Combined Imaging of Cl^- and Na^+ at 7 Tesla: First Results in Brain Tumors

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Target Audience: Scientists and physicians interested in the field of non-proton MRI

Purpose:

^{23}Na MRI has been performed for more than 25 years [1] and has evolved into a valuable tool for biomedical research [2]. Recently, also the first ^{35}Cl MR images of rat brain [3, 4] and human brain and muscle [5] were acquired. Chlorine (Cl^-) is the most abundant anion in the human body and is also involved in many physiological processes, e.g. volume regulation, regulation of electrical excitability [6] and cell migration in cancer [7]. Therefore, combined imaging of the sodium (Na^+) and Cl^- concentrations, as recently proposed [8], is highly desirable. In this work we acquired Cl^-/Na^+ ratio maps in human brain and present first results in tumor patients.

Methods:

Combined ^{35}Cl/^{23}Na MRI was conducted on a 7 T whole body MR system (MAGNETOM 7 T, Siemens AG, Healthcare Sector, Erlangen, Germany) using a dual tuned (^{35}Cl/ ^{23}Na), quadrature birdcage coil [8].

Point spread functions of ^{23}Na MRI and ^{35}Cl MRI were simulated using the standard offline image reconstruction in MATLAB (The Mathworks Inc, Natick, MA, USA). Relaxation times of brain tissue and saline solution (cerebrospinal fluid) were used for the simulations [9,10]: ^{23}Na (brain tissue): $T_{2f}^* = 4.7$ ms (33%), $T_{2s}^* = 40$ ms (67%); ^{23}Na(CSF/saline solution) = 56ms; ^{35}Cl (brain tissue): $T_{2f}^* = 1.2$ ms (41%), $T_{2s}^* = 7$ ms (59%); ^{35}Cl (CSF, saline solution).

Phantom: A spherical phantom with 2.6 L of 0.9% saline solution was used to evaluate the homogeneity of Cl^-/Na^+ maps and to normalize the Cl^-/Na^+ ratio maps.

In vivo imaging: One healthy subject and 3 patients with malignant gliomas (1 anaplastic astrocytoma (WHO °III) and 2 glioblastomas) were examined with combined ^{35}Cl and ^{23}Na MRI. Normalization was performed to the signal of cerebrospinal fluid (CSF). In CSF a Cl^-/Na^+ ratio of 0.74 is expected.

Acquisition parameters (phantom and in vivo imaging): **^{35}Cl MRI:** TE/ TR = 0.55/ 75 ms; $\alpha = 90°$; 10000 projections; Hamming filtering; $\Delta x^3 = 6$ mm^3; $T_{AQ} = 12$ min 30s; **^{23}Na MRI:** TE/ TR = 0.35/ 160 ms; $\alpha = 90°$; 4000 projections, Hamming/ Gauss filtering; $\Delta x^3 = 3$ mm^3, $T_{AQ} = 10$ min 40 s. Images were reconstructed to a field-of-view (FOV) of (300 mm)^3 and reduced to 225 mm^3.

^{23}Na MRI data was also reconstructed with a Gaussian filter ($\sigma = 5.2$ mm). This yielded a full width at half maximum (FWHM) of the point spread function (PSF) similar to the ^{35}Cl MRI data sets (cf. table 1).

Results:

In phantom imaging the acquired Cl^-/ Na^+ ratio maps showed good homogeneity. The measured ratio was 1.00 ± 0.06 (after normalization). In the area of the glioblastoma (Fig. 3) the measured Cl^-/ Na^+ ratio (0.39 ± 0.04) is markedly reduced compared to healthy brain tissue and cerebrospinal fluid. Also in the second glioblastoma (0.36 ± 0.04) and in the anaplastic astrocytoma (0.38 ± 0.03) low Cl^-/ Na^+ ratios were measured.

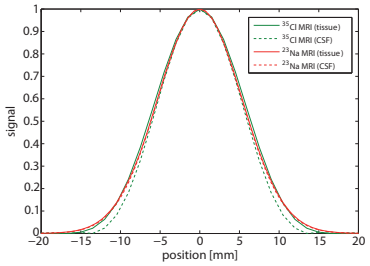

Fig. 1: Point-spread functions (PSF) of ^{23}Na MRI (Gaussian filter; $\sigma = 5.2$ mm) and ^{35}Cl MRI (Hamming filter). PSF were simulated considering relaxation times of brain tissue and filtering.

Table 1: FWHM of the point spread functions.

	brain tissue	CSF/ saline
^{35}Cl MRI (Hamming)	12.9mm	12.0mm
^{23}Na MRI (Gauss)	12.6mm	12.4mm

Discussion and Conclusion:

Combined imaging of ^{35}Cl/ ^{23}Na was performed for the first time in patients. Note, that the measured Cl^-/Na^+ ratio might by underestimated due to relaxation weighting even at the employed ultra-short echo time (TE=0.55ms), since ^{35}Cl possess inherent shorter relaxation times than ^{23}Na [10]. The Cl^-/Na^+ ratio maps showed reduced values in the area of the tumors. This might be caused by an increase in the concentration of other negatively charged ions (e.g. HCO_3^-). Cl^-/Na^+ ratio maps might contain valuable information for the characterization of tumor tissue and other diseases, in which alterations of the ion homeostasis are expected.

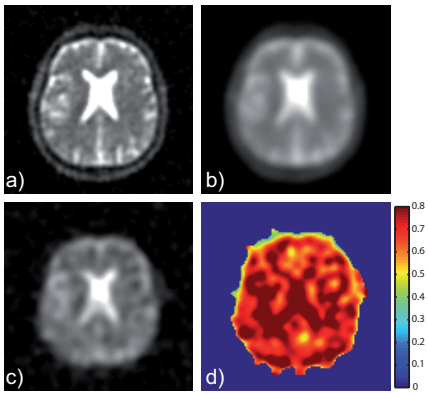

Fig. 2: a) ^{23}Na MRI of a healthy human brain (Hamming filter). b) Before the calculation of the Cl^-/Na^+ ratio maps, the ^{23}Na MRI data was reconstructed with a Gaussian filter (b) to achieve the similar actual spatial resolution than in ^{35}Cl MRI (c). d) Calculated Cl^-/Na^+ ratio maps of the healthy human brain.

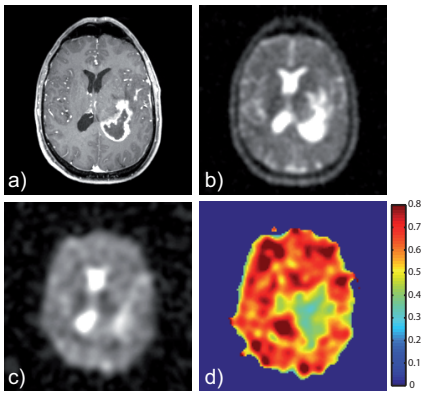

Fig. 3: Glioblastoma patient. a) Contrast-enhanced T_1-weighted MPRAGE image (B_0=3T). b) Cl^-/Na^+ ratio maps; c) ^{35}Cl MRI; d) ^{23}Na MRI. In the area affected by the glioblastoma, the measured C^-/Na^+ ratio is reduced compared to healthy brain tissue and cerebrospinal fluid.

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