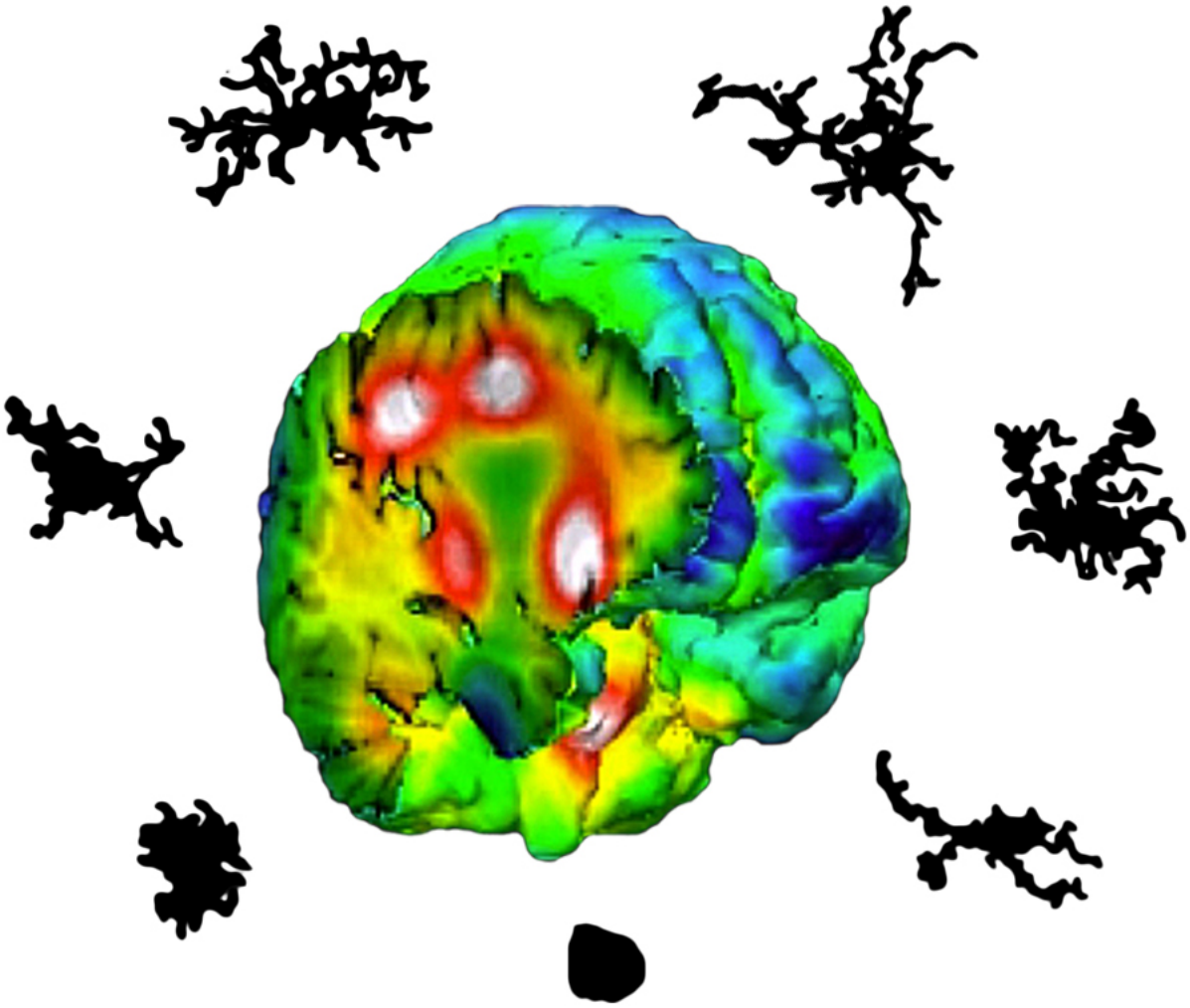
Rigshospitalet

Translocator Protein Imaging with ^{123}I-CLINDE SPECT – Method Development and Clinical Research



PhD thesis defence by Per Jensen MD

Friday, September 15th 2017 at 2 pm
Rigshospitalet Blegdamsvej, Auditorium 93

After the defence, the Neuroscience Center will host a reception at the Neurobiology Research Unit, Rigshospitalet, Juliane Maries Vej 28, 3rd floor

Evaluating Committee
Professor Olaf B. Paulson MD DMSc, Rigshospitalet, Denmark (Chair)
Dr Alexander Gerhard MD, University of Manchester, United Kingdom
Professor Leif Østergaard MD PhD DMSc, Aarhus University, Denmark

Principal Supervisor:
Associate professor Lars H. Pinborg MD DMSc, Rigshospitalet, Denmark

Thesis Summary

The translocator protein (TSPO) is upregulated in reactive glial cells and expression is increased in acute and chronic neuroinflammatory conditions. The presented work is based on four studies that describe the expression of TSPO as imaged by ^{123}I-CLINDE single photon emission computed tomography (SPECT) in different neurological disorders.

In study 1, the binding of ^{123}I-CLINDE to TSPO was investigated in a case of anti-NMDA receptor encephalitis. High binding was demonstrated at the initiation of immunotherapy in cortical and subcortical brain regions similar to the distribution of the NMDA receptor. After 7 weeks of immune suppression, symptoms had subsided and a second scan revealed almost normalized ^{123}I-CLINDE binding compared to a healthy control.

In study 2, ^{123}I-CLINDE-SPECT was compared to conventional ^{18}F-Flouro-ethyl-tyrosine positron emission tomography (^{18}F-FET PET) and gadolinium-enhanced magnetic resonance imaging (gd-MRI) in three glioma patients. Results were furthermore compared to tumor progression on contrast-enhanced structural imaging at follow-up and the results imply that TSPO imaging may be a predictor of active tumor cell proliferation and tumor progression.

Study 3 is a methodological test-retest study in the variability of ^{123}I-CLINDE SPECT imaging in healthy volunteers. 18 patients were scanned twice. Results revealed that the ^{123}I-CLINDE SPECT scanning modality showed better test-retest variability than the first generation PET tracer ^{11}C-PK11195 and comparable variability to previously tested second generation PET tracers. Furthermore, the study demonstrated the importance of immediate centrifugation of the blood-samples, as ^{123}I-CLINDE is distributed into blood cells if left in the vial, which affects the test-retest variability considerably.

In study 4, a cohort of 12 patients each patient was studied longitudinally at three time-points after ischemic stroke in the middle cerebral artery territory with ^{123}I-CLINDE SPECT, structural MRI and clinical rating. TSPO expression in stroke was furthermore compared to a cohort of 10 healthy volunteers. Results revealed an incredibly spatial and temporal dynamic TSPO expression. Findings were not correlated to clinical test-scores after stroke. Interestingly, regions un-related to the lesion were demonstrated to have lower ^{123}I-CLINDE binding to TSPO in patients compared to similar regions in healthy volunteers initially and increased to comparable values at later time-points.

In conclusion, the results of the work further the knowledge and understanding in the field of imaging neuroinflammation and demonstrate the feasibility of performing research using ^{123}I-CLINDE SPECT imaging in a variety of settings.