and grade 4 stricture/fistula related (n = 8). We investigated patient factors (age, preRT IPSS), surgical factors (clip volume, approach, margin status), and disease factors (stage, Gleason group, PSA nadir, preRT PSA, surgery to RT time). Surgical clip volume was contoured on CT and recorded in cc. Significance was determined using Mann-Whitney U test for continuous variables and Fisher's Exact test for binary variables.

Results: A higher volume of surgical clips in the prostate fossa was found to be significantly related to eventual grade ≥3 stricture/fistula related event (p = 0.05). The mean surgical clip volume was found to be 2.30 cc in those with a documented grade ≥3 stricture/fistula compared to 1.23 cc in those without. Patients with a positive margin had a 30.0% rate of grade ≥3 GU toxicity compared to 16.2% in those with a negative margin (p = 0.03). Surgical clip volume was not found to be significantly related to pathologic stage, nor to eventual biochemical failure (p = 0.799/0.897). A positive margin was associated with a lower rate of biochemical failure after salvage (p = 0.04). Grade 3 events were documented at a median of 7.7 years and grade 4 events at 12.0 years after the end of radiation.

Conclusion: Our previous study found a high rate of grade ≥3 toxicities at time points for which there is a paucity of data both in conventional and hypofractionated regimens, particularly in the era of modern surgical and radiation techniques. We also found late toxicities can occur with increasing severity for many years after salvage radiotherapy. This analysis suggests that margin positivity and volume of surgical clips might identify patients at higher risk for late grade ≥3 toxicities, although the etiologies of these toxicities, whether surgery or radiation-related, are uncertain.

Author Disclosure: **K. Ranta**: None. **A.P. Wojcieszynski**: Uncompensated; International Journal of Radiation Oncology, Biology, Physics. **T. Kruser**: Honoraria; DAVA Oncology, Radialogica LLC, AstraZeneca, Pfizer, Inc. Travel expenses; AstraZeneca. editor of thoracic section; International Journal of Radiation Biology Physics. **D. Jarrard**: Board member; Society Urology Oncology Board. **Y. Liu**: None. **M. Yu**: None. **M.A. Ritter**: None. **J.M. Floberg**: None.

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Validating a Simple Urethra Surrogate Model to Facilitate Dosimetric Analysis to Predict Genitourinary Toxicity

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Purpose/Objective(s): The urethra may be a critical structure in prostate radiotherapy planning as some studies have shown that higher urethral dose correlates with worse genitourinary (GU) toxicity. Identifying the urethra requires an MRI planning scan or foley catheter insertion at CT planning. Most surrogates have been developed and validated against the urethra identified by a foley catheter. However, the urethral position can shift with catheter placement. We, therefore, aim to validate a simple urethra surrogate model against MRI-defined urethra. The surrogate model can be used to correlate urethra dose-volume parameters (DVP) with late GU toxicity and to apply urethral constraints in those with a CT-only based workflow.

Materials/Methods: Thirty-nine MRI-defined urethras from patients in the PACE-C trial were assessed to determine the average position of the urethra in the midline sagittal prostate plane along the $^1/_4$ gland, midgland, $^3/_4$ gland, apex and 3mm below apex. Using these average positions, a Python script was developed, which places a 10mm diameter circle in the 1/4 gland, midgland, $^3/_4$ gland, apex and 3mm below the apex. The observer manually contours a 10mm circle at the prostate base (prostate-bladder neck interface) to infer the urethra position and interpolates the contours. The urethra surrogate model was compared against 20 MRI-defined urethras (within the treatment PTV) in patients treated with 36.25Gy in 5 fractions as part of the PACE-B trial. To assess the surrogate's geometric performance, the Dice similarity coefficient (DSC), Hausdorff distance (HD), mean surface distance to agreement (MDTA) and the percentage of MRI-defined urethra outside the surrogate (UOS) were calculated. The surrogate model's dosimetric performance was assessed by comparing the mean D99, D98, average dose, D50, D2 and D1 using a paired t-test. The D (n) is the dose (Gy) to (n)% of the urethra.

Results: The median results were: DSC 0.36 (IQR 0.28-0.42), HD 0.88cm (IQR, 0.70-1.04), MDTA 0.24cm (IQR, 0.21-0.28), UOS 29% (IQR, 17-52%). When comparing DVP between the MRI-defined urethra and surrogate urethra, the mean D99, D98 and D95 as 38.8Gy vs 39.1Gy (p = 0.17), 39.3Gy vs 39.5Gy (p = 0.23), 40.1Gy vs 40.4Gy (p = 0.21), respectively. The mean D50, average dose, D2 and D1 was 41.8Gy vs 41.9Gy (p = 0.03), 41.7 vs 41.8Gy (p = 0.04), 42.9Gy vs 43.0Gy (p = 0.05) and 43.0Gy vs 43.1Gy (p = 0.03), respectively.

Conclusion: While there were geometric differences between the surrogate urethra and MRI-defined urethra, there was no statistically significant difference between most urethral dose-volume parameters (D99, D98, D95, and D1). Similarly, the actual differences in urethra DVP were not clinically significant. This surrogate model could be validated in a larger cohort and then used to estimate the urethra position on CT planning scans for dosimetric analysis in those without an MRI planning scan or urinary catheter.

Author Disclosure: **R. Ratnakumaran**: Honoraria; Accuray. Salary support; Accuray. **J. Mohajer**: None. **E. Lee**: Honorary non-clinical fellow; Royal Marsden NHS Foundation Trust. **D.H. Brand**: Salary support; from Cancer Research UK RadNet City of London. **D. Loblaw**: Owner; Dr Loblaw Medicine Professional Corp. **S. Tolan**: None. **N. van As**: Grant/research funding; Accuray, Varian Medical systems. Committee member in Phase III clinical trials workstream; NCRI CTRad. Co-chairman of UK SABR consortium; UK SABR consortium. Trustee; Royal Marsden Cancer Charity. Medical Director; Royal Marsden NHS Foundation. **A. Tree**: Grant/research funding; Elekta, Accuray, Varian. Honoraria; Elekta, Janssen. Travel expenses; Elekta. Salary support; Elekta. Committee member; UK SABR consortium. Lead editor for GU at the red journal, which is financially compensated; IJROBP. I receive no direct compensation but my employer receives financial compensation to back fill my expenses.

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ADT Use and Nodal Irradiation in Men Receiving Post-Prostatectomy Salvage Radiotherapy within a Statewide Radiation Oncology Quality Consortium

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Purpose/Objective(s): For men with biochemical recurrence after radical prostatectomy, salvage radiotherapy (SRT) is a standard of care. Outcomes are improved when SRT is delivered at lower PSA levels, and there has been increased emphasis on more timely treatment. With early SRT,

however, there remains uncertainty as to the optimal use and duration of androgen deprivation therapy (ADT) and pelvic lymph node radiation (PLNRT). Moreover, PET imaging and genomic classifiers have emerged as tools to guide treatment decisions, but their uptake in routine practice is unknown. To address these questions, we analyzed a contemporary cohort treated with SRT within the Michigan Radiation Oncology Quality Consortium (MROQC). We hypothesized that ADT and PLNRT practices would reflect recent trial results in this setting.

Materials/Methods: Eligible patients receiving SRT at an MROQC center were enrolled from 06/09/20 to 11/04/22. Data was prospectively collected via patient-, physician-, and physicist-completed forms. Patients were matched to the Michigan Urological Surgery Improvement Collaborative (MUSIC) database for additional treatment- and patient-related data. Univariable (UVA) and multivariable analyses (MVA) were performed to test associations between patient/tumor factors and ADT or PLNRT use.

Results: A total of 191 patients across 26 centers were enrolled in the MROQC database. Of these, 116 were matched to the MUSIC database. Median time from RP to SRT was 17 months (IQR 8 − 33 months). The median post-RP PSA prior to SRT was 0.25 (IQR 0.16 − 0.60). Early SRT was defined as pre-SRT PSA ≤0.5, and 27% (n = 31/116) had a pre-SRT PSA >0.5. Twenty-eight were pT3b/T4, 97% were pN0/NX, and 51% had positive surgical margins. Fractionation was conventional (>28 fractions) in 58% and moderate hypofractionation (20-28 fractions) in 38%. Table 1 describes the patients receiving ADT and/or PLNRT. Median ADT duration was 6 mo (IQR 6 − 7 mo). MVA revealed pre-SRT PSA >0.5 (OR 5.05 [1.89 − 15.33]) and pT3b/T4 disease (OR 4.23 [1.40 − 14.56]) were significantly associated with ADT use (p <0.05), but not grade group (GG) or margin status. PLNRT was significantly associated with pre-SRT PSA >0.5 (OR 3.04 [1.21 − 8.42], p <0.05) but not pT stage, margin status, or GG. PET imaging was performed in 37% of men (52% negative, 21% prostate bed alone uptake, and 26% lymph node positivity) and genomic classifiers were performed in 24%.

Conclusion: Nearly 75% of biochemically recurrent prostate cancer patients within MROQC received early SRT, and about half received ADT. A pre-SRT PSA >0.5 was strongly associated with ADT and PLNRT. With prostate bed SRT alone, very few received ADT. Given the considerable heterogeneity in treatment, additional studies may help identify patients who most benefit from ADT + PLNRT, and who may be spared potential added toxicity.

Abstract 2941 − Table 1

		ADT	
		No	Yes
PLNRT	No	31%	6%
	Yes	18%	45%

Author Disclosure: **S.N. Regan**: None. **M.P. Dykstra**: None. **H. Yin**: Salary support for MROQC; Blue Cross Blue Shield of Michigan. **P.W. McLaughlin**: None. **T.P. Boike**: Honoraria; ASTRO APEx, Medivation/Astellas, Janssen, Blue Earth Diagnostics, Elekta, AstraZeneca, Myovant, Pfizer. Compensation/Payment; Boston Scientific, Lantheus, Palette Life Sciences. Board Member; Michigan Institute of Urology Foundation. Member; NCI Prostate Cancer Task Force. Co-Chair; ASTRO APEx Committee. **A.K. Bhatt**: None. **E.M. Walker**: None. **M. Zaki**: None. **D. Kendrick**: Salary support for MROQC; Blue Cross Blue Shield of Michigan. **M. Mislmani**: None. **S. Paluch**: None. **D.W. Litzenberg**: Salary support for MROQC; Blue Cross Blue Shield of Michigan. Compensation/Payment; Integrated Sensors, LLC. **M. Mietzel**: Salary support for MROQC; Blue Cross Blue Shield of Michigan. **V. Narayana**: Administrative; American Association of Medical Physics. **A. Smith**: None. **W.C. Jackson**: None. **D. K. Heimburger**: Compensation/Payment; Munson Medical Center. Clinical oversight of oncology program; Munson Healthcare. **M. Schipper**: Salary support for MROQC; Blue Cross Blue Shield of Michigan. Compensation/Payment; Innovative Analytics. **R.T. Dess**: salary support for MROQC; Blue Cross Blue Shield of Michigan. Compensation/Payment; Janssen Pharmaceuticals.

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Multidisciplinary Management of Primary Urethral Cancer with Radiotherapy

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Purpose/Objective(s): Primary urethral cancer (PUC) is a rare form of genitourinary malignancy with a paucity of data to guide management. We analyzed PUC patients for clinicopathologic characteristics and treatment approach (radiotherapy [RT] with/without consolidative surgery) to identify predictors of outcome and RT response.

Materials/Methods: We conducted a single-institution retrospective review of patients treated with RT for PUC between 2002 to 2020. Each patient underwent multidisciplinary evaluation (including cystoscopy) as well as imaging to confirm tumor origin in the urethra. The linear quadratic formula was used to calculate the biologically effective dose (BED) using an α/β of 10 for tumor. Descriptive statistics were used to characterize the cohort. Fisher's Exact test was used to compare groups. Time-to-event analyses was conducted with the Kaplan-Meier method; outcomes included overall survival (OS) and time to recurrence (TTR) from diagnosis. Cox regression analysis assessed predictors of outcomes.

Results: A total of 17 patients were identified for analysis. Median age was 63 years (range: 34-86); the majority were female (76.5%) and white (82.4%). Tumors were localized in the proximal (n = 6) or distal (n = 11) urethra. Histology included urothelial (11.8%), squamous (35.3%), adenocarcinoma (29.4%) and mixed (23.5%). Ten patients (58.8%) had cT3 or higher disease with 10 being cN0 (58.8%), 1 cN1 (5.9%), 5 cN2 (29.4%) and 1 cNx (5.9%). Median tumor size was 4.8 cm (range: 0.5-12 cm). The majority (88.2%) were treated with definitive chemoRT with 70.5% receiving platinum therapy. Median RT dose was 59.4 Gy (range: 39.6-70.2) with a median of 30 fractions. One patient underwent upfront cystourethrectomy and 6 (35.3%) underwent consolidative surgery at a median of 2.3 months after RT. Five patients (29.4%) had a complete response (CR) and 70.6% had a partial response (PR) to RT. Of the 7 patients who underwent surgical resection the final pathology was ypTis (28.5%), ypT1 (14.2%), ypT2 (14.2%), ypT4 (28.5%) and pT2 (14.2%). A median of 16 lymph nodes were removed with 1 patient having pN2 and all others pN0. Four patients (66.6%) were downstaged by chemoRT prior to surgery. At a median follow-up time of 8.4 years, the median OS was 37.9 months (range: 23.2-52.7), which was associated with a 5-year OS of 37.2%. Twelve (70.5%) patients recurred with a median TTR of 6.3 months (range 4.8-7.7). No demographics, staging methods, or tumor characteristics were associated with OS or TTR. Urothelial histology was associated with CR following chemoRT (p = 0.02). RT dose (continuous) was associated with OS (p = 0.018) as well as a BED (HR: 0.90, 95% CI: 0.84-0.97; p = 0.01). A BED > 55 Gy was associated with improved median OS (56.4 vs 9.13 months, p = 0.006).

Conclusion: Analysis of PUC patients treated with multimodal therapy found higher rates of CR in patients with urothelial histology and increased OS in patients treated with a BED > 55 Gy. Neoadjuvant chemoRT may downstage disease prior to surgical extirpation.

Author Disclosure: **A. Retzloff**: None. **R. Li**: Grant/research funding; GC Oncology. Travel expenses; GC Oncology. Research Support; Predicine Inc. Stock; Eli Lilly, Beam Therapeutics. **S.M. Gilbert**: None. **A.E. Dohm**: None. **W.J. Sexton**: Grant/research funding; Urogen Pharmaceuticals. Compensation/Payment; Urogen Pharmaceuticals, Pacific Edge. **M. Poch**: None. **L.W. Zemp**: None. **J. Pow-Sang**: None. **R. Jain**: None. **M.S. Chatwal**: Compensation/Payment; Merck. Member of several committees; American Society of Clinical Oncology. **J. Dhillon**: None. **K. Yamoah**: Honoraria; Janssen R&D, MyCareGorithm. **D.C. Fernandez**: None. **P.A.**