Quantitative Evaluation of Beta-Amyloid Brain PET Imaging in Dementia:

A comparison between both Hermes BRASS and Siemens *Syngo.VIA* Amyloid Plaque Quantification with the clinical report

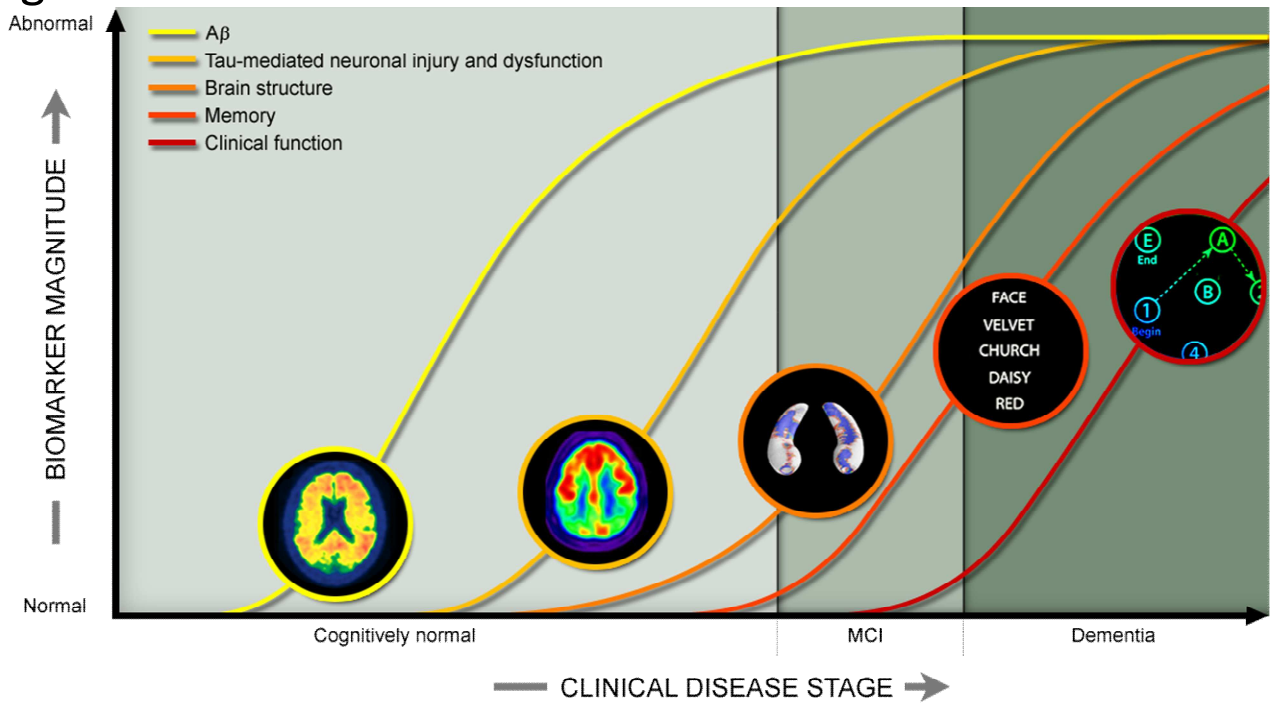
Sorcha Curry

Trainee Clinical Scientist: Imaging with Ionising Radiation
Imperial College Healthcare NHS Trust, London, UK
King's College London, London, UK

I have no conflict of interest to declare

Beta Amyloid as a Hallmark of Alzheimer's Disease

- Alzheimer's Disease is the most common form of Dementia (50-70%)
- Definitive diagnosis requires both clinical findings and neuropathological findings



- PET imaging can detect the biomarker β-amyloid in the brain
- Amyloid cascade hypothesis

adni.loni.usc.edu

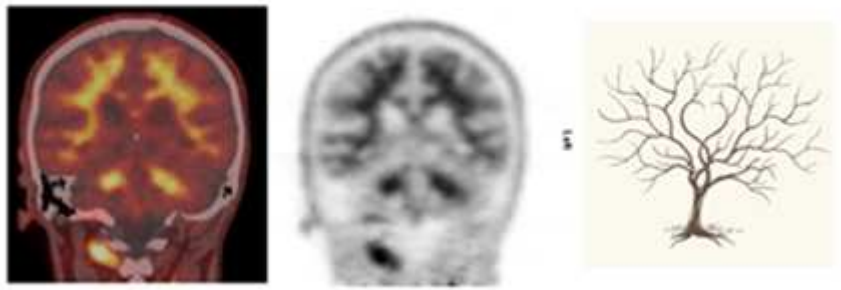
Reporting β-Amyloid Amyvid brain imaging

- Negative β-Amyloid scans have clear grey/white matter contrast
- Positive β-Amyloid scans will have 2 or more brain areas which there is reduced or absent grey/white contrast; this is the most common appearance of a positive scan

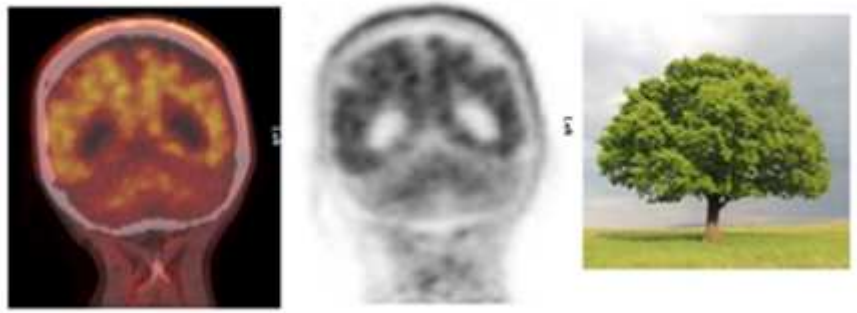
Visual delineation of the contrast is more difficult for patients with early deposition and subtle loss of grey/white contrast

Software tools developed provide support to the clinical interpretation and the visual read.

'Branching Tree' - Negative Amyvid Scan



'Tree-in-bloom' – Positive Amyvid Scan

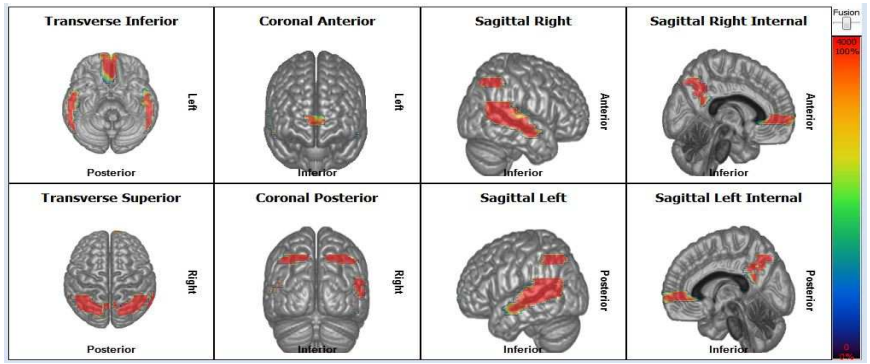


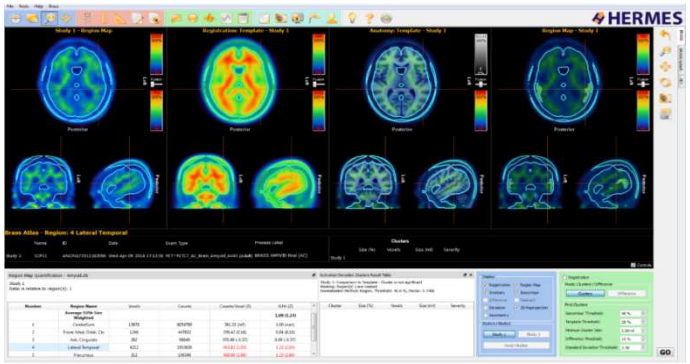
Software Packages – Hermes BRASS

- Patient study is registered to a template PET study and fused to an MRI template
- Automatic delineation of 6 cortical regions of interest (ROIs) are applied
- The standard uptake value (SUV) of each region is quantified
- The SUVr (standard uptake value ratio) is reported relative to the cerebellum

BRASS also reports the z-score (number of SD away from the mean SUVr in the database)
Previous work lead to a positive scan being classified as having z-score ≥ 2 in ROI ≥ 2

Number	Region Name	Voxels	SUVr (Z)
	Average SUVr		**1.73 (8.25)**
1	Cerebellum	15878	1.00 (nan)
2	Front. Med. Orbit. Ctx	1246	1.62 (8.71)
3	Ant. Cingulate	262	1.74 (6.95)
4	Lateral Temporal	4212	1.83 (10.34)
5	Precuneus	312	1.87 (9.88)
6	Post. Cingulate	186	1.91 (8.20)
7	Parietal	1703	1.38 (5.42)

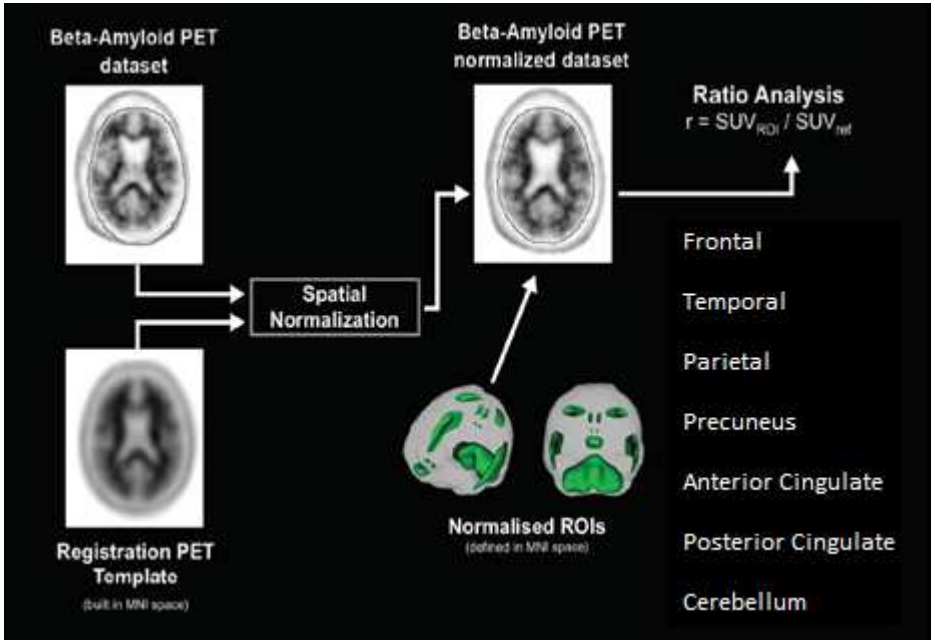


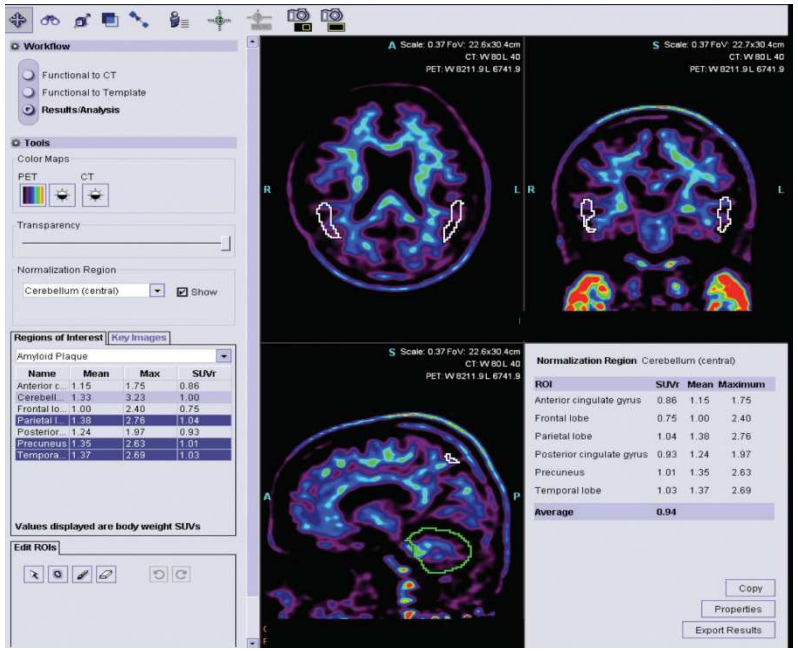


Software Packages – Siemens *Syngo.VIA*

- *Syngo.VIA* is based on a method by Fleisher et al. which demonstrates a threshold of average SUVr ≥ 1.17 as positive for pathological levels of plaque
- It also demonstrates a lower threshold of average SUVr ≥ 1.08 to indicate an identifiable level of plaque
- Final clinical diagnosis is determined by clinician

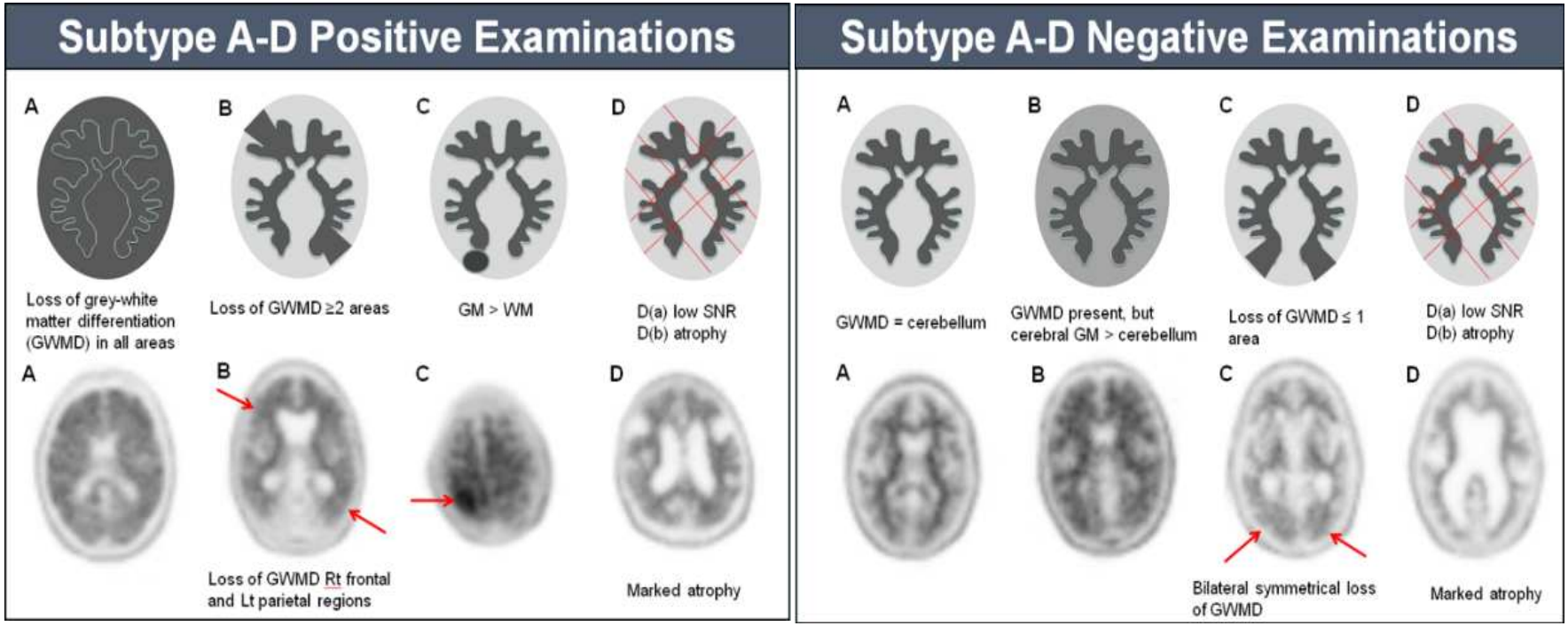
- Older health controls have typical SUVr ≈ 1.05





Scan Sub Type

- Four subtypes of Amyvid scans have been identified at ICH since 2013
- Scans are classified as Type A(typical features) or non-type A (subtypes B-D, atypical features) for both positive and negative scans according to imaging characteristics
- Non -type A scans are more difficult to interpret



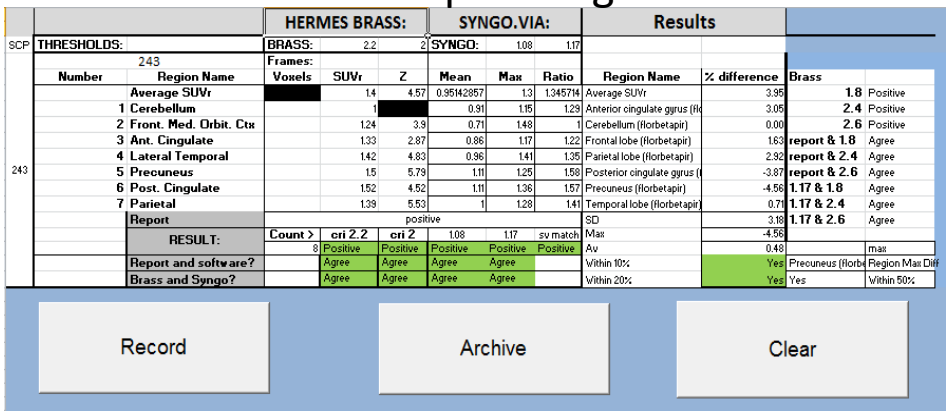
SR Khan *et al.*, Inter-reader variability of 18F-Florbetapir (Amyvid) PET/CT Brain Examinations, BNMS 2016

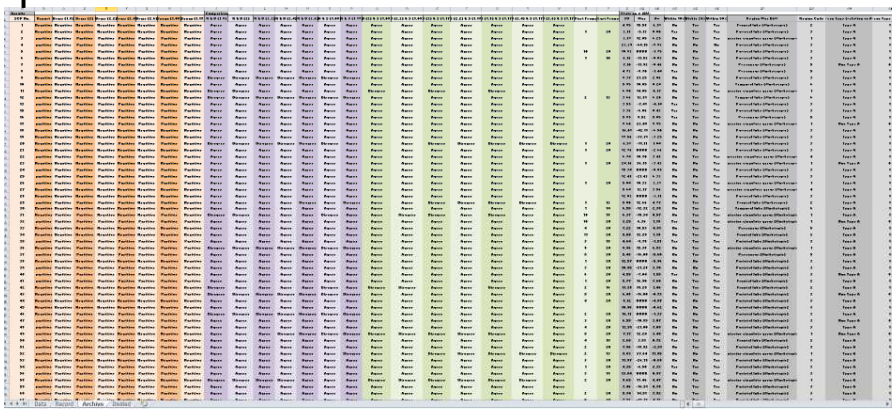
Method

- 340MBq injection of ^{18}F-Florbetapir with a 40 minute post-injection delay before imaging.
- One bed position acquired in list mode for 20 minutes over the brain.
- Reconstructed into 20x1 minute dynamic frames and assessed for motion.
- Frames with excess motion are removed to create a motion free dataset with a minimum of 10 frames.

The motion and attenuation corrected datasets were loaded into BRASS and *Syngo.VIA.* The quantitative results from 225 patients was harvested from each software package and compiled into a table.

The results were compared against the clinical report

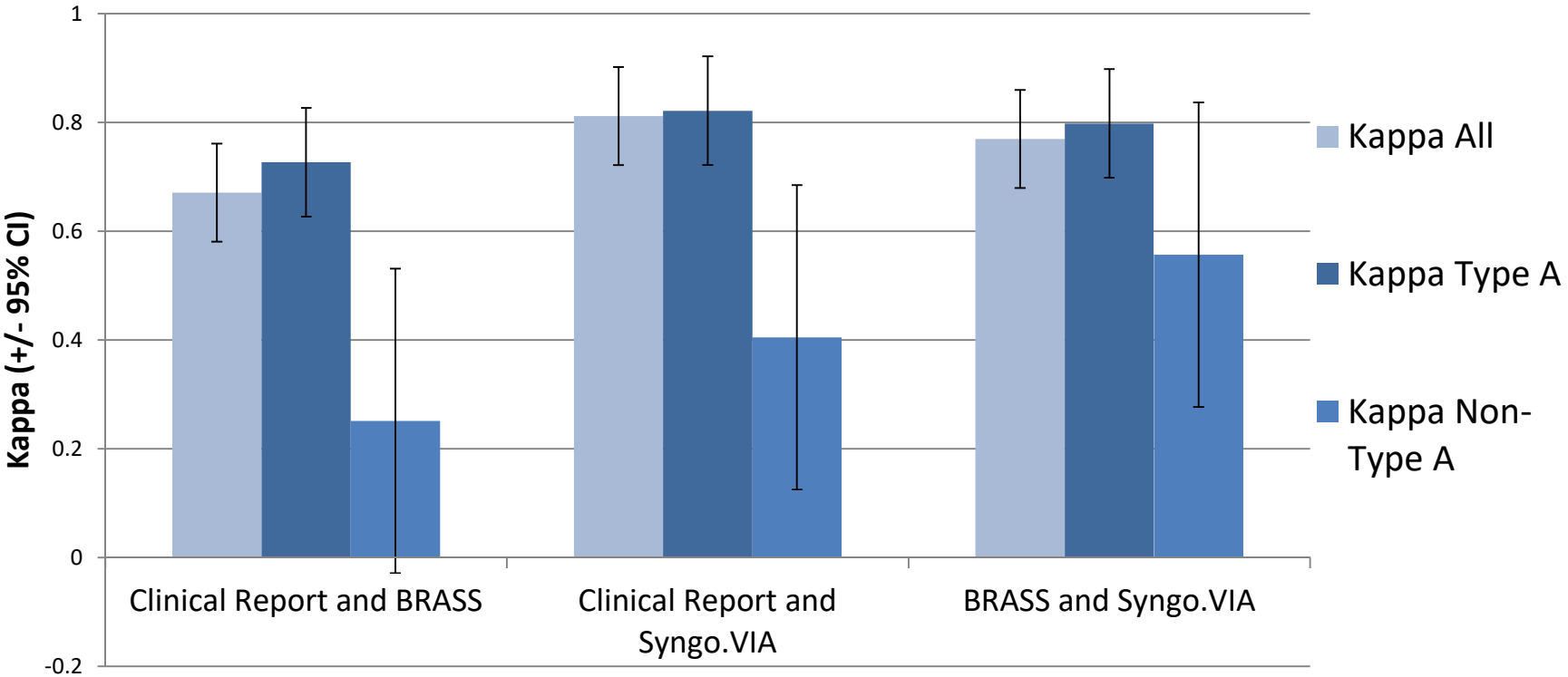




Results

	All scans (n = 225)			
	Type A (n = 182)		Non-Type A (n = 43)	
	Positive	Negative	Positive	Negative
Clinical Report	82 (45%)	100 (55%)	24 (56%)	19 (44%)
Hermes BRASS	108 (59%)	74 (41%)	35 (81%)	8 (19%)
Siemens Syngo.VIA	87 (48%)	95 (52%)	27 (63%)	16 (27%)

Agreement between Clinical Report and Software



Type A/Typical Scans

(n = 182)	Hermes BRASS	*Siemens Syngo.VIA*
Sensitivity (%)	98.8	96.3
Specificity (%)	73.0	92.0

Specificity = True negative rate

∴ The results indicate that Hermes BRASS has a high false positive rate

Possible reasons for high false positive rate:

- *Software related (alignment etc.)*
- *Analysis related (Threshold value etc.)*

Investigation into the threshold value to indicate a positive scan using Hermes BRASS

Alternative Threshold Analysis – Hermes BRASS

- A positive cut off threshold of z-score ≥ 2 in ROI ≥ 2 had been used for classifying scans using Hermes BRASS
- An alternative threshold value of SUVr > 1.18 was previously hypothesised as ICH and so this positive cut off threshold was also investigated

	Sensitivity		Specificity	
Criteria	z-score ≥ 2	SUVr > 1.18	z-score ≥ 2	SUVr > 1.18
Type A	98.8	98.8	73.0	91.0

- The original positive cut-off value was causing the low specificity

Alternative Threshold Analysis – Siemens *Syngo.VIA*

- A positive cut off value of SUVr ≥ 1.17 was used when classifying scans using Siemens *Syngo.VIA*
- A second threshold in the Fleisher method is used as to assess identifiable levels of plaque (SUVr ≥ 1.08)
- 2 of the 3 false negatives *Syngo.VIA* classified had 1.08 ≤ SUVr ≤ 1.17
- A category of medial probability was suggested (1.08 ≤ SUVr ≤ 1.17), where positive scans that fell within this category would be investigated further

Non Type A (Atypical scans)

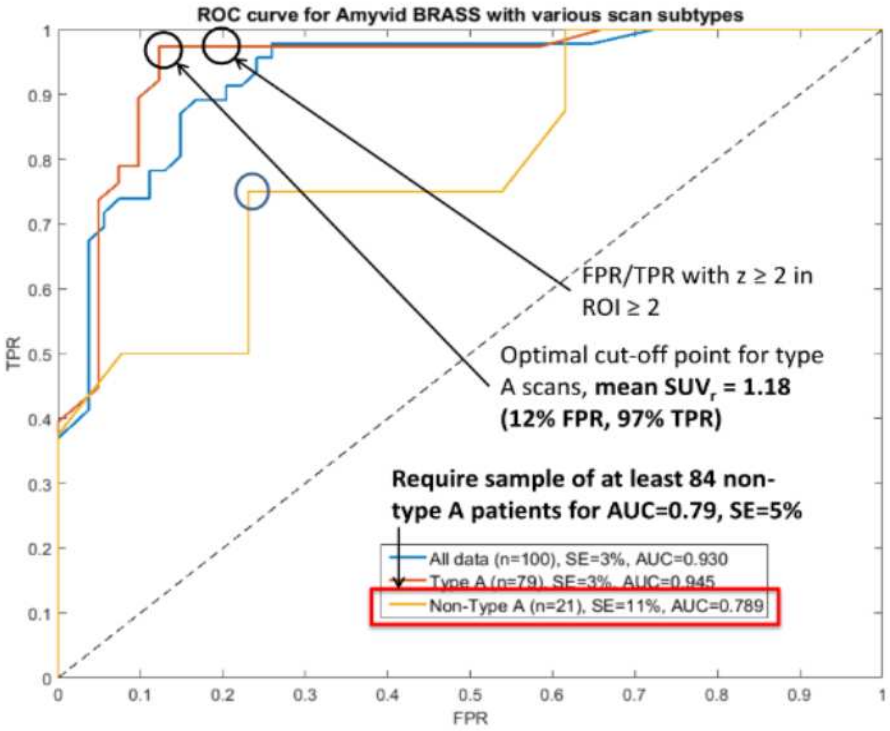
(n = 43)	Hermes BRASS	*Siemens Syngo.VIA*
Sensitivity (%)	95.8	79.2
Specificity (%)	36.8	57.9

Using the alternative threshold values with non type A scans as with Type A scans did improve specificity but not sensitivity

BRASS	Sensitivity		Specificity	
Cut off	z-score ≥ 2	SUVr > 1.18	z-score ≥ 2	SUVr > 1.18
Non-Type A	95.8	83.0	36.8	47.4

The use of the medial probability category would have brought 3 Siemens *Syngo.VIA* false negatives into this category for further investigation, potentially increasing sensitivity

Non Type A/Atypical Scans



The SUVr cut off of 1.18 was derived from Type A scans and is not optical for non Type A.

Regional analysis was also considered

Patient	Frot.MOC	Ant Cingulate	Lateral Temporal	Precuneus	Post. Cingulate	Parietal
66						
97						
159						
212						

Regional analysis of false positive Hermes BRASS scans

Conclusion

- Aim: To look at Amyloid Imaging Quantification using two software packages Hermes BRASS and Siemens *Syngo.VIA,* and how the interpretations of these different software packages compares with the final clinical report.
- Both can support the interpretation of the amyloid scans, particularly in the case of typical scans.
- A more complex solution will be needed for non-type A scans, but the software does provide valuable support.
- SUV_r based quantification could play a major supportive role for visual evaluation of beta-amyloid PET studies, particularly in cases where clinicians are less experienced.

- Must be mindful of threshold values

Future Work

- Use a larger atypical scan database for more definitive analyse
  - Better understand the role of quantification software
  - Use regional based SUVr cut-offs with ROC analysis
- Combine PET Imaging data with the MRI imaging and cognitive results
  - Work towards better predicting if a patient will develop Alzheimer's Disease
  - Possibility of applying weighting to different modalities
- Another area that is developing rapidly is the PET imaging of τau tangles, the other biomarker in AD, but this is not yet in routine clinical use at ICH.
  - Map the distribution of both AB and tau and perform regional analysis
  - Could help benefit
    - Management of disease
    - Screening of disease
    - Treatment of disease
    - Prevention of disease

Thank you.