Cohort Study

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Recent advances in three-dimensional ultrasound virtual cystoscopy in modeling and local staging for urothelial carcinoma with histopathological correlation: a cohort prospective study

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Background: Bladder urothelial carcinoma is an alarming urologic malignancy. Complex factors like modelling and local staging can affect treatment strategy. However, local staging, particularly the muscle invasion status, significantly influences decisions regarding treatment strategies. Therefore, this study aims to evaluate the novel advances of three-dimensional (3D) ultrasound (US) imaging to assess local staging in comparison with conventional cystoscopy.

Methods: Forty-three patients with painless haematuria and conventional cystoscopy findings of bladder mass underwent 3D US virtual cystoscopy. All specimens from conventional cystoscopy were processed histologically.

Results: Out of 43 participants, 18 (41.9%) patients proved to have invasive urothelial carcinoma by histopathology. The 3D US had a sensitivity of 97.5% and a specificity of 100%; however conventional cystoscopy was accurate in only 53.5% of the studied cases. Furthermore, in the case of malignant ulcers, mural extension into both the submucosal and the muscle layers was more readily appreciated in multiplanar images.

Conclusion: 3D US updates are promising for use in bladder tumour modelling and local staging; however, they can be of value in evaluating mural and extramural tumour extent and have proven accuracy.

Keywords: histopathology, local staging, teleradiology, three-dimensional ultrasound, urothelial carcinoma, virtual cystoscopy

Introduction

Urothelial carcinoma (UC) is the most common histologic subtype of urinary bladder cancer; however, accurate local staging of these tumours is crucial for the best management. Traditionally, local staging relied on a biopsy obtained during conventional cystoscopy (CC), representing the gold standard for diagnosing and managing some bladder carcinoma cases with a reported sensitivity of 87% in detecting bladder neoplasm. Its notable disadvantage is the lack of information about the mural and the extravesical extensions[1,2].

Conventional ultrasound (US) is usually the initial examination requested in cases of painless haematuria; however, it showed poor diagnostic value (from 26 to 80%) in the mapping of the bladder wall or the evaluation of extravesical mass extension[3].

However, with the increasing accuracy of the computed diagnostic modalities and techniques, other imaging modalities, such as multi detector CT and MRI, play an essential role in the multidisciplinary care of patients with this disease[4].

As an office-based modality, the latest three-dimensional (3D) US updated technology would be emerging as a noninvasive imaging procedure for evaluating urinary bladder neoplasia to visualize the bladder cavity, urinary bladder wall-layers, and

HIGHLIGHTS

- Local staging of bladder cancer influences decisions regarding prognosis and treatment strategies.
- Forty-three patients were examined by conventional cystoscopy, three-dimensional virtual cystoscopy and histopathology.
- Three-dimensional ultrasound shows promising results having a sensitivity.

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extravesical environment, which mainly depends upon the updates in the beam-former, which enable the US transducer beam to be focused with greater precision. This technology will produce less noise and better contrast resolution[3,4].

Consequently, an image of the entire structure can be produced, sliced, rotated through different planes, and viewed from many angles. It is possible for the operator to 'peel away' layers of a 3D image by using the cut mode to see the mass extension into the urinary bladder wall or its extension into the extravesical environment. Moreover, the entire volume can be stored and reviewed by the operator and other staff after the examination[5]. Moreover, this approach is highly applicable to the urinary bladder, owing to its small volume, simple luminal morphology, and absence of peristalsis, which may make it an ideal intra-abdominal organ for 3D US virtual endoscopic navigation (Fig. 1), as there is a considerable contrast gradient seen between the bladder lumen and its wall. Herein, the surface rendering algorithm can usually display sufficient detail of the urinary bladder cavity and wall, revealing a cystoscopy-like image. Furthermore, this would help in more accurate staging and overcome the low sensitivity of conventional US, which would influence decisions regarding treatment strategy.

The main aim of this research was to evaluate the potential value of the recent advances in the office-based 3D US virtual cystoscopy (VC) in modelling and staging bladder tumours in comparison with conventional cystoscopy with a correlation to the final histopathology report.

Patients and methods

This work is a prospective collaboration agreement study between the urology, uroradiology, and histopathology departments that had the approval of institutional ethics committees. Our study involved 43 patients, including 36 males and seven females, aged 36–72 years old, referred to the diagnostic imaging department from the outpatient urology clinic at Al-Azhar University Hospital from January to October 2021. All patients were referred clinically with haematuria and bladder masses, including dysuria in four patients. The evaluation of general and local examinations of all patients, included previous medications, and full laboratory reports, including urine analysis and renal function tests, were obtained. Inclusion criteria include patients attended the hospital during the study period for urinary bladder mass lesions and accepted to participate in the study and managed by the same team. Cystourethroscopy: The KARL STORZ cystoscopy set (Germany) was used. Biopsy specimens were obtained by trans-urethral approach from the urinary bladder tumours through a combined trans-urethral resection bladder tumour using a resectoscope for 37 patients and a cold cup biopsy forceps for 6 patients. The cold cup biopsy forceps was applied to avoid cautery artifact diagnostic challenges in pathology. Multiple bladder biopsies were obtained from various locations in the bladder with presented muscularis propria. Exclusion criteria included all patients with cold cp biopsies lacking muscularis propria and trans-urethral resection bladder biopsies containing marked artifacts seen at pathology examination. All patients were prepared after obtaining complete informed consent and were instructed before our procedure. Anticoagulants and drugs like aspirin were stopped 3–7 days before. However, antibiotic prophylaxis was maintained by quinolones. The first dose (500 mg of ciprofloxacin) was administered intravenously upon initiation of anaesthesia, while the second dose was administered 12 h later. Ten patients were administered general anaesthesia, while the remaining patients (33/43) underwent biopsies under spinal anaesthesia. A video system for documentation of findings was obtained, including inspection of the entire urethra, prostate, and bladder neck, followed by bladder pathology mapping.

3D US imaging

All patients with bladder masses detected by CC were referred within 2–3 days to the Uroradiology Department to identify the morphology and the mural and extramural tumour extent where the 3D US VC was performed on a fairly full bladder (average of 200 ml of urine), mainly to assess the pattern of the intravesical component, the depth of the mass lesion within the urinary bladder wall, and any extravesical extension. The 3D US VC was performed using an up-to-date Resona-6 US machine (USA-China Corporation). If Foley's catheter was inserted and not complicated, we closed it to stop urine flow with a clamp to allow the fair collection of urine within the urinary bladder before our 3D volume acquisition. Otherwise, retrograde filling of the bladder was performed through the catheter. All patients were examined in the supine position.

The study time was 7–10 min. The entire bladder and lesions were scanned with a 3D US volume scan displayed in surface-rendered images in all planes, adjusted in thin tomographic slices, which were necessary to assess the extent of a mass lesion.

All acquired volumes of images, including the whole field, were reviewed in transverse, coronal, sagittal, or free axis planes and surface rendering and then transferred to a nearby workstation and stored for further processing and interpretation.

All images within the volume range were prospectively interpreted blindly and compared to the histopathological results of the cystoscopy biopsy. Each image slice has definite image position information. Reformatted rendered images and volume-free planes (apart from axial, transverse, and oblique planes) were used to detect lesion extensions at the entire bladder layer and extravesical environment. They were used to assess tumour invasion into adjacent structures and assess lymphadenopathy.

The bladder walls were divided into six segments: the anterior, posterior, right lateral, left lateral walls, superior (dome), and inferior (base). The size, location, and morphology of the lesions were assessed.

Computed tomography (CT) and MRI: After the release of the histopathology results, further radiological investigation was conducted for the invasive lesions (18/43), where MRI imaging was performed for 7 patients, and CT examinations were requested for 13 patients (2 patients experienced both CT and MRI investigations) to detect tumour extension and metastasis of the histologically proven invasive tumours with clinical oncology consultation for the metastatic cases. Radiological examination was performed by the authors using remote examination and consultation aided by a teleradiology software system when indicated supervised by a telehealth technology expert.

All surgical procedures were done by the same team with the same level of competence (consultants with >5 years' experience) and the same was assured for the radiological examination of all studied cases.

Table 1

Demographic and morphologic distribution of cases by 3D US VC

Morphological appearance	No. lesions in VC, *n* (%)
Polypoidal mass	0
Sessile mass	38 (88.4)
Malignant ulcer	3 (7.0)
Wall thickening	1 (2.3)
Blood clot	1 (2.3)
Sex	No. patients, *n* (%)
Male	36 (83.7)
Female	7 (16.3)
Age	Mean range
	66.9 (34–77)

3D, three dimensional; US, ultrasound; VC, virtual cystoscopy.

Histopathology

All specimens were obtained during urinary bladder cystoscopy. Sections on hematoxylin and eosin-stained slides were examined histologically, and tumour type and grade were classified according to the WHO (2016) and stage according to American Joint Committee on Cancer guidelines as follows: cases of non-invasive, low-grade UC, and cases of high-grade invasive UC, with different histologic variants.

Data analysis

Cystoscopy is considered the reference standard. We independently completed detailed forms regarding the number and location of bladder tumours found at the 3D US and the biopsy-histopathology results; the latter was blind to the 3D US results. Findings from CC and the 3D US were correlated with histopathology results and with conventional cystoscopy using SPSS version 22, where the frequencies and percentages have been calculated for descriptive variables. A *t*-test was used for correlation. A *P* value of less than 0.05 was considered significant. Estimates for sensitivity / specificity were calculated from the cross tabulation of binary test results and the gold standard. They are presented with the exact 95% CIs. This work comes in line with the STROCSS guidance[6,7].

Results

This study included 43 patients, with 36 males (83.7%) and seven females (16.3%). The patient ages ranged from 34 to 77 years, with a mean of 66.9 years.

The total number of lesions detected by conventional cystoscopy only showed an accurate diagnosis in 23 out of 43 cases (53.4%) correlated with the histopathologic diagnosis performed and confirmed by at least three independent expert histopathologists using a static telepathology technique after quality assurance of the prepared slides done by histologists and pathologists.

The number of lesions according to the morphological description by 3D US VC is listed in Table 1.

Furthermore, of the 43 patients enroled in the study who presented with urinary bladder masses, 17 patients (94.4%) were approved as invasive by 3D US VC; however, out of 18 instances approved by histopathology. In addition, visual invasion evaluation could be demonstrated by 3D US VC, either mucosal or involving both the submucosa and/or the muscle layers, by combining rendered volume images and multiplanar virtual images. Two (11.1%) of 18 invasive bladder neoplasms revealed extravesical extension. One (5.5%) of 18 invasive bladder neoplasms revealed neoplasms smaller than 1 cm, proved mural extension into the submucosal layer by 3D US, and was confirmed by histopathology. Three cases were demonstrated by 3D US VC as malignant ulcers; all of them proved mural extension into both the submucosal and the muscle layers and were more readily appreciated on 3D US multiplanar images (Table 2).

The 3D US had a sensitivity of 97.5% and a specificity of 100%. In 5/43 cases, post-resection oozing (bleeding) was observed; however, after applying adequate haemostasis at the resection site using a ball loop or cauterizing loop, no extensive bleeding was observed.

Figure 1 describes the normal urinary bladder dissection anatomy, as seen by the new advances in 3D US machines. Figure 2 shows a big neoplastic mass of the urinary bladder, limited to the mucosal layer. Figures 3, 4 show different types of malignant bladder masses, ulcers, and variable invasion patterns.

Discussion

Cystoscopy is the primary modality used to diagnose urinary bladder carcinoma cases because it confers low risk by helping the urologist take biopsy specimens and resect papillary-looking tumours during the same procedure. Nevertheless, UC staging is based on how far cancer has penetrated the tissues of the bladder and whether cancer has extended beyond the bladder. The inability of conventional cystoscopic procedures to provide precise visualization of the bladder mass and the degree of mass extension necessitates further support by additional diagnostic modalities[8,9]. However, cystoscopic procedures remain the prevailing standard for mass visualization.

Ultrasonography of the abdomen and pelvis is traditionally the primary radiologic approach to assessing haematuria. However, the sensitivity of the US in detecting bladder tumours is low in some patients with small tumours or sometimes tumours located on the bladder dome or anterior wall[10].

In addition, conventional US is an operator dependent method and occasionally limited in assessing tumour extension and surrounding structures. Although it is helpful in the initial evaluation of haematuria, it is not routinely used at present for the evaluation or staging of UC and 3D US is another operator dependent diagnostic tool but the usefulness of 3D US was demonstrated in a large variety of clinical applications trying to limit the US procedure errors, indicating its role and importance in medical imaging and more accurate diagnosis. Hence, 3D US is necessary

Table 2

Accuracy of the 3D US VC and the histopathological results in the evaluation of mural invasion by the bladder mass

Stage	Cases diagnosed by 3D, n (%)	Cases diagnosed by histopathology, n (%)	*P*
Invasion (stageT1,T2,T3)			< 0.05
Total	17/43 (39.5)	18/43 (41.8)	
Submucosal	10/17 (58.8)	11/18 (61.2)	
Muscle layer	5/17 (29.4)	5 (27.7)	
Extravesical	2/17 (11.8)3	2 (11.1)	
Noninvasion (Ta, Tis)	26/43 (60.5)	25 (58.2)	

3D, three dimensional; US, ultrasound; VC, virtual cystoscopy.

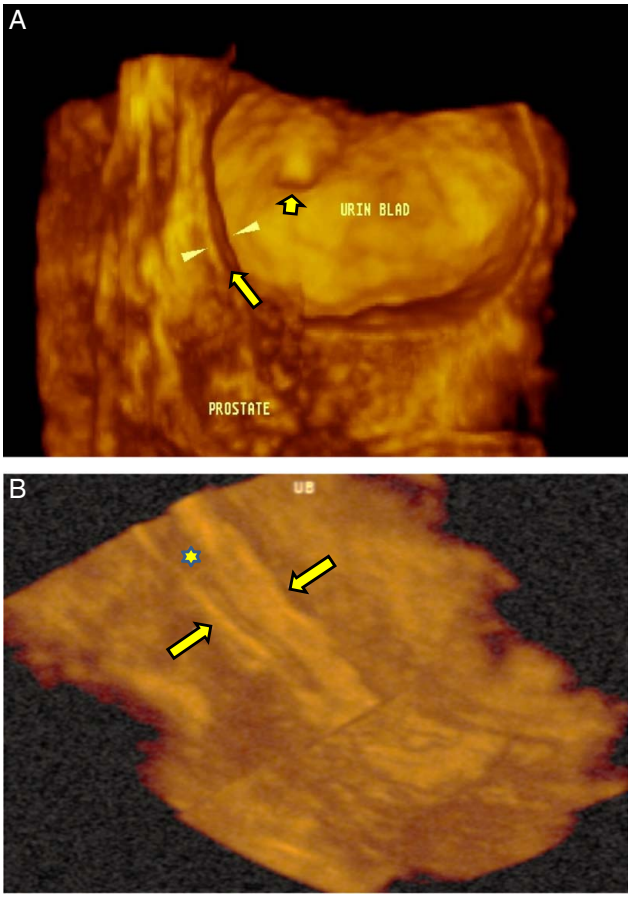

Figure 1. Three-dimensional ultrasound virtual cystoscopy normal anatomy of the urinary bladder (UB), showing its cavity and wall composition details. (A) Arrowheads = mucosal and muscle layers. Arrow = submucosal layer. The right ureteric outlet = short arrow. (B) A magnified image showing the bladder wall-layers. Arrows = mucosal and muscle layers. Asterisk = submucosal layer.

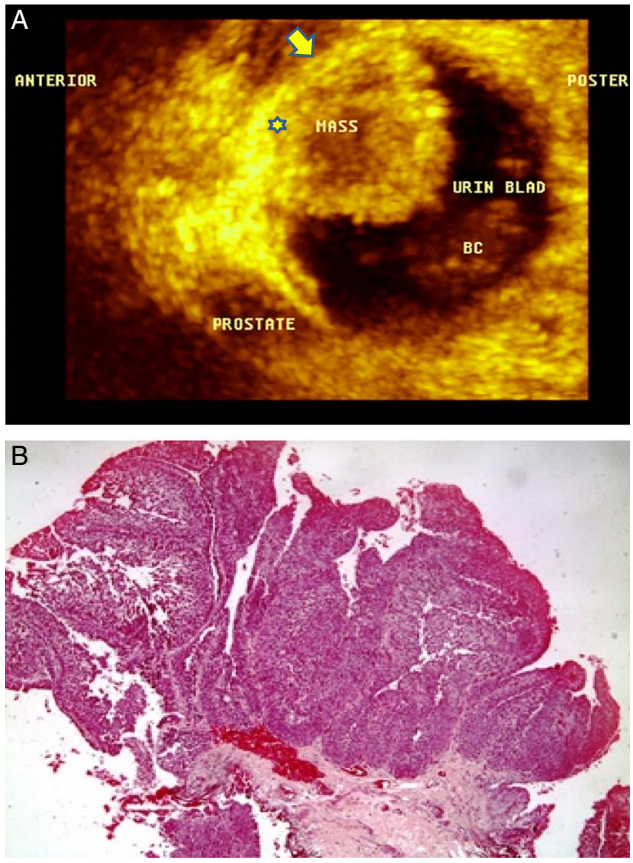

Figure 2. (A) Three-dimensional ultrasound virtual cystoscopy revealing a big mass at the anterior wall of the urinary bladder, limited to the muscle layer, not reaching the submucosal (asterisk) or the muscle layers (arrow), with some blood clots (BC) within the bladder cavity. (B) Low-grade, noninvasive urothelial carcinoma with a mild degree of cellular pleomorphism. (H&E, low power).

for urology to surmount the limitations of conventional (2D) ultrasonography[11,12]. In modern 3D volume transducers, the beamforming is digital, enabling the US beam to focus more precisely. The amount of accurate beam focusing at the correct depth can receive a composite US image from a subject and consequently leads to less noise and better contrast resolution[11]. According to some previously published studies, conventional 2D US imaging tool has been extended to the three-dimensions technique in an attempt to overcome the limitations of the former one and to allow visualization of the actual 3D anatomy with accurate repositioning of the transducer for optimal monitoring of tumour progression and accurate volume delineations and measurements[4,5]. Therefore, the previously published comparative study[13], including the 3D US, multidetector CT, and multiparametric MRI, was mainly concerned with the initial information about the urinary bladder mass, whether invasive or noninvasive.

In this study, we present the recent advances in computed 3D US imaging technology, which would change the main concept of US as an office-based hand-dependent technology regarding lesion detectability and accuracy. Furthermore, 3D US volume rendering and sectional techniques were used for image processing to interpret UC and the degree of mass extension. This approach agrees with most of the authors who preferred utilizing this technique, which provides excellent urinary bladder mass details[14,15]. In addition, the availability of layer peeling and the cut mode in the recent high-technology office-based machines allows accurate estimation of the degree of mass range within the bladder wall and/or the extravesical environment.

The results of previous studies on the 3D US stated that VC allows the assessment of the localization and morphology of bladder masses[9,16]; however, it is less precise than scored in the present study using the new updated technology.

In our study, 35 out of 43 (81.4%) bladder lesions were transitional cell carcinoma. Squamous cell carcinoma ranked second (7 out of 43; 16.3%), followed by an atypical blood clot (1 out of 43; 2.3%). Moreover, 17 cases (39.5%) of the 43 approved mural extensions, while histopathological results reported 18 cases (41.9%). Nevertheless, the ability of 3D US VC in the detection of tumour invasion proved effective in 94.4% of cases compared to histopathological investigations. The 3D US detectability of UC less than or equal to 1 cm was 7%, whereas masses greater than 1 cm were 100%, compared to CC and histopathology. This result is relatively more imposing in accuracy and image quality than reported before.

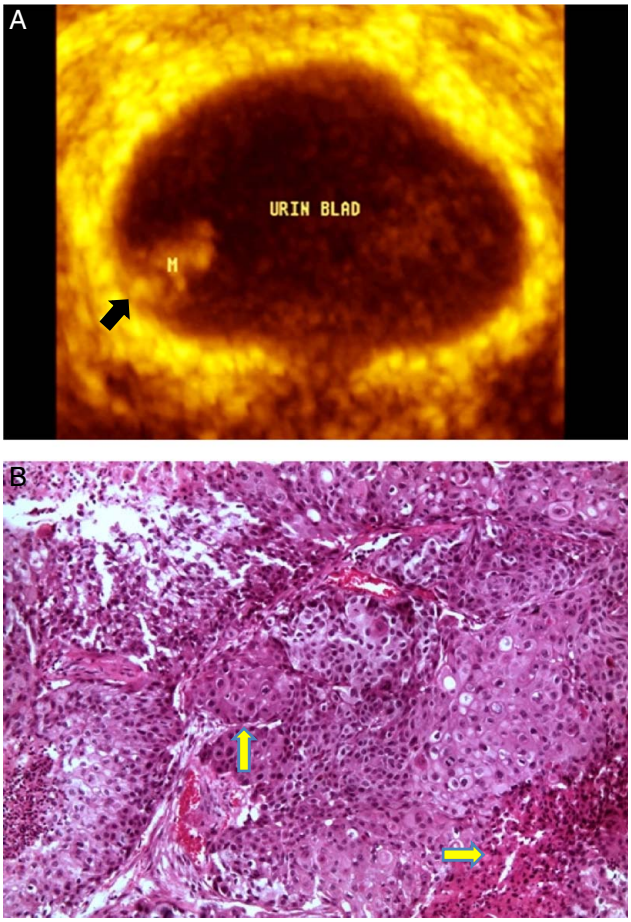

Figure 3. (A) Three-dimensional ultrasound virtual cystoscopy shows a relatively small mass at the right lateral wall of the urinary bladder, which, despite being small, has a central invasion into the submucosal layer (arrow). (B) High-grade urothelial carcinoma with squamous differentiation and tumour cell necrosis (arrows) (H&E).

Formerly, Abrol *et al.*[17] found that combining evaluated virtual rendered images with multiplanar images could provide valuable information for the mural and extraluminal mass extensions, such as mural and extravesical invasion, distal ureteral obstruction, and pressure of the neighbouring organs.

However, Vernuccio *et al.*[4] in 2021 agreed that 3D US VC is a valuable screening tool that can direct the surgeon to an appropriate area for biopsy. If normal, it may obviate the need for conventional cystoscopy and biopsy and could be helpful for the surveillance of known tumours.

On the other hand, two studies on multi detector CT ($n = 20$ and $n = 121$) comparing the urothelial and excretory phases of patients with confirmed urinary bladder cancers revealed that during the excretory phase, the intraluminal contrast material could obscure the small tumours and prevent evaluation of early tumour enhancement in dedicated urothelial phases[6,7]. The unenhanced phase is used to detect high-attenuation calcifications, stones, and blood clots. When the bladder is not filled with contrast material, a thin and enhancing bladder wall can be appreciated against low-attenuation urine in this urothelial phase. In detecting primary and recurrent urothelial carcinomas, CT urography has been reported to have an accuracy as high as 95% regarding local staging[18–20].

Multiparametric MR urography, on the other hand, is increasingly being used for staging bladder UC. MRI's high spatial resolution and soft-tissue contrast can make it possible to delineate tumours from the normal detrusor muscle of the bladder wall. Most of the references concluded that MRI is considered the imaging modality of choice in the local staging of UC, having an accuracy of 94% up to 98% in advanced stages[20,21]. Its high spatial resolution with soft-tissue contrast makes it capable of distinguishing the neoplastic process from the normal detrusor muscle of the urinary bladder wall. MRI has better diagnostic accuracy for diagnosing perivesical tumour involvement than CT.

According to our research, VC has numerous advantages. First, it is inexpensive, office-based, and proven superior in evaluating the mucosal surface of the bladder helping the operator to navigate the mucosal surface, submucosal and muscle layers, and the extravesical environment in various projections and provide interactive navigation, allowing the urosurgeon to make more confident decisions in the same setting. Second, its capability for the local staging of UC, 3D US VC can be used as a diagnostic investigation for evaluating the entire urinary tract and bladder, according to our practice. Third, 3D US VC needs short training for those interested in the field to improve the value of conventional US images and allow the utilization of the most extensive workstation data. Finally, 3D US VC helps assess urinary bladder areas that are difficult to determine using conventional cystoscopy, such as the anterior bladder neck and sometimes the bladder base.

Therefore, 3D US VC can play an essential role in the local staging of UC, having the advantages of being an office-based machine and being inexpensive to examine. Even though CT and MRI remain preferable modalities for diagnosing and staging UC in some centres, both have been increasingly used in local staging. However, machines' progress in differentiating early tumour stages remains challenging.

The bladder cold cup biopsies are usually 2–3 mm in diameter and can contain up to superficial parts of muscularis propria depending on anatomical part of the urinary bladder and the operator skill[22]. However Invasive urothelial carcinoma may present (cystoscopically and grossly) as a polypoid, sessile, ulcerated fungating and/or infiltrative lesion[23,24], Histopathological examination still the cornerstone in reaching out the most accurate diagnosis[22,25]. Different histological tumour types were reported according to the 2016 WHO[26], urinary bladder tumours classification by the authors histopathologists the correlated with the radiological features.

On histopathology, there are four defined layers for the urinary bladder wall: the urothelium (lines the bladder lumen); submucosa (the vascular lamina propria); the muscularis propria (important prognostic landmark if the tumour invades) ; and the outermost serosal[27,28].

On the imaging, three separate bladder wall-layers might be seen: the inner layer (including the mucosa and the submucosal layers together); the muscularis propria; and the perivesical fat, where the tumour invasion into the muscle may be not accurately seen[10,29].

The 3D sonography appears comparable to CT scans and MRI using in providing VC for investigating and evaluating bladder cancer.

The drawbacks and limitations of such a study include that cases in the present study were primarily subjected to conventional cystoscopy and received to evaluate tumour modelling and staging; second, adequate bladder filling was essential to evaluate the depth of the bladder wall invasion; and third, 3D US cannot

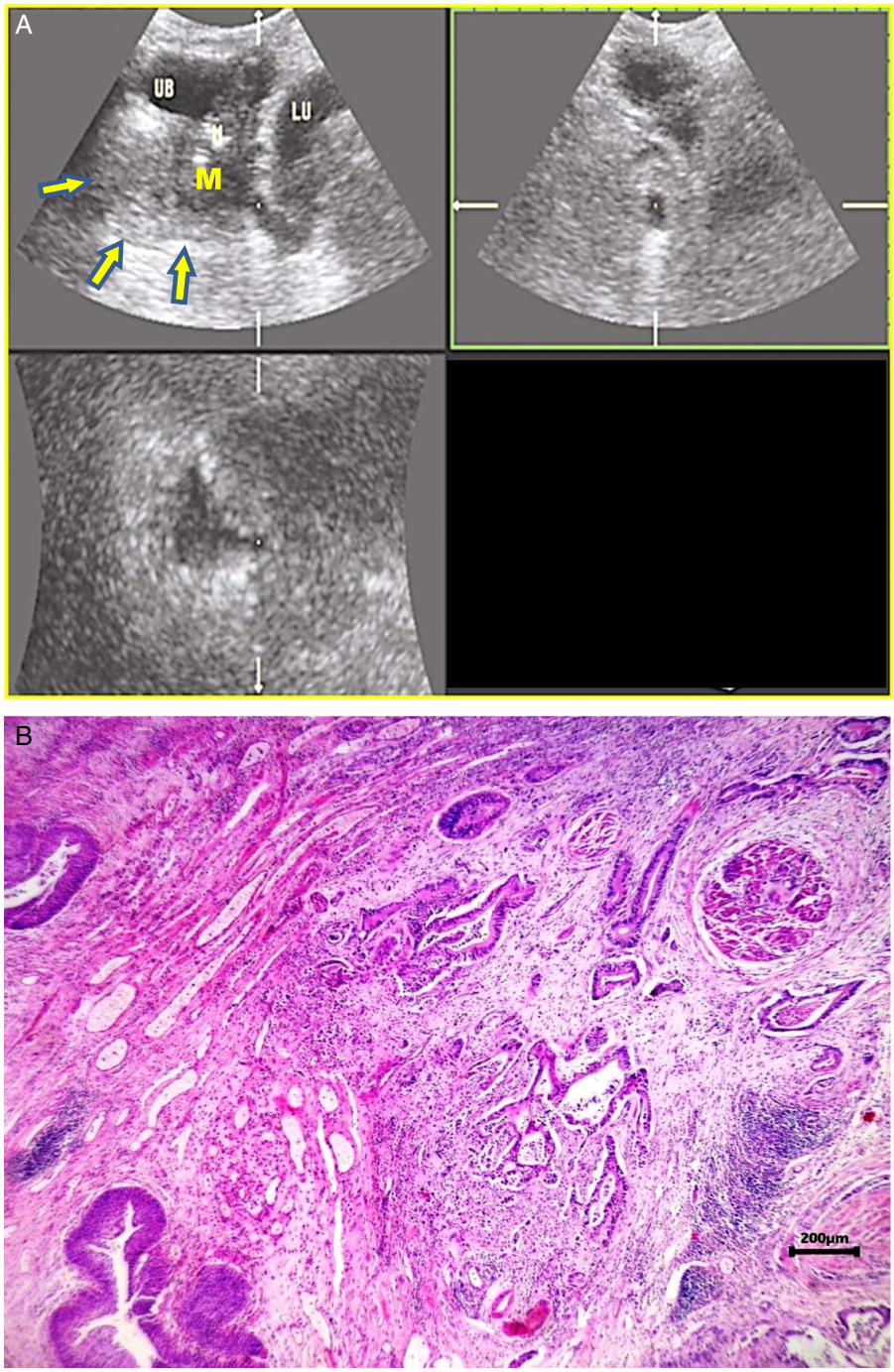

Figure 4. (A) Three-dimensional ultrasound free axis thin sectional planes showing the urinary bladder cavity (UB) and the left ureter (LU) in one plane, demonstrating an infiltrative bladder mass (M), having a relatively large extravesical exophytic extension (arrows) and significant infiltration and permeation into the left ureter. (B) High-grade invasive urothelial carcinoma infiltrating the muscle layer (H&E).

take tissue biopsy for histopathologic assessment, an ability that is available on conventional cystoscopy. The number of participants in this study was small; however, more participants in multicentered studies are highly recommended for the future studies with comparing results between the different teams ensuring the same level of competence of each study team.

Conclusion

The results of our study suggest that 3D US VC updates are promising for additional tool used in bladder tumour modelling and local staging, can be of value in evaluating mural and extramural tumour extent, and can be proven accurate.

However, it cannot completely replace conventional cystoscopy, and histopathology is still fundamental for assessing tumour type, grade, and stage. Further multicenter studies with many cases and studying the effect of other factors (such as obesity) are recommended.

Ethical approval

This study was approved by the Ethics Committee of Al-Azhar University, Faculty of Medicine under ID: His_395_Med. Research_00000110.

Consent

Provided.

Source of funding

None.

Conflicts of interest disclosure

The authors certify no conflict of interest.

Research registration unique identifying number (UIN)

None.

Guarantor

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Provenance and peer review

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Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author on reason-able request.

References

[1] Luczak M, Nowak L, Chorbińska J, *et al*. Influence of virtual reality devices on pain and anxiety in patients undergoing cystoscopy performed under local anaesthesia. J Pers Med 2021;11:1214.
[2] Lee Chau Hung, Tan Cher Heng, Faria Silvana de Castro, *et al*. Role of imaging in the local staging of urothelial carcinoma of the bladder. AJR 2017;208:1193–205.
[3] Tawfeek AM, Abd El Fattah DM, Mahmoud A, *et al*. The role of 3-dimensional sonography and virtual sonographic cystoscopy in detection of bladder tumors. Afric J Urol 2018:73–8.
[4] Vernuccio F, Cannella R, Bartolotta TV, *et al*. Advances in liver US, CT, and MRI: moving toward the future. Eur Radiol Exp 2021;5:52.
[5] Martino P, Galosi AB. Practical recommendations for performing ultrasound scanning in the urological and andrological fields. Arch Ital Urol Androl 2014;86:56–78.
[6] Mathew G, Agha R. for the STROCSS Group. STROCSS 2021: Strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery. Int J Surg 2021;96:106165.
[7] Mossanen M, Chang SL, Kimm S, *et al*. Current staging strategies for muscle-invasive UC and upper tract urothelial cell carcinoma. Urol Clin N Am 2018;45:143–54.
[8] Niazi G, Hetta WM. Role of multidetector CT virtual cystoscopy compared to conventional cystoscopy in the diagnosis of urinary bladder neoplasms. Egypt J Radiol Nucl Med 2019;50:77.
[9] Caglic I, Panebianco V, Vargas HA, *et al*. MRI of UC: local and nodal staging. J Magn Reson Imaging 2020;52:649–67.
[10] Galgano SJ, Porter KK, Burgan C, *et al*. The role of imaging in UC diagnosis and staging. Diagnostics 2020;10:703.
[11] Golemati S, Cokkinos DD. Recent advances in vascular ultrasound imaging technology and their clinical implications. Ultrasonics 2022;119:106599.
[12] Huang Q, Zeng Z. A review on real-time 3D ultrasound imaging technology. Biomed Res Int 2017;2017:6027029.
[13] Crozier J, Papa N, Perera M, *et al*. Comparative sensitivity and specificity of imaging modalities in staging UC prior to radical cystectomy: a systematic review and meta-analysis. World J Urol 2019;37:667–90.
[14] Silva-Ramos M, Louro N, Versos R, *et al*. Does 3D ultrasound enhance the diagnosis of bladder tumors in patients with haematuria? Int Sch Res Netw Urol 2012;2012:158437; doi: 10.5402/2012/158437
[15] Rokade Muktachand L. Virtual cystoscopy using 3D ultrasound. J Med Ultrasound 2013;21:146–51.
[16] Mirmomen SM, Shinagare AB, Williams KE, *et al*. Preoperative imaging for locoregional staging of UC. Abdom Radiol 2019;44:3843–57.
[17] Abrol S, Jairath A, Ganpule S, *et al*. virtual cystoscopy replace conventional cystoscopy in early detection of UC? Adv Urol 2015;2015:926590. dio:10.1155/2015/926590
[18] Schoeb DS, Wollensak C, Kretschmer S, *et al*. Ex-vivo evaluation of miniaturized probes for endoscopic optical coherence tomography in urothelial cancer diagnostics. Ann Med Surg 2022;77:103597.
[19] Sim KC, Sung DJ. Role of magnetic resonance imaging in tumor staging and follow-up for UC. Transl Androl Urol 2020;9:2890–907.
[20] Aldesouky AI, Mostafa AM, Ghanem MM, *et al*. Role of multi–detector row ct urography in the evaluation of urinary tract abnormalities. AAMJ 2012;10:2.
[21] Abouelkheir RT, Abdelhamid A, Abou El-Ghar M, *et al*. Imaging of bladder cancer: standard applications and future trends. Medicina 2021;57:220.
[22] Mazzucchelli R, Marzioni D, Tossetta G, *et al*. Bladder cancer sample handling and reporting: pathologist's point of view. Front Surg 2021;8:754741.
[23] Amin MB. Histological variants of urothelial carcinoma: diagnostic, therapeutic and prognostic implications. Mod Pathol 2009;22:S96–118.
[24] Dawood G. Urinary System. Color Atlas of Human Gross Pathology. Springer; 2022;75–91.
[25] Ali MY, Aboelsaad AY, Abdel Gawad AM, *et al*. HER2/neu expression status of post BCG recurrent non-muscle-invasive bladder urothelial carcinomas in relation to their primary ones. Arch Ital di Urol Androl 2023;95:11313.
[26] Moch H, Humphrey PA, Ulbright TM, *et al*. WHO Classification of Tumours of the Urinary System and Male Genital Organs. IARC Press; 2016:78. doi:10.1016/j.eururo.2016.02.029
[27] Verma S, Rajesh A, Prasad SR, *et al*. Urinary bladder cancer: role of MR imaging. Radiographics 2012;32:371–87.
[28] Hasan A, Mohammed Y, Basiony M, *et al*. Clinico-pathological features and immunohistochemical comparison of p16, p53, and Ki-67 expression in muscle-invasive and non-muscle-invasive conventional urothelial bladder carcinoma. Clin Pract 2023;13:806–19.
[29] Pecoraro M, Takeuchi M, Vargas HA, *et al*. Overview of VI-RADS in bladder cancer. Am J Roentgenol 2020;214:1259–68.