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

P. Thirion, D. Fitzpatrick, C. Kelly, C. Fleming, J. Armstrong. *St Lukes Hospital, Clinical Trials Resource Unit, Dublin 6, Ireland*

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

Z. Gao[1], J. Wong[1], S. Merritt[1], M. Li[1], M. Uematsu[2], C. Cheng[1].
[1]Morristown Memorial Hospital, Radiation Oncology, Morristown – NJ, USA; [2]National Defense Medical College, Radiation Oncology, Tokorozawa, Japan

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.

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

J. Armstrong[1], D. Fitzpatrick[1], J. Taylor[2], P. Thirion[3]. *[1]St. Lukes Hospital, Radiation Oncology, Dublin, Ireland; [2]St. Lukes Hospital, Nursing, Dublin, Ireland; [3]St. Lukes Hospital, Radiaiton Oncology, Dublin, Ireland*

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

G.C. Mattiucci[1], G. Mantini[1], A. Errico[1], L. Tagliaferri[1], A. Di Rito[1], S. Luzi[1], C. DiGesù[2], V. Frascino[2], A.G. Morganti[2], N. Cellini[1].
[1]"A.Gemelli" University Hospital Catholic University, Radiotherapy Department, Roma, Italy; [2]"John Paul II" Center for High Tecnology Research and Education in Biomedical Sciences Catholic University, Radiotherapy Department, Campobasso, Italy

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.