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RESEARCH ARTICLE

COMPARISON OF VIRTUAL ENDOSCOPY AND TRANSABDOMINAL ULTRASOUND WITH CONVENTIONAL ENDOSCOPY IN PATIENTS WITH HEMATURIA

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ABSTRACT

Introduction: Patients with gross haematuria have higher incidence of (30 percent) urothelial cancer. Currently recommended investigations for haematuria evaluation are CT scan, urine cytology, Cystoscopy.

Virtual endoscopy (VE) is a 3D computer rendering technique with the possibility of interactive intraluminal navigation within the bladder simulating a conventional endoscopy.

Aim and Objective: To Compare Virtual Endoscopy (VE) and Trans-abdominal ultrasound with Conventional Cystoscopy (CC), in the detection of bladder tumors in patients with haematuria.

Materials and Methods: Study was conducted from November 2007 to January 2010 in our institute of urology. All patients with haematuria were evaluated and those having a bladder tumor included in the study. Initially few patients with tumors more than 6 cm were included in the study, but later tumors less than 5 cm only were studied.

Observation and Results: Totally 106 patients were evaluated. Of these 54 patients were included in the study as they had a bladder tumor detected by cystoscopy and/or Ultrasonography and/ or Virtual cystoscopy or there were no tumor. Of the 54 patients in the study 38 (70.4 %) were males and 16 (29. 6 %) females. Most of the tumors were located in the anterior wall (18 / 51) and the posterior wall (13 / 51). Most of the tumors were papillary (82. 4 %) type, probably as we included small sized tumors in the study. Virtual cystoscopy has a high sensitivity, 92.16 % and 100 % sensitivity to tumors more than 1 cm. But this is still inferior to conventional cystoscopy.

Conclusion: Despite the obvious benefits of virtual cystoscopy in terms of less invasiveness and more comfort to the patient, it has several limitations. These include,

1. Low detection rate for lesions smaller than 1 cm
2. Not able to detect CIS.

Inferior to conventional cystoscopy in detecting bladder lesions.

So Virtual cystoscopy cannot replace conventional cystoscopy. It may have a place in the evaluation of patients with haematuria in stricture disease and surgically poor risk patients.

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INTRODUCTION

Main aim of haematuria evaluation in patients is to diagnose Urothelial cancer. The incidence of urothelial cancer in patients with haematuria is 6 to 12 %. Most of the urothelial cancer (Comparison of Virtual cystoscopy and transabdominal ultrasonography, 2008; Jones *et al*., 1988) are from the bladder, upper tract tumor incidence is only 0.5 %. Patients with haematuria can be of two types – visible or microscopic hematuria. Patients with gross haematuria have higher incidence of (30 percent) urothelial cancer. Currently recommended investigations for haematuria evaluation are

1. CT of the abdomen and pelvis (As it is more superior to IVU and Ultrasound in detecting lesions)
2. Urine cytology for malignant cells and
3. Cystoscopy

Currently cystoscopy is the 'gold standard' to rule out that the patient is not having a bladder lesion to account for the haematuria. Because it can be seen in the above table from the study by Boback *et al*. (Jones *et al*., 1988) CT (62 %) and cytology (27 %) are not as sensitive as Cystoscopy. This led the search of cost effective but highly sensitive modalities which are as sensitive as cystoscopy. This has resulted in two modalities in the horizon:

1. Molecular markers in urine
2. Virtual cystoscopy

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Boback et al study results

Test	Sensitivity (95% CI)	Specificity (95% CI)	PPV	NPV
Cytology	27% (12-48%)	100% (99-100%)	100%	95%
NMP-22	73% (52-88%)	76% (71-80%)	19%	97%
Cystoscopy	96% (79-97%)	97% (95-99%)	74%	99%
CT Urogram	62% (41-80%)	98% (96-99%)	67%	97%
All Four Tests	100% (87-100%)	74% (69-78%)	22%	100%

Similar to cystoscopy virtual evaluation of the upper tracts can also be done to rule out urothelial tumors named as virtual ureteroscopy and virtual nephroscopy. Collectively virtual cystoscopy, ureteroscopy and nephroscopy are called as Virtual endoscopy. Virtual endoscopy (VE) is a 3D computer rendering technique with the possibility of interactive intraluminal navigation within the bladder simulating a conventional endoscopy (Noriyasu Kawai *et al*., 2004). VE is possible with the routine CT images which we do for patients with haematuria when the software is available so there is no added cost to the patient. Virtual imaging is possible by the Marching cubes algorithm which is used to delineate the mucosa. It is based on the change in the attenuation values between the fluid (contrast filled urine) in the bladder lumen and the bladder wall. This results in a 3D representation of the mucosal surface. The computer mouse can be moved within the lumen as if we move the endoscope within the bladder and ureter and the entire mucosa examined systematically in an interactive manner. (Lorensen WE, Clic HE. Marching cubes:a high resolution 3D surface construction algorithm. Comput Graph 1987; 21:163 – 9) (Lorensen and Clic, 1987)

Aim and Objective

To compare virtual endoscopy (VE) and Trans-abdominal ultrasound with Conventional cystoscopy (CC), in the detection of bladder tumors in patients with haematuria.

MATERIALS AND METHODS

Study was conducted from November 2007 to January 2010 in our department of urology. All patients with haematuria were evaluated and those having a bladder tumor included in the study. Initially few patients with tumors more than 6 cm were included in the study, but later tumors less than 5 cm only were studied. Patients were first stabilised and intra venous fluids given, then blood sample taken for lab investigations and grouping - typing. The coagulation profile also checked. Patients who presented with clot retention were subjected to cystoscopic clot evacuation in the daycare cystoscopy room and a 22F urethral foley inserted and irrigation started. When the patient has stabilized and the haematuria had settled down USG KUB was done again and the findings recorded. Cytology was done. When the Sr. Creatinine was normal CECT was taken. None of the patients in the study had refractory haematuria, haematuria settled down in a maximum of 2 days. Twelve patients required blood transfusion as their haemoglobin was less than 10 gms. None of the patients were in shock at the time of presentation. Virtual endoscopic reconstruction made at the workstation by volume rendering algorithm and multiplanar image reconstruction with the Philips brilliance extended view 2 software. It took upto 1 hour for reconstruction and interpretation. Virtual endoscopic examination of the ureters and pelvis was also done in addition to the bladder. There were no associated tumors of the pelvis or ureter reported in the patients involved in the study. The image interpretation and reporting was done by a single radiology assistant. Conventional cystoscopy and tumor resection was done preferentially under Spinal anaesthesia. A preliminary cystoscopy was done using a 21F sheath and a 30 degree telescope. The site of tumor, relation to ureteric orifice, size, morphology and suspicious areas suggesting CIS were noted. Areas appearing as “red velvety” patches were biopsied with Cup Biopsy forceps and were sent separately for analysis. Following which using a 24F sheath, a 30 degree telescope and TURP working element all grossly visible tumor were resected as much as possible and specimen stored to be sent seperately. Then cold cup biopsy forceps were used to take biopsy at multiple sites in the tumor bed for muscle sample and they sent in separate container for HPE. Obturator block was used in cases were tumor was involving the lateral wall. Haemostasis was secured with loop and/or ball electrode 22F three way urethral foley was inserted for irrigation which was removed the next day if returns were clear. Mitomycin C 40 mg in 40 ml of saline was given intravesically and held for 1 hour in post op ward in small tumors which were completely resected. The procedure was done by a skilled urology assistant and the findings were recorded by the person who had operated and were later collected for analysis.

The following data were collected:

1. Site: There are 6 possible sites within the bladder where a tumor can arise. They are anterior, posterior, dome, right and left lateral wall, and base.
2. Size: largest diameter was taken
3. Morphology: sessile or papillary
4. Number of the tumors

Sensitivity of USG and Virtual cystoscopy in detecting lesions of various sizes was determined and compared with Conventional cystoscopic findings.

Also the final Histopathology of the tumor recorded.

OBSERVATION AND RESULTS

Totally 106 patients were evaluated

Of these 54 patients were included in the study as they had a bladder tumor detected by cystoscopy and/or Ultrasonography and/ or Virtual cystoscopy or there were no tumor.Those patients who had no tumor on conventional cystoscopic examination comprised the true negative group. Those lesions present on cystoscopic examination but absent on USG or Virtual cystoscopy are considered to have been missed by the above imaging modality and represent the false negative group respectively. Those lesions detected on USG and VC but not present on Conventional cystoscopy were considered as false positives for the respective imaging study. Of the 54 patients 38 had a bladder tumor on conventional cystoscopy and 16 didn’t have. Two of the bladder tumors were recurrent bladder tumors. Of the 16 patients 10 were reported to contain a bladder tumor by USG and/or VC, they comprise the false

positives. Whereas 6 patients had no lesion detected by imaging and by conventional cystoscopy. About 10 patients were were excluded from the study as they had raised renal parameters. And further 13 patients were excluded as they had large bladder growths (> 5 cm).

Patients who were found to have causes other than bladder tumor in the study were:

1. Vesical calculus :3 patients
2. Renal stone : 10 patients
3. Ureteric stones : 5 patients
4. BPH : 13 patients
5. Carcinoma of prostate : 2 patients
6. UTI : 9 patients
7. Renal cell carcinoma : 5 patients
8. Coagulopathy : 5 patients

- 3 were on heparin treatment for deep vein thrombosis
- 1 was on aspirin therapy for Ischemic heart disease
- 1 was a patient on heparin treatment for post traumatic illiac artery thrombosis

Descriptive statistical data

Of the 54 patients in the study 38 (70.4 %) were males and 16 (29. 6 %) females.

Age distribution

Age group	Frequency (n)	Percent (%)
Up to 45yrs	2	3.7
46 - 50yrs	14	25.9
51 - 55yrs	14	25.9
56 - 60yrs	16	29.6
61yrs and above	8	14.9
Total	54	100.0

Most of the patients were in the age group of 46 to 60 years.

Gender and age distribution

Gender Vs Age group	Male		Female	
	n	%	n	%
Upto 45yrs	2	5.3	0	0.0
46 - 50yrs	10	26.3	4	25.0
51 - 55yrs	12	31.6	2	12.5
56 - 60yrs	8	21.1	8	50.0
61yrs and above	6	15.8	2	12.5
Total	38	100.0	16	100.0

In males the most frequent age group is 51 – 55 years where as in females it is 56 – 60 years. (Britton *et al*., 1989)

Age (yrs)	N	Minimum	Maximum	Mean	Std. Deviation
Male	38	43	72	54.03	6.378
Female	16	46	63	55.37	5.667
Total (Both)	54	43	72	54.43	6.154

The minimum age is 43 years and the maximum was 72 years. Of the 54 patients 20 patients had microscopic haematuria on evaluation and 34 presented with gross haematuria. All the 20 patients with microscopic haematuria the main presenting complaint was storage (irritative) LUTS. (Hiatt and Ordonez, 1994) Of the 38 of 54 patients with bladder tumor 51 bladder tumors were detected as five of them had multiple bladder tumors.

Site distribution of the tumor

Site	Frequency (n)	Percent (%)
Anterior	18	35.3
Posterior	13	25.5
Base	4	7.8
Dome	5	9.8
L lateral	5	9.8
R lateral	6	11.8
Total	51	100.0

Most of the tumors were located in the anterior wall (18 / 51) and the posterior wall (13 / 51).

Morphology distribution

Papillary / Sessile	Frequency (n)	Percent (%)
Papillary	42	82.4
Sessile	9	17.6
Total	51	100.0

Most of the tumors were papillary (82. 4 %) type, probably as we included small sized tumors in the study.

Site distribution of the tumor

Site	Frequency (n)	Percent (%)
Anterior	18	35.3
Posterior	13	25.5
Base	4	7.8
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Size of the lesion is less than or equal to 1 cm (usg)

		Conventional Cystoscopy		Total
		Positive	Negative	
Ultra sonography	Positive	0	7	7
	Negative	21	9	30
Tota	l	21	16	37

P.Value = 0.003 (Significant)

Parameter	Estimate	95% CIs Lower - Upper
Sensitivity	0.0%	(0.0, 15.46)
Specificity	56.25%	(33.18, 76.90)
Positive Predictive Value	0.0%	(0.0, 35.43)
Negative Predictive Value	30.00%	(16.66, 47.88)
Diagnostic Accuracy	24.32%	(13.36, 40.12)

Ultrasound was unable to detect tumors less than/equal to 1cm.

Size of the lesion is less than or equal to 1 cm (Virtual Cystoscopy)

		Conventional Cystoscopy		Total
		Positive	Negative	
Virtual Cystoscopy	Positive	17	3	20
	Negative	4	13	17
Total		21	16	37

P.Value = <0.001 (Significant)

Parameter	Estimate	95% CIs Lower - Upper
Sensitivity	80.95%	(60.00, 92.33)
Specificity	81.25%	(56.99, 93.41)
Positive Predictive Value	85.00%	(63.96, 94.76)
Negative Predictive Value	76.47%	(52.74, 90.45)

Sensitivity falls down when the size of the lesion is below 1 cm.

Results: size of the lesion is more than 1 cm

Ultrasound:

		Conventional Cystoscopy		Total
		Positive	Negative	
Ultra sonography	Positive	25	0	25
	Negative	5	0	5
Total		30	0	30

P.Value = **Not possible**

Parameter	Estimate	95% CIs Lower - Upper
Sensitivity	83.33%	(66.44, 92.66)
Specificity	--	
Positive Predictive Value	100%	(86.68, 100)
Negative Predictive Value	0.0%	(0.0, 43.45)
Diagnostic Accuracy	83.33%	(66.44, 92.66)

Sensitivity improves when the size is more than 1cm. (83. 33 %)

Virtual Cystoscopy

		Conventional Cystoscopy		Total
		Positive	Negative	
Virtual Cystoscopy	Positive	30	0	30
	Negative	0	0	0
Total		30	0	30

P.Value = Not possible

Parameter	Estimate	95% CIs Lower - Upper
Sensitivity	100%	(88.65, 100)
Specificity	--	
Positive Predictive Value	100%	(88.65, 100)
Negative Predictive Value	--	
Diagnostic Accuracy	100%	(88.65, 100)

Virtual cystoscopy detects all the tumors above 1 cm in size. Carcinoma in situ was present in 5 patients and Virtual cystoscopy was not able to identify it. In these patients 4 had a positive cytology. Of the 38 patients who had bladder tumor only 6 patients had a positive cytology with a sensitivity of only 15.78 %. TURBx (Trans - urethral resection biopsy) was done in two patients where some residual tumor was left unresected. One was a transitional cell carcinoma and other adenocarcinoma of the bladder with obvious T3 stage. One patient had a partial cystectomy done. The patient presented as a mass abdomen and initially thought to arise from the uterus. It was an intra mural growth of bladder and cystoscopy revealed the mucosa to be intact over the growth. So a Trans – abdominal trucut biopsy was done and later the patient taken for partial cystectomy believing it to be a leiomyoma of bladder. Final specimen on immunohistochemical analysis revealed it as a mesenchyaltumor. Rest of the patients was subjected to TURBT (Trans- urethral resection of bladder tumor) where all the grossly visible tumor was resected. Two of the resected tumors were found to be benign, chronic cystitic changes. Rests were transitional cell carcinoma.

DISCUSSION

Virtual cystoscopy has a high sensitivity, 92.16 % and 100 % sensitivity to tumors more than 1 cm. But this is still inferior to conventional cystoscopy. Also it misses out carcinoma in situ. This can be overcome by combining cytology with it. Although cytology by itself has poor sensitivityfor low grade tumor it has high sensitivity for high grade lesions like CIS.

Table below sums up the results of the study.

	Sensitivity
Cytology	15.78 %
USG	49.02 %
Virtual cystoscopy	92.16 %

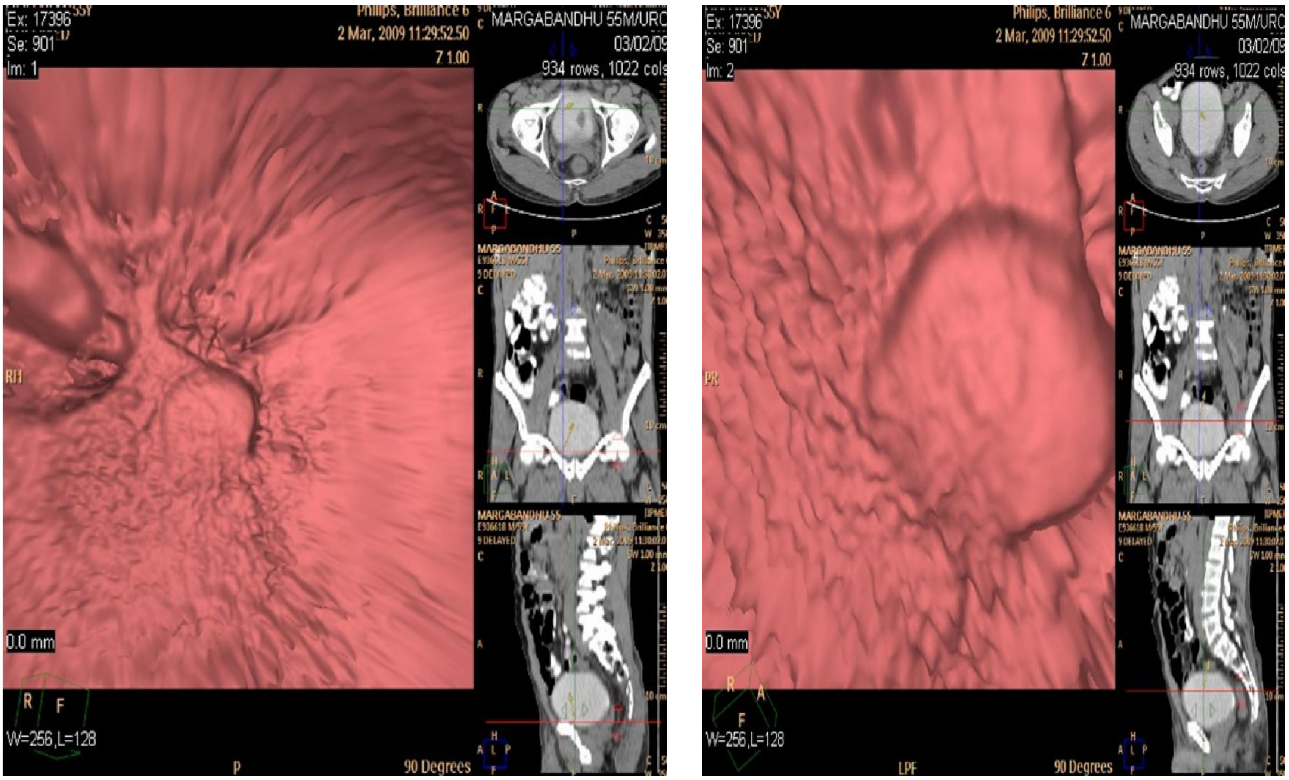
So it appears that virtual cystoscopy is not sensitive enough to replace conventional cystoscopy. So we need other modalities for screening for urothelial tumors. Lots of work is currently focused on molecular markers. Hence in the future we have to rely on molecular markers for avoiding unnecessary cystoscopy in those patients who don't have a urothelial tumor. Role of molecular was emphasized by Bryan *et al*, Goodison *et al*. and Ehdaie *et al*. "Molecular markers will become increasingly important for urothelial cancer diagnosis and prognostication as we continue through the century, with both conventional and novel experimental platforms providing robust and reproducible assays with high sensitivity and specificity, and pointof-care utility. (Bryan *et al*., 2010) Biomarkers in bladder cancer. *BJU Int* 2010; 105: 608– 1311. Goodison *et al*., 2009 Urinary proteomic profiling for diagnostic bladder cancer biomarkers.*Expert Rev Proteomics* 2009; 6 : 507–14. Ehdaie and Theodorescu, 2008 Predicting tumor outcomes in urothelial bladder carcinoma: turning pathways into clinical biomarkers of prognosis. *Expert Rev Anticancer Ther,* 2008; 8: 1103–10). I close this discussion with the quote "Finally, we think that cystoscopy will remain the 'gold standard' for ruling out bladder cancer in the haematuria patient as of now. However, conventional white light cystoscopy will evolve to embrace new imaging technologies with improved capabilities, such as narrow band and optical coherence tomography." (Vining *et al*., 1996)

Richard T. Bryan and Michael A. Wallace,

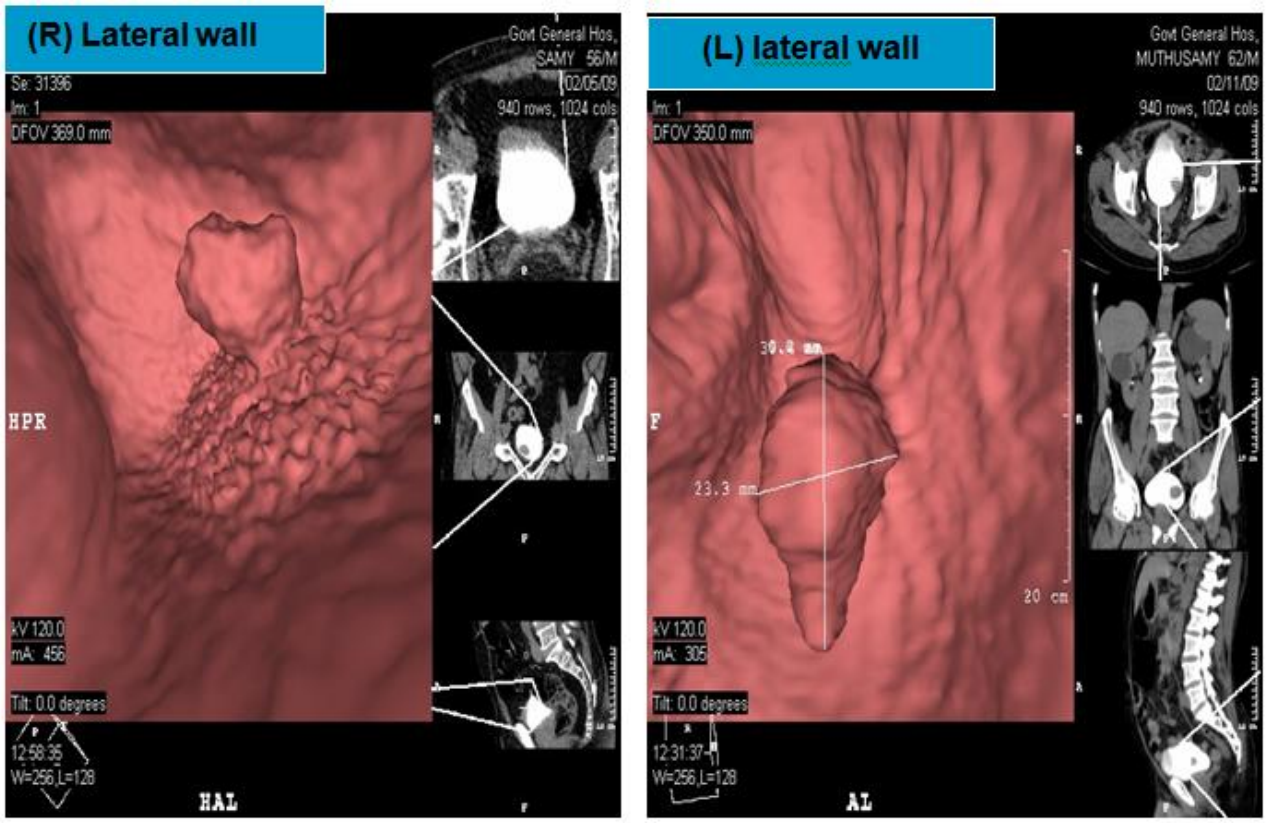
Bladder Cancer Prognosis Programme Bladder Cancer Prognosis Programme, University of Birmingham, UK

Cystoscopy is easy to teach, familiar to all urologists, reasonably accurate and performed with low morbidity around the world. It is performed in minutes, in contrast to virtual cystoscopy, which takes time.

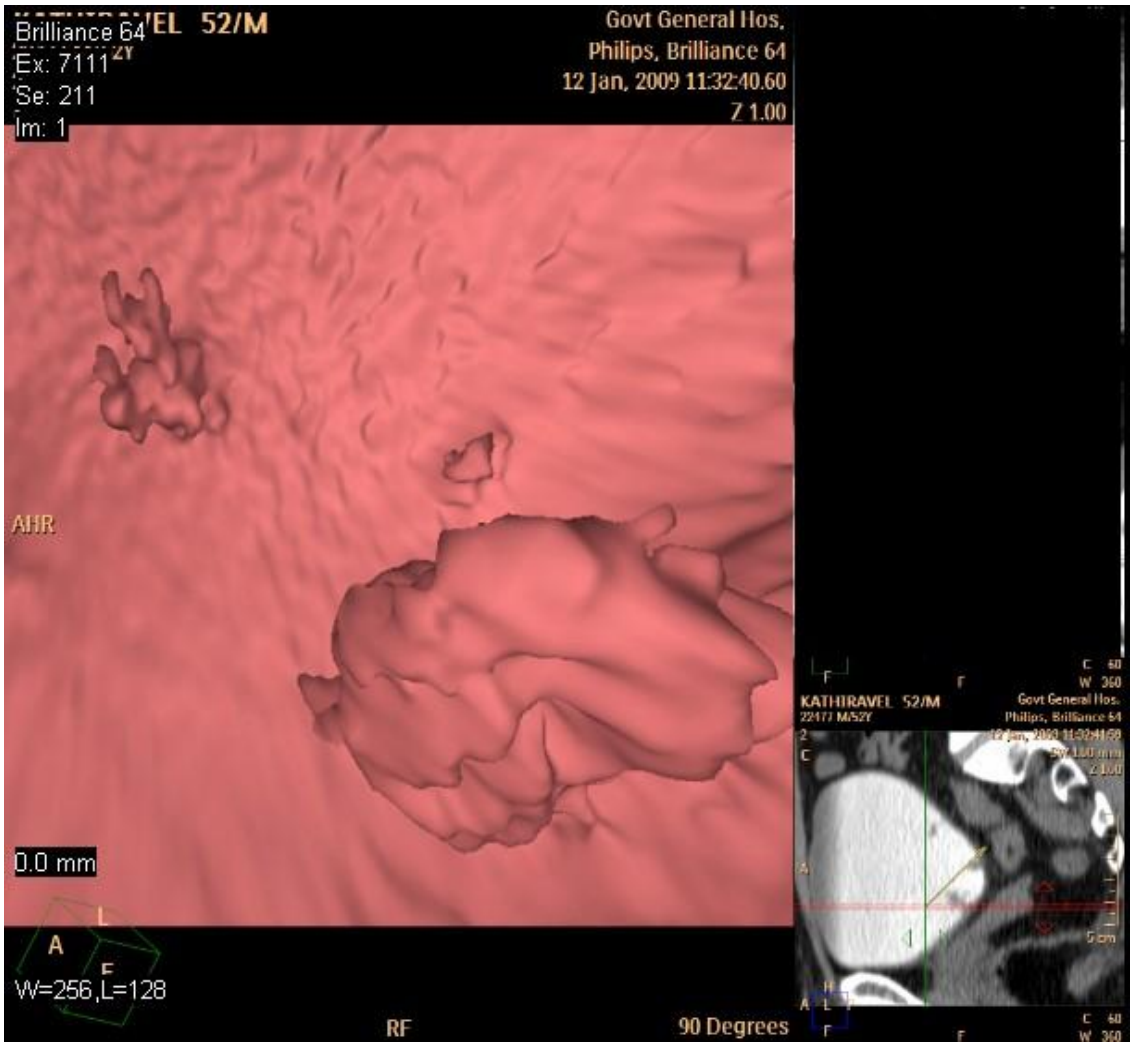
Sessile lesion (L), Lateral wall



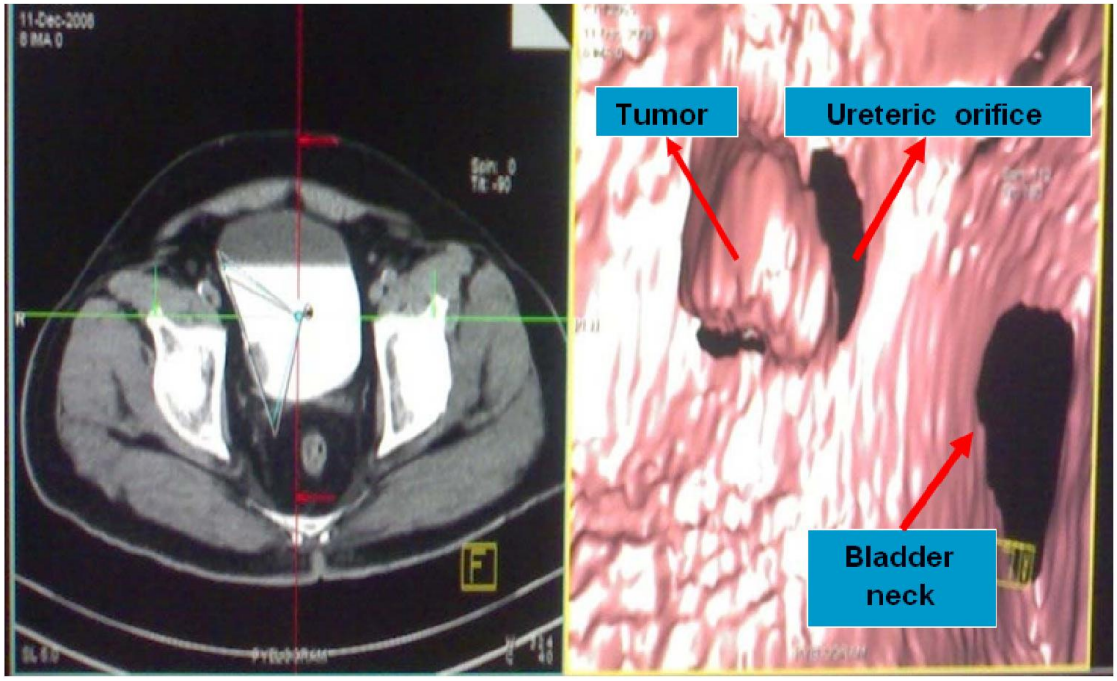
Pedunculatedtumor



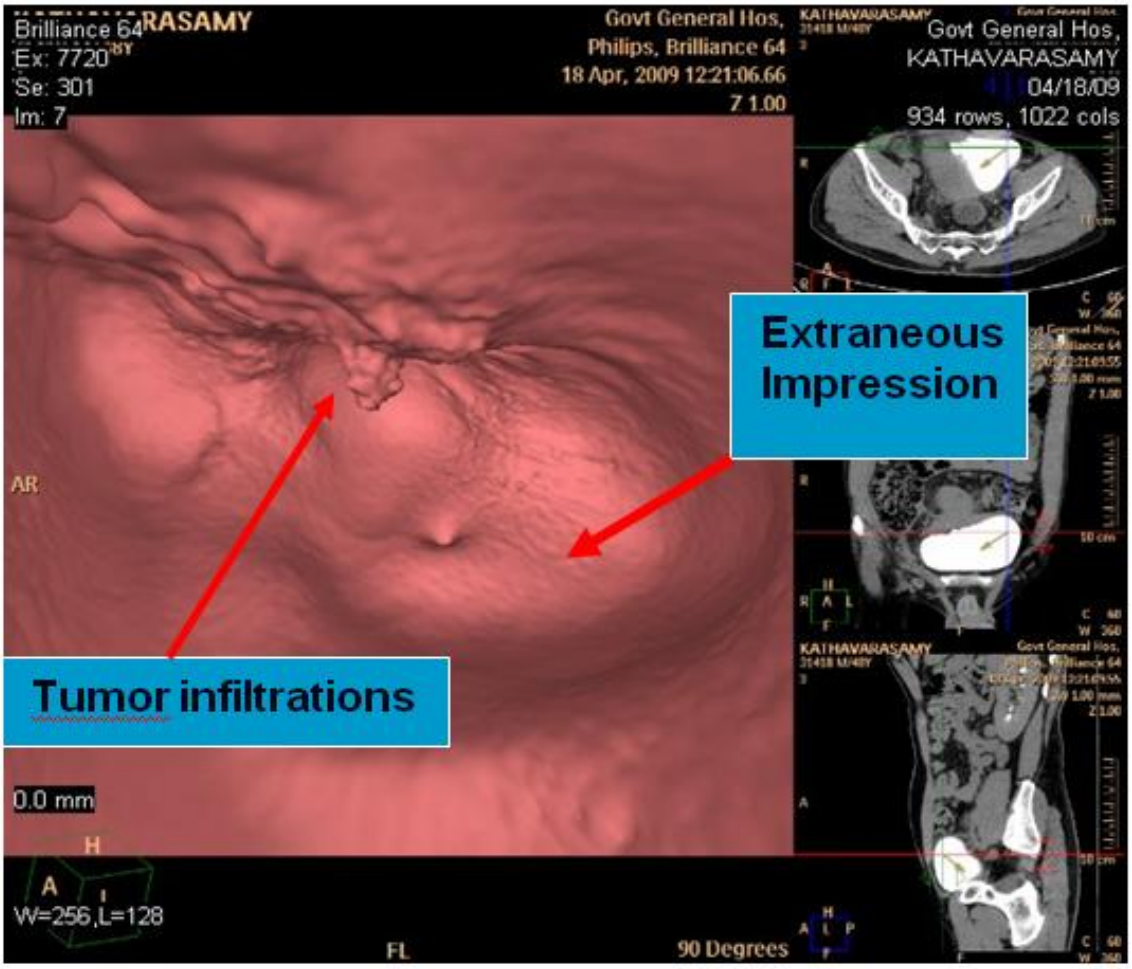
Multiple - Small tumors Posterior wall of bladder



R Ureteric orifice tumor



Sigmoid growth infiltrating the bladder (Adenocarcinoma)



Conclusion

Despite the obvious benefits of virtual cystoscopy in terms of less invasiveness and more comfort to the patient, it has several limitations. These include,

1. Low detection rate for lesions smaller than 1 cm
2. Not able to detect CIS.
3. Inferior to conventional cystoscopy in detecting bladder lesions.

So Virtual cystoscopy cannot replace conventional cystoscopy. It may have a place in the evaluation of patients with haematuria in stricture disease and surgically poor risk patients. (Campbell 9th edition)

REFERENCES

Britton JP, Dowell AC, Whelan P. Dipstick haematuria and bladder cancer in men over 60: results of a community study. *BMJ*, 1989; 299:1010-2.

Bryan RT, Zeegers MP, James ND, Wallace DM, Cheng KK. Biomarkers in bladder cancer. *BJU Int*2010; 105: 608–1311

Campbell – Walsh Urology 9th edition: vol 1: 97 – 100.

Comparison of Virtual cystoscopy and transabdominal ultrasonography with Conventional cystoscopy for Bladder tumor detection: Roberto Iglesias Lopes MD, Lucienne Nogueira MD, Cezar Jose Albertotti MD, Daniel YasumasaTakahasi MD and Roberto Nicoedes Lopes MD: *Journal of Endourology*, 2008: 8: 1725- 29.

Ehdaie B, Theodorescu D. Predictingtumor outcomes in urothelial bladder carcinoma: turning pathways into clinical biomarkers of prognosis. *Expert Rev Anticancer Ther.,* 2008;8: 1103–10.

Goodison S, Rosser CJ, Urquidi V. Urinary proteomic profiling for diagnostic bladder cancer biomarkers.*Expert Rev Proteomics* 2009; 6 :507–14

Hiatt RA, Ordonez JD. Dipstick urinalysis screening, asymptomatic microhematuria, and subsequent urological cancers in a populationbased sample. *Cancer Epidemiol Biomarkers Prev.,* 1994; 3:439-43 [Published erratum appears in Cancer Epidemiol Biomarkers Prev 1994; 3:523].

Jones DJ, Langstaff RJ, Holt SD, Morgans BT. The value of cystourethroscopy in the investigation of microscopic haematuria in adult males under 40 years.A prospective study of 100 patients. *Br J Urol.,* 1988; 62:541-5.

Lorensen WE, Clic HE. Marching cubes:a high resolution 3D surface construction algorithm. *Comput Graph*, 1987; 21:163 – 9

Noriyasu Kawai, Takeo imura, Daisuke Nagata, Keiichi Tozawa, KenjiroKohri : Intravenous urography-virtual cystoscopy is a better preliminary examination than air virtual cystoscopy : 2004 BJUI: 94:832 – 36.

Vining DJ, Zagoria RJ, Liu K, Stelts D. CT cystoscopy : An innovation in bladder imaging. *AJR,* 1996; 166: 409 – 10

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