35Cl and 23Na MRI of 9L rat glioma at 21.1 T

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Purpose

Chloride and sodium MRI are attracting attention as they can signal tumor cell alteration, apoptosis and variations in cellular energetics[1-3]. The potential of chloride MRI remains largely unexplored. However, ultra high magnetic fields provide an opportunity to expand existing MRI capabilities. Particularly ultra-high magnetic fields are favorable for low gamma nuclei where the gain in MR sensitivity is proportional to almost the power of two for the magnetic field increase. The current study was prompted by the unique capability to perform and evaluate chloride MRI in rat brain *in vivo* at ultra-high magnetic field of 21.1T and compare findings to sodium MRI. The challenges for chloride MRI are the weak MR signal (~ 20 times less than sodium), the short T_2 relaxation time which may rise the question of "visibility" and the small size of the MRI acquisition matrix which needs to be taken into consideration for correct quantification of images. Chloride and sodium MR imaging was modeled using *in vivo* MR relaxation parameters and the results were applied for detection of chloride and sodium concentration in normal rat brain and 9L rat glioma[4].

Methods

Two groups of male Fisher 344 rats (n=3 in each group, weight ~ 150 g) were used in the study. One group was implanted by 9L gliosarcoma cells and ~11 days after was participated in MRI sessions. The other group was served as control. The experiments were performed on a 21.1T magnet using Bruker MRI Avance III console (PV 5.1) and 64 mm gradient coil (RR Inc). Volume MRI coils for chloride (^{35}Cl, 88.2 MHz) and sodium (^{23}Na, 237.5 MHz) were the same size with ID/L = 33/54 mm, which allowed a direct comparison of signal intensities between nuclei from rat head. Radial center out k-space trajectories with np points were sampled using 360/nv angle increments in the plane (FOV = 64 mm) and each plane was rotated by 180/nv1 increments. Acquisition matrix for chloride was np x nv x nv1 = 40 x 84 x 42, resolution of ~ 0.8 mm, TR = 20 ms, NA = 128, TE = 0.1 ms. High resolution sodium MRI (0.4 mm) was achieved using matrix of 64x336x186, TR = 100 ms. The short readout time of ~ 2 ms was selected to reduce a partial volume effect from bi-exponential FID of chloride and sodium MR signals. Relaxation parameters T_1 and T_2^* parameters and signal to noise ratios S/N = FID(start)/STD(noise) were evaluated for both nuclei in rat head. Modeling of MRI data acquisition was performed using Matlab R2013a. All animal experiments were conducted according to the protocols approved by The Florida State University ACUC.

Results and Discussion

Chloride MR S/N ratio from whole rat head was 90 (NA=256). The corresponding ratio for sodium was 2500. The difference in sensitivity between chloride and sodium is very close to the expected value. Components of bi-exponential fit of chloride FID were T^*_{2a} = 0.4 ± 0.03 ms (41 %) and T^*_{2b} = 1.36 ± 0.03 (59 %), which were comparable to the corresponding values for sodium T^*_{2a} = 0.53 ± 0.01 ms (83%) and T^*_{2b} = 4.5 ms ± 0.08 ms (17 %). T_1 relaxation time of chloride *in vivo* was also fit by bi-exponential function T_{1a} = 4.8 ± 1 ms (70 %), T_{1b} = 24.4 ± 7 ms (30 %) while sodium T_1 relaxation was fit by mono-exponential function with T_1 = 41.4 ± 0.4 ms. T_1 relaxation of saline determined at 21.1T of 37.6 ± 0.3 ms is very comparable to the value at 9.4T (36.6 ± 2.4 ms). Thus, T_1 relaxation time of chloride being determined by quadrupolar interaction will remain the same at ultra-high magnetic fields. Chloride and sodium MR images were acquired in normal rat and in rat with glioma (Fig.1). Chloride concentration in normal brain was found to be 33 ± 4 mM and for sodium 44 ± 4 mM. Concentration of chloride in glioma was ~1.5 times more than in normal brain. Effects of short T_2 relaxation times and small sizes of acquisition matrix are demonstrated using Matlab software (Fig.2). Concentration of chloride in rat brain detected by MRI is in close correspondence with the results obtained by others[5] using ^{36}Cl radioisotope (31 mM). Chloride and sodium signals from rat head have comparable T_2 relaxation times for the quickly decaying components. Both these facts lead to the conclusion that there is no visibility problem for chloride MRI, and chloride MR signals can be detected entirely as sodium MR signals.

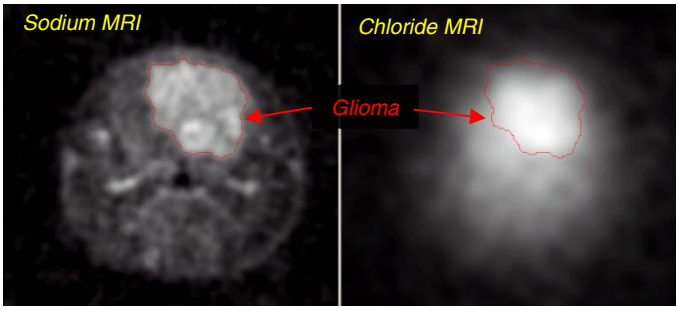

Fig. 1. Chloride concentration is increased in 9L glioma as it is usually observed in sodium MRI.

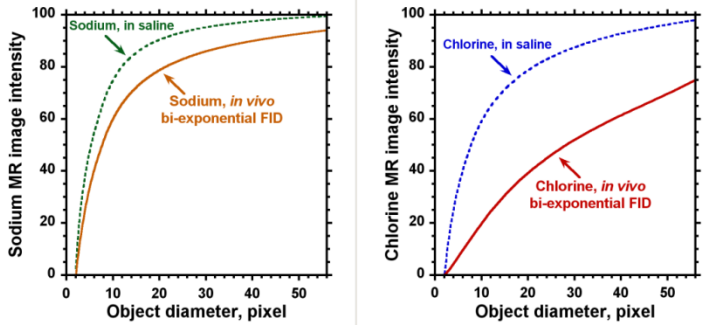

Fig. 2. Matlab modeling of changes in chloride and sodium MR image intensities due to a small acquisition matrix size and bi-exponential relaxation of FID. Note a much larger image intensity decrease for chloride MRI relative to sodium MRI.

Conclusion

The experiments performed in rat brain *in vivo* revealed that chloride *in vivo* signals are as visible as sodium MR signals. However, the bi-exponential MR signal relaxation and limited space sampling may dramatically affect quantification of the signals and need to be corrected. It is especially important if the size of the objects is changing during MRI experiments. The finding of an increased concentration of chloride in rat glioma correlates with the hypothesis stating the critical role of chloride in tumor progression[2].

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