

## RELAXATION-WEIGHTED SODIUM MRI OF BREAST LESIONS AT 7T

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**TARGET AUDIENCE:** Radiologists and physicists interested in sodium MRI for evaluation of breast lesions.

**PURPOSE:** Dynamic contrast-enhanced (DCE) MRI is an established diagnostic tool for the assessment of breast tumors with high sensitivity and good specificity. It has been demonstrated that the addition of functional MRI parameters such as diffusion-weighted imaging (DWI) improve specificity. While DWI is sensitive mainly to cellularity, sodium (<sup>23</sup>Na) MRI provides additional information on physiology and metabolism of cells in lesion. Several studies demonstrated an increased <sup>23</sup>Na concentration in malignant breast lesions compared to healthy tissue [1]. However, total <sup>23</sup>Na signal (<sup>23</sup>NaT) is a volume-weighted average of <sup>23</sup>Na in the intracellular and extracellular (interstitial fluid/edema, plasma) space. Motion restricted <sup>23</sup>Na ions, predominantly situated in cells, exhibit shorter T1 and T2\* relaxation times compared to <sup>23</sup>Na ions in fluid. This fact can be used for selective suppression of <sup>23</sup>Na signal from fluid. Relaxation-weighted (RW) <sup>23</sup>Na MRI, such as double-readout imaging, showed higher sensitivity to changes in intracellular <sup>23</sup>Na signal and were able to distinguish between low- and high-grade brain tumors [2]. Therefore, the aim of this study was to compare <sup>23</sup>NaT signal with relaxation-weighted <sup>23</sup>Na signal (<sup>23</sup>NaRW) in breast lesions at 7T.

**METHODS:** This study was approved by local ethics committee. Four patients with histologically proven breast cancer (one invasive lobular carcinoma grade II, three invasive ductal carcinoma grade II; all having MIB-1 proliferation rate of 10%; age range: 49–66 years) were measured at a 7T whole body system (Magnetom, Siemens Healthcare, Erlangen, Germany). Images were acquired with a double-resonant <sup>1</sup>H/<sup>23</sup>Na bilateral phased array breast coil (Quality Electrodynamics, Mayfield Village, OH, USA).

In all patients, DCE MR images were obtained before and after contrast agent administration using the gradient echo with k-space undersampling and data sharing time-resolved angiography with stochastic trajectories (TWIST) sequence (TR/TE= 4.6/2.4 ms, resolution= 0.7×0.7×0.7 mm<sup>3</sup>, temporal resolution= 14s, BW= 590 Hz/pix, TA= 8:36 min) (Fig. 1a). For DWI, readout-segmented echo-planar imaging with parallel imaging was performed (TR/TE1/TE2= 5500/60/102 ms, resolution= 0.9×0.9×5.0 mm<sup>3</sup>, b values= 0 & 850 s/mm<sup>2</sup>, BW= 566 Hz/pix, TA= 3:36 min) [4]. For double-readout <sup>23</sup>Na-MRI, DA-3DRP sequence was measured (TR= 103 ms, TE1/TE2= 0.58/12.0 ms, 9000 projections, nominal resolution= 4.0×4.0×4.0 mm<sup>3</sup>, BW= 100 Hz/pix, TA= 15:27 min).

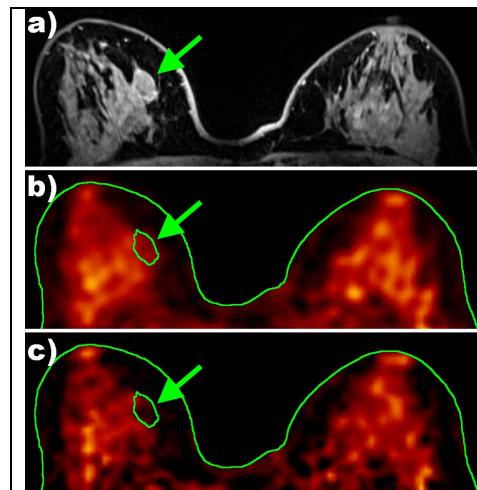
All <sup>23</sup>Na images were reconstructed offline in MATLAB (The Mathworks Inc, Natick, MA, USA). <sup>23</sup>NaT images were represented by images acquired at TE1 with double-readout <sup>23</sup>Na MRI (Fig. 1a). <sup>23</sup>NaRW images were calculated from double-readout images on a pixel-by-pixel basis using weighted subtraction of signal intensities: RW= TE1-F×TE2, where the weighting factor F= exp(TE1-TE2)/T2\*<sub>FLUID</sub> (Fig. 1c). The measured <sup>23</sup>Na T2\* in saline solution was 48 ms, which gave F=1.269. The variation of flip angle within the breast coil volume was corrected using factors calculated from <sup>23</sup>Na images obtained from homogenous saline phantom. All regions-of-interest (ROI) evaluations were performed in JiveX (VISUS GmbH, Bochum, Germany). All ROIs were drawn on DCE MRI and DWI images and subsequently transferred to corresponding <sup>23</sup>NaT and <sup>23</sup>NaRW images. For better comparison between <sup>23</sup>NaT and <sup>23</sup>NaRW, signal intensity of lesion or edema was normalized to signal of contralateral healthy breast tissue and expressed in percent as: 100×(lesion – healthy)/healthy.

**RESULTS:** While <sup>23</sup>NaT imaging obtained a signal proportional to the local <sup>23</sup>Na concentration, <sup>23</sup>Na ions with a longer T2\*, such as in a cyst, were well suppressed in <sup>23</sup>NaRW images (Fig. 1c). This is demonstrated by the decrease of mean normalized signal difference in edematous tissue from 27% in <sup>23</sup>NaT images to 11% in <sup>23</sup>NaRW images (Fig. 2). Similarly, normalized signal difference measured in cyst decreased from -27% in <sup>23</sup>NaT image to -49% in <sup>23</sup>NaRW image. Moreover, <sup>23</sup>NaRW MRI revealed increased signal in all four malignant lesions, while <sup>23</sup>NaT imaging demonstrated elevated signal in three lesions. In carcinomas, mean normalized signal difference increased from 34% in <sup>23</sup>NaT images to 44% in <sup>23</sup>NaRW images (Fig. 2).

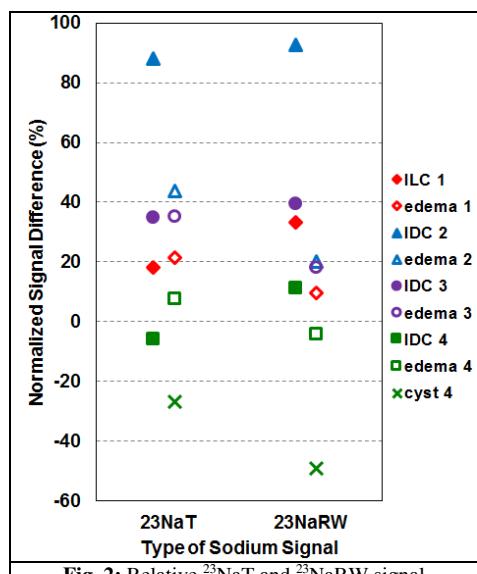
**DISCUSSION:** Our results demonstrate feasibility of double-readout <sup>23</sup>Na-MRI in patients with breast cancer with sufficient resolution and in clinically acceptable measurement time at 7T. Both <sup>23</sup>NaT and <sup>23</sup>NaRW images are obtained in one measurement. While an elevated <sup>23</sup>Na signal was observed both in malignant lesions and edema, <sup>23</sup>NaRW images demonstrated the signal increase only in malignant lesions. By suppressing <sup>23</sup>Na signal coming predominantly from fluid, <sup>23</sup>NaRW images allowed improved differentiation between edema, benign lesions and breast cancer.

**CONCLUSION:** To our best knowledge, this is the first study employing <sup>23</sup>NaRW-MRI for the evaluation of breast lesions. Further optimization of <sup>23</sup>NaRW-MRI based on relaxation times of tumor and edematous tissue might additionally improve image contrast between edema, benign and malignant lesions. Combined information from <sup>23</sup>NaT and <sup>23</sup>NaRW images may improve noninvasive evaluation of breast lesions.

**REFERENCES:** [1] Ouwerkerk R, Jacobs M.A., et al. Elevated tissue sodium... *Breast Cancer Res Treat*. 2007;106(2):151-160. [2] Nagel A.M., Bock M., et al. The Potential of Relaxation-Weighted Sodium... *Invest Radiol*. 2011;46: 539–547. [3] Nagel A.M., Laun F.B., et al. Sodium MRI using a density-adapted... *Magn Reson Med*. 2009;62:1565–1573. [4] Bogner W, Pinker K., et al. Bilateral Diffusion-weighted MR Imaging... *Radiol*. 2014; DOI: <http://dx.doi.org/10.1148/radiol.14132340>



**Fig. 1:** a) DCE image, b) color-coded <sup>23</sup>NaT image, and c) <sup>23</sup>NaRW image. Arrows indicate location of cyst with  $ADC = 2.24 \times 10^{-3} \text{ mm}^2/\text{s}$ . Please note signal suppression in cyst on <sup>23</sup>NaRW image.



**Fig. 2:** Relative <sup>23</sup>NaT and <sup>23</sup>NaRW signal intensities in edematous tissue, in cyst and in invasive lobular and ductal carcinomas.