# Validation and non-invasive kinetic modelling of [18F]BCPP-EF PET imaging in mice

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Huntington's disease (HD) is a hereditary, progressive neurodegenerative disorder with diverse clinical manifestations that evolve as the disease progresses. The main symptoms of HD are motor dysfunctions, mood disturbances and cognitive difficulties. In HD, the cellular respiratory ATP production is defective, leading to neuronal death. The mitochondrial respiratory chain (MRC), which plays a crucial role in respiratory ATP production, is located on the inner mitochondrial membrane and consists out of five mitochondrial complexes. Among these, mitochondrial complex I (MC-I) is the largest and serves as the primary entry point for electrons into the MRC, ultimately contributing to the electrochemical gradient required for ATP synthesis. Therefore, deficiencies in MC-I function lead to impaired cellular energy production and increased oxidative stress. These deficiencies can be detected using positron emission tomography (PET), a non-invasive in vivo imaging technique that can be used for the assessment of disease progression or therapeutic effects through the administration of radiolabelled tracers targeting affected molecular compounds. The aim of this study is to validate the [18F]BCPP-EF PET radiotracer, which targets MC-I, for first time use in mice. This will be done by evaluating four main aspects of the tracer: 1) characterization of the radiometabolite profile; 2) evaluation of the volume of distribution and assessment of tracer kinetics using compartmental modelling; 3) analysis of the variability and reliability of tracer quantification; 4) assessment of tracer specificity to MC-I. Successful validation of this tracer will enable its use in future studies to monitor disease progression and assessing the efficacy of therapies targeting MC-I.