

respectively. Figure 1 demonstrates relative survival by grade, extent of LN dissection, and radiotherapy treatment.

Conclusions: Despite guidelines recommending adjuvant RT for women with endometrial carcinoma with cervical involvement, more than 25% of patients received no adjuvant RT. Vaginal brachytherapy, either alone or in combination with pelvic EB, appears to be an important component of adjuvant treatment.

OR31 Presentation Time: 9:12 AM

The Impact of Smoking on Recurrence and Survival in Locally Advanced Cervical Cancer Treated with Radiation and Brachytherapy

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Purpose: We examined the effects of smoking on cervical cancer recurrence and mortality in patients undergoing radiation and brachytherapy for locally advanced cervical cancer.

Materials and Methods: Between July 2007 and September 2013, 96 patients received definitive treatment of locally advanced cervical cancer through external beam radiation therapy (EBRT) and chemotherapy and brachytherapy. A retrospective chart review was conducted to determine patient, treatment and tumor characteristics. Smoking habits were quantified based on the number of packs smoked per day multiplied by the number of years the patient smoked (pack-years). Time to event endpoints of pelvic control, disease-free survival (DFS) and overall survival (OS) were analyzed by patient and disease characteristics using multivariable Cox proportional hazards models.

Results: The study population consisted of 96 patients with an average age of 54.8 years (range, 27-91 years). Smoking history included 51 (53.1%) patients with no history of smoking, 20 (20.8%) patients with one to twenty pack-years, and 25 (26%) patients with twenty-one or more pack-years. The impact of 1 to 20 pack-years smoking history on pelvic control, DFS, and OS relative to nonsmokers was hazards ratio 1.48 (CI:0.79-2.77; P=0.226), 5.00 (CI:1.09-23.1; P=0.039), and 4.73 (CI:1.17-19.9; P=0.029, respectively. For patients with 21 or over pack-years smoking history, the impact on pelvic control, DFS, and OS was hazards ratio 0.91 (CI:0.47-1.75; P=0.772), 9.70 (CI: 2.35-40.0; P=0.002), and 4.98 (CI:1.14-21.8; P=0.033), respectively.

Conclusions: In the era of brachytherapy dose and treatment intensification strategies to improve upon cervical cancer outcomes, our study showed that smoking increases the risk of cancer recurrence and mortality. Patients who have smoked a higher number of pack-years are at increased risk of recurrence and mortality compared to those who smoked less. Intensive clinical emphasis on smoking cessation is being devised and implemented.

OR32 Presentation Time: 9:21 AM

Do Women Undergoing Image-Guided Brachytherapy Need an MR on Every Fraction?

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Purpose: Image-guided brachytherapy provides an opportunity to improve the therapeutic ratio in women being treated for cervical cancer with definitive radiation therapy. MR guidance however is a logistic challenge in many departments, and often only a single planning MR is available. It is uncertain if this has any effect of the overall implant quality when compared to a course where an MR is obtained on every fraction. Our

purpose is to compare simulations of a brachytherapy course based on a single MR to courses where MRs were available for all fractions.

Materials and Methods: Women treated with tandem and ovoid or ring brachytherapy from 2011-2013 for cervical cancer were identified, in whom a planning MR was obtained on every fraction. The dose from this "MR optimized course" was captured for the HRCTV (D90 and D98), the IRCTV (D90), and OARs (bladder, rectum, sigmoid, and bowel, calculated to D2cc). Two simulated courses were then developed. The dwell positions from the first MR guided fraction were applied to the later fractions without any edits to define a "single plan course." A "CT optimized course" was then created by developing new plans using only CT OAR anatomy from the latter fractions, with the HRCTV fused from the first fraction. If the applicator was changed, both simulations assumed that a new MR based plan would be developed with the new applicator. Doses were then calculated for the MR based HRCTVs and OARs: both simulations were compared to the MR optimized course via a two tailed Wilcoxon signed rank test for each fraction and for the entire course. Doses were converted to the equivalent dose at 2Gy per fraction (EQD2) via the BED equation ($\alpha/\beta = 10$ for target, and 3 for normal tissue).

Results: Ten women were identified; each undergoing 5 fractions of MR guided brachytherapy after 45Gy external beam with weekly cisplatin. There was no systematic deviation in the D90 or D98 dose to HRCTV in either simulated course (p>0.59 for all comparisons). The median single plan HRCTV D90 fraction was 103% of the MR optimized fraction (IQR 86-116, p=0.62); median CT optimized fraction HRCTV D90 was 100% of the MR optimized fraction (IQR 94-100, p=0.64) The IRCTV D90 was slightly lower in the CT-optimized course in fraction to fraction comparison (CT-optimized fractional dose median was 95% of the MR-optimized course, IQR 85-102%, p=0.023). Fractional doses to the rectum, sigmoid and bowel were significantly lower with the CT-optimized plan as a percent of the MR-optimized plan (Rectal D2cc 94%, IQR 71-107, p=0.037; Sigmoid 92%, IQR 78-103, p=0.022; Bowel 88%, IQR 82-100, p=0.002). 2/10 single plan courses were borderline for our clinical constraints, with HRCTV D90 of 81 and 80Gy (given a goal of D90>85Gy), and 1/10 of the CT-optimized plans (D90 83.7Gy). All OAR constraints were met in all simulated courses, though 1/10 single plan course did approach the upper rectal limit (D2cc = 74.9Gy), where both the MR-optimized (D2cc = 69.2Gy) and CT-optimized (D2cc = 69.8Gy) were under a 70Gy constraint.

Conclusions: Using a single MR-based plan on subsequent fractions resulted in clinically similar doses to organs at risk and targets in most cases. Use of CT-optimization improved on these results, both in coverage of HRCTV and sparing of OARs. This finding is reassuring for practices in which obtaining an MR with the applicator in place presents significant challenges, and may allow for improved efficiency in practices which obtain a new MR on each fraction.

PROSTATE ORAL I Friday, April 4, 2014 8:00 AM - 9:30 AM

OR33 Presentation Time: 8:00 AM

PSA Outcomes in a Single Institution, Prospective Randomized ¹³¹Cs/¹²⁵I Permanent Prostate Brachytherapy Trial

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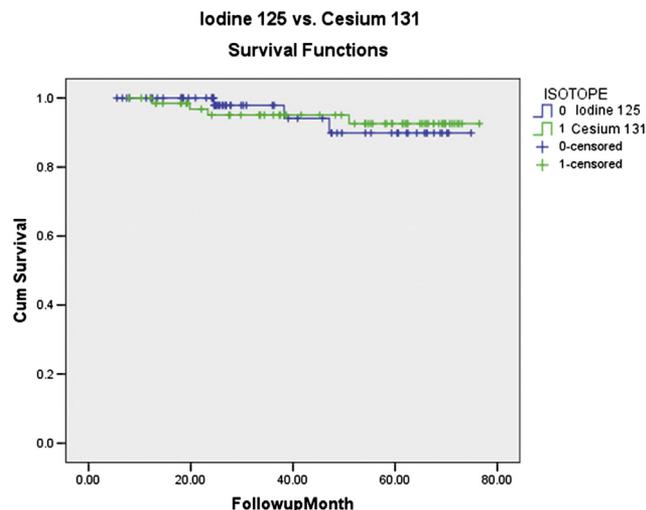
Purpose: To evaluate biochemical (PSA) outcomes in a prospectively enrolled group of patients diagnosed with low- to intermediate-risk, localized prostate cancer randomized to undergo permanent iodine-125 (I-125) or cesium-131 (Cs-131) brachytherapy.

Materials and Methods: One-hundred forty patients were randomized by random number assignment to I-125 (n=71) or Cs-131 (n=69) monotherapy. Patients were treated to a minimum prostatic dose of 144 Gy for I-125 and 115 Gy for Cesium-131. Sources were delivered via a pre-planned, template-based, pre-loaded needle technique. Biochemical relapse-free survival (BRFS) was estimated using the Kaplan-Meier

method with the Phoenix definition (nadir plus 2 ng/mL) was used to identify failures. PSA failure times were assigned “at call.”

Results: Low-risk patients made up 81.4% of the overall group while 18.6% were intermediate risk. There was no difference in risk composition between the isotopes used. A total of 833 serum PSA measurements were obtained on the 140 patients (6 per patient). Median followup was 38.5 months. At five years, BRFS was 89.8% for the I-125 group and 92.6% for the Cs-131 group, log rank $p=0.976$ (Figure 1).

Conclusions: Permanent, low-dose-rate brachytherapy provides excellent PSA-based outcomes for low to intermediate risk patients. No significant difference in BRFS between these two isotopes has been detected at this point in followup.



OR34 Presentation Time: 8:09 AM

Continued Benefit to Local Control Even in Very High-Risk Prostate Cancer

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Purpose: Recent patterns of failure analyses have suggested that even following dose-escalated external beam radiation therapy and androgen deprivation therapy (ADT) that the predominant mode of failure after radiation for high-risk prostate cancer is still local within the prostate. It is possible that as the risk for systemic spread increases, however, that local control may be less important. Therefore, we set out to report treatment outcomes in patients with very high-risk prostate cancer (VHRPC) (as defined as multiple high-risk features). In this retrospective analysis we compared clinical outcomes in those treated with combined modality radiotherapy with LDR boost as compared to dose-escalated external beam radiotherapy to identify if even in the presence of multiple high-risk features is there a potential benefit to further radiation dose-escalation.

Materials and Methods: We conducted a retrospective multi-institutional review of patients with VHRPC (those with at least 2 high-risk factors of prostate-specific antigen >20 ng/mL, Gleason score 8-10, or clinical T3-T4 stage), treated with either dose-escalated external beam radiotherapy (EBRT, minimum prescription dose 75 Gy with median 78 Gy) or combined-modality radiotherapy (CMRT) consisting of pelvic irradiation (median 45 Gy) and permanent interstitial brachytherapy. Patients were treated at either The University of Michigan Medical Center and affiliated clinics or The Schiffler Cancer Center. Biochemical progression-free survival (BPFS) was assessed using the nadir +2 definition with other

end-points including distant metastasis free survival (DMFS) and prostate cancer specific mortality (PCSM). Outcomes were analyzed by the Kaplan-Meier method and Fine and Gray cumulative incidence analysis.

Results: Two hundred thirty-eight patients with VHRPC were identified. 69% received EBRT and 31% CMRT. Eighty-eight percent received androgen-deprivation therapy (ADT), 56% for ≥ 24 months (long-term ADT). The majority (69%) of patients were >65 -years old, and were less likely to receive CMRT than younger patients (25% vs. 43%, $p=0.006$), although older men did not differ from younger patients in tumor characteristics. Median followup was 61 months (interquartile range, 38-93 months). BPFS, DMFS and PCSM for all patients at 8-years were (\pm standard error): $50.6\pm 4.7\%$, $68.5\pm 4.3\%$, $78.7\pm 3.8\%$, respectively, and were similar for patients \leq vs. >65 -years old (BPFS: HR 0.88, $p=0.56$; DMFS: HR 0.79, $p=0.40$; PCSM: HR 0.99, $p=0.99$). After adjustment for patient, tumor, and treatment-related covariates on multivariate Fine and Gray cumulative incidence analysis, even in patients with VHRPC, CMRT was associated with improved BPFS (HR 0.41 (95%CI:0.22-0.75), $p=0.004$) and with a trend for improved DMFS (HR 0.49 (95%CI:0.23-1.04), $p=0.063$) with less impact upon PCSM (HR 0.61 (95%CI:0.25-1.47), $p=0.21$). After controlling for clinical risk-features and RT treatment long-term ADT was independently associated with improved BPFS (HR 0.40, $p=0.019$), DMFS (HR 0.20, $p=0.002$) and PCSM (HR 0.25, $p=0.004$).

Conclusions: When compared to dose-escalated EBRT the use of CMRT with ADT resulted in favorable clinical outcomes for patients with VHRPC independent of age. Even in men with multiple high-risk features CMRT resulted in a significant improvement over dose-escalated EBRT and long-term ADT and thus should be considered a viable treatment option. These results support the conclusion that local failure continues to be an issue following dose-escalated EBRT for VHRPC and provide rationale for further clinical investigation of CMRT even in men with multiple high-risk features.

OR35 Presentation Time: 8:18 AM

Favorable Long-Term (10-15 Year) Results with High-Dose-Rate Brachytherapy for Prostate Cancer

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Purpose: There are numerous definitive treatments available for prostate cancer patients. Modality selection can be challenging for both the patient and their doctors. High-dose-rate (HDR) brachytherapy has been used extensively as a boost after external beam radiation therapy, but is increasingly being tested as monotherapy. We report our long-term results for HDR-monotherapy in patients with low- and intermediate-risk prostate cancer.

Methods and Materials: Patients ($n=321$) with a median age of 64 (42-90) years with low- ($n=218$) and intermediate-risk prostate cancer ($n=103$) treated at the California Endocurietherapy (CET now at UCLA) between 1994 and 2008 were analyzed. Median HDR-monotherapy dose prescription was 43.5 (35-46.5) Gy in 6 (4-9) fractions. Presenting disease characteristics were median iPSA 6.1 (0.2-17.6) ng/mL, Gleason Score ≤ 6 80% and 7 20%, median prostate volume 33 cc, androgen deprivation therapy was administered in 12% for a median of 4 months. Risk groups were defined according to the NCCN guidelines. Sustained PSA nadir+2 was used to define biochemical relapse. Statistical analyses performed were Kaplan-Meier analyses and univariate and multivariate Cox proportional analyses.

Results: The median overall followup time was 6.75 (0.5-15.25) years; the median followup time for low- and intermediate-risk patients was 7 years and 5.6 years. The 5-, 10- and 15-year overall survival (OS) rates were 93%, 77% and 66%, respectively. The median OS, distant metastases-free (DMFS), clinical progression-free (PFS) and biochemical progression-free survival (BPFS) times were not reached. The overall 10 year DMFS, CPFS and BPFS were 99%, 99% and 97%. Low-risk BPFS results at 5, 10 and 15 year were 98%, 98%, and 98%. Intermediate-risk BPFS at 5 and 10 years were 97% and 93%. Univariate Cox analysis for BPFS was