LABORATORY / RESEARCH TEAM
Laboratory of Signal and Image Processing
(LTSI - LTSI : Laboratoire Traitement du Signal et de l'Image | LTSI (univ-rennes1.fr))
UMR INSERM 1099 - Rennes 1 University
Team CINETYKS (ex-SESAME)

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GRANT
Doctoral school: MathSTIC (Rennes 1 University)
Starting date: October 2022
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SCIENTIFIC ENVIRONMENT
LTSI research lies at the interface of topics in the fields of information technology and health. Our researchers aim at developing methodological, technological and clinical tools to improve interpretation of medical imaging results or of clinical data in general and to provide decision support. The 'signal-model-image' core concept is the heart of the LTSI investigations spreading over five teams inside the laboratory. This PhD project will be part of the CINETYKS team.

The CINETYKS' research project focuses on the dynamics of large-scale pathological brain networks, in two neurological disorders: epilepsies and Parkinson's disease. In both cases, our research aims at improving diagnosis and therapy, and increasing pathophysiological knowledge. The proposed PhD will be mainly oriented towards methodological aspects in the context of research on Parkinson's disease.

PhD TITLE
Development of quantitative CEST and QSM MRI methods at 3 T in the context of Parkinson's disease.

PhD CONTEXT
The therapeutic management of neurodegenerative diseases is a major public health issue. In recent years, Parkinson's disease (PD) cases increased a lot, largely related to the aging of the population[1,2]. PD alters regions of the cortex and basal ganglia, and is characterized not only by a set of motor symptoms, but also by many sensory,

emotional and/or cognitive symptoms. First impairments can begin up to twenty years before motor abnormalities become detectable[3,4]. During this prodromal phase, several pathophysiological mechanisms are observed: **1/Abnormally high iron levels in the Substantia Nigra (SN) leading to the alteration of dopaminergic neurons**[5]. Iron has an essential neurophysiological role but its abnormal accumulation can cause a cascade of oxidative reactions and neurotoxicity leading to apoptosis of neurons; **2/Accumulation of α-synuclein proteins in neurons leading to progressive cell death that first affects dopaminergic circuits and then gradually spreads to connected areas of the cortex, inducing subtle changes in the brain connectivity**[6] and leading to a set of patient-specific motor and/or non-motor symptoms. Some patients will then progress to cognitive decline, which is a contra-indication to deep brain stimulation (DBS) while this surgery remains very effective for properly selected patients. **The search for quantitative and predictive neuromarkers from neuroimaging could improve the early diagnosis and stratification of patients based on the severity of cognitive decline and thus the identification of "good" and "bad" candidates for DBS.**

PhD OBJECTIVES

QSM MRI (Quantitative Susceptibility Mapping) quantitatively characterizes the accumulation of iron in tissues[7]. Several studies have shown a significant increase in QSM values in SN in the early stages of PD compared to control groups, as well as the possibility of differentiating patient groups according to PD stages[8]. **CEST MRI (Chemical Exchange Saturation Transfer) quantitatively characterizes the proportions of different macromolecules, peptides and circulating proteins by accessing specific chemical groups according to the frequencies used**. APT-CEST (*Amine Proton Transfer*) MRI acquisitions have targeted the accumulation of α-synuclein proteins in clinical applications in PD[9,10]. These innovative methods of quantitative neuroimaging are of great interest compared to standard methods (T_1, T_2, diffusion) and represent a major advancement in clinical research, particularly on neurodegenerative pathologies such as PD. These methodological developments will allow us to acquire clinical data at the state of the art of what is currently disseminated in the scientific community.

Our objective is therefore to develop at 3 T these two innovative quantitative MRI methods, as well as complete data processing protocols. The clinical application of such quantitative methods requires a significant work on the acquisition protocol (sequence design, optimization of acquisition parameters) as well as on the image processing methods in order to extract quantitative information related to targeted pathophysiological changes. A first phase will be carried out and validated using data acquired on healthy volunteers (3 T MRI, Neurinfo Platform, Rennes) and specific samples (1.5 T to 7 T MRI, PRISM Platform, Rennes and Angers). This work will represent a preliminary step before the acquisition at 3 T of QSM and CEST MRI data on a cohort of PD patients as part of a larger study including multimodal data (MRI, High Resolution-EEG, PET and clinical scores).

SKILLS OF THE PhD CANDIDATE

A solid knowledge of quantitative MRI acquisition methods as well as the mastery of programming tool (Matlab and/or python languages) and basic Unix commands is essential for this PhD project. The candidate will be required to use numerous tools and software for the different steps of each processing protocol (Unix and Windows systems). Knowledge of statistical data analysis methods is desirable. The candidate must also be willing to work in a hospital environment.

REFERENCES

[1] ER. Dorsey et al. *JAMA Neurol* (2018). **75**:9-10.

[2] A. Kilzheimer et al. *Front Neurol* (2019). **10**:1328.

[3] LV. Kalia et al. *Lancet* (2015). **386**:896-912.

[4] P. Mahlknecht et al. *J Park Dis* (2015). **5**:681-97.

[5] N. Tambasco *et al*. *Neurobiol Aging* (2019). **80**:91-8

[6] L. Gan et al. *Nat Neurosciences* (2018). **21**:1300-9.

[7] X. Guan et al. *NMR Biomed* (2017). **30**:e3489.

[8] GEC. Thomas et al. *J Neurol Neurosurg Psychiatry* (2020). **91**:418-25

[9] J. Zhou et al. *J Magn Reson Imaging* (2019). **50**:347-64.

[10] C. Li et al. *Frontiers Neurosc* (2017). **11**:489.