Distribution of sodium concentration in brain using sodium MRI and double inversion recovery proton MRI

Guillaume Madelin[1], Richard Kline[2], Ronn Walvick[1], Christopher Glielmi[3], Dominik Paul[4], Heiko Meyer[4], Mony de Leon[5], Henry Rusinek[1,5], and Ravinder R Regatte[1]

[1]Radiology, New York University Langone Medical Center, New York, NY, United States, [2]Anesthesiology, New York University Langone Medical Center, New York, NY, United States, [3]Siemens Medical Solutions USA, Inc, New York, NY, United States, [4]Siemens AG, Erlangen, Germany, [5]Psychiatry, New York University Langone Medical Center, New York, NY, United States

Purpose. To measure the apparent total and intracellular sodium concentrations (aTSC and aISC) in brain using a combination of quantitative sodium (^{23}Na) MRI [1] with and without fluid suppression by inversion recovery (IR) and proton (^{1}H) double inversion recovery (DIR) [2] for creating masks of the gray and white matters (GM, WM). DIR allows selective excitation of WM or GM and allows accurate tissue segmentation with minimal partial volume effect. ^{23}Na IR is used to suppress cerebrospinal fluid (CSF) and (partially) extracellular sodium signal, generating images with a stronger weighting against intracellular sodium content [3]. This methodology has been validated on healthy subjects, and will be applied to subjects with different neurological/neurodegenerative disorders such as Alzheimer's disease (AD) [4], multiple sclerosis (MS) [5] or brain cancer [6], for assessing new biochemical information non-invasively and improve early diagnosis and prognosis of these diseases through quantification of sodium content (aTSC and aISC) increase.

Methods. 5 healthy subjects (mean age 33±7 years) were scanned at 3T on a Siemens Tim Trio using a double-tuned ^{1}H/^{23}Na birdcage coil (Stark, Germany) tuned at 128/33 MHz. ^{1}H DIR MRI was performed with a DIR TSE SPACE sequence with (time unit is ms): TR=7500, TE=300, TI1=3200 and TI2=550 for WM and CSF suppression, TI1=3600 and TI2=800 for GM and CSF suppression. FOV=220×320×320 mm^3, resolution=2.5 mm, TA=4:00. ^{23}Na MRI was acquired using the FLORET sequence [7] with: TR=80, TE=0.2, FA=80°/0.5 ms, 3 hubs at 45°, 200 interleaves/hub, 14 averages, FOV=320 mm isotropic, Nyquist resolution=5 mm, TA=11:10. For IR: a 'soft' rectangular inversion pulse [8] of 180°/6 ms was added with TI=24, TR=100 and 40 averages, Nyquist resolution=6.7 mm, TA=17:00. All ^{23}Na images were reconstructed using 3D regridding with nominal isotropic resolution=2.5 mm. ^{1}H and ^{23}Na data were acquired with the same isocenter position for allowing direct co-registration. Data processing: Sodium concentration maps (aTSC, aISC) were calculated (Fig. 1) by linear regression of the signal of 5 phantoms (3% agar + 10, 30, 50, 70, 100 mM NaCl). These maps were corrected for each voxel as segmented from the DIR masks for average water fraction in WM (0.7), GM (0.85) and whole brain (GM+WM: 0.78 = average) [9].

Results and Discussion. Distributions of aTSC and aISC values from WM, GM and whole brain (Fig. 2) showed skewed to the right for aTSC and to the left for aISC. Note the tighter distribution (sharper peaks) for aTSC than aISC. The mean ± standard deviation (std) across all subjects of the statistical parameters of the distributions are given in Table 1. These values are in close agreement with values found in the literature for healthy brains (aTSC~45 mM, aISC~15 mM) [10] and across subjects (13% variation for aTSC, 18% variation for aISC). Skewness (Ske) and kurtosis (Kur) of the distributions are consistent across subjects. We speculate that the differences observed in Ske and Kur between either aTSC and aISC, or between GM and WM within aTSC, might be due to both the different water fraction and structural organization in GM and WM (higher water fraction is associated with a more 'Gaussian' distribution, with Ske≈Kur≈0, for Na^+ due to fluid environment).

Conclusion. This noninvasive ^{1}H-^{23}Na method appears to provide useful regional and statistical distribution of total and intracellular sodium content in the human brain. The method will be applied to patients with neurological pathologies (AD, MS, cancer) for assessing its utility in detecting early signs of disease. As water fraction change with pathologies, a MRI measurement of water content will also be implemented in the protocol [11].

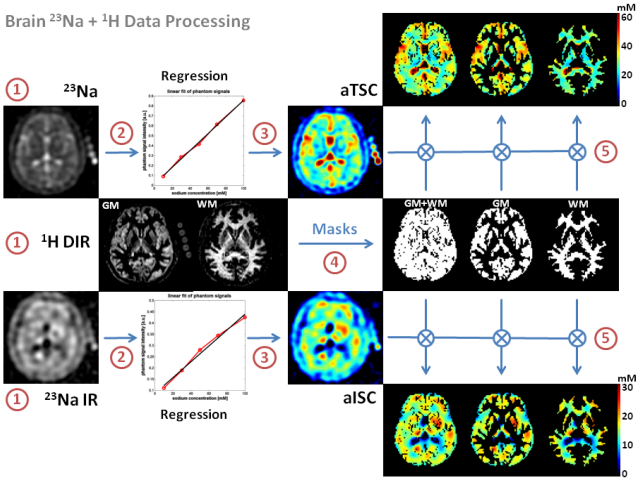

Fig. 1. Diagram of brain data processing. (1) Data acquisition: ^{23}Na with IR (fluid suppression) and without IR, and ^{1}H DIR. **(2)** Linear regression from calibration phantoms. **(3)** Calculation of aTSC and aISC maps. **(4)** WM and GM masks from segmentation with SPM8 [12]. **(5)** Multiplication of sodium maps by the masks for [Na^+] measurements in whole brain, GM and WM.

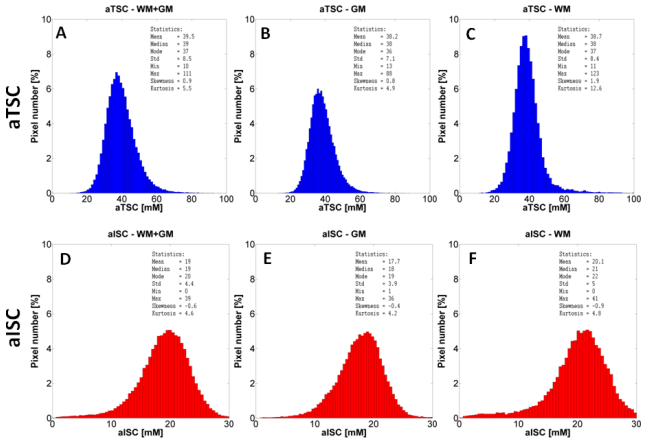

Fig. 2. [Na^+] histograms of aTSC and aISC: in whole brain (**A,D**), GM (**B,E**) and WM (**C,F**), from 1 subject. Note skews.

Table 1. Statistics of aTSC and aISC (n=5).

	Whole Brain		GM		WM	
	Mean	Std	Mean	Std	Mean	Std
aTSC (mM)						
Mean	**43.9**	6.0	**42.5**	5.4	**43.5**	5.5
Median	**42.6**	5.9	**41.6**	5.1	**42.6**	5.4
Mode	**41.2**	5.7	**40.2**	4.7	**42.4**	4.6
Std	**10.9**	1.5	**9.9**	1.4	**10.2**	1.5
Skewness	**0.9**	0.1	**0.6**	0.1	**1.5**	0.4
Kurtosis	**5.0**	0.8	**4.5**	0.6	**9.1**	2.1
aISC (mM)						
Mean	**17.6**	3.3	**16.3**	3.2	**18.3**	3.1
Median	**17.8**	3.3	**16.6**	3.2	**18.6**	3.4
Mode	**18.4**	3.2	**17.6**	3.2	**19.6**	3.3
Std	**4.5**	0.7	**4.1**	0.6	**4.8**	0.8
Skewness	**-0.3**	0.2	**-0.3**	0.2	**-0.4**	0.4
Kurtosis	**3.9**	0.5	**3.8**	0.3	**3.9**	0.7

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