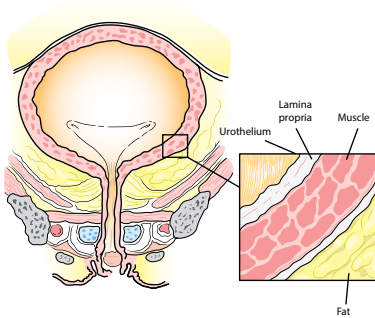


## Curing Patients with Invasive Bladder Cancer Without Surgical Removal of the Bladder

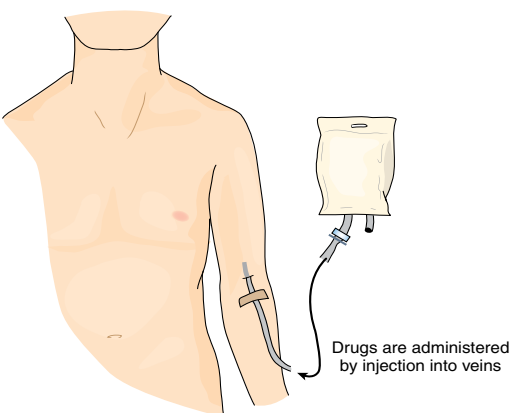
### Introduction

Nearly 70 percent of patients diagnosed with bladder cancer have disease at a very early stage affecting only the bladder lining and not yet invading the muscular layer of the bladder wall. These patients are almost always managed by transurethral resection of bladder tumor (TURBT) perhaps with the addition of immunotherapy or chemotherapy instilled in the bladder to treat its inner surface.



The remaining 30 percent of bladder cancer patients have, at diagnosis, a more deeply, muscle-invasive cancer that needs more aggressive treatment for cure. This treatment may be the surgical removal of the bladder (called radical cystectomy), including a pelvic lymph node dissection, and reconstruction of a urine collecting pouch. The long-term outcomes of cystectomy, and its complications, are well documented. Between 40 and 60 percent of patients managed with radical cystectomy are still alive five years later.

For all the sites in the body where cancer may arise our modern therapies are increasingly looking towards eradicating the cancer while at the same time preserving the affected organ and giving the patient the best possible functional outcome and thus quality of life. This is achieved by the combination of lesser surgery, with radiation, and chemotherapy, all in lower doses than if used alone. **Modern Combined-Modality Therapy (CMT)**



for bladder cancer follows just that pattern. It begins with an aggressive resection of the visible tumor then following it with Radiation Therapy (RT) given together with chemotherapy. The latter makes

the remaining tumor more sensitive to the radiation. When patients are well selected for this approach it can offer equal cure rates to treating with a cystectomy while still preserving a functioning bladder. This approach is favored for patients who are strongly motivated to maintain their bladder or in patients who have so many other medical problems that a radical cystectomy is simply not a safe option.

### Who is suitable for bladder preserving therapy by CMT and how are they to be followed?

Many factors play into the determining which patients with a muscle invading bladder cancer are suitable for CMT. Ideally these patients would have cancers with the usual urothelial histology (a small proportion have different appearance down the microscope). They would have clinical stage T2 to T3a disease, and the absence of hydronephrosis (the partial obstruction by the tumor of the ureter that transmits the urine from the kidney to the bladder). In addition, the best candidates are those with tumors small enough to have been visibly completely resected at TURBT. If a visibly complete resection is performed then the radiation and chemotherapy have only to mop up the remaining microscopic cells, a much easier prospect.

For patients who are candidates for bladder preservation, we recommend concurrent chemo-radiation follows the TURBT rather than just RT alone or chemotherapy alone. Chemotherapy that includes the drug cisplatin is preferred, although the combination of fluorouracil plus Mitomycin C is a good alternative, especially for patients whose kidneys do not work well enough for them to receive cisplatin chemotherapy.

Radiation is given daily, 5 days per week, for up to 7 weeks. The side effects are principally of inflammation to the bladder and adjacent bowel (frequent urination and bowel movements) and usually subside once the radiation is complete.



Following treatment patients must be followed closely with cystoscopy surveillance to detect any cancer recurrence or development of a new primary tumor in the bladder or elsewhere within the urogenital tract (ureters, bladder, urethra).

# Bladder Preservation with Combined Modality Therapy

A minority of patients will have cancers that do not respond completely or who develop an invasive recurrence after CMT. For them a “salvage” cystectomy is recommended and a significant number can be cured in this fashion.

## The subsequent quality of life of patients after treatment

The primary objective of a combined-modality therapy (CMT) is to cure while preserving the bladder. Bladder preservation only has merit, however, if the preserved bladder and other pelvic organs function at acceptable levels after treatment. Patients should expect some degree of temporary urinary irritative symptoms and bowel symptoms during treatment but this is to be distinguished from serious irreversible complications that the physicians now strive to avoid.



Overall, the available evidence supports the conclusion that the patients’ native bladders function well, and late pelvic toxicity remains acceptably low after CMT bladder-preservation therapy. A patient-reported quality of life and urodynamics study of long-term survivors of bladder-preserving CMT showed that 75 percent of patients had normally functioning bladders. Six percent of patients reported difficulty with urinary flow, 15 percent with urinary urgency, 19 percent with some incontinence, and 22 percent with bowel symptoms. Among men, 36 percent reported normal erections, and another 18 percent noted weaker erections that were still sufficient for intercourse.

Another study of 226 long-term survivors with muscle-invasive bladder cancer compared patient-reported quality of life in patients treated with CMT versus radical cystectomy. Patients who received CMT had significantly better general health-related quality of life than patients who had a radical cystectomy. CMT also had better bowel quality of life and equivalent urinary quality of life compared with radical cystectomy.

However, the patient’s baseline urinary function before treatment is an important consideration, since patients with very poor baseline urinary function may not have a “bladder worth sparing.”

## Consensus Guidelines



Multiple national and international medical agencies have now developed consensus guidelines and all recommend the use of combined-modality therapy (CMT) for many presentations of muscle-invasive bladder cancer. The approaches presented here are consistent with these guidelines. In addition,

BCAN is the largest community of bladder cancer survivors, and medical and research professionals and advocates that offers education and support to patients and providers and funding to advance research for bladder cancer.

## Shared decision making between patient and physician

Increasingly physicians are recognizing that the patients voice and set of values are as important, if not more important, than their own. Different individuals put a different value on the preservation of their bladder, their sexual function, or their life. Physicians thus now engage in shared decision making in which the options are placed before the patients openly and honestly, together with their risks and benefits. The patients then insert their own priorities to help them reach a determination of the best treatment. Supportive data for bladder preserving therapies has now accumulated, and the international medical societies endorse this approach in their guidelines. As a result bladder sparing can now truly be a part of the discussion for every patient presenting with a muscle invasive bladder cancer. For some, it will be favored either by them or their physicians, for some it will not, but for all, it should be discussed.



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William U. Shipley, M.D., FACR, is the Andres Soriano Professor of Radiation Oncology at the Harvard Medical School and the Head of Genito-Urinary Oncology in the Department of Radiation Oncology at the Massachusetts General Hospital. Dr. Shipley is a leader in clinical research in the area of genitourinary oncology evaluating multi-modality cancer care. He entered into a very special cooperation with his MGH colleagues in urology, in medical oncology, in radiation oncology and in pathology resulting in the implementation of seven successive national protocols for muscle-invading bladder cancer patients using a multi-modality approach which allowed over two thirds of those patients so-treated to escape without receiving radical bladder-removing surgery.