



UNDERSTANDING CYSTOSCOPY AND TURBT

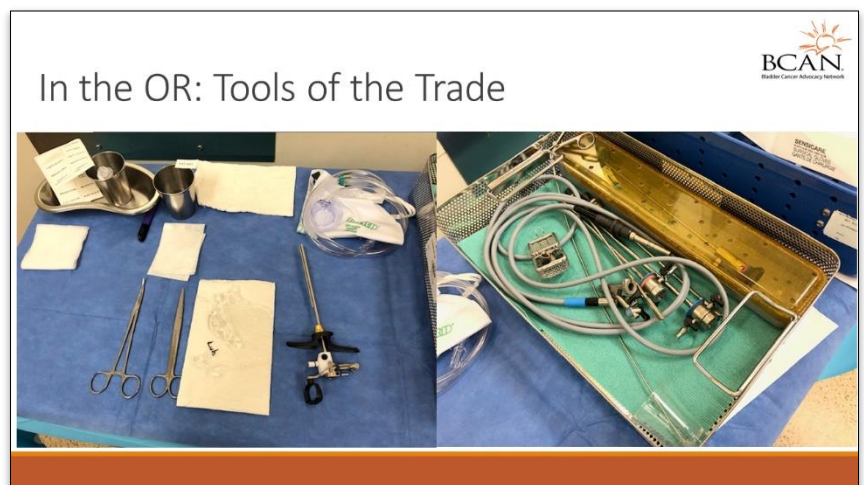
With Drs. Ken Nepple and Jeffrey Montgomery



Dr. Montgomery:

More specifics about the TURBT procedure.

These are the tools of the trade. Here is essentially the tray that we as surgeons use during the procedure. You can see, here's a light cord, here are various size sheaths of the resectoscope that go through the urethra and into the bladder. Here is a lens of the resectoscope, and this is the instrument that inserts through the working element of the resectoscope and allows us to see as we operate. This resectoscope, this is a trigger that essentially moves the loop which I'll show in subsequent slides of the resectoscope.



Dr. Montgomery:

The scope is hooked up to cautery, either what's called monopolar or bipolar cautery, and the electric energy that goes through the loop allows us to shave through the bladder tissue and remove those chips of tumor through the sheath. This instrument allows us to do a minimally invasive resection of the bladder tumor with the goals of not just getting diagnosis, but also making every effort to remove all visible of cancer cells. Another view of the resectoscope, this is the light cord.

We use a light generator in order to bring light through the scope, and then the white cord here, this is a bipolar resectoscope which is I would say most commonly used now in our field, but this cord provides the energy that will travel

through this loop and allow us to shave down the bladder tumor. This is an example of a bladder tumor on initial diagnosis before treatment.



This is the final product. This is normal bladder tissue along or around the area of resection. As you can see, this is a pretty large area of the bladder that has been removed. Importantly, this resection is into the muscle of the bladder.

We want the pathologist to have muscle in the specimen, so they can tell us if it's muscle invasive or not. Remember that important distinction, crucial distinction in bladder cancer management, is the tumor non-muscle invasive or muscle

invasive. This is an example of the chips or shavings of tissue that are removed through the scope that then are sent off to the pathologist to examine under the microscope to tell us what our diagnosis is. Next slide please. A thorough and complete and high-quality TURBT is the gateway to optimal bladder cancer management. This is the point at which all future decisions about bladder cancer care is made.

We need to not just make the diagnosis but remove as much if not all of the cancer cells as possible. An adequate TURBT shows complete resection of the tumor with assessment of the depth of invasion. An



incomplete or inadequate TURBT is a cause of early bladder cancer recurrence. One of our important time points in bladder cancer care is the 3-month cystoscopy. Three months after the initial TURBT looking back in the bladder to see if there's any remaining cancer, and you hear of people that have what's called an early recurrence. Well, if at that 3-month cystoscopy, there is bladder new bladder tumors.

Dr. Montgomery:

It's hard to know if this is truly a recurrence or if it's persistent disease. Meaning, that all of the bladder cancer was not removed at that initial resection. Ultimately, a complete TURBT is really critical for our management of bladder cancer and also in optimizing the use of intravesical therapy. Treatments in the bladder most commonly BCG which is an inactive form of tuberculosis that causes an immune response to the bladder to fight any remaining bladder cancer cells. If there is persistent bladder cancer or more importantly invasive bladder cancer left behind, BCG is likely to fail.

There are also newer enhanced cystoscopy methods, some of which I'll discuss and Dr. Nepple will as well, and newer resection techniques such as bipolar electrocautery that assist us in getting complete resections. Next slide please. This is a study by Dr. Anderson out of Columbia which we had the pleasure of participating on that essentially went through a checklist of what is necessary for a thorough and complete resection of bladder tumors, so things that we as surgeons should note with each resection. The number of tumors that are present, is it a single tumor or multiple, the size of the tumors

A crucial differentiation point in bladder cancer care is greater than or less than three centimeters. The multifocality, so is it a group of tumors that are in one spot or is it in multiple spots within the bladder? The characteristic of the tumor, is a flat or sessile? Is it firm and nodular, or is it a classic papillary tumor which looks like a shrub planted on the side of the bladder? The presence of carcinoma in situ, so carcinoma in situ is a non invasive bladder cancer, but is a high grade type of bladder cancer that is crucial to understand if that is present,

whether this tumor is recurrent. Meaning, we treated it, we thought it was gone, but it came back or is this the first tumor that the patient has experienced.

The clinical stage, so to the best of our ability understanding how large this tumor is, how deeply it invades, and the bimanual examination or the exam under anesthesia

where we palpate the abdominal wall is a crucial component. The adequacy of resection, so sometimes these tumors are located in a very challenging location or the patient's body characteristics make it just impossible to completely remove all the visible bladder cancer. That's crucial to understand, and then also any complications that resulted from the resection. The most commonly talked about complication

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A Complete and Thorough TURBT is Crucial for Optimal Bladder Cancer Outcomes

An adequate TURBT: complete resection of the tumor with adequate assessment of the depth of invasion	Incomplete TURBT: a significant cause of early bladder cancer recurrences; tumors are seen at first (3 month) surveillance cystoscopy in up to 45%	Complete TURBT is critical in management of NMIBC - accurate tumor type, staging, grading - and optimization of intravesical therapy	Enhanced cystoscopy methods and newer resection techniques, (bipolar electrocautery) may increase complete resection rates and reduce TURBT complications
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CHANG ET AL. | UROLOGY | 2016 OCT;196(4):1021-9

of a bladder tumor resection is perforation of the bladder or making an opening through the bladder wall.

Dr. Montgomery:

I get this question a lot. Why do I need to do this again? I have conversations with patients where I tell them, "Yes, we went in, we resected this tumor, but I've got to go in and do the same exact procedure in the same exact spot again." This is called a re-resection or a repeat resection, and the reason for this is that we need to better understand what's going on. I tell patients it's like a double check. A repeat resection is important for situations where we weren't able to do a complete resection, either the tumor was so big and bulky that we couldn't do it all in one procedure or was it a very challenging area that we just couldn't get to at that time.

If the tumor was non-invasive or TA but high-grade or more aggressive, but there was no muscle of the bladder within the specimen, and then also all T1 or really invasive bladder cancers require a repeat resection. This is to make sure that we are not under staging the cancer. For instance, for T1 tumors, up to 20% of repeat resection show that hey this was actually muscle invasive and that gets us into a totally different treatment algorithm. Then also as I mentioned previously for BCG to have a chance to work, all invasive components must be resected. If you have remaining T1 cancer to then give BCG, it's bound to fail, so very crucial to do a repeat resection in these situations.

Another common question is do I need the blue light. Blue light cystoscopy is a newer technique that we have at our disposal. What happens with blue light cystoscopy or blue light TURBT? A liquid is placed in the patient's bladder an hour before the procedure. This is something called Cysview, and what this does is it accumulates in cancer cells and causes the cells to light up this bright, pink color under blue lights. The classic cystoscopy or latter tumor resection is done under white light. There are filters in the scope that allows only blue light to pass out of it. In this situation, this is under white light.

This patient had Cysview placed in the bladder ahead of time. You turn on the blue light, and you can see this pink area. Again, this picture probably shows it best where this just looks like a heaped up mound of normal bladder tissue, but here under blue light, lo and behold, this lights up and is likely a

The operative steps necessary to achieve a successful TURB; identifying the factors necessary to assign disease risk

- number of tumors
- size (use the end of cutting loop as guidance; approximately 1 cm wide)
- multifocality
- Characteristics (sessile, nodular, papillary or flat)
- presence of CIS
- recurrent vs. primary tumor
- clinical stage (bimanual examination under anesthesia, assignment of clinical tumor stage)
- adequacy of the resection (visually complete resection, visualization of muscle at the resection base)
- presence of complications (assessment for perforation)

ANDERSON ET AL. J UROL. 2016; OCT; 196(4): 1024-20
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Do I need the Blue Light?

- Requires instillation of Cysview 1 hour prior to procedure
 - Causes accumulation of protoporphyrin IX in cancer cells
 - Especially helpful in identifying carcinoma in situ (CIS)
- Most studies show about a 25% reduced risk of recurrence
- Best suited for high-risk and intermediate-risk disease at 3 months then every 6 months for 2 years

Why doesn't everyone get this?

- No evidence yet that it improves survival – recurrence will eventually show up in cytology or on white light
- Requires special equipment (Karl Storz Photodynamic Diagnostic)
- Instillation 1 hour prior to procedure can be challenging to coordinate

Fig. 1: Detection of non-muscle-invasive bladder cancer with flexible white light and blue light cystoscopy with Cysview.

Blue light images depict the same area as white light cystoscopy but demonstrate pink lesions in areas of malignancy. Images are previously unpublished from the phase III multicentre trial involving Photocure®. BLC, blue light cystoscopy.

Lotan et al. Blue light cystoscopy with hexaminoleuconine in NMIBC. Nat Rev Urol. April 2019.

bladder cancer. What's the advantages of the blue light resection? Most studies show that it results in about a 25% reduced risk of recurrence. It's best suited for high risk or intermediate risk disease and can be also used in follow-up after the initial resection.

Dr. Montgomery:

It seems like a no-brainer that everyone needs to do blue light cystoscopy and blue light TURBT, so why doesn't everyone get this? Well, first off, there's not yet evidence that shows that blue light improves patient survival. The thought is that the recurrence that's caught early will eventually show up in urine cytology or looking under a microscope at the cells within the urine or eventually would show up on white light cystoscopy. What blue light is doing is it's catching those recurrences earlier on that eventually would show up as long as the patient continued on surveillance. Another barrier is that it requires special equipment.

Currently, it requires a special resectoscope and a special blue light generator in order to be able to deliver this care and finally, the installation of the Cysview one hour prior to the procedure can be challenging to coordinate. Those are some of the barriers to more widespread adoption of blue light cystoscopy. Next slide please. Another topic that comes up is the immediate post TURBT chemotherapy. What this is, is a fluid that is placed within the bladder, generally a type of chemotherapy that reduces the ability of floating tumor cells after the resection to implant in the bladder wall and cause new tumors.

It's generally done within 24 hours of resection. Most commonly right after the resection in the hospital and if the fluid is received from the pharmacy and then instilled via a catheter into the patient's bladder, and then the patient goes to the recovery and the fluid is removed approximately an hour later. This treatment is most effective in reducing the recurrence of low-grade and non-invasive bladder cancer. It's not optimal for invasive or very large bladder cancers.

Classically, a treatment called Mitomycin-C or an agent called Mitomycin-C was used for this, but Mitomycin-C is caustic and it can cause severe alterations to the bladder and very prolonged urinary dysfunction and frequency.

As an alternative now, many centers are using gemcitabine which is classically an intravenous chemotherapy for bladder cancer that is now placed in the bladder, and it is shown to decrease recurrence. It's very well-tolerated. It's a cheaper agent and is now the preferred agent for post TURBT chemotherapy according to the NCCN guidelines. Next slide please. A lot of patients ask what are my side effects, what's my healing going to be like after this procedure, and what I generally tell them is that they'll have frequent urination. They may have burning with urination. They may have the urgency to urinate, and these symptoms can last out to two weeks after the resection

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Immediate Post-TURBT Chemotherapy

- Reduces the ability of floating tumor cells to implant on the bladder wall
- Done within 24 hours of resection
- Agent instilled via a catheter, catheter is removed and patients holds fluid for at least 1 hour
- Most effective in low-grade, non-invasive bladder cancer
- Classically Mitomycin-C used, but this is caustic and can cause severe voiding dysfunction
- Single dose Gemcitabine decreased recurrence by up to 36%
 - Well-tolerated
 - Cheap
- Now the preferred agent according to NCCN guidelines

Messing et al. Effect of instillation of gemcitabine vs saline immediately following resection of suspected low-grade non-muscle-invasive bladder cancer on tumor recurrence. JAMA, 2018, 319:1880-88.

Dr. Montgomery:

Additionally, you can see occasional blood in the urine and especially around the 2-week mark, the scab or tissue healing over these resection sites can begin to fall off. Just like when you're a kid and you fell and you scabbed your knee, when that scab falls off, you can have some bleeding. You can see periodic bleeding and blood in your urine after the surgery. Now this is a very nice study that does a good job of better understanding what patients experience, so formalizing this understanding of symptoms after TURBT and the most common symptom as you can see something called pollakiuria, which is a very difficult way to just say daytime frequency.

Also, nocturia or nighttime urination is common, the urge to urinate and dysuria. As a result of the nocturia, obviously sleep disturbances are common, but importantly, there can be limitations on patient's daily activities if they feel like because of their symptoms they just can't even leave their home. It's any procedure we do, there's side effects to the patient. The vast majority of the time the side effects or symptoms after TURBT are mild and limited, but it's important to know going into it, that symptoms are expected afterwards. Next slide. How can you as the patient prepare for a TURBT? Again, I want to stress a high quality TURBT is the gateway to optimal outcome and optimal management of bladder cancer.

It's important to ask your surgeon. This is one of the most common procedures that urologists do, but some of us are more comfortable doing this. Some of us do it more frequently. Ask your surgeon how often they do this procedure and also, ask them what is their experience managing patients with bladder cancer. Is this something that they do frequently? Is this something that they have a higher understanding about what's crucial about doing this bladder tumor resection? A lot of times, patients are shy to ask or don't want to disrespect or seem like they're disrespecting their surgeon by asking these tough questions, but we as surgeons welcome these questions. We get these questions all the time, so please do not be shy about asking a surgeon's experience with the procedure.

Quality of life after TURBT

At a mean of 12 days after TURBT, almost half of the patients had symptoms that were of concern to the extent "quite a bit" or "very much".

The dominant symptoms were pollakiuria (i.e. daytime frequency) and nocturia which caused sleep disturbance, urge and dysuria with substantial impact on daily living.

All interviewed patients experienced severe voiding problems following the operation, lasting from several days to 8 months and with small to substantial impact on their daily activities.

Table 3. Frequency of symptoms.

Symptoms	"Quite a bit" or "very much"
Pollakiuria	74%
Nocturia	58%
Urge	56%
Dysuria	45%
Sleep disturbances because of voiding problems	36%
Difficulties in leaving their homes because of voiding problems	35%
Incontinence	9%
Fever	3%

Table 4. Frequency of worries.

Emotional concerns	"Quite a bit" or "very much"
Concerned about their health in the future	34%
Concerned about the results from the operation	36%
Concerned about treatments in the future	31%
Concerned about the repeated treatments	29%

MOGENSEN ET AL. SCAND J UROL 2016 JUN;50(3):170-4



How do you prepare for a TURBT?

- Ask questions of your surgeon:
 - How often do you do this procedure?
 - What is your experience managing patients with bladder cancer?
- Goldilocks Principle – Don't want the resection to be too deep or too shallow; want it to be *just* right
 - Too deep = perforation with a possible open incision to repair it
 - Too shallow = incomplete/insufficient resection of the cancer
 - Best scenario is a complete resection of the cancer cells for accurate staging and so that any intravesical therapy (if indicated) has its best chance to work




Dr. Montgomery:

Another thing about the procedure to take home is what I call the Goldilocks Principle. You don't want the resection to be too deep and perforate the bladder. You also don't want it to be too shallow. You want it to be just right. Too deep equals bladder perforation. Too shallow is an incomplete or insufficient resection of the cancer. The best scenario is a complete resection of all the cancer cells for accurate staging, so that any intravesical therapy if indicated has the best chance to work. Next slide please. Another important thing to do is to manage your expectations. We talked about some of the post-operative side-effects that patients experience, so you know that you'll have urinary frequency.

You may have some blood in the urine. You may have some burning with urination. It's important to understand what to expect after surgery. This procedure is often an outpatient procedure, but bring your toothbrush. That's what I tell patients all the time. Meaning, yes, I'm planning on this to be an outpatient procedure, but I can't guarantee it. There's a chance that I'll have to admit you to the hospital at least overnight for monitoring, and that would be the safest thing for you. Also, we know that patients prefer to go home without a catheter in the bladder, but sometimes it's for the best. There is a possibility that you do have to go home with a catheter that would then be removed in the future in the office.

Also, it's very important that you find ways to manage your stress and anxiety prior to the procedure. Finding things that work for you that help calm you is crucial for really any surgical procedure. Next slide. With that, thank you very much for your attention. I'll turn it over to Dr. Nepple.



How do you prepare for a TURBT?

- Manage your expectations:
 - Often an outpatient procedure but bring your toothbrush
 - We know patients prefer to go home without a Foley catheter but sometimes it's for your best
- Manage your stress and anxiety the best way you know how

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