Sodium and Diffusion as mediators of Tissue conductivity

L. T. Muftuler[1], M. J. Hamaura[1], and O. Nalcioglu[1]
[1]Center for Functional Onco-Imaging, University of California, Irvine, CA, United States

Introduction: Studies have shown that the electrical impedance of malignant tumors is significantly different from those of normal and benign tissues [Malich *et al Clin. Rad., 56:278-283, 2001*]. In this study, our goal was to investigate factors that contribute to this increase in tumor conductivity. Since conductivity in tissues is mediated by ion movement, increase in ion concentration and their mobility are potentially the main factors. Pethig reported that sodium and chlorine are the most abundant ions in tissue fluids and significant increase in water and sodium contents were observed in tumors [*IEEE Tr. Elect. Insulation EI-19:453-474, 1984*]. Hilal *et al* also reported significant increase in sodium content in neoplasticities [*Sodium Imaging, Mosby Year Book Inc., ch 34:1091-1110, 1992*]. On the other hand, Tuch *et al* reported a linear relationship between tissue conductivity and diffusion tensor [*PNAS 98: 11697-11701, 2001*]. Although those two phenomena are not related in a free solution, boundary conditions imposed in structured medium will force them to follow similar behavior. Therefore, we collected conductivity images based on MR-Electrical Impedance Tomography (MREIT), as well as sodium and diffusion weighted images and investigated the contribution of those factors to tumor conductivity.

Methods: Weak electrical currents that are injected into an object generate magnetic fields, the z-component of which induces additional phase information in MR images. If a modified spin-echo sequence was used with several π pulses applied during the zero-crossings of the alternating current, the phase shift accumulates across these π pulses. From this accumulated image phase, the B-fields generated by the current density can be calculated. We have developed a technique to reconstruct conductivity images from these B-field measurements using iterative reconstruction with Tikhonov regularization with Sensitivity matrix method [*Muftuler et al TCRT v 3, 599-610, 2004*]. Data were collected in a whole body 4T MRI system interfaced with a MR Solutions MR5000 spectrometer. A Sprague-Dawley rat bearing a tumor induced by the carcinogen ENU was imaged in this study. MREIT data were collected with TR=500ms, TE=50ms, FOV=10cm, BW=50kHz, matrix = 128x128, slice thickness = 5mm, NEX = 8. Two cycles of 100Hz current with 1mA peak was applied sequentially through different pairs of three electrodes, generating three different current profiles. Data were collected with both ± polarities of the currents to eliminate phase accumulation from other sources. Upon completion of MREIT experiment electrode setup was removed to avoid distortions in DWI images. Sodium images were collected using a 3D radial projection sequence [*Nielles-Vallespin et al, MRM 57:74-81, 2007*] with TR = 100ms, TE = 250us, flip angle = 90 degrees, FOV = 20cm, BW = 500kHz, number of radial lines = 5000, resample matrix = 64x64x64, NEX = 4. Finally, 2D SE pulse sequence with TR/TE = 1500/80ms, FOV = 10cm, BW = 25kHz, matrix = 128x128, slice thickness = 5mm, NEX = 1 and b=650 was used for diffusion weighted imaging (DWI).

Results: Fig.1.a shows an axial T2 weighted anatomical image from the lower abdomen of the animal. The tumor on the back of the animal was circled with a dashed red line. Sodium image and DWI from the same section of the animal were shown in Fig.1.b and Fig.1.c, respectively. Fig.1.d shows the combined sodium and diffusion image that is obtained by simple pixel-by-pixel multiplication of the two images to illustrate the areas that has high sodium concentration as well as high diffusion. Finally, Fig.2 shows the reconstructed conductivity image from MREIT.

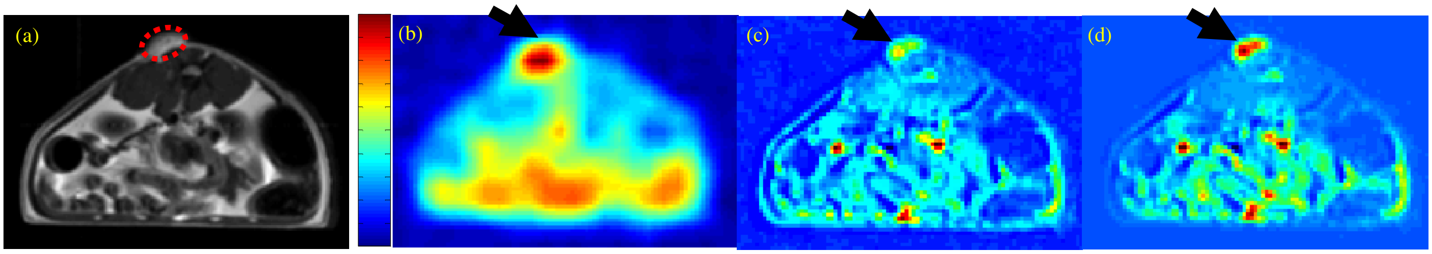

Fig.1. T2 weighted anatomic (a), 23Na (b), DWI (c) and combined 23Na*DWI image (d) from a tumor bearing rat. Tumor is encircled with the dashed red line on the anatomic image. A color bar is included to show the scale.

Discussion: In this preliminary study, we investigated sodium ion concentration and increased ion mobility demonstrated by DWI as potential factors that lead to an increased conductivity distribution in tumors. Although the results presented here are from a single animal, previous reports in the literature and our findings presented here provide evidence that those may be the major factors that mediate tissue conductivity changes. Clear boundaries of the tumor can be seen from the conductivity image in Fig.2. Other high conductivity areas seen near the electrodes are due to electrode artifacts as well as increased conductivity by the gel we apply to electrodes for better contact. Since the pressure of electrodes deformed the body of the animal, we could not do a direct correlation with the 23Na and DWI images. However, combined effect of increased sodium concentration and diffusion can be clearly seen in the tumor region. Further studies will be conducted to investigate if combined sodium and diffusion weighted images can be used as an approximation of tissue conductivity distribution. MREIT electrode setup caused image distortions in DWI images, therefore the electrodes were removed for DWI and Na imaging. This caused geometrical deformation of acquired slices between MREIT and other acquisitions. Since anatomical data was collected twice for both cases, we will be developing non-linear registrations tools to register all images.

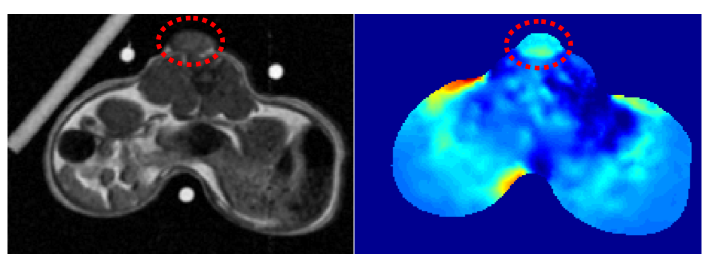

Fig.2. Anatomic image (left) and corresponding conductivity image (right) from MREIT experiment. Bright circles outside the animal are markers for electrode positions. Tumor is shown with dashed red circle.

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