Conclusions: Age and comorbidity had a significant effect on OS. Excess mortality was 13% at 10 years in our predominantly high risk population. No excess mortality was found in older patients and in the low/intermediate risk group.

4036 POSTER

Natural history of long-term radiation induced-proctopathy following localised high-dose 3-dimensional radiation therapy for prostate cancer

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Background: To report the natural history of long-term radiation-induced proctopathy following localised high-dose 3-Dimensional Conformal Radiation Therapy (3-DCRT) for prostate cancer (Pca).
Materials and Methods: From 1997 to 2001, 263 patients (pts) with localised intermediate/high risk Pca were included in a randomised trial (ICORG 97−01) comparing 4 vs. 8 months (mths) of induction maximum androgen blockage (monthly decapeptyl & daily flutamide, followed by localised 3-DCRT (Prostate & Seminal Vesicles, median dose: 73.7 Gy/35 frs). The post-radiotherapy (Post-RT) follow-up included reporting long-term rectal toxicity using the RTOG/EORTC scale. Observed toxicity rates were used to take into account the follow-up duration and the observed resolution rate.
Results: With a post-RT median follow-up of 62 mths, 249 pts were eligible for the analysis (at least 1 visit 3 mths after RT completion). 117 pts experienced rectal toxicity [Grade (Gr) 1: 73% (86 pts), Gr 2: 21.4% (25 pts), Gr 3: 3.4% (4 pts), Gr 4: 0.8% (1 pt), Gr 5: 0%]. For toxicity any grade, the time-trend analysis showed that most of the events occurred within sixth-seven year following RT [Observed rate @ 1 y = 0.8% (2/249), 2 y = 1.2% (3/240), 3 y = 4% (9/224), 4 y = 9.5% (19/199), 5 y = 23.4% (33/141), 6 y = 25.3% (22/87), 7 y = 31.2% (19/61), 8 y = 15.51% (9/58)], with a median time to onset of 67 mths. For toxicity grade $\geqslant$2, a time trend was also confirmed [Observed Gr $\geqslant$2 rate @ 1 y = 0%, 2 y = 0.4% (1/240), 3 y = 0.4% (1/224), 4 y = 2% (4/199), 5 y = 4.3% (6/141), 6 y = 9.2% (8/87), 7 y = 6.6% (4/61), 8 y = 5.2% (3/58)] with a median time to onset not reached. Among patients experiencing toxicity, 13 patients experienced a worsening of the toxicity (reaching a higher grade) with a median time to worsening of 9 months (2−72 mths). An improvement of grade $\geqslant$2 toxicity (back to 0/1) without any treatment was seen in 73% of patients (22/30 pts), with a median time from onset to resolution of 11 mths (3−50 mths). Only 4 patients (3.4%) required intervention (laser).
Conclusions: This long-term observation confirmed the need for long-term post-radiotherapy follow-up for a proper evaluation of the risk of long-term radiation induced proctopathy. Time-dependent analyses should be used when reporting or analysing long-term radiation induced proctopathy given the high resolution rate. We also confirmed a high rate of spontaneous resolution.

4037 POSTER

Clinical implementation of "quasi adaptive margin" for intensity modulated radiation therapy

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Background: In our practice, localized prostate cancers are treated by radiation via a combination of Image Guided Radiation Therapy (IGRT) followed by the conventional Intensity Modulated Radiation Therapy (IMRT). The rationale is that in the first phase using IGRT, daily movements of the prostate can be measured. This allows us to predict a "global mean shift", which defines the positioning of patient for the second phase; and the variance of daily displacements for each patient, which is incorporated into the posterior margin, which we called a "Quasi Adaptive Margin". The theoretical basis of this technique is described in this study.
Methods and Material: Based on standard statistics theory, a margin **M** to ensure 95% dose coverage on CTV with 95% confidence limit for individual patients can be prescribed as $\mathbf{M} = t(n-1)\cdot \mathrm{sd}(n)/\mathrm{sqrt}(n) + 0.7\cdot \mathrm{sd}(n) + 2$ mm, where sd(n) is the standard deviation of the n shift samples. $t(n-1)$ is a correction factor to achieve 95% confident limit for different sample size with t being 2.57, 2.23 and 2.13 for 5, 10 and 15 shifts, respectively. The number 2 is the additional margin applied to compensate for the uncertainty in IGRT.
This formula was tested for three patient groups: the first group consists of 284 patients who underwent 5 IGRT fractions, no BB shift was used; the second group consists of 114 patients, each underwent 10 IGRT fractions, one BB shift was used for fractions 6−10; the third group consists of 54 patients, each underwent 15 IGRT fractions, two BB shifts were used for setup for fractions 6−10 and 11−15, respectively.
Results: In general, the margin is reduced with the increased number of IGRT fractions. The use of 15 IGRT fractions would reduce the margin to below 10 mm for 90% of the patient population whose shift uncertainty is less than 6 mm.
The shift uncertainty was found to be 6.0, 4.4 and 3.4 mm for the three patient groups who underwent 5, 10, 15 IGRT fractions and 0, 1 and 2 BB shifts, respectively, Correspondingly, the margin would be reduced to 8.2, 6.3 mm from 13.1 mm for the second and the third patient groups.
Conclusions and Discussion: We have successfully implemented the concept of "quasi-adaptive margin" and "evidence based isocenter shift" in prostate irradiation to account for the random and systematic setup uncertainties for our prostate patients. We have shown that by performing a sufficient number of IGRT procedures (but not for the whole course of >35 fractions, which is very time and resource consuming), the patient positioning can be accurately reproduced on a daily basis, and the issues of underdosing the target or overdosing the normal adjacent tissues are addressed adequately.

4038 POSTER

Results of a randomized trial comparing short vs. protracted neoadjuvant hormonal therapy (NHT) prior to radiation therapy (RT) of localized prostate cancer

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Background: Adjuvant hormonal therapy improves survival of selected prostate cancer patients. However, there are few trials that address the variables of adjuvant hormones. This randomized trial compared short (4 months) vs. long (8 months) NHT prior to RT.
Methods: From 1997–2001, 276 pts. enrolled of whom 256 are analysed. Stratification risk factors were PSA > 20, Gleason score >7, and >T3. The intermediate-risk stratum had one factor, the high-risk stratum had >2 factors. Staging included bone scan, and CT to exclude nodal involvement. NHT consisted of monthly LHRH agonist (triptorelin – Decapeptyl) and Flutamide 250 mg 3 times daily (Drogenil). Localized RT was 66 Gy in a minority and 92% got 70 Gy using 3-D to prostate and vesicles. The primary endpoint was PSA relapse-free survival (P-RFS), calculated by the ASTRO method from the date of commencement of NHT.
Results: On multivariate analysis the Gleason score and log of the initial PSA were significant predictors of P-RFS.

	4 months	8 months
Overall	N = 128	N = 127
5 year P-RFS	45%	49%
Intermediate risk	N = 67	N = 66
5 year P-RFS	51%	51%
High risk	N = 62	N = 61
5 year P-RFS	46%	41%

All p values = NS.

Conclusions: For these intermediate and high risk patients the overall PSA relapse free survival is low, but comparable to the relevant literature. However, the ASTRO method of calling a PSA relapse overestimates true relapse and may have undermined the interpretation of this trial. Most patients had salvage hormones at relapse and did not have a chance to develop the more appropriate Phoenix failure criteria.

4039 POSTER

Optimal timing of androgen suppression in patients with high-risk prostate cancer undergoing radiation therapy

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Aim: A large number of prospective randomized trials have demonstrated that adding androgen suppression to radiation therapy improves the results for patients with locally advaced prostate cancer. However, an important question is how long time androgen suppression has to be administrated to improve biochemical disease free survival (bDFS) in this group of patients. Aim of this work is to evaluate the optimal timing of hormonal therapy in patient with high-risk prostate cancer.

Materials and Methods: 345 patients with high-risk prostate cancer (T3 or Gleason score [GS] 8−10 or PSA > 20 ng/dl) were treated with curative radiation therapy + neoadjuvant and concomitant hormonal therapy; 303 also received adjuvant androgen suppression. According to timing of hormonal therapy the patients were stratified into two group: group 1 of 285 patients received <36 months of adjuvant hormonal therapy and group 2 of 60 patients received >36 months of adjuvant hormonal therapy. Hormonal therapy was based both on LH-RH agonist (+/− antiandrogens) or high dose antiandrogen alone (bicalutamide, 150 mg/day). Total dose to the prostate ranged from 70 Gy to 74 Gy (1.8 Gy/fraction). bDFS was calculated from the time of diagnosis with Kaplan-Meier method.
Results: Median follow-up was 44 months (12–161 months). Median age of patients was 71 years (range 41−83 years). Clinical and pathological characteristics of study population were: T2 10 (2.8%), T3 330 (95.7%), T4 5 (1.5%); PSA < 10 ng/ml 152 (44.7%), PSA 10−20 ng/ml 99 (29.1%), PSA >20 ng/ml 89 (26.2%); GS 2−6 152 (44.3%), GS 7 126 (36.7%), GS 8−10 65 (19.0%). The bDFS at 5 years was 78% and 91% in patients of groups 1 and 2, respectively (p = 0.028). Considering only the patients who finished adjuvant hormonal therapy the bDFS at 5 years was statistically significant too (p = 0.032).
Conclusions: Prolonged >36 months adjuvant hormonal therapy improves biochemical desease free survival in patients with high-risk prostate carcinoma.

4040 POSTER

Salvage 3-D conformal radiation therapy for patients developing biochemical failure post prostatectomy: a single institution experience

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Background: Two recent randomized trials have shown a benefit to the use of adjuvant external beam radiation therapy (RT) post radical prostatectomy (RP) in patients presenting with high-risk features. However, residual postoperative GU toxicity, as well as fear of RT complications lead to delays in referral to radiation therapy. We retrospectively reviewed the outcome of patients presenting with biochemical relapse post RP treated with RT as salvage therapy.
Methods: Between September 1998 and July 2004, 102 patients (median age: 65 years) received salvage RT post RP biochemical failure. All patients underwent pre-RT staging using bone scan and CT scan of the abdomen and pelvis. RT typically delivered a dose of 66 Gy in 33# using 18 MV photons. A total of 25 patients received hormones given in a neoadjuvant and concomitant setting. Acute and late toxicities were graded using the CTC v3 criteria. We prospectively assessed their quality of life using the IPSS (international prostate symptom score) and SHIM (sexual health inventory for men).
Results: The median time for RT referral post RP is 24months. The median follow up time is 37 months (6–122). 44% of our patients presented with pT3 disease, 53% with positive margins and 28% with >7 Gleason score. Among them, 37% never achieved an undetectable post RP PSA level. The median pre-RT PSA is 1.00 ng/ml (range:0. 01−10.4).
Biochemical failure was defined according to SWOG criteria as any PSA > 0.5 ng/ml at least 6 months after RT. 79 patients (77%) were followed for at least one year.
28 patients (27%) developed biochemical relapse after salvage radiation, at a median time of 21 months. Of these, 22% of patients who had a pre-RT PSA < 1 ng/ml had biochemical relapse as compared to 38% with pre-RT PSA > 1 ng/ml.
Prior to RT, 41% of the patients had some degree of stress incontinence. None of our patients developed RT-induced stress incontinence. Acute and late GI/GU toxicities were minimal, 1 patient developed grade 3 urethral stenosis, one had G3 late GI and GU Toxicity.
Conclusion: Our results are comparable to others published in the literature. Post op RT was well tolerated with minimal GI and GU toxicities. As previously reported, a pre-RT PSA > 1 ng/ml was associated with higher biochemical relapse.

4041 POSTER

^{18}F-choline and/or ^{11}C-acetate positron emission tomography: detection of residual or progressive subclinical disease at very low PSA values (<1 ng/ml) after radical prostatectomy

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Background: To assess the value of PET/CT with either ^{18}F-choline and/or ^{11}C-acetate of residual or recurrent tumor after radical prostatectomy (RP) at a PSA < 1 ng/ml and referred for adjuvant or salvage radiotherapy.
Materials and Methods: 22 PET/CT studies were performed, 11 with ^{18}F-choline (group A) and 11 with ^{11}C-acetate (group B), in 20 consecutive patients (2 patients undergoing PET/CT scans with both tracers). Median PSA before PET/CT was 0.33 ng/ml (range 0.08−0.76). Endorectal MRI was performed in 18 patients. Nineteen patients were eligible for evaluation of biochemical response after salvage RT.
Results: Abnormal local tracer uptake was observed in 5/11 and 6/11 patients in group A and group B, respectively. Except for a single positive obturator lymph node, no other site of metastasis was observed. In the 2 patients evaluated with both tracers no pathologic uptake was observed. Endorectal MRI was locally positive in 15/18 patients. 12/19 patients responded with marked PSA decrease (>50% of baseline) 6 months after salvage RT.
Conclusions: Although ^{18}F-choline and ^{11}C-acetate PET/CT studies succeeded to detect local residual or recurrent disease in about half of the patients with PSA-values <1 ng/ml after RP, these studies can not yet be recommended as a standard diagnostic tool for early relapse or suspicion of subclinical minimally persistent disease after surgery. An endorectal MRI may be more helpful especially in patients with a low likelihood for distant metastases. Nevertheless, further research with ^{18}F-choline and/or ^{11}C-acetate PET with optimal spatial resolution may be needed for patients with a high risk of distant relapse after RP even at low-PSA values.

4042 POSTER

Rectal volume changes during treatment: the case for ansisotropic safety margins around the clinical tumor volume in radiotherapy for prostate cancer

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Background: To evaluate the influence of rectal volume changes (on sequential weekly CTs) on the antero-posterior (A-P) axis motion of the clinical target volume (CTV=prostate+seminal vesicles) at its apex, mid-point, and top in order to estimate for potentially anisotropic planning target volume (PTV) margins in patients undergoing 3-D conformal radiotherapy for prostate cancer.
Material and Methods: Eighty-nine patients were selected for this study. A planning CT was performed at simulation in a supine position with an empty bladder in 77 patients while 12 patients underwent, in addition, a rectal enema before simulation and before every treatment session. Weekly control CTs were implemented to all patients while on treatment (i.e., 4−7 weekly CTs per patient). The CTV and the rectum were contoured in every CT by two experienced authors (one in Geneva and one in Barcelona). Bone registrations between the simulation CT and weekly control CTs for every patient in the study was performed in order to assess for CTV A-P displacements (at the apex, mid-point, and the top) and rectal volume changes. Ideal A-P margins for the PTV were estimated at the three CTV levels.
Results: The estimated PTV A-P margins (a the CTV apex, mid-point, and top) for the 77 patients not undergoing the rectal purge, were 10, 10 and 12 mm; 12, 11, and 14 mm; and 12, 13 and 22 mm for patients with small (<60 cc), medium (60–110 cc), or large (>110 cc) rectal volumes on simulation CTs, respectively. For the 12 purged patients the estimated PTV margins were 9, 10, and 7 mm (mean rectal volume at simulation, 55 cc). A broad rectal volume distribution was observed for unpurged patients, though, a significant trend for a volume decrease was observed after the 3rd week of treatment for these patients (p = 0.017).
Conclusions: In patients with small rectal volumes at simulation, as well as in those undergoing rectal enemas as part of their preparation to simulation and treatment, PTV margins were stable and relatively small (1 cm). Contrarywise, in patients with large rectum volumes at simulation,