



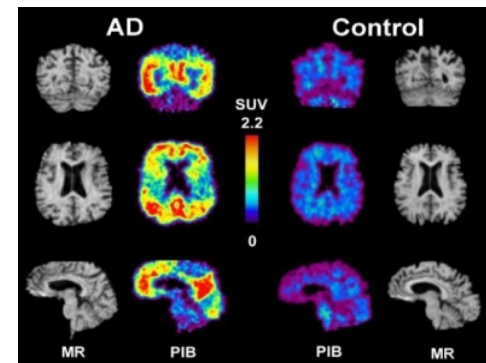
Perspectives on Amyloid Imaging from a Patient Advocacy Group

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SNMMI/AA Appropriate Use Criteria for Amyloid PET:

A report of the Amyloid Imaging Taskforce, the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association



Amyloid Imaging Taskforce

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Conflict of Interest

- AIT established a threshold for real COI
- Relationship w/industry (consulting, speaking, research etc) that exceed \$5,000 in funding over the previous 12 month period.
- Expert reviewers were cross-checked with papers included in review and cross-checked with financial and intellectual COIs

Introduction

- Premise: Amyloid imaging is not the equivalent to a clinical Dx of dementia, it is only one tool among many that clinicians should use judiciously to manage patients.
- Goal: To provide health care practitioners with the information necessary to provide their patients with optimal care, while considering the cost-effective utilization of our limited health care resources.

AUC Process

- Identification of potential indications/non-indications
- Evidence assessment and rating
- Group rating of indications/non-indications
- Open for public comment
- Discussion and re-voting
- Writing

Evidence Review

- Search strategy established by the American Academy of Neurology and Institute of Medicine
- Evaluated existing literature (adapted Fryback & Thornbury, 1991)
 - Technical efficacy
 - Diagnostic accuracy (clinical validity)
 - Clinical utility based on a change in management

Literature Review

- 408 publications were initially identified
- Exclusions:
 - *In vitro*
 - Animal toxicity
 - Biodistribution
 - Dosimetry
 - Small n
 - Reviews, editorials etc.
- Backward review cross checked literature search and review
- 23 publications used for indication guidance

AUC Indications/Non-Indications

- Group rated indications/non-indications
- 10 possible indications were rated on:
 - Amount of qualified evidence
 - Individual papers that relate to each
 - Appropriate, Uncertain or Inappropriate
- Re-voting took place

Appropriate Use Steps

- Evaluation by a dementia expert
- Referral for amyloid PET
- Performance and interpretation of amyloid PET
- Incorporation of results into clinical assessment by dementia expert
- Disclosure

Appropriate Uses

- Cognitive complaint with objectively confirmed impairment
- Alzheimer's disease as a possible diagnosis, but when uncertain after comprehensive evaluation by dementia expert
- When knowledge of the presence or absence of amyloid-beta pathology is expected to increase diagnostic certainty and alter management

- **Patients with persistent or progressive unexplained mild cognitive impairment**
 - Refers to patient that satisfied all criteria set forth and is being evaluated for persistent or progressive cognitive impairment that is still mild, e.g. MCI.
 - In these circumstances, an amyloid imaging PET finding of positivity would raise the level of certainty that the patient's impairment is based on AD pathology and represents early AD.

- Patients with unclear clinical presentation, either atypical clinical course or etiologically mixed presentation, satisfying core clinical criteria for possible AD
 - Intended to explicitly exclude the patient about whom there is little doubt as to the underlying pathology and include patients for whom uncertainty exists and for whom greater confidence would result from determining whether amyloid pathology is present or not present.

- Patients with progressive dementia and atypically early age of onset
 - Patient 50-65 years old, possibly younger with progressive impairment and features of AD
 - Goal is to manage symptomatic treatment, make appropriate employment, driving and lifestyle decisions, refer to clinical trials and plan for care.

- Patients with core clinical criteria for probable AD with typical age of onset
 - When core clinical criteria for probable AD dementia (McKhann, 2011) are satisfied
 - Uncertainty is low
 - Benefit would be low

- **To determine dementia severity**
 - Data are lacking to support use to determine severity in any cognitive disorder
 - Evidence that level of amyloid burden measured with amyloid PET does not correlate well with severity of deficits in patients with dementia

- Solely based on a positive family history of dementia or presence of APOEε4
 - There is no data available indicating that family history or APOE genotype, course or greater certainty in the cause of cognitive deficits is aided with amyloid imaging.

- Patients with cognitive complaint that is unconfirmed on clinical examinations
 - Significance of cognitive complaint in elderly person without deficits on examination is topic of investigation
 - Insufficient evidence at this time to suggest amyloid PET can aid in prognostic judgments or relieve concerns of individuals

- In lieu of genotyping for suspected autosomal mutation carriers
 - Appropriate evaluation of autosomal dominant mutation carriers is family history, genetic counseling and genetic testing

- Clinical use of amyloid PET in asymptomatic individuals is considered inappropriate at this time.
 - Prognostic value in normal elderly individuals remains investigational.
 - At present, potential harms outweigh the current minimal benefits.

- **Non-medical usage**
 - No evidence supports utility of amyloid PET in context outside of diagnostic work-up for cognitive impairment including:
 - Assessment for competency, screening for insurability, assessing employment
 - Assessment of activities of daily living such as driving, piloting aircraft or financial decision making

Impact on Patient Care

- Greater physician confidence can result in better medication management
- Reduce use of other tests which are burdensome to patients and care partners
- Minimize use of neuropsychological testing for the purpose of clinical diagnosis

Value of Knowing

- Early and documented diagnosis leads to better outcomes for individuals with AD and their families.
 - Access to appropriate treatments
 - Build a care team
 - Find support services
 - Enroll in clinical trial
 - Advance directives and financial planning
 - Address driving and safety issues

Early Stage Advisors

- Limitation of additional tests
- Eliminate other diagnosis
- Anxiety before a confident diagnosis
- Relief after confident diagnosis
- Ability to get on with the rest of life
- Action step that leads to planning
- Anticipation of difficult future moments
- Work place issues

Alzheimer's Association Recommendations

- Recommend that the Centers for Medicare and Medicaid consider coverage for PET amyloid imaging within the context of the appropriate use as determined by the AIT.
 - Patients with persistent or progressive unexplained MCI
 - Patients satisfying core clinical criteria for possible Alzheimer's disease because of unclear clinical presentation, either atypical clinical course or etiologically mixed presentation
 - Patients with progressive dementia and atypically early age of onset

SNMMI Quality & Education Initiatives

Quality

- Develop Procedure Guideline (in conjunction with European Assoc of Nuclear Medicine)
- Evidence development project: SNMMI, Alzheimer's Association and World Molecular Imaging Society

Education of Imaging Professionals

- Web-based education program consisting of
 - Core reading materials
 - Case studies for training and to assess competence in scan interpretation and reporting
- Live continuing education at SNMMI Annual, Midwinter, and Chapter meetings and AAIC
- Dissemination of clinical research results in the Journal of Nuclear Medicine (JNM), JNMT and Alzheimer's & Dementia
- Development of a microsite to serve as resource for beta-amyloid imaging information on GAIN.org and SNMMI.org

SNMMI Outreach

Referring Physicians

- Targeted session content at professional society meetings (American Academy of Neurology, American Association for Geriatric Psychiatry, American Academy of Family Physicians)
- Webinars geared toward psychiatrists, neurologists, internal medicine physicians, and family physicians
- Dedicated section on SNMMI website for referring physicians

Patients

- Collaboration with patient advocacy organizations to educate the general public
- DiscoverMI.org (public awareness campaign of SNMMI)
- Development of a fact sheet and patient-oriented webinars