Assessment of Neoadjuvant Chemotherapeutic Response of Bladder Cancer by Dynamic Contrast-Enhanced MRI at 3T

H. T. Nguyen[1,2], G. Jia[1], Z. K. Shah[1], K. S. Pohar[3], A. Mortazavi[4], D. Clark[1], M. Patel[1], D. L. Zynger[5], and M. V. Knopp[1,2]

[1]Wright Center of Innovation in Biomedical Imaging and Department of Radiology, The Ohio State University, Columbus, OH, United States, [2]Biophysics Program, The Ohio State University, Columbus, OH, United States, [3]Department of Urology, The Ohio State University, Columbus, OH, United States, [4]Department of Internal Medicine, The Ohio State University, Columbus, OH, United States, [5]Department of Pathology, The Ohio State University, Columbus, OH, United States

Introduction

Early assessment of chemotherapeutic response of bladder cancer is crucial to proper treatment strategy for bladder cancer. This on-going study is aimed at evaluating whether Dynamic Contrast-Enhanced MRI (DCE-MRI) can significantly improve the accuracy of the assessment of bladder tumor response to neoadjuvant chemotherapy. Concurrently, the study also investigates the capability of DCE-MRI to reveal changes in the microcirculation characteristics after the chemotherapy.

Materials and Methods

Subjects: 12 patients (11 males and 1 female) who had cytoscopic confirmation of bladder tumor and were treated with neoadjuvant chemotherapy have been included in the study.

MRI exams: All patient scans were performed on a 3T MRI system (Achieva, Philips Healthcare) with a phased-array surface coil.

T2-weighted MRI (T2w-MRI) was performed with a Turbo Spin Echo (TSE) sequence: number of slices = 40; slice gap = 0.3 mm; voxel size (RL/AP/FH) = 0.98/1.03/3.00 (mm); FOV (RL/AP/FH) = 350/251/132 (mm); TR/TE = 13850/80 (ms); scan time = 4 minutes; NSA = 3. DCE-MRI was performed with a 3D-spoiled gradient echo (3D-T1w-FFE) sequence: number of slices=18 or 19; voxel size (RL/AP/FH) = 1.70/1.68/5.00 (mm); FOV (RL/AP/FH) = 360/360/90 (mm); temporal resolution = 7.6(s); TR/TE/Flip angle = 5ms/2ms/20°; scan time = 8 minutes; NSA= 3.

Data Analysis: DCE-MRI data was processed with IDL (ITT)-based software by applying a linear two-compartment pharmacokinetic model [1, 2] to calculate pharmacokinetic parameters including Amp (signal enhancement amplitude), k_{ep} (exchange rate constant between the interstitial space and the plasma), kel (elimination rate constant from the plasma) for each slice. The maps of Amp+kep were parameter-coded with the same color table (Figure 1). Curve-fitting was used to display signal enhancement curves (Figure 2) that reveal the time-dependent change of the ratio of contrast-enhanced signal (S) to unenhanced signal (S_{pre}) in a region of interest (ROI).

A radiologist interpreted T2w-MRI data before reading DCE-MRI data to determine whether there was tumor residue(s) (positive case) or no identified tumor (negative case) after the neoadjuvant chemotherapy. Pathological results were used to validate the radiological interpretation of T2w-MRI and DCE-MRI data.

Results

Pathological reports confirmed 11 positive cases and 1 negative case. The results of the chemotherapeutic response assessment by T2w-MRI and DCE-MRI are summarized in Table 1. These results indicated that DCE-MRI significantly increased the accuracy of the chemotherapeutic response assessment by conventional T2w-MRI. T2w-MRI failed to assess 3 positive cases in which tumor and normal bladder wall were isointense on T2w-MR images while DCE-MRI was able to confirm these 3 positive cases with enhanced T1-weighted MR (T1w-MR) images and Amp+kep maps (Figure 1). Likewise, in the T2 false positive case, DCE-MRI was able to confirm the benign wall thickening that was identified as a tumor on T2w-MR images. In the only DCE-MRI false negative case, the tumor residue was only in microscopic size (0.7cm), thus, only several pixels large on DCE-MR images. Therefore, it was not confident to confirm the tumor residue on DCE-MR images.

In 9 out of 10 true positive cases of DCE-MRI, tumor residues showed a high Amp characteristic. The average Amp values of tumor residues range from 2.1 to 3.2 with the mean value of 2.6.

While it was impossible for T2w-MRI to assess the responsiveness of bladder tumor, DCE-MRI with color Amp+kep maps revealed that there was a correlation between the microcirculation characteristics of bladder tumor and its responsiveness. In 7 out 10 DCE-MRI true positive cases, Amp and kel of responsive tumor ROIs were significantly lower than those of nonresponsive tumor ROIs ($p<0.01$). Meanwhile, kep of responsive tumor was significantly higher than that of nonresponsive tumor ($p<0.01$). Therefore, color Amp+kep maps were able to map out responsive ROIs and nonresponsive ROIs of bladder tumor (Figure 2).

Discussions and Conclusions

The assessment of bladder cancer response to neoadjuvant chemotherapy was significantly improved by DCE-MRI. This critical improvement demonstrated the ability of DCE-MRI to investigate the change in microcirculation characteristics of bladder cancer after the chemotherapy, an important ability as no other imaging methodology has been able to achieve this in bladder cancer imaging. The promising results confirm that DCE-MRI can be an important tool to assess and predict the effectiveness of neoadjuvant chemotherapy in bladder cancer.

Sequence	True Positive	False Positive	True Negative	False Negative	Accuracy
T2w MRI	8	1	0	3	67 %
DCE-MRI	10	0	1	1	92%

Table 1: The numbers of true or false positive cases and true or false negative cases confirmed by T2w-MRI and DCE-MRI.

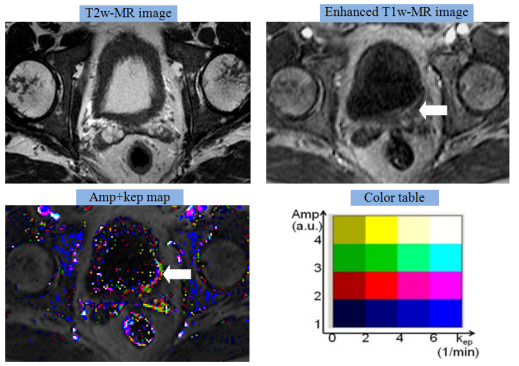

Figure 1 (a male patient, age = 47): The tumor residue indicated by arrows was isointense with the benign wall thickening on the T2w-MR image, but, identified on the enhanced T1w-MR image and the color Amp+kep map.

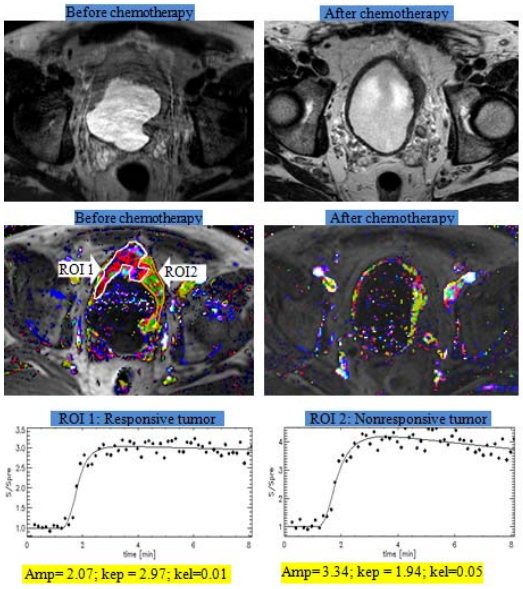

Figure 2 (a male patient, age = 59): *Row 1:* The responsive and non-responsive ROIs were isointense on the T2w-MRI images; *Row 2:* Color Amp+kel maps were able to display the two ROIs; *Row 3:* Signal enhancement curves showed the difference in perfusion characteristics of the responsive tumor ROI (lower Amp and kel, higher kep) and the non-responsive tumor ROI (higher Amp and kel, lower kep).

References

1. Tofts PS et al, J Magn Reson Imaging 1999; 10(3):223-32
2. Yang X et al, Magn Reson Med. 2008; 59(6):1448-56