DAY 1
ABSTRACT 3

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Updated Appropriate Use Criteria for Amyloid and Tau PET

Abstract:

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Background:

The Alzheimer's Association and Society for Nuclear Medicine and Molecular Imaging convened a Workgroup to update previous Appropriate Use Criteria (AUC) for amyloid PET (Johnson 2013) and develop the first AUC for tau PET. The AUC represent general guidelines and should not be considered a substitute for clinical judgment exercised in the care of individual patients.

Method:

The Workgroup included 14 researchers with multidisciplinary expertise. Meetings were held between June 2020 and August 2021. Key research questions were identified using the PICOTS framework, triggering an independent

systematic literature review. Using established methods (Fitch 2001), the Workgroup identified 17 clinical scenarios in which amyloid/tau PET may be considered. Appropriateness of amyloid and tau PET as independent, stand-alone modalities were ranked for each scenario using a 9-point scale (Table 1). Consensus was achieved using a modified Delphi process. Online surveys were completed iteratively by Workgroup members, followed by discussion, until all votes for each scenario fell within one of the following categories: Appropriate/Uncertain/Rarely Appropriate.

RESULT:

As an over-arching principle, amyloid/tau PET should be considered in patients who: (1) have undergone a comprehensive assessment by a dementia expert; (2) Alzheimer's disease (AD) is a diagnostic possibility but uncertainty remains; and (3) knowledge of amyloid/tau PET results is expected to help establish diagnosis and guide patient management. Consensus ratings for clinical scenarios are shown in Table 2. More evidence was available to inform recommendations for amyloid than tau PET. Amyloid PET was considered "Appropriate" to inform diagnosis of MCI or dementia due to suspected AD; clarify diagnosis when CSF biomarkers are equivocal; to inform prognosis in MCI; and to determine eligibility for amyloid-targeting therapies. Tau PET was considered "Appropriate" to clarify diagnosis in patients with MCI/dementia under age 65 or those with atypical presentations; and to inform prognosis in MCI or dementia due to suspected AD.

CONCLUSION:

The updated AUC highlight a growing role for amyloid PET and an emerging role for tau PET in the clinical evaluation of cognitively impaired patients. AUC are expected to further evolve based on data from ongoing studies of clinical utility and a rapidly developing therapeutic landscape.

Table 1. Rating scale for appropriateness of amyloid/tau PET in each clinical scenario.

Score of 7 to 9, Appropriate:

9 = Highly confident that the scenario is appropriate

8 = Moderately confident that the scenario is appropriate

7 = Only somewhat confident that the scenario is appropriate

Score of 4 to 6, Uncertain:

6 = Uncertain, but possibility that the scenario is appropriate

5 = Uncertain, evidence is inconclusive or lacking

4 = Uncertain, but possibility that the scenario is rarely inappropriate

Score of 1 to 3, Rarely Appropriate:

3 = Only somewhat confident that the scenario is rarely appropriate

2 = Moderately confident that scenario is rarely appropriate

1 = Highly confident that the scenario is rarely appropriate

Table 2. Clinical scenarios and consensus rankings of appropriateness of amyloid and tau PET.

Clinical Scenario	Rating	
	Amyloid PET	Tau PET
Clinical Scenario #1: Patients who are cognitively unimpaired who are not considered to be at increased risk for AD based on age, known APOE ε4 genotype, or multigenerational family history	1	1
Clinical Scenario #2: Patients who are cognitively unimpaired but considered to be at increased risk for AD based on age, known APOE ε4 genotype, or multigenerational family history	2	1
Clinical Scenario #3: Patients with subjective cognitive decline (cognitively unimpaired based on objective testing) who are not considered to be at increased risk for AD based on age, known APOE ε4 genotype, or multigenerational family history	2	1
Clinical Scenario #4: Patients with subjective cognitive decline (cognitively unimpaired based on objective testing) who are considered to be at increased risk for AD based on age, known APOE ε4 genotype, or multigenerational family history	6	2
Clinical Scenario #5: Patients presenting with mild cognitive impairment or dementia who are below 65 years and in whom AD pathology is suspected	9	8
Clinical Scenario #6: Patients presenting with mild cognitive impairment or dementia syndrome which is often consistent with AD pathology (amnestic presentation) with onset at 65 years of age or older	8	6
Clinical Scenario #7: Patients presenting with mild cognitive impairment or dementia syndrome that could be consistent with AD pathology but has atypical features (e.g., non-amnestic clinical presentation, rapid or slow progression, etiologically mixed presentation)	8	7
Clinical Scenario #8: To determine disease severity or track disease progression in patients with an established biomarker-supported diagnosis of mild cognitive impairment or dementia due to AD pathology	1	4
Clinical Scenario #9: Patients presenting with prodromal Lewy Body or dementia with Lewy Body	2	4
Clinical Scenario #10: Patients with MCI or dementia with recent CSF biomarker results that are conclusive (whether consistent or not consistent with underlying AD pathology)	3	6
Clinical Scenario #11: Patients with MCI or dementia with equivocal or inconclusive results on recent CSF biomarkers	8	6
Clinical Scenario #12: To inform the prognosis of patients presenting with mild cognitive impairment due to clinically suspected AD pathology	8	7
Clinical Scenario #13: To inform the prognosis of patients presenting with dementia due to clinically suspected AD pathology	4	7
Clinical Scenario #14: To determine eligibility for treatment with an approved amyloid targeting therapy	8	5
Clinical Scenario #15: To monitor response among patients that have received an approved amyloid targeting therapy	6	5
Clinical Scenario #16: Non-medical usage (e.g., legal, insurance coverage, or employment screening)	1	1
Clinical Scenario #17: In lieu of genotyping for suspected autosomal dominant mutation carriers	1	1