

CSI of mouse brain tumors at 7 Tesla with 0.8 μ l voxel resolution

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INTRODUCTION:

Since CSI is a major tool for the *in vivo* characterization of human brain tumor heterogeneity [1], this technique should also be of great importance for studying mouse models that try to reproduce this pathology. Nevertheless, to our knowledge no such study has been described yet.

PURPOSE:

To demonstrate that routine CSI acquisition on pathology afflicted mouse models of human disease can be carried out with a new generation of commercially available equipment.

METHODS:

Brain tumors were induced in both CD1 (30g, male, n=2) and C57BL/6J (30g, female, n=2) mice by intracranial injection of 10⁵ C6 glioma cells, essentially as described in [2]. CD1 mice underwent MR exploration at 12 days post-inoculation of C6 cells in a 7T 16 cm *PharmaScan*[®], Bruker BioSpin MRI GmbH, Ettlingen, Germany, equipped with a B-GA9S gradient coil and a 23 mm birdcage resonator whereas MR studies with C57 mice took place at day 18 post-inoculation in a 7T 30 cm *BioSpec*[®], Bruker BioSpin MRI GmbH, Ettlingen, Germany, (B-GA20S gradient coil; quadrature receive surface coil actively decoupled from a linear mini imaging resonator with 72 mm inner diameter). For this, mice were anesthetized on an animal bed with isoflurane at 1-2.5 % in O₂, maintaining the breathing pattern between 40-60 breaths/min (monitoring with SA-Instruments), and temperature controlled with a heating water blanket. Tumors were first localized both with T2 (RARE, TR/TE: 4200/41 ms, 8 echoes) and CE-T1 (TR/TE: 1500/12 ms, 4 echoes, Gd-DTPA injected either *i.v.* at 0.2 mmol/kg, or *i.p.* at 0.4 mmol/kg) MRI. For CSI studies, linear and second order shims were automatically adjusted with FASTMAP. CSI was performed with the PRESS localization method [3], positioning the CSI-PRESS selection VOI (4.5x4.5x2.0 mm) in a way that included both tumor and healthy tissue; other parameters were 2.0x2.0 cm FOV and a 32x32 CSI matrix. Water suppression was performed with a VAPOR sequence [4]. Acquisitions were performed with a 1500 ms TR, both short and long echo times (35 and 136 ms, respectively), and the signal sampled in the time domain with 2 k points. CSI grid spectra were processed in *XWIN-NMR* with a line broadening of 3.5 Hz and zero filling to 8 k points. First order phase correction was performed in the central spectra of the grid and then automatically applied to the rest. All MR measurements were performed in the application center of Bruker BioSpin MRI GmbH, Ettlingen, Germany.

RESULTS:

The FASTMAP procedure consistently produced a 14-16 Hz line width for the water resonance in the CSI-PRESS selection VOI. Tumor heterogeneity can be studied from the spectral pattern point of view with the obtained highly resolved (0.6x0.6x2 mm voxels, 0.8 μ l) CSI data (figure 1). This suggests that in the future CSI data can be correlated with tumor molecular phenotype.

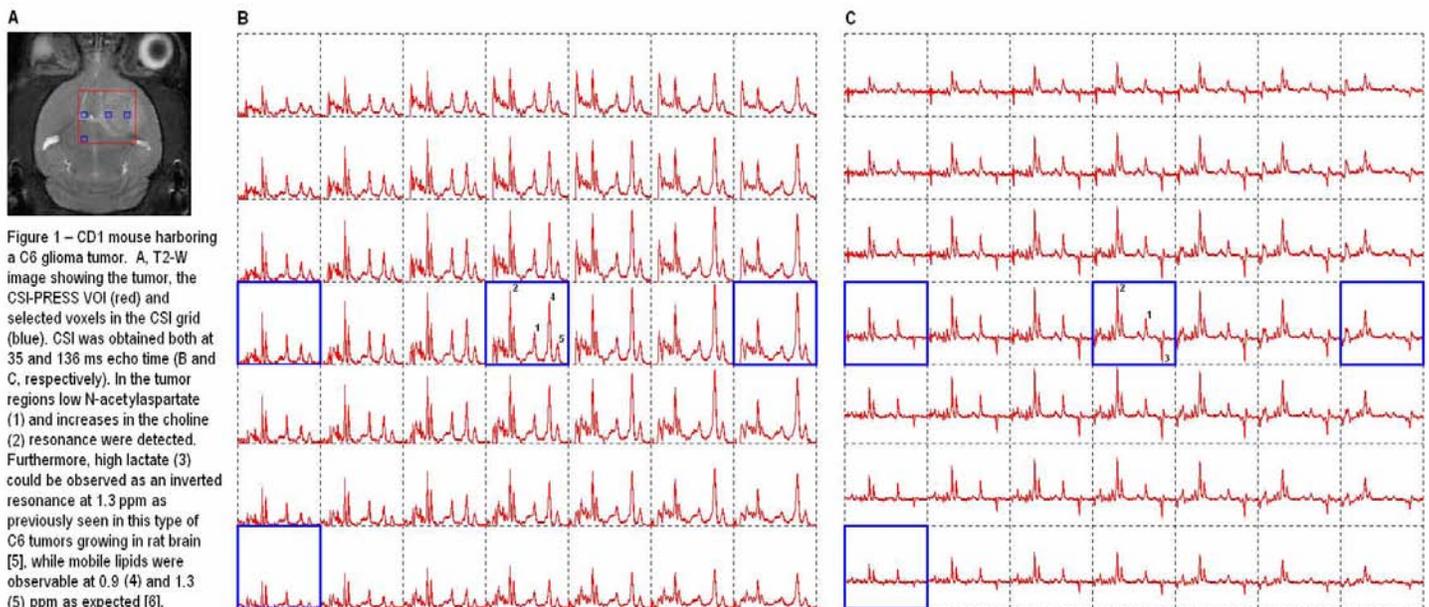


Figure 1 – CD1 mouse harboring a C6 glioma tumor. A, T2-W image showing the tumor, the CSI-PRESS VOI (red) and selected voxels in the CSI grid (blue). CSI was obtained both at 35 and 136 ms echo time (B and C, respectively). In the tumor regions low N-acetylaspartate (1) and increases in the choline (2) resonance were detected. Furthermore, high lactate (3) could be observed as an inverted resonance at 1.3 ppm as previously seen in this type of C6 tumors growing in rat brain [5], while mobile lipids were observable at 0.9 (4) and 1.3 (5) ppm as expected [6].

CONCLUSIONS:

The new generation of gradient and shim coils opens exciting avenues for new spectroscopic applications in mouse models, especially tumor models. To our knowledge this is the first described CSI study with mice harboring brain tumors, which was made possible by a novel development of shim and gradient coils, in combination with PRESS localization in the CSI method [7].

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