Regions of interest (ROIs) were delineated for NBW and tumor quantified by the asymmetry of the magnetization transfer ratio (asym). Z-spectra are shifted using a $B_0$ map to correct for $B_0$ inhomogeneity, and the adjusted spectra are often fit with high order polynomial functions to calculate an adjusted adjusted MTR$_{asym}$ value. The effect seen in CEST-MRI imaging of proteins occurs downfield from water at 3.5 ppm and 2.0 ppm frequency offsets, so the portion of the Z-spectrum upfield from water may be described by a two-pool exchange model for magnetization transfer (MT) between the bulk water pool and a bound pool of protons associated with immobile macromolecules. This study is to distinguish bladder cancer from normal bladder wall by separating the Z-spectra into upfield and downfield components and fitting these components separately.

Materials and methods

Subjects
A total of 16 bladder cancer patients (13 male, 3 female, average age 69.5 years) were evaluated with MRI prior to radical cystectomy. The stage of disease ranged from pT1 to pT4a, with eight of the patients having disease staged T3a or higher.

MRI
Patients were imaged on a 3.0 T MR system (Philips Achieva, Best, Netherlands) using a 32-channel phased array coil using a single-shot, single-slice turbo spin echo sequence (ssTSE) with a TR/TE of 6100 ms/56 ms, flip angle 90°, field of view 140 x 140 mm, acquisition matrix 80 x 65, and slice thickness 6 mm. A radiofrequency (RF) saturation pre-pulse was applied prior to image acquisition consisting of sixteen 1800° block pulses with pulse lengths of 29-31 ms. A total of 33 images were acquired with the prepulse applied at varying frequency offsets ranging from 8 to -8 ppm in 0.5 ppm increments. Additionally, one image was acquired in the absence of saturation for signal normalization, and a $B_0$ map was acquired to apply a $B_0$ inhomogeneity correction during image analysis. The total acquisition time was 3.5 minutes.

Image Analysis
Regions of interest (ROIs) were delineated for NBW and tumor based on pathology reports and T2-weighted images. Z-spectral data were acquired from each region using in-house software based on the Interactive Data Language (IDL, Exelis Visual Information Solutions, Boulder, CO). The data was separated into upfield and downfield components and fit using a non-linear least squares curve fitting package in IDL version 8.2. The data downfield from water were fit to an 8th order polynomial function, while the data upfield from water were fit to the function described by equation 1. MTR$_{asym}$ values at 3.5 ppm and 2.0 ppm frequency offsets were calculated for each ROI by evaluating MTR(-$\omega$) using the two-pool fit and MTR(+$\omega$) using the 8th order polynomial fit.

Statistical Analysis
A two-tailed, paired student’s t-test was used to test for significant differences in $A_v$, $G_{os}$, $A_b$, and MTR$_{asym}$ values between the NBW and tumor regions for all patients.

Results and Discussion
Average values for all parameters and MTR$_{asym}$ values between the NBW and tumor regions are shown in Figure 1. Pairwise statistically significant differences between the tumor and NBW regions were found for $A_v$ and MTR$_{asym}(3.5 \text{ ppm})$ ($p$-values 0.003 and 0.03, respectively). There were no statistically significant differences between the tumor and NBW regions for $A_v$, $G_{os}$, or MTR$_{asym}(2.0 \text{ ppm})$. $A_b$ is analogous to the MTR values at larger frequency offsets that are obtained from MT experiments involving transfer of magnetization from immobile macromolecules. The significant differences for $A_v$ and MTR$_{asym}(3.5 \text{ ppm})$ imply that these quantities have the potential to distinguish between NBW and bladder cancer.

Conclusion
Separately modeling the components of the Z-spectrum upfield and downfield from water can be applied in CEST-MRI experiments to distinguish bladder cancer from NBW using MTR$_{asym}(3.5 \text{ ppm})$ values. This method provides information equivalent to MTR values from classic MT-MRI experiments through the parameter $A_v$, which may also have the ability to differentiate bladder cancer from NBW.

References