Impact of Amyloid Imaging on Diagnosis

In some of the related studies, a change in diagnosis occurred more often in (amyloid-negative) subjects with a pre-scan diagnosis of AD than in (amyloid-positive) non-AD subjects. This underpins the clinical usefulness of high negative predictive value of amyloid imaging to exclude amyloid pathology, following the widely accepted rule of "no AD without amyloid load." Also of interest, in the study by Ossenkoppele et al. a change in diagnosis was observed only in cases with a pre-scan diagnostic confidence of <90% (*38*). Similarly, Sanchez-Juan et al. reported a higher diagnosis change impact in a subgroup of subjects with a pre–amyloid scan diagnostic dilemma (*41*). Also, in accordance with the above results, Weston et al. noted an amyloid imaging–related change in diagnosis, especially in atypical (young-onset) dementia or cases with borderline cerebrospinal fluid (*46*), the results which can be regarded as evidence supporting the current amyloid imaging AUC concept.

Impact of Amyloid Imaging on Diagnostic Confidence

Across the related studies, the pre-scan diagnosis or the amyloid PET result did not significantly affect the diagnostic confidence gain obtained; i.e., in most circumstances both a positive and a negative amyloid PET scan result increased diagnostic confidence regardless of the pre-scan diagnosis. This is apart from a recent ^{18}F-flutemetamol bi-center study by Zwan et al., who included 211 subjects with early-onset cognitive impairment and a diagnostic confidence of <90%. In that study, no gain in diagnostic confidence was—somewhat surprisingly—found in subjects with a pre-scan diagnosis of AD and a negative PET, or in subjects with a pre-scan diagnosis of other dementia (*17*). It was further reported by Boccardi et al. that the gain in diagnostic confidence by amyloid imaging is independent from whether the imaging result affected diagnosis (*10,34*).

Impact of Amyloid Imaging on Patient Management

Changes in planned diagnostic follow-up after amyloid imaging were reported in three related studies for 10%–26% of cases (*17,39,46*), and changes in care plans via amyloid imaging were reported for 11% and 39% of cases, respectively (*17,45*). Finally, Grundman et al. observed changes in the plan to refer subjects to clinical trials in 16% of cases (*39*). Also of interest, it was noted in two studies that the impact of amyloid imaging on patient management was higher for PET-positive than PET-negative subjects (*17,44*) and that medication changes occurred more often in PET-positives than in PET-negatives, while the opposite was the case for care plan changes (*45*).

Supplemental Table 1: Criteria for appropriate and inappropriate use of amyloid imaging

Amyloid imaging appropriate	Amyloid imaging inappropriate
Persistent or progressive unexplained MCI	Core clinical criteria for probable AD with typical age of onset
Core clinical criteria for possible AD because of unclear clinical presentation*	To determine dementia severity
Progressive dementia and atypically early age of onset	Solely positive family history of dementia or presence of APOE4
	Solely subjective cognitive complaint
	In lieu of genotyping in suspected autosomal mutation carriers
	Nonmedical use**

Adapted from (*13*). MCI = mild cognitive impairment, AD = Alzheimer dementia, APOE4 = apolipoprotein ε4. *Either atypical clinical course or etiologically mixed presentation. **Legal, insurance coverage, employment screening etc.

Supplemental Table 2: Recommendations for disclosure of amyloid imaging results to MCI subjects

Offer pretest counseling
Use clear graphics
Review the brain PET images during disclosure
Offer take-home materials
Call after disclosure to address emerging questions
Communicate seamlessly with primary care providers

As proposed by (*31*). MCI = mild cognitive impairment.

Supplemental Table 3: Studies on Clinical Utility of Amyloid PET Imaging

Reference	Cases (*n*)	Pre–amyloid PET diagnosis	Amyloid tracer	PET positivity (% of cases)	Comments
Frederiksen et al. 2012 (*34*)	57	Cognitive impairment with diagnostic uncertainty	^{11}C-PIB	47	—
Schipke et al. 2012 (*35*)	201	Probable AD vs. HC	^{18}F-Florbetaben	56	Retrospective "intended change" survey of phase 2 clinical tracer development study
Degerman Gunnarsson et al. 2013 (*37*)	18	Probable AD vs. FTD	^{11}C-PIB	39	Amyloid PET + FDG + repeated NEUROPSYCH
Ossenkoppele et al. 2013 (*38*)	154	Cognitive impairment with diagnostic uncertainty	^{11}C-PIB	48	Amyloid PET + FDG
Grundman et al. 2013 (*39*)	229	Cognitive impairment (diagnostic confidence of AD = 15%–85%)	^{18}F-Florbetapir	49	—
Mitsis et al. 2014 (*40*)	30	Cognitive impairment with diagnostic uncertainty	^{18}F-Florbetapir	50	—
Sanchez-Juan et al. 2014 (*41*)	140	Cognitive impairment (19% with diagnostic uncertainty)	^{11}C-PIB	49	Amyloid PET + FDG
Zannas et al. 2014 (*42*)	11	Cognitive impairment (diagnostic confidence of AD = 15%–85%)	^{18}F-Florbetapir	55	Subset of cohort in (*39*)
Boccardi et al. 2016 (*10*)	228	Cognitive impairment (diagnostic confidence of AD = 15%–85%)	^{18}F-Florbetapir	60	—
Bensaïdane et al. 2016 (*45*)	28	Atypical* dementia	^{18}F-NAV4694	50	—
Weston et al. 2016 (*46*)	20	Different dementia syndromes	^{18}F-Florbetapir	90	—
Schönecker et al. 2016 (*47*)	33	Cognitive impairment	^{18}F-Florbetaben	52	—
Zwan et al. 2017 (*17*)	211	Cognitive impairment (diagnostic confidence < 90%)	^{18}F-Flutemetamol	63	Early-onset or mild dementia

AD = Alzheimer disease, HC = Healthy control, FTD = Frontotemporal dementia, NEUROPSYCH = Neuropsychological testing. *In the opinion of expert behavioral neurologists after review of history, basic lab, MRI, and ^{18}F-FDG PET.