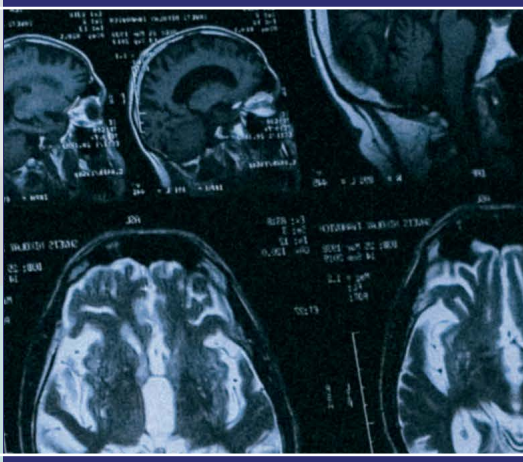


Your Imaging Analysis & Operations Experts in Alzheimer's Disease Clinical Research

IXICO

IXICO.com

Transforming clinical research in Alzheimer's disease

At IXICO, we are dedicated to revolutionizing clinical research in Alzheimer's disease (AD) through our advanced neuroimaging solutions. With over 20 years of expertise, we leverage cutting-edge technology and a robust scientific network to facilitate the development of investigational therapies.

Our mission is to provide biopharma companies with the confidence and technical expertise needed to navigate the complexities of clinical trials.

IXICO's Alzheimer's Disease Footprint at a Glance

Pioneering Precision in AD Imaging

IXICO excels in AD image analysis with advanced imaging biomarkers to quantify markers such as amyloid plaques, tau tangles, and brain atrophy. Our AI-driven IXIQ.Ai platform enhances the accuracy and efficiency of brain image measurements. We have supported over 100,000 brain scans collected through various AD research initiatives, driving innovation and harmonizing imaging data for better clinical trial outcomes.

Seamless Global Imaging Solutions

We offer comprehensive imaging support with global site management, a regulatory-compliant platform and processes, and rapid Amyloid and Tau PET eligibility read reports within three days. Our services include centralized radiology reads, AD-specific workflows, advanced analytics, and tailored solutions to meet diverse clinical trial needs, ensuring seamless data collection and analysis.

Proven Excellence in AD Clinical Trials

With over 25 sponsors supported across 55 clinical studies, IXICO collaborates with leading institutions and initiatives like ADNI, GAP, AMYPAD and EPAD to name a few. Our proven expertise ensures high-quality deliverables and successful trial outcomes, making us a trusted partner in advancing AD research and clinical trials.

Key Imaging Biomarkers

Key imaging biomarkers, such as Amyloid PET, Tau PET, and volumetric MRI, are crucial for accurately diagnosing and monitoring Alzheimer's disease. These biomarkers are essential for safety monitoring, eligibility, and assessing drug efficacy.

They provide critical insights into disease progression, enabling researchers to make informed decisions in clinical trials. Our centralized radiology reads ensure consistent and high-quality evaluations across all imaging data. By quantifying amyloid plaques, tau tangles, and structural brain changes, these biomarkers help identify patients at various stages of the disease, ultimately guiding therapeutic strategies and improving patient outcomes.

Our well-defined discordance resolution workflow addresses discrepancies between local and central reads, minimizing delays in trial enrollment. Our tailored radiological read solutions allow for customizable read reports and reading paradigms to meet the specific needs of each clinical trial, such as single, dual, consensus or adjudication workflows.

Centralized MRI Eligibility Reads: 01

Importance: Conducted by our expert neuroradiologists with expertise in diagnostic imaging and identification of comorbidities.

Service: Reviewing Study MRI-related exclusion criteria at screening.

Centralized MRI Safety Reads: 02

Importance: Conducted by our expert neuroradiologists with expertise in clinical trial safety monitoring and particularly ARIA-E and ARIA-H monitoring.

Service: Review of presence, number and location of new or changed findings such as ARIA-E, microhaemorrhages, macrohaemorrhages, and superficial siderosis.

Centralised Amyloid PET Reads: 03

Importance: Conducted by expert nuclear medicine physicians to support eligibility decisions.

Service: Read can be performed as a visual only read and/or a VisQ read (where reader is provided with supporting SUVr information) to visually determine Amyloid classification.

Centralised Tau PET Reads: 04

Importance: Conducted by expert nuclear medicine physicians to support eligibility decisions.

Service: Read workflow and criteria are tailored to specific Tau tracer(s) in use to visually determine Tau classification.

Key Radiological Read Outcomes

Amyloid PET for Eligibility and Efficacy	Visual Read & Quantitative Analysis Amyloid classification, longitudinal analysis
MRI for Eligibility	Alzheimer's Disease Exclusion criteria
Tau PET for Eligibility and Efficacy	Visual Read & Quantitative Analysis Tau classification, longitudinal analysis
MRI for Safety Monitoring Presence, number, and location of new or changed findings	ARIA-E Microhaemorrhages Macrohaemorrhages Superficial siderosis White matter lesions

Quantitative Imaging Endpoints in Alzheimer's Disease (AD)

Amyloid PET

Importance: Essential for determining eligibility and monitoring disease progression and target engagement by visualizing amyloid plaques.

Imaging Analysis:

SUVR: Quantifies amyloid burden

Centiloid Scale: Standardizes results across different tracers.

Tau PET

Importance: Provides insights into tau tangles to monitor disease progression and target engagement, correlating with cognitive decline.

Imaging Analysis:

SUVR: Quantifies tau pathology.

Structural MRI

Importance: Assesses structural changes, particularly in the hippocampus.

Imaging Analysis:

Volumetric Analysis: Measures brain regional atrophy.

Vascular pathology

Importance: Assesses vascular pathology changes due to ageing or comorbidities

Imaging Analysis:

White Matter Hyperintensity: Measures white matter hyperintensity volume, a marker of neuroinflammation and cerebral small vessel disease.

ASL (Arterial Spin Labelling) MRI

Importance: Measures tissue perfusion (cerebral blood flow).

Imaging Analysis:

Regional CBF Measurement: Quantifies tissue perfusion (e.g. hypoperfusion) in brain regions.

Diffusion MRI:

Importance: Evaluates white and grey matter tissue microstructural integrity and connectivity.

Imaging Analysis:

Diffusion Tensor Imaging (DTI): Assesses microstructural integrity of grey and white matter tissue.

Neurite Orientation Dispersion and Density Imaging (NODDI): Multi-compartment model to provide further detail on microstructural tissue integrity.

Free Water Imaging (FWI): Multi-compartment model used to quantify changes in intra- and extra-cellular water, which could be due neuroinflammation.

Structural Connectivity: Measures loss of white matter pathways due to neurodegeneration

Functional MRI:

Resting-State fMRI (rs-fMRI): Measures tissue perfusion (cerebral blood flow).

QSM (Quantitative Susceptibility Mapping)

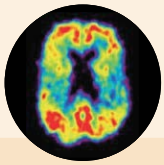
Importance: Provides insights into iron deposition by quantifying magnetic susceptibility in brain tissue, which can be altered in Alzheimer's disease.

Imaging Analysis:

Susceptibility Mapping: Quantifies magnetic susceptibility, an indicator of inflammation and neurodegeneration.

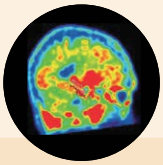
IXICO

Key Biomarkers



Amyloid

Central Read	Eligibilty Efficacy
Standardized Uptake Value Ratio(SUVR)	Eligibilty Efficacy
Semi-quantitative Analysis	Eligibilty Efficacy
Centiloid	Eligibilty Efficacy



Tau

Central Read	Safety Eligibilty Efficacy
Standardized Uptake Value Ratio (SUVR)	Safety Eligibilty Efficacy
Tracer Harmonisation	Safety Eligibilty Efficacy

Structural MRI

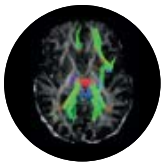
Volumetrics (Cross-sectional and Longitudinal)	Safety Eligibilty Efficacy
Central Read	Safety Eligibilty Efficacy
Hippocampal subfields	Efficacy

White matter hyperintensities (FLAIR)

Volume by Region Normal Appearing White Matter	Safety Eligibilty Efficacy

Perfusion MRI (ASL)

Regional Cerebral Blood Flow (CBF)	Efficacy



Diffusion MRI (dMRI)

DTI Analysis	Efficacy
Structural Connectivity	Efficacy
NODDI Analysis	Efficacy
Free Water Analysis	Efficacy

Functional MRI (fMRI)

Resting State fMRI	Efficacy
ICA network analysis	Efficacy
Seed-Based Network Analysis	Efficacy
Graph Theory Summary Metrics	Efficacy

Susceptibility (SWI, QSM)

Radiological Read (incl. CMB) (SWI)	Safety
ROI segmentations (SWI, QSM)	Safety
Regional Susceptibility Metrics (QSM)	Safety

PET Tracer Management & Coordination

Our Tracer Management services oversee the provision of Amyloid and Tau PET tracers to the sites and covers the following:

- Contracting for supply and transportation
- Supply invoice reconciliation and passthrough financial administration
- Imaging site onboarding and training for tracer supply ordering and handling
- Ongoing tracer coordination management oversight and supply monitoring

Advanced Analytics and Technology

Our advanced analytics capabilities are designed to enhance trial outcomes:

AI-Driven Analysis: We employ sophisticated AI pipelines for quantifying imaging endpoints, ensuring rapid and accurate results.

TrialTracker™ Platform: A GCP and 21 CFR compliant infrastructure that centralizes imaging data, streamlining the workflow from image acquisition to reporting.

Comprehensive Imaging Support

End-to-End Services: IXICO delivers complete clinical imaging support for neurological diseases, collaborating with specialty biotech firms, CROs, and top pharmaceutical companies.

Global Site Support: Our extensive network of sites across multiple countries ensures that we can efficiently manage and support clinical trials worldwide. We have the operational capacity to onboard and manage 100s of sites, facilitating seamless data collection and analysis across diverse geographies.

In collaboration with the wider Alzheimer's Disease Network

Global Alzheimer's Platform (GAP): Supporting the Bio-Hermes 001 and 002 trials to develop a comprehensive biomarker database.

Alzheimer's Disease Neuroimaging Initiative (ADNI): Contributing to the development of clinical and imaging biomarkers.

EPAD/AMYPAD: Enhancing understanding of early-stage AD and prevention strategies through collaborative research, where extensive data access allows for development and validation of our cutting-edge analysis methodologies.

Key Contributions in AD Research

Extensive Experience: Over 25 sponsors supported across 55 AD clinical studies, with more than 100,000 brain scans analysed globally.

Rapid Turnaround: Average turnaround time of three days for PET reads, ensuring timely results for trial progression.

Global Reach: A network of 2,000+ imaging sites across 50+ countries, facilitating diverse and inclusive clinical trials.

Proven Track Record

IXICO has established a strong reputation in AD research:

Successful Trials: Participation in high-profile studies, including the Bio-Hermes and AMYPAD initiatives, demonstrating our commitment to advancing AD research.

In both the **EPAD** and **AMYPAD** initiatives, our expertise in MRI and PET image data standardisation and our TrialTracker™ platform are being deployed to collect 1000's of MRI and PET scans from people recruited from clinical centres all over Europe

Our partnership with the **Global Alzheimer's Platform Foundation** in the **Bio-Hermes** study involved using beta amyloid PET scans to create a comprehensive biomarker database, exploring correlations between amyloid PET and digital assessments and blood biomarkers. We had recent podium presentations at CTAD 2023 and 2024

Collaboration with Acumen: Recently, we partnered with Acumen in their Phase 1 INTERCEPT-AD trial of ACU193, utilizing semi-quantitative amyloid classification for eligibility and ASL perfusion analysis. This collaboration highlights our ability to support innovative therapies in the AD space.

We openly worked with **Acumen** in their recently completed Phase1 **INTERCEPT-AD** trial of ACU193 using semi-quantitative amyloid classification for eligibility, and ASL perfusion analysis. We had recent co-presentations at AAIC 2023

Expert Team: Our central reading team comprises of leading neuroradiologists such as Prof Frederik Barkhof for MRI and Dr Elsmarieke van de Giessen for PET, ensuring high-quality assessments and compliance with regulatory standards.

Why Choose IXICO?

Choosing IXICO means partnering with a leader in neuroimaging for Alzheimer's disease:

Expertise: Deep knowledge of AD biomarkers and imaging techniques, backed by a proven track record.

Innovation: Commitment to advancing imaging methodologies through ongoing research and development.

Collaboration: Strong ties with academic and industry leaders, fostering a collaborative approach to tackling the challenges of AD research.

For more information on how IXICO can support your imaging analysis needs in clinical trials for Alzheimer's disease, please contact us at **www.ixico.com.**

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