(SUV) were compared using linear-mixed modeling at baseline and at four weeks after RT for target and non-target lesions.
Results: Eleven patients were eligible for analysis. There were 13 target lesions (two irradiated target lesions in two patients) and 12 non-target lesions (treated with sorafenib alone). Two patients experienced severe toxicity: one developed hand-foot syndrome and another died during treatment from unrelated causes. There were no severe side effects directly attributable to the combination of RT and sorafenib. The BPI mean 'present' pain scores at baseline, 7 weeks and 12 weeks were 3.9, 1.6, and 1.6 respectively ($p = 0.07$ for 7 weeks vs. baseline; $p = 0.13$ for 12 weeks versus baseline). There was a significant difference in the metabolic response of target lesions versus non-target lesions ($p=0.002$). For target lesions, SUV decreased after RT and sorafenib ($p=0.003$). However, for non-target lesions, there was a trend towards an increase in SUV ($p=0.09$). Only two patients required re-irradiation of a previously treated index lesion. Seven other patients required subsequent RT for symptomatic progression of previously untreated lesions.
Conclusions: The combination RT and sorafenib is feasible and well tolerated as a treatment for palliation of painful bone metastases in patients with metastatic RCC. Both the re-treatment and PET results suggest that RT provides additional palliative benefit in this patient population and should be considered even in those receiving tyrosine-kinase inhibitors like sorafenib.

OC-0050
Linac based SBRT for prostate cancer in 5 fractions: Preliminary report of a Phase II study with FFF delivery
F. Alongi[1], C. Iftode[1], S. Arcangeli[1], E. Villa[1], L. Liardo[1], A. Tozzi[1], P. Mancosu[1], S. Tomatis[1], L. Cozzi[2], M. Scorsetti[1]
[1]*Istituto Clinico Humanitas Cancer Center, Radiotherapy and Radiosurgery, Rozzano (Milan), Italy*
[2]*IOSI, Phyisics, Bellinzona, Switzerland*

Purpose/Objective: End point of the present study is to evaluate the technical feasibility and early side effects of a short course hypofractionated high dose LINAC based SBRT delivered with Flattened Filter Free (FFF) beams, and SpaceOAR as a spacer between rectum and prostate.
Materials and Methods: This is a prospective phase-I-II pilot feasibility study, started on February 2012. Inclusion criteria were: age ≤ 80 years, WHO PS ≤ 2, PSA ≤ 20 ng/ml, histologically proven prostate adenocarcinoma(risk of microscopic nodal involvement ≤ 15%), T1-T2 stage, no distant metastases, no previous prostate surgery other than TURP, no malignant tumours in the previous 5 years, IPSS 0-7. The schedule was 5 x 7 Gy = 35 Gy, delivered in 5 alternative days (NTD2 between 70 and 85 Gy for an α/ß between 3 and 1.5 Gy, respectively). SBRT was delivered using the volumetric modulated arc technique by RapidArc, with photon beam energy of 10 MV FFF (Filter Flattening Free) and maximum dose rate of 2400 MU/min. Physical examinations and toxicity assessments were performed during and after SBRT according to CTCAE v4.0 toxicity scale. EPIC questionnaires were used for Quality of Life assessing. Tumour response was evaluated on ASTRO PHOENIX definition (+2 from Nadir of PSA). Neo-adjuvant/concomitant hormonal therapy was prescribed based on the risk according to NCCN classification. SpaceOAR was implanted by intraperineal injection as a spacer to enlarge the minimum distance between prostate and anterior rectal wall. The SpaceOAR implant was optional and based on clinician decision for each case.
Results: With a median follow-up of 6 months(1-9),40 patients were treated with this schedule and were evaluable for the current analysis. 34/40 patients were officially recruited in the protocol and met perfectly all inclusion criteria. Other 6/40 'out of trial' were treated with the same protocol. In the trial, according to NCCN criteria, 21/34 patients were low-risk and 12/34 were Intermediate risk. Median Age was 69.6(56-80), median initial PSA was 6.33 ng/ml(range:0.50-12 ng/ml). Median Gleason score was 6.33(6-7). Median treatment duration was 11.8 days(9-22). All patients completed the treatment as programmed. Acute Toxicities were as follow: Rectum G0 in 21/34 cases(62%), G1 in 11/34(33%); G2 in 2/34(5%). Genito-urinary G0 in 15/34 cases(45%), G1 in 7/34(20%), G2 in 12/34(35%). In two G2 urinary retention cases, the placement of intermittent catheter was needed(in both cases prostate dimension was superior than100cc). No acute G3-5 was found in the trial and 'out of trial'patients. Median treatment time was 109 seconds(63-124). SpaceOAR was implanted in 9 patients with a single case of rectal fascia infection resolved with antibiotics. During Follow-up, PSA reduction was documented in all treated patients.
Conclusions: Our early findings suggest that LINAC based SBRT FFF treatment for prostate cancer in 5 fractions is feasible, fast and well tolerated in acute setting for the first 40 treated patients. Longer follow-up is needed for definitive assessment of late toxicity and clinical outcome.

OC-0051
GU outcomes & toxicity 5 years after protons for low- & intermediate-risk prostate cancer: Two prospective trials
R. Henderson[1], B.S. Hoppe[1], W.M. Mendenhall[2], R.C. Nichols[1], Z. Li[1], Z. Su[1], C.G. Morris[1], C.R. Williams[2], J. Costa[2], N.P. Mendenhall[1]
[1]*University of Florida Proton Therapy Institute, Radiation Oncology, Jacksonville, USA*
[2]*University of Florida, Urology, Jacksonville, USA*

Purpose/Objective: To assess urinary (GU) function and toxicity in patients treated with image-guided proton therapy (PT) for early- and intermediate-risk prostate cancer and to analyze the impact of pretreatment urinary obstructive symptoms on urinary function after PT.
Materials and Methods: Two prospective trials accrued 171 prostate cancer patients from August 2006 to September 2007. Low-risk patients received 78 cobalt gray equivalent (CGE) in 39 fractions and intermediate-risk patients received 78 to 82 CGE. Median follow-up was 5 years. The International Prostate Symptom Score (IPSS) and GU toxicities (per CTCAE v3.0 and v4.0) were documented prospectively.
Results: Five transient GU events were scored Gr 3 per CTCAE v4.0, for a cumulative late GU toxicity rate of 2.9% at 5 years. There were no Gr 4 or 5 events. On multivariate analysis (MVA), the only factor predictive of Gr 2+ GU toxicity was pretreatment GU symptom management ($p=0.0058$).
Patients with pretreatment IPSS of 15-25 had a decline (clinical improvement) in median IPSS from 18 before treatment to 10 at their 60-month follow-up. At last follow-up,18 (54.5%) patients had a ≥ 5-point decline, 14 (42.5%) remained stable, and 2 patients (3%) had a ≥ 5-point rise (deterioration) in IPSS. Patients with IPSS <15 had a stable median IPSS of 6 before treatment and at 60 months.
Conclusions: Urologic toxicity at 5 years with image-guided PT has been uncommon and transient. Patients with pretreatment IPSS of < 15 had stable urinary function 5 years after PT, but patients with 15-25 showed substantial improvement (decline) in median IPSS, a finding not explained by initiation or dose adjustment of alpha blockers. This suggests that PT provides a minimally toxic and effective treatment for low and intermediate prostate cancer patients, including those with significant pretreatment GU dysfunction (IPSS15-25).

OC-0052
Late toxicity in the randomized phase III Dutch Hypofractionation Trial for prostate cancer patients (HYPRO).
S. Aluwini[1], F. pos[2], E. Schimmel[3], E. van Lin[4], A. krol[5], P.P. van der Toorn[6], H. de Jager[7], M. Dirkx[1], W. Ghidey[8], L. Incrocci[1]
[1]*Erasmus Medical Center Rotterdam, Radiation Oncology, Rotterdam, The Netherlands*
[2]*Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Radiation Oncology, Amsterdam, The Netherlands*
[3]*Institute for Radiation Oncology, Radiation Oncology, Arnhem, The Netherlands*
[4]*University Medical Centre Nijmegen, Radiation Oncology, Nijmegen, The Netherlands*
[5]*Leiden University Medical Centre, Radiation Oncology, Leiden, The Netherlands*
[6]*Catharina Hospital Eindhoven, Radiation Oncology, Eindhoven, The Netherlands*
[7]*Radiotherapy Centre West, Radiation Oncology, The Hage, The Netherlands*
[8]*Erasmus MC- Daniel den Hoed Cancer Centre, Department of Trial and Statistics, Rotterdam, The Netherlands*

Purpose/Objective: Accumulating evidence demonstrates the sensitivity of prostate cancer to fractionation, estimating a low α/ß ratio. This suggests a significant therapeutic benefit of hypofractionation, delivering a higher biological dose to the prostate without increasing toxicity. To test this hypothesis a randomized multicenter phase III Hypofractionation Trial was performed in The Netherland. Here we report on the first results of late toxicity.
Materials and Methods: Between April 2007 and January 2011, 820 men with localized prostate cancer were included. They were randomly assigned to a standard fractionation (SF) arm of 39x2 Gy (5 fractions a week), or a hypofractionated (HF) arm of 19x3.4 Gy (3 fractions a week). Primary endpoints were relapse-free survival (RFS) and toxicity scores. The late toxicity scores were measured twice a year after finishing the radiation course (RC) using RTOG/EORTC criteria. The highest grade scored in the follow-up was considered. Analyses were done based on the intention to treat.
Results: To each fractionation arm 410 patients were randomly assigned. The median follow-up was 27 months (range 2.3-57 months). A grade ≥ 2 late gastrointestinal toxicity (GI) after finishing the RC was reported by 15% of the patients treated with SF and by 20% of the

patients treated with HF, respectively (*p=0.154*). Grade ≥ 2 late genitourinary (GU) toxicity was experienced by 41% and 43% of patients treated with SF and HF, respectively (*p=0.532*).
From 3 months after RC, only 2% of patients experienced a grade 3 late GI toxicity in the SF arm versus 1% in the HF arm (*p=0.337*). Grade 4 late GI toxicity was reported in 1 patient in the SF arm versus 4 patients in the HF arm *(p=0.373*). Late GU grade 3 toxicity was reported by 9% and 14% in the SF- and HF arm, respectively (*p=123*). No grade 4 late GU toxicity was reported in the SF arm versus 1 patient in the HF arm.
A multivariable analysis evaluating the effect of age, PSA, Gleason-score, T-stage, use of hormonal therapy, previous TURP, smoking and the presence of acute GI/GU toxicity showed that only the presence of acute toxicity significantly increased the risk of developing late GI toxicity (*p=0.000*) . For the late GU toxicity, the age >70 (*p=0.001*), the presence of acute GU toxicity (*p=0.000*) and smoking (*p=0.046*) were significant factors increasing the risk of developing late GU toxicity.
Conclusions: Our initial results on late toxicity, after a median follow-up of 27 months, show that the hypofractionated treatment is well tolerated. No significant differences in late GI and GU toxicity were observed compared to the standard fractionation arm. The presence of acute GI and GU toxicity were significant prognostic factors for late toxicity. Age and smoking were significant prognostic factors for late GU toxicity as well.

OC-0053
Factors predicting Grade 3-4 late urinary toxicity in 1176 patients treated with post-prostatectomy irradiation.
C. Cozzarini[1], C. Fiorino[2], C. Deantoni[1], F. Zerbetto[1], B. Noris Chiorda[1], M. La Macchia[1], A. Briganti[3], N. Suardi[3], F. Montorsi[3], N. Di Muzio[1]
[1]*San Raffaele Scientific Institute, Radiotherapy, Milano, Italy*
[2]*San Raffaele Scientific Institute, Medical Physics, Milano, Italy*
[3]*San Raffaele Scientific Institute, Urology, Milano, Italy*

Purpose/Objective: Moderate dose escalation and hypofractionation (HYPO) have a possible role in the postprostatectomy (POSTOP) setting, both adjuvant (ADV) and salvage (SALV). This analysis focused on possible clinical and physico-dosimetric predictors of most severe (Grade ≥3) genitourinary toxicity (GU TOX) after POSTOP RT for prostate cancer (PCa).
Materials and Methods: A cohort of 1176 consecutive patients (pts) was submitted to POSTOP ADV (n=804) or SALV (n=372) RT between 1993 and 2010 in a single Institution with conventionally fractionated (CF, 1.8 Gy/fraction, fr) non conformal (NC, n=169), 3DCRT (n=657) or IMRT (n=103) technique, or moderately HYPO (median 2.50 Gy/fr) helical Tomotherapy (n=247). The whole-pelvis (WP) was irradiated in 345 pts. The median dose to the prostatic bed and WP was 70.2 Gy and 50.4 Gy, respectively, in the CF group. For the HYPO group, 3 cohorts were identified: 116 treated at a median of 65.8 Gy (2.35 Gy x 28), 76 at 71.4 Gy (2.5-2.6 x 28) and 49 at 58 Gy in 20 Gy. In the HYPO group the most common WPRT schedule was 51.8 Gy/28 fr. Total doses were also converted in biological equivalent doses (BED) following the linear quadratic model (LQ) taking a/b = 3 or 5. We focused on Grade ≥3 toxicity, retrospectively graded according to CTCAE v 4.0.
Results: After a median follow-up of 95 months (60 for HYPO), 121 pts experienced Grade 3 late TOX (57 urethral or bladder neck strictures requiring interventions ± 49 severe urinary incontinence onset/worsened after RT ± 25 gross haematuria) and 5 underwent cystectomy (Grade 4). Patients were grouped in 3 classes, according to the dose/fr received: A=1.8-2.0 Gy, B=2.3-2.4 Gy, C=2.5-2.9 Gy. At univariate analysis, the 5-year risk of TOX G≥3 was predicted by fractionation (7% vs 15% vs 21% for groups A, B and C, respectively, p<0.0001), acute Grade ≥2 TOX (18% vs 8%, p=0.0001) and use of anti-hypertensives (HYPERT, 12% vs 7%, p=0.04). At multivariate analysis (MVA) the only predictive covariate of Grade≥3 TOX in the overall population was acute Grade ≥2 TOX (HR 2.49, p=0.0002), while fractionation (p=0.06) and HYPERT (p=0.09) were found to be of only borderline significance. In the HYPO subgroup, the only significant variable at MVA was HYPERT (HR 8.15, p=0.008). Overall, BED was not predictive.
Conclusions: This is the largest data set focusing on the impact of different doses and fractionations on severe GU toxicity after POSTOP RT for PCa, suggesting the existence of an important 'consequential' component for the onset of severe late GU toxicity, and an important role of HYPERT. Moreover, the impact of an increased daily dose effect (from 1.8-2 to 2.3-2.9 Gy/fr) is completely inconsistent with the linear-quadratic model, suggesting that HYPO exacerbates severe GU TOX far more than would be expected from BED calculation. This effect may suggest an increased incomplete repair effect of the urothelium, possibly enhanced by the previous surgery.

JOINT SYMPOSIUM: ESTRO-CARO: MANAGEMENT OF LUNG OLIGO-METASTATIC DISEASE

SP-0054
Management of lung metastases: Stereotactic body radiotherapy as a non-invasive option
M. Guckenberger[1]
[1]*University Hospital Würzburg, Department of Radiation Oncology, Würzburg, Germany*

Based on prospective trials, stereotacticbody radiotherapy (SBRT) has become the standard of care for early stage non-small cell lung cancer (NSCLC): high accuracy of the whole radiotherapy work-flow allowed safe delivery of escalated irradiation doses, which significantly improved local tumor control and overall survival compared to conventionally fractionated radiotherapy. Local surgical treatment of oligo-metastatic lung and / or liver lesions has shown promising long term overall survival with cure in a proportion of the patients and these results were the rational for exploring the role of SBRT in the setting of pulmonary metastases. Until today, several prospective trials have investigated safety and efficacy of SBRT in this metastatic setting. The majority of the studies limited the number of treated pulmonary lesions or lesions anywhere in the body to 3 – 5 and SBRT irradiation doses were similar to experiences in SBRT for stage I NSCLC, mostly higher than 100Gy BED. However, lesions were rather small in the majority of the studies and risk-adapted fractionation with larger number of treatment fractions and lower total doses are recommended in the situation of multiple large-volume disease. Integration of SBRT into systemic chemotherapy is still poorly investigated but the majority of the studies did not allow simultaneous chemotherapy and recommended a chemotherapy-free interval of several weeks prior to and after SBRT. Clinical outcome of SBRT for pulmonary metastases is promising with toxicity grade >2 of <10%: radiation induced pneumonitis and chest wall pain were the most frequently observed toxicities. Local tumor control was consistently achieved in 80-90% of the patients. Despite the majority of the patients developed progressive systemic disease, long term overall survival was observed in a similar proportion of the patients as in the surgical series. Despite these promising results, a better understanding of how to select patients, which benefit most from this local treatment, is warranted. Additionally, the combination of SBRT with concurrent chemotherapy and targeted therapy is poorly investigated. Finally, endpoints other than overall survival like prolonging a chemotherapy-free interval with improved quality-of-live are worth to evaluate in future prospective trials.

SP-0055
Surgery in pulmonary oligometastases
P. Granone[1]
[1]*Università Cattolica del Sacro Cuore, Surgery, Rome, Italy*

Resection of pulmonary metastases is commonly performed in patients whose primary disease is controlled. Lung metastases from a primary extra pulmonary malignancy are often a manifestation of widespread dissemination; however, some patients have no other evidence of disease. The largest number of solitary metastases survivors had metastases primarily in the lung and/or liver. With innovations in molecular imaging and advances in molecular oncology, the stage is set to detect truly solitary metastases early.Then, aggressive treatment by surgical excision, stereotactic body radiosurgery, targeted chemotherapy, or immunotherapy could eradicate the lesion. A broader staging system is recommended to encompass a solitary metastasis(M1) and oligometastases (M2) as distinct from multiple metastases (M3). Even if nonresectional therapies such as radio frequency ablation and stereotactic body radiation therapy are being used in centers for patients with oligometastases to the lungs, extensive experience with pulmonary metastasectomy in a number of different cancers has confirmed that resection can substantially prolong survival and cure some patients. Based upon these observations, aggressive resection of isolated pulmonary metastases has become a widely accepted treatment for appropriately selected patients. In addition, technological improvements in radiological screening of pulmonary metastases and thoracoscopic resection are fundamentally altering the management of these patients and their surgery. Despite high resolution computed tomography scan and positron emission tomography-computed tomography remain the preferred imaging modalities for pulmonary metastases, the sensitivity of the technique is 100% for lesions larger than 1 cm, but it decreases according to the size of the metastases (<5 mm). Indeed, there is a real problem of missing small metastatic lesions in the video-assisted thoracic surgery approach; complete manual