The Declining Use of Brachytherapy Boost for Prostate Cancer Despite Associated Survival Advantage
Scott M. Glaser, MD\textsuperscript{1}, Goundappa K. Balasubramani, PhD\textsuperscript{2}, Ronald M. Benoit, MD\textsuperscript{3}, Ryan P. Smith, MD\textsuperscript{4}, Sushil Beriwal, MD\textsuperscript{1}.
\textsuperscript{1}Radiation Oncology, University of Pittsburgh Cancer Institute, Pittsburgh, PA, USA, \textsuperscript{2}Epidemiology, University of Pittsburgh School of Public Health, Pittsburgh, PA, USA, \textsuperscript{1}Urology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

\textbf{Purpose:} Dose-escalated external beam radiotherapy (DE-EBRT) has been demonstrated to improve outcomes in men with intermediate-high risk prostate cancer. Brachytherapy represents the optimal modality for conformal dose escalation. A recent randomized trial demonstrated an improved biochemical-failure free survival in men who received EBRT plus a brachytherapy boost (BB) compared to DE-EBRT. 

\textbf{Materials and Methods:} We queried the National Cancer Data Base from 2004-2013 and identified 113,719 men with non-metastatic, non-operative, intermediate-high risk prostate cancer who were treated with EBRT+BB (44-54 Gy of EBRT followed by a brachytherapy boost) or DE-EBRT (75.6-81 Gy of EBRT at 1.8-2.0 Gy per fraction). We performed univariate analysis of all available factors potentially predictive of receipt of treatment selection for intermediate risk and high risk patients. Significant factors were then entered into a multivariate logistic regression model and factors significant on multivariable analysis were used to generate a propensity score corresponding to likelihood of treatment selection. Likewise, parsimonious survival analysis was conducted both with and without inclusion of the propensity score. Cox-Proportional Hazards modelling was used for the multivariate component of survival analysis and log-rank statistics were used for the univariate portion.

\textbf{Results:} Median follow-up was 54 months (IQR=33-78). Utilization of BB declined significantly over time both in an absolute sense and in relation to use of DE-EBRT. For intermediate-risk patients utilization of BB decreased from 33.1\% (n=1,742) in 2004 to 12.5\% (n=766) in 2013, with a similar decrease for Gleason 3+4 and 4+3. For high-risk patients utilization of BB dropped from 27.6\% (n=879) in 2004 to 10.8\% (n=479) in 2013. On multivariate analysis, factors predictive for preferential use of EBRT+BB boost for both intermediate and high risk patients were: earlier year of diagnosis, younger age, Charlson-Deyo comorbidity score <2, race other than white or black, private insurance, higher residential area median income, treatment at a non-academic facility, geographical location (South for both intermediate and high risk and West for high risk), higher facility volume, higher T stage (except 2C for high risk), PSA ≤ 10, Gleason score (7 for intermediate-risk and 7-8 for high-risk), and primary Gleason pattern of 4; for intermediate-risk higher alone: residential area graduation rate; and for high-risk alone: metropolitan residential setting, increased distance from facility to residence, and no receipt of hormonal therapy. For intermediate-risk patients, unadjusted 5 and 10-yr OS for DE-EBRT vs. EBRT+BB were 87.3\% (95\% CI = 86.9-87.7) vs. 91.6\% (95\% CI = 91.0-92.2) and 58.0\% (95\% CI=56.4-59.6) vs. 71.6\% (95\% CI = 69.4-73.8) respectively (p<0.0005). For high-risk patients, unadjusted 5 and 10-yr OS for DE-EBRT vs. EBRT+BB were 82.0\% (95\% CI = 81.4-82.6) vs. 88.7\% (95\% CI = 87.9-89.5) and 50.4\% (95\% CI = 48.6-52.2) vs. 63.0\% (60.0-66.0) respectively (p<0.0005). On multivariate analysis of factors predictive for survival, this correlated to a HR of 0.71 (95\% CI = 0.67-0.75, p<0.0005) for intermediate-risk patients.
and 0.73 (95% CI = 0.68-0.78, p<0.0005) for high-risk patients. With incorporation of propensity score into the model, HR=0.73 (95% CI = 0.68-0.77, p<0.0005) for intermediate-risk patients and HR=0.74 (95% CI = 0.69-0.79, p<0.0005) for high-risk patients. **Conclusions:** Using a hospital-based national data set, we have demonstrated a concerning decline in the utilization of brachytherapy boost for intermediate and high risk prostate cancer patients. This is especially worrisome as brachytherapy boost is associated with a survival advantage as compared to DE-EBRT on both multivariate analysis and propensity-adjusted multivariate analysis. Furthermore, we have described numerous factors associated with preferential use of brachytherapy boost.

**PP02**

**Presentation Time: 9:09 AM**

**Comparing Academic and Non-Academic Treatment Trends for Unfavorable Risk Localized Prostate Cancer: Are We Prepared to Boost Our Academic Standard?**

Peter F. Orio, DO, YU-Wei Chen, MD, Paul Nguyen, MD.

*Radiation Oncology, Dana Farber/Brigham and Women's Cancer Center, Boston, MA, USA.*

**Purpose:** The Canadian ASCENDE-RT trial randomized men with intermediate and high-risk adenocarcinoma of the prostate to dose-escalated external beam radiation therapy (EBRT) alone versus EBRT plus a brachytherapy boost. Patients receiving a brachytherapy boost had a 50% reduction in PSA progression. Considering this significant result and the recent trends of the decreasing use of prostate brachytherapy in academic centers, we sought to determine how men with identical inclusion criteria to the ASCENDE-RT trial were being treated in academic and non-academic Radiation Oncology centers in the United States. **Material and Methods:** We used the National Cancer Database (NCDB) to identify prostate cancer patients treated with radiation from 2004 through 2012 who met the inclusion criteria of the ASCENDE-RT trial (intermediate/high-risk prostate cancer, excluding patients with PSA >40 or tumor stage T3b/T4). Radiation therapy was categorized as EBRT alone, brachytherapy alone, or EBRT plus brachytherapy. Center types were categorized as academic versus non-academic. The Mantel-Haenszel test was used to investigate the trend for type of radiation modality used over the study period. **Results:** A cohort of 180,303 patients was identified. Of those, 120,372 men (67%) were treated with EBRT alone, 35,503 (20%) with brachytherapy alone and 24,428 (14%) with EBRT plus brachytherapy. Thirty percent of patients were treated at academic and 70% at non-academic centers. There was a steady rise in the use of EBRT in both academic and non-academic Radiation Oncology centers, increasing from 66% and 56% in 2004 to 80% and 71% in 2012, respectively (Figure 1). During this same period there was a steady decline in the use of brachytherapy alone in academic and non-academic centers from 18.7% and 24.8% to 11.6% and 17%, respectively. EBRT plus a brachytherapy boost demonstrated the lowest utilization from 2004 to 2012 in both academic and non-academic centers, declining from 14.8% and 19% to 8% and 11%, respectively (P-value for trend <.0001 for academic and non-academic). Academic centers treated this patient cohort significantly more often with EBRT alone than with EBRT plus a brachytherapy boost (p=x). Figure 1 graphs the utilization rates over time. **Conclusions:** The ASCENDE-RT trial provided level one randomized evidence for a significant improvement in biochemical control of intermediate and high-risk prostate cancer with the use of EBRT plus a brachytherapy boost. Despite this finding, both academic and non-academic Radiation Oncology practices have demonstrated a significant reduction in the use of this superior treatment option over the time period 2004-2012, with the lowest utilization in academic centers, in favor of dose-escalated EBRT alone. As practice patterns shift, the question becomes whether academic centers are prepared to train the next generation of residents in this treatment modality.
Multiparametric MRI Guided Salvage Low Dose Rate Brachytherapy for Locally Recurrent Prostate Cancer - The 15 Year Richmond Experience
Drew Moghanaki, MD, MPH1, Emily Harris, BS2, Alfredo Urdaneta, MD3, Matthew Williams, BS4, Priyanka Kapoor, MS5, Jinxing Yu, MD6, Matthew Schutzer, MD1, Michael Chang, MD1, Michael Hagan, MD, PhD7.

1Radiation Oncology Service, Hunter Holmes McGurie VA Medical Center, Richmond, VA, USA, 2University of Virginia, Charlottesville, VA, USA, 3Radiation Oncology, Virginia Commonwealth University Massey Cancer Center, Richmond, VA, USA, 4Johns Hopkins University, Baltimore, MD, USA, 5Radiation Oncology Service, Virginia Commonwealth University Massey Cancer Center, Richmond, VA,
Purpose: Salvage permanent low dose rate brachytherapy (LDR-BT) has long been offered at our institution with mpMRI guidance for patients who develop locally recurrent prostate cancer following external beam radiotherapy (EBRT) or prior LDR-BT. It was hypothesized that this approach is associated with a delay and/or avoidance of androgen deprivation therapy (ADT) in the majority of patients, and might be associated with only rare occurrences of severe late toxicities. Materials and Methods: As part of a quality improvement project, we reviewed the patient, tumor, and treatment characteristics for all patients who underwent a salvage LDR-BT between 2001-2015 at our institution. All patients had undergone a restaging mpMRI scan with T2-weighted imaging, diffusion weighted imaging, and dynamic contrast enhancement with or without spectroscopy (1.5-Tesla with endorectal coil or 3-Tesla with transabdominal phase array coil). Concerning lesions were biopsied via mpMRI-guidance. Salvage LDR-BT plans were developed to encompass the suspicious regions on the mpMRI images and implanted under anesthesia with either I-125 or Pd-103. Post-implant dosimetry was available for all patients except for two who underwent salvage LDR-BT after prior LDR-BT. Genitourinary and gastrointestinal toxicities were retrospectively coded using CTCAE 4.0. The Kaplan-Meier method was used to estimate the time to re-recurrence, which was defined as the post-LDR-BT PSA nadir + 2 ng/mL, or initiation of ADT. Results: A total of 39 patients were identified with a median follow-up time of 55 months. The median age at relapse was 72 (range: 52-91). The initial course of radiotherapy had been EBRT, LDR-BT, or a combination in 77%, 15%, and 8%, respectively. The median time from initial radiotherapy to salvage LDR-BT was 80 months (range: 22 - 156 months). The median rPSA and rPSA doubling times were 5.8 ng/mL (range: 1.2-26.4 ng/mL) and 18.1 months (range: 1.9-36.3 months), respectively. Restaging biopsies with mpMRI guidance were performed in 33 patients and identified Gleason’s score (GS) 8-10, GS 7, GS ≤6, PIN and benign changes in 39%, 33%, 6%, 12%, and 9%. Following salvage LDR-BT, the PSA response rate was 100%. The K-M adjusted freedom from re-recurrence was 46% at 55 months. All failures occurred between 3-44 months with a median time to failure of 21.9 months. Four patients developed grade 3 toxicities (incontinence = 2; rectal ulcer = 2). There were no grade 4-5 toxicities. Two patients developed metastasis at 55 and 98 months. Among 13 deceased patients, 1 died as a result of relapse, 5 with recurrence but not from relapse, and 7 died without relapse. Conclusions: Nearly half of all patients who underwent mpMRI-guided salvage LDR-BT had long-term PSA control and avoided ADT. This likely improves patient health, but its impact on metastases, prostate cancer mortality, and overall survival cannot be determined from this retrospective study. Improved ultrasound imaging, planning techniques, and the introduction of injectable rectal spacers over the study period have eliminated grade 3 toxicities. However, our experience provides a reminder that they are to always be discussed with patients whenever offering this treatment.
Purpose: HDR brachytherapy boost is utilized for dose escalation in the treatment of clinically localized intermediate to high risk prostate cancer, but long term clinical outcome data continues to mature. This report examines long term clinical outcome in a large cohort of patients treated in a single institution, extending an initial 7 year follow-up (Zwahlen, 2010) to a median follow-up of 11.9 years.

Materials and Methods: We reviewed data of the men treated for clinically localized prostate cancer with curative intent between 1998 to 2004 at our institution. A total of 655 patients received either 3-dimensional conformal radiotherapy (median 46Gy) in combination with a HDR (median18Gy in 3 fractions) boost (‘3DCRT+HDR’; 215 patients) or 3DCRT alone (‘3DCRT’; median 70Gy; 440 patients). Men with National Comprehensive Cancer Network (NCCN) intermediate risk disease were offered neoadjuvant androgen deprivation (AD) and those in the high risk category were also offered adjuvant AD. Data collection included serial questionnaire based assessment of acute and long term adverse effects.

Results: The median age was 68.9yrs and 70.8yrs for the 3DCRT+HDR and 3DCRT groups, respectively, and the median presenting PSA (iPSA) was 12.2ng/mL and 9.9ng/mL, respectively. 15.3% of the 3DCRT+HDR group had a Gleason score >7, with 29.3% presenting with clinical category > cT2. This compared to 12.5% of the 3DCRT group who had a Gleason score > 7, with 25.7% of that group presenting with > cT2 category. The 3DCRT+HDR group had an expected lower proportion of NCCN low risk patients (4.3% vs 20.9%) and higher proportion of NCCN high risk patients (50.7% versus 37.5%) compared to the 3DCRT group. The 5 and 10 year overall survival was superior at 90.7% and 80.3%, respectively for the 3DCRT+HDR group, compared to 87.2% and 69.9%, respectively in the 3DCRT group (p<0.001). The 5 and 10 year cause specific survival also favoured the HDR boost group with survival of 95.7% and 92.5% (3DCRT+HDR) and 94.5% and 87.9% (3DCRT), respectively (p<0.042).

Conclusions: HDR brachytherapy boost in conjunction with 3DCRT offered superior overall survival and cause specific
survival in our large patient population, with extended follow-up identifying late divergence of the survival curves suggestive of a persisting benefit.

PP05 Presentation Time: 9:36 AM
Low-Dose-Rate Brachytherapy for Low- and Intermediate-Risk Prostate Cancer: A Dose-Response Analysis for 3392 Consecutive 125-Iodine Monotherapy Patients
William James Morris, MD, FRCPC, Ingrid Spadinger, PhD, FCCPM, Ross Halperin, MD, FRCPC.
1Vancouver Cancer Centre, Vancouver, BC, Canada, 2Cancer Center for the Southern Interior, Kelowna, BC, Canada.

Purpose: To investigate the effect of D90 on biochemical failure in a large consecutive cohort of 125-Iodine monotherapy patients. Materials and Methods: Between 07/1998 and 09/2011, 3436 men with NCCN low- and intermediate-risk prostate cancer underwent 125-Iodine monotherapy, 3392 (98.6%) of whom had post-implant, CT-based dose metrics recorded. Sixty percent had intermediate-risk disease and 46% had 6 months of neoadjuvant/concomitant androgen deprivation therapy (ADT). The median D90 was 153 Gy (mean 154 Gy, SD 15.9, range 86.5-223 Gy). The median follow up was 5.48 years (mean 6.12, SD 3.95, range 0-16.9); 648 men have been followed for at least 10 years. Results: As of 09/2015, there have been 222 biochemical relapse events (nadir+2ng/mL threshold) yielding 5- and 10-year K-M biochemical progression free survival (b-PFS) estimates of 94.9% (±1.0%) and 89.9% (±1.6%) respectively. Intermediate-risk patients were more than twice as likely to experience biochemical failure compared to low-risk (HR 2.13, p <0.001). In a multivariate Cox model, Gleason sum 7 versus ≤6 (HR 2.2, p <0.001), pre-treatment PSA (HR 1.14 per unit increase, p <0.001) and clinical T2b-c versus T1c-T2a (HR 1.8, p <0.001) were each strongly associated with increased risk of biochemical failure. The use of ADT reduced the risk of biochemical failure (HR 0.51, p <0.001). Post-implant D90 values, age and percent positive cores were not statistically associated with biochemical relapse in MVA. Although not reaching statistical significance, a small dose effect was identified when comparing the annualized risk of relapse for years 4-9 post-implant permitting a quantitative estimate of the impact of D90 on b-PFS. For
intermediate-risk patients who did not receive ADT (N =929), D90 had no measurable impact on the risk of biochemical failure. However, for the intermediate-risk patients who did receive ADT (N =1085), there was a 1.8% improvement in the 10-year b-PFS for each 10 Gy increase in D90. For the low-risk patients, there was a 1.4% improvement in the 10-year b-PFS for each 10 Gy increase in D90. **Conclusions:** The three conventional prognostic factors (Gleason sum, pre-treatment PSA and clinical T-Stage) as well as the use of ADT were all strongly associated with biochemical failure in MVA. D90 did not reach statistical significance in MVA, but a small beneficial effect of increased D90 values was identified.

**PP06**

**Presentation Time: 9:45 AM**

**Prospective Cohort of Permanent Seed Implantation Prostate Brachytherapy for Intermediate Risk Prostate Cancer: Patient Reported Outcomes and Comparison of Toxicity Profiles between 125-iodine, 131-cesium and 103-palladium**

Pierre Blanchard, MD PhD, Thomas J. Pugh, MD, David A. Swanson, MD, Usama X. Mahmood, MD, Hsiang-Chun Chang, MSc, Xuemei Wang, MSc, William J. Graber, MD, Rajat J. Kudchadker, PhD, Teresa Bruno, CMD, Maria C. Occena, RN, Toweilla G. Henry, RN, Steven J. Frank, MD. MD Anderson Cancer Center, Houston, TX, USA.

**Purpose:** Different radioactive isotopes can be used for permanent seed implantation of the prostate, but their differences in side effect profile are unknown. We have conducted a prospective cohort of intermediate risk cancer patients in which 125-Iodine, 131-Cesium and 103-Palladium were used each in a third of the patients. We report the patient reported outcomes overall and the differences between the three isotopes. **Materials and Methods:** This prospective single center cohort aimed at evaluating the efficacy and toxicity of prostate brachytherapy in intermediate risk prostate cancer patients. Eligible patients had a non-pretreated prostate cancer with intermediate risk prostate cancer as determined by one of the following combinations: Gleason < 7 and PSA 10-15; Gleason 7 and PSA must be < 10. T stage had to be ≤ T2b. Hormonal therapy was not allowed. All patients provided written informed consent. Follow-up was scheduled every 4 months for the first year, every 6 months up to 5 years and yearly afterwards. At each time point physician reported outcomes were measured, and patient filled the Expanded Prostate Cancer Index Composite (EPIC), the American Urology Association Symptom Index (AUA-SI), the SF-12, and a questionnaire on the use of sexual medical devices. **Results:** From August 2006 to August 2013, 300 intermediate risk patients were included. Three cohorts were treated successively with 125-Iodine (n=98, prescribed dose=145 Gy), 103-Palladium (n=102, prescribed dose=125 Gy) and 131-Cesium (n=100, prescribed dose=115 Gy). Median age was 64.9 (range: 44.2, 86.3). The median follow-up of the last cohort was 2.6 years, results are only presented up to two years following treatment. Rate of EPIC completion at baseline, one and two years were respectively 11.2%/4.1%/4.3% for the I-125 cohort, 14%/11.6%/13.2% for the Pd-103 cohort and 12%/11.1%/22.8% for the Cs-131 cohort. On the overall population, all quality of life domains show an initial drop at three months post treatment. While bowel and hormonal scores quickly return to baseline values (respective p-values for clinically meaningful difference at one/two years of 0.49/0.48 and 0.99/0.99), urinary and sexual impairment in quality of life never fully return to baseline, the difference being clinically meaningful for the urinary domain (with respective p-values for clinically meaningful difference at one/two years for sexual and urinary summary scores of 0.98/0.79 and <0.001/<0.001). When comparing between isotopes, there were no differences in terms of bowel and hormonal scores at baseline, but I-125 patients had a poorer sexual function and Pd-103 patients a better urinary score at baseline. At twelve months post implant, the decrease from baseline in bowel score was statistically and clinically significantly higher for Cs-131 patients (p=0.03), but no significant difference was observed in hormonal (p=0.33), sexual (p=0.14) or urinary (p=0.07) scores or between the three isotope groups. Compared to baseline, the decrease in bowel, hormonal, sexual or urinary scores at two years post implant were not...
differences according to the isotope used. Both at one and two years, the decreases in EPIC scores were always numerically larger in patients treated with Cs-131, intermediate with I-125 and smaller with Pd-103. Out of the patients who had erections firm enough for intercourse at baseline, 90% of I-125 patients, 66% of Pd-103 patients and 35% of Cs-131 patients remained potent at two years post implant.

Conclusions: This prospective analysis patient reported outcomes following prostate brachytherapy shows long lasting and clinically significant decrements in urinary and sexual domains. Comparison of the different isotopes shows a favorable toxicity profile favoring Pd-103.

PP07 Presentation Time: 9:54 AM
Long Term PSA Stability and Predictive Factors of Failure after Permanent Seed Prostate Brachytherapy
Audrey Tetreault-Laflamme, MD FRCPC\textsuperscript{1}, Juanita Crook, MD FRCPC\textsuperscript{1}, Jeremy Hamm, PhD\textsuperscript{2}, Tom Pickles, MD FRCPC\textsuperscript{2}, Mira Keyes, MD FRCPC\textsuperscript{3}, Michael McKenzie, MD FRCPC\textsuperscript{3}, Howard Pai, MD FRCPC\textsuperscript{3}, Francois Bachand, MD FRCPC\textsuperscript{4}, James Morris, MD FRCPC\textsuperscript{3}.
\textsuperscript{1}BC Cancer Agency, Kelowna, BC, Canada, \textsuperscript{2}Cancer Surveillance and Outcomes, BC Cancer Agency, Vancouver, BC, Canada, \textsuperscript{3}BC Cancer Agency, Vancouver, BC, Canada, \textsuperscript{4}BC Cancer Agency, Victoria, BC, Canada.

Purpose: The Phoenix definition of biochemical failure (BF) (nadir+2) may overestimate cure rates after low dose rate prostate brachytherapy (LDR-PB). The purpose of this study is to assess long term PSA stability after LDR-PB and predictive factors of eventual BF for those with a slowly rising PSA.

Materials and Methods: 2772 low or intermediate risk prostate cancers underwent Iodine-125 LDR-PB monotherapy between 1998 and 2010. 49.7% received androgen deprivation (ADT) prior to LDR-PB (treatment policy: 6 months). Patients with less than 36 months follow-up were excluded (n=433). Clinical characteristics, dosimetric parameters and sequential PSA readings were retrieved from a prospective provincial database. A rising PSA was considered to be PSA $\geq 0.2 \text{ ng/mL}$ with an increase $\geq 0.1 \text{ ng/mL}$ over previous 2 years. The Phoenix definition was used to identify BF. Patients were classified as (1) stable PSA (cured), (2) rising PSA (without BF) or (3) BF. The three groups were compared according to clinical, dosimetric and post-treatment parameters. Multivariate analysis was performed on the cured and failed groups to determine variables predicting for failure. Logistic regression model was applied with cross validation to test for model accuracy. ROC curves were obtained for patients with and without ADT to determine predictive cut-offs for BF. Results: Median follow-up is 89 months (37-199); median age at implant 66 years (43-84). Majority of patients (80.7%) had clinical stage T1-T2a, 55% had Gleason score $\leq 6$ and median baseline PSA was 6.5 ng/mL (0.3-40 ng/mL). 59% were intermediate risk. Among the 2339 patients analyzed, 2004 (85.7%) had a stable PSA and were considered cured [median PSA at 60 months (PSA-60): 0.04ng/mL], 145 (6.2%) had a rising PSA (PSA-60: 0.27ng/mL) and 190 (8.1%) had BF. PSA nadirs for the 3 groups were respectively 0.03 (cured), 0.16 (rising PSA) and 0.51ng/mL (BF) ($p<0.0001$). For patients with no prior ADT, the variables associated with failure are PSA nadir (OR: 20.6 $p<0.0001$) and PSA-60 (OR: 18.3 $p<0.0001$). If the model is applied to the rising PSA group, using a PSA-60 cut-off of 0.3ng/mL (sensitivity:85%, specificity: 98.1%), the risk of failure is 9.8% (8/82) for patients not having received ADT. For patients who received ADT, the predictive factors of failure are PSA-60 (OR:53.9 $p<0.0001$) and T-stage (OR:0.25 $p=0.0008$). Using this model and a PSA-60 cut-off of 0.1ng/mL (sensitivity: 85%, specificity: 92.9%), the predicted risk of BF in the rising PSA group is 53.7% (36/56). Taking into account the two predictive models, the anticipated cure rate for the entire cohort is 89.7%. Conclusions: Patients treated with LDR-PB monotherapy and whose PSA-60 is $\leq 0.3\text{ng/mL}$ are highly likely to be cured even if they experienced a slight PSA rise. However, for patients who also received ADT, a stricter cut-off of 0.1ng/mL may be appropriate.