

Quantitative Strategies for Detecting Off-Target Signal and Image Noise in ADNI NAV4694 PET Imaging

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Background

- 18F-flutafuranol (NAV4694) is an amyloid PET tracer, with some studies suggesting higher dynamic range and high cortical binding specificity compared to other F-18 tracers [1].
- However off-target uptake and increased levels of image noise have been reported and may complicate interpretation, particularly in amyloid-negative cases [2].
- We explored quantitative metrics to complement traditional visual quality control (QC) and improve detection of potential atypical patterns.

OBJECTIVES

- Develop quantitative and visual QC metrics to assess extracerebral binding and noise level
- Examine associations between quantitative and visual metrics
- Determine if any differences in rating proportions and quantitative metrics between tracers

Methods

- Study population: All ADNI participants with [18F]NAV-4694 PET data. Additional groups of individuals with [18F]AV45 and [18F]FBB, matched by age, sex, and Centiloid value, were selected.
- Processing pipeline: MRI parcellation [3], co-registration to PET using NiftyReg [4], regional Standardized Uptake Value Ratio (SUVR) calculated using a whole cerebellar reference region
- Visual rating: Three raters independently rated each scan for noise level and extracerebral binding using a four-point scale (Figure 1). Interrater reliability for both scales were moderate to good (3-way Fleiss Kappa: noise=0.52, extracerebral=0.59)
- Estimate of Noise: The subcortical WM region, a large region with homogeneous uptake, was eroded once in PET space and intensities were normalized to have mean intensity of 1. The white matter standard deviation (WMSD) was extracted as a proxy for noise level
- Extracerebral binding: SUVR of a non-brain ROI derived from the MRI parcellation (Figure 2)

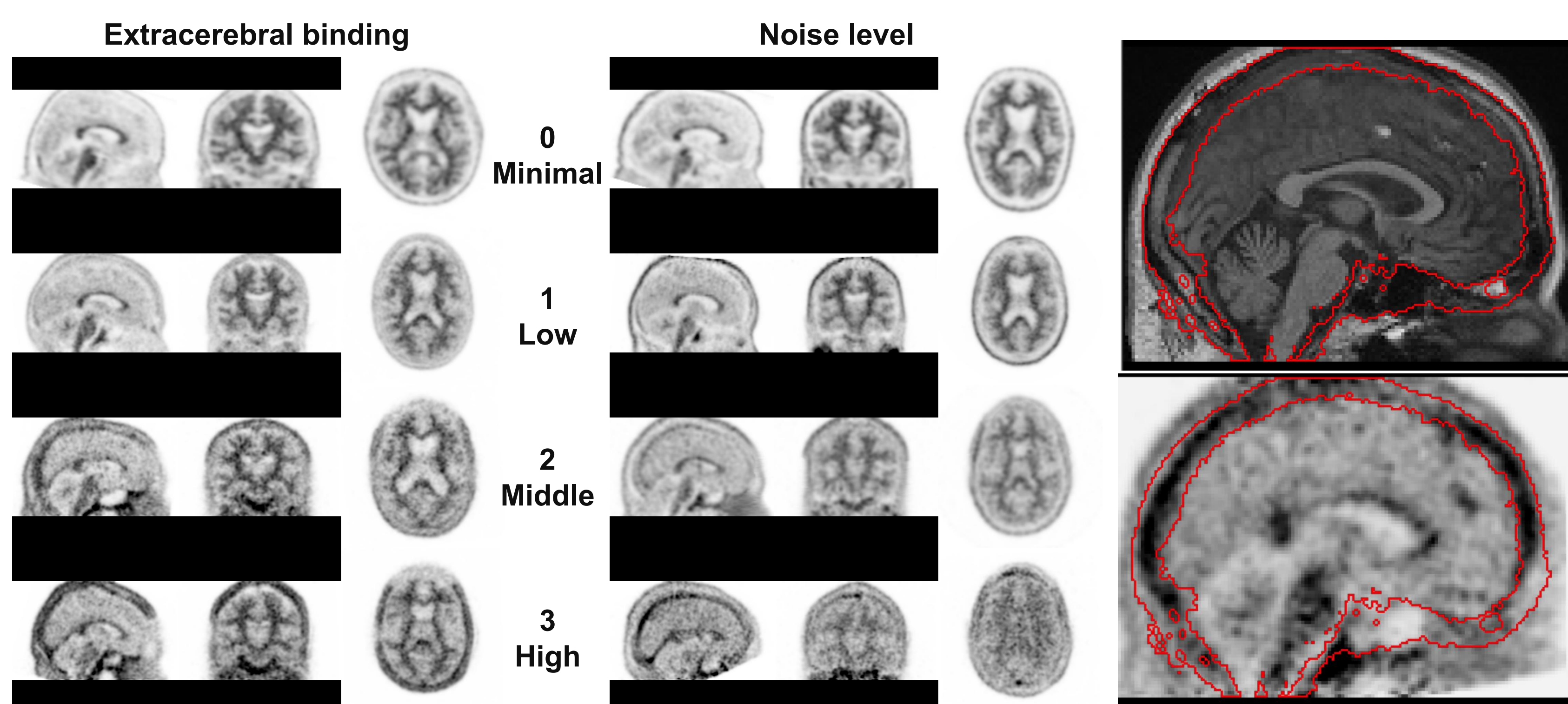


Figure 1 Example scans from each of the four visual rating levels for extracerebral binding (left) and noise level (right)

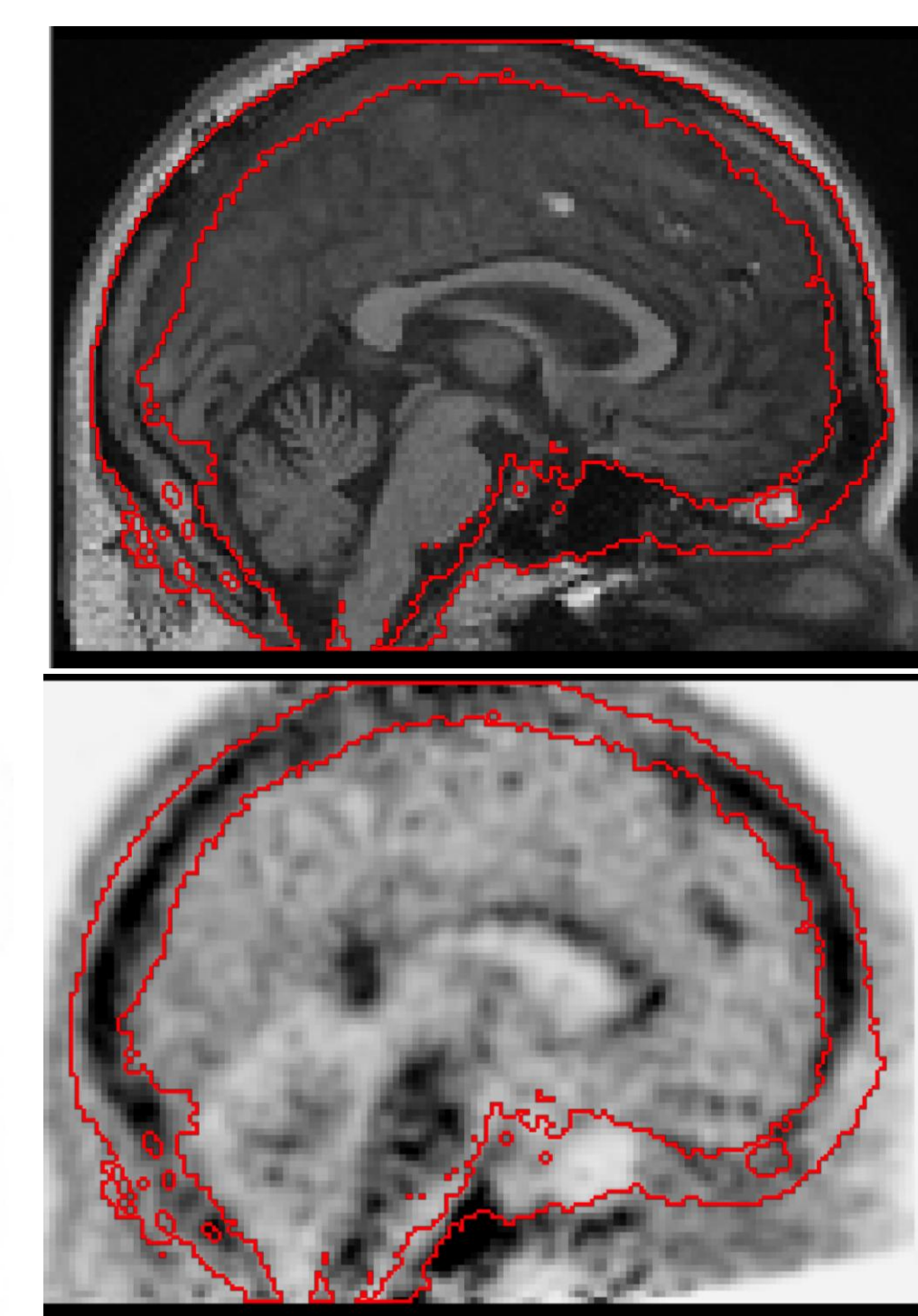


Figure 2 Example of non-brain region overlaid on MRI and co-registered PET images

Take-home messages

- Automated quantitative metrics of noise and extracerebral binding associate with qualitative visual ratings of image quality
- NAV4695 scans exhibit higher levels of noise (as measured by WMSD) across all ratings, which may be counteracted by higher cortical specificity
- NAV4694 scans exhibit higher rates of extracerebral binding and higher SUVR in non-brain regions.

Results

- Significant higher WMSD was observed with increasing visual rating scores for noise. Individuals with high extracerebral binding also showed increased WMSD.
- Across tracers, there were significant differences in the visual rating proportions (χ^2 test between groups, $p=0.021$ for noise level and $p=0.007$ for extracerebral). The AV45 group had higher noise and NAV4694 had higher extracerebral binding.
- Across all visual rating levels, NAV4694 had higher WMSD than the other tracers ($\beta_{NAV4694}=0.02$, $p < 0.001$) and higher non-brain SUVR ($\beta_{NAV4694}=0.3$, $p < 0.001$).
- Significant increases in non-brain SUVR were observed with increasing visual rating levels for extracerebral binding. Individuals with high noise level also showed increased non-brain SUVR. Differences in global composite SUVR between visual ratings were mixed and less frequent.

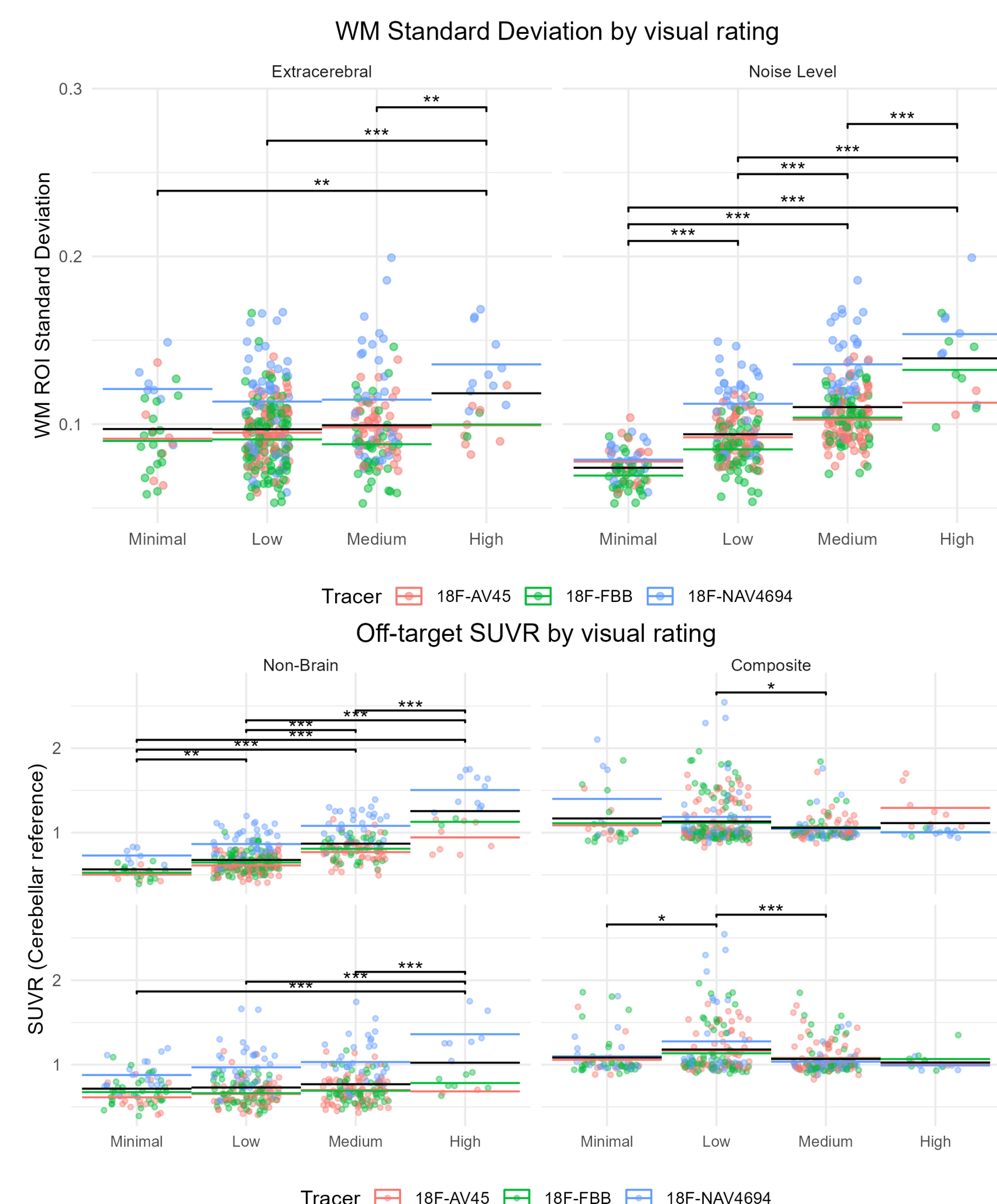


Figure 3 Quantitative metrics with respect to visual rating levels. (Top) WMSD, which serves as a proxy for noise and (Bottom) non-brain and global composite SUVR. The color of points indicate the Amyloid PET tracer group

Table Study demographics of the three radiotracer groups. 15 of the data sets came from an ADNI site where the data was subsequently removed from the study. It was agreed that the PET data could be included for assessment of image quality, but the clinical and cognitive data was excluded and marked as missing. * indicates that there were significant differences between groups using ANOVA (continuous) or chi-squared test (categorical) at a threshold of $p < 0.05$

		AV45 (N=150)	FBB (N=150)	NAV4694 (N=101)
Age, years	Mean (SD)	68.9 (8.3)	69.6 (7.2)	69.7 (8.2)
	N-Miss	0	0	15
Education, years	Mean (SD)	15.8 (2.7)	16.4 (2.4)	16.0 (2.5)
	N-Miss	0	0	15
Race*	Asian	8 (6%)	12 (8%)	6 (7%)
	African American	22 (16%)	25 (17%)	37 (43%)
	White	108 (77%)	108 (74%)	42 (49%)
	Unknown	3 (2%)	1 (1%)	1 (1%)
	N-Miss	9	4	15
Diagnosis	NC	79 (53%)	82 (55%)	48 (56%)
	MCI	51 (34%)	58 (39%)	33 (38%)
	AD	20 (13%)	10 (7%)	5 (6%)
	N-Miss	0	0	15
MMSE	Mean (SD)	28.1 (2.4)	28.3 (2.5)	27.7 (2.5)
	N-Miss	0	0	17
CDR Sum of Boxes	Mean (SD)	1.2 (1.8)	0.9 (1.4)	1.0 (1.4)
	N-Miss	0	0	16
Noise Level Visual Rating*	Minimal	17 (11%)	33 (22%)	20 (20%)
	Low	58 (39%)	59 (39%)	37 (37%)
	Medium	73 (49%)	51 (34%)	37 (37%)
	High	2 (1%)	7 (5%)	7 (7%)
Extra-cerebral Visual Rating*	Minimal	8 (5%)	17 (11%)	8 (8%)
	Low	89 (59%)	93 (62%)	48 (48%)
	Medium	45 (30%)	38 (25%)	34 (34%)
	High	8 (5%)	2 (1%)	11 (11%)

1. Rowe C et al. *J Nuclear Medicine*, (2013). DOI: 10.2967/jnumed.112.114785
2. La Joie R et al. *Human Amyloid Imaging*, San Juan, Puerto Rick 12-14 Jun 2026
3. Cardoso MJ et al, *IEEE TMI*, (2015). DOI: 10.1109/TMI.2015.2418298
4. Modat et al. *J Medical Imaging*, (2014). DOI: 10.1117/1.JMI.1.2.024003

