Quantitative measurement of water concentration in the brain, a mouse model.

MR Spectroscopy (MRS)

MRS allows for particular chemical compounds or metabolites in living organisms to be observed. The technique is based on mobile protons that are resonant when they exposed to a large externally applied magnetic field (B_0). The resonance (*Larmor*) frequency of a proton e.g. 1H (or other resonating atomic nuclei) can be disturbed by the small electrical field produced by the electrons surrounding the nucleus. The phenomenon produces what is known as the chemical shift (shift in the *Larmor* frequency) and can be utilized in MR spectroscopy to identify different chemical components e.g. metabolites in brain.

MRS can generate a spectrum (figure 1), where the concentration of a given metabolite is proportional to its spectroscopic peak area although the constant of proportionality is not straightforward to determine.

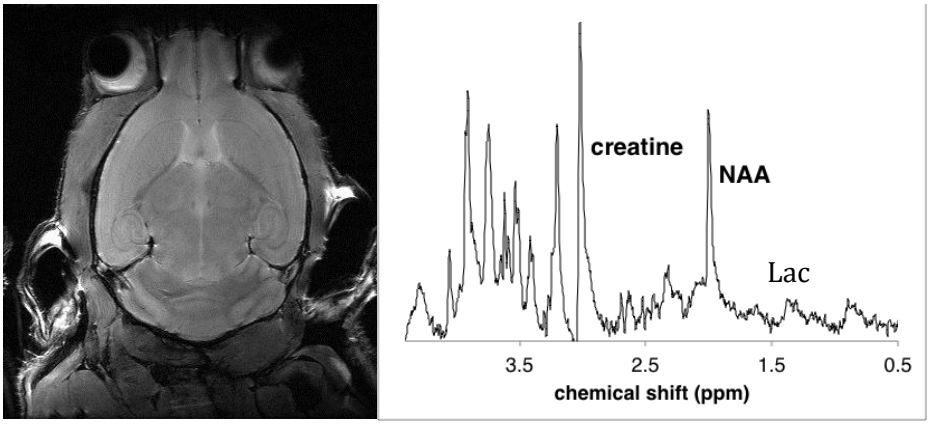

Fig. 1: A T_2 weighted image and an in vivo localized 1H-spectruscopy from a mouse brain

Peak area however, depends on characteristics such as relaxation times T_1, T_2, B1 non-uniformity, the receiver gain (which can be determined in principle), the coil loading (which depends on the subject or sample), the voxel size (since the peak area is actually proportional to the number of protons in the voxel), tissue inhomogeneity and the temperature of the interrogated volume.

Proper corrections for these factors are necessary in order to obtain absolute concentrations of the metabolites (in millimolar units, mM).

Referencing to a Standard Concentration

Peak Ratio

The absolute concentration can be obtained only if one metabolite peak in the spectra is known not to vary in concentration. In most cases there is no such metabolite, and

the biological interpretation of any change in a peak ratio becomes very difficult, since it could be caused by a change in the metabolite of interest or by a change in the 'standard', which forms the denominator in the ratio, or by both.

A metabolite from a known concentration can be measured in a separate acquisition from a phantom as an external referencing. The results is not accurate however since the phantom does not have the exact same geometry as the sample, causing alterations in coil sensitivity. Furthermore, the temperature of a phantom is typically ill-defined.

An internal reference such as water is preferable since it is easy to collect a rapid brain spectrum that includes the water peak as an internal standard. If the water concentration is known, then a link between proton concentration and peak area can be established. Furthermore, non-uniformity in the receive sensitivity is the same for the water and metabolite, and therefore need not be corrected.

The water signal has a high SNR, therefore only a few averages are required. The difficulty is that the water concentration is not known exactly. It depends on the proportions of white matter, grey matter and CSF in the voxel, and is age dependent and is often increased in disease (oedema).

The aim of this project is to measure the exact concentration of the water in mouse brain to be able to calculate the absolute concentration of the brain metabolites such as N-acetyl aspartate (NAA), Creatine (Cr), Choline (cho) and MyoInositol (MI).

Materials and methods:

- Mice with and without infarct
- Advanced MR technology to identify and characterize infarct areas and the metabolites of interest. The Bruker BioSpec 94/30, 9.4 T USR Preclinical MRI System at Panum NMR Center, equipped with a high sensitive transmitter and receiver mouse brain coil is used.
- After measurements of brain volume and metabolites concentration based on MRI and MRS respectively, the animals will be scarified and the brains are harvested. Brain volume (based on in vivo MRI) and weight are determined before - and brain weight alone is determined after - placement in a dry oven in order to estimate the water content in the brain. The blood volume and the CSF volumes are assumed to be minimal when cutting the brain in "four" pieces.
- Other MRI sequences such as inversion recovery could also be applied *in vivo* estimation and comparison of the water contents in the brain.

Required qualifications:

The project is suited for medical student interested in research (research year)

Responsible institution:

Biomedical Institute, Panum NMR Center

Contact information:

Associate prof. Henrik EL ALI, helali@sund.ku.dk

Associate Prof. Jens Christian Brings Jacobsen jcbrings@sund.ku.dk