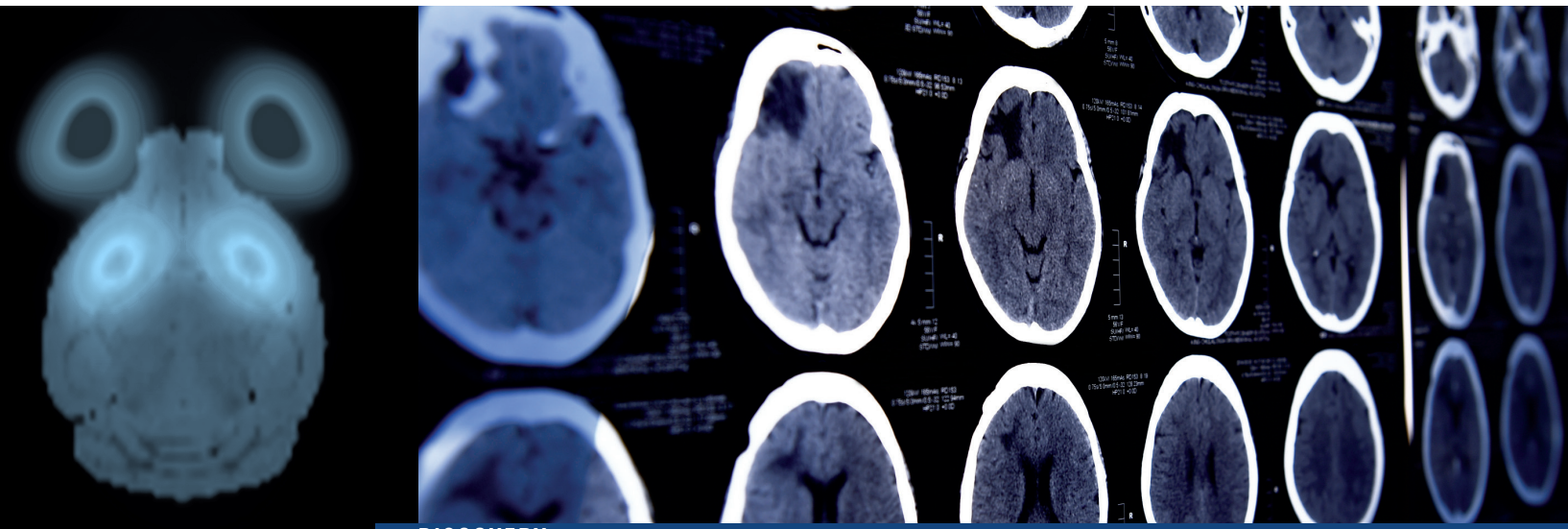
charles river



DISCOVERY

# Preclinical Imaging Capabilities for Neurological Diseases

## Available Technologies

- Magnetic resonance imaging (MRI)
  - Structural MRI
  - Diffusion MRI (DWI) and diffusion tensor MRI (DTI)
  - Pharmacological MRI (phMRI) and functional MRI (fMRI)
  - Magnetic resonance spectroscopy (MRS)
- Positron emission tomography (PET)
- Single photon emission computed tomography (SPECT)
- Autoradiography

Imaging modalities are used to noninvasively study disease pathophysiology in the brain. Different modalities are used to assess gross anatomical structures, as well as changes in cellular and molecular structure and function. Advances in imaging techniques have allowed improved sensitivity and specificity for clinical and biomarker endpoints, consequently supporting early diagnosis and more efficient disease monitoring. MRI, PET and SPECT are translational methodologies that serve as a bridge between preclinical studies and clinical endpoints. Within drug discovery, imaging can increase the efficiency of lead candidate selection by providing earlier and more predictive data that translate to the clinic. Charles River's *in vivo* imaging capabilities include high-field MRI, PET/CT and SPECT/CT scanners for radionuclide-based applications. These platforms are applicable for longitudinal studies with multiple imaging endpoints to study phenotype progression and treatment efficacy, as well as biodistribution or tissue activity changes.

Nuclear imaging provides translational and noninvasive *in vivo* methodologies to reliably quantify pathological changes during disease progression. Currently at Charles River, we apply nuclear imaging technologies in drug discovery studies to evaluate efficacy and mechanism of action of novel candidates in animal models of neurological diseases. Unique access to a cyclotron at our facility in Kuopio, Finland supports the production of short-lived positron-emitting isotopes suitable for PET imaging. In addition to enhanced radioligand availability, we offer arterial input function (AIF) generation from rodents for precise quantification of radioligand binding for cases where reference tissue modeling is not applicable. AIF is considered the gold standard analysis for dynamic PET imaging. The historical expertise with PET, MRI, SPECT, and associated *ex vivo* techniques, combined with new capabilities such as AIF, provides a comprehensive, translational toolkit to evaluate pathophysiology and drug effects in animal models of neurological disorders.

## Utility of specific imaging modalities available at Charles River:

| Imaging Modality | Purpose/Research Application | Agents |
|---|---|---|
| Structural MRI | Studies shape, volume, integrity and developmental changes in brain tissues, integrity of blood-brain barrier<br>Stroke (ischemia/hemorrhagia), neurodegeneration (atrophy) | Gadolinium (Gd) – for rCBV mapping, BBB integrity |
| Diffusion (DWI) and Diffusion Tensor Imaging (DTI) | Quantitative assessment of water movement due to diffusion in brain tissues<br>Stroke and demyelination models; traumatic brain injury models | |
| Pharmacological and Functional MRI (phMRI and fMRI) | Measures brain activity by detecting changes in blood flow, volume and oxygen levels when stimulated with a somatosensory (fMRI) or pharmacological (phMRI) agent<br>Target engagement studies | Superparamagnetic iron oxide particles (SPIO) – for rCBV phMRI |
| Magnetic Resonance Spectroscopy (MRS) | Measure concentrations of brain metabolites for neurochemical profiling and response to compounds.<br>Neurodegenerative disease model characterization, efficacy studies | |
| Positron Emission Tomography (PET) | Measures metabolic activity, neuroinflammation, receptor occupancy and dopaminergic system<br>Used across all neurological disease models to study metabolic changes, blood flow and oxygen levels. | $^{18}$F-FDG, $^{18}$F-FEPPA, $^{18}$F-PE-2I, $^{18}$F-Fallypride, $^{68}$Ga-PSMA, $^{68}$Ga-DOTA-NOC, $^{11}$C-PIB |
| Single Photon Emission Computed Tomography (SPECT) | Measures brain perfusion, inflammation and dopaminergic system, biodistribution of novel compounds or cells<br>Used across all neurological disease models to study metabolic changes, blood flow and oxygen levels. | $^{99m}$Tc-HMPAO, $^{111}$In-oxine<br>$^{123}$I-β-CIT, $^{123}$I-CLINDE |
| Autoradiography | Measures receptor density and occupancy, activation of G-protein coupled receptors (GPCR)<br>Used to measure radioactive compound distribution in *ex vivo* brain tissues | Tritiated radioligands for different receptors, $^{35}$S-GTPγS |

To learn more, visit our website - www.criver.com.product-services/drug-discovery/platforms/imaging/

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