

preservation of sexual potency. Previous trials have not demonstrated inferior survival in patients with T3 bladder cancer managed by radical radiotherapy reserving salvage cystectomy for those who recur. However, these trials have not been large. We have recently re-analysed the Institute of Urology trial which registered 189 patients between 1965 and 1976 to determine long-term results. The 5 year survival in 91 patients randomised to radical radiotherapy was 27.9% (19.1–37.8%). Whereas for 98 patients randomised to radiotherapy + cystectomy, the 5 year survival was 39.8% (30.3–49.8%). Since this trial, there have been advances in both radiotherapy and surgery. Conformal radiotherapy offers the potential for reducing radiation side-effects. Additionally, we have completed a study of accelerated fractionation treated to doses between 57.6 and 64 Gy in 32 fractions over 26 days. Eighty five patients were treated in this study and of 70 who had check cystoscopy at 3–6 months, a pathological complete response was seen in 80% with 2 further patients demonstrating carcinoma *in situ* only. We conclude that a trial is required based on modern staging and treatment techniques to compare radiotherapy and cystectomy for localised muscle invasive bladder cancer.

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#### BLADDER CONSERVATION USING COMBINED EXTERNAL IRRADIATION AND IRIIDIUM 192 IMPLANTATION

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For selected bladder carcinomas we consider iridium 192 implantation as the treatment of choice. Selection criteria that we use are:

1. Stages T1G3, T2 and T3a.
2. Solitary tumours.
3. Diameter not exceeding 5 cm.
4. No previous tumour elsewhere in the bladder.

From 1987 to 1994 63 patients have been treated. Results can be summarized as follows:

- Incidence of bladder recurrence at 5 years is 36%.
- About one half of the bladder relapses consist of secondary tumours.
- Isolated bladder relapses can be salvaged in the majority of the patients, many times with conservation of the bladder.
- Incidence of distant metastases at 5 years is 33%.
- In about one half of the cases distant metastases are combined with a bladder recurrence.
- Distant metastases are the major cause of death.
- Acute toxicity is limited and mainly related to the surgical procedure.
- Late toxicity is very limited.

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#### NEOADJUVANT CHEMOTHERAPY AND ITS ROLE IN BLADDER CONSERVATION

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Radiation therapy (RT) has been employed in the treatment of bladder cancer since the early 1900's, but its role in the curative management of bladder cancer is still controversial. Effects of RT are limited by cellular RT resistance, tolerance of normal tissues and the risk of systemic dissemination. Chemotherapy is active systemically, but few agents or combinations equal the antitumour activity of RT. The study of combined chemotherapy and RT is confounded by factors such as: specific tumour type, type of normal tissue involved, drugs selected, drug dosage and scheduling, RT dose, RT fractionation and overall treatment time and sequence of administration of each modality. Strategies for combining the two modalities include the use of drugs and RT concurrently, neoadjuvant chemotherapy or adjuvant chemotherapy. The first two approaches have been investigated in bladder cancer as CT delivered prior to or with RT also has the potential to improve local control beyond that achieved with RT alone. Current experience using concurrent and neoadjuvant chemotherapy in invasive bladder cancer will be reviewed with emphasis on the bladder conservation aspect of such management.

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#### CHEMOTHERAPY AND RADIATION THERAPY WITH SELECTIVE ORGAN-SPARING TREATMENT OF INVASIVE BLADDER CANCER

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Several recent (1–4) reports supply new overall survival data for transurethral surgery and chemoradiotherapy as good as any reported cystectomy series which supports its safe and selective use for clinical stage T2–T3a patients. One likely important key to the improved success is the early identification of incomplete responders to chemoradiotherapy by prompt re-cystoscopy. This allows for prompt cystectomy before local regrowth (and a second chance for metastases) occurs.

Series	Pts	5 yr Overall Survival	5 yr Survival with Bladder Preservation
Mass Gen Hosp (4)	53	48%	38%
U of Erlangen (1)	197	45%	36%
RTOG (4 yr data, 3)	42	54%	45%

This multimodality and selective (by initial response) approach may, for stage T2–T3a patients, now become a standard treatment option in the US. Patients with tumor-associated hydronephrosis are not good candidates for bladder sparing.

1. Dunst J, Sauer R *et al.* *Int J Radiat Oncol* 1994,30,261. 2. Housset M, Maulard C *et al.* *J Clin Oncol* 1993,11,2150. 3. Tester W, Porter A *et al.* *Int J Radiat Oncol* 1993,25,783. 4. Kaufman DS, Shipley WU *et al.* *N Engl J Med* 1993,329,1377.

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#### RESECTION OF UNRESECTABLE HEPATIC METASTASES FROM COLORECTAL CANCER WITH NEOADJUVANT CHRONOTHERAPY

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In this study, we report a 6-year experience of the management of patients (pts) with hepatic metastases initially considered as unresectable and subsequently submitted to a resection following an efficient chemotherapy. From Apr. 1988 to Dec. 1994, 53 out of 330 pts (16%) with liver metastases initially considered unresectable underwent hepatic resection with a curative intent. All pts have been treated by intravenous chronomodulated chemotherapy combining 5 Fluorouracil, Folinic acid and Oxaliplatin using an ambulatory programmable-in-time pump. Initial unresectability assessed by the same surgical team was related to large (n = 10), multinodular (n = 22), centrally located tumors (n = 8) or to the presence of extrahepatic disease (n = 13) with peritoneum (n = 6), epiploon (n = 3), lungs (n = 4). Pts received 3 to 29 courses of chemotherapy (mean = 9) for 2 to 21 months (mean = 7).

**Results:** An objective reduction of tumour size was observed following chemotherapy in all pts subsequently submitted to liver resection. A significant reduction of tumor markers was also demonstrated for CEA and CA 19-9. Mean follow up is currently 24 months for the whole group (range 4–68). Patient survival rate is 55% at 3 years similar to that of pts submitted to liver resection as a first treatment. Survival rate is higher in those 40 pts with technically unresectable lesions (large or multinodular or centrally-located) than in those 13 with extrahepatic disease, 58% vs 39% respectively.

**Conclusion:** A second-step resection may be achieved in some unresectable pts with the help of an efficient chemotherapy. The benefit in survival seems comparable to that obtained with liver resection as a first intent. This therapeutic strategy involves a multimodality approach including repeat hepatectomy and extrahepatic surgery.

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#### NOVEL METHOD FOR DETECTING LIVER METASTASES

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All patients undergoing curative surgery for colorectal cancer should have an accurate staging of their liver prior to treatment. However, conventional radiological methods which rely on the differences of density of neoplastic tissue and normal liver have limits in their resolution rarely detecting lesions less than 1 cm in diameter. An alternative approach is