Methods: From 1987 to 1995,415 patients from 26 centers were randomized.377 patients were assessable for long term toxicity. Median age was 70 years. At the time of this analysis, median follow-up is 42(3-136) months. Toxicity was evaluated according to extensive review based on follow-up information and additional details of the severity and evolution of the adverse events obtained by comprehensive queries. Urinary and intestinal late toxicity and leg edema were graded according to modified RTOG scale on the basis their severity and impact on patients' performance status. Significant late treatment toxicity was classified as moderate (grade2) when symptoms required brief hospitalization or minor surgical procedures; severe (grade3) when they required a major surgical procedure or prolonged hospitalization;and fatal (grade4). Late SAE, that included cases with late treatment toxicity, were also assessed and grouped according to their relation to the treatment as; 'likely-related', 'not assessable' and 'unrelated' to treatment.

Results: 291 patients(77%) had either no or mild (grade1) late toxicity. Of the 86 patients with ≥grade 2 late toxicity;72 had grade 2, 10 grade 3 and 4 grade 4.The most frequent major urinary and intestinal complications were urethral stricture and proctitis, respectively. All 14 events of ≥ grade 3 toxicity except 2 (intestinal toxicity; small bowel obstructions) were due to urinary complications. The most frequent ≥grade 3 urinary toxicity was urethral stricture (9),followed by urinary incontinence (2) and cystitis (2). Late SAE were reported in 34 patients (9%) as likely-related(15 cases; 14 with≥grade 3 late toxicity and 1 with severe proctitis requiring blood transfusion), unrelated (7)and not assessable (12).

Conclusion: In our series,the overall toxicity is comparable to those reported in the literature, except for 4 patients, died due to urinary complications. Our analysis includes comprehensive queries which might have led to a more complete data collection than other series. It seems relevant to address carefully the occurrence of adverse events that are not clearly related to treatment, since the symptoms attributed to concomitant pathologies are, at least partially, due to the treatment side-effects.

847 POSTER

HDR vs. IDR brachytherapy for bladder cancer: disappointing local control and unexpected late toxicity

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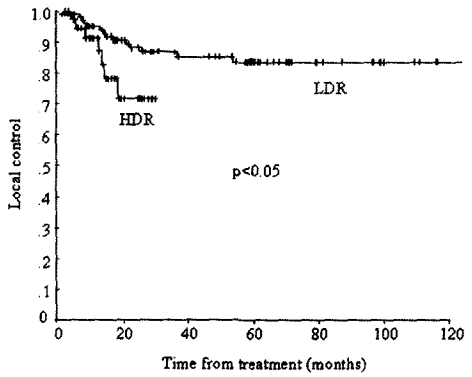
Objective: To analyze of the efficacy and toxicity of a high dose rate (HDR) brachytherapy schedule of 10 x 3.2 Gy for T1G3 and T2 bladder carcinoma and to compare these results with a previously used schedule of 40 Gy low dose rate (LDR) brachytherapy.

Patients and methods: Between 2000 and 2002 40 patients with T1G3 and T2 bladder carcinoma have been treated with 30 Gy external beam radiotherapy (EBRT) followed by interstitial HDR brachytherapy 32 Gy, 10 x 3.2 Gy/2 fractions per day with 6 hr interval. Local control rate and toxicity is compared with a historical group of 108 patients treated with 30 Gy EBRT followed by 40 Gy interstitial LDR brachytherapy. The HDR schedule was designed to be biologically equivalent to the previously used LDR schedule with the linear quadratic model including incomplete mono-exponential repair. The following parameters were used: for late responding normal tissue a/b ratio = 3 Gy and half time of repair = 1.5 hr; for tumor a/b ratio = 10 Gy and half time of repair =0.5 hr.

Results: After a median follow up of 14 months 7/40 HDR patients developed a local recurrence, at 20 months of follow up local control was 72% for HDR vs. 91% for LDR LDR ($p<0.05$). The incidence and pattern of late toxicity EORTC/RTOG > G3 was different for the two treatment groups. In the HDR group 5/30 evaluable patients encountered serious late toxicity, 4 patients developed global bladder dysfunction and one patient developed a local ulcer at the site of implant. In the LDR group 2/84 evaluable patients developed serious late toxicity, one patient developed a persisting vesico-cutaneous fistula and the other a urethral stricture due to fibrosis, both because of local problems at the site of implant. The difference in observed late toxicity HDR vs. LDR was highly significant (p=0.006).



Conclusions: Local control of HDR brachytherapy for bladder cancer was disappointing and late toxicity unexpectedly high when compared with the originally used LDR schedule. The results can be explained by the selection of the values for a/b ratio and repair half time when calculating equivalent schedules. The lack of reliable data on human tissue repair kinetics and repair capacity, the heterogeneity of LDR dose rates and essential differences in biological dose distribution make the calculation of equivalent HDR schedules hazardous.

848 POSTER

Does the clinical outcome correlate to altered expression of the EGF Receptor-family in renal cell carcinoma?

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Background: The EGFR family is involved in the development of many tumors. EGFR (ErbB1, HER1) is believed to be involved in the tumorogenesis of renal cell carcinoma (RCC). ErbB2 (HER2, neu), ErbB3 (HER3) and ErbB4 (HER4) has been poorly or not at all investigated in RCC. EGFR and ErbB2 are known to act as oncogenes in many tumors. Data on ErbB4 suggest that it acts as an oncogene in some tumors (colon cancer, medulloblastoma) but counteracts tumor progression in some (breast cancer).

Aim: To evaluate the expression of the EGFR family members in RCC, and correlate the levels to various clinical parameters.

Material and methods: Tissue samples from 100 patients with RCC and samples of non-neoplastic kidney cortex from the affected kidney were analyzed by real-time RT-PCR. Immunohistochemistry with antibodies against the EGFR and ErbB4 was performed on tumor tissues and kidney cortex in 8 cases.

Results: Results from the 20 cases with tumor and matched non-neoplastic kidney tissue showed that EGFR is up-regulated, ErbB2 and ErbB4 is down-regulated in the tumors. ErbB3 expression was not significantly altered. The immunohistochemical results correlated with the RT-PCR results.

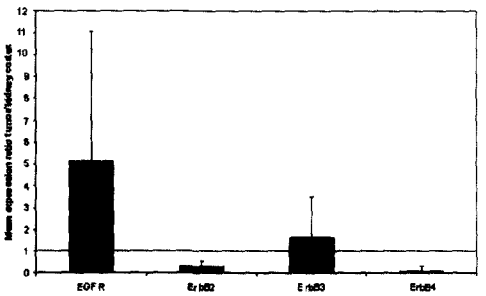

Figure: Ratio of EGFR-family members expression between tumor and matched non-neoplastic kidney cortex. Mean and stadard deviation from 20 cases.

Conclusions: The results confirmed the up-regulation of EGFR in RCC. ErbB2 was down-regulated in RCC. The marked down-regulation of ErbB4 suggests that it may be an important tumor suppressor in RCC. More investigation is needed to elucidate the role of these proteins in RCC. Data on analysis of 100 tumors with correlation to clinical parameters will be presented.