

68 INTERMEDIATE-RISK PROSTATE CANCER, ANDROGEN DEPRIVATION THERAPY AND THE RISK OF DEATH

Tom Pickles, Scott Tyldesley, Mira Keyes, W James Morris
University of British Columbia, Vancouver, BC

Purpose: Intermediate-risk prostate cancer comprises a heterogeneous group, whose management includes external radiation (EBRT), brachytherapy (brachy), or surgery. Androgen deprivation therapy (ADT) has been shown to improve survival in IR prostate cancer when combined with standard dose EBRT (RTOG 9408). Its role with brachy is unclear, but appears to add 10-15% absolute improvement in biochemical control (as presented at CARO 2015). In our practice the use of ADT in this context has declined from 91% in 1990 to 21% in 2015, because of uncertainty of its role, and concerns of toxicity. The aim of this study was to examine the effect of ADT on subsequent survival of men treated for IR with brachy.

Methods and Materials: Men treated for IR prostate cancer 1998-2011 were prospectively followed in an outcomes database. They were risk grouped using the ProCars scheme into low- and high-IR. Endpoints were biochemical control (bNED, by the Phoenix, nadir + 2 definition) and survival. Death information was obtained from the provincial cancer registry. Cause of death was ascribed to prostate cancer, cardiovascular disease, other cause, or unknown. bNED and survival were calculated using the Kaplan-Meier method with log-rank statistics, and multivariable analysis performed.

Results: 2232 men form the study cohort. Eighty-seven percent had low-IR cancer, and 13% high-IR. Six months of neoadjuvant and concurrent ADT was used in 50%. Ninety-nine percent received 125I low dose rate permanent brachytherapy monotherapy (144 Gy) and 1% received 115 Gy plus pelvic EBRT, (46 Gy). Median follow up for bNED is five years (range 0-17) and for survival seven years (4-17, with 23% followed for more than 10 years). Actuarial biochemical control at 10 years is 74% without, and 88% with ADT ($p < 0.001$), and both low-IR (77% versus 86%) and high-IR (68% versus 83% at six years) show this improvement. Overall survival is 89% without ADT and 85% with ADT at 10 years ($p = 0.041$). Cardiovascular deaths were significantly increased with ADT (5% versus 2.3% at 10 years, $p = 0.015$), and contribute to the decreased overall survival observed. Prostate cancer deaths occurred in 0.5% and 1.5% without and with ADT, at 10 years. Multivariable analysis shows that the excess cardiac deaths are due to comorbidity and age.

Conclusions: Although bNED is improved by the addition of six months of ADT, overall survival is worse when examined in a mature dataset. This detriment is due to excess non-prostate causes, including cardiovascular deaths. The main drivers of the latter appear to be presence of cardiac risk factors, other comorbidity, and age. The use of ADT may be a particular concern in patients with such risk factors. Benefits, risks, and patient preference should be considered when determining the addition of ADT with BT for IR prostate cancer.

69 ACUTE COMPLICATIONS OF PERINEAL INTERSTITIAL BRACHYTHERAPY (ISBT) IMPLANTS IN GYNECOLOGICAL CANCER PATIENTS: PROSPECTIVE ANALYSIS OF ORGAN INJURY AND INFECTION

Lucas C. Mendez¹, Lisa Barbera², David D'Souza³, Laura D'Alimonte², Eric Leung²

¹University of São Paulo, São Paulo, Brazil

²University of Toronto, Toronto, ON

³University of Western Ontario, London, ON

Purpose: Brachytherapy is an integral component of radiation treatment of gynecological malignancies. Many locally-advanced pelvic tumours may not be adequately controlled with intracavitary techniques due to challenges in dose conformality. ISBT can improve dosimetry through the insertion of catheter needles directly into tumour tissue. However, due to its invasiveness and potential risks of complications, there is a lack

of expertise in ISBT. The goal is to evaluate the safety of ISBT by studying the acute complications with a perineal applicator technique.

Methods and Materials: Thirty-nine patients at a single institution treated with high-dose rate perineal ISBT from September 2014 to January 2016 were included in a prospective registry trial. Median age was 65 (range 23-88) with 13 cervical cancer patients, 11 vaginal, 11 recurrent endometrial, one vulvar. Three patients were treated palliatively. No bowel preparation was used prior to implant and no antibiotics were given perioperatively. Post-procedure, patients were imaged with CT or MRI with no attempt to adjust needle depth or position after review of imaging. First follow up visit occurred within 6 weeks after treatment and then 2-3 months later. Post-operative adverse events were graded with CTCAE V3.0 and radiation related toxicity with RTOG common criteria.

Results: Median follow up time was three months. Thirty-four patients were initially treated with external beam radiation therapy to the pelvis with a dose of 45 Gy (median). A total of 56 implants were performed; 22 patients received one implant while 17 had two. Median hospital stay was two days (1-5). The median number of needles for each implantation was 17 (8-26). The most commonly invaded organ by the interstitial catheters was the bladder (13) followed by bowel (10) and rectum (nine). Eighteen patients had radiological evidence of needle intrusion to a pelvic organ and six patients had more than one pelvic organ punctured by the catheters. Two acute organ complications attributable to needle intrusion to the bladder were found. One patient developed G1 hematuria and was discharged without delay and another had G2 hematuria requiring manual saline irrigation. No GI complications were found. Three patients developed perineal cellulitis post-ISBT. Acute radiation-related toxicities were seen in six patients with Grade 1 GI and/or GU.

Conclusions: ISBT is a safe and feasible treatment for locally-advanced gynecological cancers. With no attempted post-treatment adjustment, radiological evidence of needle intrusion into pelvic organs is a common finding. No severe organ complications were found and the rate of acute complications are low. Vulva and perineal infection post-ISBT was the most common complication related to needle implantation. The development of real-time image-guidance may improve implant positioning for tumour coverage but likely will not affect the existing low rate of acute organ complications.

70 COMPARING RADICAL PROSTATECTOMY AND PERMANENT SEED BRACHYTHERAPY FOR LOW AND INTERMEDIATE-RISK CANCER

Guila Delouya¹, Daniel Tausky², Veronique Ouellet², Fred Saad²
¹CHUM-Hôpital Notre-Dame, Montreal, QC
²Université de Montréal, Montreal, QC

Purpose: To compare results of radical prostatectomy (RP) and permanent seed prostate brachytherapy (PB) is difficult because of different definitions for recurrence and differences in baseline characteristics. We analyzed treatment results of both treatments in low- and low-intermediate prostate cancer patients from a single tertiary centre using similar definitions for biochemical recurrence.

Methods and Materials: Patients were selected from each department's internal database based on pre-operative selection criteria from NCCN guidelines (2015) for low- and low-intermediate-risk patients. All selected patients had complete data on Gleason score, clinical staging and pre-treatment prostate specific antigen (PSA) value and none had received any neo-adjuvant androgen deprivation therapy. The end point was biochemical recurrence (BCR) or any salvage treatment for both RP and PB at 48 (± 4) months after treatment. The biochemical relapse threshold was set at PSA ≥ 0.5 ng/mL for PB and two PSA values ≥ 0.2 ng/mL for RP. Patients from both treatment groups were compared using non-parametric tests. A binary logistic regression analysis was done to test an association of treatment and pre-treatment factors with a BCR at 48 months.

Results: Five hundred and seventy-five patients were included, 254 treated with RP and 321 with PB. At RP, 24% had pT3 disease. The positive surgical margin rate was 50% and 21% for patients with pT3 and pT2 respectively. The median D90 (dose [Gy] that covers 90% of the prostate volume) in this study was 159.1 Gy (IQR 140.9-176.7 Gy). The D90 was < 130 Gy in 14% of implants. Patients who had RP were compared to patients treated with PB: RP patients were significantly younger, had less positive pre-treatment biopsies but a lower rate of Gleason 7 disease. The mean PSA was not different. The rate of patients with BCR was not different between both groups ($p = 0.24$) and occurred in 21.2% after RP and in 20.6% after PB. On univariate and multivariate logistic regression analysis, younger age, higher percentage of positive biopsies and initial PSA were predictive of BCR. Treatment modality was not predictive in either univariate (OR 0.96, 95%CI 0.64-1.44 $p = 0.58$) or multivariate (OR 1.42, 95%CI 0.88-2.28, $p = 0.42$) analyses.

Conclusions: Both RP and PB result in similarly good results at four years post treatment with about 20% experiencing BCR, as measured with similar PSA-thresholds. Clinical T-Stage, age, percentage of positive biopsies and Gleason score are predictive of outcome. However, it is possible that study power is inadequate and/or follow up is too short to detect a difference between both treatments.

71

LOW-DOSE-RATE BRACHYTHERAPY FOR LOW- AND INTERMEDIATE-RISK PROSTATE CANCER: A DOSE-RESPONSE ANALYSIS FOR 3392 CONSECUTIVE 125-IODINE MONOTHERAPY PATIENTS

W James Morris, Ingrid Spadinger, Ross Halperin
British Columbia Cancer Agency, Vancouver, BC

Purpose: To investigate the effect of D90 on biochemical failure in a large consecutive cohort of 1125 monotherapy patients.

Methods and Materials: Between July 1998 and September 2011, 3436 men with NCCN low- and intermediate-risk prostate cancer underwent 1125 brachytherapy monotherapy, 3392 (98.6%) of whom had post-implant, CT-based dose metrics recorded. Sixty percent had intermediate-risk disease and 46% had six 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 September 2015, there have been 222 biochemical relapse events (nadir+2 ng/mL threshold) yielding five- and 10-year K-M biochemical progression free survival (b-PFS) estimates of 94.9% ($\pm 1.0\%$) and 89.9% ($\pm 1.6\%$) 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 ($n = 1019$), 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 ten-year b-PFS for each 10 Gy increase in D90. For the low-risk patients, there was a 1.4% improvement in the ten-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.

72

FOCAL SALVAGE HDR BRACHYTHERAPY FOR LOCALLY RECURRENT PROSTATE CANCER - EARLY REPORT FROM A PROSPECTIVE STUDY
Peter Chung, Alejandro Berlin, Alexandra Rink, Marco Carlone, Andrew Bayley, Charles Catton, Jessamine Abed, Bernadeth Lao, Gerald O'Leary, Pdraig Warde, Robert Bristow, Cynthia Menard
Princess Margaret Cancer Centre, Toronto, ON

Purpose: To report preliminary outcomes of focal salvage HDR brachytherapy for locally recurrent prostate cancer after external beam radiotherapy (RT).

Methods and Materials: All 15 patients entered on a prospective study had biopsy proven locally recurrent prostate carcinoma visible on MRI, at least 18 months after definitive RT, with > 6 months PSA doubling time. The GTV was defined using multiparametric MRI (T2-weighted, diffusion-weighted, dynamic contrast-enhanced). The prostate gland and GTV contours were deformably co-registered to T2w images at time of brachytherapy after catheter placement using deformable image registration. CTV margin expansion (5 mm in all directions) was restricted to adjacent OARs and 2 mm beyond the prostate boundary where applicable. PTV margins of 2 mm cranio-caudally and 1mm elsewhere were then applied. A total dose of 26 Gy in two separate implants 7-14 days apart was delivered. No patient received androgen deprivation therapy.

Results: Median follow up was 12 months (range, 3-24). The median age at time of enrollment was 72 years (range, 62-77). The median pre-brachytherapy PSA was 3.96 ng/ml (range, 1.68 - 8.39). All patients had a single GTV. Median GTV and PTV volumes were 1.45 cc (range, 0.66-6.76) and 6.45 cc (range 3.5-17.39), respectively. A median of eight catheters (range, 4-12) were used. Initial biochemical response after salvage brachytherapy was seen in all patients with 14 having > 50% reduction from baseline. To date 10 have achieved PSA < 1 ng/ml, while 10 of 12 patients with > 12 months follow up have PSA level < 1 ng/ml. Of two patients who have experienced biochemical failure, one had imaging and biopsy evidence of a marginal recurrence. Acute toxicity (CTCAE v4.0) was mild. Only one patient had Grade 2 toxicity (temporary urinary catheterization after his second implant). All acute toxicity has resolved in patients who have greater than three months of follow up.

Conclusions: MR-guided focal salvage HDR brachytherapy in patients treated with previous RT is associated with minimal acute toxicity and initial biochemical response appears promising. Further follow up will determine if this approach results in acceptable local/biochemical control and late toxicity.

73

PRELIMINARY RESULTS FROM A PILOT STUDY ON THE ROLE OF DUAL SOURCE COMPUTED TOMOGRAPHY FOR CARDIAC SPARING IN LEFT BREAST RADIOTHERAPY

Houda Bahig, Toni Vu, Nhu Tram Nguyen, Jacques de Guise, Martin Lebeau, Carl Chartrand-Lefebvre, Danis Blais, Stephane Bedwani, David Roberge
Centre Hospitalier de l'Université de Montréal, Montreal, QC

Purpose: Exposure of the heart to radiation during radiotherapy for breast cancer has been shown to increase the rate of ischemic heart disease, with the increase being proportional to the mean dose to the heart. Although a significant reduction of heart dose has been shown with respiratory-gated irradiation of the left breast, there is currently no data on heart dose variation through the cardiac cycle. The purpose of this study was to assess dose variation to left coronary artery, left ventricle and heart during the cardiac cycle using dual source computed tomography (DSCT). 4D cardiac motion was used to investigate the potential dosimetric advantage of cardiac-gated radiotherapy.

Methods and Materials: This is a prospective pilot study of patients with left-sided breast cancer treated with tangential breast irradiation. A planning scan and a contrast-injected