

Radiation

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Online patient's guide to bladder radiation, from the NHS:

Bladder Radiotherapy

March, 2005: Researchers in The Netherlands conclude, "...bladder preservation with brachytherapy is an excellent alternative to radical cystectomy and combined modality treatment. " PubMed Abstract

2007: Free online article from world experts: Radiotherapy for Bladder Cancer

Michael Milosevica, Mary Gospodarowicza, Anthony Zietmanb, Farhat Abbasc, Karin Haustermansd, Luc Moonene, Claus Rödelf, Mark Schoenbergg and William Shipley Urology Volume 69, Issue 1, Supplement 1, January 2007, Pages 80-92

{/niftybox}as first line treatment / bladder sparing protocol

For info on the radiation+chemotherapy for bladder sparing, see our page on "Combined Modalities"

Radiation uses high-energy x-rays to destroy cancer cells. External beam radiation is emitted from a machine outside the body. Internal radiation is emitted from radioactive "seeds" implanted into the tumor, also known as brachytherapy [see below]. Either type of radiation therapy may be used after surgery to destroy cancer cells that may remain. Radiation therapy is also used to relieve symptoms (called palliative treatment) of advanced bladder.

Side effects include inflammation of the rectum (proctitis), incontinence, skin irritation, hematuria, fibrosis (buildup of fibrous tissue), and impotence (erectile dysfunction). 1

There is some concern that radiation may cause long term complications in up to 20% of people who receive pelvic radiotherapy. Cystitis (a painful bladder condition causing inflammation, and occurring mainly in women) and contracted bladder (shrinkage) were the most common side effects, and the ureter and the gut are particularly vulnerable to radiation damage, whereas the bladder and gynecological internal organs are relatively radio insensitive. Tissue damage after pelvic radiation can also impede the creation of internal urinary reservoirs after cystectomy.¹ 5-year survival rates are generally much lower in radiation-treated patients than in those who undergo surgical therapy. Although local reappearance of bladder cancer occurs in up to one-half of all individuals who receive radiation therapy, people who experience complete tumor regression after radiation therapy tend to do well.

In spite of it's potential drawbacks, under certain circumstances radiation is preferable to other modalities and may be advised as first line treatment. For a good description of radiation treatments, see this UK site; <http://telescan.nki.nl/bladder2.html> under heading ‘Radiotherapy’.

External and/or interstitial radiation is more often used in Europe as a first line treatment than in the US, where primary radiation therapy usually is reserved for people who are not be good candidates for, or refuse surgery. US researchers have also concluded that it can be a very effective approach to controlling invasive TCC in some cases, as well as being technically simple with acceptable morbidity. 3

Preoperative radiation therapy is another strategy that has been used, the rationale being that radiation exposure will "sterilize" tumor outgrowths, regional lymph node metastases, and any tumor cells that are spread during the process of cystectomy. Radiation therapy also is used to shrink the tumor before surgery, though this sometimes causes a significant delay. Therefore, there is a tendency for American physicians to omit radiotherapy prior to cystectomy in patients with invasive bladder cancer. Exceptions to this include patients with invasive squamous cell carcinoma (SCC) or bilharzial bladder cancer. 1

Although the use of concurrent chemotherapy appears to contribute to better local control of invasive bladder cancer, it is uncertain whether it is actually improving long term survival. One German study which compared results of TUR+radiotherapy as definitive treatment vs. TUR+chemoradiotherapy after 10 years of follow up suggests that it does not. The authors state; "Chemotherapy increased the rate of complete remission, but had no impact on 5-year survival (52% vs. 50%). The most important single prognostic factor was the amount of residual tumor after TUR."4

In a 1999 review from the UK, Bell and colleagues assessed the current efficacy and safety of definitive external beam radiotherapy (EBRT) in the treatment of invasive bladder TCC in a district general hospital with cancer-centre status. The case notes of all patients with bladder TCC undergoing EBRT with curative intent over an 8-year period (1988-95) were reviewed, 120 patients in all. Sixty-seven patients (59%) developed a local recurrence and in 36 (30%) this was invasive. The overall median survival was 60 months. Thirty- three patients underwent salvage cystectomy with a subsequent median survival of 12.5 months. The authors concluded that modern radical multifraction EBRT in invasive bladder TCC has a low morbidity, with an overall median survival of 5 years.5

Brachytherapy

In a review of a combined approach consisting of a transurethral resection, a course of external irradiation to the bladder and an Iridium-192 implant procedure, a Dutch study led by Moonen investigated the efficacy and safety of conservative treatment for T1G3 and T2-T3a bladder carcinoma on 63 patients with tumors less than 5 cm in size. After a mean follow-up of 4.2 years (range 3 months to 7.2 years) 42 patients were alive without tumour. The 5 year actuarial survival was 66%. The authors concluded that bladder conservation using Iridium-192 implantation is an effective and safe procedure and in selected group of patients with bladder cancer and is a good alternative to radical cystectomy.6

In another Dutch study which evaluated the use the bladder sparing protocol mentioned above (TUR followed by external beam radiotherapy (EBRT), and interstitial radiation (IRT) with iridium-192), on 66 patients with primary, solitary muscle invasive bladder cancer, Wijnmaalen and associates looked at the results after six years (median follow up of 26 months); The probability of remaining bladder relapse free at 5 years was 88%. The bladder was preserved in 98% of the surviving patients. Metastases developed in 16 patients, and the probability of remaining metastasis free at 5 years was 66%. The cumulative 5-year overall and bladder and distant relapse free survival were 48% and 69%, respectively. Acute toxicity was not serious in the majority of cases; CONCLUSIONS: Interstitial radiation preceded by TUR and EBRT, in a selected group of patients with muscle invasive bladder cancer, yields an excellent bladder tumor control rate with a high probability of bladder preservation. Survival was mainly dependent on the development of distant metastases. Serious acute and late toxicity was rare.7

Updates: 2005

"Organ preservation in invasive bladder cancer: brachytherapy, an alternative to cystectomy and combined modality treatment?"

Dutch researchers recently published long-term results of bladder preservation with brachytherapy in the treatment of bladder cancer:

METHODS AND MATERIALS: Between 1987 and 2000, 108 patients with T1-G3 and T2-T3a stages of bladder cancer were treated with a transurethral resection (TUR) and a course of external beam radiotherapy (30 Gy in 15 fractions) followed by brachytherapy (40 Gy). All tumors were solitary lesions with a diameter \leq 5 cm. Median follow-up was 54 months (range, 1-178 months).

RESULTS: The 5-year and 10-year overall survival rates were 62% and 50%, respectively. The 5-year and 10-year disease-specific survival rates were 73% and 67%, respectively. The actuarial local control rate was 73% at 5 and 73% at 10 years, respectively. The 5-year and 10-year disease-specific survival rates for patients with a preserved bladder were 68% and 59%, respectively. Of all long-term surviving patients, 90% preserved their native bladders. The treatment was well tolerated. Acute toxicity was mild. Two patients experienced serious late toxicity: 1 patient developed a persisting vesicocutaneous fistula and the other a stricture of the urethra and ureters.

CONCLUSION: For patients with solitary, organ confined invasive bladder cancer \leq 5 cm, bladder preservation with brachytherapy is an excellent alternative to radical cystectomy and combined modality treatment.

Int J Radiat Oncol Biol Phys. 2005 Mar 1;61(3):678-86. Organ preservation in invasive bladder cancer: brachytherapy, an alternative to cystectomy and combined modality treatment?

Pos F, Horenblas S, Dom P, Moonen L, Bartelink H.

Department of Radiotherapy, The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands. PMID: 15708245

Update: 2002

" Saving bladders with brachytherapy: implantation technique and results."

PURPOSE: To analyze and report the treatment results of brachytherapy for solitary bladder cancer in the Arnhem Radiotherapy Institute.

METHODS AND MATERIALS: Between January 1983 and October 1998, 63 patients with a solitary bladder tumor were treated with a combination of transurethral resection, external beam radiotherapy (EBRT), and interstitial radiotherapy. The indications for bladder-conserving treatment were tumor \leq 5 cm, T1G3 (n = 14), T2G2 (n = 8), T2G3 (n = 37),

and T3a (n = 4). The prescribed implant dose was either 55 Gy (range 50-65 Gy) in combination with small pelvis external beam RT, 3-4 fractions of 3.5 Gy (n = 58), or 30 Gy in combination with 20 fractions of 2 Gy external beam radiotherapy (n = 5). Brachytherapy was performed with 2-8 ¹³⁷Cs needles until 1995 (n = 48) and 2-5 afterloading catheters (¹⁹²Ir) since 1996 (n = 15). Follow-up cystoscopies were performed at 3-month intervals during the first 2 years, then every 6 months for 3 years, and annually after the fifth year. The median follow-up was 4.9 years.

RESULTS: Twenty patients developed local recurrences, of which 6 were "true in-implant recurrences," 12 were in second bladder locations, and 2 were urethral recurrences. All recurrences developed within 2.5 years after treatment. Of these 20 patients, 13 underwent cystectomy: 6 stayed disease-free, 1 died of postoperative complications, 2 developed regional metastases, and 4 developed distant metastases. The 5-year disease-specific survival rate was 80% for patients with Stage T1 and 60% for those with Stage T2 disease. The local control rate was 70% in the whole patient population and 80% after salvage cystectomy. Forty-four bladders were saved. Acute complications were seen in 14 patients, and no significant late complications occurred.

CONCLUSION: Using this treatment technique, a high cure rate with conservation of the bladder and only minor toxicity can be obtained in a selected patient population having a solitary tumor < or =5 cm.

Van der Steen-Banasik EM, Visser AG, Reinders JG, Heijbroek RP, Idema JG, Janssen TG, Leer JW. Joint Center for Radiation Oncology, Arnhem-Nijmegen, Radian-Arti, Wagnerlaan 47, 6815 AD Arnhem, The Netherlands. *Int J Radiat Oncol Biol Phys.* 2002 Jul 1;53(3):622-9.PMID: 12062605

Biomarkers

In a 1998 study from Spain, the authors assessed whether the antibody Ki67 had any predictive value as a biomarker for local control in bladder cancer patients treated by radiotherapy. Fifty-five patients with invasive bladder carcinoma recommended for radical radiotherapy were included in this study. Paraffin-embedded biopsy specimens were stained with the Ki67 antibody and the percentage of Ki67-positive nuclei was correlated with established prognostic factors, local control and survival. Patients with tumours with a very low Ki67 index had better local control at 5 years (69%) than patients with tumours with greater Ki67 expression indices (31.5%). The authors concluded that Ki67 immunostaining was a feasible method to estimate tumour proliferation and that patients with very low proliferating tumours seemed to achieve better local control after fractionated radiotherapy compared to other patients, but that further studies are needed with a greater number of patients to accurately define the role of Ki67 expression in predicting response to fractionated radiotherapy. 8

In another Spanish study from 1999, Drs. Lara and Perez state; The search for biological parameters that could select patients who will respond to radiation treatment has become essential. The aim of this study is to assess whether the pretreatment apoptotic index is useful in predicting local control and survival in a group of bladder cancer patients treated by radiotherapy." 55 patients treated between 1983 and 1996 were included; after comparing the relationship of clinicopathological tumor characteristics to the apoptotic index, they found that patients with tumors showing low pretreatment apoptotic indexes had better local control (p < 0.037) and survival (p < 0.01) than highly apoptotic tumors. The five year actuarial local control for the whole group was 45%. Tumor stage (T2 vs. T3-4) and the pretreatment apoptotic index were significant predictive factors for local control and survival in multivariate analysis. Assessment of biological tumor characteristics could allow the selection of patients for different treatment strategies.9

MD Anderson researchers conducted a study in 1996 which looked at the relationship between pretreatment apoptosis levels and clinical-to-pathologic downstaging resulting from preoperative radiotherapy in 158 patients. When the analysis of the distribution of patients by radiation response and AI was segregated by stage, a significant correlation was observed only for those with Stage T3b disease; 93% of T3b patients with an AI > 3 were downstaged. A trend was seen for improved survival when AI was > 3 (71% vs. 41%, p = 0.09) for Stage T3b patients. "Further investigation of

pretreatment apoptosis levels as a marker of anticancer response is needed, especially for patients treated with chemotherapy and radiotherapy with the goal of bladder preservation." 10

A Finnish retrospective analysis of 203 patients which looked at outcome, survival and prognostic factors showed that initial response to radiotherapy was obtained in 26.7% of the patients, and the actuarial 5-year survival was 24% for patients treated with definitive radiotherapy only. The most important factors associated with survival in this radiotherapy group were stage (T- class), performance status and serum creatinine. Acute side-effects were common and in 18% of the patients deviation from the planned treatment was necessary.¹¹

A 1999 Norwegian retrospective study which included 135 patients who had undergone either cystectomy or radiation therapy compared results; after cystectomy 10-year overall survival rates for superficial and muscle-infiltrating tumours were 67 and 26%; after radiotherapy, the corresponding survival rates for superficial and muscle-infiltrating tumours were 26 and 5%, respectively.¹²

A Canadian study reviewed the results of 121 people treated with radiation between 1981 and 1985, which suggested that factors other than stage and grade influence prognosis in invasive bladder cancer and should be considered in interpreting treatment results. The rate free of local relapse was significantly influenced by stage and presence of coexistent carcinoma in situ. Over-all actuarial survival of the patient population (median age 70 years) was 31.6% at 5 years and cause-specific survival was 44.8%. At analysis 33 of 121 patients (27.3%) were alive with preserved bladder function.¹³

Additional info:<http://www.cancerbacup.org.uk/info/radiotherapy.htm> About internal RT

<http://www.cancerbacup.org.uk/info/bladder.htm> External RT
http://oncolink.upenn.edu/specialty/rad_onc/general/xrt_intro.html

New Advance In Radiation Therapy May Improve Bladder Cancer Treatment

A significant advance in radiation therapy known as intensity modulated radiotherapy (IMRT), is a new technique which enables physicians to deliver greater amounts of radiation to the precise location of a tumor while minimizing the dose to the healthy tissue that surrounds it.

[back to invasive bladder cancer](#)

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