fractionation, but also the exploration of hypo-fractionated regimes for prostate cancer given its suggested low alpha/beta ratio. We report the long term efficacy of radiotherapy using a hypo-fractionated 50 Gy in 16 fractions (3.13 Gy per fraction) in men with localised prostate cancer.
Materials and Methods: A retrospective review of men with localised prostate cancer treated consecutively with conformal radiotherapy at a single institution between January 1995 and May 2001 was performed. Only patient's in the good prognostic group (PSA $\leqslant$ 10 ng/ml and Gleason $\leqslant$ 6 and Clinical stage T1/2) were included in the study. A conformal external beam radiotherapy dose of 50 Gy in 16 fractions over 22 days was deliverd using a 4 field arrangement on a linear accelerator with energy $\geqslant$6MV. The planning target volume (PTV) was defined as GTV (Prostate +/− base of seminal vesicles) + 1 cm in all directions except posteriorly were 7 mm was used. Patients treated with neo-adjuvant, concurrent or adjuvant hormonal therapies were excluded. Biochemical failure was defined using both the American Society for Therapeutic Radiology and Oncology (ASTRO) consensus definition and Phoenix definition (Nadir + 2 ng/ml).
Results: One hundred and ninety-nine men were identified. 73 with clinical T1 and 126 with clinical T2 disease at presentation. The median age at presentation was 67.9 years (49.9−81.6 years) and median initial PSA was 5.9 ng/ml (0.1−10 ng/ml). Histological review demonstrated that 78, 49 and 72 patients had Gleason scores of 4, 5 and 6 respectively. At a median follow-up of 84 months (4.6–134.9 months), the 7 year actuarial overall survival was 83.2% and the biochemical failure free survival was 55% and 76.8% as defined by the ASTRO consensus and Phoenix definitions respectively.
Conclusion: This data demonstrtates the efficacy of a hypofractionated regime for good prognosis patients. It provides similar levels of biochemical control when compared with other reported long term outcomes with conventional radiotherapy fractionation (2 Gy per fraction).

4033 POSTER

Preliminary results of late rectal and urinary toxicity in a phase II randomized study of conventional fractionation vs. hypofractionation on patients with high risk prostate cancer

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Background: Several recent studies suggested a great sensitivity of prostate cancer to high dose fractions due to an estimated α/β ratio of 1.5−2 Gy. With estimated α/β values of 3 to 5 Gy in late responding normal tissues of the pelvis, theoretical modeling shows a stronger enhancement of tumor effect than of late complications for larger (and fewer) fractions in prostate tumours. The purpose of this study is to test this hypothesis by comparing the late complication rate of a conventional fractionation and a biologically equivalent hypofractionated regimen in the radiotherapy of prostate cancer.
Material and Methods: From January 2003 to March 2007, 144 patients with histologically proven, high risk prostate cancer were recruited to this study. All patients received a total androgen deprivation (AD) for 9 months. A 3D conformal radiotherapy to prostate and seminal vesicles was started after two months of AD. Patients were randomized to receive 80 Gy in 40 fractions in 8 weeks (control arm A) or 62 Gy in 20 fractions in 5 weeks, 4 fractions per week (hypofractionation arm B). Late toxicities were defined as those detected 6 or more months after the end of radiation treament, and were evaluated following the EORTC/RTOG score system. The rectal mucosa damage was also evaluated in all patients with a 3 grade score scale (slight edema and rare telangectasia, moderate edema and confluent telangectasia, and necrosis) by means of pre- and post-treatment recto-sigmoidoscopies performed every six months after the end of radiation treatment.
Results: One hundred thirty seven patients with a follow-up longer than 6 months, 70 in the control and 67 in the hypofractionation arm were evaluated for late toxicity. Grade $\geqslant$3 toxicity was experienced by 4 patients of arm A, 2 (1.5%) rectal and 2 (1.5%) urinary toxicity, and in 1 patient of arm B (1.5%) who experienced an urinary incontinence.
The actuarial 2-year G $\geqslant$ 2 late rectal toxicity was 11.6% and 12% in the hypofractionated and control arm, respectively ($p = 0.89$). The actuarial 2-year G $\geqslant$ 2 rectal mucosa damage was 18% and 20% in the former and latter arm, respectively. The actuarial 2 year G2 late urinary toxicity was 2.3% and 9.3%, respectively, for the experimental and control arm, respectively ($p = 0.2$).
Conclusions: From these preliminary results, the hypofractionation schedule seems to be as safe as the conventional fractionation for both rectal and urinary tissues, with a slight but not significant trend in favor of hypofractionation, thus confirming the hypothesis of the theoretical modeling.

4034 POSTER

High or low dose rate in the radiation treatment of prostate cancer: different results and toxicity rates?

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Background: to analyse results after shifting from low dose rate (LDR) brachytherapy (BT) to high dose rate (HDR) treatment as a boost to external beam radiotherapy (EBRT).
Materials and Methods: From 1997 to 2005, 328 patients with locally advanced prostatic adenocarcinoma were consecutively and prospectively treated with BT as a boost to 3D conformal EBRT. All over the study, BT technics remained unchanged unless dose delivery. Until 07/2002, 201 patients received 40 Gy EBRT and a 42 Gy LDR BT boost with 192Ir wires. Afterwards to introduce the stepping source technologies, we shifted to a HDR BT boost for the last consecutive 127 patients. To shorten BT procedures, we delivered only one fraction of 10 Gy while increasing the EBRT dose up to 60 Gy to maintain a same Extrapolated Response Dose (ERD) of 143 Gy3. The ERD to the 20% most anterior region of the rectum were thus126 Gy3 and 117 Gy3, respectively for the HDR and LDR patients.
Results: The median follow up are 60 months for the LDR group and 31 months for the HDR group. No difference in initial prognostic factors was present (initial PSA, Gleason score, clinical Stage) between the two groups of patients. Recurrence rates of 23% and 27% at 33 months are not different ($p = 0.88$). However, late severe grade 3 rectal toxicity at 2 and 3 years are respectively 2.36% and 3.15% for the HDR group but 0% for the LDR group ($p = 0.01$).
Conclusions: With identical EBRT and BT technics and a same 143 Gy3 dose, the control rate of the disease at 31 months was similar in the two different groups. Our experience confirms thus the low α/β ratio of prostatic adenocarcinoma. However, rectal toxicity was significantly greater in the HDR arm. So, as opposed to what is commonly believed when the α/β of a tumor is low, shifting from LDR to hypofractionation can be similar in terms of disease control but not in terms of late toxicity. This observation can have significant impact on designing future protocols based on hypofractionation.

4035 POSTER

Effect of comorbidity on overall survival in patients with prostate cancer

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Background: The use of biochemical failure free survival in prostate cancer is controversial because mortality due to other causes is not taken into account. The aim of this study is to evaluate the impact of age and comorbidity on the overall survival (OS) and calculate the relative survival, which is important for patient counseling and clinical decision making.
Materials and Methods: All patients were selected with localized (T1−3NX-0M0) prostate carcinoma primarily treated with curative radiotherapy in our hospital between 1991 and 2000. Information on T-, N- and M-stage, age, performance score, Gleason score/grade, PSA-value, comorbidity and prior malignancies was abstracted from the charts. Comorbidity was measured using the Adult Comorbidity Evaluation index (ACE-27). The prognostic value of these variables on OS and disease specific survival (DSS) was studied. The OS of the patients was compared to an age- and period matched cohort of men from the Dutch population.
Results: Of the 395 patients treated, 217 died after a median follow up of 6.0 years, 94 due to prostate cancer, 30 due to other tumors, 66 due to intercurrent disease, and in 27 the cause of death was unknown. 130 patients developed a recurrence: 119 distant metastases, 27 loco-regional recurrences.
Mean age at diagnosis: 70.2 years (SD 6.2), median pretreatment PSA level: 19.0 ng/ml. The median radiation dose was 66 Gy (60−70 Gy). 18.7% received hormonal therapy during RT. The ACE-27 score was 0 in 38.9% of the patients, 1 in 22.2%, 2 in 24.1%, 3 in 3.8%. T1: 13.9%, T2: 54.2%, T3: 31.9%. Grade 1: 26.8%, 2: 46.3%, 3: 23.5%. 47 prior malignancies were found in 43 patients (10.9%).
The 5-year OS was 74.2%, the 5-year DSS 83.4%. ACE27, age, grade and PSA were independent prognostic factors for OS. The mean OS was 8.9 years compared to 10.1 years for the matched controls ($p < 0.0001$). Relative survival analysis showed excess mortality in the third to tenth year of follow up of $\pm$2% per year. For the low/intermediate risk group and patients aged >80 years no excess mortality was seen. In the age group 71−80 excess mortality started after 6 years.
Late grade 3 or 4 complications of the rectum were found in 18 patients (4.6%), of the bladder in 24 patients (6.1%).