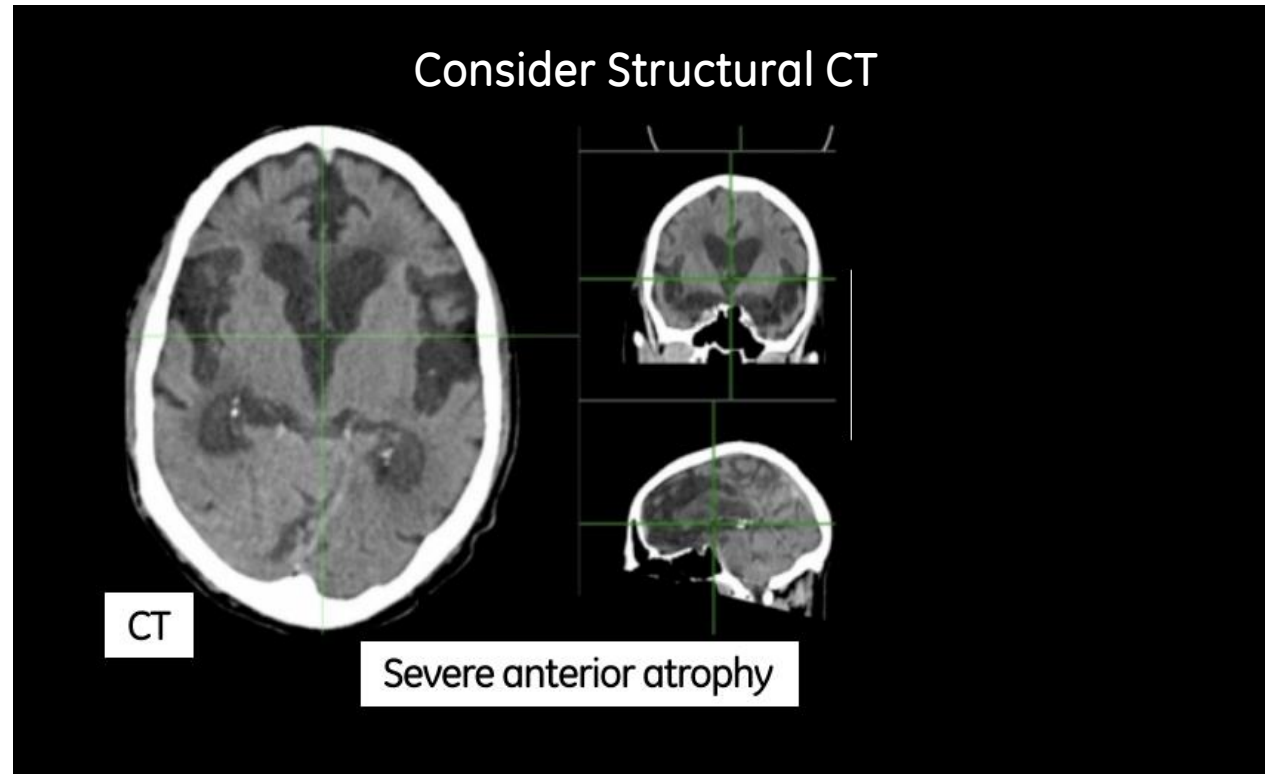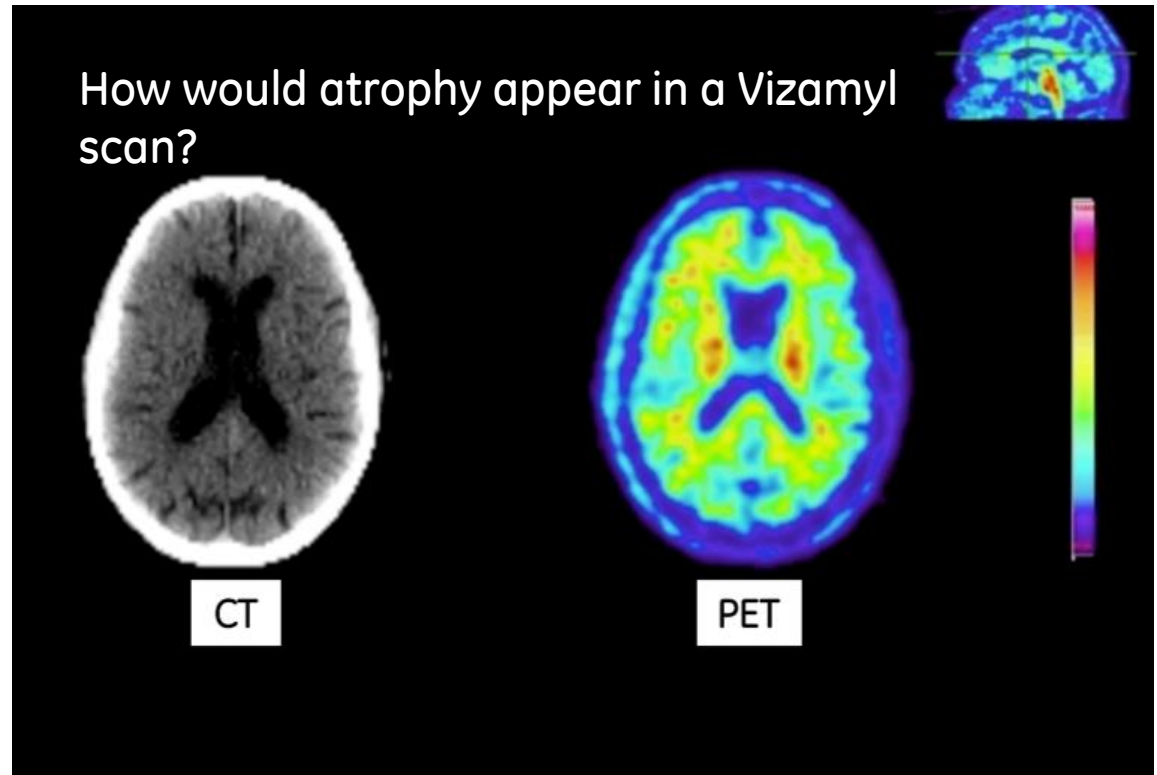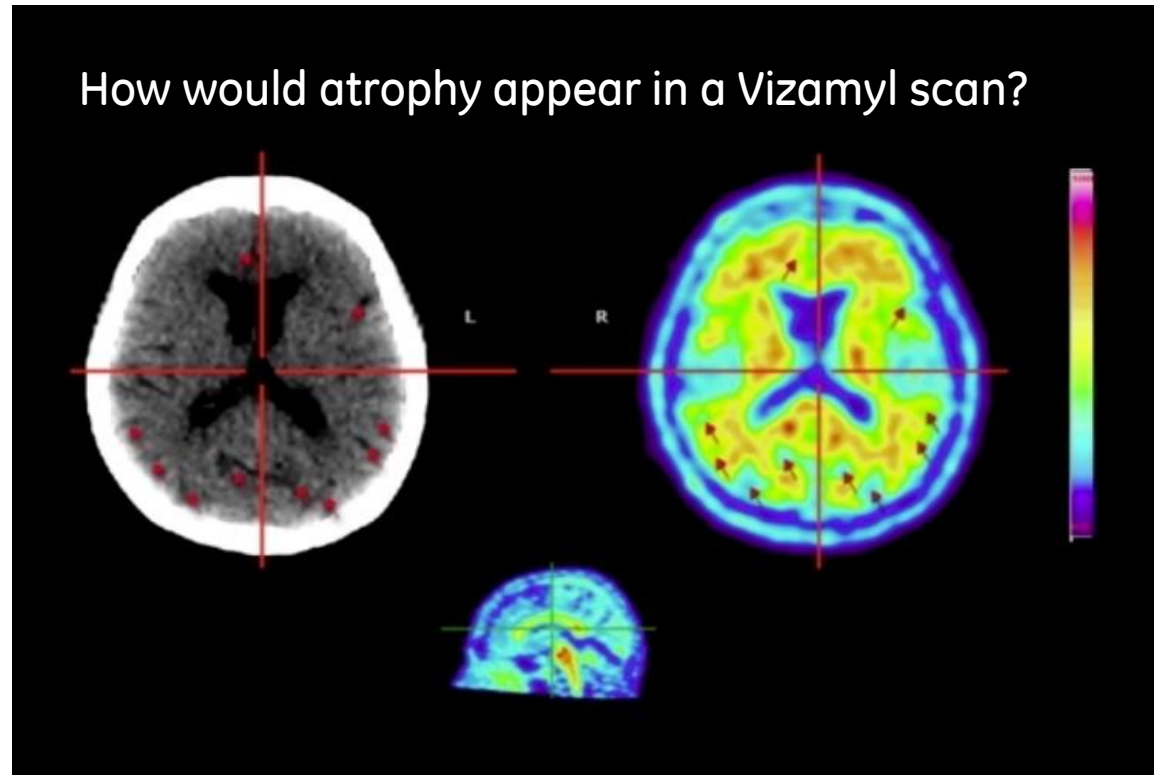
Abbreviations:
CT: computed tomography
PET: positron emission tomography

Use of CT with PET images

Positive case

Use of other anatomical images

MRI or diagnostic CT

- Display them so that you can inspect the white and grey matter distribution

- Display orientations and slice locations that match those of the Vizamyl PET Image

- Inspect the anatomical images for atrophy

- If atrophy is present in the anatomical images, consider if this is producing lower intensity in the PET image

- Try to find regions not affected by atrophy and review the Vizamyl images in these regions

Abbreviations:
MRI: magnetic resonance imaging
CT: computed tomography

Challenging cases: Classification

Your classification of positive should
be based on:

- Increased intensity in grey matter regions

- Loss of the white matter sulcal pattern

Recall that the most robust regions are the frontal lobe and the posterior cingulate and
precuneus. The other regions are supportive, particularly in cases where you suspect atrophy

Quantitative assessment of VIZAMYL™ images

Scope: Supplemental training module to guide the adjunctive use of quantitation for image interpretation by visual inspection. This module is intended to demonstrate some basic principles governing the use of quantitation in image interpretation but is not intended to replace the training given by individual manufacturers of CE marked software for amyloid quantitation.

The reader should also have completed the overall training for the visual interpretation of Vizamyl.

Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

Key labelling language included in European SmPC regarding the use of quantification

- Quantitative assessment of cortical radioactive signal intensity using validated and CE marked computer software may be used **to assist in the visual estimate of radioactive signal distribution**

- **An SUVR threshold value of 0.59 to 0.61 derived from CE marked software using the pons as a reference** has been determined to give very high concordance with dichotomous visual reads validated against the boundary between sparse and moderate neuritic plaque densities

- Readers should **interpret the scan visually and then perform quantitation analysis according to manufacturer's instructions including quality checks for the quantitation process**

- In case of **discordance of visual read and quantitation result** the reader should
  - Check the **placement of the regions of interest (ROIs)** and **reference regions ROIs**

- If the visual read is positive and the quantitative result is negative, **check for focal uptake** or **atrophy**

- If the visual read is negative and the quantitative result is positive, **check ROI placement accuracy of the reference region** and determine **if white matter is sampled in the cortical region of interest (ROI)**

Please refer to the SmPC for complete labelling language

When might quantitation supplement visual inspection of Flutemetamol (18F) Images?

- New readers

- Lower confidence in image interpretation

- Cases close to the pathology threshold

- Assessing regional vs global cortical uptake
  (for example when the majority of regions are visually negative but one region is positive)

Units for amyloid quantitation: SUVr

Standardised Uptake Volume Ratios (SUVr)

- A simplified method based on computation of the ratio between a target region and a reference region in a late static image (SUVr)*

- Target regions may be a composite of cortical regions or individual regions

- Reference regions have minimal amyloid pathology and may include cerebellar cortex, whole cerebellum or pons
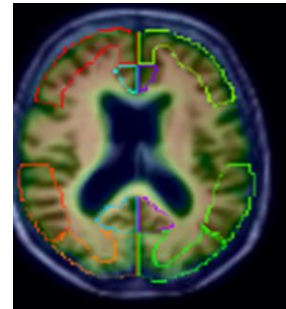
Target Regions
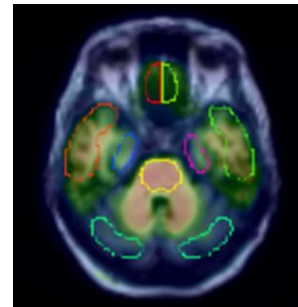
Reference Region

$$Frontal_{SUVR} = \frac{Frontal_{counts}}{Reference_{counts}}$$

*Lopresti et al., J Nucl Med. 2005 Dec;46(12):1959-72.

Units for amyloid quantitation: Z-scores

Z-score: Uptake of amyloid in numerical terms relative to the mean of a set of normal images. The measurement represents numbers of standard deviations from the mean

- Based on a set of negative normals, an average image (NID_{Ave}) and a standard deviation image (NID_{SD}) is created

- The patient scan (*Pat*) is then compared to this reference normals database

- Z scores are based upon SUVr units and can be calculated for both composite cortical regions or individual regions
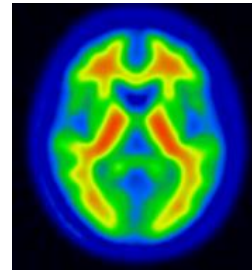
Average negative image (NID_{Ave})
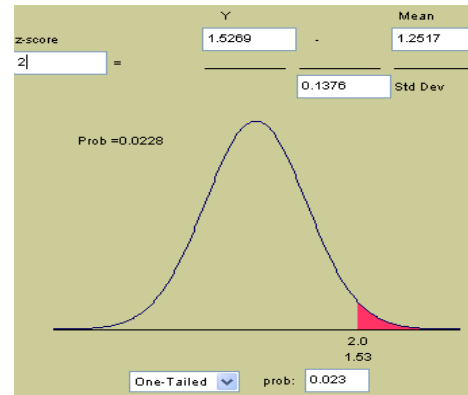
Normal Distribution of PET SUVr data from negative scans

$$Pat_{Zscore} = \frac{Pat_{SUVR} - NID_{Ave}}{NID_{SD}}$$
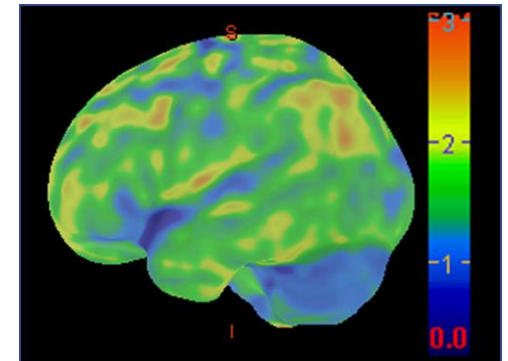
A Z-score of >2.5 is consistent with a positive visual read for a given region

Summary of Visual Read versus Quantitation for Clinical Studies using CE Marked Software

	Thurfjell et al 2014	**Leuzy et al 2019**	
Study Population	Healthy controls Mild Cognitive Impairment Probable Alzheimers Disease	Patients attending the memory clinic	
n	172	207	Total = 379
% agreement between visual and quantitation results	170/172 = 98.8%	205/207 = 99%	
CE Marked Software	Cortex ID	Hermes Brass	

Thurfjell et al., J Nucl Med. 2014 Aug 21;46(12):1959-72
Leuzy et al., EJNMMI. 2019 Jun;46(6):1276-1286

Examples of CE Marked Image Quantitation Software

- CortexID Suite (GE Healthcare)

- Hermes Brass^{TM} (Hermes Medical Solution)

- MIMneuro® (MIM)

- NeuroQ^{TM} (Syntermed)

Examples of CE marked software packages as of February 2020. Information is subject to change as technology evolves.
Hermes Brass, MIMneuro and NeuroQ are trademarks of the respective software manufacturers.

Generic Steps Performed when using Image Analysis Software

Transform PET image to standard space (e.g. MNI ***)	Application of cortical and reference volumes of interest (VOIs) to amyloid PET image	Cortical uptake divided by reference region uptake provides SUV ratio (SUVR)	If software contains a normal database, Z-scores (regional and voxelwise) can be calculated and may be displayed on a surface of the brain	Report is generated for both regional and composite measures

Nb. This supplemental training module is to guide the adjunctive use of quantitation in supporting image interpretation by visual inspection. The intent of this training module is to demonstrate some basic principles governing the use of quantitation in image interpretation but not replace the training given by individual manufacturers of CE marked software for amyloid quantitation.

Flutemetamol (18F) Image Interpretation Guidance for Visual Inspection and Adjunctive Use of Quantitation

	Issue	Detail	Remedial Action	Image Interpretation Guidance
1	Volume of interest placement	Incorrect placement of the volume of interest (VOI) for either the region of interest or the reference region can render the quantitative assessment incorrect relative to the image read	Check accurate placement of VOI on both region of interest and reference region	Quantitation can support visual inspection in these cases once checks on both region of interest and reference region have been made
2	Local atrophy	Atrophy of the cortex can reduce regional PET signal and therefore quantitation may underrepresent Flutemetamol (18F) uptake	Use of anatomical MRI or CT image to identify areas of atrophy and correct VOI placement. Refer to Image Interpretation training where regions less susceptible to atrophy can be visually examined.	Visual inspection of image can confirm presence of atrophy. Automated quantitative methods maybe less helpful.
3	Enlarged Ventricles	Ventriculomegaly/enlarged ventricles cause thinning of the cortical ribbon which makes the overall cortical signal difficult to examine	Use of anatomical MRI or CT image to assist in differentiating white matter versus grey matter. Extra checks on placement of VOIs for excluding non-specific white matter uptake	Quantitation can support visual inspection in these cases once MRI/CT and VOI placement is checked
4	Regional versus global uptake of amyloid	A few subjects show positive uptake of Flutemetamol (18F) in only a single region (for example in striatum or precuneus / posterior cingulate). An average global quantitative measure may fall below the threshold with an overall negative result which fails to take account of the positive region by visual inspection.	As per the Image Interpretation training all 5 read regions should always be visually inspected in all the recommended review planes before rendering a scan visually positive or negative.	If only a quantitative measure was used in this instance, the scan would be rendered negative when there is regional positive uptake. Recommended that visual inspection is the primary method of interpretation and quantitation is supportive
5	Equivocal amyloid uptake	Amyloid levels close to the boundary between negative and positive levels may lower the confidence of image inspection alone	Check placement of VOIs as above to optimise accuracy of quantitative result	Quantitation can support visual inspection in these cases

1. VOI placement
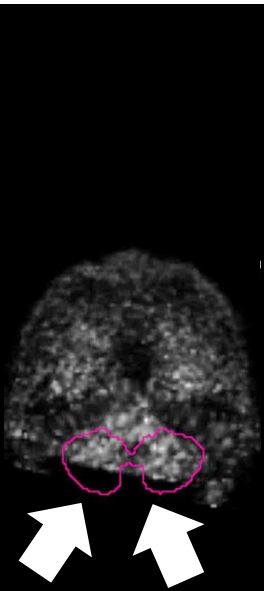
2. Focal Atrophy
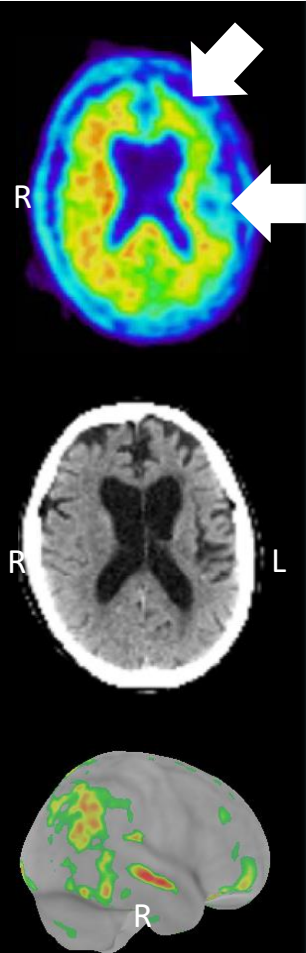
3. Enlarged ventricles
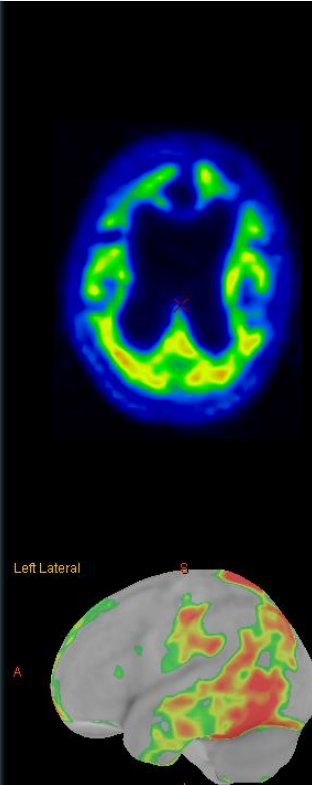
4. Regional vs global
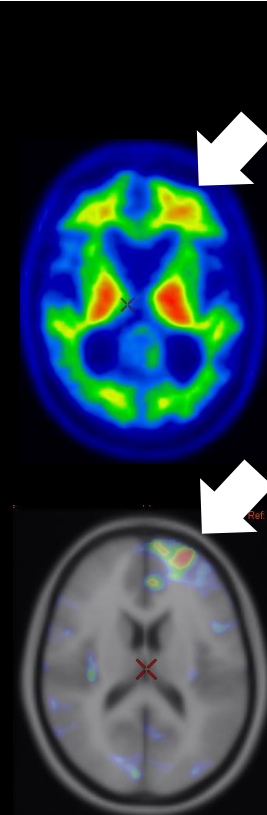
5. Equivocal uptake
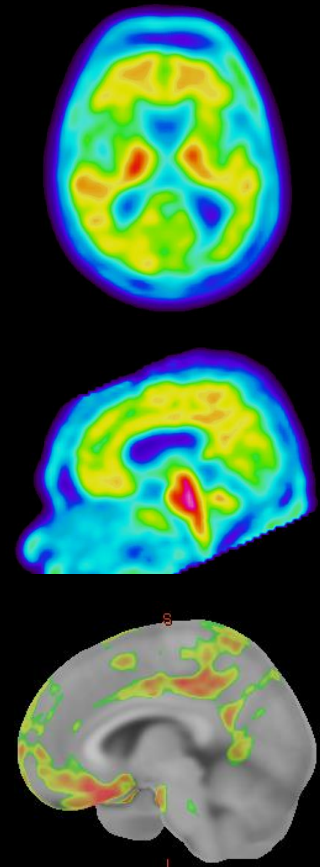
Summary

1. Quantitation may be used as an adjunct to visual inspection

2. Agreement between visual and quantitation is generally very high

3. Users should refer to software manufacturers training for detailed instructions when adding quantitation to their image interpretation

4. In the case of discordant visual and quantitative image interpretation users should follow the guidance given at the end of this module

VIZAMYL^{TM} Flutemetamol (^{18}F)
Refresher Training

Version 3.0 September 2022

GE HealthCare
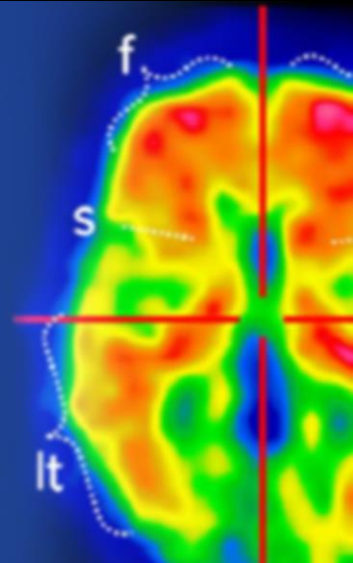
Welcome to the Vizamyl Refresher Training which supplements the Vizamyl Image Reader Training that you have already taken. This refresher training will take approximately 30 minutes of your time and there will be a questionnaire on the content at the end of the course. We hope you will find this training useful.

Reminder of Basic Steps

Additional tips and learnings have been added for each step

1 Choice of colour scale

2 Image orientation

3 Scaling the pons to 90% of maximum image intensity

4 Recognising the white matter pattern in the negative scan and differentiating normal and abnormal cortical uptake

5 Systematic review of read regions

This training will provide a reminder of the five basic steps for image interpretation with Vizamyl.
We will also share tips and learnings that may help you gain a better understanding of the methodology.

The five basic steps that we will cover are:
1) Choice of an appropriate colour scale
2) The importance of image orientation and alignment
3) Scaling the pons to 90% of maximum image intensity
4) Recognising the white matter pattern and being able to differentiate normal and abnormal cortical uptake
and finally
5) The systematic review of the five read regions
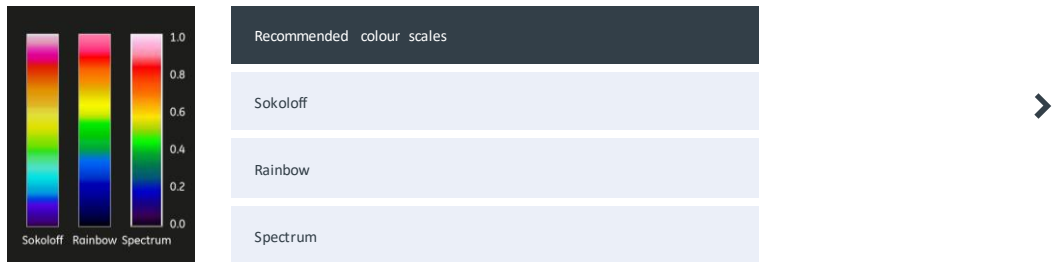
- Basic step number one is that Vizamyl PET images should be read using an appropriate colour scale.
- Usable colour scales provide a clear intensity range for negative grey matter as well as an identifiable band of high intensity, that can clearly discriminate intensity levels above and below the intensity level of the pons
- Sokoloff, Rainbow or Spectrum are examples of such colour scales

Basic step number two is to ensure correct orientation of the images in all three review planes: axial, coronal and sagittal. After confirming a correct field of view and the absence of motion artefacts, check the images for any rotation or tilt and realign as necessary in all three planes.

Basic Step 2: Image Orientation
Tips & Learnings

1 Even though care is taken to position the patient on the camera bed, images need to be checked and realigned if required

2 Image alignment in all three planes is essential for all images prior to review

3 The correct differentiation of white matter from cortical grey matter depends upon accurate image orientation

4 False positive reads from white matter may be observed if images are incorrectly aligned

Remember:
- Images need to be checked and realigned as part of the image processing steps rather than just relying on patient positioning on the camera bed.
- Alignment needs to take place for all three planes as this is important for the correct differentiation of white matter from cortical grey matter.
- A consequence of incorrectly aligned images could be false positive reads, where the reader is picking up white matter signal and falsely attributing it to increased cortical uptake

Vizamyl Refresher Training

Basic Step 2: Image Orientation

Tips & Learnings: Avoiding a false positive read
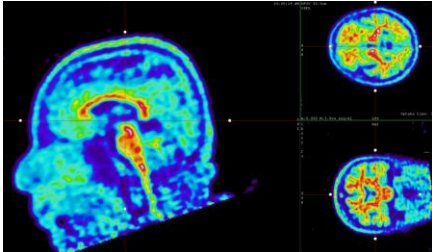
Correct Image Alignment

- Sagittal Review of medial surface
- No signal in posterior cingulate/precuneus regions
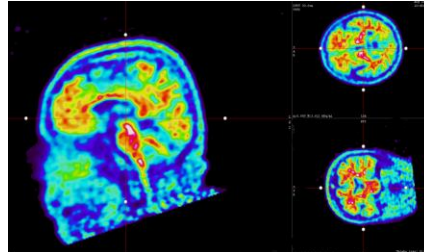
Incorrect Image Alignment

- Sagittal review of medial surface
- White matter signal in both frontal region and posterior cingulate/precuneus could be mistaken for cortical amyloid signal

These images demonstrate this specific learning. On the left, the image is correctly aligned and shows a negative posterior cingulate/precuneus area when reviewing the medial surface of the sagittal plane. On the right side however, the same image is incorrectly aligned and shows white matter signal pushing into the review plane in the frontal and posterior cingulate/precuneus area areas. This signal might be incorrectly perceived to be grey matter uptake and could possibly lead to a false positive assessment.

Basic Step 3: Scaling the pons to 90% of maximum image intensity

90%

Images scaled with pons set to **90%** of maximum image intensity

Pons always mainly red/pink in both negative and positive cases

No difference in pons uptake between negative and positive scans
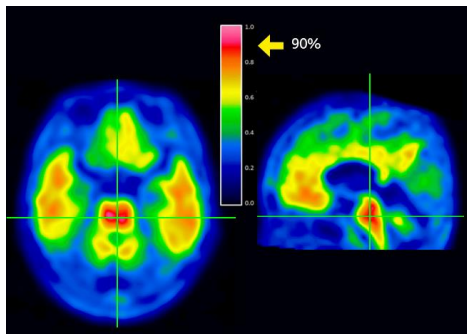
Example images will use the Rainbow colour scale

Basic step number three is scaling the pons to approximately 90% of maximum image intensity. This step is required for all images and should always be performed irrespective of whether the images are normal or abnormal. The pons should be clearly seen as a red or pink structure when an appropriate colour scale is used. There is no difference in pons uptake between negative and positive scans.

Vizamyl Refresher Training

Basic Step 4: Recognising the white matter pattern in the negative PET scan

Negative scan
white matter pattern

Positive scan
white and grey
matter pattern

MRI Structural image shows the negative PET scan is
consistent with white matter uptake

MRI structural image · *Fused MRI and Vizamyl images* · *Vizamyl PET image*
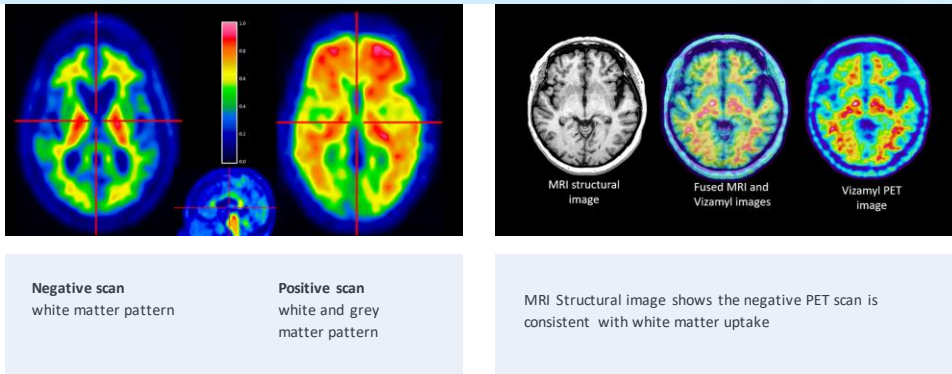
Basic step number four is to recognise the white matter pattern in the negative scan
in order to differentiate normal and abnormal cortical uptake.
Interpretation of the images is performed visually. To do this, we compare the activity
in cortical grey matter with activity in adjacent white matter.
In panel on the left, the negative scan on the left side has a typical white matter
pattern. However, in the positive scan on the right, the white matter signal is
augmented by tracer signal in the cortical regions with similar or even higher intensity
In the right panel the overlay of MRI and PET scan illustrates the white matter uptake
of a negative scan.

Example of frontal uptake showing white matter uptake pattern (left) and cortical uptake pattern (right)
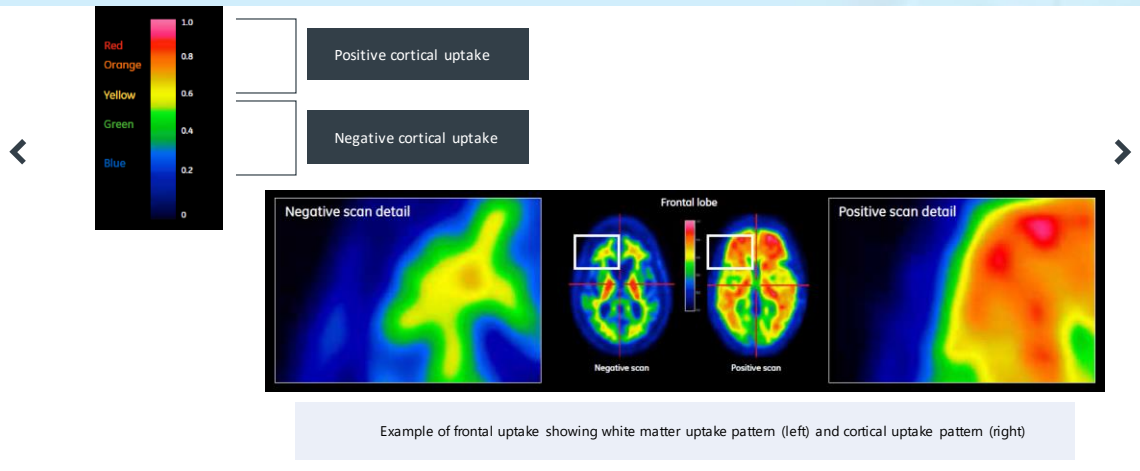
Here you can see a more detailed view of cortical and non-cortical uptake.
On the left, the white matter pattern in the frontal lobe with the sulcal and gyral structures can be seen in the normal image. In the positive image on the right, the signal radiates out to the edge of the brain in a convex pattern due to cortical uptake. As a reminder from a colour perspective: positive cortical update is observed with yellow, orange and red colours whilst negative uptake would show as blues and greens when using an appropriate colour scale.
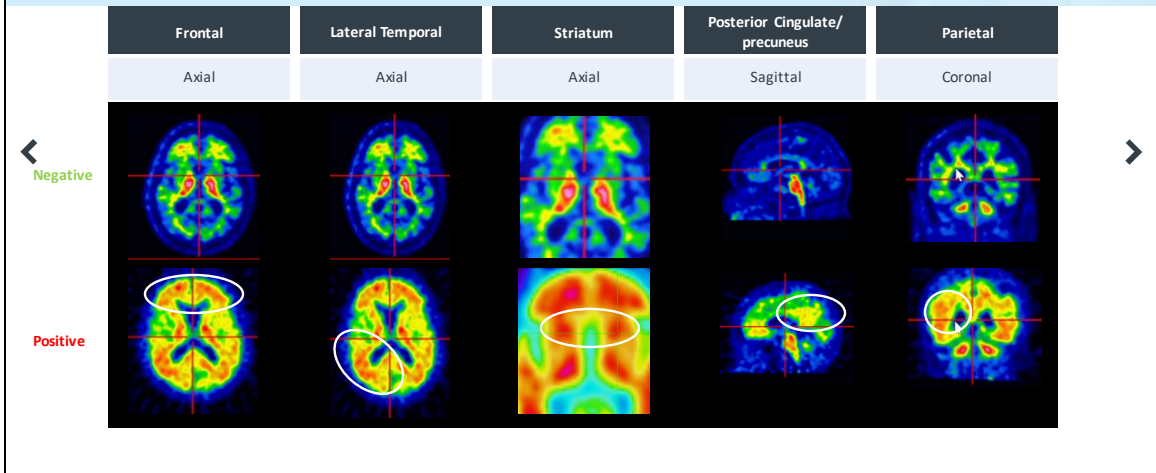
The fifth and final basic step is the systematic review of the read regions.
Axial is the primary review plane for the frontal, lateral temporal and striatum regions
whilst the posterior cingulate is read on the medial surface of the sagittal plane.
Finally, the parietal lobes are read in coronal review. It is recommended to read the
image in this order: axial followed by sagittal and then finally coronal.

Vizamyl Refresher Training

Step 5: Systematic Review of Read Regions

Tips & Learnings: Scrolling is valuable to gain an overall impression of a region
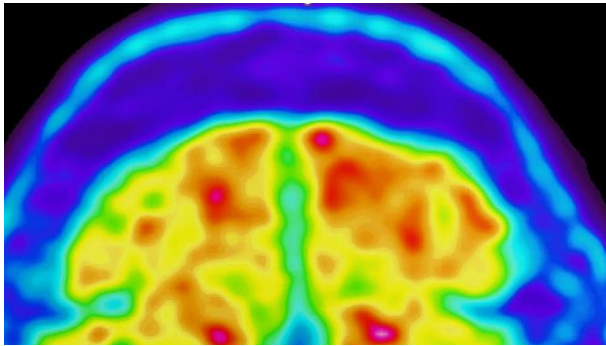
Scrolling in axial view around the AC-PC plane is valuable to confirm positive Vizamyl uptake in both frontal lobes in this case

This video demonstrates the value of scrolling the image as it is useful to get an overall impression of a region rather than just looking at a single plane. Scrolling around the AC-PC plane in the axial view can give a fuller picture of the uptake patterns, in particular when there is some uncertainty around the image interpretation.
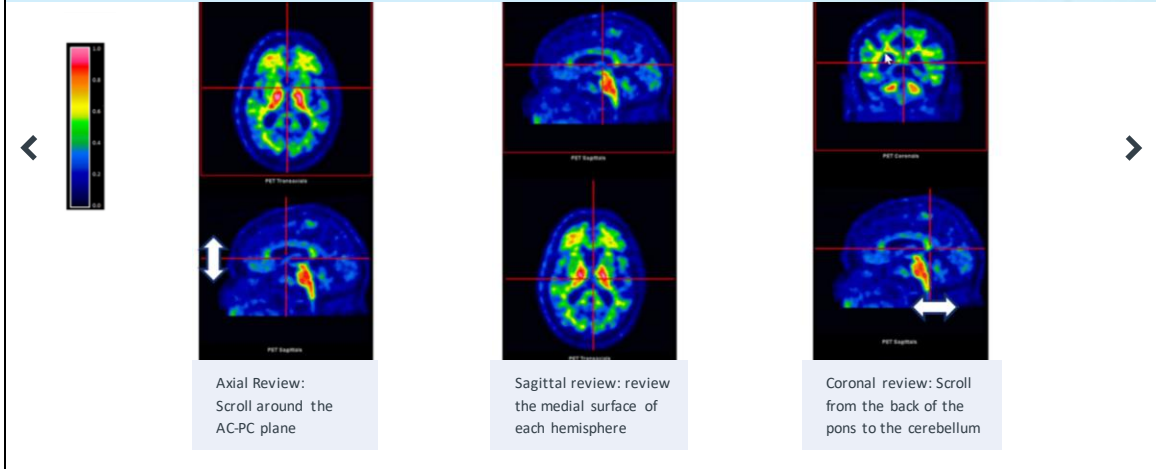
As previously mentioned, there are some optimal review planes for each read region. In axial the image can be scrolled around the AC-PC plane.
In the sagittal view the medial surfaces of both hemispheres are assessed, whilst finally for the coronal view the optimal position is to scroll from the back of the pons to the cerebellum
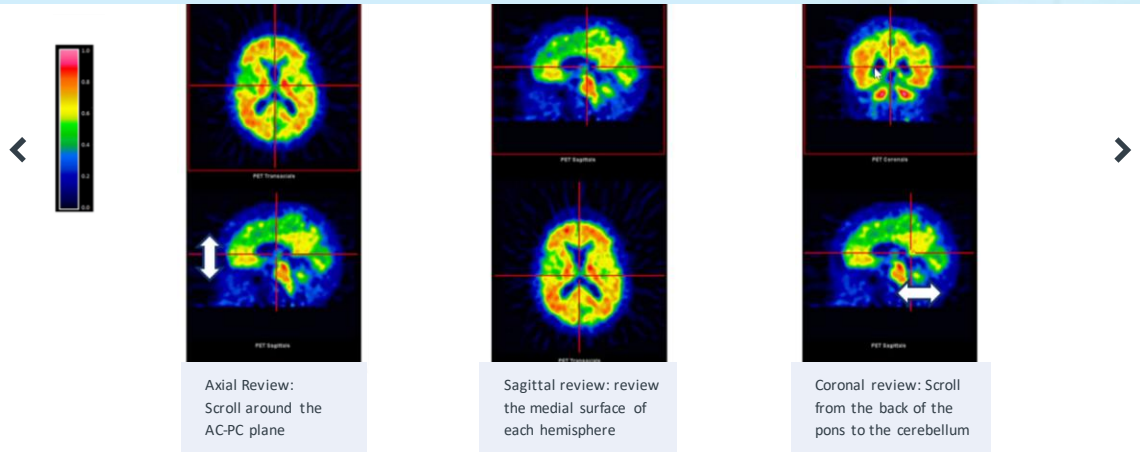
Here in a positive image, the same optimal review planes are demonstrated

Step 5: Systematic Review of Read Regions

Tips & Learnings: A coronal review alone is not sufficient to examine a Vizamyl scan
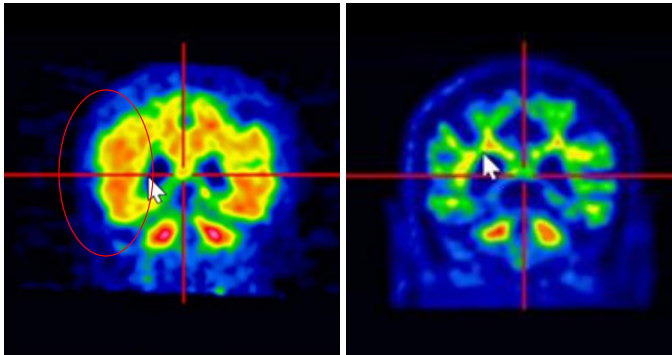
The coronal review is good for examining the temporo-parietal lobe, but axial and sagittal reviews are always recommended for other regions

As a reminder, amyloid PET scans have a different read methodology to FDG (i.e., the coronal view is less central compared to axial and sagittal review)

It is important to not solely rely on a coronal review. The coronal review is useful for examining the temporo-parietal lobes, but axial and sagittal reviews are always recommended for the other four regions. Indeed, it is recommended recommend to review these planes first, with the coronal assessment at the end.

Remember: the read methodology is specific for amyloid PET and methods used for other tracers such as FDG should not be employed.

Step 5: Systematic Review of Read Regions

Tips & Learnings: Atrophy may impact image interpretation
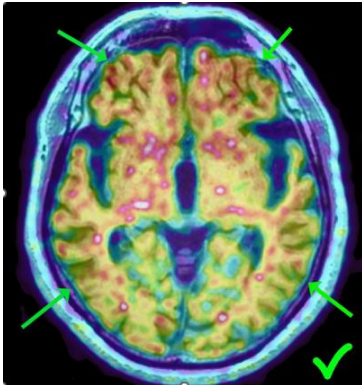
Co-registered MRI/CT scan can help show more robust read regions

Video demonstrates an image with bilateral atrophy in the frontal lobes whereas the lateral temporal lobes are spared

Another factor which may impact interpretation of Vizamyl images is the presence of atrophy. Atrophy may result in the uptake pattern of a positive scan having the appearance of sulcal and gyral structures. This may give the appearance of a negative pattern in that region due to the missing white matter. Co-registered MRI or CT scans can help with the structural delineation of the image.

A further tip is to assess the contralateral regions as the atrophy may be asymmetrical. Also, the striatum is less prone to atrophy.

The striatum may be easily overcalled. This may occur as illustrated in the top image when the axial review is too superior of the AC-PC plane. In this case signal from the white matter rich internal capsule may be picked up. In the correct review plane on the AC-PC level, in the bottom image the 'striatal gap' can be seen between the thalamus and the frontal white matter indicating a negative striatal region.
This is another situation where scrolling around the AC-PC plane is very valuable to avoid any over calling or false positive read.
We would like to point out that positivity in the striatum in isolation with negative uptake in the remaining cortical regions is only rarely observed.

Step 5: Systematic Review of Read Regions

Tips & Learnings: Regional positivity observed in 4-5 regions in most positive Vizamyl images

Images are rarely only positive in one region

In approximately 90% of clinical MCI cases positive uptake was observed in either 4 or 5 regions. It is rare to see only one or two regions positive, including the striatum in isolation.

Combinations of positive regions (red) in positive [18F]Flutemetamol cases: aMCI study (97 amyloid positive cases)[1] Majority read results of 5 expert readers

Frontal	Temporal	Insula	Posterior Cingulate & Precuneus	Striatum	N	%
red	red	red	red	red	84/97	87%
red	red	green	red	red	3/97	3%
red	red	red	red	green	1/97	1%
red	green	red	red	red	1/97	1%
green	red	red	red	red	2/97	2%
red	green	green	red	red	1/97	1%
green	green	red	red	red	2/97	2%
green	green	red	green	red	1/97	1%
green	green	green	green	red	2/97	2%
93%	93%	91%	97%	98%		

MCI - Mild Cognitive Impairment
aMCI – amnestic Mild Cognitive Impairment

[1]Farrar G, Molinuevo JL, Zanette M. , Eur J Nucl Med Mol Imaging. 2019;46(6):1299-1308

Indeed, clinical cases that are amyloid positive typically show uptake in four to five regions. In this example taken from a cohort of 97 amyloid positive amnestic mild cognitive impairment cases you can see that regional positivity in all five regions was observed in 87% of cases, with a further 5% of cases being positive in four regions. Note also that in this cohort a positive striatum in the absence of any other positive region occurred in only in 2% of the cases

1 Scroll across the entire brain first to get a general impression

2 In each review plane there is an optimal position for image review

3 Scrolling around these optimal review planes is recommended

4 Review plane order: axial → sagittal → coronal

5 Secondary review planes may be supportive if the primary review plane is equivocal
e.g. frontal signal may also be observed in the sagittal review if the axial review is equivocal

To summarise some of the important learnings, we would advise the following:
Review the whole brain first to get a general impression of the uptake pattern
Remember that for each review plane there is an optimal position for image review
Don't forget the value of scrolling in the review planes
We recommend to review the image in the order of axial review, then sagittal and lastly coronal
Secondary review planes, such as observing frontal uptake in the sagittal review can be supportive particularly when a more careful inspection is warranted

Other Tips & Learnings:

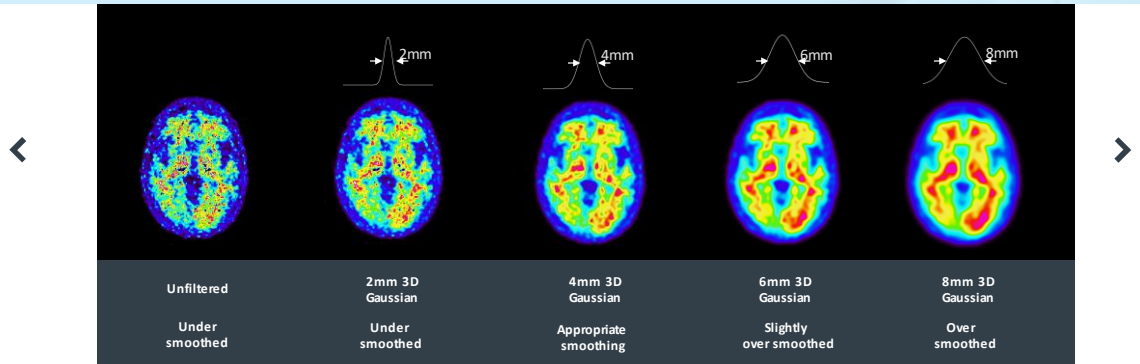Optimise reconstruction settings
to reduce image noise

There are also some additional tips to share:
The first is how to optimize reconstruction settings to reduce image noise which may
impact your visual inspection.

Vizamyl Refresher Training

Reducing image noise by post filtering
Scrolling and use of quantitation can help too

| | 2mm | 4mm | 6mm | 8mm |

Unfiltered	2mm 3D Gaussian	4mm 3D Gaussian	6mm 3D Gaussian	8mm 3D Gaussian
Under smoothed	Under smoothed	Appropriate smoothing	Slightly over smoothed	Over smoothed

Reminder from SmPC: Iterative or filtered back projection reconstruction is recommended with a slice thickness of 2 to 4 mm, and an axial matrix size of 128 x 128 with pixel sizes of approximately 2 mm. Where a post-smoothing filter may be applied with a full width half maximum (FWHM) of not more than 5 mm, the filter FWHM should be chosen to optimize the signal-to-noise ratio while preserving the sharpness of the reconstructed image.

Post filtering the image can be helpful to reduce noise. You can see in the example shown that a 4mm Gaussian filter appropriately smooths the image whereas a 6mm filter slightly over smooths the image but still renders it suitable for image inspection. The 2mm filter however renders the image with some noise in this case.
Scrolling the image may also help when the image is slightly noisy. In addition, quantitation can help as well, as an SUVr or Centiloid measure is less impacted by noise.

Adjunctive Value of Quantitation

We also like to briefly mention the adjunctive value of quantitation. There is a specific training module available which covers this topic in more detail

Quantitation can supplement visual inspection of Vizamyl images

- New readers or readers who infrequently perform the scan
  - Inexperienced readers may also consider obtaining a second opinion from an experienced reader if quantitation is not available
- To increase confidence in image interpretation
- Cases close to the pathology threshold
- In case of a noisy image

KEY LEARNINGS

Remember that even when using quantitative tools, all images should be inspected visually first

Agreement between experienced visual readers and quantitation is generally very high at over 95%[1]

[1] Bucci M, Savitcheva I, Farrar G, et al., Eur J Nucl Med Mol Imaging. 2021;48(7):2183-2199

Quantitation can supplement the visual inspection of Vizamyl.
It can be particularly valuable for new readers or readers who infrequently perform the scan. Readers may also consider obtaining a second opinion from a more experienced reader if quantitative methodology is not available.
Quantitation can increase reader confidence and help with equivocal or noisy images.
It should be emphasised that visual inspection is the primary method for image interpretation and all images should be inspected visually first.
The agreement between experienced visual readers and quantitation is generally very high at over 95%

SUMMARY

1 Correct alignment in all 3 review planes is important

2 Recommend to systematically read axial, sagittal and coronal planes

3 Use MRI/CT if atrophy impacts PET image interpretation

4 Majority of positive images are positive in 4-5 regions

5 Scrolling and secondary review planes can be helpful if regional read is equivocal

6 Quantitation can supplement visual read

In summary:
Correct alignment in all three review planes is important and it is recommended to systematically read in the axial plane followed by sagittal and lastly coronal.
We recommend to use structural MRI or CT if atrophy impacts the image interpretation and to remember that most positive scans are positive in 4-5 regions in routine clinical cases.
Scrolling and the use of secondary review planes can be helpful if the regional read is equivocal, and quantitation can supplement the visual read