iDEAS
Imaging Dementia—Evidence For Amyloid Scanning

ACR
American College of Radiology

alzheimer's association

IRB#201504940
IDEAS Study

- Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study: A Coverage with Evidence Development Longitudinal Cohort Study

- Directed by: Alzheimer’s Association
- Sponsored & Managed by: American College of Radiology Imaging Network (ACRIN)
- Advised by: Centers for Medicare & Medicaid Services (CMS)
- Tracer Agnostic: All tracers can be used
  - florbetaben (*Neuraceq*, Piramal Imaging)
  - florbetapir (*Amyvid*, Eli Lilly and Company)
  - flutemetamol (*Vizamyl*, GE Healthcare)

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# IDEAS Research Team

## IDEAS Steering Committee

<table>
<thead>
<tr>
<th>Core Science Team</th>
<th>Additional Committee Members</th>
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<tbody>
<tr>
<td>Gil Rabinovici, UCSF, Principal Investigator</td>
<td>William Abbott, Piramal Imaging</td>
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<td>Maria Carrillo, Alzheimer’s Association</td>
<td>Rosemarie Hakim, CMS</td>
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<td>Constantine Gatsonis, Brown University</td>
<td>Meridith Johnson, GE Healthcare</td>
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<td>Bruce Hillner, Virginia Commonwealth U</td>
<td>Mark Mintun, Avid</td>
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<td>Barry Siegel, Washington University</td>
<td>Radiopharmaceuticals/Lilly</td>
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<td>Rachel Whitmer, Kaiser Permanente</td>
<td>Charlie Apgar, Don Rosen, ACR</td>
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<td>Terri Wilson, Medical Imaging &amp; Technology Alliance (MITA)</td>
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## IDEAS Management/Support Team

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<thead>
<tr>
<th>American College of Radiology (ACR) Operations</th>
<th>Biostatistics Center (Brown U)</th>
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<tr>
<td>Cynthia Olson, Leslie Sears</td>
<td>Ilana Gareen, Roee Gutman</td>
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<td>Glenna Gabrielli, King Lo</td>
<td>Erin Greco, Lucy Hanna</td>
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<td>Benjamin Herman, Rajesh Makineni</td>
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<td><strong>Scientific and logistical support</strong></td>
<td><strong>Consultant</strong></td>
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<td>Jim Hendrix, Alzheimer’s Assn.</td>
<td>Brian Carey, Foley Hoag LLP</td>
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![IDEAS Logo](IDEAS-Logo.png)
Study Overview

- An open-label, longitudinal cohort study that will assess the impact of brain amyloid PET imaging on patient outcomes under Coverage with Evidence Development (CED) in patients meeting Appropriate Use Criteria (AUC)\(^1,2\)

- The primary hypothesis is that, in diagnostically uncertain cases, knowledge of amyloid status as determined by brain amyloid PET will lead to significant changes in patient management, and this will translate into improved medical outcomes

IDEAS Aim 1

- To assess the impact of brain amyloid PET imaging on the management of patients meeting Appropriate Use Criteria (AUC) at 90 days
  - Patient management plans recorded in pre and post-PET case report forms completed by the Dementia Specialist
Aim 1 Study Primary Objective

- Test whether amyloid PET imaging will lead to a \( \geq 30\% \) change between *intended* and *actual* patient management within \(~90\) days in a composite measure of at least one of the following:
  - AD drug therapy;
  - Other drug therapy; and
  - Counseling about safety and future planning

- The hypothesis will be tested separately for MCI and dementia.
Impact on Management in the Literature (Aim 1)

- 31% change in AD drug therapy and 7% change in non AD drug therapy in 229 patients (intended management)\(^1\)
- 35% change in cholinesterase inhibitor or memantine use in 140 patients (retrospective) \(^2\)
- 37% change in patient management (prospective study of 211 patients) \(^3\)
- Prospective study of 618 patients randomly assigned to immediate or delayed (1 y) disclosure of brain amyloid PET showed immediate disclosure lead to significantly more changes in management vs delayed. \(^4\)


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IDEAS Aim 2

- To assess the impact of brain amyloid PET on hospital admissions and emergency room visits in study patients (amyloid PET-known) compared to matched patients not in the study (amyloid PET-naïve) over 12 months

  - CMS Claims Data to address Aim 2 will be collected for all study participants and from concurrent controls matched according to a validated algorithm
Aim 2 - Rationale

- Individuals with dementia at increased risk for hospitalizations & ED visits compared to those without dementia\(^1\)
  - Annual hospitalizations: 26.7% vs. 18.7%\(^1\)
  - Annual ED visits: 34.5% vs. 24.5%\(^1\)
  - Two-thirds deemed preventable (CHF exacerbation, bacterial pneumonia, UTI)\(^2\)
- Dementia associated with increased mortality and shorter survival after hospitalizations
- Preliminary data from Kaiser shows targeted dementia plan led to 18% reduction in ED visits and 11% reduction in hospitalizations\(^3\)

3. Whitmer RA. Unpublished data.
Overall Rationale (Aim 1 and 2)

Diagnostic clarity helps:

- Prompts physicians, individuals and their families to develop targeted strategies to manage medical co-morbidities
- Develop care plan to better protect personal safety in the setting of cognitive impairment

Increased diagnostic clarity will lead to targeted care plan, which will translate into decreased hospitalizations and ER visits
When should brain amyloid imaging be considered per the AUC?

For patients with all of the following core elements:\(^1,^2\)

1. A cognitive complaint with objectively confirmed impairment.

2. Alzheimer’s disease is a possible diagnosis, but the diagnosis remains uncertain upon comprehensive evaluation by a Dementia Specialist.

3. The presence or absence of amyloid would increase certainty in the diagnosis and alter the treatment plan.

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Appropriate Clinical Indications

- Patients with progressive unexplained MCI
- Patients with possible AD but unclear clinical presentation due to an atypical course or comorbid conditions
Disclaimer

• Brain amyloid PET imaging detects one of the key pathologic processes in Alzheimer’s disease – Beta-amyloid

• Brain amyloid PET (alone) does not diagnose AD nor predict the risk or rate of progression to AD dementia

• Negative brain amyloid PET indicates few to no amyloid plaques. If there is cognitive impairment, the cause is likely to be something other than AD.
IDEAS Operational Model

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IDEAS Operational Model

- Screen
- Consent and register
- Pre-PET *Intended management plan*
- Order PET scan

IDEAS Project Team

**IDEAS-Project Team**

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IDEAS Operational Model

- Patients
- PET Imaging Centers
- Dementia Specialists
- IDEAS Project Team

- +90 Days
- Post-PET (ACTUAL management plan)

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IDEAS Operational Model

Data Analysis
- Impact on management plan
- 12 month outcomes assessment of longitudinal cohort and CMS matching cohort

PET Imaging Centers

Dementia Specialists

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IDEAS Study Flow

Qualified Dementia Specialists and PET Facilities register at ideas-study.org
(Registration opened on Sept. 30, 2015)

Dementia Specialist: Screen and Consent Participants (T1)
Enrollment to start Jan 2016

Refer for Amyloid PET Scan

Amyloid PET Scan within 30 Days after T1 (T2)

Treating Physician: Visit with Pt to Complete 90-Day Post-Amyloid PET Assessment (T3)

Submit Pre-PET CRFs within 30 Days before Amyloid PET Scan (Aims 1 & 2)

Submit PET Report and PET CRF and PET images within 7 Days after Amyloid PET (Aims 1 & 2)

Submit Post-PET CRF within 15 Days after T3 Visit (Aim 1)
IDEAS Study Data Analysis

Goal = 18,488 study patients over 24 months
- Aim 1 and Aim 2 = 11,050
- Aim 2 = 18,488
  - Additional 7,438 for Aim 2; 90-day visit clinical assessment not required
- At least 400 Dementia Specialists refer 2-3 cases/month

All eCRFs and images will be collected via the IDEAS website and stored by ACRIN in a secure database

ACRIN will request CMS claims data 12 months after Visit 1

Study Team performs study analysis (analysis complete ~ 2019)

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Clinical Site Locations

- Patients referred by Dementia Specialists must have access to a study PET Imaging facility.
- PET Imaging facility must be within 3-4 hours of an amyloid tracer supplier.
- Upon patient enrollment (January 2016), a listing of Dementia Specialists and Imaging sites will be available.
## Amyloid PET Radiotracer Locations

PET Imaging Centers located within 3-4 hours of location may have access to radiotracers. (Updated 10.20.2015.)

<table>
<thead>
<tr>
<th>Beta Amyloid Tracer Availability</th>
<th>Phoenix</th>
<th>AZ</th>
<th>Chicago</th>
<th>IL</th>
<th>Hackensack</th>
<th>NJ</th>
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<td>NC</td>
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PET Facility Qualifications

- Experience with brain PET imaging
- Free-standing PET facilities: accreditation for PET brain imaging by the ACR, Intersocietal Accreditation Commission (IAC), or RadSite
- PET facilities located in hospitals: Medicare-approved accreditation for hospitals (e.g., Joint Commission)
- Interpreting physicians: board-certified and completion of vendor-provided reader training
IDEAS: Dementia Specialist Criteria (also known as Referring Physicians)

- Physicians who self-identify as being trained and board certified in neurology, psychiatry, or geriatric medicine
- Physician also must devote a substantial proportion of patient contact time (≥25%) to the evaluation and care of adults with acquired cognitive impairment or dementia\(^1,2\)
- Required online training (Alzheimer’s Assn site)
- Informed Consent (investigator is research subject)
- Other online training on eCRF will be offered

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(Dementia Specialists Known as Referring Physicians)

Alzheimer's research → another step forward

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What is the Incentive For Dementia Specialists and PET Facilities to Participate?

- A brain amyloid PET scan will be covered for their patients with cognitive decline in whom the diagnosis is not clear
- Case reimbursement will be provided to participating Dementia Specialists for completion of required case report forms for each patient enrolled
- PET facilities will be reimbursed for the PET scans under CMS CED, which requires research study participation as a condition of payment
How Do Patients Enroll in the IDEAS Study?

• Patients may be enrolled through a Dementia Specialist who is participating in the study.

• Once enrollment begins (expected Jan 2016), a list of Dementia Specialists and Imaging Sites will be available.
For Information and Registration

Go to:
ideas-study.org
Supplemental Slides
IDEAS Study Timeline

- CMS Approval
- Accrual Phase
- CMS Claims data for last POS
- Publish/Request Reconsideration
- Develop Phase
- Last POS final claim
- Completed Analysis
- CMS Coverage Decision

- March 2015
- 6-9 months
- 30 months
- 42+ months
- 48+ months
- 50+ months
- 54+ months
- 66+ months

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Sample Size

Aim 1.
The projected prospectively-recruited sample size is 11,050
  • 30% change in composite endpoint
  • Assumes 60% MCI, 40% dementia
  • \( \beta=0.80, \alpha=0.025 \) (Bonferroni corrected)

Aim 2.
The projected prospectively-recruited sample size is 18,488 (additional 7,438 beyond Aim 1)
  • 10% relative reduction in hospitalizations, ED visits
  • Similar number of controls, identified in CMS database
  • \( \beta=0.90, \alpha=0.025 \) (Bonferroni corrected)
Study Patient Inclusion Criteria

- 65 or older
- Medicare beneficiaries referred by qualified Dementia Specialists
- Diagnosis of MCI or dementia verified by Dementia Specialist in last 24 months
- Meets Appropriate Use Criteria: Etiology of cognitive impairment is uncertain after a comprehensive evaluation by a dementia Specialist (neuro exam, mental status testing (e.g. Mini Mental State Exam [MMSE] or Montreal Cognitive Assessment), lab tests for toxic-metabolic disturbances, structural neuroimaging (CT or MRI).
- Alzheimer’s disease (AD) is a diagnostic consideration
- Amyloid PET status is expected to alter diagnosis and management
- Head MRI and/or CT within 24 months prior to enrollment
- Clinical lab assessment
- Able to tolerate PET required by protocol
- English or Spanish speaking (for the purposes of informed consent)
- Willing and able to provide consent. May be provided by proxy.

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Study Patient Exclusion Criteria

- Normal cognition or subjective complaints that are not verified by cognitive testing.
- Knowledge of amyloid status, in the opinion of the referring dementia Specialist, may cause significant psychological harm or otherwise negatively impact the patient or family.
- Amyloid status already known to patient or referring clinician based on prior amyloid imaging or cerebrospinal fluid analysis.
- Current or previous enrollment in an anti-amyloid therapeutic trial.
- Scan is being ordered solely based on a family history of dementia, presence of apolipoprotein E (APOE) 4, or in lieu of genotyping for suspected autosomal mutation carriers.
- Scan being ordered for nonmedical purposes (e.g., legal, insurance coverage, or employment screening).
- Cancer requiring active therapy (excluding non-melanoma skin cancer);
- Hip/pelvic fracture within the 12 months prior to enrollment;
- Body weight exceeds PET scanner weight limit;
- Life expectancy less than 24 months based on medical co-morbidities;
- Residence in a skilled nursing facility.