Role Of Dynamic Contrast-Enhanced & Diffusion weighted Magnetic Resonance Imaging in Local Staging & Grading of Urinary Bladder Carcinoma

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Aims and objectives

Urinary bladder cancer is a relatively common malignancy, especially in elderly patients. Treatment outcome and prognosis are strongly related to adequate local and regional tumor staging. Unfortunately, clinical understating frequently occurs, which negatively influences prognosis. Therefore, advanced imaging techniques are needed to adequately stage bladder cancer patients. Dynamic contrast-enhanced and diffusion-weighted MRI has been introduced in clinical MRI protocols of bladder cancer because of its accuracy in local staging and grading.

Our air in the current study was to evaluate the accuracy of Dynamic contrast enhanced (DCE) MRI and Diffusion weighted (DW) MRI for preoperative T staging of bladder cancer and find correlation between apparent diffusion coefficient (ADC) of urinary bladder carcinoma and its histological grade.
Methods and materials

Current Prospective study conducted from June 2015 through August 2016 upon fifty patients with a presumed diagnosis of bladder cancer either clinically or by other radiologic investigations. Examination protocol was approved by the institutional medical ethics committee, and informed consent was obtained from all patients.

Exclusion criteria included patients with general contraindications for MR examination (as d.t pacemaker or metallic prosthesis) or contraindications for cystoscopy (patients unfit for anesthesia or d.t urethral stricture), patients with high renal function tests & patients refusing consent.

Pelvic MRI was performed in the supine position with a 1.5-T MRI scanner (Magnetom Avanto, Siemens) with 18-channel & phased array pelvic coil. The entire pelvis was imaged from the aortic bifurcation to the inferior margin of pubic symphysis.

DW-MRI was performed during free breathing with axial plane fat suppressed water-excited single-shot spin echo echo-planar sequence (TR/TE, 4000/78, slice thickness 4mm & 0.4 mm intersection gap and b values of 0, 500 and 1000 s/mm²).

DCE-MRI acquired with an axial fat-suppressed 3D volumetric spoiled gradient-echo sequence (TR/TE 180-300/1.7- 4.2; flip angle 70°, slice thickness 6 mm & intersection gap 2 mm) before and after IV injection of 0.1 mL/kg of gado-pentetate-dimeglumine (Magnevist, Bayer Schering Pharma) at 2 ml/s. Contrast-enhanced images obtained at 20 sec.(arterial phase), followed by 70 sec. (venous phase) and 3 minutes (delayed phase) as axial enhanced T1-W SE imaging.

Image analysis:

DW MRI; image interpretation was referred to T1 and T2 images. Stage T1 showed hyperintense tumor is within the bladder lumen, stage T2 showed hyperintense tumor partially seen in bladder wall, stage T3 showed hyperintense tumor disrupting the bladder wall and stage T4 showed hyperintense tumor extending into the adjacent organs, abdominal or pelvic wall.

DCE-MRI; bladder tumor, mucosa, and submucosa enhanced early, but the muscle layer maintains its hypointensity and enhanced late. Intact submucosal linear enhancement indicates stage T1 or lower lesions. So stage T1 showed intact muscle layer at the base
of the tumor showing low signal intensity, stage T2 showed disrupted hypointense line and early enhancement without perivesical fat infiltration, stage T3 showed disrupted hypointense line & enhancing streaky areas in perivesical fat and stage T4 showed lesion extending into adjacent organs or abdominal and pelvic side walls.

The time-intensity curves were constructed from signal intensity values obtained from regions of greatest enhancement selected from the lesions. Grade 1 show enhancement, followed by a slow increase. Grade 2: show enhancement, followed by a plateau. Grade 3: show enhancement, followed by washout.

Receiver operating characteristic curve (ROC) analysis was used to calculate the area under the curve (AUC) for identification of ADC cut off values differentiating normal values from bladder cancer & differentiating low grade from high grade cancers.
Results

The study was performed on 50 patients (46 (92%) were males and 4 patients (8%) were females). Age ranged between 30-82 years (mean age was 59.72± 9.08 years).

22 out of 32 patients (69%) with PT1 bladder carcinoma showed preserved submucosal enhancement in DCE-MRI confirming superficial non muscle invasive disease.

20 of 32 (63%) patients with stage PT1 carcinoma showed the positive inchworm sign in the DW-MRI confirming superficial non muscle invasive disease.

DCE-MRI time-intensity curves produced three types of curves. Grade 3 curve [29/50 patients (58%)]. Grade 2 curve [15/50 patients (30 %)]. Grade 1 curve (6/50 patients 12%). Grade 1 curve only identified in patients with low grade urinary bladder carcinomas (40%). Grade 3 curve mostly identified in high grade carcinomas (68.6 %).

As regards DW-MRI, all 50 carcinomas (100%) were detected as high signal intensity relative to the surrounding structures. ADC values of UB carcinomas were measured & compared with the pathological tumor grades revealing 40/50 (80%) of patients were correctly graded, 6 patients (12%) were over-graded & 4 patients (8%) were under-graded.

ADC values were significantly lower in high-grade (median 0.73×10^{-3} mm^2/s) than in low-grade carcinomas (median 1.24×10^{-3} mm^2/s); (P1<0.001 & P2<0.001 & P3<0.001 & P4<0.001)

ADC values were significantly lower in higher stage carcinomas # stage T1 (median 0.70×10^{-3} mm^2/s) than in superficial stage T1 carcinomas (median 0.97 ×10^{-3} mm^2/s); (P<0.001, denoting statistical significance between the higher tumor stages and their lower ADC values). (Figures 1 & 2)

A receiver operating characteristics (ROC) curve based on the ADC values demonstrated an excellent AUC of 0.996. A cut-off ADC value of # 1.36×10^{-3} mm^2/s best differentiated normal bladder wall from urinary bladder carcinoma with a sensitivity of 98%, a specificity of 94%, PPV of 94% and NPV of 97%. (Figure 3).

A receiver operating characteristics (ROC) curve based on ADC values demonstrated a perfect AUC of 1.000. A cut-off ADC value of < 1.012 ×10^{-3} mm^2/s best differentiated high grade from low grade carcinomas with a sensitivity of 100 %, a specificity of 6.7%%, PPV of 71 % and NPV of 100%. (Figure 4)
The extent of agreement between the radiologic staging and histopathological staging was relatively greater with the DW-MRI ($r=0.669$) than DCE-MRI ($r=0.619$). Diagnostic accuracy of DW-MRI for local (T) staging found to be 76.7% & staging accuracy of DCE-MRI found to be 73.3%. The overall diagnostic accuracy of DWI (ADC criteria) tumor grading was found to be 80%.
Fig. 1: Box plots show comparison between the studied cases according to the ADC values of urinary bladder carcinomas (high & low grades), the normal bladder wall and urine.

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**Fig. 2:** Box plots show the comparison between the measured ADC values & their corresponding pathological stages (stage #T1 and higher stages carcinomas #T2)

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Fig. 3: ROC curve for ADC value differentiating low & high grades of urinary bladder carcinomas.

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Fig. 4: 51 years male patient with history of recurrent hematuria. (A) T2 WI showed large solitary papillary mass, seen at the left side of the posterior wall & showing intermediate signal intensity with interruption of the underlying muscle layer. (B) DW-MRI showed restricted diffusion of the mass with intact underlying muscle layer (Positive inchworm sign) is identified on the b1000 DWI. (C) ADC value of the UB mass 1.20, for normal bladder wall 1.24 & urine 3.14 x 10^-3 mm2 sec); ADC mapping consistent with low grade neoplastic process. (D) DCE-MRI showed early enhancement of the mass with intact underlying muscle layer & preserved submucosal linear enhancement (SLE). (E) Time-intensity curve showed grade 2 curve with early enhancement & plateau pattern. (F) Histopathology matched with low grade PT1 T.C.C. ....Multiparametric MRI features of low grade stage T1 non muscle invasive urinary bladder carcinoma. Histopathological assessment showed low grade TCC stage PT1 (non muscle invasive tumor).

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Fig. 5: 67 years male patient with history of hematuria. (A) T1 WI showed multiple large papillary masses, the largest is seen at the posterior wall measuring 3.0 x 3.5 cm & showing intermediate signal intensity. (B) T2WI showed intact underlying muscle layer. (C) DW-MRI showed marked restriction of the mass lesions with no involvement of the underlying muscle layer (Positive inchworm sign) is noted on the b 1000 DWI. (D) ADC values of the UB mass 0.720 - The normal bladder wall 1.68 & urine 3.19 x 10^{-3} mm² sec; ADC mapping consistent with high grade neoplastic process. (E) DCE-MRI showed marked early enhancement of the masses with no involvement of the underlying muscle layer & preserved submucosal linear enhancement (SLE). (F) Time-intensity curve showed grade 2 curve with plateau enhancement pattern.....Multiparametric MRI features of multicentric High grade stage T1 non muscle invasive urinary bladder carcinoma. Histopathological assessment showed multicentric high grade TCC stage PT1 (non muscle invasive tumor).

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Fig. 6: 45 years male patient with history of recurrent hematuria. (A) T1 WI showed flat infiltrating UB mass, seen at the base, trigone & the left lateral wall; measured 5.3 x 1.4 cm & showed intermediate signal intensity. (B) T2WI showed involvement of the underlying muscle layer by the mass lesion. (C) DW-MRI showed marked restriction of the mass lesion with involvement of the underlying muscle layer. (D) ADC values of the UB mass 0.582 - The normal bladder wall 1.66 & urine 2.75 x 10^-3 mm2 sec; ADC mapping consistent with high grade neoplastic process. (E,F) Bilateral enlarged restricted iliac lymph nodes are noted measuring 2.6 x 1.4 cm & showing ADC values 0.701; suggesting metastatic LNS. (G) DCE-MRI showed marked enhancement of the mass with focal involvement of the underlying muscle layer. (H) Time-intensity curve showed grade 3 curve with early enhancement & wash out pattern..... Multiparametric MRI features of High grade stage T2 N2 muscle invasive urinary bladder carcinoma with metastatic LNS. Histopathological assessment showed high grade TCC stage PT2 N2 (muscle invasive tumor with metastatic LNS).

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Fig. 7: 62 years male had history of recurrent hematuria. (A) T1 WI showed multiple fungating UB masses, the largest is seen at the base measuring 2.9 x 2.9 cm showing intermediate signal intensity & perivesical extension. (B) T2WI showed focal interruption of the hypointense muscle layer, involvement of the left seminal vesicle & the prostate. (C) DW-MRI showed marked resriction of the mass lesions with involvement of the underlying muscle layer, left seminal vesicle & prostatic involvement. (D) ADC values of the UB mass 0.539 - The normal bladder wall 1.89 & urine 2.99 x 10^-3 mm2 sec ; ADC mapping consistent with high grade neoplastic process. (E) DCE-MRI showed marked early enhancement of the mass with involvement of the underlying muscle layer, the left seminal vesicel & the prostate. (F) Time-intensity curve showed grade 3 curve with early enhancement & wash out pattern. No enlarged lymph nodes….Multiparametric MRI features of High grade stage T4aN0 multicentric muscle invasive urinary bladder carcinoma. Histopathological assessment showed multicentric high grade TCC stage PT4aN0 (muscle invasive tumor).

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**Fig. 8:** 50 years male patient having with history of hematuria & frequency. (A) T1 WI showed multiple papillary masses seen at the base & posterior wall; the largest is measuring 2.9 x 4.0 cm & showing intermediate signal intensity. (B) T2 WI showed no interruption of the underlying muscle layer. (C) DW-MRI showed marked restriction of the mass lesions with no involvement of the underlying muscle layer. Positive inchworm sign is identified. (D) ADC values of the UB mass 1.24 - The normal bladder wall 1.65 & urine 3.04 x 10^{-3} mm^2 sec; ADC mapping consistent with low grade neoplastic process. (E) DCE-MRI showed early enhancement of the masses with no involvement of the underlying muscle layer & preserved submucosal linear enhancement. (F) Time-intensity curve showed grade 1 curve with progressive enhancement pattern. (G) Histopathological slides confirmed low grade TCC PT1…. Multiparametric MRI features of multicentric low grade stage T1 Non muscle invasive urinary bladder carcinoma. Histopathological assessment showed multicentric low grade TCC stage PT1 (non muscle invasive tumor).

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Conclusion

MRI is an effective tool for determining T stage and histological grade of urinary bladder cancers. Results were more accurate when both DW-MRI including ADC and DCE-MRI were used together and hence a combined approach is suggested.
References


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