Virtual Cystoscopy Versus Conventional Cystoscopy In Diagnosis of Vesical Masses.

A Thesis Submitted for Fulfillment of M.D. degree in Radiodiagnosis

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2010
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LIST OF ABBREVIATIONS

2-D: Two – Dimensional
3-D: Three – Dimensional
4-D: Four – Dimensional
AP: Anteroposterior
ADC: Adenocarcinoma
BC: Bladder Carcinoma
Ca: Cancer
CIS: Carcinoma in Situ
CT: Computed Tomography
CTVE: CT Virtual Endoscope
Conv. Cyst: Conventional Cystoscopy
EBCT: Electron Beam CT
FNAC: Fine needle aspiration cytology
G (I, II, III): Grade (I, II, III)
GM-CSF: Granulocyte – Macrophage Colony Stimulating Factor
IV: Intravenous
IVU: IV Urography
Lat: Lateral
LN: Lymph node
Lt: Left
MIP: Maximum intensity projection
MPR: Multiplanar reconstruction
MRI: Magnetic Resonance Imaging
MSCT: Multislice CT
PET: Positron emission tomography
PLND: Pelvic Lymph Node Dissection
PR: Per Rectal (examination)
Rt: Right
Rb: Retinoblastoma gene
SCC: Squamous cell carcinoma
SSD: Surface shaded display
TCC: Transitional cell carcinoma
Ts: Transverse
TUR: Trans Urethral Resection
UICC: Union International Center of Cancer
US: Ultrasound
VC: Virtual Cystoscopy
VE: Virtual Endoscope
VR: Volume rendering
Introduction

Bladder cancer is the fourth leading cause of cancer in American men, accounting for more than 12,000 deaths annually. It was one of the first malignancies in which carcinogens were recognized as an important factor in its cause. Currently, cigarette smoking is by far the most common cause of bladder cancer, although occupational exposure to arylamines has been implicated in the past. Gross or microscopic hematuria is the most common sign at presentation (Amling, 2001).

The urinary bladder is the commonest site of malignant neoplasia in the genitourinary tract. An early metastatic spread, with a high mortality rate, is the typical course of the disease. There are a few reports regarding the CT features of bladder neoplasia, as advanced-stage, large, broad-based, heterogeneous bladder masses. However, the preoperative characterization of the nature of bladder neoplasm based on the imaging findings is difficult. Differential diagnosis of large-sized, advanced-stage bladder malignancies should include a high-grade urothelial carcinoma, undifferentiated carcinoma, like small cell carcinoma, primary or secondary lymphoma, metastasis from SCC outside the bladder and sarcoma (Kim et al., 2003).

Bladder cancer is a common problem facing urologists worldwide. The gold standard for its diagnosis and follow-up is the direct visualization of the tumor using conventional cystoscopy. Despite having high sensitivity and specificity for detecting bladder cancer, conventional cystoscopy is regarded as an invasive procedure which is associated with several complications. In addition, regular follow-up of patients with bladder cancer is a financial burden on the health system (Mohammed et al., 2008).
Carcinoma of the bladder can be a serious and complex condition that is not always easy to diagnose with radiological methods (Bernhardt and Rapp – Bernhardt, 2001).

Ultrasonography has been proposed as the initial test for detection of bladder carcinomas in patients presenting with hematuria. For ultrasonography, the sensitivity, specificity, positive and negative predictive values were good but not as good as cystoscopy. While the tolerability of cystoscopy is relatively low, it is still superior to ultrasonography in the evaluation of the bladder as a possible source of hematuria (Stamatiou et al., 2009).

Computed tomography (CT) and magnetic resonance (MR) imaging are used mainly to demonstrate extra vesicles extension and distant metastasis (Song et al., 2001).

Virtual Cystoscopy using Volume Ultrasound is an emerging application used to detect bladder lesions. This technique is useful for diagnosing urinary bladder pathology. Benefits include a more comprehensive understanding of pathology when correlating 2D and volume information, thus providing increased diagnostic confidence. An additional benefit is the reduction of patient discomfort and the cost savings of potentially eliminating the need for an invasive examination. This is especially true when considering follow up cystoscopy after a therapeutic cystoscopy or surgery (Dahiya et al., 2004).

CT urography and virtual endoscopy images are generated from dedicated multislice helical CT data sets and various three-dimensional reconstruction techniques. These imaging techniques can provide external and endoscopic images of the urinary tract and also provide high spatial resolution images helping overcome some of the limitations of intravenous urography and ultrasound. Conventional cystoscopy is the standard method for the detection of urinary bladder neoplasm, but the technique is invasive and uncomfortable. Other drawbacks are the inability to evaluate extravesical pathology and a 5-15% risk of urinary tract infection (Song et al., 2001).
With the progressive development in diagnostic imaging and medical computer software technologies, it was possible to generate virtual reality images to aid the clinician to inspect the interior of the bladder in real time. This technology is considered as a safe test for bladder cancer diagnosis and follow-up, and it is associated with cancer detection rates comparable with conventional cystoscopy. However, it is associated with some drawbacks that limit its use in routine clinical practice at the current time (Mohammed et al., 2008).

Technological breakthroughs have advanced the temporal and spatial resolutions of diagnostic imaging, and 3 dimensional (3-D) reconstruction techniques have been introduced into everyday clinical practice. Virtual endoscopy is a non-invasive technique that amplifies the perception of cross-sectional images in the 3-D space, providing precise spatial relationships of pathological regions and their surrounding structures. A variety of computer algorithms can be used to generate 3-D images, taking advantage of the information inherent in either spiral computed tomography or magnetic resonance imaging (Kagadis et al., 2006).

One of the important advantages of virtual CT cystoscopy is the minimal invasiveness of the technique. The evaluation of intravesical and extravesical pathology is possible with the same study. Although CT data interpretation was based mainly on the axial images, the combined evaluation of transverse and virtual cystoscopic images has been proved mandatory in CT cystoscopy, since small-sized tumors may be detected only or predominantly on virtual images (Tsampoulas et al., 2008).

In the assessment of recurrent bladder tumors, diagnostic efficiency of virtual cystoscopy carried out by multidetector computed tomography was investigated and compared with the criterion standard of conventional cystoscopy (Mohammed et al., 2008).
As a minimally invasive procedure, virtual cystoscopy provides many advantages. It allows accurate localization of a lesion due to its wide field of view and depiction of extravesical abnormality, landmarks the size of tumor, and virtual cystoscopy can be used to monitor treatment response in a patient with a non–resectable tumor. Patients with a severe urethral stricture or marked prostatic hypertrophy, who may be poor candidates for conventional cystoscopy, can safely undergo virtual cystoscopy (Song et al., 2001).

Virtual endoscopy images enable endoluminal navigation through hollow organs, thus simulating conventional endoscopy. Several clinical studies have validated the diagnostic utility of virtual cystoscopy, which has high sensitivity and specificity rates in the detection of bladder tumor (Kagadis et al., 2006).

Virtual CT cystoscopy for now remains a complementary examination. Its main limitations are the inability to provide biopsy tissue specimens for histopathologic examination, something that is possible with conventional cystoscopy, providing a basis for optimal therapeutic planning. Another disadvantage is the difficulty to depict carcinoma in situ and flat lesions or small-sized tumors. The introduction of multidetector CT scanners improved the feasibility of virtual CT cystoscopy in detecting tumors smaller than 5 mm (Arslan et al., 2006).

Use of virtual cystoscopy should be considered in patients who present with hematuria or have histories of bladder carcinoma operation and are for follow-up because of its lesser complication risk and its being a less invasive, easily applied procedure without need of anesthesia (Basak et al., 2009).
REVIEW OF LITERATURE

Anatomy of the Urinary Bladder

The urinary bladder is the largest potential space in the pelvis. It is a hollow muscular organ situated extraperitoneal posterior to the pubic symphysis (Tortora, 1999).

The shape of the bladder (Fig. 1 & 2) varies according to its degree of fullness but, when empty, it can be considered for descriptive purposes as a tetrahedron, having neck, apex, superior and two infero-lateral surfaces with a base posteriorly. Angles of the tetrahedron are situated inferiorly at the bladder neck, postero – laterally at the site of entry of the ureters and anteriorly at attachment of fibrous remnant of the urachus, when the bladder is full it has more rounded contours because its surfaces become stretched and reaches the abdominal cavity (Ritchie, 1998).

The fundus or Base:

It is triangular and postero – inferior in females, it is closely related to the anterior vaginal wall. In males, it is related to the rectum but its upper part is separated from the rectum by the recto-vesical pouch of peritoneum, and below that by seminal vesicles and deferent ducts which separate the two viscera (Williams and Dyson, 1992).
Fig. (1) Illustration of mid-sagittal plane through urinary bladder

(Quoted from Netter 1980)
Fig. (2) Illustration of coronal plane through urinary bladder

(Quoted from Netter 1980)
The Neck:

It is lowest and also the least mobile part of the bladder. It is firmly anchored to the pelvic diaphragm. It is pierced by internal urethral orifice. In the male, it is continuous with the prostate, although a groove separates the two organs externally. The neck of the female bladder is lower than that of the male, and it rests on pubococcygeal parts of the lavatory ani (O'Rahilly, 1986).

The Apex:

The apex is the most superior and anterior portion of the bladder. It is the site of the urachus, which is fetal connection between urogenital sinus and the allantois (Cher and Carroll, 1997).

The Superior surface:

It is triangular in shape. Its lateral borders run from the apex to ureteric entrances and its posterior border joining the ureteric entrances. In males the superior surface is completely covered by peritoneum, extending slightly on to the base and continued posteriorly into the rectovesical pouch, laterally into the para-vesical fossae and anteriorly into the median umbilical fold. It is in contact with the sigmoid colon and the terminal coils of the ileum.

In females, the superior surface is also largely covered by peritoneum, but posteriorly this is reflected to the uterus at the level of the internal Os, forming the vesico-uterine pouch. The posterior part of the superior surface, devoid of peritoneum, is separated from
supravaginal part of uterine cervix by fibro areolar tissue (*Williams and Dyson, 1992*).

**The inferolateral Surfaces:**

Each inferolateral surface slopes downwards and medially to meet its fellow, lying against the front part of pelvic diaphragm and obturator internus. Where the surfaces meet below the apex, there is a (retroperitoneal) space behind the pubic bones and symphysis, the retro peritoneal space of Retzius, containing loose fatty tissue and also denser condensations that form the pubovesical and puboprostatic ligaments in the male and pubovesical ligaments in the females (*McMinn, 1994*).

**Histology of the urinary Bladder:**

The bladder wall is composed of four layers:

1- The inner mucosa is a mucous membrane composed of transitional epitheliums arranged in five to seven layers from basal cells to the surface. The urothelium is continuous with that of ureters and urethra, its histological appearance depends on degree of distention. A basal lamina is present beneath the urothelium separating it from the richly vascularized subjacent lamina propria.

2- The submucosa (the lamina propria) composed of loose collagen, vessels, lymphatic and nerves, is interspersed between the mucosa and deeper muscularis layer.

3- The muscularis (detrusor muscle), consists of three layers of smooth muscle fibers: inner longitudinal, middle circular, and
outer longitudinal. Around the opening of the urethra the circular fibers form an internal urethral sphincter. Inferior to the internal sphincter is the external urethral sphincter, which is composed of skeletal muscle and is a modification of the urogenital diaphragm muscle.

4- The adventitia is the outer coat of the urinary bladder which is a layer of areolar connective tissue that is continuous with that of the ureters. Over the superior surface the urinary bladder is a layer of visceral peritoneum called the Serosa (Tortora, 1999).

**Blood supply (Fig. 3):**

The superior and inferior vesical arteries which are branches of internal iliac artery provide most of the arterial blood. Occasionally branches of obturator, inferior gluteal, uterine and vaginal arteries contribute to supply the bladder.

The veins of the bladder do not follow the arteries. They form a plexus of veins communicating with prostatic venous plexus and drain to internal iliac veins. There is similar plexus of veins in females, communicating with veins in the base of broad ligament (McMinn, 1994).
Lymphatic drainage (Fig. 4):

Numerous anastomosing lymph channels drain the prostate and the bladder neck, base, and body. A rich lymphatic network within the bladder wall collects lymph from mucosa. These vessels drain into larger channels in the adventitia. Small lymph nodes are often present within the adventitia of the bladder. Ultimately, these lymphatic channels lead to the obturator, internal iliac and external iliac lymph nodes (Cher and Carroll, 1997).
Nerve Supply (Fig. 5):

Sympathetic and parasympathetic nerve fibers innervate the bladder after forming the vesical plexus of autonomic nerves. This plexus is derived from pelvic splanchnic nerves which carry parasympathetic fibers originating in the 2nd, 3rd and 4th sacral segments of the spinal cord and from the inferior hypogastric nerves which carry sympathetic fibers from lower thoracic and upper lumbar segment (T10-12). The final pathway of these fibers to the bladder is along the arteries. Sensory (visceral afferent) fibers travel in the opposite direction to the efferent sympathetic and
parasympathetic fibers, but have their cell bodies in the dorsal root ganglia. Stimulation of the parasympathetic causes detrusor contraction, but the role of the sympathetic nerves in relation to detrusor functions is uncertain \textbf{(Ritchie, 1998)}.

\textit{Fig. (5)Nerve supply of urinary bladder}

\textit{(Quoted from Netter 1980)}
4D Ultrasound Anatomy of Urinary Bladder

The bladder is an ovoid structure lying in the pelvic cavity. The ureters enter the bladder and the urethra leaves it at the three corners of the trigone. The trigone itself is a triangular area that is smoother than the surrounding muscles on cystoscopy but has no distinguishing features in the B mode ultrasound.

On the 3D and 4D ultrasound we can use the hollow viscus filled with urine to render the internal mucosa and thus comment on changes seen in the morphology. 4D sonography gives a virtual cystoscopic view which can show similarity to conventional cystoscopy. The ureteric orifices may be seen, their position can be identified by ureteric jets. The position of urethra can be rendered on 4D ultrasound and its position seen as a small depression at bladder base. The bladder must be distended, although not too much (Ashok & Nirvikar, 2004).

The full bladder has the shape of a rounded triangle in sagittal plane and a rounded oblong in transverse scan. In female patients the ureters bulge into the posterior wall of the bladder; in male, the prostate causes an impression of the bladder base.

The bladder wall is of even thickness of 4 to 6mm. the normal bladder empties completely on micturition. Urine however starts to refill the bladder immediately but at a rate of up to 2ml/min. even a short delay in taking post micturition measurements may result in small bladder residue (Ashok & Nirvikar, 2004).
Also some normal people do not empty their bladder completely. Generally a post void that is 10% of the pre void or lesser is insignificant clinically (Fig. 6). In all post void residual urine calculations 4D ultrasound has been found to be superior to the 2D method of volume calculation (Ashok & Nirvikar, 2004).

**Fig. (6) Measurement of bladder volume by 4D ultrasound**

*(Quoted from Ashok & Nirvikar, 2004)*
CT Anatomy of Urinary Bladder

The urinary bladder is a hollow muscular organ for storing urine temporarily. Bladder is higher in position in children and slightly higher in males than females. It is relatively larger in children than in adults. Size and shape vary considerably. When empty, it is completely within the pelvis.

Inferior aspect projects 5-10 mm above the symphysis pubis, separated from pubic bones by retropubic space. Floor is parallel to superior aspect of the pubic rami. The bladder dome is rounded in male and flat or slightly concave in female (Fig. 7).

Bladder is relatively free to move except at the neck which is fixed by the puboprostatic ligaments (males) and pubovesical ligaments (females) (www.radiology.rsna.org).

Fig. (7) CT pelvis and urinary bladder without and with contrast
(Quoted from www.radiology.rsna.org)
On CT scans, bladder appears as a homogenous midline structure of the pelvis, whose size and configuration vary greatly depending on the amount of urine inside (Lee, 1985).

When empty, it is flattened against the posterior aspect of pubis, confined to the true pelvis and only a small portion of it would be visible on CT scans (Schneck et al, 1990).

As the bladder distends, it expands postero-superiorly to fill more of the true pelvis and antero-superiorly to extend across the plane of pelvic inlet into the lower abdomen, gaining more close relationship to rectus abdominus muscles anteriorly, psoas muscles and external iliac vessels antero-laterally, and the obturator internus laterally (Wegener, 1992).
Endoscopic Anatomy of Urinary Bladder

The mucosa is formed of transitional epithelial cells that flatten and form a single epithelial layer during bladder distension. In the distensible portions of the bladder, the mucosa is only loosely attached to the submucosa but is more firmly attached directly to the muscular layer over the trigone. It remains smooth in this area regardless of the state of distension since the trifocal area does not distend. In the distensible areas, the mucosal pattern can be related to the degree of filling. The mucosa appears flat when the bladder is filled but can appear redundant or wrinkled when the bladder contains a lesser volume. The normal bladder mucosa is pale, creamy red in color showing small blood vessels radiating and branching underneath (Fig. 8). Points of orientation are the bladder neck with the trigone and ureteric orifices in one hand and bladder roof on the other hand (Reuter, 1987).

Fig. (8) Normal mucosal pattern of urinary bladder on cystoscopy
www.urologyinformation.co.uk
The vesical neck, which limits the bladder inferiorly and distally, appears as a funnel–shaped opening of the urethra into the bladder.

Endoscopically, the vesical neck is seen when the instrument passes proximally into the bladder. From that point, the vesical neck appears as a concentric muscular ring.

If the bladder neck is viewed from the superior aspect, either with the bladder opened or with an endoscopy placed through a suprapubic tract, the vesical neck remains, the major landmark and reference point in the anatomy of the bladder.

The trigone is formed of two muscle layers superimposed on the detrusor muscle. The superficial trigone is formed as a direct continuation of fibres in the roof and the floor of the intravesical ureter.

The deep trigone is formed by direct continuation of Waldeyer's sheath, a fibromuscular structure that completely encircles the distal 3 to 4 cm of the juxtavesical ureter and follows the ureter through the ureteral canal.

The sheath (now the deep trigone) continues under the superficial trigone. The trigone and the dense ventral condensation, the middle circular layer of the detrusor, surround the bladder outlet (Tanagho and Pugh, 1963).
The trigone is subjected to many variations with respect to the position of ureteric orifices, its surface area, and angulation. In the male, it frequently extends with several longitudinal urethral folds as far as the verumontanum. Its mucosa is velvety and more strongly colored than that of the remaining bladder; there are no muscular makings of any kind (including spastic or pathologic ones, such as in trabeculation) (Reuter, 1987).

The interureteric ridge is an elevation extending between the ureteral orifices. It is more prominent in males than females, in whom it may be poorly defined. The ureteral orifices are located along the interureteric ridge symmetrically, usually 1 to 2 cm from the midline. There is great variation in the appearance of the normal ureteral orifice (Fig.9).

In the adult, a normal, non-refluxing orifice may have the configuration described as a volcano, a horseshoe, slit-like or some other variation. The orifice may either be quite prominent and obvious on endoscopic examination or appears as an inconspicuous slit distinguishable from the surrounding mucosa only through careful inspection.

The ureteral orifice is often surrounded by a characteristic mucosal vascular pattern. Prominent mucosal vessels course in an area medial, inferior, and lateral to the orifice. This pattern is often obscured in the presence of generalized mucosal inflammation (Bagley et al., 1985).
The base or the fundus of the bladder is located posterior to the trigone. The lateral walls of the bladder extend superiority to the dome or vertex as do the anterior and posterior walls.

The normal vascular pattern and topographic appearance of the mucosa can be seen over the bladder musculature in these areas. When the bladder is distended, this pattern becomes relatively smooth unless there is prominent trabeculation (*Bagley et al., 1985*).

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*Fig. (9)* Normal ureteral orifice with notable ridge on cystoscopy

*(Quoted from www.urologyinformation.co.uk)*
Pathology of Urinary Bladder

About 95% of bladder tumors are of epithelial origin, the remainder being mesenchymal tumors (table 1). Most epithelial tumors are composed of urothelial (transitional cell) type and are thus interchangeably called urothelial or transitional tumors, but squamous and glandular carcinomas also occur (Cotran et al., 1999).

In Egypt, bladder cancer is the most common cancer; squamous cell carcinoma is the most common type of bladder cancer but recently transitional cell carcinoma show definite rise over the years (Fettouh, 1994).

Superficial tumors represent 30% of transitional cell carcinoma in bilharzial patients (Shoukry and El – Bolkainy, 1995).

A) Benign Proliferative and metaplastic lesions:

A spectrum of hyperplastic and metaplastic changes of urothelium occurs throughout the urinary tract, from the renal pelvis to the urethra. These non-neoplastic lesions of urothelium are characterized either by hyperplasia or by combined hyperplasia and metaplasia. Mucosal lesions that are only hyperplastic include simple hyperplasia, Brunn's invaginations nests, and cystitis cystica. The urothelial changes that combine hyperplasia and concurrent metaplasia include cystitis glandularis, mucinous metaplasia, nephrogenic metaplasia, and squamous metaplasia. The proliferative and metaplastic lesions are found in association with chronic
inflammation, caused by urinary tract infections, calculi and neurogenic bladder (Peterson, 1994).

**Simple hyperplasia:**

It refers to an increased number of cell layers in mucosal transitional epithelium. This change has a flat configuration, with neither papillary features nor invaginations into lamina propria (Peterson, 2001).

**Brunn's buds:**

These are bulbous invaginations of the surface urothelium into lamina propria (Peterson, 2001).

**Brunn's nests:**

They are similar to Brunn's buds, but in this case, the urothelial cells have detached from the surface and are seen within the lamina propria (Peterson, 2001).

**Cystitis cystica:**

Are characterized by small slits or round spaces in otherwise solid brunn's nests. Cystitis Cystica is actually very common occurring in 60% of otherwise normal adult bladders (Peterson, 2001).

**Cystitis Glandularis:**

Refers to a lesion of the bladder mucosa characterized by metaplastic glandular structures lined by mucin – secreting columnar epithelial cells. Cystitis glandularis differs from cystitis cystica only
in the nature of the lining cells. In fact, structures with the columnar cells of cystitis glandularis and the transitional cells of cystitis cystica are not a common. In cystitis glandularis, the overlying surface epithelia usually remain one of transitional cells, yet, metaplastic mucus-secreting columnar cells (Fig. 10) similar to those in the underlying glandular structures may also be observed in the surface epithelium (Peterson, 2001).

![Image](image-url)

**Fig. (10) Cystitis, Proliferative cystitis**

*(Quoted from www.wordpress.com)*

**Mucinous (Colonic) metaplasia:**

Particularly conspicuous glandular metaplasia of the urinary tract is referred to as mucinous metaplasia and occurs most frequently in the bladder. In this condition the glands are lined by an epithelium resembling that of the colon, composed of goblet cells and occasionally paneth cells.
Squamous Metaplasia:

The urinary tract may react to chronic injury and inflammation with squamous metaplasia, particularly when associated with calculi (Peterson, 1994).

Nephrogenic Metaplasia:

Nephrogenic Metaplasia, which occurs most frequently in the urinary bladder, consists of a papillary exophytic nodule containing numerous small tubules clustered in the lamina propria. Nephrogenic metaplasia is often associated with chronic cystitis. It has no age predilection and is reported from infancy to the eighth decade of life.

There is a pronounced male predominance (3: 1). Transurethral resection is the most common form of therapy, but recurrences are not uncommon.

Patients with proliferative and metaplastic lesions of the urothelium have a significantly increased risk for the development of transitional cell carcinoma of the bladder, and in the case of cystitis glandularis adenocarcinoma as well.

However, there is no evidence to suggest that these lesions are preneoplastic. Rather, Persistence of the Injury related to the development of proliferative and metaplastic urothelial lesions is more likely the important factor in the pathogenesis of bladder cancer (Peterson, 2001).
A) Inflammatory conditions:
- Non specific inflammatory masses:

  **Follicular cystitis:** Chronic cystitis with many follicles; it has a characteristic cystoscopic appearance, with small whitish nodules, in a mucosa varying from normal to diffuse edema and hyperemia (*Bernstein et al., 1992*). Variable number of lymph follicles is seen within the lamina propria and they may coalesce to form large nodules (*Koss, 1983*).

  **Polypoid cystitis:** Is strongly associated with indwelling catheters. It is characterized cystoscopically by multiple sessile or stalked Polypoid projections of the mucosa; these projections are covered by normal urothelium, which may be ulcerated; the stroma is edematous and infiltrated with mononuclear leucocytes and granulocytes (*Bernstein et al., 1992*).

  **Eosinophilic cystitis:** Severe and persistent symptoms including dysuria, frequency and hematuria, with a histopathology picture of strong transmural eosinophilic infiltration and detrusor muscle necrosis; the patients may show allergic symptoms (*Such as bronchial asthma, mainly among women and children*) or may not.

  Cystoscopy shows mucosal edema and polyps (or nodules) resembling tumors; eosinophils may be numerous in acute and chronic cases; the characteristic mixture of eosinophils and histiocytes is diagnostic (*Bernstein et al., 1992*).
**Malacoplakia:** Is rare and it has been described in immunosuppressed patients. Symptoms are nonspecifically those of chronic cystitis; the classical lesions are yellow plaques somehow soft, in all parts of the bladder; however the differential diagnosis of cystoscopy includes bladder tumor, because the plaques may be nodular or polypoid. They consist of large collections of histiocytes called von Hansemann cells, with eosinophilic cytoplasmic granules staining heavily with PAS *(Bernstein et al., 1992).*

- **Specific inflammatory masses:**

**Shistosomal bladder (Fig. 11):** The early clinical phase is marked by hematuria and dysuria; this represents the reaction against egg deposition, it takes the form of a granulomatous inflammation mainly in the lamina propria.

The primary lesions include Bilharzial tubercles which appear as seed like yellowish specks, and Bilharzial polypi which represent sessile pedunculated lesions resulting from a denser granulomatous reaction *(El Bolkainy, 1983).*

Three types of polypi are recognized. Granulomatous polypi are the most common which appear red, inflamed and later become yellow brown with coarse granular surface; fibrocalcific polypi seen in old patients are composed of healed granulomas with calcified eggs, fibrosis and atrophic surface epithelium; the villous polyp is indistinguishable from bladder papilloma by cystoscopy, however biopsy will reveal the bilharzial granuloma at
the polyp pedicle; they respond to antibilharzial therapy but resection may be indicated. Secondary lesions represent epithelial reaction to the initial lesions, (Include bilharzial sand patches, and bilharzial ulcers) and also include cystitis cystica and glandularis. Late complication include contracted bladder with reduction of its functional capacity due to healing by fibrosis, with possibility of obstructive uropathies at this stage; leucoplakia may also be seen, with greater incidence of carcinoma in situ and invasive carcinoma later on (El Bolkainy et al., 1981).

![Ultrasound and CT demonstrating extensive bladder wall calcifications](Quoted from www.emedicine.medscape.com)

**Fig. (11) Ultrasound and CT demonstrating extensive bladder wall calcifications**

**Viral infections:** (rare cases); Human papilloma virus gives rise to condyloma acuminatum which is common in the urethra and rare in the bladder; the lesion may be single or multiple; they form sessile or stalked papilloma with branching cores of connective
tissue covered by multilayered squamous epithelium; simple condyloma should be distinguished from papillary urothelial tumors and from verrucous squamous carcinomas of the bladder.

Herpes eruptions with typical vesicles rarely occur in the bladder and urethra (Bernstein et al., 1992).

**Tuberculosis of the bladder** (Fig. 12): caused by mycobacterium tuberculosis, occurs in association with renal TB, as a result of descending infection (May also be associated with genital TB, often in men).

The characteristic appearance in the active stage is that of disseminated, pale nodules, the so called tubercles, isolated or confluent; when confluent, they form coarse nodules (that may give rise to ulcers covered by caseous material with ragged undermined edges.

The tubercles are surrounded by hyperemic mucosa. Microscopically, the tubercles are formed of granulomas with rims of epithelioid cells and multinucleated langhans giant cells, surrounding necrotic centers; and the tubercles are surrounded by dense lymphocytic infiltrates; acid – fast bacteria are detected in the area of necrosis.

Late stages show fibrous scarring of the bladder leading to contracted thick – walled bladder. This classical picture of vesical TB
is rarely, if ever, seen today in developed countries (Bernstein et al., 1992).

![Image](image_url)

Fig. (12) CECT and IVU demonstrate thickened, contracted and deformed bladder with enhancing wall and minimal dilatation of ureters. There is extension of the inflammatory process to the anterior abdominal wall.

*(Quoted from Amling, 2010)*

**Iatrogenic Granulomas**: these are usually following transurethral resection of bladder tumors; they are of two types: the foreign body type appears as circumscribed lesions composed of multinucleate giant cells; the other type resembles a rheumatoid nodule displaying an ovoid, elongated configuration, with central fibrinoid necrosis surrounded by multinucleate cells, lymphocytes and histiocytes (Bernstein et al., 1992).
Table 1 Classification of bladder tumors (Bernstein et al., 1992)

I. Epithelial tumors.
A. Transitional cell
   * Inverted papilloma.
   * Papilloma grade 0
   * Carcinoma grades, 1, 2, and 3.
   * Carcinoma undifferentiated grade 4.
   * Carcinoma in – situ
B. Squamous cell:
   * Carcinoma.
   * Verrucous carcinoma.
C. Glandular
   * Vesical adenocarcinomas.
   * Urachal adenocarcinoma.
   * Signet – ring cell adenocarcinoma.
   * Clear- cell adenocarcinoma
D-Mixed histological Pattern:
   * Combinations of transitional cell, squamous cell and adenocarcinoma.
E. others:
   * Spindle – cell carcinoma.
   * Small – cell undifferentiated carcinoma.
   * Carcinoid tumor.

II. Mesenchymal tumors:
A. Benign
   * Leiomyoma
   * Hemangioma
   * Neurofibroma
   * Granular cell tumor
B-Malignant
   * Embryonal rhabdomyosarcoma.
   * Pleomorphic rhabdomyosarcoma.
   * Leiomyosarcoma.
   * Osteosarcoma and chondrosarcoma.
   * Carcinosarcoma.

III. Miscellaneous tumors
* A. paraganglioma
* B. Germ cell tumors.
* C. Malignant lymphoma and plasmacytoma.
* D. Malignant melanoma.

IV. Secondary Tumors
* A. Carcinoma Direct extension (e.g. from colon, ovary, prostate).
  * B From distant primary (e.g. stomach, breast, lung).
* C. Malignant lymphoma.
* D. Malignant melanoma.

V. Tumor – like lesions:
* A. Nephrogenic adenoma.
   * B. Inflammatory pseudotumor.
   * B. Condyloma acuminatum.
C) Urothelial Dysplasia

Preneoplastic Proliferative Abnormalities

Atypical hyperplasia is similar to epithelial hyperplasia except that there are also nuclear abnormalities and partial derangement of the umbrella cell layer (Koss et al., 1974). In patients with superficial bladder cancer, the presence of atypia in adjacent urothelium is associated with a 35% to 40% risk of developing invasive disease (Althausen et al., 1976).

Dysplasia:

The term dysplasia denotes epithelial changes that are intermediate between normal urothelium and carcinoma in situ. There are three categories of dysplasia: Mild, moderate and severe. Dysplastic cells have large round notched basally situated nuclei that do not exhibit the normal epithelial polarity (Murphy and Soloway, 1982). It is difficult to make a sharp distinction between severe dysplasia and carcinoma in situ (Friedell et al., 1986). As a general rule, mild and moderate dysplasia, even when associated with a history of bladder cancer, warrant careful follow up but no particular specific therapy, whereas severe dysplasia/carcinoma in situ requires aggressive treatment (Messing and Catalina, 1998).

Inverted papilloma:

An inverted papilloma is a benign proliferative lesion caused by chronic inflammations or bladder outlet obstruction. Most
commonly it occurs in the trigone and bladder neck areas in men with prostatitis (*De messter et al., 1975*).

Papillary fronds project into the fibrovascular stoma of the bladder rather than into the bladder lumen. The lesion is usually covered by a thin layer of normal urothelium. Two different types of inverted papilloma occur: Trabecular and glandular. Rare cases of malignant transformation of inverted papillomas have been reported (*Lazarevic and Garret, 1978*). There is a more common association of inverted papilloma, however, occurring in patients with coexistent transitional cell carcinoma elsewhere in the bladder or with histories of such tumors (*Cheon et al., 1995*). Because the overlying epithelium is normal, inverted papilloma appears as small raised nodules rather than as papillary or frond-like tumors (*Messing and Cataluña, 1998*).

**Vesical leucoplakia:**

Leucoplakia is defined as cornification of a normally noncornified epithelium. The histopathologic criteria include squamous metaplasia with marked keratinization downgrowth of the rete pegs (acanthosis), cellular atypia, and dysplasia. Leucoplakia is believed to be a response of the normal urothelium to noxious stimuli and generally is considered a premalignant lesion or a lesion that heralds the presence of malignant disease elsewhere in the bladder (*Benson et al., 1984*).

Vesical leucoplakia may progress to squamous cell carcinoma in up to 20% of patients (*Dekock et al., 1981*).
Leucoplakia is frequently found in patients with chronic cystic, bladder calculi, long-term indwelling catheters, or schistosomiasis (Messing and Catalina, 1998).

D) Urothelial Carcinoma

Carcinoma in Situ:

Carcinoma in situ may appear as a velvety patch of erythematous mucosa on cystoscopic examination, although quite often it is endoscopically invisible. Histologically, it consists of poorly differentiated transitional cell carcinoma confined to the urothelium. Carcinoma in situ may be asymptomatic or may produce severe symptoms of urinary frequency, urgency, and dysuria (Utz et al., 1970). Urine cytopathology study results are positive in 80% to 90% of patients with carcinoma in situ because of the poor cohesiveness of the tumor cells. Carcinoma in situ occurs more commonly in men its symptoms may be mistaken for prostates', urinary tract infection, neurogenic bladder, or interstitials cystitis (Utz and Farrow, 1984).

Carcinoma in situ occurs only rarely in patients with well – differentiated, superficial bladder tumors, but it is present in 25% or more of patients with high – grade superficial tumors (Koss et al., 1974).

It presents a poor prognosis. Patients with carcinoma in situ have higher tumor recurrence rates (Flamm and Dona, 1989).
With just endoscopic resection as treatment, between 40% and 83% progress to muscle – invasive cancer by different studies (Althausen et al., 1976).

Some patients have protracted courses lasting for more than a decade without developing muscle – invasive bladder cancer (Riddle et al., 1976).

Others progress rapidly to invasive bladder cancer that has a poor prognosis despite definitive therapy (Utz et al., 1970).

Some investigators have characterized carcinoma in situ as a peculiar cancer with aggressive morphologic features but having a limited capacity to invade and metastasize (Weinstein et al., 1980).

Patients with marked urinary symptoms generally have a shorter interval preceding the development of muscle invasive cancer. About 20% patients treated with cystectomy for diffuse carcinoma in situ are found to have microscopic muscle – invasive cancer (Farrow et al., 1976).

**Transitional Cell papilloma:**

Transitional cell papilloma of the urinary bladder is an uncommon benign lesion, which is often encountered incidentally or after painless hematuria. Papillomas comprise 2% to 3% of bladder epithelial tumors and occur most frequently in men older than the age of 50 years. The papillary fronds of this tumor are lined by a transitional epithelium that is virtually indistinguishable from normal urothelium. Papillary tumors that meet this criterion are
uncommon, and they have been accepted as papillomas, rather than as low–grade transitional cell carcinomas, only in the past 2 decades. On cystoscopy, the majority of cases show single lesions, 2 to 5 cm in diameter, but multiple lesions are not unusual. Recurrent papillomas are common (70%) and invasive carcinoma are developed in 7% of patients.

Although transitional cell papillomas are not malignant, they arise in an urothelial mucosa that is not at rest and evolving tumors can be detected only by repeated examinations for many years. In most instances, "recurrences" represent new tumors that develop elsewhere in the urinary bladder (Peterson, 1994).

**Transitional cell carcinoma:**

- **Epidemiology and risk factors:**

  The incidence of carcinoma of the bladder resembles that of bronchogenic carcinoma, being more common in men than in women, in industrialized than in developing nations, and in urban than in rural dwellers, the male to female ratio for transitional cell tumors is approximately 3: 1. About 80% of patients are between the ages of 50 and 80 years (Cotran et al., 1999).

  A number of factors have been implicated in the causation of transitional cell carcinoma. Some of the more important contributors include the following:

  - Cigarettes' smoking is clearly the most important influence, increasing the risk threefold to sevenfold, depending on the
packs – years and smoking habits. Fifty per cent to 80% of all bladder cancers among men are associated with the use of cigarettes, cigars and pipes whereas smokeless tobacco invokes a much smaller risk (Cotran et al., 1999).

- Occupational exposure to certain organic chemicals among workers in the German aniline dye industry was described in 1895, and it was subsequently confirmed among similar workers in the United States. Later, an increased risk of bladder cancer was identified among workers in the leather, rubber paint, and organic chemical industries (Peterson, 2001).

- *Schistosoma haematobium* infections in areas where these are endemic (Egypt, Sudan) are an established risk. The ova are deposited in the bladder wall and incite a brisk chronic inflammatory response that induces progressive mucosal squamous metaplasia and dysplasia and, in some instances, neoplasia. Seventy per cent of the cancers are squamous, the remainder being transitional cell carcinoma (Cotran et al., 1999).

- Transitional cell cancers of the bladder, ureters, and renal pelvis have been reported in the setting of analgesic abuse, particularly with phenacetin. Most cases, however, are not associated with known risk factors (Peterson, 2001).

- Heavy long-term exposure to cyclophosphamide an immunosuppressive agent, induces as noted hemorrhagic cystitis and increases the risk of bladder cancer (Cotran et al., 1999)
- **Pathogenesis:**

Two variants of urothelial bladder carcinomas are recognized with distinctly different histogenetic origin and biologic profile, namely: the superficial papillary and the muscle invasive types. Superficial papillary transitional carcinomas are tumors arising from papillary non-invasive (Ta) tumors, show exophytic growth and exhibit 9q deletions, a recurrence rate of 60%, but low progression rate of 10% and 10 years survival of 98%. Conversely, invasive transitional carcinomas are aggressive tumors arising from carcinoma in situ (CIS), exhibit endophytic growth and show Rb and P53 tumor Suppressor genes mutations, with a high recurrence rate of 85% ad 10 year survival of 30% (El-Bolkainy, 1998).

One or more defects in chromosome 9 or in the P or the q arms are frequently detected in non-invasive, low – grade, papillary TCC. In contrast, high – grade invasive TCC usually contains a defect on chromosome 17p, which represents an abnormality in the p 53 gene (Olumi et al., 1990).

Two different pathways leading to the development of non-invasive bladder cancer are suggested. P 53 gene inactivation seems to occur early in CIS, an observation supported by the fact that P 53 mutations were found in patients with CIS without any previous history of bladder cancer, many of whom did not have detectable loss of either chromosome 9 or 17. In contrast, chromosome 9 alterations may be sufficient for superficial papillary tumors to develop. The progression of superficial papillary tumors and CIS
may require subsequent acquisition of defects in P 53 or additional defects in chromosome 9 (Spruck et al., 1994).

Other chromosomal alterations have been observed in bladder tumors particularly in high – grade, invasive TTC, most frequently involving chromosomes 3, 5, 7, 8, 10, 11 and 13. Some of these most likely represent late, secondary changes related to the increasing genetic instability of DNA with progressing malignancy (Knowles et al., 1994).

Abnormalities in tumor – suppressor genes have also been identified in bladder cancer. Abnormalities in the retinoblastoma gene (Rb) are frequently observed. Nevertheless, none of the alterations in oncogenes or suppressor genes have so far led to clinically useful markets for diagnosis, Prognosis or therapy.

Epidermal growth factor (EGF) is present in relatively large amounts in urine and acts as an endogenous enhancer of bladder tumor development. EGF receptors appear to increase with higher – grade urothelial tumors and recently a significant correlation between EGF receptor expression, high tumor stage and poor patient outcome was reported, though EGF expression was not independent of stage (Nguyen et al., 1994).

- **Macroscopic Appearance** (Fig. 13):

  The gross pattern of urothelial cell tumors vary from purely papillary, nodular or flat to mixed papillary and nodular. The tumors may also be invasive or non- invasive.
The papillary lesions appear as red elevated excrescences varying in size from less than 1 cm in diameter to large masses up to 5 cm in diameter. Multicentric origins may produce separated tumors. As noted, the histological changes encompass a spectrum from benign papilloma to high aggressive anaplastic cancers. Overall, about half of bladder cancers are high grade lesions. Most arise from lateral or posterior at the bladder base (Cotran et al., 1999).

*Fig. (13) Gross pathology specimen of TCC*

*(Quoted from Van Tilborg and van Rhijn, 2003)*

- **Microscopic appearance:**

  Transitional cell carcinoma of bladder is classifieds according to world health organization grading system.

  1) Papillary projections lined by neoplastic transitional epithelial cells that show minimal nuclear pleomorphism and mitotic activity. The papillae are long and delicate, and fusion of papillae is focal and limited.
2) The histological and cytologic features are intermediate between those of grade 1 (the best differentiated) and grade 3 (the poorest differentiated).

3) Significant nuclear pleomorphism, frequent mitoses, and fusion of papillae are typical. Occasional bizarre cells may be present, and focal sites of squamous differentiation are often seen. Although invasion of the underlying bladder wall may occur with any grade of transitional cell carcinoma, it is most frequent in grade 3 tumors (Peterson, 1994).

A more recent classification, based on consensus reached at a conference by the International Society of Urologic Pathology (ISUP) in 1998, is currently being prepared (Table 2). It recognizes a rare benign papilloma, a group of papillary urothelial neoplasms of low malignant potential, and two grades of carcinoma (low and high grade).

Table (2) A comparison of the WHO grading and the ISUP consensus (Cotran et al., 1999).

<table>
<thead>
<tr>
<th>WHO Grading</th>
<th>ISUP CONSENSUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papilloma</td>
<td>Urothelial papilloma</td>
</tr>
<tr>
<td>TCC Grade I</td>
<td>Urothelial neoplasm of low malignant potential</td>
</tr>
<tr>
<td>TCC Grade II</td>
<td>Urothelial carcinoma, low grade.</td>
</tr>
<tr>
<td>TCC Grade III</td>
<td>Urothelial carcinoma, high grade.</td>
</tr>
</tbody>
</table>
Squamous Cell Carcinoma

Carcinoma of the bladder is one of the most common malignant diseases in Egypt. It also occurs in high frequency in some parts of Africa and the Middle East. Because of the geographic coincidence of bladder cancer and endemic bilharziasis, a causal relationship has long been speculated and established between the tumor and Schistosoma haematobium infestation. This association defines a distinct clinicopathologic entity quite different from that experienced in the western world. The tumor is found mostly in relatively young age groups. It is usually consisting of solitary fungating masses. It is commonly a well – differentiated squamous carcinoma with a limited tendency to lymphatic and blood stream spread. The patients usually present in an advanced stage of the disease with the symptoms of cystitis (El Sebai, 1981).

These are virtually always invasive at the time of diagnosis, and the majorities have invaded deep into the muscle layer or beyond (T3 and T4) (Peterson, 1992).

Squamous carcinomas probably account for no more than 5% of bladder carcinomas where schistosomiasis is not endemic nonschistosomal squamous carcinoma of the bladder is often associated with chronic urinary tract infection or bladder calculi. It may also arise in bladder diverticulae.

Squamous carcinoma of the bladder may be of low or high grades, that is showing marked keratinization, prickle cell differentiation, and limited cellular pleomorphism on one hand, or
showing obvious anaplasia with numerous mitoses and only slight keratinization on the other hand (Bernstein et al., 1992).

**Adenocarcinoma**

Adenocarcinoma of the bladder is uncommon and most cases have been reported in the past 2 decades. As with the other forms of bladder carcinoma, adenocarcinoma shows a pronounced male predilection. Bladder adenocarcinoma must be distinguished from urachal adenocarcinoma and from prostatic carcinoma. The histological patterns encountered in primary adenocarcinoma of the bladder include papillary, glandular, mucinous, adenoid cystic, signet ring cell and clear cell types. Foci of transitional cell with or without areas of squamous cell carcinoma may be observed. An association with cystitis cystica and cystitis glandularis have been reported in a minority of cases of bladder adenocarcinoma (mixed histological pattern). The majorities of adenocarcinomas are deeply invasive at time of initial presentation and are not curable (Peterson, 1994).

**Metastatic Spread**

Roughly 5% of patients with well–differentiated and moderately differentiated superficial papillary cancer and approximately 20% with high–grade superficial disease (including carcinoma in situ) have vascular or lymphatic spread. Presumably metastases occur with superficial tumors because of invasion into lymphatic and vascular channels within the lamina propria. Although, realistically, some patients with superficial malignancies
already have developed latent metastases, the vast majorities of such individuals have their bladder lesion pathologically under staged and already harbor muscle-invasive lesions (Freeman et al., 1995).

**Lymphatic spread:**

Lymphatic metastases occur earlier and independent of hematogenous metastases in some patients (Lerner et al., 1993).

The most common sites of metastases in bladder cancer are the pelvic lymph nodes (LNs), occurring in about 78% of patients with nodal metastases. Among these, paravesical LNs are involved in 16%, the obturator nodes in 74%, the external iliac nodes in 65% and presacral nodes in roughly 25%. Juxtaregional common iliac lymph nodes are involved in about 20% of patients, but almost always with involvements of the above mentioned regional sites as well (Smith and Whitmore, 1981).

**Vascular Spread:**

The common sites of vascular metastases in bladder cancer are liver 30%, lung 36%, Bone 27%, adrenal glands 2% and ingesting 13% any other organ may be involved (Babaian et al., 1980).

**Implantation:**

Bladder cancer also spreads by implantation in abdominal wounds, denuded urothelium, the resected prostatic fossa, or traumatized urethra (Weldon and Solway, 1975).
Implantation occurs more commonly with high – grade tumors (*Van der werf – messing, 1984*).

**Staging of Bladder Cancer**

Jewett and strong in 1946 examined autopsy material from 107 patients and analyzed the reaction of depth of penetration (Stage) to the incidence of local extensions and metastases. From these studies, they concluded that: (1) stage A (Submucosal infiltration) disease was not associated with dissemination (2) stage B (Muscular infiltration) disease was associated with dissemination in 13% of cases (2 of 15 patients); and (3) stage C (perivesical infiltration) exhibited dissemination in 74% of cases (64 of 89 patients).

In 1952, Jewett refined his initial staging system based on 80 patients who had complete excision of the primary tumor. The bladder muscle was arbitrarily divided at the midway level into superficial (stage B1) and deep (Stage B2).

In 1950, the Union International Center of Cancer (UICC) appointed a committee on tumor nomenclature and statistics to develop a classification system that embraced the status of the primary tumor, lymph nodes and metastases (T.N.M. Classification). The American joint Committee on cancer approved this staging that comprises both clinical and pathological staging (**Fig.14** & **Table 3**) (*Droller, 1997*).
A comparison of the UICC classification and the Jewett-Strong Marshall staging system is shown in (Table 4) (Cummings et al., 1992)

Superficial bladder tumors are largely grade I or II papillary transitional cell carcinoma that may or may not invade the lamina propria. Approximately 70% of the tumors are non invasive (Stage 0; Ta) and 30% invade the lamina propria (Stage A; T1) (Anderstrome et al., 1989).

<table>
<thead>
<tr>
<th>TNM</th>
<th>TIS</th>
<th>T_3</th>
<th>T_1</th>
<th>T_{2A}</th>
<th>T_{2B}</th>
<th>T_{3B}</th>
<th>T_{4A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>JSM</td>
<td>0</td>
<td>0</td>
<td>A</td>
<td>B_1</td>
<td>B_2</td>
<td>C</td>
<td>D_1</td>
</tr>
</tbody>
</table>

Fig. (14) Diagram for staging of bladder carcinoma (Quoted from Nat Pernick, 2011)
Table (3) AJCC-UICC TNM staging protocol for bladder carcinoma, (Droller, 1997).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Extent of invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>T : primary</td>
<td></td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ, (Flat tumor).</td>
</tr>
<tr>
<td>Ta</td>
<td>Papillary non invasive carcinoma</td>
</tr>
<tr>
<td>To</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Invasion limited to lamina propria</td>
</tr>
<tr>
<td>T2</td>
<td>Invasion limited to superficial muscle</td>
</tr>
<tr>
<td>T2a</td>
<td>Invasion to superficial muscle (inner half)</td>
</tr>
<tr>
<td>T2b</td>
<td>Invasion to superficial muscle (outer half)</td>
</tr>
<tr>
<td>T3</td>
<td>Invasion to deep muscle or perivesical fat</td>
</tr>
<tr>
<td>T3a</td>
<td>Invasion to deep muscle (outer half)</td>
</tr>
<tr>
<td>T3b</td>
<td>Invasion to perivesical fat</td>
</tr>
<tr>
<td>T4</td>
<td>Contiguous spread to adjacent organs</td>
</tr>
<tr>
<td>T4a</td>
<td>Uterus, vagina, prostate</td>
</tr>
<tr>
<td>T4b</td>
<td>Pelvic or abdominal wall</td>
</tr>
<tr>
<td>Tx</td>
<td>Extent of invasion cannot be determined.</td>
</tr>
</tbody>
</table>

N : regional and Juxtaregional Lymph nodes

| No | No regional lymph node metastases |
| N1 | Metastases in single lymph node that is 2 cm or smaller in greatest dimension |
| N2 | Metastases in a single lymph node that is larger than 2 cm but not larger than 5 cm in greatest dimension or multiple lymph node none of which is larger than 5 cm |
| N3 | Metastases in a lymph node that is larger than 5 cm in greatest dimension |
| Nx | Lymph node metastases cannot be Assessed |

M : Distant Metastases

| Mo | No evidence of distant metastases |
| M1 | Evidence of distant metastases |
| Mx | Distant metastases cannot be determined |

<table>
<thead>
<tr>
<th>Level of infiltration</th>
<th>Jewett–Strong Marshall</th>
<th>UICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial only</td>
<td>0</td>
<td>Tis, Ta Papillary Carcinoma Confined to Mucosa</td>
</tr>
<tr>
<td>Lamina Propria</td>
<td>A</td>
<td>T1</td>
</tr>
<tr>
<td>Superficial Muscle</td>
<td>B1</td>
<td>T2</td>
</tr>
<tr>
<td>Deep muscle</td>
<td>B2</td>
<td>T3a</td>
</tr>
<tr>
<td>Perivesical fat</td>
<td>C</td>
<td>T3b</td>
</tr>
<tr>
<td>Adjacent organ, Lymph nodes</td>
<td>D1</td>
<td>T4 Adjacent organ N1-3 Pelvic Lymph node metastases</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>D2</td>
<td>Juxtaregional Lymph Node metastases + Metastatic Lesion other than Lymph nodes.</td>
</tr>
</tbody>
</table>

Prognostics Factors:

The probability of tumor extension and subsequent recurrence is associated with a number of factors.

- Large size.
- High stage.
- High grade.
- The presence of multiple tumors.
- Vascular or lymphatic invasion.
- Urothelial dysplasia, including carcinoma in situ, at other sites in the bladder (Peterson, 1994).

The prognosis depends on the histological grade of the tumor and on the stage when it is first diagnosed. Papillomas and grade I
cancers (those of low malignant potential) yield a 98% 10-year survival rate regardless of the number of recurrences; only a few patients (<10%) have progression of their disease to higher grade lesions. In contrast, only about 40% of individuals with a grade III cancer survive 10 years; the tumor is progressive in 65%, approximately 70% of patients with squamous cell carcinomas are dead within the year (Cotran et al., 1999).

E) Mesenchymal Tumors

Benign: A great variety of benign mesenchymal tumors may arise in the bladder. Collectively they are rare, the most common is leiomyoma. They all tend to grow as isolated, intramural, encapsulated, oval to spherical masses, and varying in diameter up to several centimeters. On occasion, they involve submucosa pedunculated positions. They have the histological features of their counterparts elsewhere.

Sarcomas: True sarcomas are distinctly uncommon in the bladder. As a group, sarcomas tend to produce large masses (varying up to 10 to 15 cm in diameter) that protrude into the vesical lumen. Their soft, fleshy, grey-white gross appearances suggest sarcomatous nature. Rhabdomyosarcoma takes one of two forms: The "adult" form occurs mostly in adults older than 40 years and shows a rare form of histology similar to rhabdomyosarcomas of striated muscle. The other variant is the embryonal rhabdomyosarcoma, or sarcoma botryoides, encountered chiefly in infancy or childhood, and similar to tumors those occur in the female genital tract (Cotran et al., 1999).
Bladder rhabdomyosarcoma of childhood is an edematous mucosal polypoid mass, which has appearance like a cluster of grapes. Recent advances in combined treatment with radiation therapy and chemotherapy have resulted in greatly increased survival rates (Peterson, 1994).

**F) Secondary Tumors of the Urinary Bladder**

Secondary tumors may invade by direct extension from neighboring structures (cervix, uterus, prostate, and rectum) or by discrete, usually blood – born metastases. Prostatic carcinoma often involves the base of the urinary bladder by direct extension. This should not, as a rule, be a diagnostic problem, because immunohistochemical of the bladder (in both males and females) may show imunoreactitivy to prostate- specific acid phosphatase, and this fact needs to be borne in mind when determine the origin of a tumor at this site.

Direct spread may also occur from ovarian carcinoma or adenocarcinoma of colon. Urinary symptoms are occasionally the first manifestation.

Apart from direct spread, the bladder may be the site of metastases from primary tumors (e.g., lung or bronchus, stomach, and breast). There is predilection for infiltrating lobular carcinoma of the breast to metastasize to unusual sites (including the bladder), with diffuse infiltration (Bernstein et al., 1992).
TECHNIQUE OF VIRTUAL CYSTOSCOPY USING VOLUME ULTRASOUND

Volume Ultrasound deals with the acquisition of large volumes of ultrasound data. This block of information can be viewed in many ways such as sagittal, transverse and coronal, or as a complete volume-rendered image. To render a surface, it is necessary to have fluid in front of it. For example, the urinary bladder mucosa must be rendered while the bladder is full of urine. The resulting image lets us to look at the mucosal surface, and also allows a complete view of the bladder base (Fig 15). This is significant because it allows us to virtually image the bladder trigone sonographically for the first time (Dahiya et al., 2005).

Fig 15: 4D ultrasound surface rendering of the bladder base shows the “bird’s-eye” view of the bladder base at the trigone (Quoted from Dahiya et al., 2005)
In males, it is easier to visualize the urethral opening in the sagittal view, since the prostate can be used to orient the bladder base. In females, a very acute angulation behind the pubic bone is required to visualize the urethral orifice. This is problematic in 2D imaging due to the difficulty of positioning the probe, but this problem is overcome when using volume imaging.

Volume Ultrasound not only helps us to look at the trigone of the bladder, ureteric ridges and urethral openings but also allows us to study in detail the ureteric orifices, especially when they are patulous in nature. Lesions that arise from the bladder wall can be better characterized, and more clearly show their spatial relationship.

Additionally, the bladder can be sectioned in any plane to visualize structures behind or below the bladder. This gives better visualization of pathologies extending to or involving adjacent structures (Dahiya et al., 2005).

Four-dimensional (4D) ultrasound volumes were generated by the automatic rotation of the transducer. 4D data acquisition was based on high quality 2D US images of the UB with the sample window encompassing the prostate in men and the cervix in women. Rotational angles ranged from 45 to 90 degrees, with a rotational field width of 5 to 10 cm. The quality of the data collected was set at High or Extreme for better delineation of the tumors and internal bladder surfaces (Kocakoc et al., 2008).
Small artifacts were trimmed from the 4D data by increasing or decreasing the threshold, allowing better appreciation of the image. We also improved the quality of US images by application of a special algorithm for speckle reduction and edge enhancement. For each patient, the 4D sonographic examination and image reconstruction procedures were completed within 10 to 15 minutes (Kocakoc et al., 2008).

**The 4D US protocol included:**

1 - Acquisition of 3D transabdominal scan through the whole urinary bladder for detection of possible UBTs, finding locations and interactions with ureteric jets, bladder necks and trigones and calculating their numbers.

2 - Voiding 4D VEUS cystourethrography in patients with more than 1 UBT, and with tumors in the trigone region. 4D Virtual reconstructions of the urethra were constructed during micturition for exclusion of possible additional tumors.

3 - 4D virtual endocavitary ultrasound through the minimally distended urinary bladder was performed for detection of small UB lesions. The tumor size, volume and overall basement area of the tumor lesion were calculated for the surgery planning. Also, all the tumors were studied with Power Doppler for evaluation of vascularity (Kocakoc et al., 2008).
Postprocessing was performed after collecting the 4D data. Surface rendering was used to obtain cystoscopic-like US volumetric images of the urinary bladder, and a Multi-Slice View special program was used for reslicing the 4D data. All 2D, static 3D volumes and live 4D cineloops (4D real-time clips) based on surface renderings were recorded on the hardware for further evaluation.

Tumor locations, numbers, sizes and tumor basement areas were estimated during cystoscopy for TUR planning. US results were compared with cystoscopy findings which served as a “gold standard.” Two-dimensional (2D) sonographic results were compared with the findings of 4D sonography and with conventional cystoscopy (Kocakoc et al., 2008).
TECHNIQUE OF CT VIRTUAL CYSTOSCOPY

Introduction (CT Technique):

Different CT protocols are used for visualization of bladder lesions; however imaging should be done with filled bladder, as configuration and thickness of the bladder wall depends on degree of filling (Kraus et al., 1992).

But over distension of the urinary bladder should be avoided to detect early irregularity and mural lesions (Walsh, 1994).

Husband (1992) insisted that CT should be carried out following or during rapid injection of IV contrast medium in order to enhance the primary tumor and opacify the pelvic vessels, and to help assessment of adjacent organ invasion.

Kraus et al., (1992) completed pelvic examination by delayed images after excretion of contrast into the bladder for better delineation of the mucosa.

Kraus et al., (1992) mentioned however that routine CT technique should be altered according to bladder lesion to improve diagnostic capabilities.

When fully distended, the normal bladder wall is several millimeter thick. Thickness exceeding 0.5 cm must be considered pathological (Wegener, 1992).
Basis and Technical Issues of Virtual Imaging

Introduction:

In recent years the computerized post-processing of image data from cross-sectional imaging modalities has received progressively increasing recognition in the field of medicine. This development has various reasons: First, the technical developments of examination modalities such as CT and MRI, as well as SPECT, PET, and ultrasound; Second rapidly growing capturer performance has created the opportunity to dimply complex relations, anatomical structures of functional information, in a simplified and comprehensible manner.

Virtual endoscopy is one of the most recent innovations in the spectrum of post processing techniques. The predominant motive here is similarly, to present the image data included in the original slices in such a fashion that the viewer or radiologist is able to differentiate between that which is healthy and that which is pathological (Scheltinga, 2001).

Virtual endoscopy or "flight through" method that combines the features of endoscopic viewing and cross-sectional volumetric imaging may provide an advance in diagnosis methods. Nevertheless, virtual endoscopy presentation of image data enables the operator not only to explore the inner wall surfaces but also to navigate inside the virtual organs extracted from CT scans or MR images. In addition, interactive display of correlated two-dimensional (2D) and 3D data in a multi-window format may help
the endoscopies in performing various images – guided procedures. This interactive and real – time aspect of virtual endoscopy may contribute to a significant change in the execution of endoscopic procedures (Jolesz, et al., 1997).

**Volume Data**

Modern CT and MRI scanners produce a set of contiguous cross sectional images. When these individual slices are combined a great level volumetric data set of voxels is formed. Voxels (volume elements) are the basic element of volumetric data, similar to picture elements which are called pixels. Volume visualization techniques visualize such a volumetric data set as a whole, predicting a single projected image of the volume data (Scheltinga, 2001).

The volume data can be regarded as a discrete sampling of a continuous intensity field, which can be reconstructed by an interpolation function. By selecting only one specific intensity value it is possible to define an iso surface in this continuous field. This is the basic thought that is used to select the visible data from the volume data. In certain instances, an iso surface selection may not be sufficient, for example, when certain structures are blocking the view. In this situation, the iso surface selection can be restricted solely to the structures of interest, thereby making the struts that originally obstructed the view invisible. This is handled via a segmentation process (Scheltinga, 2001).
Interpolation (Fig. 16):

The voxels in the volume data are positioned on a grid. When intermediate intensity values are needed, the surrounding voxels are used to calculate this intensity value. This interpolation reconstructs a continuous function, from discrete sample points. It ranges from very simple technique e.g. replication to higher order interpolation techniques, e.g., cubic splints give even better results, but are computationally very expensive as the number of predation increases rapidly for 3D interpolation (Scheltinga, 2001).

![Fig. (16) The black line in the 3D plot on the left shows linearly interpolated data points. The surface is a linear interpolation of the black curves.](Quoted from sertac.scripts.mit.edu)

Segmentation (Fig. 17):

To display specific structures present in the volume data, they first need to be identified. The intensity value is often a good indicator for the presence of a structure. Thus a basic selection method is thresholding; the voxels or points with intensity values within an intensity range are selected. Sometimes this thresholding is
part of revering methods itself, so that no explicit segmentation step is required. When only a threshold is used an iso surface image is generated.

Thresholding is often just the basis for further segmentation based on this initial selection. Well-known techniques are selecting connected regions via a seed point. Regions can be expanded (via a dilation operation) or shrunken (via an erosion operation). Other post processing operations include or exclude regions based on properties like size, shape, location or other characteristics, or by manual editing (Levoy, 1988).

Segmentation methods often label individual voxels as belonging to a certain region or not. These binary segmentation methods approach difficulties at the borders of regions. Because only a fraction of each voxel at the border is occupied (the partial volume effect), the internet of such a border voxels quickly falls outside the selected threshold range. As a result such a border voxel is not included in the selection. This may translate into a false appearance of holes in thin structures (Scheltinga, 2001).

Advanced segmentation methods not only include or exclude voxels, but are also able to label individual voxels as partly occupied by a certain reconstruction. This probabilistic segmentation is often used in volume rendering methods (Scheltinga, 2001).
Fig. (17) 3D segmentation
(Quoted from Schwartz et al, 2003)

View Projections

Since the volume data are three-dimensional, they cannot be viewed directly. In order to visualize the volume data in a single 2D image, a projection of the volume data onto a projection plane is needed. This projection plane is similar to a film in a camera. Every point of the volume data is transformed to a point on the projection plane. This transformation is defined by a straight projection ray (projector) which starts at center of projection and passes through the volume point that is projected. The intersection point of this projector, or ray, with the projection plane is the projected position. Under certain circumstances parts of the volume data may not be visible; this occurs when the projector does not intersect with the projection plane. Normally the center or projection, or viewpoint, is positioned at a certain distance on a line perpendicular to the projection plane and through its center. So the viewpoint, together with the position, orientation and size of the projection plane, define the view (Foley et al., 1990).
View projections can be divided into two basic classes: parallel projection, where the viewpoint is positioned at an infinite distance, and perspective projection. When separate view projections for both eyes are used, this is called stereoscopic projection (Scheltinga, 2001).

- **Parallel Projection:**

  When the viewpoint is positioned at an infinite distance, the projection rays are parallel to each other. Parallel projection has certain characteristics. The projection is generally faster than perspective projection, as it is simpler to perform. Furthermore, the relative sizes and angles of objects are preserved in the final image. For example, parallel lines remain parallel in the projected image. This absence of distortion in the produced images is an advantage of parallel projection because it allows measurements to be performed on the projection plane (Scheltinga, 2001).

- **Perspective projection:**

  With perspective projection, objects are projected towards a single point behind the projection plane. This is referred to as the center of projection or the viewpoint. Perspective projection causes a distortion of object shapes. The reason for the distortion is that objects that are located closer to the viewpoint appear larger in the projected image than objects that are located further away. In this respect, perspective projection is similar to viewing in the real life in realistic images and can provide essential depth cues. However, the
perspective distortion precludes accurate measurements of objects in the projected plane (Scheltinga, 2001).

- **Stereoscopic projection (Fig. 18):**

Stereoscopic projection is a combination of two normal perspectives instead of one. In the human visual system, the eyes view a scene from slightly different positions. The two projection planes mainly overlap each other, but are shifted partially to the left and right because the viewpoints are positioned at slightly different locations, the objects are seen from somewhat different angles. These left and rig images are fused in the brain, thereby giving the perception of depth.

Several techniques exist to view such a pair of stereoscopic images. A well–known technique is to use glasses with polarizing filters. Another technique is using a screen where the image seen is dependent on the angle from which it is viewed (Scheltinga, 2001).

*Fig. (18) Stereoscopic 3D projection*

*(Quoted from www.wikipedia.org)*
Surface Shading

The intensity and color visible at a specific surface location is determined by the surface shading model. This process of surface shading adds realism to an image, so it is a very important aspect of volume visualization. The absence of surface shading makes it very difficult to guess the surface orientation, or relative positions of surfaces (Lorenson and Cline, 1987).

Depth Cueing:

A simple but effective means to enhance the sensation of depth is called depth cueing. In fact, in the early days of volume visualization, this was the only method available for surface shading. With depth cueing; Points closer to the viewer appear brighter than points farther away. This simulates the effect of atmospheric attenuation. It is also possible to simulate fog by extending this model with an atmospheric color (Herman and Udupa, 1981).

As it is very complicated to signify small intensity changes, visualization of small depth differences is poor. However, depth cueing is a useful technique to view or enhance visualization of global surface structure (Scheltinga, 2001).

Phong Illumination Model:

Surface illumination imitates the interaction of light with a surface. A very popular surface illumination model is the phong model (Phong, 1975). This model consists of three components:
ambient, diffuse and specular reflection. Although the various existing deviates of the phong model give similar results they allow for a more efficient implementation than that which is possible in the original model (*Blinn, 1977 and Schick, 1994*).

**Ambient Light:**

The ambient component models indirect light, reflected from other surfaces in the environment. It is independent of the surface orientation, as the light is arriving from all directions. Because the ambient light is assumed uniform in the environment, the ambient component is modeled as a constant value (*Gordon and Roland, 1985*).

**Diffuse Reflections:**

The diffuse component models the direct light, which is scattered on the surface into all directions. It is dependent on the angle between the surface normal (N) and direction to the light source (L). As the intensity depends on the orientation of the surface towards the light source, it provides vital clues about the surface orientation (*Scheltinga, 2001*).

**Specular Reflection:**

It models the mirror – like reflection of light on a surface. On a perfect mirror, incoming light is reflected in a single direction. This direction of reflection (R) is the light vector (L) mirrored about the surface normal (N) but usually a shiny surface is not a perfect mirror, and the light is not reflected in this reflection direction only,
but also in other directions with a lower intensity. The angle \( A \) between the reflection vector and the vector to the viewpoint \( V \) specifies the intensity of the reflection. Because the specular reflection is only visible form a certain direction, it is dependent on the viewer's position. Especially with motion, this gives important hints about the surface orientation (Scheltinga, 2001).

**Surface Illumination:**

The total illumination of a surface point is given by the additional ambient, diffuse and specular components (Scheltinga, 2001).

**Material Properties:**

The material properties define the appearance of a surface. A logical parameter is, of course, the surface color. It can for example, be used to distinguish (segmented) surfaces from each other. Another property is whether the surface looks dull (for example, chalk) or shiny (for example, polished metal). This is defined by the phong parameters.

The ambient component of the phong model can be regarded as the brightness parameter of a material, the diffuse component as the contrast parameter, while the specular component is a shininess parameter. The specular component controls the extent of the highlighting, in which case higher values result in a weaker highlighting (Scheltinga, 2001).
3D Rendering

For interpreting volume data, two classes of rendering techniques are applicable. Surface rendering requires a surface description, which is extracted from the volume data. Volume rendering directly renders the volume data, without the need for such an intermediate description (*Schroeder, et al., 1992*).

Surface Rendering

Surface rendering is a conventional computer graphics technique that is widely supported by specialized graphics hardware. It uses a surface description to model the object surface. This description normally consists of a mesh of polygons. To visualize this surface, individual polygons are project and combined with previously projected polygons, resulting in the final image which depicts the surface.

To visualize volume data, a surface description needs to be extracted. This process could be based on a segmentation performed earlier or on iso value segmentation (*Schroeder, et al., 1992*).

Surface Description:

The most common surface description is a set of connected planar polygons, or a polygon mesh. As a polygon is flat, the points forming the boundary of a polygon (called vertices) must lie in one plane. To avoid a violation of this requirement, triangles are often used, as the three vertices of a triangle always form a plane (*Lorensen, 2010*).
A widely used surface extraction method algorithm is the marching cubes algorithm. Considering the production of a set of triangles this process is called triangulation. The marching cubes algorithm creates triangle meshes by examining basic cells (cubes bounded by eight voxels) in the volume data. A threshold value selects an iso surface for which a description is generated. Once the surface description is obtained, the original volume data is no longer needed, however, if the threshold value is changed, a complete new surface description must be regenerated (Lorensen, 2010).

A cube is defined by the inclusion of eight contiguous voxels from two adjacent slices. Each vertex of this cube is classified as inside or outside the surface by comparing its intensity value with the iso surface value. The edge list is then used to define the triangles present in the cube by subscribing which three of the 12 cube edges delimit a triangle. The position of the intersection along the edge is found by interpolations of the vertex intensities. Up to four triangles may be needed to describe the iso surface in the cube. Finally surface normal for each triangle vertex are calculated by interpolating the volume gradients at the cube vertices. Using the symmetry of the cube, the 256 possible cases of iso surface intersection can be reduced to 14 (Woo et al., 1997).

**Rendering the surface Description:**

When the surface normal is interpolated over the polygon, and the shading is performed for every pixel, accurate results can be
achieved. The Polygon mesh surface description can be rendered using a standard software library interface (Woo et al., 1997).

Multiple polygons can overlap each other in the image, but only the parts of polygons in front of others are visible. Therefore the visibility of a part of the polygon needs to be determined before it is actually scored in the image. This is called hidden–surface removal (Schroeder et al., 1992).

**Depth Buffer:**

To determine whether a newly projected pixel is visible compared to previously rendered pixels, a depth buffer is used. This depth buffer (or Z-buffer) has the same size as the image, and contains a depth value for each image pixel. The depth of every new surface pixel is compared to the corresponding depth value stored in the depth buffer. Only when the pixel is in front of a previously rendered pixel, pixel stored in the image, and the depth buffer is adjusted accordingly.

With a depth buffer, the polygons can be projected in an arbitrary order. Furthermore, potential intersections of polygons are irrelevant. If a rough front–to–back depth sorting of polygons is performed, then most of the hidden surfaces will require no expensive shading. The depth buffer is useful not only during the rendering stage itself, but also for merging other objects or images afterwards (Scheltinga, 2001).
**Volume Rendering**

With volume rendering, the volume data itself is directly interpreted. Without an explicit surface representation, a classification function defines the visible and invisible parts of a volume, based on the intensity value in the volume. Many variants of volume rendering exist, so there is not a single true volume rendering method. Although volume rendering is often associated with translucent images, it is also capable of creating surface shaded images. The known methods of volume rendering are classification, splitting and Ray casting (*Shirely and Tuchman, 1990*).

- **Classifications:**

  The classification function defines the visibility of materials present in the data set. It is commonly assumed that different materials map to different intensity levels; therefore, the classification function maps intensity levels to opacity values. A low opacity value results in a translucent or even invisible object while a high opacity value results in a clearly visible object. When the classic tone is restricted to segmented regions, only these regions are visualized (*Levoy, 1988*).

  When a simple thresholds is used to select an iso surface, the classification maps all intensity values below the threshold to a low or zero opacity, and all intensities above this threshold to a high opacity. The classification function is often smoothed, which generates a fuzzy classification (*Scheltinga et al., 1996*).
- **Splatting:**

  Volume rendering method projects the volume data in voxel order onto the projection plane. With splitting, each voxel is projected onto the projection Plane (Westover, 1990).

  A voxel contributes to multiple image pixels, which is defined by a footprint. The contribution of the voxel to an image pixel is highest at the center of the footprint. The footprints of adjacent voxels overlap each other; hence, an individual image pixel is normally the result of an accumulation of several projected voxels. Because the resolution of splitting is restricted to the voxel size, and because the footprint causes blurring of the image, splitting is of limited use (Levoy, 1990).

- **Ray Casting:**

  A commonly used volume rendering method to project the volume data is ray casting (Levoy, 1988). With ray casting the volume data is processed in image (pixel) order. A ray is cast through the volume data for each pixel of the output image. Along this ray, opacity and color values are calculated at evenly spaced sample positions. When all sample points of the ray are composited, the result is a single image pixel (Scheltinga et al, 1996).

**Rendering artifacts**

**Starcasing:**

When the slice distance is large compared to the pixel size a starcasing effect may occur. Normally interpolation of the volume
data results in a smooth iso surface, but with a large slice distance this is a problem. To prevent this starcasing effect the slice distance of the volume data should be similar to the slice pixel size. Another possibility is to use a specialized interpolation technique aimed at reducing this effect (Scheltinga, 2001).

**Aliasing:**

Aliasing occurs as a result of interference between the sample grid and the voxel grid. When the sample grid resolution with ray casting is too small with respect to the voxel grid, ringing artifacts can occur. Enlarging the resolution of the image can prevent this. With virtual endoscopy aliasing is not a problem, as the images are normally zoomed and thus have a high resolution compared to the volume data (Scheltinga, 2001).

**Rippling:**

With volume rendering individual voxels are sometimes visible via rippling artifacts when an image is zoomed – in these artifacts are caused by an incorrect order of operations. The voxels show up in the image. But this rippling disappears when first the volume data is interpolated to the sample location, and then classification and shading is performed (Scheltinga, 2001).

**Slicing:**

When ray casting the sampling distance along a ray is too large, slices may appear in the image; the discrete depth locations at which samples are taken then become visible as slices. This effect
occurs when the sample rate is not adjusted while zooming – in on the image. It is solved by increasing the sample rate at higher zoom rates, but these results in a slower rendering speed as more samples are taken along each ray (Scheltinga, 2001).

**Highlights Flashing:**

With surface rendering, the specular highlights may suddenly flash on or off during interaction because shading is only performed at vertices, specular shading is not always correct for the other pixels of the polygon. Instead of interpolating colors over the polygon, the surface normal should be interpolated. But this also requires shading for every polygon pixel, a costly affair (Scheltinga, 2001).

**Virtual Endoscopy**

Virtual endoscopy visualizes the inner surfaces of structures present in volumetric data in 3D images. To simulate true endoscopy, surface shaded images are generated using a perspective projection. As navigating through the inner structures quickly becomes a complicated procedure, often a (Possible branched) path through the structure is used. This path can be used to interactively investigate the inner structure or to generate an animation along the path (Paik et al., 1998).

**Visualizations settings:**

To visualize the interior surface of tubular structures, the visible surface needs to be sleeted. Normally, a simple threshold is sufficient, resulting in an iso surface display. A segmentation step
may sometimes be necessary, however, to remove blocking structures.

For virtual endoscopy, the parallel projection is not very useful. The explanation is that only a small part of the surface wall is visualized, and it is very hard to observed depth in such images. Because branches are hardly detectable, they are easily missed. The perspective projections show much more of the surface of tubular structures, than the parallel projections (*Scheltinga, 2001*).

Surface shading results in images similar to true endoscopic images. This is essential for virtual endoscopy, as it shows subtle changes in surface orientation, which are not seen otherwise. The light source is normally positioned at the viewpoint, as this ensures a satisfactory illumination of all visible surfaces.

With virtual endoscopy large zoom factors are often needed. Consequently, the individual voxels become easily noticeable, especially when surface rendering is used. The reason is that only a limited amount of triangles are created for each voxel. With the large zoom factors used, these individual (flat) triangles easily show up in images. As volume rendering generates images from the volume data itself, it allows rendering at a higher spatial resolution when zoomed-in on voxels. Therefore, volume rendered images show details present in surface rendered images. Thus although surface rendering is capable of providing interactive frame rates, volume rendering is the preferred rendering technique for virtual endoscopy (*Parker et al., 1998*).
Path Planning:

Navigating through the inner structures is often a problem, especially when these structures are strongly curved. With full control over a camera, it is easily moved out of this inner structure. Comparatively, a simple solution is to use a guidance path for easy navigation. The path adds constraints, which are useful in guiding the viewer through structure. An effective path needs to have certain properties.

The path must remain inside the structure and avoid collision with the wall. It should follow the centerline of the structure as closely as possible, as this provides the best visualization of the surrounding wall. The path should also be smooth without unnecessary kinks.

Once a path is created, navigating is simply a matter of positioning the view along the path. The viewing direction adjusted to the local path orientation. It remains possible to look around by adjusting this viewing direction, in order to obtain a better impression of interesting features. To generate an animation, a series of images is generated along the path at small distances (Paik et al., 1998)

Step for Creating Virtual Cystoscopy

Helically acquired CT data sets of the bladder used to perform virtual cystoscopy. This requires several manipulations of the data utilizing computer technology, which was originally developed for special effects in the movie industry. The steps after acquiring the
data include data transfer, volume formation, image segmentation, 3D rendering and video recording. The images are transferred to a Silicon Graphics work station computer via software program generates 3D surface rendered images of the bladder. These images can be viewed from any projection with the bladder lumen thus simulating a cystoscopic exam. The software and the real time rendering capabilities of the computer allow the user to navigate through video images of the bladder with a computer cursor directed by a mouse. So the steps for creating virtual cystoscopy include:

- Patient preparation and image acquisition.
- Image processing.
- Segmentation.
- Fly through (Creating virtual reality).
- Image analysis.
- Image display. (*Vining et al., 1996*)

**Patient preparation and Image acquisitions:**

One of the most important parts of the examination is to assure the complete filling and distention of the bladder as a hollow organ, to prevent the appearance of pseudo – lesions due to incomplete distention (*Olcott et al., 1998*).  

Beside the requirement to distend the bladder, it is important to increase the contrast difference between the bladder wall and the lumen in order to optimize the virtual endoscopy independently of the reconstruction technique using surface or volume rendering algorithms (*Fleiter, et al., 2001*).
For computed tomography:

There are two different principles for distending the urinary bladder and increasing the contrast difference between bladder wall and lumen: retrograde via a Foley catheter with insufflation of air or contrast medium (Vining, 1997) or using the excretory Function of the urinary system to fill the bladder with intravenously injected contrast material (Merkle et al., 1998). As the second method does not require placement of any tubes it is less invasive and is the preferred one for daily routine work but it requires detailed preparation and timing (Fenlon et al., 1997).

Using the urine – filled bladder for virtual endoscopy were unsuccessful because the low contrast attenuation between the urine and the bladder resulted in noisy images that were unusable for diagnostic purposes in 90% of the cases (Fleiter et al., 1997).

Various protocols of examination are available for example (Bernhardt et al., 2003) suggested that patient is laying supine in the CT table, adequacy of bladder distention is assessed with review antero-posterior tomograms image obtained prior to axial CT data. The examination is performed using helical CT scanner. Images are obtained with a 3-mm collimation and a pitch of 1. Reconstructions are performed at 1-mm increments (Jolesz et al., 1997).

Image processing:

The cross – sectional image data are processed and the signal intensities are converted into anatomic surfaces for later display. The first step toward surface rendering is segmentation. The imaging
technique and anatomic location of the study dictate the choice of segmentation \((Jolesz \ et \ al., \ 1997)\).

Virtual cystoscopy of the bladder is not limited to a specific reconstruction technique if the contrast attenuation between the bladder wall and the contrast filled lumen is sufficient. Volume and surface rendering can both be used to calculate the internal views of the bladder and possible tumor masses \((Fleiter \ et \ al., \ 2001)\).

However, volume rendered images are "data rich"; they use 100% of available cross sectional data for three – dimensional reconstruction and have a fluoroscopic appearance rather than the flat opaque appearance image created with surface shaded display \((Fenlon \ et \ al., \ 1997)\).

The frits step in achieving virtual cystoscopy of the urinary bladder is to detect the surface of the bladder mucosa in the scan data set. This can be done by manual control for surface rendering or using a specific attenuation class for volume rendering \((Fleiter \ et \ al., \ 2001)\).

**Fly Through – Navigation:**

Manually specifying the path is possible by defining key points along the path. Intermediate path positions are then automatically determined by fitting a smooth curve through these manually defined points. This is a well – know technique in computer animation \((Hong \ et \ al., \ 1997)\). But defining satisfying key points is often difficult and time consuming. Another possibility is to
use a computer assisted path generation algorithm (Paik et al., 1998).

Unlike virtual colonoscopy; interactive navigation is a must to create complete virtual cystoscopy. The changeable perspective of the virtual camera can be used to generate "fisheye" perspectives of the balder lumen and this improves orientation compared to fibro optic examinations. User controls could rotate the camera about its origin or its focal point and controlling the field of view of the camera. Multilane images corresponding to the position of the virtual camera are useful to provide the examiner with adequate orientation during the workup (Fleiter et al., 2001).

**Image Display:**

Optional approaches to viewing the images generated have included the review of computer monitor, scans, or still photographs of bladder abnormalities and regions of interest, video presentations of the simulated endoscopic examination, and real – time interaction with the data set at the computer workstation. To facilitate this process and to limit disorientation within the hollow organ, several navigational aids have been developed (Haponik et al., 1999).

(Jolesz et al., 1997) used a relatively simple physical model of an endoscope. The camera was represented by a cylindrical object and the viewing direction followed the longitudinal axis (Z-axis). The virtual camera had three functions simulating the translations and rotations of a real endoscope: it advanced along the Z-axis, it rotated around the Y-axis and it pivoted around the X-axis. They
implement this simulation on a silicon graphics workstation. On the monitor, three windows simultaneously displayed the global view, the local view, and the nearest CT or MR imaging slice with the camera positioned as indicated. Both the global (Surface – rendered outside surface) and the local (Virtual endoscopy view of the inside surface) views could be displayed from various angles, and details could be zoomed in (Jolesz et al., 1997).

With the surface models of the desired anatomy and a path (or means to generate one); (Jolesz et al., 1997) used various display techniques to present endoscopy – like views of the cross – sectional data.

**Navigation Aids and display Techniques For Real – Time Virtual Endoscopy**

Single – image display is traditional surface rendering. The triangle lists of the organs can be readily rendered using commercial polygon acceleration hardware. Transparent renderings of large enclosing tissue (such as the skin) allow an unobstructed view of the interior while providing a 3D environment for the user (Jolesz et al., 1997).

**Stereoscopic Images:**

Many methods used to enhance the perception of 3D images with three different types of stereoscopic display hardware: videotapes viewed, liquid crystal display shutter glasses, and large – screen projection using polarized glasses. All three techniques
require two separate images: one corresponds to the left eye image and one corresponds to the right eye image (Jolesz et al., 1997).

**Split Screen Display:**

Split – screen display presented two images simultaneously. One was an image from a user – specified location that served as a localizer for the endoscope. This overview uses a geometric clipping technique to cut a hole through any anatomy between the overview camera and the endoscopic camera. The other image was a simulated endoscopic view (Jolesz et al., 1997).

**Camera tracking on cross – sectional slices:**

Camera tracking on cross – sectional slices is achieved with an auxiliary window that shows the location of the endoscope as a marker on the original CT or MR imaging slices. This view localizes the endoscope within the familiar cross sectional image (Jolesz et al., 1997).

**Pointer Display:**

Pointer display presents an overview with a pointer showing the location of the endoscope. While moving along a generated path, the user can press the "Where am I?" button to change to the pointer display (Jolesz et al., 1997).
CONVENTIONAL CYSTOURETHROSCOPY

Cystoscopy is the use of a scope (Cystoscopies) to examine the bladder. The examination includes the following.

- Urethra or urinary channel, which includes the prostate in men.
- Bladder and ureters.

This is done either to look at the bladder for abnormalities or to help with surgery being performed on the inside of the urinary tract (Transurethral surgery) (Gaynes, 2001).

Indications:

1) Lower urinary tract disease:

The primary indication for cystourethroscopy is the diagnosis of lower urinary tract disease.

With regard to the diagnosis of lower urinary tract disorders, signs and symptoms that may be related to the urinary tract are evaluated with cystourethroscopy to directly visualize lower urinary tract anatomy and macroscopic pathology, which may be responsible for the clinical picture under evaluation.

One of the most common indications for cystourethroscopy is in the evaluation of microscopic and gross hematuria (Carter, 1998).

By combining radiographic and endoscopic techniques, one can usually determine the source of bleeding in the upper or lower
urinary tract. Other indications for cystourethroscopy include evaluation of voiding symptoms (Obstructive and irrelative), repeated urinary tract infections or incontinence, which may be the result of neurologic, inflammatory, neoplastic, or congenital abnormalities.

In addition, materials for both cytology and histologic examinations can be obtained through cystourethoscopic techniques (Carter, 1998).

2) Upper urinary tract disease:

Access to the upper urinary tract can be obtained cystoscopically. Diagnostic contrast examination of the entire upper urinary tract is accomplished by retrograde injection of contrast agents through small catheters passed cystoscopically. Ureteral stents to bypass or prevent ureteral obstruction as well as ureteral catheters and brushes can be passed cystoscopically to obtain material for cytological and histologic examination from the upper urinary tract. In most cases, fluoroscopy is used in conjunction with these diagnostic and therapeutic procedures of the upper urinary tract (Pollack, 1990).

Instrumentation:

Cystourethroscopy can be performed with either: 1-the rigid cystoscopies with an optical system and accessory instruments. 2-Flexible fibro-optic cystoscopy with accessory equipment(Carter, 1998).
- **Rigid Instruments**

Modern rigid cystourethroscopes consist of:

1. A metal sheath connected with irrigant fluid.
2. An obturator that provide a method of easy direct visual passage of the endoscope.
3. A bridge that allows both passage of the telescope and access to the working channel of the sheath for passage of accessory instruments.
4. A deflector system (Albarran lever) can be placed through the sheath to allow passage and controlled deflection of catheters through the working channel.
5. Telescopes: The telescopic lens is placed through the sheath by attaching a bridge to the sheath. Telescopes consist of illuminating and imaging systems. Modern telescopes use fibro-optic illumination and a rod – lens imaging system. The objective lens at the tip of the instrument collects the light of the image and transmits the image to the eyepiece through the rod – lens system. Telescopes are available with different angles of view for urethroscopy and bladder inspection (*Carter, 1998*).

**Advantages of the rigid endoscope:**

1. Better optics because of the use of a rod – lens system in rigid instruments, in contrast to the fibro-optic system in flexible instruments.

2. Larger working channel that allows the urologist greater versatility in passage of accessory instruments as resectoscope.

3. Larger lumen for water flow, thus improving visualization.

4. Ease of manipulation and maintaining orientation during inspection within the bladder (*Carter, 1998*).
- **Flexible instruments**

Flexible cystourethroscopes contain fibro-optic bundles within a flexible shaft for illumination and visualization. The shaft has an irrigating channel and a working channel for passage of accessory instruments. The tip of a flexible endoscope can be deflected 180 to 220 degrees by a thumb control located near the eyepiece (*Carter, 1998*).

**The advantages of flexible endoscopes:**

1) Greater comfort for the patient.

2) The ability to perform the procedure in the supine position.

3) The ease of passing the instrument over an elevated bladder neck.

4) The ability to inspect at any angle with deflection of the tip of the instrument.

The size of cystourethroscopes in usually given according to the French scale and refers to the outside circumference of the instrument in millimeters. Instruments of different sizes are available to accommodate pediatrics patients (No. 8 to 12 Fr.) and adults (No. 16 to 25 Fr.) (*Carter, 1998*).

**Video – cystourethroscopy**

The image from a rigid or flexible endoscope can be transmitted to a TV monitor with the use of a video camera (video – cystourethroscopy). Modern video cameras may contain an optical
device that divides the light into two paths (beam – splitter) to provide simultaneous video – monitor projection and direct viewing through the endoscope. Endoscopic images can be transferred to a video recording device and tapped, allowing documentation and review of a procedure. With a video – cystoscopic unit, the endoscopist can perform the procedure by using the image on the TV monitor to guide movement of the endoscope instead of looking through the eyepiece of the endoscope (Carter, 1998).

The advantages of the approach include:

1- Avoidance of contact with body fluids.

2- Documentation of the procedure by using a video recorder.

3- Use of the TV monitor for teaching purposes (Carter, 1998).

Patient Preparation:

It is important to ensure that the patient does not have an active urinary tract infection before cystourethroscopy, because of the possibility of exacerbating the infection by instrumentation of the urinary tract. After the patient has been counseled regarding the style of the procedure, the preparation is the same as for urethral catheterization. It is important to ensure sterilization and obtain adequate urethral anesthesia for diagnostic cystourethroscopy. With local urethral anesthesia biopsy and cauterization of the urethral and bladder mucosa can be accomplished cystoscopically. In addition, upper urinary tract instrumentation can be performed. More
extensive endoscopic procedures should be performed with general or regional anesthesia. *(Pollack, 1990).*

**Technique**

Any urologic non-irritant fluid can be used for cystourethroscopy; most often, sterile water or saline is used. If electrocoagulation is planned, it is necessary to avoid solutions containing electrolytes.

If diagnostic cystourethroscopy is being performed, a small instrument (No 17 Fr) is adequate. If a larger working channel is needed for accessory equipment (e.g., a biopsy device), a larger endoscope is chosen.

Systematic inspection of the entire urethra and bladder should be performed during cystourethroscopy. Before insertion of the instrument, the urethral meatus should be inspected if this has not already been accomplished. If the meatal size appears inadequate to accept the endoscope, it can be dilated with metal sounds. After the sheath of the cystourethroscope is generously lubricated with water–soluble anesthetic lubricant, the endoscope can be passed under direct vision with a 0 to 30–degree lens *(Reuter, 1987).*

- **Urethra:**

In the male, the penis should be grasped and straightened so that it forms almost a right angle to the abdominal wall. The endoscope is passed through the fossa navicularis, and the anterior urethra is inspected as the instrument is gently passed. Any mucosal
abnormality should be noted, and the diameter of the urethra should be evaluated. If there is resistance to the passage of the endoscope, a smaller instrument should be used or the urethra should be dilated.

As the instrument is advanced and enters the bulbar urethra with its greater diameter, the endoscope and penis are lowered while the instrument is passed until the penis is parallel with the floor. This allows passage of the instrument through the membranous urethra. The external sphincter is easily identifiable at the level of the membranous urethra by the mucosal folds radiating from a narrow lumen ahead of the endoscope. Gentle pressure facilitates passage of the endoscope through this area. When the instrument passes into the prostatic urethra, the verumontanum is noted. The prostatic urethra is inspected, and the size of the prostatic lobes is evaluated together with the length of the prostatic urethra, which can be elongated with prostatic hyperplasia (Reuter, 1987).

At the level of the bladder neck, it may be necessary to depress the endoscope gently in order to pass the instrument into the bladder over the bladder neck. An alternative techniques is pass the rigid endoscope "blindly" into the bladder as one would pass a metal dilator, with inspection of the urethra on withdrawal of the endoscope.

Inspection of the female urethra is easily performed by inserting the endoscope under direct vision into the urethral meatus and by directing the instrument cephalad toward the umbilicus. (Reuter, 1987).
**Bladder:**

Once the endoscope is inside the bladder, a systematic evaluation of the entire bladder surface is performed. Using the 30-degree lens with the bladder only slightly filled, one can identify the interureteric ridge just inside the bladder neck along the trigone. Next, the ureteral orifices are visually located several centimeters lateral from the center of the interureteric ridge and should be observed as passage of clear urine occurs bilaterally. The floor of the bladder behind the trigone and posterior bladder wall are inspected. Using the 70 to 90 degree lens, one can systematically inspect the lateral walls of the bladder by moving the endoscope from anterior to posterior and back as the bladder fills slowly. Finally, the dome and anterior bladder wall are evaluated with the 70 to 90 degree lens, with the bladder air bubble instilled at the time of instrumentation as a landmark on the dome of the bladder. The anterior bladder wall just behind the bladder neck is best seen with the bladder only partially filled and with one hand exerting suprapubic pressure to depress the anterior bladder wall. After complete inspection of the urethra and bladder has been accomplished, the bladder is drained and the instrument is gently removed.

It is important to document the procedure in a systematic fashion as it was performed. The urologist should have a systematic method of performing cystourethroscopy that allows careful inspection of the entire lower urinary tract from the urethral meatus to the bladder and that at the same time causes minimal discomfort for the patient *(Carter, 1998).*
Complications and Sequels of cystoscopy:

As with any surgical procedure there are some risks involved with a cystoscopy complications may include:

1- Profuse bleeding.

2- Damaged urethra.

3- Perforated bladder.

4- Urinary tract infection.

5- Injured penis.

6- Cystoscopic procedures can also create scar tissue. This tissue can cause a stricture, or narrowing, in the urethra, which may cause difficulties during urination (Gaynes, 2001).
Diagnosis of Urinary Bladder Cancer

1-Signs and Symptoms:

The most common presenting symptom of bladder carcinoma (BC) is painless gross hematuria, which is often intermittent, leading to occasional delays in consultation. Bladder cancer will be found in approximately 25% of adult patients with gross hematuria (Jung et al., 2001).

In almost all patients with cystoscopically detected cancer, microhematuria will be found if enough consecutive testings are performed. On the other hand, BC will be detected in only 2% to 4% of all adult patients presenting with microhematuria which represents a dilemma to physicians in recommending invasive investigation for such low yield (Brad et al., 1988).

The same is true for the second most common presenting symptoms of bladder: irritability, urinary frequency, urgency and dysuria. Although this symptom complex will be most commonly associated with diffuse carcinoma in situ or invasive BC, depending on the severity of the symptoms, BC will only be found in approximately 5% of these patients. Bladder cancer will more rarely present with flank pain from ureteral obstruction or other symptoms of more advanced disease such as weight loss and abdominal or bone pain (Jung et al., 2001).
2-Urine Cytological Studies:

Microscopic cytology is more sensitive in high grade tumors as cells from well differentiated tumors are more cohesive and do not shed easily. Even in high grade tumors, urine cytology may be falsely negative in 20% of cases whereas false positive results may occur in 1-12% (Koshikawa et al., 1989).

False positive results are usually due to severe atypia. Inflammation or changes caused by radiation or chemotherapy. These changes usually appear after several months of therapy and may persist for more than a year after therapy (Jung et al., 2001).

Cytology specimens obtained by bladder barbotage are more accurate than voided samples. In a study; sensitivity of urinary cytology was 59% but increased to 66% using bladder washing cytology (Gregoire et al., 1997).

The urine specimen should be fresh and morning samples are avoided. The accuracy of urine cytology in CIS exceeds 80% in all lesions and more than 90% in symptomatic lesions (Murphy, 1986).

A cytology specimen obtained by bladder barbotage would be expected to be positive in 10% of patients with G I tumors, 50% of those with G II and 90% of those with G III tumors (Soloway et al., 1985).

Cytologic examination of urine provides an accurate means for the diagnosis of carcinoma in the bilharzial bladder. The sensitivity of the test in different bilharzial series varies from 26.1 % to 91.3%,
this compares favorably with data of the non–bilharzial bladder cancer reported from western countries. In such cases, the sensitivity of the test varies between 44.7% and 97.3% (El-Bolkainy et al., 1981).

Cytology is not a cost–effective means of screening unless high risk populations are evaluated (Gamarra and Zein, 1984).

3-Cystoscopy and Biopsy:

The diagnosis of bladder cancer ultimately depends on cystoscopic examination of the bladder and pathologic evaluation of the resected lesion. Cystoscopy may initially be performed without anesthesia in assessing a patient for bladder cancer. If a bladder cancer has been visualized on earlier imaging studies, or if urinary cytology has previously been found to be positive, diagnostic cystoscopy can be omitted and the patient scheduled instead for cystoscopy and biopsy or tumor resection under anesthesia (Droller, 1997).

With the patient anesthetized, a bimanual examination should be performed first to assess whether a mass is palpable in the bladder and, if so, whether it is fixed to the pelvic wall (Fossa et al., 1991).

Bimanual examination may be performed both before and after transurethral resection. The presence of a palpable mass after resection implies that there is extravesical tumor to a greater extent than the residual endophytic tumor that can be visualized endoscopically. Conversely, negative bimanual examination or only the impression of induration without a palpable mass implies that the
invasive tumor may be more superficial and potentially associated with a better outcome. Previous pelvic surgery, irradiation, or inflammatory disease may limit interpretation of bimanual examinations. Moreover, small tumors may not be palpated, even if they extend extravesically. Obesity and areas that are inaccessible to palpation can also compromise bimanual examination (Gospodarowics, et al., 1991).

Cystoscopy can then be used to examine the gross appearance of the tumor (i.e., papillary or nodular), the extent and multiplicity of the tumor, and the presence of any other abnormal areas in the bladder or prostatic urethra. Papillary tumors generally are more superficial, even when invasive, than nodular tumors. In addition, papillary tumors that are confined to the bladder mucosa are generally associated with normal bladder wall thickness, whereas more deeply invasive nodular or papillonodular tumors are often associated with a thicker bladder wall in addition to assisting in the assessment of the potential behavior of the cancer. These considerations may aid in determining how aggressive transurethral resection should be (Droller, 1997).

High grade tumors are more likely to be associated with abnormal areas elsewhere in the bladder, whether these areas appear normal or abnormal endoscopically. Biopsy specimens of abnormal areas in the bladder may assist in defining the diffuseness of malignant urothelial changes in these instances. Systematic biopsy of endoscopically normal area of the bladder mucosa may also be useful in this regard. It should include specimens of mucosa
immediately lateral to each ureteral orifice, of the posterior bladder floor, of the lateral walls on each side posteriorly, and of the prostatic urethra when done. A clinical staging can be obtained by bimanual palpation and positive biopsy (*Table 5*) (*Vicente et al.*, 1991).

It is important to realize that cystoscopy is not 100% sensitive or specific. For example, it will not recognize carcinoma in situ that does not have the typical red velvety appearance. It may also miss some tumors when performed in patients who are actively bleeding or with enlarged prostates and trabeculated bladders (*Jung et al.*, 2001).

Transurethral resection of the bladder tumor should be done so as to maximize the preservation of architectural detail and the relation of the tumor to the various layers of the bladder wall. It is primarily the extent to which the tumor involves the various layers of the bladder wall that has traditionally been used as a means of staging bladder cancer and determining prognosis. For pathologic evaluation, the more superficial component of the tumor should be resected separately from its deeper component. Use of cautery current should be minimized to preserve pathologic detail and avoid cautery artifact (*Droller, 1997*).

For tumors that appear to be papillary and superficial, complete resection may require only resection into the lamina propria or possibly into the superficial muscularis to provide sufficient material for accurate staging assessment. In contrast,
tumors that appear to be more nodular may require a more extensive resection that extends deeply into the muscularis and even into the perivesical fat. This will not only provide more accurate staging information but may also serve adjunctively in the treatments of this type of malignancy (Droller, 1997).

Some surgeons suggest that a second transurethral resection should be performed in patients thought to have superficial disease who are found on pathologic evaluation of the initial resection specimen to assess if we have tumor infiltration into the lamina propria. In this regard, tumor grade has also been considered as an important indicator of potential understandings by initial transurethral resection (Klan et al., 1991).

In a review of 238 cases, it was observed that more than one half of tumors that were thought to be superficial but were actually high grade were found on subsequent transurethral resection to have invaded the muscularis. Moreover, 90% of tumors that were high grade and underwent cystectomy were actually found to be muscle invasive. Understaging by transurethral resection is therefore an important consideration in the overall assessment of the staging of a patient with bladder cancer, especially in the setting of high – grade, papillonodular or nodular disease (Droller, 1997).
Table (5): A Clinical Staging (Bimanual Palpation and Positive biopsy) of urinary bladder tumors (Mehta and Bansal, 2004).

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tumor restricted to the mucosa</td>
</tr>
<tr>
<td>Stage I</td>
<td>Tumor freely movable within the bladder, and soft in palpation</td>
</tr>
<tr>
<td>Stage II</td>
<td>Induration of the bladder wall as revealed by palpation and / or with biopsy evidence of superficial muscular infiltration.</td>
</tr>
<tr>
<td>Stage III</td>
<td>Hard nodular tumor movable in all directions and / or with biopsy evidence of deep muscular infiltration.</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Fixed tumor with involvement of adjoining structures or organs.</td>
</tr>
</tbody>
</table>

4-Diagnostic Imaging:

A. Conventional Urography:

Evaluation of hematuria includes imaging of the kidneys and ureters, cystoscopy and urinary cytology. Intravenous pyelography (IVP) can be used to detect the presence of a renal cortical mass, filling defects in the renal pelvis and ureters, and hydronephrosis, which may indicate the presence of a ureteral cancer or muscle-evasive bladder cancer at the ureteral orifice (See and Fuller, 1992).
Since small urothelial neoplasms of the collecting system and ureter may occur synchronously with a bladder tumor, it is important to demonstrate these structures. Urography (**Fig. 19**) remains a sensitive method for detection of small upper tract lesions that are often clinically occult. Since urography provides visualization of the lumen of the bladder it is not as effective as CT, ultrasound, and MRI for showing the extent of disease. Urography findings such as hydronephrosis and ureteral displacements are generally associated with more advanced disease. Papillary tumors produce intraluminal filling defects that have an irregular surface which has been described as stipple. This appearance is due to the presence of contrast material between the fronds of tissue. In fact, an attempt to demonstrate small bladder lesions urographically is rarely made since they are usually directly visualized at cystoscopy. Tumors that are more infiltrative tend to produce a contour defect in the balder wall which is manifested as a flattening at the site of tumor growth (**Ladetsky, et al., 2001**).

![Bladder mass by IVP](image)

**Fig. (19) Bladder mass by IVP**

*(Quoted from Machele Donat, 2006)*
B. Ultrasound:

Transabdominal, transurethral, transvaginal and trans rectal ultrasound have been used to stage bladder cancer, although non-invasive, transabdominal ultrasound (Fig.20) is seldom used today because the results are inaccurate in the assessment of tumor spread beyond the bladder wall and visualization of the tumor is often obscured in obese patients, and by air – containing bowel loops adjacent to the bladder wall.

Further problems relate to inaccessibility of tumors arising in the region of the bladder neck and to the evaluation of lymph node metastases (Husband, 1998).

Distensibility of the bladder wall is assessed during filling of the bladder with irrigation fluid. Superficial tumors do not cause fixation or distortion of the wall. Muscle invasive tumors limit the distensibility of the bladder wall and cause fixation and distortion of the bladder wall.

Bladder tumors appear on ultrasound as echogenic lesions. The bladder wall has a more intense echo pattern than tumor tissue, thus permitting distinction of early superficial lesions form those invading the deeper layers of the bladder wall.

Superficial tumors appear as masses projecting into the bladder lumen and are nonmobile as opposed to stones and clots. Invasion of muscle layers appears as interruption of the smooth and curved echo pattern of the bladder wall (Ladetsky et al., 2001).
One particular advantage of transurethral ultrasound is the detection of tumor within diverticulae, which might not be seen with cystoscopy (Ladetsky et al., 2001).

Fig. (20) Bladder mass by ultrasonography
(Quoted from www.msdlatinamerica.com)
C. COMPUTED TOMOGRAPHY:

There is currently no role for diagnostic imaging in screening for bladder carcinoma or staging superficial disease. Cystoscopy, transurethral resection and bimanual examination are more accurate than imaging for staging T1 and T2 lesions. However once invasive bladder carcinoma is detected there is a role for imaging; traditionally this has been performed with CT. Both CT and magnetic resonance imaging overstage tumor. CT is usually more accessible and better cost effective than MRI. A major drawback of CT is its inability to depict the extent of internal invasion due to the similar attenuation of the bladder wall and carcinoma (Ladetsky et al., 2001).

On CT, bladder tumors appear as soft tissue density lesions. Tumor may be represented as a localized area of thickening of the bladder wall or as a definite sessile or pedunculated soft tissue mass arising from the bladder wall with or without perivesical extension. Occasionally, the surface of the tumor may be encrusted with calcium or with blood clot (Husband, 1997).

Tumors enhance following injection of intravenous contrast medium (Fig. 21), usually to a greater degree than the adjacent normal bladder wall. Early tumors confined to mucosal layer of the bladder can only be identified on CT if scanning is undertaken before cystoscopic resection particularly at the bladder base (Husband, 1998).
Bladder cancers invading superficial and deep muscle usually produce bladder wall thickening but distinction between T2a and T2b lesions is impossible on CT. Residual bladder wall thickening, following resection of Ta and T1 lesions due to oedema or inflammatory reaction, is also indistinguishable from muscle invasive disease (Husband et al., 1992).

The most important role of CT is to distinguish those tumors confined to the bladder wall from those which spread into the perivesical fat. An irregular ill – defined outer edge of the bladder wall with soft tissue stranding into the perivesical fat is highly suspicious of perivesical disease (Stage – T3b) (Husband, 1998).

Tumor enhancement is helpful for delineating such early perivesical spread because contrast enhancement increases the tissue
contrast between tumor and fat. In more advanced disease, an obvious soft tissue mass extending beyond the bladder wall is seen as well as infiltrating strands of tumor tissue (*Husband, 1998*).

Spread to the pelvic side wall is diagnosed if tumor extends through the pelvic fat and is contiguous with the pelvic side wall, muscles may even be enlarged by tumor infiltration or oedema.

Early organ invasion can be difficult to detect if the only sign is loss of the fat plane between the bladder wall and an indecent structure. Enlargement of the structure of organ and contrast enhancement of tissue within the organ in direct contiguity with the primary tumor are strong evidence of tumor invasion (*Husband et al., 1989*).

However, Invasion of the seminal vesicles is identified because the fat angle between the posterior bladder wall and the anterior surface of the seminal vesicles is lost. It is not a reliable sign of tumor extension as overdistension of the rectum may cause the angle to be distorted in some normal patients. False positive results may occur when a distinct fat plane between contiguous organs is not visualized and early invasion is suspected. Perivesical inflammation and fibrosis is indistinguishable from tumor and a frequent cause of over staging. The overall staging accuracy for primary tumors with CT ranges from 40-92% (Mean 74%).

Finally, CT plays an important role in detection of lymph node and distant metastases. Lymph nodes measuring less than 1 Cm are
considered normal, nodes measuring 1 and 1.5 cm are indeterminate and nodes greater than 1.5 cm are abnormal (Ladetsky et al., 2001).

CT Picture of Bladder Masses:

I-CT Picture of Tumors:

(1) CT Picture of carcinomas (Fig. 22):

Mass confined to the bladder wall: 25% bladder cancers are multifocal. The lateral wall is involved in 40-50%, the trigone and neck of bladder 25%, and the fundus 10-15%. As a rule, the base and vault of the bladder are inadequately demonstrated on axial CT cuts (Wegener, 1992).

Fig. (22) Axial CT image shows an urothelial tumor within a bladder diverticulum

(Quoted from Jade et al, 2006)
On the other hand, CT is not accurate in staging early tumors, and its major advantage lies in the ability to distinguish extravesical spread from those tumors confined to the bladder wall (Husband, 1997).

However according to TNM staging system: a pedunculated tumor is considered T1, a sessile tumor is considered T2, and a sessile tumor with wall thickening is considered T3 (Tanimoto et al., 1992).

Nodal spread: carcinoma of the bladder spreads initially to the regional pelvic LNs; those first involved include the anterior and lateral paravesical nodes and the hypogastric, obturator, external iliac, and lateral sacral nodes. In more advanced disease, LNs in the common iliac, Para aortic and inguinal chains are involved.

The incidence of LN metastases increases with advancing disease. CT can identify enlarged LNs, but unlike lymphangiography, they cannot provide any information on the internal architecture of the enlarged nodes. Thus tumor cannot be distinguished from benign causes of nodal enlargement.

Nevertheless CT is considered equally effective as lymphography in identification of nodal metastasis. For CT, the accuracy rates reported range usually from 70-96% (Husband, 1997).

On CT, enlarged nodes appear as soft tissue density structures, they may show uniform or heterogenous enhancement after IV
injection of contrast, and occasionally they may opacify to such an extent that they are difficult to distinguish from opacified blood vessels.

Because enlargement is the only criterion for detecting LN metastasis with CT, the size is of critical importance. As suspicious and upper limit of normal for the internal iliac group and obturator groups should be taken as 7-8 mm respectively. If more than one LN is enlarged, the likelihood that those nodes contain metastases increases; but if doubt exists, FNABC (CT guided), can be undertaken (Husband, 1997).

Distant Spread: Because hematogenous spread usually occurs late in bladder cancer, investigation for metastatic disease is usually carried out when symptoms and signs develop in a particular site.

These metastases are frequently in the pelvic bones and CT must cover the whole of these pelvic bones, so such metastases are not missed.

In patients with involved pelvic LNs, the likelihood of paraaortic LN involvement and of liver metastasis increases, and all patients should undergo, pelvic and abdominal CT for staging.

Lung metastases are usually diagnosed on plain chest radiographs and CT is not routinely indicated as part of the initial staging procedure unless cystectomy is being considered (Husband, 1997).
Bladder wall leiomyosarcomas are muscle density masses that are enhanced with intravenous contrast administration. Low – density unenhancing necrosis may be present; large necrotic regions favor its diagnosis. Calcifications may be seen with it.

The border, with the urine filled bladder, is usually smooth, except that some leiomyosarcomas ulcerate. All mesenchymal neoplasms appear similar to leiomyomas/leiomyosarcomas, on CT, (except for dermoid, in which the characteristic appearance of fat suggests the diagnosis) (Seidmon and Friedman, 1990).
3- Secondaries CT Picture (Fig. 24):

![CT image of metastasis from esophageal carcinoma](image)

*Fig. (24) metastasis from esophageal carcinoma*

*(Quoted from Schuurman et al, 2012)*

Primary tumors invading the bladder directly, such as cancer colon, or cervix, can be easily distinguished from the primary bladder tumors, because the major component of the mass lies outside the bladder wall.

However, a diagnostic problem exists, concerning the distinction of a primary prostatic cancer from a primary bladder tumor; in this situation CT is usually unhelpful, because a large prostate cancer invading the bladder may have identical appearance to a bladder cancer invading the prostate.

Other metastases to the bladder, for example from melanomas or lymphomas, have similar appearance to primary bladder tumors *(Husband, 1997)*.
Limitations of CT in tumors detection and staging:

The major limitations of CT for detection and staging of bladder tumors, relate to the inability to detect early tumors, to difficulties in identifying minimal extravesical tumor spread, and adjacent organ invasion.

Other problems include edema and inflammation following cystoscopy, that may be misinterpreted for tumor, (therefore CT staging should be carried out either before cystoscopy or after 2 weeks interval); so patients previously treated with radiotherapy present a particular problem, due to irradiation fibrosis, with thickening and irregularity of bladder wall, in addition to edema and fibrosis within the perivesical fat making the diagnosis of residual or recurrent tumors impossible.

However CT is the most widely used technique for evaluating bladder cancer. The range of accuracy of CT for staging bladder cancer varies from 64-92%, despite improvements in CT scanning techniques (Husband, 1997).

5-CT monitoring of treatment response:

CT can be used to assess treatment response either to radiotherapy or to chemotherapy. The CT findings of radiotherapy include edema of subcutaneous tissues and perivesical fat, thickening of the bladder wall, reduction in bladder capacity, and thickening of pelvic ligaments. Such finding may mask the presence of recurrent disease, as distinction of tumor from fibrosis is one of the most challenging issues in radiology (Husband, 1997).
After chemotherapy, reduction in tumor volume is more readily assessed (Husband, 1997).

II- CT Picture of inflammatory and some proliferative conditions:

In acute infections, the filling capacity of the bladder is usually not restricted, and the wall thickness is borderline; on post contrast scans a small hyperdense rim is seen on the interior sides of the cystitis (Wegener, 1992).

Lumen reduction and wall thickening are primary signs of chronic infections. These changes are uniform sometimes, as in bilharziasis, and irregular sometimes, as in tuberculosis.

Focal wall thickening may be observed in patients with granuloma related bilharziasis and tuberculosis, and in cystitis cystica (which appear as thin walled water – dense cysts in a diameter of 1 mm to a maximum of 10mm).

Calcification is frequently found in conjunction with bilharziasis and tuberculosis. These conditions must be differentiated from tumors of the urinary bladder (Wegener, 1992).
D. Magnetic resonance imaging:

MRI has unique advantages, including multiplanar capabilities and superior tissue contrast. Because the bladder wall and the perivesical fat are well defined and have characteristic signals on different sequences (Fig. 25). Bladder wall invasion of tumor and extension into perivesical fat can be well visualized. Multiplanar capabilities allow three dimensional lymph node measurements as well as better visualization of tumor involving the bladder dome or base (Ladetsky et al., 2001).

Fig. (25) Bladder mass by Coronal T2 MRI
(Quoted from www.radrounds.com)
Treatments of the Urinary Bladder Cancer

The type of treatment called for is governed by: (a) the grade and stage of the lesion and (b) multicentricity of the tumor. Curability is directly related to the depth of penetration of the cancer into the bladder musculature. Transurethral resection is the treatment of choice in almost all patients with superficial transitional cell carcinoma of the urinary bladder (stage A & B1). Management of resectable muscle–infiltrating tumors or tumors invading the perivesical fat is debatable, multimodal treatment is generally considered.

Treatment should be considered separately for the three different types of clinical presentation (a) low grade, early cancer (b) high grade, invasive cancer and (c) advanced cancer (Mehta and Basal, 2004).

Management of Early Disease (Stages A and B1):

- Carcinoma in situ:

These patients should receive intensive intravesical therapy (BCG or anticancer drugs). The risk of tumor recurrence, progression and other prognostic factors are evaluated at initial endoscopy, which help determine further therapy. A radical treatment is reserved for patients who are non responders (Mehta and Bansal, 2004).
Superficial bladder cancer:

a) Transurethral Resection (TUR): Transurethral resection should be the primary line of treatment for T1 (0-A), and for low grade T2 (B1) tumors. Endoscopic Control of these lesions is carried out by electrosection or by endoscopic laser fulguration; the latter technique is used to destroy lesions less than 5mm; Big tumors had no contraindication to transurethral resection, however, they may require more than one session of resection with few days of interval (Ghoneim and Shoukry, 1981).

The overall 5- year survival rate is around 70%, 10 to 15 patients ultimately need nevermore aggressive therapy due to repeated recurrence. Small single tumors are removed by transurethral resection (TUR) however freedom from recurrence is dependent on the remainder of the urothelium being normal both by random biopsy and by urinary cytology. If multiple foci of transitional cell cancer are found in the bladder, more aggressive therapeutics approaches are indicated. The first check cystoscopy is performed 3 months after the initial TUR and is repeated every 3 months for two years. It is then carried out every six months for a period of two more years and then yearly. Survival of patients with solitary, low – grade, low – stage tumors approaches normal life expectancy. Even if there a recurrence, progression is unlikely and treatment with repeat TUR is successful (Mehta and Bansal, 2004).

Neodymium – YAG laser may be used in this setting to treats mall tumors (<1.5 cm); the laser is used as a "Paintbrush" with its power kept below 45 watts. A further refinement is to use lasers in
bladder tumors that have been sensitized to photoradiation by administration of haematoporphyrins. Lasers are also used to treat the tumor bed following TUR of larger tumors. Lasers do, however, have their drawbacks; There is a risk of optical damage to the operator; it may occasionally cause bladder injury or bowel perforation and limited tumor is available for histopathology (Hisazumi et al., 1983).

b) Adjuvant intravesical therapy: Intravesical therapy is used for patients at high risk of tumor recurrence e.g. recurrent tumors, multiple and high – grade tumors with urothelial atypia, tumor penetration into the lamina propria and patients with CIS. Tumor eradication rates of 30-95 have been obtained with Thiotepa, Doxorubicin, Mitomycin C and BCG which is currently the most effective agent (Weinstein et al., 1993).

C) Cystectomy: Total cystectomy in superficial bladder cancer may be required for symptomatic, diffuse, recurrent, high grade papillary tumors or CIS not responding to intravesical therapy. Patients treated with cystectomy for stages Ta and T1; bladder cancers have survival rates comparable to those in the age – matched population (Mehta and Bansal, 2004).

Management of Invasive Bladder Cancer (Stages B, C and D1)

There are essentially two treatment approaches available for muscle invasive bladder cancer (1) bladder preservation and (2) bladder reconstruction. Bladder preservation aims at elimination of cancer while at the same time maintaining adequate bladder
function. Bladder salvage protocols are best suited for patients with mislay invasive cancer of pure transitional cell histology (Mehta and Bansal, 2004).

a) Bladder Salvage:

Bladder salvage protocols include (1) definite TUR alone; (2) definitive Radiotherapy alone; (3) neoadjuvant chemotherapy followed by cystectomy only when necessary and (4) neoadjuvant chemotherapy plus Radiotherapy followed by cystectomy when necessary. Patients are treated with Cisplatin based combination chemotherapy (usually two cycles), which is followed with full course radiotherapy. These regimens produce local objective response rates of 55 to 75% (Herr and Scher, 1994).

b) Radical Cystectomy with Urine Diversion and Pelvic Lymph Node Dissection (PLND):

Radical cystectomy and PLND provide excellent control of the primary tumor and are superior to either radiation therapy alone or bladder sparing approach. However, approximately half of all patients with high – grade tumors have unrecognized distant metastasis and they die of disseminated disease within 2 years of presentation. The rationale for cystectomy in these patients therefore remains debatable (Mehta and Bansal, 2004).

- Urinary Diversion Techniques
  - Retro – cutaneous anastmosis
  - Uretero – sigmoidostomy
- Ileal Conduits
- Continent Urinary Diversions.
- Other Techniques as Kock pouch and Mainz pouch (Holmang et al., 1997).

c) External – beam radiation therapy (EBRT)

Selection criteria for primary radiotherapy include papillary tumors; complete TUR prior to radiotherapy, tumor size less than 5 cm, and low stage tumors. The radical radiation treatment for stages T2 and T3 had a high (84%) rate of persistent tumor, or local recurrence or a contracted balder. The median survival for stages T2 and T3 was 16 months (Holmang et al., 1997).

Combining interstitial iridium – 192 (192Ir) and external beam radiation therapy provides a higher radiation dose to the tumor. This combination has been previously reported to increase survival but substantially increase morbidity. As a primary treatment of muscle – invasive bladder cancer, radiation alone, does not provide survival rates comparable to radical cystectomy, even when combined with salvage cystectomy. In patients who fail to respond, the survival rates are lower than those achieved with primary radical cystectomy (Mehta and Bansal, 2004).

d) Neoadjuvant Chemotherapy:

Neoadjuvant chemotherapy is used to shrink locally advanced disease and to eradicate occult distant metastases. It is indicated in patients with perivesical extension or lymph node metastases. The M-VAC regimen (combination of methotrexate, vinblastine,
doxorubicin and cisplatin) has been the most promising (Scattoni et al., 1995).

e) Combined Modality:

Combined modality therapy combines TUR, Electron Beam CT (EBCT), and concurrent chemotherapy for bladder preservation in patients with invasive bladder cancer. While TUR, radiation therapy, or chemotherapy used alone does not result in significant local control, clinical evidence suggests that a combination of all three treatments could be effective in carefully selected patients. Radiation therapy and chemotherapy were combined to achieve improved local control based on the synergistic effect of radiation therapy and chemotherapy (Kim et al., 2005).

Management of Metastatic Disease (Stage D2):

a) Chemotherapy:

Metastatic transitional cell carcinoma is treated with systemic M–VAC chemotherapy with a 25% CR, however, 2/3 of patients with CR relapse within two years. M-VAC chemotherapy causes significant morbidity. Recombinant granulocyte – macrophage colony stimulating factor (GM-CSF) is being investigated to enable the use of high – dose M-VAC chemotherapy. Several drugs are active in metastatic bladder carcinoma with variable response rate but in all cases the response is temporary (Scattoni et al., 1995).
b) Palliative Radiation Therapy:

Pain from bony metastases can be relieved by radiation therapy (RT) in doses of 3000 – 3500 cGy given in 10 fractions. Weight bearing bones like the spine or neck of the femur, with minimally symptomatic metastases, should undergo prophylactic radiation. Prevention or treatment of pathological fractures may require internal fixation. Symptoms due to the primary may be reduced by palliative radiotherapy in doses of 4000 – 4500 cGy, but on the other hand, symptoms like urgency, frequency, haematuria and dysuria may be aggravated (Mehta and Bansal, 2004).
Patients and methods

The inclusion criteria for patients in this study will be hematuria with suspected bladder wall thickening or mass lesion by pelvic sonography.

Exclusion criteria included acute abdominal/pelvic pain, fever, known bladder perforation, inability to tolerate distention of the bladder, women of child-bearing age, and inability to undergo conventional cystoscopy.

Sixty patients (10 control patients will be included) with urinary bladder masses detected by ultrasound examination will be subjected to CT pelvis by multi-detector CT in non-enhanced and enhanced phases, and then virtual cystoscopic reconstruction will take place.

Twenty eight patients with known bladder lesions underwent Virtual Cystoscopy using Volume Ultrasound and a conventional cystoscopy protocol. A distended bladder was used to obtain a good acoustic window.

The study group included 12 women and 48 men, with an age range of 52–78 years (mean age 65 years); informed consent was obtained from each patient.

The study was worked upon starting from October 2010 to October 2012. Written informed consent was obtained from each patient.
Approximately an hour before the US examination, 500 ml of water was given to each patient orally. The examination was performed with the bladder filled up to 350 ml, or up to each patient’s tolerance.

Routine 2D scanning with documentation of the longitudinal and transverse planes of the bladder was recorded.

Three-dimensional ultrasound volumes were generated by the automatic rotation of the transducer. 3D data acquisition was based on high quality 2D US images of the UB with the sample window encompassing the prostate in men and the cervix in women.

A volume transducer (4D3C) at 4 MHz on a LOGIQ ultrasound system (GE Healthcare) was used for the acquisitions. A surface rendering of the lumen was obtained. The rendering settings used were a combination of surface smooth and surface texture.

Rotational angles ranged from 60 to 70 degrees, with a rotational field width of 5 to 10 cm. The quality of the data collected was set at High or Extreme for better delineation of the tumors and internal bladder surfaces.

Small artifacts were trimmed from the 3D data by increasing or decreasing the threshold, allowing better appreciation of the image. We also improved the quality of US images by application of a special algorithm for speckle reduction and edge.
For each patient, the 3D sonographic examination and image reconstruction procedures were completed within 10 to 15 minutes.

- The 3D US protocol included:

1 - Acquisition of 3D transabdominal scans through the whole urinary bladder for detection of possible UBTs, finding locations and interactions with ureteric jets, bladder necks and trigones and calculating their numbers.

2 - The tumor size, volume and overall basement area of the tumor lesion were calculated for the surgery planning. Also, all the tumors were studied with Power Doppler for evaluation of vascularity. Postprocessing was performed after collecting the 3D data. Surface rendering was used to obtain cystoscopic-like US volumetric images of the urinary bladder, and a Multi-Slice View special program was used for reslicing the 3D data.
CT VIRTUAL CYSTOSCOPY

The technique for CT cystoscopy began with the placement of a 12-F Foley catheter into the bladder to drain residual urine only by gravity. The bladder was then insufflated with room air by slow hand injection through the Foley catheter. About 300 –500 ml of air is insufflated or whatever volume the patient could tolerate, whichever came first.

After a scout view was obtained with the patient in the supine position to locate the bladder and confirm its adequate distention, single–breath-hold helical CT was performed with (TOSHIBA ACTIVION16), with 3-mm collimation, pitch of 1:1, 120 kVp, and 220 mA. Images were reconstructed at 1-mm intervals by using the minimal field of view.

The patient was then turned to the prone position, and helical CT of the bladder was repeated with use of the same parameters after a repeat scout view was obtained.

Additional bladder distention with approximately 100 ml of air was necessary in about half of the patients, since repositioning lead to leakage of some of the insufflated gas from the bladder.

Virtual cystoscopy time, including catheter placement, was approximately 30 minutes. The data were downloaded to an independent workstation (Vitrea 2; Toshiba Medical Systems) equipped with software for interactive intraluminal navigation with a surface-rendering algorithm.
IMAGE GENERATION:

The observers used the Advantage Windows workstation Navigator to scroll through the axial images alongside reconstructed coronal, sagittal, and 3D endoluminal perspective images. The observer interpreted the axial images and used the reconstructed projections and endoluminal views as optional problem-solving tools.

The data files were volume rendered with the rendering package. The opacity look-up table was set to render the air–tissue interface only, leaving both air and tissue transparent so that it could be examined from either side. Series of renderings were done which progressively cut away the surfaces closest to the viewer, allowing previously obscured areas to be revealed.

A series was created for each of the six orthogonal directions (anterior and posterior, left and right, superior and inferior). The viewer allowed the observer to scan back and forth through each series at will.

IMAGE ANALYSIS:

The images were initially viewed with a window of 2000 HU and a level of 2250 HU, but the operator was permitted to adjust the settings as desired.

The number, size, location, and morphologic features of the lesions were evaluated on transverse and virtual images obtained
with the patients in both the supine and prone positions. Each lesion was characterized as a focal polypoid lesion, a sessile mass, or wall thickening.

A discrete lesion was considered polypoid if it was taller than it was wide, while a sessile mass was defined as a lesion that was wider at the base. A lesion was characterized as wall thickening when there was elevation of the bladder wall without a discrete mass.

Lesions were measured using an electronic cursor on the axial images for the Conventional 2D data with 3D problem solving. When using the surface-shaded display, the lesion sizes were quantified as small (<1 cm), medium (1–2 cm), and large (>2 cm).
CONVENTIONAL CYSTOSCOPY

Cystoscopy was performed within three days after the CT examination by an attending urologist. Mass sizes were estimated by comparison with the scope tip or were measured ex vivo from pathologic specimens if removed in total. Masses not directly measured were stratified into small, medium, or large, as defined previously.

Sterile water or saline is used as urologic non-irritant fluid for cystourethroscopy.

In most of cases No 17 Fr is adequate. If a larger working channel is needed for accessory equipment, larger endoscopes are chosen.

Systematic inspection of the entire urethra and bladder is performed during cystourethroscopy. Before insertion of the instrument, the urethral meatus is inspected. If the meatal size appears inadequate to accept the endoscope, it is dilated with metal sounds. After the sheath of the cystourethroscope is generously lubricated with water – soluble anesthetic lubricant, the endoscope is passed under direct vision with a 0 to 30 –degree lens.

The cystoscopic findings were considered to be the gold standard and correlated with the CT findings jointly with a result unblinded radiologist and urologist with regard to lesion number, location, size, and morphology, regardless of the histopathology. We analyzed our data by patient and by total number of masses
independent of the patient. The pathology report in each patient was also reviewed for further correlation.

Inspection of the urethra during the passage of cystoscope takes place for detection of any pathology.

Once the endoscope is inside the bladder, a systematic evaluation of the entire bladder surface is performed. Using the 30-degree lens with the bladder only slightly filled, the interureteric ridge is identified just inside the bladder neck along the trigone.

Next, the ureteral orifices are visually located several centimeters lateral from the center of the interureteric ridge and observed as passage of clear urine occurs bilaterally. The floor of the bladder behind the trigone and posterior bladder wall are inspected.

By using the 70 to 90 degree lens, we inspect the lateral walls of the bladder by moving the endoscope from anterior to posterior and back as the bladder fills slowly. Finally, the dome and anterior bladder wall are evaluated with the 70 to 90 degree lens.

The anterior bladder wall just behind the bladder neck is best seen with the bladder only partially filled and with one hand exerting suprapubic pressure to depress the anterior bladder wall.

After complete inspection of the urethra and bladder has been accomplished, the bladder is drained and the instrument is gently removed.
STATISTICAL ANALYSIS

Statistical analysis was performed according to the number of the lesions (not the number of patients) because each patient had one or multiple lesions.

Using the conventional cystoscopic findings as the reference standard, the presence or absence of a bladder lesion at each site was evaluated on the virtual cystoscopies together with multiplanar reconstruction images. We calculated the sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV), and accuracy of virtual cystoscopy. NPV and PPV were calculated on a per patient basis: if at least one tumor per patient was detected on both virtual and conventional cystoscopy, the patient was counted as a true-positive. When tumors were not detected with either diagnostic method, we considered patients as true-negatives. If a tumor or tumor-like lesion was detected by virtual cystoscopy but not detected by conventional cystoscopy, the patient was counted as a false-positive. The patient was counted a false-negative if the opposite findings were recorded.
Results

Site of involvement: Table (6) provide a comparative study between cystoscopy, VC, spiral CT regarding detection of tumor location as found by gross pathology.

Table 6: Results obtained regarding tumor localization by Cystoscopy, VC, CT and Pathology:

<table>
<thead>
<tr>
<th>Cases</th>
<th>Conventional Cystoscopy</th>
<th>Virtual Cystoscopy</th>
<th>CT</th>
<th>Gross pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dome</td>
<td>RT lat wall</td>
<td>Lt lat wall</td>
<td>Base</td>
</tr>
<tr>
<td>60 cases &amp; 92 lesions</td>
<td>40</td>
<td>40</td>
<td>52</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lateral walls of the urinary bladder showed more than 50% of bladder masses, followed by bladder base and not far from the dome.

Age Distribution:

Table 7: Number and percentage of patients according to their age.

<table>
<thead>
<tr>
<th>Age by decades</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20th</td>
<td>1</td>
<td>1.67</td>
</tr>
<tr>
<td>30th</td>
<td>1</td>
<td>1.67</td>
</tr>
<tr>
<td>40th</td>
<td>5</td>
<td>8.33</td>
</tr>
<tr>
<td>50th</td>
<td>23</td>
<td>38.33</td>
</tr>
<tr>
<td>60th</td>
<td>25</td>
<td>41.67</td>
</tr>
<tr>
<td>70th</td>
<td>5</td>
<td>8.33</td>
</tr>
</tbody>
</table>
Old ages are more vulnerable to develop bladder masses, most evident at 5th and 6th decades. The young adults and middle ages are less probably had bladder neoplasia. The mean age in our study was 56 years.

Size:

Table 8: Number of masses detected by Cystoscopy, VC and Spiral CT according to its size out of a total number of 92 masses from 60 cases.

<table>
<thead>
<tr>
<th>Size of the mass</th>
<th>Mass ≥ 10mm</th>
<th>5mm &lt; Mass &lt; 10mm</th>
<th>Total number of masses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conv. Cyst</td>
<td>68</td>
<td>24</td>
<td>92</td>
</tr>
<tr>
<td>VC</td>
<td>68</td>
<td>24</td>
<td>92</td>
</tr>
<tr>
<td>CT</td>
<td>68</td>
<td>16</td>
<td>84</td>
</tr>
<tr>
<td>Gross Pathology</td>
<td>68</td>
<td>24</td>
<td>92</td>
</tr>
</tbody>
</table>
The smaller the lesion, the less ability to be discovered by axial CT, while larger masses are easily discovered by all modalities in our study. Lesions less than 5mm are not encountered in this study.

Table 9: Comparison between sensitivity of Cystoscopy, VC and CT in detection of the mass according to its size:

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mass ≥ 10 mm</td>
</tr>
<tr>
<td>Conv. Cyst</td>
<td>100%</td>
</tr>
<tr>
<td>VC</td>
<td>100%</td>
</tr>
<tr>
<td>CT</td>
<td>100%</td>
</tr>
</tbody>
</table>

VC showed excellent sensitivity (100%) in detection of bladder masses greater than 5mm, comparable to that of Conventional Cystoscopy; while sensitivity of spiral CT, in detection of bladder masses comprised between 10 to 5mm, decreased to 66.7%.
Table 10: Comparison between sensitivity and specificity of Cystoscopy, VC and CT in detection of tumor location

<table>
<thead>
<tr>
<th>Tech</th>
<th>Wall</th>
<th>Conv. Cyst.</th>
<th>VC</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Dome</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Rt Lat</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Lt lat.</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Base</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conventional Cystoscopy and VC showed equal sensitivity (100%) and specificity (100%) in identification of the walls involved by the tumor.

Again CT showed a certain deficiency in exact localization of the tumor.

**Morphology:** A comparative study between Cystoscopy, VC and Spiral CT was undertaken, regarding morphology description of the tumor as found by Gross pathology; the following sensitivity and specificity rates were obtained.

Table 11: Comparison between sensitivity and specificity of Cystoscopy, VC and CT in morphology description of the tumor.

<table>
<thead>
<tr>
<th>Tech</th>
<th>Morphology</th>
<th>Conv. Cyst.</th>
<th>VC</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Papillary</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Polypoidal</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Wall thickening</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
VC was always able to depict the morphology of the bladder pathology in all these 15 cases, with 100% sensitivity and specificity; CT was somehow deficient in morphology description of the bladder lesions, with decreased sensitivity to papillary lesions.

**T-staging:** tables (12/13) provide a statistical evaluation of T – staging of bladder neoplasms by spiral CT.

**Table 12: Results of –T-staging by CT, and pathology.**

<table>
<thead>
<tr>
<th>Technique</th>
<th>CT</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ta</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>T2</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>T3a</td>
<td>20</td>
<td>29</td>
</tr>
<tr>
<td>T3b</td>
<td>29</td>
<td>23</td>
</tr>
<tr>
<td>T4a</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>T4b</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 13: Number of cases correctly staged, over- and understaged by CT.**
There were 48 cases correctly staged, 12 cases under staged and 12 case overstaged, by CT.

The overall sensitivity of CT in T-staging was about 80.95% according to our results.

**N- Staging:** Tables (13/14/15) provide a statistical evaluation of pelvic nodal staging by spiral CT for the studied cases.

**Table 14: Results of pelvic nodal staging by CT and pathology.**

<table>
<thead>
<tr>
<th>Technique</th>
<th>CT</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-staging</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td>N1</td>
<td>8</td>
<td>29</td>
</tr>
<tr>
<td>N2</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>N3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 15: Number of cases correctly staged and understated by Ct.**

<table>
<thead>
<tr>
<th>Technique</th>
<th>True +ve</th>
<th>False +ve</th>
<th>False -ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>36</td>
<td>0</td>
<td>24</td>
</tr>
</tbody>
</table>
Table 16: sensitivity, specificity and accuracy of CT in pelvic N- staging.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>33.3%</td>
<td>100%</td>
<td>62%</td>
</tr>
</tbody>
</table>

There were 36 cases correctly staged and 24 cases understaged, by CT. CT showed 100% specificity and only 33.3% sensitivity in pelvic N- staging, thus the overall accuracy of CT in pelvic nodal staging was 62% in our study.
For results of virtual sonographic cystoscopy:

Twenty-eight (90%) of 31 4D VEUS studies had good or excellent image quality.

Conventional cystoscopy revealed 47 lesions in 28 patients; 4D VEUS showed 41 (87.2%) of 47 lesions.

Nineteen (69%) patients had solitary and nine (31%) had multiple tumors. Morphologically, the most frequent type of tumor was polypoids in 40 (85% of lesions) cases, followed by infiltrating in seven (15%) cases.

The trigone region of the bladder and the distal ureters can also be seen in greater detail. The Multi-Slice View available in the system gave a more precise assessment of the basement of the tumor. With this technology intact, submucosa was clearly shown in different resliced images. Infiltrating tumors were detected in seven cases. Five of them were accurately found on 4D VEUS better than on 2D grey scale.

Using 3D surface rendering, 3D reconstructions of the organ, including virtual cystoscopic views, multiple, tiny, polypoid lesions that presented as focal mural thickening on the corresponding 2D images were revealed in our study in five cases.

The possibility to perform multislice reformatting in three orthogonal planes helped to define invasions in the muscularis propria of the tumors at the T2a stage. No evidence of the
hyperechoic line of the mucosa was highly predictive for muscle invasion in our study.

Gray scale 2D sonography had a sensitivity of 92%, and a specificity of 76.7% for tumor detection. Three-dimensional virtual sonography alone had sensitivity of 96.2%, specificity of 70.6%, a positive predictive value of 93.9%, and a negative predictive value of 80% for tumor detection.

The combination of gray scale sonography, multiplanar reconstruction, and 3D virtual sonography had sensitivity of 96.4%, specificity of 88.8%, a positive predictive value of 97.6%, and a negative predictive value of 84.2% for tumor detection.
Cases

Case 1

Female patient 45 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A Polypoidal mass lesion is seen measuring 18mm in maximum diameter arising from the bladder base, anteriorly.

No extra-vesical infiltration.

No lymphadenopathy or metastasis.

Stage T3a N0 M0

![Image](image-url)

**Conventional cystoscopy**

A muscle invasive polypoid tumor with nodular appearance, measuring 25mm diameter is seen arising from the bladder base, anteriorly. Other smaller 4 polypoidal lesions are seen adjacent to the previous one measuring 6mm and 7mm diameters.

Stage T3
Virtual cystoscopy

A pedunculated mass lesion is seen measuring 25mm in maximum diameter arising from the bladder base, anteriorly showing nodular surface. Other smaller 4 polypoidal lesions are seen adjacent to the previous one measuring 6mm and 7mm diameters.

Stage T3

Pathology

Transitional cell carcinoma grade 2

Stage T3a N0 M0
Case 2

Male patient 65 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A sessile cauliflower ulcerating mass lesion is seen measuring 45mm in maximum diameter arising from the anterior wall and extending to right lateral wall.

Extra-vesical infiltration is noted.

Multiple right inguinal enlarged lymph nodes.

No metastasis.

Stage T3b N1 M0

**Conventional cystoscopy**

A muscle invasive fungating ulcerating tumor with nodular appearance, measuring 45mm diameter is seen arising from the anterior bladder wall with extension to right lateral wall.

Stage T3
**Virtual cystoscopy**

A large sessile nodular mass with ulcerations is seen measuring 45mm in maximum diameter arising from the anterior wall, extending to right lateral wall.

Stage T3

**Pathology**

Transitional cell carcinoma grade 2

Stage T3b N1 M0
Case 3

Male patient 60 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A sessile mass lesion is seen measuring 54mm in maximum diameter arising from the anterior wall.

Extra-vesical infiltration is noted.

Single right inguinal enlarged lymph node.

No metastasis.

Stage T3b N1 M0

---

**Conventional cystoscopy**

A muscle invasive tumor, measuring 36 mm diameter is seen arising from the anterior bladder wall.

Stage T3
Virtual cystoscopy

A large sessile mass is seen measuring 38mm in maximum diameter arising from the anterior wall.

Stage T3

Pathology

Transitional cell carcinoma grade 1

Stage T3b N0 M0
Case 4

Male patient 44 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A large polypoidal ulcerating mass lesion is seen measuring 64mm in maximum diameter arising from the posterior and left lateral walls. The mass encroaches upon both vesico-ureteric junctions causing bilateral mild hydro-ureteronephrosis

Extra-vesical infiltration is noted.

Multiple regional enlarged lymph nodes.

No metastasis.

Stage T3b N2 M0

**Conventional cystoscopy**

- A muscle invasive polypoidal ulcerating tumor, measuring 77 mm diameter is seen arising from the posterior and left lateral walls.
- Another smaller similar mass is noted adjacent to former lesion.
- Stage T3

**Virtual cystoscopy**
A large pedunculated ulcerative mass is seen measuring 78mm in maximum diameter arising from posterior and left lateral walls. Another smaller similar mass is noted adjacent to former lesion.

Stage T3

**Sonocystoscopy**

A large polypoidal mass lesion is seen at the posterior wall, more inclined to left side

**Pathology**

Transitional cell carcinoma grade 1

Stage T3b N2 M0
Case 5

Male patient 77 years old presenting by hematuria and frequency

**CEPT abdomen and pelvis**

A large exophytic mass lesion is seen originating from anterior and right lateral walls of urinary bladder, measuring 62mm in maximum diameter.

Extra-vesical infiltration is noted with involvement of anterior abdominal wall.

Single regional enlarged lymph node.

No metastasis.

Stage T4 N1 M0

**Conventional cystoscopy**

A muscle invasive fungating tumor, measuring 65 mm diameter is seen arising from the anterior wall.

Stage T3
Virtual cystoscopy

A large mass lesion is seen involving the anterior wall of urinary bladder measuring 66 mm in maximum diameter. The mass is seen appearing as ridges in the anterior bladder wall

Stage T3

Pathology

Squamous cell carcinoma

Stage T4 N1 M0
Case 6

Female patient 50 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A large sessile fungating and ulcerating mass lesion is seen originating from right lateral wall, extending to anterior wall and roof of urinary bladder.

Extra-vesical infiltration is noted.

No regional enlarged lymph nodes.

No metastasis.

Stage T3b N0 M0

**Conventional cystoscopy**

A muscle invasive ulcerating tumor is seen arising from the right lateral, anterior wall and roof of urinary bladder.

Stage T3
**Virtual cystoscopy**

A large sessile fungating and ulcerating mass is seen arising from right lateral wall with extension into anterior wall and roof of urinary bladder.

Stage T3

**Pathology**

Transitional cell carcinoma grade 1

Stage T3b N0 M0
Case 7

Female patient 23 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

A polypoidal mass lesion is seen originating from anterior wall, inferiorly.

No extra-vesical infiltration is noted.

No regional enlarged lymph nodes.

No metastasis.

Stage T2 N0 M0

---

**Conventional cystoscopy**

A muscle invasive polyp is seen arising from the anterior wall of urinary bladder.

Stage T3

**Virtual cystoscopy**
A polypoidal irregular mass is seen arising from bladder base anteriorly

Stage T2

**Pathology**

Transitional cell carcinoma grade 1

Stage T2 N0 M0
Case 8

Male patient 48 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

No detected abnormal wall thickening, sessile or polypoidal masses.
No regional enlarged lymph nodes.
No metastasis.

**Conventional cystoscopy**

A small polyp is noted in bladder base.
Stage T2

**Sonocystoscopy**

A small polypoidal mass lesion is seen at the bladder base, demonstrated in two different thresholds
**Virtual cystoscopy**

A small 7mm diameter polyp is seen originating from bladder base with notable peri-lesional wall thickening and irregularity.

Stage T3

**Pathology**

Transitional cell carcinoma grade 2

Stage T3a N0 M0
Case 9

Male patient 72 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

Apart from mild wall irregularity, no definite masses seen in urinary bladder.

No extra-vesical infiltration is noted.

No regional enlarged lymph nodes.

No metastasis.

---

**Conventional cystoscopy**

- A muscle invasive infiltrative neoplasm is seen in anterior bladder wall.
- A smaller polyp is also noted.
- Stage T3
**Virtual cystoscopy**

A large area of wall irregularity and thickening is seen in anterior bladder wall. A small polyp is also noted.

Stage T3

**Sonocystoscopy**

Wall irregularity of the anterior bladder wall, yet with no definitive masses

**Pathology**

Transitional cell carcinoma grade 1

Stage T3b N0 M0
Case 10

Male patient 53 years old presenting by hematuria and frequency

**CECT abdomen and pelvis**

Two polypoidal ulcerating masses are seen in right lateral and posterior aspect of bladder base

Extra-vesical infiltration is noted.

Multiple regional and inguinal enlarged lymph nodes.

Multiple hepatic metastatic lesions are captured.

Stage T3b N2 M1

![CT scans]

**Conventional cystoscopy**

- Two muscle invasive polypoidal ulcerating tumors, larger measured 37 mm diameter are seen arising from the right lateral wall and bladder base.
- Stage T3
**Virtual cystoscopy**

Two large pedunculated ulcerative masses are seen arising from right lateral and posterior walls.

Stage T3

![Virtual cystoscopy images](image1)

**Sonocystoscopy**

Two large polypoidal masses are seen, more inclined to left side

![Sonocystoscopy image](image2)

**Pathology**

Transitional cell carcinoma grade 1

Stage T4 N2 M1
Discussion

Among the different pathologically described bladder masses, whether tumoral, proliferate, inflammatory masses or others, the most commonly encountered are bladder tumors and precisely the primary epithelial malignant tumors which are carcinomas of the urinary bladder. Carcinoma of the urinary bladder is the most common malignant tumor of the urinary tract, accounting for approximately 7% of all malignant tumors in men and about 4% in women (Parker et al., 1996).

In Egypt the condition is more serious as a result of prevalence of bilharziasis. Bilharziasis is not only endemic in our country but also considered to be a historical (El Bolkainy et al., 1981).

About 90% of all malignant epithelial tumors of bladder are transitional cell carcinoma. Adenocarcinomas account for only 2% of bladder cancers, and squamous cell carcinoma accounts for 5-10% (Teeger and Sica, 1996). The later is predominant with schistosomal bladder cystitis (El Bolkainy et al., 1981).

The major factors influencing prognosis and management of bladder neoplasms are: Depth of bladder wall invasion, grade of malignancy, tumor size, growth pattern, and presence or not of lymphatic and/or distant metastases (Husband, 1995).

The most important characteristics of the tumor which influences its curability are the depth of wall infiltration and the extent of metastases (Putman et al., 1994).
The correct evaluation and staging of the bladder tumors is essential in planning therapy, establishing prognosis and assessing the results of therapy (Bullock et al., 1990).

Radiologists and urologists alike have frequently studied and compared the accuracy of many clinical and radiological tools used for assessment of bladder masses. Various imaging methods including ultrasonography, CT and other imaging modalities have been introduced to improve the assessment of bladder lesions (Kim et al., 1994).

Yet not reliable radiological technique is available for use in bladder lesions detection (Rubin et al., 1996). Cystoscopy remains the mainstay for diagnosis, proper evaluation and follow – up of bladder lesions. Once the diagnosis of a bladder tumor has been established US, CT, and MRI are performed for staging (Hayshi et al., 2000).

Recent studies reported the feasibility of 3-D rendering of the bladder, which provides an image format familiar to the urologist (Fenlon et al., 1997).

The recent production of virtual endoscope adds to the imaging armamentarium for use in bladder evaluation. The volumetric data obtained with 4D ultrasound and helical CT (or MR) imaging are computer rendered to generate 3-Dimensional images and with commercially available software, intraluminal navigation through any hollow viscous is possible (Calhoun et al., 1999).
Ryan et al (1999) stated that CTVE could demonstrate normal anatomical structures and reproduce the views produced by standard conventional endoscopy.

Since the original article by Vining et al (1996) there have been several studies of the utility of virtual endoscopy of the bladder. Although the reports published about virtual cystoscopy, the indications are still limited (Narumi et al, 1996).

As cystoscopy still plays the key-roll in the diagnosis of tumors of bladder, virtual cystoscopy may be the less invasive alternative in diagnostic work up (Olcott et al, 1998).

In our Study, we tried to demonstrate that virtual cystoscopy is a feasible technique for use in the detection of bladder masses, and to compare between it and real cystoscopy.

Whatever the used protocol and parameters, an AP scout view of the pelvis is first obtained with the patient in supine position to plan for helical CT scan; this is followed by helical CT scanning, of the distended bladder (Song et al, 2001). Scanning should be performed during one breath hold to prevent breathing artifacts (Fleiter et al, 2000).

Certain authors (such as Song et al, 2001/ Bernhardt and Rapp - Bernhardt, 2001/ Heinz-Peer et al, 2003) claimed that, for proper evaluation of the bladder and detection of bladder lesions, scanning of the air distended bladder in both supine and prone positions is preferred. Performing cystoscopy in prone and supine positions will shift retained fluids into other segments of the bladder as Fletcher et al (1999) show in their study.
Moreover the internal structure of the bladder is rather complicated due to the functional status and the filling. That is why repositioning is performed, since there is always, despite of the drainage, a minimal amount of urine in the bladder. Also adequate distention with air has to be controlled after repositioning, since the repositioning maneuver between supine and prone may lead to leakage of the insufflated air (Bernhardt and Rapp - Bernhardt, 2001).

Multiplanar reformation (MPR): Is the most simple and allows viewing of single scans in multiple planes (Coronal and Sagittal) others than axial scans (Heinz-Peer et al, 2003).

Maximum intensity projection (MIP): The entire volume is projected into one viewing plane with depiction of only the highest density value in the viewing direction. The limitation is that MIP offers just a 2-D character of the image (Heinz-Peer et al, 2003).

Surface shaded display (SSD): Computer processing in SSD involves manipulation of CT data by means of marching cubes algorithm to create a «wire frame» model the surface of which is filled in. Depending on the CT attenuation threshold selected, tissues of different densities can be either included or removed. The net effect is the display of a tissue interface that simulates a flat opaque anatomic specimen. Light and shade from a simulated light source are used to achieve a 3-D perspection.

Although SSD allows a rapid 3-D reconstruction and is less demanding computationally than volume rendering, SSD uses only 10 % of the available helical CT data and compared
with volume-rendered images, lacks depth and details (Heinz-Peer et al, 2003).

Volume rendering (VR): VR images are "data rich"; they use 100% of the available CT data for 3-D reconstruction and have a "fluoroscopic" appearance rather than the flat opaque appearance of images created with SSD. In addition to showing greater anatomic details, volume rendered images contain fewer smoothing and blurring artifacts.

A sense of depth, distance, and motion is also, achieved by using perspective algorithm (perspective volume rendering). This algorithm is a computer graphics technique that causes the object to grow larger as the observer approaches. When combined with real time viewing (5-30 frames/second), use of this technique conveys the effect of travelling through the bladder lumen in-vivo. Volume rendering algorithms generate a tissue volume by assigning varying degrees of opacity based on CT attenuation coefficient of each voxel (Heinz-Peer et al, 2003).

The changeable perspective of the virtual camera can be used to generate "fish eye" perspectives of the bladder lumen and this improves orientation compared to conventional cystoscopy (Fleiter et al, 2000).

In addition Schreyer et al (2000) developed an algorithm for color mapping the thickness of the bladder wall, and by using a color range, even subtle thickness changes appeared very clearly. However although volume rendered images provide more information than surface rendering since the entire datasets are used, this technique requires more powerful
computers, which would increase the cost of virtual endoscopy (Rapp-Bernhardt et al, 2000).

On the other hand, technical advances regarding 3-D workstations have led to a considerable reduction of the post-processing time required for production of virtual endoscopy views, including interactive intraluminal navigation through the bladder (Hussain et al, 1997). Variation of post processing times ranging from 7 to 8 hours, and 12 to 15 min. has been reported in literature and is dependent on the available 3-D hard and software. Today post processing can be performed in few minutes after transfer of the 3-D datasets to the workstation (Heinz-Peer et al, 2003).

In our study, the required time to produce virtual endoscopy imaging may be distributed as follows: 10-15 min. to perform spiral CT scanning of abdomen and pelvis, 5-10 min. to transfer the axial CT data to the specialized workstation and 15-30 min. for post processing work up to obtain virtual endoscopic views.

Results of most of the carried out studies indicated that virtual cystoscopy allows the accurate assessment of localization and morphology of bladder masses (Heinz-Peer et al, 2003).

In our study, the obtained results for the sixty patients, demonstrated excellent sensitivity and specificity scores (up to 100%) of VE, in localization and morphology description of bladder tumors; the results were comparable to those of real conventional cystoscopy, and superior to spiral CT of the bladder.

Concerning the size (depth) of the mass, many different studies reported different results. Narumi et al (1996) found
detection and characterization of masses less than 10 mm to be
difficult with 3-D display of helical CT data, while Fenlon et al
(1997) reported that all of bladder masses detected at
conventional cystoscopy were visualized at CT cystoscopy, and
pointed out in their study that all tumors less than 10 mm were
identified, although this group did not report how many of their
masses were less than 5 mm. In their study, Song et al (2001)
demonstrated that virtual cystoscopy is a feasible technique for
use in detection of bladder masses greater than 5 mm, but for
lesions less than or equal to 5 mm, the detection rate was 60%.

Our study demonstrated a sensitivity of 100% in detection
of bladder masses including those smaller than 10 mm and
greater than 5 mm by VE in all cases, (while spiral CT was
sometimes defective in depiction of masses ranging from 5-
10 mm in size). But actually, sensitivity of VE to masses smaller
than 5 mm could not be evaluated since no such small lesions
were encountered in the studied cases.

However, the majority of the authors concluded that
reliable and consistent visualization of lesions less than 5 mm
was problematic (Narumi et al, 1996 / Fenlon et al, 1997 /

But recently, many studies have been introduced that
change these findings. Kim et al (2002) demonstrated excellent
agreement between virtual cystoscopy and conventional
cystoscopy with high sensitivity and specificity, and the
detection rate for lesions smaller than 5 mm was 88% in their
study.

In the other hand, virtual cystoscopy at different mass
settings has been compared to conventional cystoscopy in
patients with tumors of the bladder; for the protocol with reduced radiation exposure, the authors reported a sensitivity and specificity of 96.5% and 100% respectively, for tumor detection; preliminary results of these studies show excellent detection rates, including for lesions less than 5 mm (Bernhardt et al, 2003 / Mang et al, 2003).

Still virtual cystoscopy is unable to depict mucosal color changes (such as leucoplakia..) detected only on conventional cystoscopy, as reported also by Song et al (2001) and Heinz-Peer et al (2003).

In addition, the calcifications associated with masses were seen only on the axial images but not on the virtual images due to the threshold selection optimized to depict soft tissue abnormalities as reported also by Song et al (2001).

Another important fact is that virtual cystoscopy cannot make sure of the nature, or the origin of the mass. Song et al (2001) reported that extravesical pseudolesions that simulated intraluminal masses on virtual views, were then correctly identified as a phlebolith and an enlarged median lobe of the prostate gland on the axial images; and Heinz-Peer et al (2003), reported that mucosal thickening secondary to fibrosis cannot be distinguished from neoplasm.

Therefore, although Song et al (2001) and others reported that the sensitivity of virtual cystoscopy is higher than that of axial images due to the different way of image presentation, the authors agreed that transverse axial together with virtual images are complementary for lesion detection and characterization, and to obtain optimum results (Heinz-Peer et al, 2003).
Spiral CT gave an adequate sensitivity (80.95%) for T-staging and an acceptable accuracy (62%) for pelvic N-staging, in bladder neoplasms.

It is known that the T-stage is the most important factor influencing management and prognosis of bladder tumors; However virtual cystoscopy fails to assess bladder wall invasion, while conventional cystoscopy is properly able to estimate wall infiltration by the tumor (Song et al, 2001).

But when interpreted together, in a complementary way, virtual cystoscopy with axial CT images become comparable to conventional cystoscopy in tumor detection and evaluation of bladder wall invasion.

In addition, CT is adequately able to evaluate extravesical tumor extension and presence or not of regional pelvic lymphadenopathies, an advantage that conventional and virtual cystoscopies lack.

Generally speaking, as one of the most important innovations in the spectrum of the post processing diagnostic techniques, virtual CT cystoscopy provides many advantages:

- Non-invasive, or minimally invasive technique, with minimum discomfort and risks for the patients, especially that there is no requirements for anesthesia (Song et al, 2001).
- Much less time consuming (Heinz-Peer et al, 2003).
- Virtual CT cystoscopy improves the value of axial CT images and allows utilization of the largest amount of CT data (Song et al, 2001).
- Ability of imaging of the bladder in multiple planes and intraluminal viewing of the bladder from any angle (the 360°
view an impression not available on conventional cystoscopy): the virtual camera can be maneuvered 360° to improve orientation and bypass any obstruction (Bernhardt and Rapp - Bernhardt, 2001).

- High accuracy in detection of bladder lesions, despite its size (even those less than 5 mm), as well as wall thickening, as recently reported by Bernhardt et al (2003), Mang et al (2003) and Heinz-Peer et al (2003).
- Adequate capacity of evaluation of the normal internal anatomy of the bladder (Heinz-Peer et al, 2003).

**However virtual CT cystoscopy has its limitations:**

- It is unable to depict flat lesions and subtle mucosal color changes (such as leucoplakia, and carcinoma in situ) that are only seen on conventional cystoscopy (Heinz-Peer et al, 2003).
- It lacks of course the ability to take biopsy and provide tissue for histopathology (Heinz-Peer et al, 2003).
- It could not evaluate deep space viscous wall invasion (Ryan et al, 1999 / Heinz-Peer et al, 2003).
- It lacks ability to identify origin and nature of bladder masses (Heinz-Peer et al, 2003).
- In addition, the exposure to X-ray and the possibility of hypersensitivity reactions to contrast media should not be neglected (Song et al, 2001).
The cost: Virtual endoscopy requires specialized software and hardware that are expensive (Rodenwaldt et al, 1997).

Recent advances in computed tomography (CT) hardware and software have led to the development of various forms of virtual reality of imaging techniques.

Since Vining et al (1996) first described the method, virtual endoscopy of the urogenital tract has enormously improved; contributing to this progress is the advent of multislice CT (MSCT). Recently commercially available highly advanced 3-D workstations have been introduced.
Conclusion

Many investigators have evaluated the usefulness of virtual cystoscopy for detecting bladder lesions.

In our study we tried to investigate the utility of 4D ultrasound VE, CT virtual cystoscopy in the detection of bladder masses, as compared to the gold-standard conventional cystoscopy.

Four-dimensional sonography is a promising alternative noninvasive technique for use in detection of bladder tumors, their localization, and perivesical spreading. The location, size, and morphologic features of the tumors shown on 4D sonography agreed well with the findings of conventional cystoscopy.

Virtual Cystoscopy using Volume Ultrasound is an emerging application used to detect bladder lesions. This technique is useful for diagnosing urinary bladder pathology as demonstrated in the cases presented. Benefits include a more comprehensive understanding of pathology when correlating 2D and volume information, thus providing increased diagnostic confidence.

Using Volume Ultrasound provided the information necessary to make the diagnosis. In our practice Volume Ultrasound has proven to us to be a valuable diagnostic tool adjunct to 2D ultrasound. In addition, it has the potential to reduce the number of invasive procedures in the future, with significant impaction the efficacy and efficiency of urological patient care.
At present virtual cystoscopy based on volumetric data obtained with thin section multislice CT and the use of perspective volume rendering technique, seems to be the most accurate method regarding lesion detection in the urinary bladder.

An excellent overview of the bladder masses was obtained in all the cases and the results of virtual cystoscopy and conventional cystoscopy were comparable with excellent sensitivity rates of VC in detection, localization and morphology description of the bladder masses.

Our results corresponded to a great extent to those reported by many authors such as Vining et al (1996), Fenlon et al (1997), Song et al (2001), Bernhardt and Rapp - Bernhardt (2001), and many others that stated that virtual CT cystoscopy is a useful technique in detection and localization of bladder masses, with high sensitivity, specificity and accuracy rates.

An additional benefit is the reduction of patient discomfort and the cost savings of potentially eliminating the need for an invasive examination. This is especially true when considering follow up cystoscopies after a therapeutic cystoscopy or surgery. In a different series of patients, we were able to cancel 7 out of 10 cases scheduled for a follow-up conventional cystoscopy after Virtual Cystoscopy.

Generally speaking virtual cystoscopy has several advantages over conventional cystoscopy (specially after the technical advances of 3-D workstations that reduced markedly the post processing time): It is much less invasive, much less time consuming, requiring less equipment, with fewer patient preparation steps, allowing intraluminal viewing of the bladder.
from any angle ("fisheye" perspective of the bladder lumen) and bypassing any obstruction if present.

On the other hand, it allows access to some areas which may be sometimes inaccessible by conventional cystoscopy (within bladder diverticulosis for example).

However adequate preparation of the bladder is necessary for CT virtual cystoscopy performance: Beside the requirement of proper bladder distension, there must be an adequate contrast difference between bladder wall and lumen by distending the bladder with air.

In addition, scanning of the bladder in both supine and prone positions is preferred for optimal evaluation.

Complementary analysis of both transverse and virtual CT images is always necessary for proper diagnosis.

CT virtual cystoscopy has still some limitations: in addition to the exposure to radiations and risk of allergic reactions to contrast media, the cost of such specialized workstations is an important limiting factor.

It is unable to depict flat lesions or mucosal color changes; it also lacks the ability to provide tissue for histopathology; it is unable to identify the origin and nature of the bladder masses; it cannot evaluate deep space invasion in case of neoplasm, thus it is alone impractical in T-staging of bladder cancer.

Therefore the complementary interpretation of VC and axial CT informations is essential, allowing us to obtain adequate results comparable, and even sometimes superior, to those of conventional cystoscopy.
Despite the great improvement recently in the virtual CT cystoscopy techniques, it cannot yet supplement real conventional cystoscopy that remains the basis for diagnosis and follow up of bladder lesions.

So far, virtual cystoscopy may be an alternative or a complementary examination, when conventional cystoscopy is difficult to perform or contraindicated: in patients with cystitis, urethritis, obstructive prostatic hypertrophy, stricture or rupture urethra, and for those who are at risk of complications (such as injury, perforation of the bladder or urethra, hemorrhage, and risks of anesthesia).

It may serve as a follow up examination between conventional cystoscopies in bladder cancer patients who are under treatment.

As a minimally invasive procedure it is easily acceptable and could be performed on the patient's request, or if he refuses to undergo the classical conventional cystoscopy.
REFERENCES


9.


5:117.


86. **Lee JKT** (1985): Staging of pelvic neoplasm in contemporary imaging, in Henny, Goldberg, Higging and Ring (eds). California Univ. USA.
87. **Lerner S.P., Skiner D.G., Lieskovski G. et al. (1993):**


Allelic loss of chromosome 17p distinguishes high grade from low grade transitional cell carcinoma of the bladder Cancer. 50:7081.


115. **Putman CE, Ravin CE and Louvrie CA (1994)**: Textbook of diagnostic imaging; 2011-2029;.


162. www.urolgyinformation.co.uk. Last update may 2012


الملخص العربي

المثانة البولية هو المكان الأكثر شيوعاً من الأورام الخبيثة في الجهاز البولي التناسلي. سرطان المثانة مشكلة مشتركة تواجه جراحى المحال البولية في جميع أنحاء العالم. نتائج المراقبة التقليدية هو المعيار الأساسي في تشخيص ومتابعة تطور الأورام، وعلى الرغم من وجود حساسية عالية وخصوصية للكشف عن سرطان المثانة، يعتبر النظام التقليدي إجراء غازي يرتبط بتعقيدات عدة وعلاوة على ذلك، يمثل متابعة منتظمة للأفراد المصابين بسرطان المثانة عبء مالي على النظام الصحي.

النظام التقليدي هو الطريقة القياسية للكشف عن أورام المثانة البولية، ولكن هذه التقنية غازية وغير مريحة بالإضافة إلى كونها تزيد إحتمالية عدوى المحال البولية وعدم قدرتها على تقييم الأمراض خارج المثانة.

إن التقدم العلمي في الأجهزة الطبية والتكنولوجيا الحديثة بالإضافة إلى التطور السريع في أجهزة الكمبيوتر والبرامج الحديثة وإمكانية تطبيقها في المجال الطبي بالإضافة إلى انتشار استخدام المقطعية الطبية أدى إلى إمكانية تصوير المثانة من الداخل باستخدام الأشعة المقطعية ثلاثية الأبعاد مما اتفق عملياً على تسميته بالنظام التقني (التخيلي) للمثانة.

مع التطور التدريجي في التصوير التشخيصي وتقنيات برامج الكمبيوتر الطبية، كان من الممكن إنشاء صور الواقع الافتراضي لفحص الجزء الداخلي من المثانة. هذه التكنولوجيا تعتبر بمثابة اختيار آمن لتشخيص سرطان المثانة والمتابعة، خاصة وأنها مرتبطية بمعدلات للكشف عن السرطان قابلة للمقارنة بالنظام التقليدية. وعلى الرغم من ذلك، فإنه يرتبط ببعض العوائق التي تحد من استعماله في الممارسة السريرية الروتينية في الوقت الحالي.
صور المناظير الظاهري تتولد من مجموعات مخصصة للبيانات وتقنيات مختلفة لإعادة البناء ثلاثي الأبعاد. تقنيات التصوير هذه يمكن أن توفر الصور الخارجية وتنظير الباطن للمسالك البولية وكذلك تقديم صور عالية الدقة التي تساعد في التغلب على بعض المشاكل لفحوصات عن طريق الحقن الوريدي والموجات فوق الصوتية.

واحدة من المزايا الهامة للمنظار الظاهري هو أنها غير غازية ومن الممكن تقييم الأمراض داخل وخارج المثانة في نفس الدراسة. هذا الفحص أثبت قيمة كبيرة في تقييم أورام المثانة المتكررة بعد مقارنة نتائج التشخيص من المنظار الظاهري التي تقوم بها أجهزة الأشعة المقطعية المتعددة المقاطع محسوبة ومقارنة مع المستوى المعياري من تشخيص المنظار التقليدي.

الهدف من هذه الدراسة هو تقييم دور المنظار التقديري للمثانة مقارنة بالمنظار التقليدي (الحقيقي) في تشخيص ودراسة كتل المثانة. وقد اشتملت الدراسة على 60 مريضاً تتركز شكلهم في وجود كتل بالمنطقة وقد تمت بالتحليل الباثولوجي للعينات التي تم الحصول عليها باستخدام المنظار التقديري إصابتهم جميعاً بسرطان المثانة.

تمت الدراسة بوحدة الأشعة التشخيصية بمستشفى بنها الجامعي باستخدام جهاز الأشعة المقطعية الحلزونية حيث تم تصوير البطن والحوض لجميع الحالات ثم نقلت الصور إلى جهاز كمبيوتر خاص مزود ببرنامج خاص بعمل المنظار التقديري للمثانة من الداخل تضايماً ما أمكن الحصول عليه باستخدام المنظار التقليدي.

وقد استغرقت الدراسة الفترة من أكتوبر 2010 إلى أكتوبر 2012 وأثبتت إيجابية النتائج وبالرغم من أن المنظار التقليدي يعتبر من أهم الفحوص التي تجري لتشخيص كتل المثانة حيث يتميز بإمكانية رؤية الورم بصورة مباشرة وكذلك رؤية التغييرات التي تحدث لجدار المثانة والحصول على عينة للتحليل الباثولوجي إلا أن المنظار التقديري يتميز بقدرته الفائقة على تصوير المثانة من جميع الزوايا والأبعاد كذلك يمكنه فحص المثانة بعد مرحلة الضيق أو الانسداد الناتج عن الأورام أو الأسباب
الباثولوجية المختلفة والتي يعجز المنظار التقليدي عن المرور خلاله.

ومن أهم مزايا الفحص التقديري هو أنه فحص آمن لذا فإنه من الممكن استخدامه في الأطفال وفي الحالات التي يصعب أو يحظر فيها استخدام المنظار التقليدي مثل وجود التهابات أو ضيق أو لمتابعة حالات سرطان المثانة خاصة التي خضعت لتدخلات جراحية.

ليس من المتوقع أن يحل المنظار التقديري للمثانية محل المنظار التقليدي الذي يعطي صورة حية ديناميكية للمثانية كذلك يتيح فرصة للحصول على عينة للتحليل الباثولوجي من الكتلة الموجودة ولكن من المتوقع أن يكون هذا الفحص روتيني خاصة للمتابعة في حالات سرطان المثانة لما له من فوائد متعددة كذلك يعتبر إضافة جديدة لمزايا الأشعة المقطعية في دراسة وتقييم كتل المثانة.
منظار المثانة الإفتراضى مقارنة بالمنظار التقليدى فى تشخيص أورام المثانة

رسالة
للحصول على درجة الدكتوراه
في الأشعة التشخيصية
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