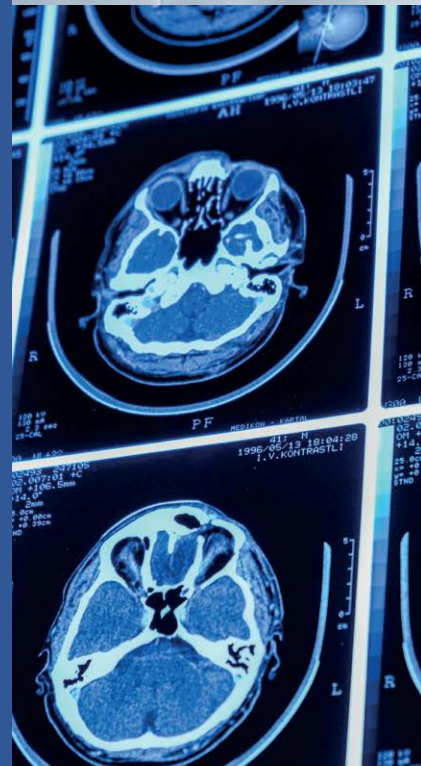




# Your Partner in Huntington's Disease Imaging Analysis & Operations Solutions



# Transforming clinical research in Huntington's disease

Established for over 20 years, IXICO is the leading provider of neuroimaging services for Huntington's disease (HD) clinical trials.

Our mission is to advance investigational therapies through innovative imaging solutions that comply with global regulatory standards.



## IXICO's Huntington's disease footprint at a glance

### Pioneering Precision in HD Imaging

IXICO excels in HD imaging with advanced imaging biomarkers like caudate nucleus and putamen atrophy, white matter tissue integrity changes, and striatal susceptibility changes. Our AI-driven IXIQ.Ai platform enhances accuracy and efficiency of volumetric measurements. We have led the analysis of over 6,000 MRIs through the HD Imaging Harmonization Consortium (HD-IH), 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 rapid reports. Our services include central radiology reads, HD-specific workflows, advanced analytics, and tailored solutions to meet diverse clinical trial needs, ensuring seamless data collection and analysis.

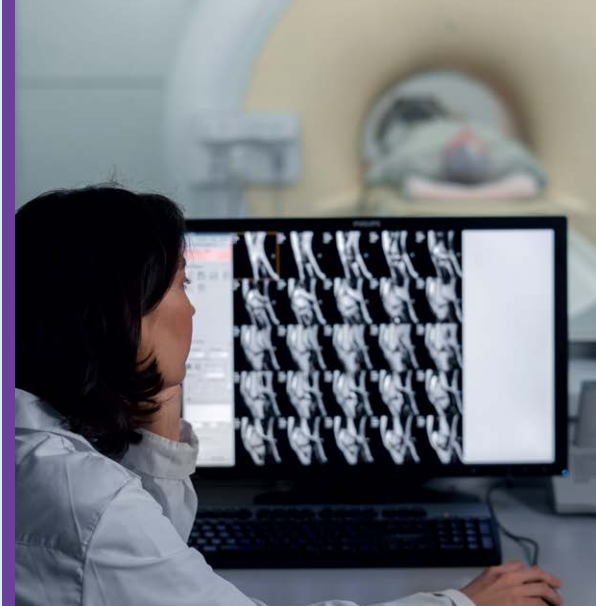
### Proven Excellence in HD Clinical Trials

With over 60 CNS trials supported globally, including 28 HD trials over 20 years, IXICO collaborates with leading institutions like University College London (UCL) and the CHDI Foundation. Our proven expertise ensures high-quality deliverables and successful trial outcomes, making us a trusted partner in advancing HD research and clinical trials.







## Key Imaging Biomarkers


Understanding and measuring the progression of HD relies heavily on specific imaging biomarkers. IXICO focuses on the following key biomarkers:



### Regional Brain Atrophy:


-  **Caudate Nucleus:** Atrophy in this region is a hallmark of HD progression and one of the landmarks included in the HD-Integrated Staging System (HD-ISS).
-  **Putamen:** We have developed highly accurate methods for segmenting this important, but difficult to segment, region in HD. This region is also one of the landmarks included in the HD-ISS.
-  **Whole Brain:** Whole brain atrophy is another sensitive marker of HD progression.
-  **Lateral Ventricles:** Increased volume is a sensitive marker of inflammation and neurodegeneration.

### Magnetic Resonance Spectroscopy (MRS):





-  **Brain Metabolite Levels:** Evaluates concentrations of metabolites like N-acetylaspartate (NAA) and choline, which are crucial for understanding neuronal function.

## Other Imaging Biomarkers


### Functional Connectivity:

-  **Resting-State fMRI (rs-fMRI):** Measures altered functional connectivity patterns due to re-organisation and neurodegeneration.


### Diffusion MRI:

-  **Diffusion Tensor Imaging (DTI):** Assesses microstructural integrity of gray 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, that could be due to neuroinflammation.
-  **Structural Connectivity:** Measures loss of white matter pathways due to neurodegeneration.

### Quantitative Susceptibility Mapping (QSM):

-  **Regional Susceptibility:** Increased susceptibility in the caudate, putamen and globus pallidus, is an indicator of inflammation and neurodegeneration.

### Metabolism:

-  **Positron Emission Tomography (PET):** FDG-PET is used to quantify metabolic changes in HD. Other research tracers such as PDE10A can also be used to quantify functional changes in HD.



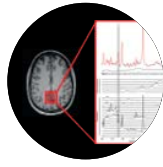
### Structural MRI

Volumetrics  
(Cross-sectional  
and Longitudinal)

Safety  
Eligibility  
Efficacy

Central Read

Safety  
Eligibility  
Efficacy



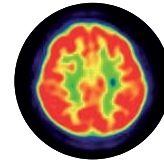
### Magnetic Resonance Spectroscopy (MRS)

PRESS /  
SEMI-LASER

Efficacy

N-acetylaspartate,  
Myo-Inositol, Choline,  
Glucose, GABA,  
Glutamate, Lactate

Efficacy



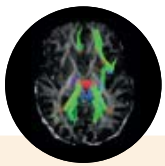
### Glucose (FDG)

Visual Read

Efficacy

Standardized  
Uptake Value Ratio  
(SUVR)

Efficacy



### Diffusion MRI (dMRI)

DTI Analysis

Efficacy

Structural  
Connectivity

Efficacy

NODDI

Efficacy

Free Water  
Analysis

Efficacy



### Functional MRI (fMRI)

Resting State  
fMRI

Efficacy

ICA network  
analysis

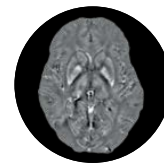
Efficacy

Seed-Based  
Network Analysis

Efficacy

Graph Theory  
Summary Metrics

Efficacy



### Susceptibility (SWI, QSM)

Radiological Read  
(incl. CMB) (SWI)

Efficacy

ROI segmentations  
(SWI, QSM)

Efficacy

Regional  
Susceptibility  
Metrics (QSM)

Efficacy

#### Efficacy and Safety

Striatal Atrophy, Whole brain  
atrophy and Ventricular  
Enlargement

Longitudinal volume  
Analysis using Boundary  
Shift Integral

Fully- and semi-automated  
(manual) options

#### Eligibility

HD-ISS staging and  
Volumetric reports within  
5-day TAT



### Key Operations

#### Central radiology read

Study specific training  
HD specific workflows  
Assessment of hydrocephalus



#### Gene therapy read

Intraparenchymal Injection specific workflows  
Blinded and unblinded read report versions



## Advanced Analytics and Technology



**Expert Team:** Our highly qualified professionals understand HD biology and imaging biomarkers, advising on advanced techniques to ensure reproducible analytics for MRI and PET endpoints.



**AI-Driven Analytics:** Our IXIQ.Ai platform provides high-quality, automated segmentation and analysis, enhancing the accuracy and efficiency of imaging metrics.



**Solutions to Meet your Needs:** We have a number of image analyses solutions to suit your needs. Our in-house team of imaging engineers can also assist with developing custom solutions, if needed.



**Regulatory Compliant Platform:** Our TrialTracker platform is fully regulatory compliant providing a single environment for image upload, central reads and image analyses.

## Comprehensive Imaging Support



**End-to-End Services:** IXICO delivers complete neurology clinical trial imaging support for imaging centres, collaborating with specialty biopharma, CROs, and top pharmaceutical companies.



**Global Site Support:** We efficiently manage and support clinical trials worldwide with our extensive global network of imaging sites across multiple countries. We have the operational capacity to scale up to onboard and manage 100s of sites, facilitating seamless data collection and analysis across diverse geographies.

## In collaboration with the wider Huntington's Disease Research Community

### HD Imaging Harmonization Consortium (HD-IH)



**Driving Innovation:** IXICO is a founding member of the HD-IH Consortium, which aims to harmonize imaging data and develop reliable biomarkers to accelerate drug development. This consortium includes key players such as uniQure, AskBio, PTC Therapeutics, and the CHDI Foundation.



**Extensive Data Collection:** With over 6,000 MRIs collected, our consortium is paving the way for targeted therapies and enhanced clinical trials. This effort supports the validation of imaging biomarkers linked to detailed phenotypic and non-imaging biomarker data.

### Key Contributions to HD Research



**Harmonization of Imaging:** IXICO played a pivotal role in harmonizing MRI data acquisition and validating imaging biomarkers during the TRACK-HD studies.



**Development of Imaging Biomarkers:** In collaboration with UCL we have deployed validated imaging analyses methods like the Boundary Shift Integral (BSI) in multiple clinical trials. In collaboration with CHDI we are working on the qualification of imaging biomarkers as reasonably likely surrogate endpoints.

### Proven Track Record



**Strong Industry Relationships:** We have collaborated with key academic, clinical partners and leading KOLs, including the CHDI Foundation and leading researchers at UCL, to enhance imaging capabilities in HD trials.



**Successful Trials:** IXICO has supported over 60 CNS trials globally, with more than 28 focused on HD, including 10 current studies for major biopharma companies



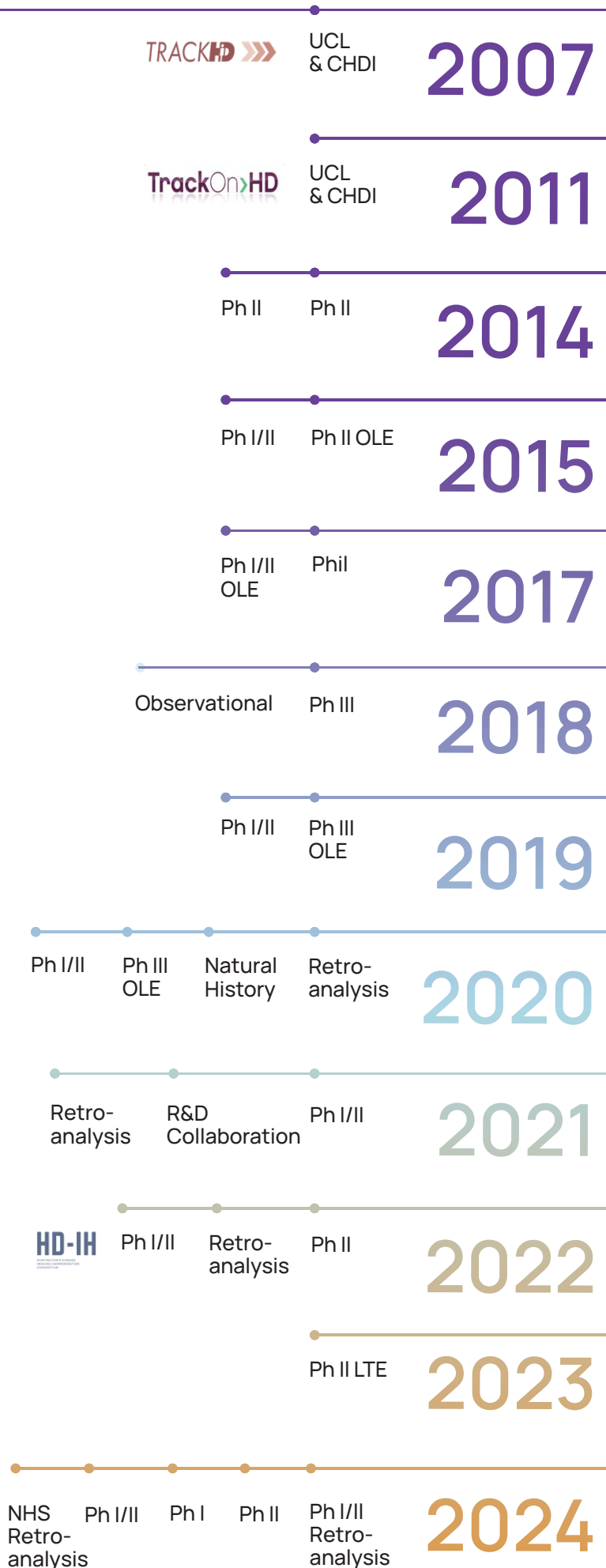
# IXICO's neuroimaging services in Huntington's Disease (HD)

Delivered 28 HD trials over **20 years**

## Why Choose IXICO?

**Expertise in HD:** Our in-house team has extensive experience in optimising quantitative MRI and PET image analysis and standardising image acquisition protocols for multi-center trials.

**Regulatory Robustness:** We continuously strive to translate academic innovations into clinical settings, ensuring compliance and high-quality deliverables





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