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# Diagnostic Value of Diffusion-Weighted MR Imaging in Differentiating T- Stage of Urinary Bladder Cancer: With Histopathological Correlation

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**Abstract**

Urinary bladder cancer is the second most prevalent kind of cancer affecting the urinary tract. Magnetic resonance imaging (MRI) is a useful imaging modality for the radiological examination of the urinary bladder and the prostate gland because of its high tissue contrast, multiplanar imaging capabilities, and the potential of tissue characterisation. The purpose of this research was to examine the relationship between the apparent diffusion coefficient (ADC) and the histologic grade of bladder cancer and to assess the use of DW-MRI as a staging tool for this disease. Thirty individuals with bladder mass were included in this trial. It was discovered that DWI has a higher overall accuracy (stage by stage) than T2WI and post contrast image (83.3% vs. 56.7% and 42.9%, respectively). In low grade tumours, the mean ADC value is high, whereas in high grade tumours it is low, with a cut off value of 0.83 mm2/s x10-3. Our research led us to the conclusion that DW-MRI is a reliable and secure tool for detecting and locally staging urinary bladder cancer. The histological grade of a tumour may be predicted using the ADC value as well. As a result, DWI may become a standard procedure for imaging malignancies in the urinary bladder.

**Keywords:** Bladder Cancer, DW-MRI, post contrast MRI

## 1. Introduction

Urinary bladder cancer is the second most frequent kind of genitourinary cancer. With its excellent tissue contrast, multiplanar imaging capabilities, and potential for tissue characterisation, magnetic resonance imaging (MRI) is a useful imaging modality for the radiological examination of the urinary bladder and prostate gland [1].

Differentiating between muscle-invasive and superficial tumours (stage T1 or below) is crucial for clinical therapy of urinary bladder cancer (stageT2 or higher). Significant differences exist between treatment choices for stages 1 and 2. [2].

Therefore, if preoperative imaging tests could be utilised to accurately distinguish between the two types of bladder cancer, they would serve a significant diagnostic function [3].

With no ionising radiation involved, dynamic magnetic resonance (MR) imaging was thought to be a more effective and safer diagnostic technique than contrast enhanced CT for staging of bladder cancer [4].

Over-staging, however, has been proven to be a typical issue with the use of dynamic MR imaging. Nephrogenic systemic fibrosis is one potential side effect of contrast media (NSF). Though transurethral endoscopic ultrasonography (TUEUS) may be a less invasive option for locoregional staging, it is still an invasive technology [5].

Diffusion-weighted imaging (DWI) has been more popular for the assessment of different abdominal lesions in recent years. High tissue contrast versus a normally subdued background signal allows this method to clearly outline pathogenic lesions. According to certain studies, the apparent diffusion coefficient (ADC) value may be used to objectively differentiate malignant from benign lesions [3].

The study's goal is to examine the relationship between the apparent diffusion coefficient (ADC) and histologic grade in order to prospectively assess the value of diffusion weighted magnetic resonance imaging (DW-MRI) in diagnosing the T stage of bladder cancer.

## 2. Patients And Method

**Type of study:**

This prospective, non-controlled diagnostic accuracy study was carried out on thirty patients presenting with urinary bladder masses or wall thickening to the urology clinics in New Cairo police hospital.

**We exclude patients with following properties:**

Impaired renal function (serum creatinine > 2 mg/dl), Contraindications to MRI (e.g. caustrophobia and metallic implants…), and patient with masses or wall thickening proven to be benign by histopathology.

The study was conducted in accordance with Helsinki Standards as revised in 2020 [6]**.** After obtaining the approval from the local ethics committee, Faculty of Medicine, Benha University. The included cases were voluntirly give written informed consent.

**Patients were subjected to the following:**

**1- Imaging assessment:**

The exam was done in radiology departments of benha university hospital and radiology department of new cairo police hospital using Siemens Magnetom aera 1.5-T MRI machines in both departments.

**A- Protocol include**

- Axial T1WIs,T2WIs and STIR
- Coronal and sagittal T2WIs
- DW images will be obtained in the axial and sagittal planes.
- ADC value map will be obtained with ( B values 0 and 500 and 1000 s/mm$^2$).

- In most of the patients (28 patients), Gadolinium enhanced T1WIs were obtainned in axial, coronal and sagittal planes.
- The ADC map images were sent to the work station to calculate the ADC value.
- parameters of the sequences

**Table( 1)** showed the parameters of the MRI protocol used in the current study

| Parameter setting at 1.5 T | T1WI SE | T2WI | DWI |
|---|---|---|---|
| TR (ms) | 450-640 | 4600-8200 | 2400-4700 |
| TE (ms) | 8.9 | 120 | 75 |
| Flip angle (degree) | 180 | 90 | 90 |
| FOV (cm) | 40 | 23 | 25-33 |
| Matrix | 214 x 256 | 256 × 189–256 | 128 × 109 |
| Slice thickness (mm) | 5 | 4 | 4 |
| Slice gap (mm) | 1.25 | 0–0.4 | 0–0.4 |
| Number of Slices | 25 | 19-24 | 19-24 |
| b values | | | 0–500–1000 |

**B- Staging:**

According to Takeuchi et al., [5] we use the following MRI DW imaging staging

Stage T1: A thin, flat, high SI area corresponding to the tumor or a high SI tumor with a low SI submucosal stalk or a thickened submucosa .

Stage T2 : A high SI tumor without a submucosal stalk and with a smooth tumor margin.

Stage T3 : Extension into the perivesical fat with an irregular margin.

Stage T4 : Extension into adjacent organs .

The MR images were assessed by two consultants (15- and 10-years experience in MR interpretation) and one specialist (5years experience) radiologists in a double-blind manner and the staging of the tumor according to T2WIs, DWIs and T1WIs post contrast (if present) were obtained. The ADC value was also calculated for each case. The staging was accepted if it is approved by atleast two of the observers

**2- Histopathological correlation:**

- All the patients were underwent histopathology for their masses either after cystoscopic biopsy or radical cystectomy (According to indicated proper treatment for the estimated tumor stage ).
- The T2WIs and T1WIs pos contrast MRI and the histopathological findings were compared with the DWIs findings. The calculated ADC values were correlated the tumor grade.

**Statistical Analysis**

The following statistical methods were used for analysis of results of the present study. Data were checked, entered and analyzed using SPSS version 13 for data processing and statistics.

Data were expressed as number and percentage for qualitative variables and mean ± standard deviation for quantitative one. the threshold of significance was fixed at 5% level (P-value).

**3.Results**

This study included 30 patients with bladder mass. They were 21 males (70%) and 9 females (30%). Their ages ranged from 52 to 70 years (64.1± 32).

**Table (2)** showed the tumor staging by the different MR sequences (T2 WI, DWI and T1WIs pos contrast) and the histopathology

| | T2 weighted(30) | | post contrast MRI (28) | | DWI (30) | | Tumor histopathology stage (30) | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % |
| ≤T1 | 8 | 26.7 | 8 | 28.6 | 11 | 33.7 | 10 | 33.3 |
| T2 | 15 | 50 | 14 | 50 | 15 | 50 | 14 | 46.7 |
| T3 | 7 | 23.3 | 6 | 21.4 | 4 | 16.3 | 6 | 20 |
| T4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

In present study all patients (30) undergoing T2WI weighted, DWI and Histopathology. Only 28 patients undergoing post-contrast MRI.

**Table (3)** Comparison between DWI Staging and histopathological staging of the urinary bladder tumors on a stage-by-stage basis

| DW imaging stage | Histopathology stage | | | | |
|---|---|---|---|---|---|
| | ≤ T1 | T2 | T3 | T4 | Total |
| ≤ T1 | 9 | 2 | 0 | 0 | 11 |
| T2 | 1 | 12 | 2 | 0 | 15 |
| T3 | 0 | 0 | 4 | 0 | 4 |

| | | | | | |
|---|---|---|---|---|---|
| T4 | 0 | 0 | 0 | 0 | 0 |
| Total | 10 | 14 | 6 | 0 | 30 |

**Table (4)** Accuracy of staging tumors ≤ T1 by different imaging sets

| | **T2 Weighted** | | **DWI** | | **post Contrast- Enhanced** | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | **No.** | % |
| Accurate staging | 4/10 | 40 | 9/10 | 90 | 4/10 | 40 |
| Over staging | 6/10 | 60 | 1/10 | 10 | 6/10 | 60 |
| Under staging | 0 | 0 | 0 | 0 | 0 | 0 |

This table showed that DWI is more accurate than T2 WI and post contrast image in staging superficial bladder tumors (≤ T1), 90%, 40% and 40% respectively).

**Table (5)** Accuracy of staging tumors T2 by different imaging sets

| | **T2 Weighted** | | **DWI** | | **post Contrast- Enhanced** | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | **No.** | % |
| Accurate staging | 10/14 | 71.4 | 12/14 | 85.7 | 6/14 | 42.9 |
| Over staging | 0/14 | 0 | 0 | 0 | 5/14 | 35.7 |
| Under staging | 4/14 | 28.6 | 2/14 | 14.3 | 2/14 | 14.3 |

DWI was more accurate than T2 WI and post contrast T1WIs image in the staging T2 bladder tumors, 85.7%, 71.4% and 42.9% respectively).

**Table (6)** Accuracy of staging tumors T3 by different imaging sequences

| | **T2 Weighted** | | **DWI** | | **post Contrast- Enhanced** | |
|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | **No.** | % |
| Accurate staging | 3/6 | 50 | 4/6 | 66.7 | 2/6 | 33.3 |
| Over staging | 0 | 0 | 0 | 0 | 0 | 0 |
| Under staging | 3/6 | 50 | 2/6 | 33.3 | 4/6 | 71.4 |

This table showed that DWI and T2 WI were more accurate than post contrast TWIs image in staging T3 bladder tumors, 66.7%, 50%and 33.3% respectively).
The over all accuracy (stage by stage) of the DWIS in the tumor stagning was much better than T2WI and post contrast T1WIs image, 83.3%, 56.7% and40% respectively.

**Table (7)** Overall Accuracy stage by stage

| **Image** | **Accuracy** | **Percent %** |
|---|---|---|
| T2 WI | 17/30 | 56.7 |
| DWI | 25/30 | 83.3 |
| Post Contrast- Enhanced | 12/28 | 42.9 |

**Table (8)** ADC values and histopathological grade correlation

| | **Low grade(G1) tumors** | **High grade(G2, G3) tumors** | **P value** |
|---|---|---|---|
| Mean$x10^{-3}$ $mm^2/s$ ± SD | 0.97 ± 0.04 | 0.71 ± 0.03 | 0.0001 |

This table shows that mean ADC value iswas significantly higher in low grade tumors compared to the high grade tumors (P value 0.0001).
The ROC curve analysis revealed cut off ADC value of 0.83 $mm^2/s$ $x10^{-3}$ at a highest specificity and sensitivity of 100% for each. Area under the curve (AUC) =0.83

**Table (9)** Cut off ADC value between low grade (G1) and high grade (G2, G3) tumor

| | **Cut off value (b=1000 $s/mm^2$)** | **Sensitivity** | **specificity** | **P value** |
|---|---|---|---|---|
| Low grade VS high gradeBenign | 0.83 | 100.0 | 100.0 | 0.001 |

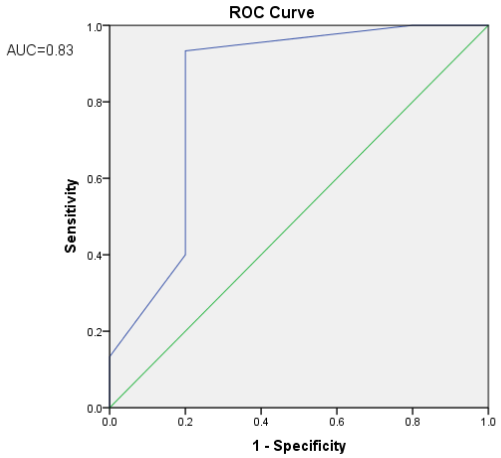


**Fig. (1)** ROC curve for Cut off value between low grade (G1) and high grade (G2, G3) tumor

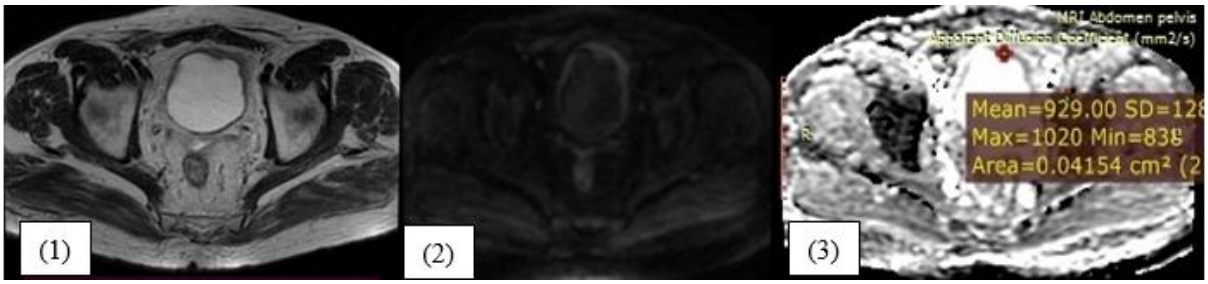


**Fig. (1,2 and 3)** Male patient aged 56 years old diagnosied with Transitional cell carcinoma, staged T1, low grade (G1) (1) Axial T2-weighted images, shows polypoidal soft tissue mass lesion is seen involving the left anterolateral wall of the urinary bladder measuring about 1 cm in maximum diameter. The mass with intermediate SI infiltrating the hypo intense line of muscle layer at base of the mass denoting (Stage T2). (2)DW images, shows soft tissue mass lesion showed evidence of restricted diffusion evident by high signal intensity in the diffusion weighted images and urinary bladder walls are seen clearly identified with no disruption denoting stage (T1). (3)ADC value, was 0.93 $x10^{-3}$ $mm^2/s$ denoting low grade (G1) tumor.

## 4. Discussion

A staggering three to four times more frequent in males than women, bladder cancer ranks as the fourth most common cancer in men in the United States [7].

Traditional methods of detecting and staging bladder cancer include a cystoscopy and biopsy. Its drawbacks include of its invasive nature, its inability to diagnose flat lesions, and its inability to evaluate extravesical invasion of bladder cancers. Those two men, Amin and Abd El Hamid [8].

MRI has the potential to provide more accurate bladder cancer staging than other imaging modalities because of its low radiation exposure, high spatial resolution, high soft tissue contrast, multi-planar imaging, and functional imaging capabilities, including diffusion-weighted MRI (DWI) and dynamic-contrast enhanced MRI (DCE-MRI) [7].

Our research aimed to correlate the computed ADC value with the histologic grade of urinary bladder cancer to determine the use of diffusion-weighted magnetic resonance imaging (DW-MRI) in staging this disease.

There were few publications in the literature assessing the usefulness of DWI for the detection of bladder malignancies. The ADC value of bladder malignancies has been found by Matsuki et al. to be lower than that of the normal bladder wall, the prostate, and the seminal vesicles [9].

Thirty patients were enrolled in the present investigation, and their ages varied from 52 to 70. Urinary bladder tumours are more common in those over the age of 50, as reported by Rozanec [10].

Our findings corroborated those of Wong-You-Cheong et al. [11], who found a ratio of 3:1 for urinary bladder carcinoma, showing a higher incidence of the disease in men than females (2.4:1).

The total effectiveness for all kinds ranges from 52 to 93% [5].

Post contrast dynamic T1WIs sequences were shown to be 86% sensitive and 84% specific in differentiating between T2 and T3 stages by Tekes et al.[12]. Post-contrast T1WIs performed somewhat poorly in this investigation, with an accuracy of 75% for distinguishing tumours at T1 stage or below from those at T2 stage or above, and 70% for distinguishing tumours at T2 stage or below from those at higher than T2 stage.

For the identification of superficial bladder cancers, El-Assmy et al. [13] showed that DWI had a

sensitivity, specificity, and positive predictive value of 100% in a research including 43 patients.

DWI has a sensitivity and specificity of 90% for detecting superficial bladder cancers, according to our research. Unfortunately, neither El Assmy et al. nor Matsuki et al. evaluated the reliability of DWIs in staging urinary bladder cancer, nor did they compare the reliability of DWIs to that of other MR characteristics (T2WIs and contrast enhanced T1WIs). However, we compared the precision of DWIs to that of T2WIs and contrast-enhanced T1WIs in our prospective analysis, in which all patients were scanned before the biopsy.

In their meta-analysis, Huang et al. [14] analysed data from 1449 individuals with bladder cancer. High diagnostic performance of MR imaging was shown; the sensitivity and specificity were 90% and 88%, respectively, for distinguishing tumours with T1 or lower grades from those with T2 or higher grades. Diffusion-weighted imaging was shown to modestly increase sensitivity and specificity to 92% and 96%, respectively.

According to Kobayashi et al. [15], DWI has greater interobserver agreement and diagnostic efficacy than T2WIs and contrast enhanced T1WIs when it comes to identifying bladder cancer. They hypothesised that the high contrast seen in DWI, where signals of bladder cancer are extremely bright and pictures of adjacent tissues seem muted regardless of tumour location, may be to blame.

In the present investigation, bladder carcinomas were shown on DWI in all patients (100 percent), but on T2WIs and post contrast MRI images in only 24 of 30 patients (80%).

T2WIs alone, as validated by Takeuchi et al.[5], had the lowest accuracy (67%) in diagnosing the T stage of bladder cancer. In addition, the diagnostic efficacy of T2 weighted plus contrast enhanced and diffusion weighted imaging was 92%, higher than that of T2 weighted plus DWI (88%) and T2 weighted plus contrast enhanced (79%). Our findings were consistent with the above three research.

Accuracy of DWI for identifying particular tumour stages has been reported by El-Assmy et al. [13]. DWI was reported to have an accuracy of 63.6%, 75.7%, 93.7%, and 87.5% for diagnosing tumour stages T1, T2, T3, and T4, respectively.

According to Abdel-Rahman et al. [16], DWI's accuracy in tumour staging ranged from 85.7% to 77.8% to 50% across stages T1 and T3.

In comparison to El-Assmy et al.[13] and Abdel-Rahman et al. [16], the present study's findings indicated considerably better accuracy for T1 and T2 staging, at 90% and 85.7% respectively, and accuracy for T3 staging, at 66.7%.

In order to evaluate the pathophysiological features of bladder cancer, tissue Apparent Diffusion Coefficient (ADC) quantification has been more popular in recent years. Cancerous tissues may be distinguished from benign ones by using ADC, as established by previous research of Avcu et al [17].

When comparing tumours of different grades, high-grade tumours were shown to have much lower ADC levels Kobayashi et al [15].

Urinary bladder tumours had lower ADCs than their surroundings, according to research by Al Johi et al.[2].

The average ADCs we found were 0.97 x 10-3 mm2/s, 0.71 x 10-3 mm2/s. Specifically, 0.83 mm2/s x10-3 for tumours in the G1 phase and (G2& G3).

This is consistent with the findings of Settein et al. [4], who used DW-MRI for T-stage prediction and ADC for tumour grade prediction. High-grade cancers have lower average dilution coefficients (ADC). With an ADC cutoff value of 0.95 103mm2/s, grade III lesions were shown to have significantly lower ADC values compared to grades I and II.

In addition, Al Johi et al.[2] found that a threshold ADC value of 0.9 x 10-3 mm2/s could distinguish high-grade from low-grade cancers with a sensitivity of 94.5% and a specificity of 87.5%.

Sherif also observed an inverse correlation between ADC readings and tumour grade [3].

Although their sensitivity and specificity (94.1% and 95.7%, respectively) were close to ours, Avcu et al. (2) reported a higher cut-off ADC value (1.5 x 103 mm2/s) than ours.

**5.Conclusion:**

It is our opinion that DW-MRI is a reliable and secure tool for detecting and locally staging urinary bladder cancer. The histological grade of a tumour may be predicted using the ADC value as well. As a result, DWI may become a standard procedure for imaging malignancies in the urinary bladder.

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