A review on the accuracy of bladder cancer detection methods, their advantages and disadvantages

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Abstract

Background and purpose: Bladder cancer is the most common malignant tumor in the urinary system, with a high incidence and recurrence rate. While the incidence of bladder cancer has been rising in recent years, the prevalence of bladder carcinoma is showing a tendency in the younger age group. There are several methods to detect bladder cancer, but different methods have varying degrees of accuracy which intrinsically depends on the method's sensitivity and specificity. Our aim was to comprehensively summarize the current detection methods for bladder cancer based on a large number of literature, and at the same time, to find the best combination of different effective methods which can produce a high degree of accuracy in detecting the presence of cancerous cells.
Materials and methods: We used key-word retrieval method for searching related references in English that had been published in PubMed and Medline.
Results and discussions: This paper discussed the detection methods and their sensitivities/specificities as well as advantages and disadvantages. We summarized the best identified cancer cell detection methods with higher sensitivity/specificity.
Conclusion: The results of this review can positively help to identify accurate methods for detecting cancer and can be further improved for future research work.

Keywords: Bladder cancer, Methods, Sensitivity, Specificity, Advantages and disadvantages

1. Background

Bladder cancer is the sixth most common malignant tumor cancer in men and the 17th most common malignant tumor cancer in women[1]. It is a relatively common disease and is the most common malignant tumor of the urinary system. Its incidence ranks at first place among malignant cancers of the urinary system, second only to prostate cancer in Western countries. In recent years, the incidence of bladder cancer has risen steadily. The pathologic histology shows that over 90% bladder cancer patients have bladder transitional cell carcinoma, 5% have bladder squamous cell carcinoma, and less than 2% have bladder adenocarcinoma [2]. Moreover, the incidence of bladder cancer among males is three to four times that of females [3, 4]. Among patients who are first diagnosed with bladder cancer, 70% to 85% are diagnosed as having nonmuscle-invasive bladder cancer (NMIBC), while 15% to 30% are muscle-invasive bladder cancer (MIBC) [5]. NMIBC is known as superficial bladder cancer, where the pathological stages include Ta (papillary), T1 (infiltration lamina propria) and carcinoma in situ (CIS). Ta patients comprise 70% of cases, T1 roughly 20% and CIS about 10%. MIBC is known as invasive bladder cancer, where the pathological stages include T2, T3 and T4 [5, 6]. Up to 80% of NMIBC patients relapse within five years; 30% of Ta patients develop to MIBC; whileT1 and CIS patients are more likely to develop to MIBC [7, 8]. The standard treatment for NMIBC is transurethral resection of the bladder tumor (TURBT), where the treatment for MIBC is RC and/or chemotherapy [5, 9].

The incidence of bladder cancer is a complex and multifactorial pathologic process, either due to intrinsic genetic factors or external environmental factors. At present, two major confirmed factors are smoking and prolonged exposure to aromatic amines chemical substances. Smoking is the most confirmed pathogenic factor, as about 30% to 50% of bladder cancers can be ascribed to smoking which can amplify the incidence of bladder cancer by two to four times. The incidence rate is in proportion to the intensity and duration of smoking. Hematuria is the most common and the earliest symptom of primary bladder cancer. The nature of hematuria includes full-course, intermittent and painless gross hematuria, sometimes accompanied by blood clots [8, 10]. Other clinical manifestations of initial diagnosis include microscopic hematuria, lower urinary tract symptoms and urinary tract infection [11]. Statistics show that bladder cancer has a high incidence rate, high progression rate and high recurrence rate. Therefore, in clinical work it is extremely important to accurately diagnose and assess early emerging bladder cancer patients, and particularly to monitor high-risk postoperative bladder cancer patients. The most common ways to diagnose bladder cancer include biopsy, cystoscopy, imaging methods, urinary cytology, fluorescence in situ hybridization (FISH), and urine protein detection (BTA-STAT, BTA-TRAK, NMP22 and ACCU-DX), etc., [8, 12]. Currently, cystoscopy and urinary cytology are the golden standard for diagnosis of bladder cancer. However, cystoscopy is an invasive examination and can cause pain, bleeding, urethral mucosa, urinary tract infections and other complications on the patients. Additionally, it is sometimes difficult for cystoscopy to detect tumors on the top and forearm of the bladder, which constrains its clinical application. Cytology is a non-invasive test that can directly identify tumor cells shed in urine. It is simple to use, low cost and performs well, although it has low sensitivity and low diagnostic efficiency.

2. Materials and Methods

The method adopted in this paper is the “keyword” information retrieval method. After collecting references related to bladder cancer detection, the references were summarized and organized, so as to select representative and reliable research literature that matched the study’s requirements. In this article, PubMed and Medline complete were used for systematic retrieval from 2008 to 2018. Firstly, we set two keywords (bladder cancer, detection) as abstract retrieval, resulting in 2,783 relevant

English-language papers in the literature. Secondly, the inclusion criteria for this study were that 297 full texts must include results of detection of bladder cancer with clinical trial or without clinical trial. Then, we took "bladder cancer, detection" as abstracts that had been reviewed and "clinical trial, accuracy" as full articles that had been reviewed. After all exclusions, 28 relevant articles. The main exclusion criterion for this study was that they should not have been used for clinical diagnosis. Other publications of urinary problems and other cancers were also excluded. The flowchart for the entire article search is presented in Fig. 1.

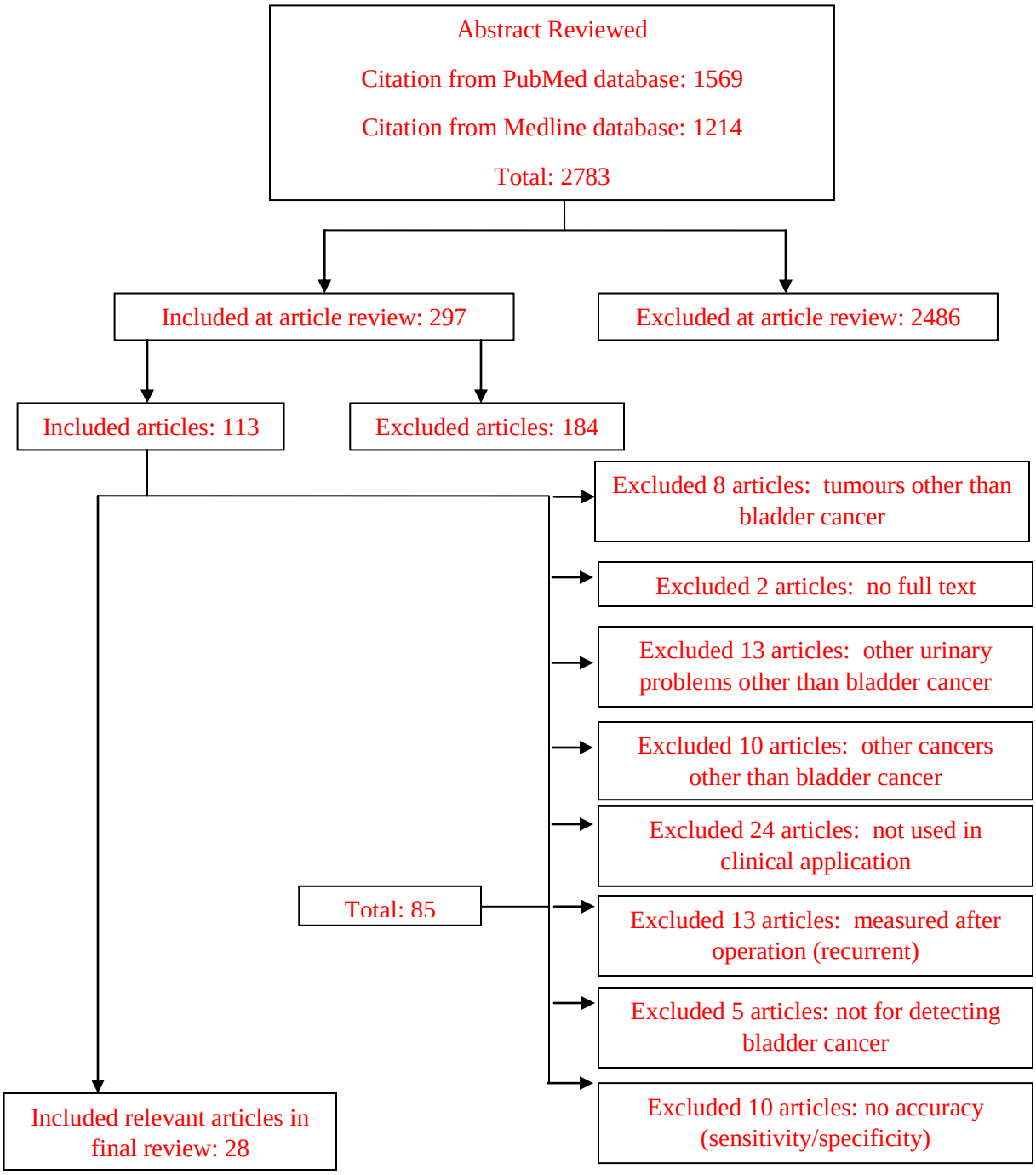

Fig. 1. Flowchart of literature search results using Medline complete and PubMed from 2008 to 2018.

All diagnostic methods for clinical use have their own pros and cons. Therefore, it becomes a top priority to find a detection and diagnosis method for bladder cancer, which is characterized by high sensitivity, high specificity, low cost, non-invasive, ease of use and repeatability. In the area of medical diagnosis, sensitivity and specificity are the most widely employed in statistics used to describe a diagnostic test. Test specificity is the capacity for the test to correctly identify those without the disease (true negative rate), while test sensitivity is the capacity for the test to correctly identify those with the disease (true positive rate). Therefore, in this article, using sensitivity and specificity to compare several different diagnostic methods can enable patients get more intuitive judgments. In this study, we compared the accuracy of different methods, thus, any article that was in-accurate was excluded. In the end, we used 11 articles from PubMed database, and 17 articles from Medline complete database.

3. Results and Discussions

The clinical stage and grade are the two most vital determinants of the destiny of bladder growth. Albeit hard to demonstrate in forthcoming studies, it is truly clear that the deferrals experienced during the time spent making conclusion and performing treatment of the bladder disease will subsequently lead to inadmissible results. The postponement could be multifactorial in the sense that it could be a lack of awareness about the imperative reality of this illness amongst the all-inclusive community and non-urology doctors, due to delay in seeing the doctor, delay in the referral and management (doctor's facility) which consequently contributes to delay in the treatment. Basic leadership on matters of top priority, such as when to treat forcefully and to recognize the high-chance gathering according to hazard stratification, can likewise be a main element in the treatment result of the bladder growth. A proportion of recent studies have highlighted less than ideal referral designs for hematuria in the current practice [13].

There is constantly a conflict among those who feel that early recognizable proof may not translate into improved survival. Regardless of the advances in the progression of surgery and chemotherapy, the 5-year disease free survival rate in the muscle-prominent bladder tumor has not improved and is still in the extent of 50 to 60% success [14]. There could be various clarifications behind this. Elements, such as, non-regulation of the arrangement of cystectomy and neighborhood lymph center elbowroom, no comprehensive simultaneousness on perioperative chemotherapy, lack of further progress in new pharmaceutical developments and lack of data regarding the natural behavior of bladder disease could well be the reason for poor results. Thus, early recognition as well as reasonable and propitious treatment of bladder symptoms is fundamental to improve the outcome of bladder cancer. Bladder cancer is the fourth most common cancer among men in the Western world, after prostate, lung, and colon malignancies.

Bladder growth is an illness brought on by synthetic cancer-causing agents and might have variable normal history. Although shallow bladder tumors repeat more often than not, they likewise tend to advance and be fatal for the patient. This article summarizes the detection methods and their sensitivities/specificities as well as advantages and disadvantages and the best identified cancer cell detection methods with highest sensitivity/specificity. The discussion above looks at the world-wide rates of bladder cancer. The statistics show that bladder cancer is mostly found among men. In Europe and the United States, those below 75 years old are at risk of bladder cancer [1].

3.1 Urine microscopy

Urine microscopy is an important device for the determination and administration of a few conditions that influence the kidneys and the urinary tract. Microscopic examination of urine is a joint

responsibility of the nephrologists and the pathologists. The former, if sufficiently trained and equipped, are able to obtain important diagnostic information about the individual patients under their care. However, increasingly, a lack of appropriate resources, including time, equipment, biologically safe environments, and, in the United States, legislative barriers, are making this procedure more difficult [15].

Urine tests for microscopy should be acquired from the relevant examining centre using an aseptic method. Tests should not be taken using the outlet tap, as small colonies of microscopic organisms live inside the stagnant urine or around the outlet tap, and may produce false results. Table 1 shows a review of urine microscopy sequence and their sensitivity and specificity. This investigation will help explain the accuracy of this method. Based on the review, Table 2 shows the advantages and disadvantages of the above detection methods.

Table 1: Sensitivity and specificity of urine microscopy.

Authors	Year	Urine Microscopy Sequence(s)	Sensitivity/specificity (%)	References
Becker et al.,	2016	Urine RBCs and Glomerular disease	85 / NA 87.5 / NA	[16]
Roche Diagnostics Ltd	2011	Multiview Microscopy	95 and 80	[17]
Williams et al.,	2010	Gram-stained bacteria	91 and 96	[18]

Table 2: Advantages and disadvantages of urine microscopy [19].

Advantages	Disadvantages
No risk (e.g., trauma, bacterial infection) to patient. Avoids iatrogenic hematuria.	May contain debris (e.g. bacteria, exudate) from lower urinary and genital tract. If bacterial growth appears on urine culture, must differentiate between urethral contamination and urinary tract infection. Quantitative urine culture required.
Provides method to obtain urine sample when voluntary micturition has not occurred.	May induce trauma to urinary tract, resulting in hematuria. May be stressful for patient, especially if bladder is in painful condition. If bacterial growth appears on urine culture, must differentiate between urethral contamination and urinary tract infection. Quantitative urine culture required.
Provides method to obtain urine sample when other methods of collection have failed.	Potential for trauma to urinary tract, especially urethra. More invasive than other methods; sedation may be required. Risk of introducing bladder infection. If bacterial growth appears on urine culture, must differentiate between urethral contamination and urinary tract infection. Quantitative urine culture required. Least desirable method of

	urine collection.
Preferred method of collection for urine culture. Avoids contamination of sample from lower urinary tract.	Potential risk of trauma if performed incorrectly or patient moves during procedure. Potential for iatrogenic hematuria. More invasive than spontaneous micturition. Potential for bacterial contamination of sample if needle penetrates colon during procedure.

3.2 Urine cytology

Urine tests have been performed to recognize bladder cancer. A case in point is pee tests, for instance, the UroVysion test, ImmunoCyt test and NMP-22 test. These tests recognize chemicals, proteins and chromosomal changes in urine that are caused by bladder infection. However, these tests are not routinely done, in spite of the fact that their utilization is expanding in a few doctors' facilities [20]. Table 3 shows a review of urine cytology sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method.

Table 3: Sensitivity and specificity of urine cytology.

Authors	Year	Urine cytology Sequence(s)	Sensitivity/specificity (%)	References
Lee et al.,	2015	High Grade Urothelial Carcinoma (HGUC)	86 and 73	[21]
Yafi et al.,	2015	Cytology	84.6 and 100	[22]
Rosser er al.,	2014			
Anai et al.,	2014	MP22-17 and 5-aminolevulinic acid	83 / NA	[23]
Shen et al.,	2012	NBI or WLI cystoscopy	87.8 and 77.1 (NBI) 68.3 and 82.9 (WLI)	[24]
van Rhijn et al.,	2009	urethra-cystoscopy (UCS)	75 and 83	[25]

As a rule, the specificity was lower for low-and-high-review sores in voided samples or in a subsequent setting, and this was summarily considered as the edge of a positive cytological analysis. Then again, the affectability for poor quality injuries was higher in voided specimens interestingly with high review sores, which were identified all the more frequently on instrumented examples [26]. Based on the review, Table 4 shows the advantages and disadvantages of the above detection methods.

Table 4: Advantages and disadvantages of urine cytology [27].

Specimen Type	Advantages	Disadvantages
Voided urine	Non-invasive No instrumentation artifact	Low cellularity Vaginal contamination Poor preservation
Catheterized	High cellularity	Invasive

		Instrumentation artifact Poor preservation
Bladder washing	High cellularity Good cell preservation	Invasive Instrumentation artifact
Upper tract washing	High cellularity Good preservation Selective sampling	Invasive Instrumentation artifact
Brush cytology	Selective sampling	Invasive Air drying possible (if direct smear)
Heal loop	Permits screening for recurrent bladder cancer	Low cellularity Poor preservation

3.3 Urine markers

Urine markers are a combined method for bladder cancer diagnosis. More than 30 urinary biomarkers have been identified for use in bladder disease diagnosis, however, just a few industrially accessible; the rest are still being tested [28]. Financially accessible tests include:

- Urine cytology
- Fluorescence in situ hybridization (FISH)
- Nuclear matrix protein (NMP-22)
- BTA *stat*
- BTA TRAK
- ImmunoCyt/uCyt+
- CertNDx
- CxBladder

While surveying the execution of a marker, one must be careful in order to consider the study population, as it will influence the execution of the marker if it is associated with as an advanced stage of disease. Although low in number, some of these markers have undergone focused studies, and we have tried to segregate these data in Table 5, keeping in mind that uniform data are not available for each marker [29]. Table 6 shows a particular review of urine markers sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method. Based on the review, Table 7 shows the advantages and the disadvantages of the above detection methods.

Table 5: Sensitivity and specificity of urinary markers for bladder cancer [29].

	Surveillance*		**Screening**	
Test	**Sensitivity (%)**	**Specificity (%)**	**Sensitivity (%)**	**Specificity (%)**
Cytology	52	98	55	99
BLCA -4	96	100	–	–
BTA stat®	83	72	90	76
BTA TRAK®	72	75	–	–
CYFRA 21 -1	97	89	79	89

DD23	81	60	–	86
NMP22/	100	90	97	85
Bladder Chek®	100	93	–	–
SurvivinUBC™	82	90	–	–
ImmunoCyt™/uCyt+™	100	79	–	–
UroVysion™	100	98	–	–

*Also includes mixed cohorts

Table 6: Sensitivity and specificity of urine markers.

Authors	Year	Urine markers Sequence(s)	Sensitivity/specificity (%)	References
Aprikian and Chen	2010	TMPRSS2:ERGFusion	45.4 and 34.8	[30]
Babjuk et al.,	2008	BTA TRAK	90 and 24.8	[31]

Table 7: Advantages and disadvantages of urine markers [32].

Advantage	Disadvantage
Detection of low grade tumour	Labour intensive and expensive
Sensitivity	Complex and expensive
More choices	High inter-observer variability
Less painful	Influenced by inflammation and age
	Needs further study

3.4 Cystoscopy

This is the most vital test for diagnosing bladder. The patient can have this test done under a special or a general sedation. During a cystoscopy under sedation, the patient's specialist will analyze the bladder. In the event that the patient needs tissue tests taken, these will require a cystoscopy under general anaesthesia [33].

For a cystoscopy, the specialist will clean the skin around the patients urethra (tube turning out from the bladder) and use a topical gel to numb the region. A delicate tube with a light will be plaves inside the patients' bladder. The tube has fiber optic connections inside it. This allows the patients' specialist to see inside the bladder. The cystoscope will be embedded into the patients' urethra and up into the bladder. A few patients will feel the desire to urinate. The specialist will deplete the patient's urine into a sterile holder, and then evacuate the catheter. The procedure carries a small risk of infection or bleeding in the bladder. The doctor will send the urine sample to a laboratory for analysis and will then receive a subsequent report of the result. The cystoscopy test can be made available at the patient's first appointment on the grounds that it should be performed rapidly. The specialist will press some sedative inject into the patient's urethra and leave it for a couple of minutes for it to work. This can be uncomfortable, however, it should not be painful [34].

Once the sedative has worked, the specialist will put the cystocopy tube (cystoscope) into the patient's bladder and move it around to inspect the entire inside view of the bladder which will just take a couple of minutes. In the event that any irregular features are glimpsed inside the patient's bladder, the specialist will need to take tissue tests (biopsies). Thus, the patient will require another appointment to have a cystoscopy under a general sedative. Table 8 shows a review of cystoscopy sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method.

Table 8: Sensitivity and specificity of cystoscopy.

Authors	Year	Cystoscopy Sequence(s)	Sensitivity/specificity (%)	References
Ciudin et al.,	2015	Air cystoscopy	88 and 97	[35]
Horstmann et al.,	2014	PDD cystoscopy	92 and 57	[36]
Tatsugami et al.,	2010	NBI over WLC	92.7 and 70.9	[37]
Allam et al.,	2009	Cystoscopy	100 and 94.4	[38]

Based on the review here, we see some advantages and disadvantages of the above detection methods. One of the advantages of this system is that it can be performed over and over again with negligible danger to the patient and with favorable results. There is not exactly a 100% danger of disease or harm to the bladder, and both are effectively correctable [39]. There are favorable circumstances and detrimental effects to every kind of activity. Every alternative method should be examined and evaluated with the doctor who can confirm which choice will work best for the patients. Table 9 shows conservation and with their advantages and disadvantages [35].

Table 9: A few Systems for Conservation, and their Favorable advantages and disadvantages[35].

Advantages	Disadvantages
No chemical Interference	Use for a short period of time (3-6 hours).
For specimen transport	For prolonged periods additional preservatives must be used
Preserves acetone	May destroy formed elements
Reducing Substances	Flammable
Preserves most constitiuents	Can cause false positives for proteins
Preserves urine aldosterole level	Settles to the bottom of the urine containers
Preserves formed elements	Interferes with glucose evaluation
Stabilizes steroides, catecolamines	Formed elements are destroyed,
Preserves chemicals formed elements	Precipitate uric acid
Preserves porphyrines and urobilinogen	Interferes with other urine constituents

3.5 CT scan

Computed tomography (CT) scan (comment: this is not a "screening test"; it is used for staging once the bladder cancer is diagnosed, most commonly by cystoscopy and biopsy/TURBT). Another test called CT urogram is a unique sort of CT sweep that acquires photos of the patient's urinary tract. This is occasionally done to search for a bladder tumor. A CT examination takes a progression of X-ray beams which develop a three-dimensional photo of the inside of the body. A CT urogram is a CT sweep of the bladder, ureters and kidneys. The sweep is simple and takes 10 to 30 minutes. It uses a small measure of radiation, which is far below the permissible level and is not harmful even with contact. The patient should not eat for no less than four hours before the treatment using the CT urogram is carried out[33].

The patient may be given a colored drink (contrast medium, dye) which permits their bladder, ureters and kidneys to be seen clearly. This may make the patient to feel warm all over for a couple of minutes. It is essential to follow the specialist's advice whether the patient is adversely affected by iodine and if he has asthma, so that he can genuinely respond to the infusion. The patient will most likely be able to go home when the treatment is over [40]. Table 10 shows a review of CT scan sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method. There are advantages and disadvantages of CT treatment as shown in Table 11.

Table 10: Sensitivity and specificity of CT scan.

Authors	Year	CT scan Sequence(s)	Sensitivity/specificity (%)	References
Ahmed et al.,	2013	CT scan and angiogram	76.6 and 100	[41]
Perry et al.,	2011	Third generation computed tomography	92.9 and 100	[42]
Cortnum et al.,	2010	CT scanning techniques	99.7 and 100	[43]
Asha and Cooke	2009	CT images on ‘‘lung window’’ settings	89.9 and 81.9	[44]

Table 11: CT advantages and disadvantages [45].

Advantage	Disadvantage
First, CT completely eliminates the superimposition of images of structures outside the area of interest.	Small increased risk of cancer in future from exposure to ionising radiation (X-rays). Risk is greater for children.
Second, because of the inherent high-contrast resolution of CT, differences between tissues that differ in physical density by less than 1% can be distinguished.	Uses higher doses of radiation than plain X-ray, so the risks (while still small) are generally greater than for other imaging types.
Finally, data from a single CT imaging procedure consisting of either multiple contiguous or one helical scan can be viewed as images in	Injection of a contrast medium (dye) can cause kidney problems or result in allergic or injection-site reactions in some

the axial, coronal, or sagittal planes, depending on the diagnostic task. This is referred to as multiplanar reformatted imaging.	people. Some procedures require anaesthesia.

3.6 MR imaging

A magnetic resonance imaging (MRI) scan is an easy technique that may take 15 minutes up to an hour and a half, contingent upon the area being checked and the quantity of pictures being taken. MRI uses a powerful magnetic field, radio recurrence beats and a PC to deliver point by point pictures of organs, delicate tissues, bone and for all intents and purposes all other interior body structures [46]. As the MRI scanner produces solid magnetic fields, it is essential to remove any metal articles from your body (eg. watches, jewellery, piercings and so on) [46]. Table 12 shows a review of MRI sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method. Based on the review, Table 13 shows the advantages and disadvantages of the above detection methods.

Table 12: Sensitivity and specificity of MRI.

Authors	Year	MRI Sequence(s)	Sensitivity/specificity (%)	References
Lee M	2017	MRI	80.8 and 77.8	[47]
Laoruengthana and Jarusriwanna	2012	1.5 Tesla MRI	90.9 and 84.6	[48]
Abdel-Wanis et al.,	2011	MRI to assess the underlying pathology	97 and 98	[49]
Chambers et al.,	2010	MRI	91 and 90	[50]

Table 13: MRI advantages and disadvantages [51].

Advantages	Disadvantages
MRI is particularly useful for the scanning and detection of abnormalities in soft tissue structures in the body like the cartilage tissues and soft organs like the brain or the heart.	MRI scan is done in an enclosed space, so people who are claustrophobic i.e., fearful of being in a closely enclosed space, will face problems with having an MRI done.
There is no radiation used in MRI, so it is safe for people who can be vulnerable to the effects of radiation such as pregnant women or babies.	MRI scans are very noisy because they involve a very high amount of electric current .
MRI scan can provide information about the blood circulation throughout the body and blood vessels and also enables the detection of problems related to the blood circulation.	MRI scanners are usually expensive

3. 7 Ultrasound scanning

Ultrasound filters use high recurrent sound waves to develop a photo within the body. These outputs are typically done in the X-ray department of hospital. The ultrasound scanner has a mouthpiece which emits sound waves. The sound waves bounce off the organs inside the body, and are captured again by the receiver. The receiver is connected to a PC and transforms the reflected sound waves into a photo [52]. Ultrasound or ultrasonography is a therapeutic imaging method that uses high recurrent sound

waves and their echoes. The principle is similar to that of echolocation use by bats, whales and dolphins, or SONAR used by submarine [53].

An ultrasound scanner comprises a console containing a PC and hardware, a video screen and a transducer that is used in scanning. The transducer is a small hand-held gadget that looks like an amplifier, attached to the scanner by a cable. Some scanners may use distinctive transducers (with various capacities) during a solitary scan. The transducer conveys indistinct, high-recurrent sound waves into the body and then listens for the returning echoes from the tissues in the body [54]. The normal technique of ultrasound examinations can analyze an assortment of conditions related to the body's organs which have been affected by diseases. Table 14 shows a review of ultrasound sequence and their sensitivity and specificity. This investigation will help to explain the accuracy of this method. Based on the review, we can see some advantages and disadvantages of the above detection methods in Table 15 [55].

Table 14: Sensitivity and specificity of ultrasound.

Authors	Year	Ultrasound Sequence(s)	Sensitivity/specificity (%)	References
Gupta et al.,	2016	Ultrasound	90 and 93	[56]
Pinto et al.,	2013	Ultrasound technique	100 and 99	[57]
Al -Ajerami	2012	Ultrasound	84.8 and 83.3	[58]
Fowler et al.,	2011	Ultrasound	95 and 86	[59]
Menon et al.,	2009	Ultrasound screening	89.4 and 99.8	[60]
Kocakoc et al.,	2008	3D ultrasoud	96.2 and 70.6	[61]

Table 15: Ultrasoud advantages and disadvantages [55].

Advantages	Disadvantages
Usually non-invasive, safe and relatively painless	Quality and interpretation of the image highly depends on the skill of the person doing the scan
Uses no ionising radiation	Other factors can affect image quality, including the presence of air and calcified areas in the body (e.g. bones, plaques and hardened arteries), and a person's body size
Does not usually require injection of a contrast medium (dye)	Use of a special probe (e.g. for the oesophagus, rectum or vagina) is required in some ultrasounds
Can help diagnose a range of conditions in different parts of the body, such as, the abdomen, pelvis, blood vessels, breast, kidneys, muscles, bones and joints	Special preparations may be required before a procedure (e.g. fasting or a full bladder)
Can be used to check on the health of a baby during pregnancy	

3. 8 Combined method

A combined method diagnosis system is a system that combines one, two or three methods. These combined systems will increase the accuracy of detection of the cancer or other particular problems in the human body.

3.8.1 Urine Markers and Urine Cytology

The sensitivity and specificity of some detection methods are compared in Table 16 and Table 17 [62, 63][75].

Table 16: Strip-based Adjunct Markers for Urine Cytology (all FDA-approved) [62].

Markers	Sensitivity/ Specificity (%)	Comment
NMP 22	73 and 90	Good sensitivity in low grade lesions
BTA Stat	93 and 90	Benign hematuria lowers specificity
BTA TRAK	68 and 75	Better sensitivity, specificity still low
FDP	68 and 78	Currently not being produced

Table 17: Sensitivity and Specificity of urinary markers [62,63],[75].

Markers	Sensitivity (%)	Specificity (%)
BTAstat	100	93
BTA TRAK	78	98
NMP22	100	95
ImmunoCyt	100	86
UroVysion	87	96

Along these lines, the choice of a financially available bladder tumor marker would add to the armamentarium of bladder illness area [64]. The ideal screening and perception test should be non-prominent, quick, adequately accessible to suppliers and patients, be effective and have and specificity. Since urine comes into direct contact with bladder tumors, urinary markers have been of excellent use in this field. Be that as it may, urine cytology is hampered by administrator reliance and low effectiveness, especially for poor quality sores [25]. However, a few have gone through clinical trials and are ready for clinical use [29].

3.8.2 CT scan and MRI

The combination method of CT and MRI has sensitivity and specificity is shown in Table 18 [65, 66].

Table 18: Diagnostic sensitivity and specificity of CT and MRI, where MRI is ‘‘Gold Standard’’ [65, 66]

Diagnostic accuracy	Senior consulting radiologist		Resident in radiology		Resident in orthopaedic surgery	
	MRI	CT	MRI	CT	MRI	CT
Sensitivity (%)	100	87 95	87 95	67 95	80 95	47 95
Specificity (%)	100	100 95	88 95	96 95	90 95	96 95

Positive predictive value	100	100 95	68 95	83 95	71 95	78 95
Negative predictive value	100	96 95	96 95	91 95	94 95	86 95

3.8.4 MRI, cystoscopy, DCE, DW and T2W

Nodal arrangement of BCa with MRI is restricted since it now depends entirely on the extent of the hubs. Extensive hubs can just be hyperplastic and dangerous hubs are not generally extended, prompting false positive and false negative results when estimate alone is utilized as the model for design of hubs. Ultrasmall Superparamagnetic Iron-Oxide (USPIO) (Ferumoxtran-10) upgraded MRI has been identified to enhance lymph hub organizing in a few concentrates, however, this operator is no longer accessible for human use. Thoeny et al. [67] surveyed 21 BCa and/or prostate disease patients with USPIO upgraded MRI and DW MRI. They reported an indicative accuracy of 90% for identifying metastatic lymph hubs. Without the accessibility of this specialist, analysts are examining whether ferumoxytol, a comparative compound which is confirmed for use as an iron supplanting treatment in patients, may be substituted with ferumoxtran-10. Table 19 summarizes the MRI studies which can be incorporated into this audit [68]. A comparison of the accuracy of pelvic construction during PET/MRI in bladder cancer patients was reported [69].

Table 19: MRI studies included in the review [68].

Authors	Year	MRI Sequence(s)	Sensitivity/specificity (%)	PPV/NPV (%)	References
Avcu et al.	2011	DW MRI	1 and 76	NA	[70]
Kobayashi et al.	2011	DW MRI	92 and 90	NA	[71]
Watanabe et al.	2009	DW MRI	80 and 79	NA	[72]
Abou El-Ghar et al.	2009	DW MRI	98 and 92	1 and 92	[73]
Takeuchi et al.	2009	DW MRI	80 and 94	NA	[74]
El-Assmy et al.	2009	DW MRI	98 (sensitivity)	1 (PPV)	[75]

4. Conclusion

According to this study, it is clear that the methods have their own respective accuracies. The sensitivity and specificity data were collected from different patients. We can understand the higher detection performance by using those methods. The best accuracy can also be compared between the single and the combined methods. Table 20 and Table 21 show the methods and the highest percentages of sensitivity and specificity for each method. Below is the summary of the above study.

Table 20: Highest percentage of sensitivity and specificity in single detection method

Methods	Sensitivity (%)	Specificity (%)
Urine microscopy	95	96
Urine cytology	100	99
Urine makers	90	34.8
Cystoscopy	100	97
CT scan	99.7	100
MRI	97	98
Ultrasound	100	99.8

Table 21: Highest percentage of sensitivity and specificity in combined method

Combined methods	Sensitivity (%)	Specificity (%)
Urine Markers and Urine Cytology	100	98
CT scan and MRI	100	100
MR cystoscopy, DCE, DW and T2W	98	94

It can be concluded that the methods for detecting bladder cancer can be performed with different modes of varying characteristics. Some methods produce high accuracy whereas some do not. But it can be observed that every method has its own advantages and disadvantages, which can be understood from the detection method benefits. Based on this review it can be seen that Urine cytology has low sensitivity but higher specificity.

From Table 20, it can be seen that Urine microscopy and MRI have sensitivity of 95% and 100%, and specificity of 96% and 99%, respectively. However, Urine cytology, Cystoscopy and Ultrasound have the same sensitivity but specificity of 99%, 97% and 99.8% respectively. It also shows the combined methods, where the most accurate sensitivity and specificity are found in Urine markers and Urine cytology. Other combined methods, such as, CT scan and MRI have 100% sensitivity and specificity, while MR cystoscopy, DCE, DW and T2W have 98% sensitivity and 94% specificity (Table 21). Bladder growth is a condition brought about by a combination of cancer-causing agents and might have a variable regular history. Although shallow bladder tumors occur more often than not, they have the tendency to develop. Each examination should be taken to guarantee proper diagnosis, arrangement, and evaluation. This article support the conclusions obtained from the study on disease transmission, Organizing and Evaluating, and Analysis Board of trustees of the Bladder Tumor.

Those systems may overcome the constraints of the present routines and be of worth in a few clinical situations since they are inadmissible for screening the whole bladder, while PDD and NBI do not provide a histopathological conclusion. Along these lines, a combination of strategies should be utilized as a part of the system without limitations. Future work should consider the test situations where the reception apparatus is placed adjoining to, or on the skin, with a definite objective of adding to a wearable bladder volume screen. There is an urgent need to improve the overall existing system by using advanced equipment for detecting bladder cancer. Such studies will promote more research and construct more precise plans to realize the basic preconditions of proper data collection so that it can produce a solid reliable-model of a detection system by applying different methods.

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Authors' contributions
Chao-Zhe Zhu wrote the manuscript. Hua-Nong Ting, Kwan-Hoong Ng and Teng-Aik Ong revised the manuscript.

Disclosure statement
No potential conflict of interest was reported by the authors.

Ethics and consent
This review is comprised of articles which included established ethical clearance procured for the research, or if that was not apparent, the informed consent process was described clearly within the article thus implying that the statement of ethical consent need not be published directly, merely accompanying the submission of the article to prove the ethical quality. Therefore, this review examined and included articles if it was clear that the studies were performed in an ethical manner.

Paper Context
Bladder cancer is the most common malignant tumor in urinary system, which is high incidence and recurrence rate. This article review complied the most recent common research and its advantages and disadvantages. The results of this review can positively help to identify the accurate method for detecting cancer and can be further improved for future research works.

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