CASE STUDY · CENTRAL NERVOUS SYSTEM

# Phase II Alzheimer's Amyloid PET and MRI

55 sites · 3T MRI, amyloid PET · Volumetric and visual PET endpoints

## Challenge

Intrinsic Imaging supported this study’s imaging activities, addressing the scientific and operational considerations that inform the work of an imaging CRO and imaging core lab. In this Phase II Alzheimer's disease program, the biomarker endpoints depended on detecting subtle longitudinal change in brain volume and amyloid burden. Yet the 55 participating academic and commercial imaging centers operated scanners from multiple vendors, each introducing its own measurement variability into volumetric MRI quantification and amyloid PET assessment. Left uncontrolled, that cross-site variability could obscure treatment-related change and compromise interpretation of both the secondary and exploratory biomarker endpoints on which dose and go-forward decisions would rest.

Longitudinal consistency posed a further difficulty. Participants would be imaged repeatedly, and any change in scanner hardware, software or acquisition practice at a site could introduce artificial shifts in measured brain volume or amyloid signal indistinguishable from biology. The sponsor therefore required prospective control of technical variability, continued verification throughout follow-up and transparent documentation of acquisition and processing, so that change between baseline and follow-up could be interpreted in relation to disease and treatment rather than equipment. Visual amyloid interpretation and volumetric measurement provide complementary evidence, but neither should be treated as interchangeable with clinical improvement. Their usefulness depends on maintaining the acquisition and processing conditions that give longitudinal differences a consistent meaning.

## Intrinsic Imaging’s Solution

Intrinsic Imaging developed vendor-specific acquisition protocols for MRI and amyloid PET, aligning parameters as closely as each platform permitted, and implemented phantom-based site qualification to characterize and calibrate every scanner before subject imaging began. Sites were trained on the protocols before activation, and each submission was automatically verified against the prescribed parameters and checked for image quality and completeness before entering analysis, with prompt feedback to sites when correction was required.

Central assessment paired quantitative volumetric analysis of regional atrophy with standardized visual PET scoring, both performed under a single charter so that quantitative and qualitative endpoints were derived under uniform conditions across vendors and sites. Visual PET readers were trained and calibrated against reference cases before reading began; quantitative analysts followed documented procedures for image processing, region definition and quality review, and documented any correction to automated output so that every reported value could be traced to its source images and processing history.

Our project team monitored sites for scanner upgrades and software changes throughout the study, requiring requalification where necessary to preserve longitudinal comparability. Results were reviewed for consistency across timepoints before release to the sponsor, and any value departing from the expected longitudinal course was examined for technical cause before being accepted as biological change.

## Intrinsic Imaging’s Results

- 38% reduction in cross-site measurement variation, achieved through phantom-based qualification, automated parameter verification and requalification whenever site equipment or software changed
- 55 sites operating scanners from multiple vendors delivered volumetric MRI and amyloid PET data sufficiently comparable for pooled longitudinal analysis across the full program
- Secondary and exploratory biomarker endpoints reported with technical noise controlled closely enough to interpret longitudinal change in relation to biology and treatment
- Site qualification procedures, acquisition protocols and analysis conventions carried forward by the sponsor into later-phase Alzheimer's development with minimal redesign or revalidation required

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Read the full study online: https://intrinsicimaging.com/case-studies/central-nervous-system

### About Intrinsic Imaging, LLC

Intrinsic Imaging is an ISO certified medical imaging CRO and imaging core lab providing comprehensive services in support of Phase I-IV clinical trials and Class I, II, III medical device trials. Intrinsic Imaging is also a world leader in conducting Artificial Intelligence studies. With its team of more than 650 board-certified and fellowship-trained physicians, Intrinsic Imaging’s team has sub-specialization in all therapeutic areas, including Cardiovascular, Central Nervous System,Gastroenterology, Musculoskeletal, Oncology and Ophthalmology. Certified by the British Standards Institution (BSI), Intrinsic Imaging is the only company in the world to hold five ISO certifications specifically for providing imaging core lab services on clinical trials. For more information, please visit www.IntrinsicImaging.com.

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