Tạp chí Sức khỏe và Lão hóa
Journal of Health and Aging
Published online at https://tcsuckhoelaohoa.vn

Review

THE ROLE OF AMYLOID POSITRON EMISSION TOMOGRAPHY (PET) IMAGING IN THE EARLY DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE: A LITERATURE REVIEW

Truong Diep Van Anh[1,*]

1. Can Tho University of Medicine and Pharmacy, Can Tho City, Vietnam

* *Corresponding author: Truong Diep Van Anh* ✉ *tvanh@ctump.edu.vn*

ABSTRACT: Alzheimer's disease (AD) is becoming a global health burden, necessitating a shift in diagnostic models from traditional clinical criteria to biomarkers based on the ATN classification system. This review synthesizes scientific evidence on the role of amyloid positron emission tomography (PET) in the early diagnosis and management of AD. Amyloid PET enables quantification of amyloid-beta (Aβ) plaque deposition in the living brain, a biological process that begins 15–20 years before symptom onset. The article reviews the development from the first-generation compound ^{11}C-PiB to ^{18}F-labe^{le}d radiotr^{ac}ers (Florbetapir, Flutemetamol, Florbetaben), which have made this technique feasible in routine clinical practice. Amyloid PET has become an indispensable "gold standard" for patient selection and for monitoring the plaque-clearing efficacy of novel immunotherapies such as Lecanemab and Donanemab. Finally, the paper discusses challenges in Vietnam and proposes a multimodal model that uses blood-based biomarkers for screening followed by amyloid PET for confirmation, to optimize costs and improve diagnostic efficiency in the local context.

Keywords: Amyloid PET; Alzheimer's disease; biomarkers; ATN framework; immunotherapy.

Received: 03/06/2026 Accepted: 15/09/2026 Published: 01/10/2026
Copyright: © Author(s). Published by *Journal of Health and Aging*.

1. INTRODUCTION

Alzheimer's disease (AD) is currently the leading cause of dementia and is fast becoming one of the deadliest and most costly diseases of this century, with one of the largest health burdens. According to epidemiological reports, about 50 million people worldwide were living with dementia in 2018, and this number is expected to triple by 2050. Two-thirds of those affected live in low- and middle-income countries such as Vietnam. The rapid rise in the number of cases puts enormous pressure on health systems and also has serious economic consequences because of the very high costs of care and treatment [1].

The traditional diagnostic model for Alzheimer's disease, which relies only on clinical symptoms of cognitive decline, has considerable limitations. Studies of biomarker dynamics have shown that pathological changes in the brain develop silently 10 to 20 years before the first clinical symptoms appear. Therefore, by the time clinical signs become evident and patients reach the diagnostic threshold for dementia, neural damage is often at a late and irreversible stage [2, 3]. Moreover, relying on clinical presentation alone leads to misdiagnosis rates of 10% to 30% because symptoms overlap with those of other types of dementia [3, 4].

Against this background, Alzheimer's disease has been redefined as a biological disease rather than a clinical syndrome. The NIA-AA Research Framework (2018) formalized the ATN classification system, in which A (amyloid) represents amyloid-β plaque deposition, T (tau) represents tau pathology, and N (neurodegeneration) represents neurodegeneration or neuronal injury. This system allows a definitive diagnosis of Alzheimer's disease even in people who have no clinical symptoms but already show evidence of the biological disease on imaging and cerebrospinal fluid testing [3, 4].

This review aims to synthesize the scientific evidence on the role of amyloid PET, from its biological basis in the ATN classification system to its practical clinical applications and the prospects for introducing the technique in Vietnam, to give clinicians and researchers in the country a comprehensive overview.

2. PATHOPHYSIOLOGICAL BASIS OF THE AMYLOID HYPOTHESIS IN ALZHEIMER'S DISEASE

2.1. Processing and cleavage of the amyloid precursor protein (APP) to generate $A\beta_{42}$ fragments

The etiology of Alzheimer's disease is closely linked to abnormal metabolism of the amyloid precursor protein. In the amyloidogenic pathway, APP is cleaved by β-secretase (BACE1) and the γ-secretase complex to release amyloid-beta (Aβ) peptides. Of these, Aβ42 is a highly hydrophobic fragment with a stronger tendency to aggregate than Aβ40 and is considered the main initiator of extracellular plaques. The radiotracers used in amyloid PET (such as Florbetapir, Florbetaben, and Flutemetamol) are designed to have high affinity and selectivity for these fibrillar Aβ structures [5].

2.2. Mechanisms of extracellular amyloid-beta plaque accumulation and neurotoxicity

Aβ accumulates through a sequence of steps: monomers convert into soluble oligomers, which then grow into fibrils and are finally deposited as extracellular amyloid plaques. Soluble oligomers are considered the most toxic form, causing synaptic dysfunction and neuronal injury. Aβ plaques activate an inflammatory response in microglia and trigger a cascade of pathological events, including the formation of intracellular tau neurofibrillary tangles. This synergistic interaction between Aβ and tau is thought to drive widespread neurodegeneration and cell death.

Longitudinal studies (such as AIBL) estimate that Aβ accumulation takes about 12 years to rise from normal levels to the positivity threshold (1.5 SUVR) and about another 17 years to reach the levels typically seen in patients with clinical-stage AD [6].

3. RADIOTRACERS FOR AMYLOID PET IMAGING

On amyloid PET, tracer uptake is usually highest in the prefrontal, posterior cingulate, and temporal cortices, accurately reflecting the distribution of Aβ plaques found at neuropathology [5].

3.1. First-generation compound: ^{11}C-PiB (Pittsburgh Compound B)

Mechanism: ^{11}C-PiB is a neutral benzothiazole derivative of the dye thioflavin-T. It crosses the blood-brain barrier rapidly and binds with very high affinity and specificity to the β-pleated sheets of fibrillar amyloid (aggregated fibrils). Postmortem and in vivo studies have confirmed that PiB accumulates mainly in amyloid plaques in the cortex and striatum but does not bind significantly to tau neurofibrillary tangles.

Advantages:

High contrast: PiB clearly distinguishes patients with Alzheimer's disease from healthy individuals. In patients with AD, PiB retention increases most in the prefrontal cortex (1.94-fold compared with controls), followed by the parietal and temporal cortices and the deep gray matter nuclei [7].

Gold standard: PiB was the first compound to show that amyloid plaques could be quantified in living people. It laid the foundation for the entire amyloid biomarker system and is the reference against which later-generation radiotracers are compared.

Clean kinetics: PiB is cleared very rapidly from normal brain tissue that contains no amyloid (such as the cerebellum), which optimizes the signal-to-noise ratio.

Disadvantages:

Short half-life: Because it is labeled with the radioisotope carbon-11, PiB has a half-life of only about 20 minutes.

Limited availability: This physicochemical property requires medical centers to have an on-site cyclotron and radiochemistry synthesis system so that the tracer can be produced and used immediately. This creates major cost and infrastructure barriers, so ^{11}C-PiB cannot be commercialized on a large scale or transported to hospitals far from the production site [7].

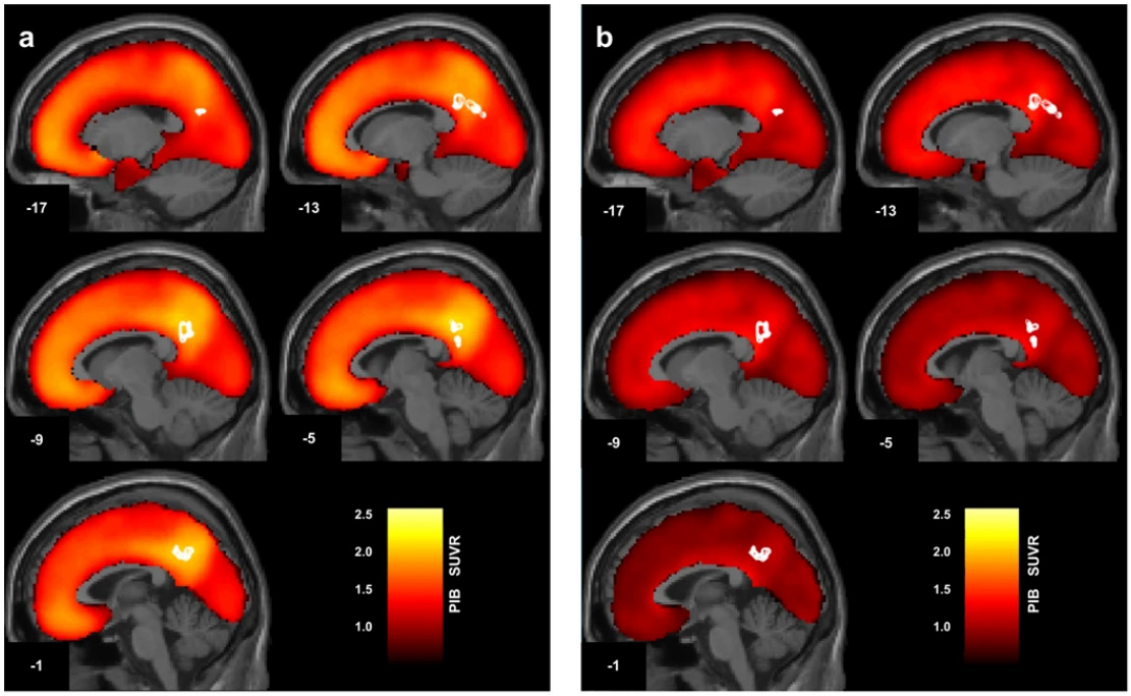


Figure 1. Mean SUVR maps of Aβ-PET with ^{11}C-PiB in patients with Alzheimer's disease (a) and controls (b). S^{ou}rce: Nádia et al, Nature, 2022 [8]

3.2. New-generation ^{18}F-labeled compounds (the commercial option)

To overcome the short half-life of ^{11}C-PiB, fluorine-18-labeled radiotracers were developed. The most important property of these compounds is their considerably longer half-life (~110 minutes). This allows the tracers to be produced at centralized facilities (central cyclotrons) and transported to satellite hospitals over a wide radius, making amyloid PET feasible in routine clinical practice [9, 10].

Florbetapir (Amyvid): This was the first ^{18}F tracer to be studied extensively. Florbetapir showed excellent accuracy in studies that compared it directly with autopsy findings. PET images acquired during life correlated closely with amyloid plaque burden after death (measured by immunohistochemistry and silver staining), with agreement of up to 96% [9].

Flutemetamol (Vizamyl): As a direct ^{18}F-labeled derivative of PiB, Flutemetamol has a chemical structure and binding properties similar to those of the "gold standard" PiB. Phase 3 trials confirmed its sensitivity for detecting advanced phases of amyloid pathology (Thal phases 4 and 5), allowing accurate differentiation of Alzheimer's disease from other non-amyloid dementias [11].

Florbetaben (Neuraceq): The efficacy of Florbetaben was established in a multicenter phase 2 trial, with a sensitivity of 80% and a specificity of 91% for distinguishing people with AD from healthy individuals. The posterior cingulate cortex gave the best discriminating signal [9]. Later studies showed that Florbetaben had a sensitivity and specificity of up to 96% against the histopathological gold standard [12].

Comparison of diagnostic performance: In clinical practice, the three ^{18}F tracers above (Florbetapir, Flutemetamol, and Florbetaben) are considered diagnostically equivalent. All show high reproducibility, and visual reading has been standardized across PET centers [11]. However, because each tracer has different kinetics and positivity thresholds, direct comparison of quantitative measures (such as SUVR) is difficult. To address this, the Centiloid project established a standard scale from 0 (equivalent to the amyloid level in young healthy people) to 100 (equivalent to the level in typical AD patients). The

Centiloid scale converts data from different tracers and analysis software into a single unit, making it easier for clinicians to define the pathological threshold (usually >19–24 Centiloid, depending on the tracer) and to accurately monitor plaque clearance with new therapies [13].

4. CLINICAL APPLICATIONS IN THE EARLY DIAGNOSIS AND TREATMENT OF ALZHEIMER'S DISEASE

4.1. Diagnosis at the mild cognitive impairment (MCI) and preclinical AD stages

Differential diagnosis and prediction of the risk of progression in patients with mild cognitive impairment (MCI) are particularly important in clinical practice. According to the epidemiological review by Tahami Monfared et al. (2022), an estimated 40% to 75% of MCI cases are biologically due to Alzheimer's disease, depending on the diagnostic criteria (clinical only or combined with biomarkers) and the study population. Establishing amyloid positivity allows accurate prediction of clinical progression: longitudinal studies have shown that among patients with MCI and positive amyloid biomarkers, the rate of conversion to AD dementia reaches 50%–61% after 3 years of follow-up (IWG-1 and IWG-2 criteria) and 59% in the high-likelihood group under NIA-AA. This is much higher than in MCI with negative biomarkers (only about 5%–24% progress after 3 years). In MCI populations diagnosed on clinical grounds alone, progression to AD dementia averages 38.7% after 31 months of follow-up, and the conversion rate is markedly higher among patients seen at specialist centers (31%) than in community samples (13%). This difference confirms the central role of biomarkers such as amyloid PET in accurately stratifying the risk of progression from the early stages [14].

Under the most recent criteria (2024), AD is defined as a biological process that begins asymptomatically with pathological changes in the brain, and amyloid PET is sufficient for a definitive diagnosis and for clinical decision-making [15, 16].

Preclinical staging according to NIA-AA 2011, based on amyloid PET combined with markers of neuronal injury:

Table 1: Preclinical staging of Alzheimer's disease according to NIA-AA 2011

Stage	Description	Amyloid PET	Evidence of neurodegeneration	Cognitive/clinical presentation
Stage 1	Asymptomatic cerebral amyloidosis	Positive	None	Normal (asymptomatic).
Stage 2	Amyloidosis + neurodegeneration	Positive	Present (e.g., elevated CSF tau or brain atrophy on MRI)	Normal.
Stage 3	Amyloidosis + neurodegeneration + subtle cognitive decline	Positive	Present (e.g., elevated CSF tau or brain atrophy on MRI)	Very mild cognitive change from the individual's own baseline, not yet meeting criteria for MCI.

Clinical staging according to NIA-AA 2018, based on the ATN classification system:

Table 2: Clinical staging of Alzheimer's disease based on the ATN system (NIA-AA 2018)

Stage	Stage name	Objective cognitive assessment	Clinical features & level of independence
Stage 1	Asymptomatic	Cognitive test performance within normal limits.	Fully asymptomatic, but with biomarker (ATN) evidence in the brain.
Stage 2	Transitional cognitive decline	Performance on objective cognitive tests still within normal limits.	Subjective memory complaints or subtle decline on longitudinal testing.

Stage 3	Mild cognitive impairment (MCI)	Objective cognitive performance in the impaired/ abnormal range; evidence of decline from baseline.	Mild impact on complex activities of daily living.
Stage 4, 5, 6	Dementia (mild, moderate, severe)	Marked, progressive decline on cognitive tests.	Dementia severity increases from mild (Stage 4) to moderate (Stage 5) and severe (Stage 6); marked by gradual loss of independence and complete dependence on caregivers in the final stage.

4.2. Criteria for selecting patients for new anti-amyloid immunotherapies

The arrival of monoclonal antibody therapies targeting amyloid-beta has raised amyloid PET from a diagnostic tool to a mandatory standard for selecting patients and monitoring treatment response in clinical trials and current practice.

Lecanemab (Leqembi): In the phase 3 Clarity AD trial, confirmation of "amyloid positivity" by PET or cerebrospinal fluid testing (Aβ1–42) was a prerequisite for patient screening. Amyloid PET was used not only for enrollment but also to assess drug efficacy: Lecanemab reduced amyloid burden by a mean of 59.1 centiloids relative to placebo at 18 months. At that point, the mean amyloid level in the treatment group had fallen to about 22.99 centiloids, below the usual positivity threshold (~30 centiloids), showing marked plaque clearance confirmed directly by imaging [17].

Donanemab (Kisunla): The TRAILBLAZER-ALZ trial broke new ground by using amyloid PET to individualize treatment according to each patient's biological response. Instead of continuing infusions indefinitely, amyloid PET was performed periodically (at weeks 24 and 52) to monitor amyloid plaque dynamics. Based on these results, clinicians could make an important clinical decision: stop infusions once amyloid plaque had been cleared from the brain (<11 centiloids, or 11–25 centiloids on two consecutive scans). By week 76, about 67.8% of patients receiving Donanemab had become amyloid-negative [18].

Table 3: Role of amyloid PET from enrollment to treatment monitoring in clinical trials.

Criterion	Clarity AD trial (Lecanemab)	TRAILBLAZER-ALZ trial (Donanemab)
Study drug	Lecanemab, a monoclonal antibody (targeting soluble Aβ protofibrils).	Donanemab, a monoclonal antibody (targeting deposited N3pG Aβ plaques).
Study population	1,795 patients with early AD (MCI due to AD or mild AD dementia), aged 50–90 years; baseline CDR-SB about 3.2; MMSE 22–30.	1,736 patients (phase 3) with early symptomatic AD (MCI or mild dementia due to AD); baseline MMSE 20–28.
Role of amyloid PET in enrollment criteria	Mandatory inclusion criterion: positive amyloid-β plaque on amyloid PET (or CSF Aβ1–42) to confirm AD biology.	Mandatory inclusion criterion: amyloid positivity confirmed by Florbetapir amyloid PET, combined with Flortaucipir tau PET to stratify tau burden (patients with very low or very high tau excluded).
PET assessment time points	PET substudy (n=698) at baseline, 3, 6, 12, and 18 months (week 79).	Amyloid PET at baseline, week 24, week 52, and week 76.
PET response criterion	Reduction in cortical Aβ plaque burden versus placebo on the standardized Centiloid scale.	Plaque burden (Centiloid) and time to meeting "plaque clearance" criteria (<11 Centiloid, or 11–25 Centiloid on 2 consecutive scans).
Main amyloid PET results	Mean change of -55.48 Centiloid with Lecanemab vs +3.64 Centiloid with placebo (difference -59.12 Centiloid, $p < 0.001$) at month 18.	Reduction of -85.06 Centiloid vs placebo at week 76; 67.8% of patients amyloid-negative (<24.1 Centiloid) at week 76.

PET-based clinical decision	Target engagement confirmed; dosing continued on a fixed schedule.	Treatment discontinuation: 54.7% of patients switched to placebo at week 56 after PET confirmed plaque clearance from the brain.
Main clinical results	27% slowing of cognitive/functional decline on CDR-SB at month 18 (difference -0.45 points, $p < 0.001$); secondary endpoints ADAS-cog14, ADCOMS, and ADCS-MCI-ADL met.	32%–35% slowing of decline in cognition and activities of daily living on iADRS and CDR-SB at week 76.

4.3. Impact of amyloid PET on patient management decisions and Appropriate Use Criteria (AUC) in clinical practice

Beyond confirming the biological nature of the disease, the real-world impact of amyloid PET results on diagnostic changes and clinical management was demonstrated in the IDEAS study (Imaging Dementia—Evidence for Amyloid Scanning). This was the largest prospective clinical study of its kind, conducted in 11,409 older patients (60.5% with mild cognitive impairment [MCI] and 39.5% with dementia of uncertain cause) at 595 medical centers in the United States. All participants met the appropriate use criteria, under which the cause of cognitive impairment could not be determined with certainty after a comprehensive specialist evaluation. IDEAS showed that access to amyloid PET changed overall clinical management (including treatment with Alzheimer's drugs, other drugs affecting cognition or mental health, and counseling on safety and future planning) in 60.2% of patients with MCI (95% CI: 59.1%–61.4%) and 63.5% of patients with dementia (95% CI: 62.1%–64.9%) after 90 days36. This change was significantly greater than the hypothesized target of 30% ($P < 0.001$). Clinicians judged that PET results made a central contribution to the new management decision in 85.2% of cases with a change. Regarding etiological diagnosis, amyloid PET changed the diagnosis from Alzheimer's disease to non-Alzheimer's disease (non-AD) in 25.1% of patients (2,860/11,409) and from non-AD to Alzheimer's disease in 10.5% (1,201/11,409). As a result, the proportion of cases in which clinicians reported uncertain diagnostic confidence (scores 4–7 on a Likert scale) fell sharply, from 72.4% before PET to 16.2% after the results were available. Regarding drug therapy, among patients with positive amyloid PET, prescription of symptomatic Alzheimer's drugs (acetylcholinesterase inhibitors and memantine) rose from 40.4% to 81.5% in the MCI group and from 63.2% to 91.2% in the dementia group ($P < 0.001$). Conversely, in patients with negative PET, clinicians discontinued unnecessary Alzheimer's drugs and cut back on other costly or invasive diagnostic tests, such as follow-up MRI or lumbar puncture. In addition, accurate determination of amyloid status increased the proportion of correctly selected amyloid-positive participants enrolled in clinical trials from 65.5% to 92.9% [19].

To move from simply describing technical capability to defining the exact place of amyloid PET in patient care, the Alzheimer's Association (AA) and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) developed, and have continually updated, the Appropriate Use Criteria (AUC). According to the latest AUC report, amyloid PET should not be ordered indiscriminately; it must meet two prerequisite principles:

The cause of cognitive impairment remains uncertain after a comprehensive, in-depth evaluation by a dementia specialist (including history, neurological examination, objective cognitive assessment, blood tests to exclude reversible causes, and structural imaging with MRI/CT).

Knowing whether amyloid plaque pathology is present in the brain is expected to directly change the diagnostic plan, prognostic counseling, or medical treatment of the patient.

Table 4: Summary of the Appropriate Use Criteria (AUC) for amyloid PET (AA-SNMMI 2025 / Rabinovici GD et al.) [20]

AUC category	Delphi score	Clinical scenario	Impact on clinical management
Appropriate	9 / 9	Selection for anti-amyloid therapy: determining eligibility to start monoclonal antibodies (Lecanemab, Donanemab).	Mandatory confirmation of Aβ plaque before costly targeted therapy.
	9 / 9	MCI or early-onset dementia (<65 years) with suspected AD pathology.	High rate of atypical disease; confirmatory PET guides early treatment and reduces misdiagnosis.
	8 / 9	Monitoring response to anti-amyloid therapy: quantifying Aβ reduction on the Centiloid scale in patients receiving infusions.	Helps clinicians decide to stop or reduce dosing once the brain is cleared of plaque.
	8 / 9	MCI or dementia with atypical presentation: non-amnestic variants (PCA, lvPPA, dysexecutive syndrome), unusually rapid/slow progression.	Distinguishes Alzheimer's disease from frontotemporal lobar degeneration (FTLD), prion disease, or mixed causes.
	8 / 9	MCI or dementia with typical symptoms (<65 years) but uncertain cause after specialist evaluation.	Confirms coexisting AD pathology; excludes vascular or LATE causes that mimic Alzheimer's disease.
	8 / 9	MCI or dementia with unclear or discordant fluid/blood biomarker results	PET gives direct evidence of the extent and location of insoluble plaque deposition.
Rarely appropriate	1–2 / 9	Cognitively asymptomatic individuals, or those with subjective complaints without high risk.	Avoids unnecessary anxiety; Aβ in older people does not necessarily mean imminent clinical symptoms.
	1 / 9	Assessing severity or monitoring progression in people with a prior biological diagnosis of AD.	Aβ plaque reaches a plateau at the dementia stage; PET does not reflect clinical severity.
	1 / 9	Non-medical purposes: legal assessment, behavioral capacity, driving ability, or insurance/ employment screening.	PET signal does not correlate directly with behavioral capacity or current cognitive function.

5. CHALLENGES AND FUTURE DIRECTIONS IN VIETNAM

Although amyloid PET is a powerful diagnostic tool, its implementation in Vietnam currently faces major infrastructure and economic challenges. In real-world clinical practice, the number of PET/CT scanners and of centers with cyclotrons able to produce ^{18}F-labeled radiotracers is still very limited, and these are concentrated mainly in large cities such as Hanoi and Ho Chi Minh City. Apart from infrastructure, the cost of an amyloid PET scan remains very high relative to average income and is not widely covered by health insurance. These barriers make access to modern imaging-based diagnosis a considerable financial burden, delaying early diagnosis and timely intervention for patients.

With limited resources, combining amyloid PET with other biomarkers is the inevitable way to optimize the diagnostic pathway:

Cerebrospinal fluid (CSF) testing: CSF measures are highly accurate and correlate closely with amyloid PET results. The main barrier is that lumbar puncture is invasive and often makes patients and their families reluctant [3].

Blood-based biomarkers: New-generation markers such as p-tau217 and the Aβ42/ Aβ40 ratio offer the prospect of a breakthrough because of their low cost and simple blood sampling. In particular, plasma p-tau217 has shown excellent diagnostic accuracy, comparable to that of expensive imaging methods for identifying Alzheimer's pathology [3].

Proposed model for clinical practice in Vietnam: Based on the latest advances in the NIA-AA 2024 criteria, we propose a multimodal pathway suited to local practice:

Screening: Blood tests (such as p-tau217) are used as the first filter at lower-level health facilities or specialist clinics for broad screening of people with memory complaints.

Confirmation: Only cases with blood test results in the "gray zone" (indeterminate), or cases that require precise quantification of plaque burden before starting targeted therapy, are referred to central-level hospitals for amyloid PET.

This model would both optimize costs for the health system and ensure that patients have accurate and safe access to new immunotherapies based on solid biological evidence. It is fully consistent with the global shift toward an era of personalized diagnosis and treatment based on core biomarkers.

6. CONCLUSION

Amyloid PET is more than an advanced imaging tool. It has become the only "biological visual key" that can locate and quantify amyloid-β plaque burden, a core pathological feature of Alzheimer's disease, in living people. With high sensitivity and specificity against the histopathological gold standard, the technique helps eliminate errors in diagnosis based purely on clinical findings, which often overlap with other forms of dementia.

In the era of targeted disease-modifying therapies, amyloid PET is an essential bridge to precision medicine. The success of monoclonal antibodies such as Lecanemab and Donanemab rests entirely on the use of amyloid PET as a strict screening criterion, which ensures that the drugs reach patients with biological evidence of amyloid accumulation. Amyloid PET also allows plaque dynamics to be monitored in real time, helping clinicians determine when to adjust the dose or stop infusions once the brain has been cleared of plaque, which optimizes treatment efficacy and minimizes adverse effects.

REFERENCES

[1] Scheltens P, De Strooper B, Kivipelto M, Holstege H, Chételat G, Teunissen CE, Cummings J, Van Der Flier WM. Alzheimer's disease. The Lancet. 2021;397(10284):1577–1590. doi:10.1016/S0140-6736(20)32205-4

[2] Jack CR, Knopman DS, Jagust WJ, Petersen RC, Weiner MW, Aisen PS, Shaw LM, Vemuri P, Wiste HJ, Weigand SD, et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. The Lancet Neurology. 2013;12(2):207–216. doi:10.1016/S1474-4422(12)70291-0

[3] Hansson O, Blennow K, Zetterberg H, Dage J. Blood biomarkers for Alzheimer's disease in clinical practice and trials. Nature Aging. 2023;3(5):506–519. doi:10.1038/s43587-023-00403-3

[4] Jack CR, Bennett DA, Blennow K, Carrillo MC, Dunn B, Haeberlein SB, Holtzman DM, Jagust W, Jessen F, Karlawish J, et al. NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease. Alzheimer's & Dementia. 2018;14(4):535–562. doi:10.1016/j.jalz.2018.02.018

[5] Villemagne VL, Doré V, Burnham SC, Masters CL, Rowe CC. Imaging tau and amyloid-β proteinopathies in Alzheimer disease and other conditions. Nature Reviews Neurology. 2018;14(4):225–236. doi:10.1038/nrneurol.2018.9

[6] Villemagne VL, Burnham S, Bourgeat P, Brown B, Ellis KA, Salvado O, Szoeke C, Macaulay SL, Martins R, Maruff P, et al. Amyloid β deposition, neurodegeneration, and cognitive decline in sporadic Alzheimer's disease: a prospective cohort study. The Lancet Neurology. 2013;12(4):357–367. doi:10.1016/S1474-4422(13)70044-9

[7] Klunk WE, Engler H, Nordberg A, Wang Y, Blomqvist G, Holt DP, Bergström M, Savitcheva I, Huang G, Estrada S, et al. Imaging brain amyloid in Alzheimer's disease with Pittsburgh Compound-B. Annals of Neurology. 2004;55(3):306–319. doi:10.1002/ana.20009

[8] Nádia Canário, Lília Jorge, Ricardo Martins & Miguel Castelo-Branco. Dual PET-fMRI reveals a link between neuroinflammation, amyloid binding and compensatory task-related brain activity in Alzheimer's disease. Commun Biol. 2022;5:801. doi:10.1038/s42003-022-03761-7

[9] Clark CM. Use of Florbetapir-PET for Imaging β-Amyloid Pathology. JAMA. 2011;305(3):275. doi:10.1001/jama.2010.2008

[10] Barthel H, Gertz H-J, Dresel S, Peters O, Bartenstein P, Buerger K, Hiemeyer F, Wittemer-Rump SM, Seibyl J, Reininger C, et al. Cerebral amyloid-β PET with florbetaben (18F) in patients with Alzheimer's disease and healthy controls: a multicentre phase 2 diagnostic study. The Lancet Neurology. 2011;10(5):424–435. doi:10.1016/S1474-4422(11)70077-1

[11] Thal DR, Beach TG, Zanette M, Heurling K, Chakrabarty A, Ismail A, Smith APL, Buckley C. [^{18} F] flutemetamol amyloid positron emission tomography in preclinical and symptomatic Alzheimer's disease: Specific detection of advanced phases of amyloid-β pathology. Alzheimer's & Dementia. 2015;11(8):975–985. doi:10.1016/j.jalz.2015.05.018

[12] Chételat G, Arbizu J, Barthel H, Garibotto V, Law I, Morbelli S, Van De Giessen E, Agosta F, Barkhof F, Brooks DJ, et al. Amyloid-PET and 18F-FDG-PET in the diagnostic investigation of Alzheimer's disease and other dementias. The Lancet Neurology. 2020;19(11):951–962. doi:10.1016/S1474-4422(20)30314-8

[13] Doré V, Bullich S, Rowe CC, Bourgeat P, Konate S, Sabri O, Stephens AW, Barthel H, Fripp J, Masters CL, et al. Comparison of^{18} F-florbetaben quantification results using the standard Centiloid, MR-based, and MR-less CapAIBL® approaches: Validation against histopathology. Alzheimer's & Dementia. 2019;15(6):807–816. doi:10.1016/j.jalz.2019.02.005

[14] Tahami Monfared AA, Byrnes MJ, White LA, Zhang Q. Alzheimer's Disease: Epidemiology and Clinical Progression. Neurol Ther. 2022;11(2):553-569. doi:10.1007/s40120-022-00338-8

[15] Jack CR, Andrews JS, Beach TG, et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimers Dement. 2024;20:5143-69. doi:10.1002/alz.13859

[16] Safiri S, Ghaffari Jolfayi A, Fazlollahi A, Morsali S, Sarkesh A, Daei Sorkhabi A, Golabi B, Aletaha R, Motlagh Asghari K, Hamidi S, et al. Alzheimer's disease: a comprehensive review of epidemiology, risk factors, symptoms diagnosis, management, caregiving, advanced treatments and associated challenges. Frontiers in Medicine. 2024;11:1474043. doi:10.3389/fmed.2024.1474043

[17] Van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, Kanekiyo M, Li D, Reyderman L, Cohen S, et al. Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine.

2023;388(1):9–21. doi:10.1056/NEJMoa2212948

[18] Mintun MA, Lo AC, Duggan Evans C, Wessels AM, Ardayfio PA, Andersen SW, Shcherbinin S, Sparks J, Sims JR, Brys M, et al. Donanemab in Early Alzheimer's Disease. New England Journal of Medicine. 2021;384(18):1691–1704. doi:10.1056/NEJMoa2100708

[19] Rabinovici GD, Gatsonis C, Apgar C, Chaudhary K, Gareen IF, Hanna L, et al. Association of Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia. JAMA. 2019;321(13):1286-1294. doi:10.1001/jama.2019.2000

[20] Rabinovici GD, Knopman DS, Arbizu J, Benzinger TLS, Donohoe KJ, Hansson O, et al. Updated appropriate use criteria for amyloid and tau PET: A report from the Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging Workgroup. Alzheimers Dement. 2025;21(1):e14338. doi:10.1002/alz.14338