

49

## ORGAN PRESERVATION OF BLADDER CANCER

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One method of treating localised muscle invasive transitional carcinoma of the bladder is by radical cystectomy however, the alternative organ conserving approach is based on radical radiotherapy. Trials suggest that patient survival is equivalent with these two approaches and reported results for radical radiotherapy would indicate a 40%-50% 5 year survival for T2 tumours and a 20%-30% 5 year survival for T3 tumours. The use of radical radiotherapy requires continued monitoring of the bladder both to detect local recurrence and to detect the development of new urothelial tumours. These are then usually treated by salvage cystectomy.

The first trial of the Cooperative Urological Cancer Group compared radical radiotherapy at a dose of 60Gy and 30Gy over 6 weeks with pre-operative radiotherapy + cystectomy. Overall survival of these two treatments was not significantly different however, in patients under 60 years, surgery was more effective. Amongst those patients treated with cystectomy, the best prognostic group had histological evidence of "down-staging" by the pre-operative radiotherapy.

This led to the second CUCG trial to attempt down-staging using neoadjuvant single agent methotrexate. Three moderately high dose injections were given at weekly intervals prior to radical local therapy and then 9 monthly injections of methotrexate were given following the local treatment. Local therapy could either be radical radiotherapy or pre-operative radiotherapy and cystectomy. Analysis of disease-free survival and local disease-free survival did not demonstrate any significant difference between the two treatments.

There remains a significant problem of local control when organ preserving techniques are used and this may be addressed by increasing the aggressiveness of therapy. Approaches which have been studied include concomitant cisplatin chemotherapy as a radiation sensitizer, accelerated fractionation of radiotherapy, since transitional carcinoma of the bladder when poorly differentiated is one of the most rapidly proliferative of human tumours. We have pursued a pilot study for accelerated fractionation in approximately 80 patients for various stages of bladder cancer. This shows greatly improved short term disease free survival however, the final evaluation of this protocol requires further follow up.

51

## ORGAN PRESERVATION IN RECTAL CANCER

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The standard surgical treatment for patients with invasive, resectable, distal rectal cancer who are unable to undergo a low anterior resection is an abdominoperineal resection. Given the morbidity of an abdominoperineal resection and the need for adjuvant therapy for many rectal cancers, the concept of using radiation in conjunction with sphincter preserving surgery is reasonable. The sphincter preserving approach for this group of patients depends on the clinical stage of the tumor. In the setting of a clinical T3 and/or node positive tumor, the preferred approach is pre-operative radiation therapy + 5-FU based chemotherapy followed by a low anterior resection/coloanal anastomosis. For patients with clinical T1-2 tumors who are technically able to undergo a local excision, a full thickness local excision and pre- or post-operative radiation therapy ± 5-FU chemotherapy is recommended.

53

## LIMB PRESERVATION IN SOFT TISSUE SARCOMA (STS)

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Between 1974 and 1990, 369 pts. with STS were treated in the Dpt. of Radiooncology. 267 of those received neutrons or palliative irradiation leaving 102 pts. (median age: 51 yrs.) for a curative photon treatment. 55% of the tumours were located at the extremities and 90% had a stage II-IV. The median total target absorbed dose (TAD) was 59Gy with weekly doses of 5x2Gy or 4x2.5Gy. The second and first order treatment volumes received 40-50Gy and 45-72Gy, respectively. Only one third of all tumours had adequate surgery. Local failures occurred in 18%. They increased from 10% (IA/B) to 33% (IVA) and were strongly correlated with primary or recurrent tumours, total TAD, tumour site, mode of surgery and chemotherapy ( $p < 0.05$ , multi- and univariate analyses). The stage (grading and tumour size) had no prognostic impact on local tumour control. The rate of distant metastasis depended exclusively on the grading and tumour extension ( $p < 0.05$ ) and increased with tumour size from 5.4% to 33.3% (5cm to >15cm). For overall survival the occurrence of local failures and distant metastases, tumour size (multi- and univariate), total TAD and grading (univariate) were prognostic parameters. The grade-III late radiation damage (WHO) was 22% in the period of 1974-1982 and only 10.5% from 1983-1990. The local relapse-free survival (5 yrs.) for stages respectively grades I-III were 85.7%, 85.1%, 75.9% and 87.5%, 85.1% and 73.7%. Recurrent tumours had a worse prognosis even though the median tumour size was significantly smaller (4.5cm vs. 8cm). The 5yr. local control rates after inadequate resection was about 70% compared with 94.4% after wide excision. The overall survival rates at 10 yrs. were 100%, 85.6% and 49.7% for grade I, II and III/IV tumours. Perioperative radiotherapy in STS allows functional integrity and limb salvation in STS without compromising local control.

50

## PRIMARY CHEMOTHERAPY FOR RESECTABLE BREAST CANCER.

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In 227 women with breast cancer who were candidates for mastectomy because the largest diameter of the tumor was 3 cm or more, primary chemotherapy was administered in the attempt to substitute conservative surgery for mutilating surgery. Tumor reduction was then systematically quantitated by clinical, radiologic and histopathologic evaluations. In response to primary chemotherapy, 78% of patients showed either complete or partial response; 15% achieved only minor response, while progressive disease was documented in 7 patients (3%). Tumor shrinkage to less than 3 cm was documented in 83% of the 220 women subjected to surgery (87% with initial tumors measuring up to 5 cm and 62% with initial tumors measuring > 5 cm). Histopathologic complete remission was documented in 8 patients. Conservative surgery became feasible in 91% of patients. Tumor response was unrelated to age, menopausal status, drug regimen used, or number of treatment cycles, but the frequency of response was greater in receptor-negative tumors. Present results challenge the classical indication for primary mastectomy by showing that use of full-dose primary chemotherapy, sequentially combined with conservative surgery and radiation, can offer an effective and safe alternative to women concerned about the preservation of body integrity.

52

## LARYNX PRESERVATION

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Undoubtedly, chemotherapy (CT) has tremendously changed the therapeutic approach of Head and Neck SCC over the past decade. If some disappointment has succeeded to the initial enthusiasm, it remains undisputable that the organ preservation, in particular for the larynx, is a real advance thanks to CT. It is clear, from the literature, that the policy of the use of induction CT with the goal of larynx preservation does not compromise the survival rates, whatever the larynx could have been spared or not. In contrast, it is more difficult to assess the actual preservation rates since some studies mix tumors suitable for partial and for total laryngectomy and in some others the subsequent treatment is modified in the case of objective response to CT or only in the case of complete response. It seems reasonable to assert that one third of total laryngectomies could be avoided. In addition, some studies suggest that if the loco-regional control is slightly lower with CT, in contrast the incidence of distant metastases could be higher without CT. These results are, obviously, encouraging but this CT strategy should not lead to forget the place of conservative surgery nor the results of definitive radiotherapy alone.

54

## THE IMPORTANCE OF REPORTING COMPLICATIONS IN SELECTING TREATMENT STRATEGY.

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Careful registration of morbidity after cancer therapy provides the basis for choosing among equally effective treatments and for a thorough patient information. There is yet no internationally accepted system for reporting complications. The recording of each event used in the definition of each specific complication grade would allow a rescoring of grades. Thereby a comparison of late morbidity in studies applying different systems would be possible. Treatment results and radiotherapeutic morbidity in 442 consecutive patients with locally advanced cervical cancer treated according to two different strategies (continuous vs split course radiotherapy) will be presented. The results from this study elucidate some important items in the recording and reporting of late morbidity. Actuarial estimates of late morbidity continue to increase the first three years after treatment. Cumulated frequencies are up to 25% lower than actuarial estimates and almost unchanged after one year. The recording of the maximal damage implies loss of information about early morbidity and less troublesome complications, which may influence the patients' quality of life. The long latency of late morbidity necessitates the reporting of actuarial estimates and especially so in cancer patients with a poor prognosis.