High resolution spectroscopic imaging of the mouse brain using a cryogenic 2x2 phased array coil at 9.4T

Aline Seuwen[1], Sandra Bürgi[1], Aileen Schröter[1], and Markus Rudin[1,2]

[1]*Institute for Biomedical Engineering, University and ETH, Zürich, Switzerland,* [2]*institute of pharmacology and toxicology, University Zürich, Switzerland*

Introduction Spectroscopic imaging (SI) is a useful non-invasive tool to investigate the concentrations of metabolites in different tissues (e.g. brain), which might be linked to pathologies, disease status or therapeutic treatment effects [1]. SI on mouse brain is attractive in view of the many transgenic lines available for mechanistic studies. Due to the intrinsically low signal-to-noise ratio (SNR) resulting in very long acquisition times, the spatial resolution is limited. The use of cryogenic transceiver coils for *in vivo* imaging of the mouse brain revealed a SNR enhancement by a factor of about 2.5 at high field [2]. However, the inhomogeneous transmit B_1-Field across the field of view (FOV) hampered the use for SI applications. In the present study, we show preliminary results of SI data of the mouse brain acquired with a novel cryogenic receive-only phased array coil in combination with a volume resonator for homogeneous excitation. The SNR enhancement according to the cryogenic receiver coil was reinvested into improved spatial resolution, enabling for the first time the acquisition of spectroscopic data with voxel sizes of 0.47 µl in the establishment phase and finally down to 0.32 µl in a pilot study using a glioblastoma mouse model.

Methods All experiments were carried out using a BioSpec 94/30 (Bruker BioSpin MRI GmbH, Ettlingen, Germany) small animal MR system operating at 400 MHz. A four-element receive-only cryogenic phased array coil (2x2 geometry, overall coil size 20x27mm^2) was used in combination with a linearly polarized room temperature volume resonator for transmission. The cryogenic array coil was provided by Bruker BioSpin AG, Fällanden, Switzerland. All *in vivo* experiments were carried out in strict adherence with the Swiss law for animal protection. All mice were anesthetized using 1.5% isoflurane in an oxygen/air (20% / 80%) mixture, intubated and artificially ventilated. SI experiments used a PRESS excitation scheme with: TR/TE: 2000/26ms. Scans were performed using VAPOR water suppression interleaved with six saturation slices for fat suppression. Field maps were used for shimming. The acquisition scheme was weighted in k-space following a Hanning filter function. In the establishment phase, we acquired SI datasets on 6 C57Bl/6 mice with following parameters: FOV: 1.7x1.7cm^2; slice thickness: 1.5 mm; acquisition matrix: 4096x29x31; reconstruction size: 4096x32x32; scan time: 1.5h; resulting in a nominal voxel size of 0.47µl, while we increased the resolution in the pilot study (acquisition matrix: 4096x37x37, 0.32µl voxels). The pilot study consisted of 5 nude mice which were imaged 17 days after injection of GL261 brain tumor cells. For data analyses spectra from different coil elements were weighted for each voxel using a water reference scan and individually phase corrected to ensure optimal SNR during reconstruction. The phase correction needed for each coil element in each location was calculated by multiplying the FID signal by the normalized complex conjugate of the highest point in the reference FID. All the corrections and the summation of the spectra were performed in the time domain [3]. Post-processing of spectra: 5Hz Lorentzian filter, jMRUI [4].

Results The metabolite distributions resulting from SI data acquired with a resolution of 0.47µl reflect the anatomy of the brain: Cortical structures and basal ganglia (striatum, thalamus) display high metabolite levels (creatine: Cre, choline: Cho, N-acetylacetate: NAA, glutamate: Glu, taurin: Tau), while the respective levels were low in ventricular structures (Figure 1). The distribution of myo-inositol (Ins) is characterized by high levels in thalamus and hippocampus. The spectra acquired in each position of the FOV revealed at least 10 metabolite signals (Figure 2). The SNR for the Cre signal was estimated to be >10 for all voxels recorded in all 6 C57Bl/6 mice (Figure 3). SI in 5 glioma bearing nude mice performed 17 days after injection of GL261 brain cells with voxel sizes of 0.32µl revealed aberrations from the normal metabolite distribution (Figure 4). Cho and Ins levels were found to be strongly increased in the tumor tissue, while NAA and Cre levels were decreased (Figure 5). The different metabolites were fitted in the time domain using AMARES [5] (jMRUI). The Cramer-Rao lower bounds reveal that accurate quantification of high-resolution mouse SI data is possible (Figure 6). The quantification of data is ongoing.

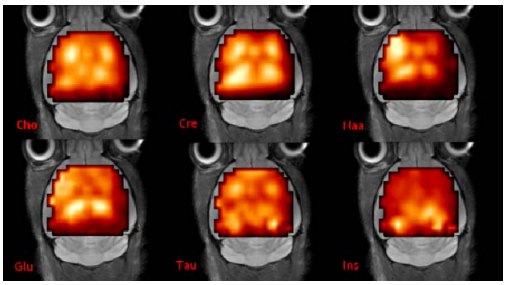

Figure 1: Metabolite maps acquired on a healthy mouse brain with 0.47µl voxel size in 1.5h. No correction for chemical shift was performed here.

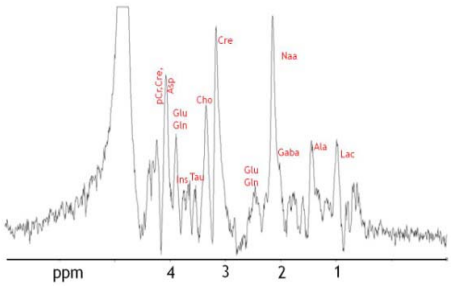

Figure 2: Spectrum located in the right striatum (5Hz Lorentzian filter).

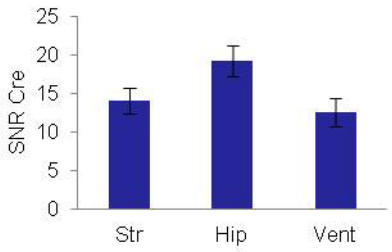

Figure 3: Signal to noise ratio of Cre for different brain structures (striatum, hippocampus, ventricle).

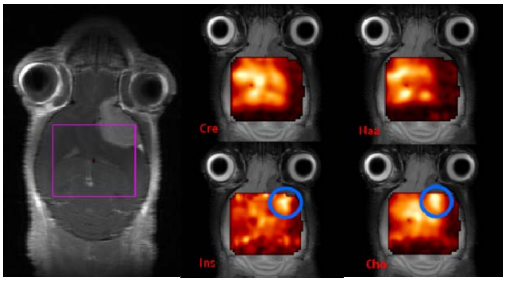

Figure 4: Metabolite maps acquired on a mouse, 17 days post-injection of GL261 brain tumor cells. In all 5 animals, the tumor was clearly visible in the Ins and Cho maps. Resolution: 0.32 µl, 2h acquisition.

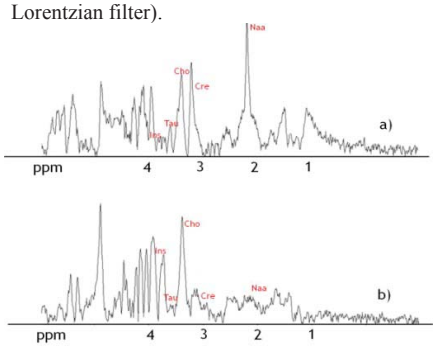

Figure 5: Spectra located in the tumor tissue (b) and in the contra lateral region (a). NAA and Cre level are strongly reduced, while Cho and Ins level are increased.

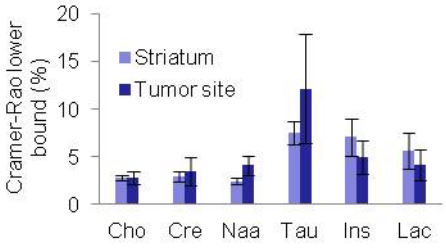

Figure 6: Cramer-Rao lower bound of the curve-fit performed in jMRUI.

Conclusion The use of a receive-only cryogenic phased array coil yielded excellent spectral quality in SI experiments with a resolution of down to 0.32 µl per voxel. All experiments could be performed in less than 2h. The metabolite distributions over the FOV strongly correlate with brain structures allowing the localization of a tumor and a detailed resolution of the metabolite composition in tumor tissue. Using the established protocol we aim to resolve and characterize compartments of tumor tissue in terms of metabolite content.

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