PhD student position

Location : EPFL AVP-CP CIBM-AIT, Bâtiment CH F.
Dates: 1st of November 2022 to 31 October 2026
Duration: 4 years

Developments of innovative fast acquisition and metabolic modelling strategies for clinical and preclinical deuterium MR imaging in the brain at ultra-high field

Dr Bernard Lanz from the MRI EPFL Animal Imaging and Technology Section is looking for a highly motivated PhD candidate in the area of metabolic imaging using dynamic quantitative **deuterium magnetic resonance spectroscopic imaging (^{2}H-MRSI) and cross-validation with dynamic ^{13}C-MRS and FDG-PET** (Fig 1): advanced methodological ^{2}H-MRSI developments (i.e. pulse sequence development and implementation, reconstruction, post-processing, denoising techniques), implementation and acquisition of *in vivo* dynamic ^{13}C-MRS and FDG-PET, development of adapted metabolic models to analyse the different dynamic metabolic data, validate and combine the obtained metabolic fluxes and applications in a rat model of epilepsy.

Background

Developments of novel, accelerated and translational *in vivo* imaging techniques are necessary for studying healthy and diseased brain. The brain is an organ with a particularly high and continuous energy consumption, relying essentially on glucose for its energy supply. As such, glucose metabolism plays an important role in several diseases, such as epilepsy.

Although ^{18}F-fluorodeoxyglucose (^{18}F-FDG) for positron emission tomography (FDG-PET) can provide information about brain glucose metabolism, it cannot distinguish between the oxidative and non-oxidative pathway (1). Carbon-13 magnetic resonance spectroscopy (^{13}C-MRS) is able to distinguish between those, but has an intrinsically low sensitivity (2). As such, *in vivo* non-invasive methods and metabolic models allowing the 3D mapping of brain glucose metabolism through a quantitative analysis of oxidative and non-oxidative metabolic rates of glucose (CMRglc(ox) and CMRglc(non-ox) in micromole/gram minute) are needed, something we are proposing in the current project.

Project description

Deuterium magnetic resonance imaging (^{2}H-MRSI) has emerged as a technique providing a much higher sensitivity, and can also distinguish between the oxidative and non-oxidative pathway by detecting brain glutamate, glutamine, and lactate turnovers (3). However, to achieve high-resolution, whole-brain mapping of the glucose metabolism, current ^{2}H-MRSI acquisitions and reconstructions have to be improved, as well as the modelling of the oxidative and non-oxidative glucose pathways. Our project will build on our previous work in accelerated MRSI techniques at ultra-high field, with the collaboration and expertise of the group from Vienna and with our recognised expertise in multimodal preclinical acquisitions (^{1}H-MRSI, ^{13}C-MRS, FDG-PET) and advanced metabolic modelling of glucose metabolism, to fill in the current gaps in ^{2}H-MRSI methodology with regards to acceleration and denoising techniques and advanced metabolic modelling (4). Finally, as a proof of concept we will apply our novel ^{2}H-MRSI methodology in a rat model of epilepsy to gain additional insights into local brain metabolism during epilepsy, as well as a tool for localizing the epileptogenic zone (5).

Therefore, *we aim to build on the ^{2}H-MRSI methodological advancements implemented during this project to obtain quantitative measurements of oxidative and non-oxidative glucose metabolism in micromole/g/min as 3D metabolic maps, to validate this quantitative approach with ^{13}C-MRS and FDG-PET and finally probe deeper into the local glucose metabolic alterations encountered in epileptogenic zones.*

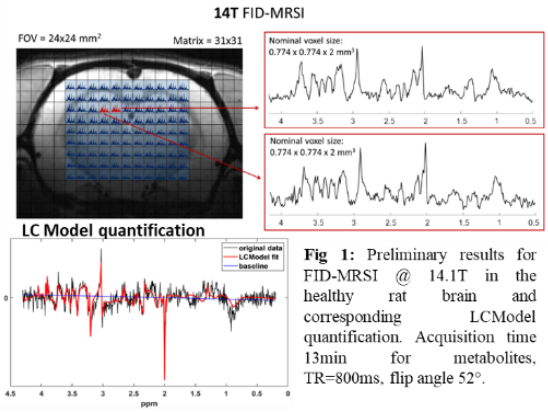
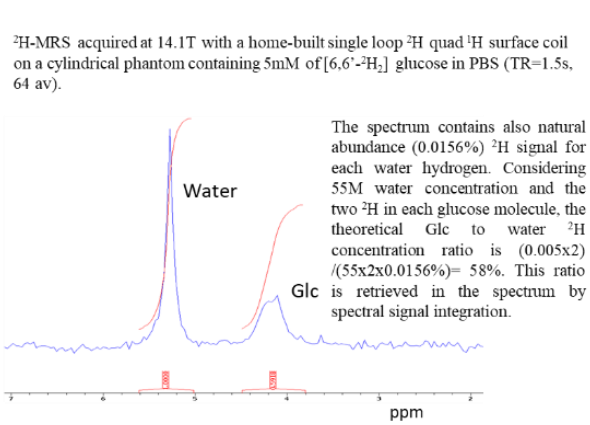


Fig 1: Preliminary results for FID-MRSI @ 14.1T in the healthy rat brain and corresponding LCModel quantification. Acquisition time 13min for metabolites, TR=800ms, flip angle 52°.



^{2}H-MRS acquired at 14.1T with a home-built single loop ^{2}H quad ^{1}H surface coil on a cylindrical phantom containing 5mM of [6,6'-$^{2}H_2$] glucose in PBS (TR=1.5s, 64 av).

The spectrum contains also natural abundance (0.0156%) ^{2}H signal for each water hydrogen. Considering 55M water concentration and the two ^{2}H in each glucose molecule, the theoretical Glc to water ^{2}H concentration ratio is (0.005x2) /(55x2x0.0156%)= 58%. This ratio is retrieved in the spectrum by spectral signal integration.

The PhD candidate will first familiarize himself/herself with the MRS/MRSI part of the project. Working directly on the preclinical 14.1T magnet and the small animal LabPET scanner, she/he **will develop a fast dynamic ^{2}H-MRSI acquisition sequence with full brain coverage. She/he will also implement and perform dynamic ^{13}C-MRS acquisitions and FDG-PET measurements.** Furthermore, she/he **will develop adapted metabolic models to analyse the different dynamic metabolic data, validate and combine the obtained metabolic fluxes.**

References

1. Mosso J, Yin T, Poitry-Yamate C, Simicic D, Lepore M, McLin VA, et al. PET CMRglc mapping and 1H-MRS show altered glucose uptake and neurometabolic profiles in BDL rats. Analytical Biochemistry. 2022 Jun 15;647:114606.

2. Lanz B, Gruetter R, Duarte JMN. Metabolic Flux and Compartmentation Analysis in the Brain In vivo. Front Endocrinol (Lausanne). 2013 Oct 28;4:156.

3. De Feyter HM, Behar KL, Corbin ZA, Fulbright RK, Brown PB, McIntyre S, et al. Deuterium metabolic imaging (DMI) for MRI-based 3D mapping of metabolism in vivo. Sci Adv. 2018 Aug;4(8):eaat7314.

4. Lai M, Lanz B, Poitry-Yamate C, Romero JF, Berset CM, Cudalbu C, et al. In vivo 13C MRS in the mouse brain at 14.1 Tesla and metabolic flux quantification under infusion of [1,6-13C2]glucose. J Cereb Blood Flow Metab. 2018;38(10):1701–14.

5. Ryvlin P, Ravier C, Bouvard S, Mauguire F, Le Bars D, Arzimanoglou A, et al. Positron emission tomography in epileptogenic hypothalamic hamartomas. Epileptic Disord. 2003 Dec;5(4):219–27.

Supervisors:

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Skills: Master's degree in (biomedical) physics, bioengineering, neuroscience or a similar degree. Experience in programming (i.e. Matlab, Python) is desirable. Ready to work in a multidisciplinary research field requiring extension of his/her own expertise and collaboration with researchers from various backgrounds. Open to work on animal and translational research. Proficient in English, both verbal and in writing.

We offer:

- A dynamic, interdisciplinary, and international team of very motivated people.
- A stimulating working environment based at CIBM in Lausanne, Switzerland.
- Participation in one of the world's leading transitional brain ultra-high field MRS efforts.
- Access to cutting-edge technology and state-of-the-art resources.
- Salary in compliance with Swiss National Science Foundation guidelines.

How to apply: Applications will be considered until the position is filled, so interested candidates are encouraged to apply early. Please send your CV and motivation letter to bernard.lanz@epfl.ch

About CIBM

The CIBM Center for Biomedical Imaging was founded in 2004 and is the result of a major research and teaching initiative of the partners in the Science-Vie-Société (SVS) project between the Ecole Polytechnique Fédérale de Lausanne (EPFL), the Université de Lausanne (UNIL), Université de Genève (UNIGE), the Hôpitaux Universitaires de Genève (HUG) and the Centre Hospitalier Universitaire Vaudois (CHUV), with the generous support from the Fondation Leenaards and Fondation Louis-Jeantet.
CIBM brings together highly qualified, diverse, complementary and multidisciplinary groups of people with common interest in biomedical imaging.
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