INTRODUCTION: Frequency shift of proton MRI have been recently used to generate unique image contrast between gray and white matter (1, 2). This frequency shift has been largely attributed to magnetic susceptibility arising from varying chemical composition and microstructure of the tissue (3-7). While proton is the most abundant element in the body in the form of water molecules, about 70-80% of the water protons are in the intracellular space. It is thus reasonably to believe that the susceptibility measured by proton MRI is dominated by intracellular susceptibility even with the consideration of water exchange between intra- and extracellular space. Sodium, on the other hand, resides primarily in the extracellular space with a ratio of 142:10 between extra- and intracellular sodium concentration. In addition, sodium exists in the form of ion; thus it is generally considered not influenced by chemical binding and associated exchange effect as in the case of proton. In this study, we found that sodium MRI exhibits different susceptibility contrast compared to proton. The typical gray and white matter contrast is largely absent and the quantitative values differ significantly. Measuring susceptibility from sodium MRI may thus provide additional insights into cellular and sub-cellular susceptibility distribution and the complex mechanisms involved in tissue susceptibility contrast.

METHODS: A sodium ($^{23}$Na) MRI experiment was conducted on a healthy adult volunteer with a whole-body human 9.4T MRI scanner. A 3D flexible twisted projection imaging (flexTPI) sequence was used for data acquisition (8). Two sets of images were collected with TE values of 0.26 ms and 2.26 ms for mapping the B0 field. The transmit power level was manually adjusted to achieve a global 90 degree excitation. Other acquisition parameters were: FOV = 20 cm, nominal resolution = 3.3 mm isotropic, TR= 160 ms, radial fraction = 0.32, and scan time = 9 minutes and 40 seconds. Images were reconstructed to 256 x 256 x 256 matrix and phase images were extracted from the complex 3D data. Phase wraps were removed with a Laplacian-based algorithm (5). Background phases that were generated by magnetic sources outside the brain were eliminated by a spherical-mean-value (SMV) based algorithm (9). Quantitative susceptibility values were calculated based on an LSQR algorithm which resulted in high-quality susceptibility maps with few artifacts.

As a comparison, a second adult subject was scanned for proton ($^1$H) MRI on a 3T scanner with a 3D gradient-echo sequence with the same FOV and image resolution. Other parameters were: TE = 40 ms, TR = 70 ms and flip angle = 30°. Phase and susceptibility maps were processed identically to those of sodium.

RESULTS: Figure 1 compares the frequency and susceptibility contrast between $^{23}$Na and $^1$H MRI in the cortical region. While $^1$H frequency and susceptibility have the characteristic high contrast, this contrast is absent in those of $^{23}$Na in various regions of the cortex. Both white matter and gray matter may appear paramagnetic in $^{23}$Na, contrary to the diamagnetic white matter seen in $^1$H (line profile plot in Fig. 1a). In addition, the susceptibility values of $^{23}$Na are approximately six times larger than those of $^1$H.

Figure 2 shows $^{23}$Na magnitude, frequency and susceptibility maps of one axial slice in the midbrain. Overall, white matter (e.g. the genu of the corpus callosum) appears paramagnetic. However, significant heterogeneity exists in the white and gray matter regions with some isolated spots appearing diamagnetic. No clear gray and white matter boundaries can be delineated. CSF, in general, appears diamagnetic, consistent with $^1$H results.

DISCUSSIONS AND CONCLUSIONS: Our study made three surprising findings. First, both white matter and gray matter may appear paramagnetic in $^{23}$Na frequency and susceptibility maps. Second, the susceptibility values are significantly larger than those of $^1$H. Third, susceptibility of white matter exhibits larger heterogeneity that that of $^1$H. The first finding could suggest that extracellular susceptibility in the white matter may be paramagnetic considering $^{23}$Na resides mainly in the extracellular space. This would further suggest that there is a large susceptibility gradient between extra- and intracellular space with the latter being diamagnetic. The lack of gray and white matter contrast in $^{23}$Na susceptibility maps seems to support extracellular space being magnetically similar in gray and white matter. However, there is no obvious explanation why the $^{23}$Na susceptibility in the CSF is much larger than the $^1$H susceptibility. One potential source of the discrepancy could be the difference in the reference frequency due to the different distribution patterns of $^{23}$Na and $^1$H. Our study is limited due to the low resolution and low sensitivity of $^{23}$Na MRI. The unusually large susceptibility may result in significant phase wraps within one voxel that cannot be recovered. Nevertheless, the direct comparison between $^{23}$Na and $^1$H of identical resolution suggests that our findings are not simply a consequence of the image resolution. Further studies of the same subjects at the same field would be necessary to further verify the results.

The unique location of Na in the body makes it an attractive tool for probing cellular susceptibility distribution. In the diseased states when the cell membranes break down, our data would predict a reduced and more diamagnetic susceptibility. Similarly, during neuronal activation when the sodium channels open, our data would also suggest decreased $^{23}$Na susceptibility. This change would be a potential useful way to study energy metabolism involving sodium channels. Further studies of $^{23}$Pd could be used to verify the predicted susceptibility gradients between extra- and intracellular space as phosphate mostly resides in the intracellular space.