HIPRO (Hypofractionated Dose Escalation utilising Intensity Modulated Radiotherapy in Carcinoma of the Prostate) study (UKCRN ID 1272).
Materials and Methods: Sixty men, median age 75 years (50−87), with localised adenocarcinoma of prostate (T1−3N0M0) and either Gleason score ⩾7 or PSA 20−50 ng/l received 57 Gy in 19 fractions (n = 30) or 60 Gy in 20 fractions (n = 30) using 5-field inverse-planned IMRT. All patients received neoadjuvant hormone therapy, continuing for up to 6 months after treatment. Late toxicity was assessed at 7 years follow-up using RTOG criteria and a validated LENT/SOMA patient questionnaire. Overall survival, cause-specific survival and biochemical progression-free survival defined using Phoenix criteria (bPFS) were assessed at 5 years.
Results: Median follow-up was 84 months (13−93 months) and forty-four (73%) patients were alive at 7 years. Nine patients (21%) reported RTOG grade 1 bowel or bladder toxicity; there was no grade 2 toxicity or above. There was no difference between the fractionation schedules. LENT/SOMA questionnaires were returned by 31/44 patients. At 7 years, mean and median scores were less than one for bowel and urinary symptoms. Compared with baseline assessment prior to radiotherapy, the proportion of all patients with significant (maximum LENT/SOMA ⩾2) urinary symptoms remained similar (76% vs. 75%), problems with sexual function had decreased (98% vs. 84%) but bowel symptoms increased (25% vs. 62%). At 5 years, overall survival was 83% and 74%, cause-specific survival 83% and 84% and bPFS 50% and 58% in the 57 Gy and 60 Gy groups respectively.
Conclusions: Dose-escalated hypofractionated IMRT for prostate cancer is well tolerated with acceptable levels of late toxicity compared to the published literature. Although this study predominantly included high risk patients (D'Amico classification), survival outcomes are promising. This study served as a precursor for CHHiP (Conventional or Hypofractionated High Dose Intensity Modulated Radiotherapy for Prostate Cancer), a large multicentre Phase III clinical trial which will further assess long-term disease control and toxicity with these regimens.

7039 POSTER

Establishing a Dose Response Relationship for the Treatment of Prostate Cancer With External Beam Radiotherapy: a Meta-analysis

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Background: Randomized trials have shown the benefit of radiation dose-escalation in prostate cancer, however, the exact quantitative relationship remains unclear. We aim to quantify a relationship between radiotherapy dose and freedom from biochemical failure (FFBF) in low and intermediate risk prostate cancer. To reduce confounding, we used data with a standardised endpoint, mature follow-up, low competing risk of metastatic failure via exclusion of high risk patients, conventional fractionation and separate reporting for outcomes with hormonal therapy.
Materials and Methods: A systemic review of the literature from was carried out in EMBASE, Pubmed and the Cochrane library, as well as proceedings of annual ASTRO meetings and publication bibliographies. Studies that reported the use of radiotherapy alone in 1.8−2 Gy fractions in low and intermediate risk prostate cancer were included. The primary endpoint was Phoenix definition 5-year FFBF. A logistic regression was used to model the dose-response relationship. The dose required to achieve 50% biochemical tumour control (TCD50) and the slope of the dose-response curve at TCD50 (γ50) were calculated.
Results: Data from 14 studies with 2704 patients met the inclusion criteria. The data from 1255 low risk patients (591 patients without hormone therapy and 664 patients treated with hormone therapy) and 1449 intermediate risk patients without hormone therapy were analysed. A strong correlation between radiotherapy dose and FFBF were found in low and intermediate risk patients managed with radiotherapy alone. In low risk patient not treated with hormone therapy the TCD50 is 49.5 Gy and the γ50 is 1.8%/Gy ($p = 0.0003$). At 78 Gy this represents a FFBF of 88.8%. In intermediate risk patients not treated with hormone therapy, the TCD50 is 64.7 Gy and the γ50 is 3.2%/Gy ($p < 0.0001$). At 78 Gy this translated into a FFBF of 84.5%. Hormonal therapy had a borderline significant effect in low risk patients with a relative risk reduction of 27% in FFBF at 78 Gy ($p = 0.07$), equivalent to an absolute risk reduction of 3%.
Conclusions: A strong correlation was found between radiation dose and biochemical outcome in both low and intermediate risk patients. There is a FFBF benefit for hormonal therapy for men with low risk disease, but in absolute terms this is small in the presence of dose escalated radiotherapy. With image guided radiotherapy and conformal planning techniques providing more accurate prostate dose delivery than what was achieved in some of the studies included in this analysis, the models may underestimate FFBF rates achievable in the modern era.

7040 POSTER

Treatment of Prostate Cancer With Intensity Modulated Radiation Therapy Using an Empty Bladder Protocol − Treatment Outcomes and Toxicity Profile

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Background: To examine the acute and late toxicities, and biochemical relapse-free-survival (bRFS) after moderate dose-escalation using Intensity Modulated Radiation Therapy (IMRT) in Stage cT1−4cN0 prostate cancer patients on an empty-bladder protocol.
Materials and Methods: We retrospectively analyzed all (n = 95) patients with prostate cancer treated with IMRT at the National Cancer Centre Singapore from 2004 to 2006 using a modified bladder-filling protocol. Patients were instructed to empty their bladder before simulation and treatment. After completion of treatment, patients were scored for late-urinary and bowel toxicities using the Common Terminology Criteria for Adverse Events version 3.0. Late toxicity data was compared to that published from other IMRT studies using a full-bladder protocol. Overall-Survival (OS) and bRFS were estimated by the Kaplan–Meier method.
Results: Ninety-one patients (95.8%) completed IMRT. Median age was 68 years (range = 51−82). 71% of patients had clinical stage cT1 and cT2 disease. Median presenting PSA was 13.8 ng/dL (range = 2.5–483). Median Gleason score was 7 (range 4−10). Fifty-eight patients (70%) received 74 Gy to the prostate gland. 4.8% and 50% of patients exceeded the dose-constraints for rectum and bladder, respectively. Median follow-up time was 51 months (range = 3.6–144). Twelve (14.5%) and 10 (12.8%) patients had hematuria and rectal bleeding. 5-year OS and bRFS was 89.7% and 80.5%.
Conclusions: Moderate dose-escalation with IMRT using a modified empty-bladder protocol is feasible and produces late-toxicity rates and treatment outcomes comparable to treatments using a conventional full bladder protocol.

Table: Comparison of treatment outcomes and toxicity profile of patients in study with published results

	Current study	MSKCC (Alicikus et al., 2010)	MSKCC (Zelefsky et al., 2008)			Koh et al., 2009	Storey et al., 2000		Al-Mamgani et al., 2008	
Radiation technique	IMRT	IMRT	3D CRT, IMRT (n = 170)	3D CRT	3D CRT	IMRT	3D CRT	3D CRT	3D CRT, IMRT (n = 41)	3D CRT
Bladder during RT	Empty	Empty	Empty	Empty	Empty	Full	Full	Full	Full	Full
No. of patients	91	170	741	358	472	76	91	98	333	331
Median follow-up, months	50.3	99	120	78		7.9	42	40	71	70.3
Radiation dose, Gy (fraction size)	66−74 (2)	81 (1.8)	81 (1.8)	70.2 (1.8)	75.6 (1.8)	73.8 (1.8)	78 (2)	70 (2)	78 (2)	68 (2)
Survival rate, %										
5-year OS, %	91.3	–	–	–	–	–	–	–	–	–
7-year OS	–	–	–	–	–	–	–	–	75%	75%
5-year bRFS, %	73.2	–	85%	61%,	74%	–	–	–	67%	61%
7-year bRFS, %	–	–	78%	68%	50%	–	–	–	56%	45%
10-yr Risk groups										
Fav		81%								
Mod		78%								
Poor		62%								
G.U. Toxicity										
⩾Gr 2, %	15.4	9	20	10	15	3.9	20	9	40%	41%
⩾Gr 3, %	2.2	5	5	3	3	1.3	–	–	12%	13%
G.I. Toxicity										
Gr 1	12.1	19	–	–	–	–	–	–	–	–
⩾Gr 2, %	1.1	2	5	7	18	2.6	21	14	35%	25%
⩾=Gr 3, %	0	1	1	1	1	1.3	–	–	4%	6%