

statistical differences were observed concerning interest in sex ($p = 0.016$) and sexual activity ($p < 0.001$), urinary incontinence ($p < 0.001$) and cystitis ($p = 0.01$). No major digestive complications were observed among patients. When morbidity was reported by patients, physicians generally underestimated it (from 69% for incontinence to 96% for pelvic pain).

Conclusion: The study demonstrates that survivors from LPC treated with an association of EBI and brachytherapy have good global health status. Major problems that persist are sexual disorders, urinary incontinence and cystitis without severe digestive complications. The association of EBI and brachytherapy could be considered an alternative to exclusive EBI. The exact benefit that can be expected from this technique should be explored in randomized trials.

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POSTER

Fibronectin is a prognostic factor in malignancy: An ultrastructural and immunofluorescence study of carcinoma of the bladder

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Purpose: Fibronectin (FN) is a major adhesive glycoprotein of extracellular matrix that is implicated in neoplasia. FN expression in benign and malignant lesions of the bladder were studied, as a trial to assess the value of FN staining in relation to grading and staging of bladder tumours, for the prediction of their biological behavior.

Material and Methods: 60 cases of carcinoma of the bladder, 23 cases of benign inflammatory lesions and 7 normal control specimens were subjected to indirect immunofluorescence staining using antifibronectin monoclonal antibody and were also studied ultrastructurally in addition to routine histopathology.

Results: The FN distribution pattern found in squamous and transitional cell tumours, was eminently different from that observed in benign lesions. Immunofluorescence staining for FN revealed a prominent intracellular reaction in grade I tumours both squamous (Sq.C.C.) and transitional cell carcinoma (Tr.C.C.). This could be attributed to the early damage of Golgi complex noticed ultrastructurally. This intracellular FN accumulation in grade I tumours decreased significantly with the increase of tumour grade ($p < 0.05$). This could be explained by the marked decrease in amount of rough endoplasmic reticulum revealed by electron microscopic examination in grade II & III tumours. The diffuse stromal FN decreased significantly with the increase of tumour grade ($p < 0.05$) in cases of Tr.C.C. Whereas in Sq.C.C. the pericellular stromal FN increased significantly with increase of tumour grade ($p < 0.05$).

Conclusion: We suggest that FN expression in the stroma of Sq.C.C. and Tr.C.C. cell carcinoma may have clinical prognostic implications regarding their invasive behavior and their radio and chemotherapeutic resistance.

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Strong correlation of basement membrane degradation with up-regulation of metalloproteinases by functional p53 loss

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Purposes: We investigated the relationships between the degradation of basement membrane underlying superficial urothelial carcinomas and functional p53 loss.

Methods: Nuclear accumulations of p53 and mdm2, and up-regulation of metalloproteinases (MMPs) were examined immunohistochemically for 60 transitional cell carcinomas and 13 concomitant CIS lesions. Degradation of the basement membrane was defined as the reduction or total loss of type IV collagen expression.

Results: The frequency of the degradation of basement membrane underlying grade 1 pTa tumors was 0%, grade 2-3 pTa tumors 57.1%, and primary CIS lesions 83.3%. Nuclear over-accumulation of p53 was found in 48.3% and of mdm2 in 23.3% of the primary tumors. In pTa-pT1 carcinomas, nuclear staining of p53, mdm2, or both was highly correlated with degradation of the basement membrane ($p = 0.00002$). In the CIS lesions, the association of p53 nuclear staining with the destruction of type IV collagen expression was of borderline significance ($p = 0.03$). When mdm2 overexpression was considered as a molecular abnormality together with p53 inactivation, the correlation with the degradation of the basement membrane was highly significant ($p = 0.00006$). Moreover, the functional p53

loss was strongly associated with the up-regulation of MMPs ($p = 0.0005$). This finding was well correlated with the strong association of basement membrane degradation with up-regulation of MMPs ($p = 0.000004$).

Conclusion: Degradation of basement membranes was significantly related to functional p53 loss.

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POSTER

Role of radical radiotherapy (RRT) in the treatment of inoperable invasive bladder cancer in the elderly

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Introduction: currently the standard therapy for muscle invasive bladder cancer is cystectomy, but in elderly unfit pts. alternative therapies are required. In the bladder cancer treated with RRT we achieve an overall survival between 0-59% at 5 years in relation to stage disease. Numerous prognostic factors have been shown to affect treatment results: T-N status; grading; papillary vs solid tumor; presents of ureteral obstruction; pretreatment hemoglobin level; TURB radicality; total dose. We have reviewed the records of 24 pts with age > 65 yrs., unfit for surgical approach because of coexistent illness. Overall survival was the only endpoint.

Patients and Methods: from 5/90 to 12/94, 24 pts. (19 M, 5 F), median age 71 yrs. (range 65-83) with bladder cancer stage 2-4 (MO) were treated with RRT using an isocenter box technique with shrinking field at 46 Gy. Minimal dose at T was 50 Gy (range 50-54).

Results: the overall actuarial survival of 24 pts: was 9.5% at 5 yrs., with a cause specific survival of 17.2%. Complete response was achieved in 15 pts. (62.5%). At our multivariate analysis there were no apparent differences in the outcome of pts. treated with total dose < 60 Gy. Only hemoglobin level > 12 gr% vs < 12 gr% ($p = 0.02$) and complete response vs. partial response ($p = 0.0004$) had statistical significance. Our data show high initial response rate with a very poor overall actuarial survival at 5 yrs. Therefore, on this set of pts., we believe that before planning RRT it is necessary evaluate carefully the prognostic factors in order to personalize the management.

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POSTER

Loss of E-cadherin expression has a prognostic value for bladder carcinoma patients

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Loss of E-cadherin-mediated cell-cell adhesion (E-CD) is associated with the progression of many carcinomas. Indeed, the invasion of the surrounding tissues and metastatic spread require the detachment from the primary lesion which is favoured by reduction of E-CD expression.

In the present study we have studied the expression of E-CD in human bladder cancer by immunohistochemistry. Tissue samples ($n = 46$) from superficial ($n = 23$) and invasive ($n = 19$) tumors and corresponding normal urothelium were obtained from surgical resections. E-CD expression was evaluated at the invasive front and found reduced or absent in 66% of the tumor samples tested compared to normal urothelium. Reduced expression was also significantly correlated with tumor grade ($p < 0.01$) and stage ($p < 0.01$). Immunostaining was divided into three tiles (positive, positive focally and negative) and when comparing them significant differences in overall survival were found ($p < 0.01$; log rank test). Proportional hazard regression analysis (Cox's multiple variant regression analysis) showed that loss of E-CD has an independent predictive value. In conclusion, we show that E-CD expression has a prognostic value for patients with bladder cancer and its effect on prognosis will be discussed in comparison to other known factors such as the presence of p53 mutations. The expression of a- and b-catenin which couple E-CD molecules to the cytoskeleton is currently under investigation.