the prostate with the planning GTV. Prostate and rectum were segmented on each daily pre-treatment MVCT and doses recalculated. To simulate positioning of the patient based on alignment of the pelvic bones (for example with daily x-ray) a software algorithm was used that matches the bones on the daily MVCT to the bones of the planning CT. Doses of the prostate and the rectum for this theoretical bone match position were calculated. Actual treatment and treatment in bone match position were compared with respect to the calculated dose of 95% of the prostate (D95) and absolute rectal volume with dose over 1.5 Gy (rV1.5) in a single fraction. Currently 109 out of 363 fractions are evaluated.
Results: Comparing actual treatment position and theoretical bone match position: average ($\pm$SD) shift between both positions for each fraction was 2.4$\pm$1.7 mm, difference of roll was −0.35$\pm$0.56. Average difference between treatment position and bone match position for D95 was 0.35% and for rV1.5 was 1.6%, both not significant ($p = 0.01$). The confidence interval for the difference of D95 was [0.2%, 0.9%] and for rV1.5 was [16%, 19%] ($p = 0.01$). However improvement of >100% for rV1.5 in treatment versus bone match was possible in 2% of fractions.
Conclusion: Average differences found of delivered dose between positioning based on daily MVCT and positioning based on pelvic bones are small for two reasons: (1) The soft tissue contrast of MVCT is small, which limits GTV alignment during treatment and dose recalculation of GTV after treatment. (2) Interfractional movements of prostate and rectum are complex and sufficient compensation with table shift and rotation is difficult in a number of fractions. However, daily MVCT can avoid high dose rectum radiation of >1.5 Gy in a number of fractions.

4054 POSTER

Placebo-controlled, randomized, phase II study of radium-223 in metastatic hormone refractory prostate cancer (HRPC)

S. Nilsson[1], L. Franzén[2], C. Tyrrell[3], R. Blom[4], J. Tennvall[5], B. Lennernäs[6], D.C. Johannessen[7], M. Sokal[8], C. Parker[9], O.S. Bruland[10]. *[1]Karolinska Hospital and Institute, Radiumhemmet, Stockholm, Sweden; [2]Länssjukhuset Sundsvall-Härnösand, Oncology, Sundsvall, Sweden; [3]Plymouth General Hospital, Oncology, Plymouth, United Kingdom; [4]University Hospital Linköping, Oncology, Linköping, Sweden; [5]University Hospital Lund, Oncology, Lund, Sweden; [6]Sahlgrenska University Hospital, Oncology, Gothenburg, Sweden; [7]Haukeland University Hospital, Oncology, Bergen, Norway; [8]Nottingham City Hospital, Oncology, Nottingham, United Kingdom; [9]Royal Marsden Hospital, Oncology, Sutton, United Kingdom; [10]The Norwegian Radium Hospital and Algeta ASA, Oncology, Oslo, Norway*

Background: The alpha emitter radium-223 (Alpharadin^{TM}) is a bone-seeking radionuclide studied as a novel treatment for patients with HRPC and skeletal metastases. Ra-223 showed minimal toxicity in a phase I study [1]. Here we present outcome data from a randomised phase II study with 18 months follow up.
Methods: Patients with CRPC and bone pain requiring external beam radiotherapy were randomized to treatment with 4 injections of either Ra-223 (50 kBq/kg b.w.) or saline (placebo) every 4 weeks. The primary endpoints were change in bone-alkaline phosphatase (ALP) levels from baseline to 4 weeks after last injection (previously reported [2]), and time to occurrence of Skeletal Related Events (SREs). Secondary endpoints included toxicity, PSA progression and overall survival.
Results: 33 patients were randomised to Ra-223 and 31 to placebo. The two groups were well balanced with respect to standard prognostic factors. Mild, transient haematological toxicity was seen after Ra-223. Long term toxicity was not observed. SAEs were reported in 8 patients in the Ra-223 group versus 14 in the placebo group. Based on intention to treat analysis, the median time to PSA progression was 26 versus 8 weeks ($p = 0.048$) for Ra-223 versus placebo, respectively. The median time to first SRE was 14 versus 11 weeks ($p = 0.257$). The hazard ratio (HR) adjusted for baseline covariates was 1.75 (95% CI: 0.97−3.19, $p = 0.065$). The median overall survival was 65.3 weeks versus 46.4 weeks ($p = 0.066$). The HR adjusted for baseline covariates was 2.12 (95% CI: 1.13−3.98, $p = 0.020$). At 18 months, 15 (45%) versus 8 (26%) patients were still alive. Two years survival and long term safety data will be presented at the meeting.
Conclusions: Four injections of Alpharadin were well tolerated, with minimal myelotoxicity, and demonstrated encouraging evidence of efficacy. Larger clinical trials are warranted to study the impact of Alpharadin on the prevention of SREs and on overall survival in CRPC. The bone targeting properties of Alpharadin, may also be applicable to the treatment of skeletal metastasis from other primary cancers.

References

[1] Nilsson S, et al., Clin Cancer Res 2005; 11 (12): 4451−59.
[2] Bruland ØS, et al. Clin Cancer Res 2006; 12: 6250s–6257s.

4055 POSTER

Hypofractionated stereotactic intensity modulated radiotherapy (IMRT) for prostate cancer with low-metastasic potential

M. Molla, D. Linero, J.I. Toscas, L. Escude, R. Miralbell. *Instituto Oncologico Teknon, Radiation Oncology, Barcelona, Spain*

Introduction: To assess the feasibility, outcome, and toxicity of hypofractionated IMRT in patients with low- to intermediate-risk prostate cancer with <20% risk of metastases.
Material and Methods: From December 2003 to December 2005, 63 patients with non-metastasic prostate cancer and a Roach index [RI% = 2/3PSA + 10(Gleason score − 6)] of <20% were treated with an hypofractionated IMRT protocol using an extracraneal stereotactic repositioning system (Exatrac, BrainLAB) and 6MV X-ray beams from a micro-multileaf collimator-based linear accelerator (Novalis, BrainLAB). A total dose of 56 Gy (14$\times$4 Gy, 2 days a week for a total elpased time of 7 weeks) was delivered to the prostate with or without the seminal vesicles (equivalent to 88 Gy in 2 Gy daily fractions, $\alpha/\beta = 1.5$ Gy). Acute ($\leqslant$6 months) and late ($\geqslant$6 months) genitourinary (GU) and low-gastrointestinal (low-GI) toxicities were scored according to the LENT-SOMA and RTOG scoring systems, respectively. Five-year biochemical disease-free survival (bDFS) was calculated according to the Houston definition for failure (i.e., PSA nadir +2 ng/ml).
Results: Feasibility was optimal as well as preliminary results on tolerance (see table) and bDFS: 89% (5-year) after a median follow-up of 33 months (range, 13−90).

Toxicity	GU		low-GI	
Grade	1	$\geqslant$2	1	$\geqslant$2
Acute	12 (19%)	6 (9.5%)	5 (7.9%)	5 (7.9%)
Late	7 (11%)	2 (3.2%)	12 (19%)	2 (3.2%)

Conclusions: Hypofractionated RT using 56 Gy/14 fractions using stereotactic IMRT is feasible and is associated with a very low risk of $\geqslant$grade 2 acute (<10%) and late toxicity (<5%). Preliminary data may suggest, in addition, optimal bDFS similar to normofractionated treatments with equivalent doses for a similar risk group of patients.

4056 POSTER

Clinical validation of PTV margins used during dose escalated loco-regional IMRT to prostate, seminal vesicles and pelvic lymph nodes

J. Yan, A.J. Bayley, V. Kelly, P. Chung, C.N. Catton, P. Warde, T. Rosewall. *Princess Margaret Hospital, Radiation Medicine, Toronto Ontario, Canada*

Background: Determining appropriate PTV margin size is difficult when multiple CTVs move independently. This is particularly challenging when small margins are necessary to limit dose to the adjacent organs at risk. We describe the clinical efficacy of the PTV expansions used during a Phase II clinical trial of escalated-dose IMRT to prostate/seminal vesicles (P+SV) and pelvic lymph nodes (PLN) for high-risk prostate cancer.
Materials and Methods: This retrospective review included data from the first 14 patients treated in the clinical trial. Patients were treated supine and in a vac-cushion with full bladder/empty rectum preparation. PTV margins were: PLN (5 mm), prostate (10 mm except 7 mm posterior) and seminal vesicles (10 mm). Daily isocentre adjustment was performed, by incorporated both offline and online EPI analysis. Twenty-nine daily orthogonal EPIs were reviewed for each patient. The proportion of treatment fractions where the CTVs could not be encompassed within the PTV was determined using pelvic bony anatomy (BA) as a surrogate for PLN position and the centre of 3 intra-prostatic fiducial markers (COM) as a surrogate for P+SV position.
Results: The distribution of CTV excursions outside the PTV for BA and COM is summarised in Table 1. Without any correction strategy, frequent Anterior/Posterior (AP) excursions of the CTVs outside the PTVs occurred. After offline correction of systematic errors, COM excursions were reduced to 2.6%, but BA excursions remained common due to the smaller PTV margin used. Online correction resulted $\leqslant$3% of fractions with an excursion outside the PTVs. Data revealed that excursions for the 2 CTVs were reasonably well correlated ($r^2 = 0.94$ Left/Right [LR], 0.60 Superior/Inferior [SI], 0.82 [AP]) and this allowed the matching strategy to routinely accommodate the displacements of both CTVs.
Conclusions: The PTV margins used here during dose escalated loco-regional IMRT to prostate, SV & pelvic lymph nodes are able to accommodate $\geqslant$97% of CTV displacements when online image guidance is used.