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.

Table 1. Fractions where CTV is displaced outside the PTV

	Centre of markers			Bony anatomy		
	LR	SI	AP	LR	SI	AP
Before off-line (Number)	3	6	48	59	20	121
Percentage	0.8%	1.6%	12.4%	15.1%	5.1%	31%
After off-line (Number)	0	0	10	34	20	27
Percentage	0%	0%	2.6%	8.7%	5.2%	7%
After on-line (Number)	1	0	0	4	9	10
Percentage	0.3%	0%	0%	1.0%	2.3%	3%

4057 POSTER

Tomotherapy in patients with prostate cancer

R. Schwarz[1], D. Hornung[1], F. Cremers[2], W. Rapp[2], V. Platz[2], D. Albers[2], A. Bajrovic[1], G. Matnjani[1], R. Schmidt[3], A. Krüll[1]. *[1]Ambulanzzentrum des UKE, Radiation Oncology, Hamburg, Germany; [2]University Hospital, Radiation Oncology, Hamburg, Germany; [3]University Hospital, Radiation Oncology, Hamburg, Germany*

Background: Tomotherapy is a new technique for image guided radiotherapy in patients with prostate cancer. By this technique dose escalation up to 80 Gy is possible.The treatment of patients with tomotherapy was analysed.
Material and Methods: Since December 2006 13 patients with prostate cancer were treated with tomotherapy, nine of them for primary tumors and four patients for salvage after prostatectomy. In 8 cases small volumes (prostate +/− seminal vesicles) and in 5 cases also larger volumes including the pelvis were treated. A comparative treatment planning was done for tomotherapy, 3D-conformal and intensity modulated radiotherapy (IMRT). Daily adjustments in the optimisation process by matching KV-CT and MV-CT and table and treatment times were analysed. Acute toxicity was documented.
Results: In all cases tomotherapy showed a reduction of dose to the rectum and the femoral heads in the dose-volume-analyses in comparison to 3D-conformal and intensity-modulated radiotherapy. By these dose-reductions a dose-escalation of 76−80 Gy was possible in primary radiotherapy. Tabletimes and treatment times were 26 and 4 minutes for small volumes and 28 and 6.7 minutes for large volumes. Daily adjustments for translations (*x, y, z*, roll) were 4.9±3.4 mm, 2.1±1.3 mm, 7.3±3 mm, 0.350±0.30 for small volumes and 3.1±2.1 mm, 1.4±1.4 mm, 5.5±2.7 mm, 0.250±0.230. Acute toxicity (CTC-score) for rectum and bladder was maximal grade 2.
Conclusions: Tomotherapy had better dose-volume-parameters in comparison to IMRT and 3d-conformal radiotherapy. Median table times for the patients were 26 and 28 minutes. Median adjustments for *x, y, z* were under 10 mm. Acute toxicity was tolerable.

4058 POSTER

Survival and PSA relapse data after hypofractionated radiotherapy for early stage prostate cancer

A. Law, G.S. Higgins, G.R. Kerr, D.B. Mclaren, G.C.W. Howard. *Edinburgh Cancer Centre, Oncology, Edinburgh, United Kingdom*

Background: Radiotherapy is often used for localised early stage prostate cancer. Radiation schedules vary and hypofractionated regimes aim to exploit a potential radiobiological advantage of low α/β ratio. The use of neoadjuvant hormone treatment has been shown to increase control. We report the results from radical treatment of early prostate carcinoma (T 1 and 2) with 3 months of neoadjuvant hormone therapy and then 5250 cGy in 20 fractions to prostate +/− seminal vesicles.
Methods: Using the Edinburgh database we identified 201 patients treated for T1/T2 prostate cancer from 1996 to 2001. Results were analysed for survival and PSA relapse free survival. The results were analysed according to pre-treatment prognostic groups – good (PSA $\leqslant$ 10, Gleason $\leqslant$ 6), poor (PSA $\geqslant$ 10, Gleason $\geqslant$ 6) or intermediate (one of prognostic indicators raised).
Results: *Survival*: Minimum follow up was 47 months. 64 patients have died, giving an overall actuarial 5-year survival rate of 77.6%, 56.5% at 10 years. Good Prognostic group 97.1% (95% CI 91.1–100.0); Intermediate 92.2% (86.6−97.8); Poor 75.4% (64.8−85.9).
PSA Relapse: 110 patients have had a PSA relapse. The actuarial rates were 6.0%, 21.1%, 34.5%, 44.7% and 48.8% at 1, 2, 3, 4 and 5 years, respectively. The 5-year relapse rate was 22.8% for the good prognosis group, 44.2% for the intermediate prognosis group and 71.0% for the poor prognosis group.

PSA relapse 5 years

Group	Relapse	95% CI
Overall	48.8%	41.6−55.9
Prognostic group		
Good	22.8%	8.9−36.7
Intermediate	43.2%	32.9−53.5
Poor	71.0	59.8−82.3

Discussion: Overall PSA relapse free survival and overall survival is poorer in this series compared to other series using longer fractionation. It is likely that the hypofractionated dose used may be too low (equivalent dose in 2 Gy fractions is 61.9 Gy if α/β ratio is 1.5). The use of neoadjuvant hormones does not seem to compensate for this low dose.
Compared to the Canadian study (Lukka et al) that used the same dose fractionation in one arm but without neoadjuvant hormone treatment, our results are worse [their PSA relapse rate (defined by Houston criteria) at 5 years was 42%, ours is 49%]. The Gleason score were similar in both studies (60% had Gleason $\leqslant$6) though mean PSA was less in Canadian study (10.6 vs 23.6).
The margins in the Canadian study were larger (1.5 cm compared to 1 cm anteriorly and laterally) and (1 and 0.6 cm posteriorly) respectively. Also all the patients were CT planned in the Canadian study, whilst only 30% were CT planned in our series in this time period. These differences and the higher average PSA may explain the lack of improvement in our series despite the addition of neoadjuvant hormone treatment.
Conclusion: The results of this series are not as good as other published results and we have subsequently increased our radiotherapy dose to 55 Gy in 20 fractions. We also now CT plan all radical prostate patients.

4059 POSTER

Confirmation of proton beam by positron emission tomography apparatus in patients with prostate cancer

M. Shimizu[1], R. Sasaki[2], D. Miyawaki[3], H. Nishimura[2], Y. Demizu[3], T. Akagi[4], D. Suga[1], M. Murakami[3], K. Sugimura[2], Y. Hishikawa[3]. *[1]Hyogo Ion Beam Medical Center, Radiation Technology, Hyogo, Japan; [2]Kobe University Graduate School of Medicine, Radiology, Hyogo, Japan; [3]Hyogo Ion Beam Medical Center, Radiology, Hyogo, Japan; [4]Hyogo Ion Beam Medical Center, Medical Physics, Hyogo, Japan*

Background: Proton therapy is promising and sophisticated treatment modalities against prostate cancer and other malignancies. The proton-irradiated area can be confirmed by coincidence detection of pair annihilation gamma rays from positron emitting isotopes generated by nuclear reaction of irradiated proton nuclei and nuclei in the irradiation target, called autoactivation. Thus, the purposes of this study are to investigate which positron emitting isotopes are detected in our clinical settings, and to evaluate whether anatomical or physiological factors affected or not in patients with prostate cancer treated with proton therapy.
Methods and Materials: Autoactivation data were evaluated in thirty patients treated with 210 MeV proton beam to a fraction dose of 2 Gy equivalent (GyE). Those patients were received totally 74 GyE. Doses were calculated on the basis of the pencil beam algorithm. Beam parameters including width of spread-out Bragg peak (SOBP) and degrader thickness were adequately selected with 3D treatment-planning system. Calculation of radioactivity induced by the autoactivation started at 5 min after proton irradiation for 10 min by using a PET apparatus and a vendor-provided software for interpreting image data. Regions of interest were set in following 5 portions; PTV center, urinary bladder within PTV, urinary bladder outside PTV, rectum (outside PTV), and contra-lateral femoral head (outside PTV). Experimentally, 6 GyE of proton beam was irradiated to following materials containing certain percentage of several target nuclei for positron emitting: Tough water phantom (^{12}C, ^{16}O), charcoal (^{12}C), blood sample (^{12}C, ^{16}O). Diffusion effect of water in the autoactivation was compared to that of ice-block ($20\times20\times20$ cm^3) both with setting a 6 cm width of SOBP.
Result: Isodose curve (95%) and distribution of the autoactivation were well-matched in terms of beam range in axial image of PTV center level in all patients. However, in sagital and coronal image, and axial image of bladder level, the autoactivation spread out of 95% of the isodose curve. Mean calculated radioactivities in those 30 patients with prostate cancer were 39 Bq in PTV center, 36 Bq in urinary bladder within PTV, 19 Bq in urinary bladder outside PTV, 4 in rectum (outside PTV), and 2 in contra-lateral femoral head, respectively. From this result, urine in the urinary bladder seemed to be a major diffusion mediator of autoactivation after the proton irradiation. In our experimental setting and time point, the major