**POD 3.1**

**Leveraging artificial intelligence to predict 5-year progression risk in non-muscle-invasive bladder cancer and improve stratification of intermediate-risk patients: A Canada-wide study**

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**Introduction:** Current prognostic tools in non-muscle-invasive bladder cancer (NMIBC) perform poorly and do not fully reflect contemporary practices. We aimed to develop, externally validate, and conduct an algorithmic audit of a progression risk assessment tool using artificial intelligence approaches (PROGRxN-Bca).

**Methods:** PROGRxN-Bca, based on a random survival forest, was trained on the NMIBC patients treated from January 1, 2005, to June 30, 2022, at four Canadian academic or community hospitals. External validation was performed on patients treated from November 1, 2011, to September 11, 2023, across 13 institutions from the Canadian Bladder Cancer information system. The primary outcome was time to progression, defined as first development of muscle-invasive or metastatic disease. PROGRxN-Bca was compared to the European Association of Urology risk calculator and a LASSO Cox model using identical variables as PROGRxN-Bca. Model performance in predicting five-year progression risk was characterized using c-index, calibration plots, decision curve analysis, and an algorithmic audit.

**Results:** Overall, 999 of 7032 patients (14%) developed progression during a median follow-up of 3.0 years (IQR 1.4–5.4). PROGRxN-Bca had the highest c-index overall (training: 0.83, 95% CI 0.81–0.84; validation: 0.76, 95% CI 0.74–0.77) and across different subgroups. It was well-calibrated and had the highest net benefit for clinically relevant thresholds from 15–40%. False negatives occurred in only 2–6% of all predictions, most commonly found in patients with Ta disease. PROGRxN-Bca could better stratify intermediate-risk patients compared to current guideline recommendations, reclassifying 12% of these patients with an observed five-year progression risk of 31.6% who otherwise would not have been considered for treatment intensification or clinical trial enrollment (Figure 1).

**Conclusions:** PROGRxN-Bca outperformed current prognostication tools and improved stratification of the heterogeneous intermediate-risk group.

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**POD 3.2**

**Radiomics and renal mass histology prediction**

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**Introduction:** The increasing use of abdominal imaging has led to a greater number of incidental renal masses. Unfortunately, physicians cannot rely on CT scans to accurately determine their histology. Radiomics have shown to be a promising avenue to solve this conundrum. Our main objective was to build a prediction model using CT scan radiomics and clinical features to distinguish clear-cell renal cell carcinoma (ccRCC) from non-ccRCC (nccRCC).

**Methods:** This single-center, retrospective study used the Canadian Kidney Cancer information system to identify patients who were operated for a localized RCC between 2011 and 2021. Clinical data was extracted and for each patient, the renal mass was manually segmented on CT (without contrast) and CECT (contrast-enhanced CT) by three trained readers. Then, 173 radiomics features were extracted using a Python code. The dataset was split into a learning set (80%) and a hold-out set (20%). The learning set was used to train and test five independent machine-learning models with an XGBoost algorithm. Once the best model was chosen, its performance was independently tested on the hold-out set.

**Results:** A total of 326 patients were included, of which 76% were ccRCC. The mean tumor size was 5.1 ± 3.2 cm. For the clinical T stage: 66% were T1, 7% T2, 23% T3, and 4% T4. After analyzing the five models, the one using CECT radiomics showed the best results (Table 1). The final prediction model, only the best seven features were included. The model’s AUC was 0.90, with 86% sensitivity and 80% specificity. Size subgroup analysis was performed (Table 2). Inter-reader correlation was assessed using 15 masses. The segmentations were overall similar, and S/I features had a strong correlation between readers.

**Conclusions:** Our radiomics-based prediction model showed good performance and the distinction of cccRCC vs. ncccRCC in similar patient characteristics and inter-reader correlation was strong overall. This supports the use of radiomics as a clinical tool to help guide the management of kidney cancer.

**Acknowledgements:** 1. KCRN-CKC-CUASF Research Grant: Canadian Urology Association Scholarship Foundation – Kidney Cancer Research Network of Canada; 2.
POD 3.2. Table 1. Performance of the 5 independent models

<table>
<thead>
<tr>
<th>Model</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CECT radiomics</td>
<td>0.83 (0.76, 0.88)</td>
<td>0.91 (0.81, 0.97)</td>
<td>0.48 (0.30, 0.80)</td>
</tr>
<tr>
<td>CECT radiomics + clinical data</td>
<td>0.84 (0.77, 0.88)</td>
<td>0.92 (0.8, 1)</td>
<td>0.45 (0.19, 0.68)</td>
</tr>
<tr>
<td>CT radiomics</td>
<td>0.54 (0.43, 0.63)</td>
<td>0.90 (0.83, 1.0)</td>
<td>0.16 (0, 0.35)</td>
</tr>
<tr>
<td>CT radiomics + clinical data</td>
<td>0.53 (0.35, 0.62)</td>
<td>0.87 (0.77, 0.99)</td>
<td>0.17 (0, 0.34)</td>
</tr>
<tr>
<td>Clinical data only</td>
<td>0.58 (0.50, 0.68)</td>
<td>0.88 (0.79, 1.0)</td>
<td>0.16 (0, 0.44)</td>
</tr>
</tbody>
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POD 3.3
Natural history of patients with regional lymph node positive renal cell carcinoma: Results from the Canadian Kidney Cancer Collaboration

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Introduction: The presence of lymph nodes (LN) in renal cell carcinoma (RCC) is a known poor prognostic factor. The natural history of pT(1-4)N1M0 renal cell carcinoma has been difficult to study due to low sample sizes. For instance, a large, multi-institutional, prospective trial (EORTC 30881) had only 4% pN1M0 patients in their analysis of patients undergoing radical nephrectomy with and without LN dissection. This study aimed to analyze the natural history of patients with pN1M0 RCC using a multi-institutional Canadian cohort.

Methods: The Canadian Kidney Cancer information system (CKCiS), a multi-institutional, prospective cohort database, was used to identify patients with pT(1-4)N1M0 disease since January 2011. Patients underwent surgical resection (partial or radical nephrectomy) with or without formal retroperitoneal lymph node dissection (RPLND). Primary outcomes included overall recurrence-free survival (RFS), cancer-specific survival (CSS), and overall survival (OS).

Results: Of 10 641 cM0 surgical RCC patients, 113 (1.1%) patients had pT(1-4) pN1M0 disease (64.42% with clear-cell histology, 5.77% with chromophobe, 27.89% with papillary, and 1.92% with clear-cell papillary histology), with a median followup of 3.1 years (IQR 1.2–6). Mean (SD) age was 63 (+12) years and 69% (n=78) were male. Of the 113 pN1 patients, 37 (35.58%) had clinical adenopathy on preoperative images. Pathologic stages T1/T2 were seen in 12 patients (10.71%), and 100 patients (89.29%) had pT3/T4 disease. Grade 3/4 RCC was observed in 94 patients (86.68%). Tumor necrosis of the primary lesion was seen in 78 patients (69.64%). Disease recurrence was identified in 76.99% (n=87) of patients, with a median time to recurrence of 4.8 months (IQR 3.6–7.2). Almost half (49.4%) had non-LN distant metastases, 20.7% had LN-only metastases, 18.4% had both local and distant non-LN metastases, and 11.5% had only local metastases. The median OS was 4.4 years (IQR 3.4–6.5) and the median CSS was 5.5 years (IQR 3.8–non-estimable).

Conclusions: This study highlights the unfavorable natural history of patients with renal cell carcinoma pT(1-4)N1M0 in a contemporary Canadian cohort. The results are particularly important in the era of adjuvant and salvage use of immune checkpoint inhibitors and highlight the need to closely monitor these patients, as their prognosis is poor with high rates of recurrence within the first year.

Acknowledgements: The Kidney Cancer Research Network of Canada (KRCNC) and The Canadian Kidney Cancer information system (CKCiS) have received unrestricted funding from: BMS, Eisai, EMD Serono, GSK, Jansen, Merck, Novartis, Pfizer, and Roche. There is no direct role or influence from this funding on this work. This abstract will also be presented at the American Urologic Association (2024) meeting and the Canadian Kidney Cancer Forum (2024).


POD 3.4
Does enhanced audit and feedback to urologist improve quality and reduce recurrence after transurethral resection of bladder tumor? Results from the RESECT study

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Introduction: Transurethral resection of bladder tumor (TURBT) is central in the diagnosis and treatment of non-muscle-invasive bladder cancer (NMIBC). We aimed to determine if auditing with subsequent feedback to the urologists improves TURBT quality and reduces recurrence.

Methods: RESECT is a global, prospective, observational study with an embedded cluster randomized trial of site-targeted performance feedback (intervention) vs. no feedback (control). Consecutive patients having primary TURBT for presumed NMIBC were included. Baseline data was obtained retrospectively prior to randomization. Primary outcomes were four predetermined TURBT quality indices (QI): detrusor muscle sampling (DM+), single instillation of intravesical chemotherapy (SI-IVC+), and documentation of resection completeness (RES-DOC) and key tumor features (TMF-DOC). Secondary outcomes were recurrence at first cystoscopy. Sites not meeting minimum contribution (20 cases) were excluded. Ethical approval was obtained at each site prior to the start of study.

Results: From May 2021 to March 2023, 219 sites were randomized. Data from 15 879 patients were included in the final analysis. Sites randomized to feedback (n=100) had significantly greater achievement of both documentation outcomes (adjusted mean difference, 95% CI: RES-DOC 5.6% [1.6, 9.6], p=0.006; TMF-DOC 6.1% [1.8,10.3], p=0.005). There was no difference in DM+, SI-IVC+, or recurrence rate at first cystoscopy. In control sites, the recurrence rate was significantly lower during the study compared to baseline after adjusting for tumor characteristics (Figure 1).
Of the benign tumors, 31% were sex cord-stromal (six Leydig and two Sertoli GCTs, 27 (67.5%) had seminoma and 13 (32.5%) had non-seminomatous GCTs. Of the patients with age was 38.5 years, median tumor size was 13.5 mm (9–19), and 74% and 12% underwent radical and partial orchiectomy, respectively. Of the patients with confirmed GCTs, 22 with benign histology, and four patients who had been on the Wilcoxon rank-sum test. Comparison of pre-orchiectomy miRNA and surgical pathology was done using the area under the receiver operating characteristic curve. We used the Wilcoxon rank-sum test. Conclusions: Enhanced audit and feedback on TURBT performance improve documentation quality, but not DI-M or SI-IVC+ in this setting. Participating in a global study of TURBT practice resulted in significant reduction in recurrence rates even in sites without feedback, presumably related to the Hawthorne effect. This study would support the conduct of organized audits of TURBT practice.

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POD 3.5
miRNA as a liquid biomarker to detect malignancy in small testicular masses
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Introduction: Approximately 1–4% of individuals undergoing scrotal ultrasounds are found with incidental small (<2 cm) testicular masses (STMs), with the vast majority being benign (≈13–21% malignant). Distinguishing between malignant and benign STMs remains a challenge, as neither serum tumor markers nor imaging methods offer reliable predictive capabilities. This study explored the potential of miRNAs as liquid biomarkers for predicting germ cell tumors (GCTs) in STMs.

Methods: Pre-orchiectomy serum/plasma samples, drawn between one day and <6 months before surgery, were analyzed using different miRNA extraction methods (qRT-PCR, DdPCR) and platforms across three research laboratory facilities in three different centers (Portugal, Vancouver, Toronto). The primary endpoint of our study was the association between miRNA (miR-371a-3p) and the presence of GCTs. Additionally, we analyzed miRNAs 372, 373, and 367, aiming to improve the diagnostic performance of miRNA to predict GCTs in STMs. Our research laboratories used quantitative Ct value (<40) and qualitative analysis. We used the area under the receiver operating characteristic curve (AUROC) calculations to establish optimal thresholds for miRNAs. A comparison of pre-orchiectomy miRNA and surgical pathology was done using the Wilcoxon rank-sum test.

Results: From 2009–2023, we identified 66 patients with STMs who had banked serum/plasma prior to orchiectomy. Our cohort included 40 patients with confirmed GCTs, 22 with benign histology, and four patients who had been on surveillance for >12 months and were deemed to have benign STMs. The median age was 38.5 years, median tumor size was 13.5 mm (9–19), and 74% and 12% underwent radical and partial orchiectomy, respectively. Of the patients with GCTs, 27 (67.5%) had seminoma and 13 (32.5%) had non-seminomatous GCTs. Of the benign tumors, 31% were sex cord-stromal (six Leydig and two Sertoli cell tumors). Our first lab used magnetic beads-based for extraction on serum, miR371a-3p showed a sensitivity and specificity of 67.5% and 100%, respectively. The AUROC was 0.774. We examined plasma with a qRT-PCR extraction kit in our second research laboratory. Using the qualitative analysis method and a Ct mean threshold of >12.6, miR371a-3p showed a sensitivity and specificity of 96% and 77.9%, respectively, the AUROC was 0.912. Other miRNAs were not informative for either of these two labs. Finally, our third laboratory examined serum using DdPCR, miR371a-3p showed a sensitivity and specificity of 56.1% and 47.8%, respectively; the AUROC was 0.53 when establishing a threshold of >0.6346 copy numbers. Using a multiple regression analysis, the resulting AUC value exhibits significant improvement and was reported to be 0.656.

Conclusions: This is the largest study of STMs which have banked blood/sperm to date. Our unique interlaboratory comparison represents a meaningful contribution to the field. miR-371a-3p appears sensitive to detect the presence of GCTs in STMs. Further research in this area is needed and could revolutionize the approach to managing incidental STMs.

POD 3.6
Stenting vs. nephrostomy tubes for bladder cancer associated with hydronephrosis: Does stenting increase the incidence of upper tract urothelial carcinoma by retrograde tumor cell seeding?
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Introduction: Hydronephrosis in the setting of bladder cancer is not uncommon. It can be either caused by tumor-related compression of the ureter/ureteric orifice or by transurethral resection-associated periorificial tissue swelling/edema. It is possible that decompression of the hydronephrosis by stenting instead of nephrostomy tube insertion is associated with an increased incidence of upper tract urothelial carcinoma (UTUC) due to potential retrograde tumor cell seeding; however, prior evidence is conflicting. Hence, our study aimed to investigate the association between type of decompression and UTUC incidence during followup.

Methods: We designed an observational study based on bladder cancer pathology reports linked to health administrative databases within the province of Ontario, Canada. Patients who underwent transurethral resection/biopsy of a urothelial bladder cancer between January 2001 and December 2015 that received upper tract decompression by stenting or nephrostomy insertion within seven days were included. We excluded patients who underwent UTUC between three years of the index date up to seven days after the index date and followed the cohort for the occurrence of UTUCs by querying the Ontario Cancer Registry. The association between the type of decompression (reference: nephrostomy tube) and time to UTUC was quantified by unadjusted and adjusted Cox proportional hazards regression analysis. Patients were censored at the date of death or at the date of the last contact with the healthcare system. Effect estimates are presented as hazard ratios (HR, 95% confidence intervals).

Results: We identified 973 patients diagnosed with bladder cancer but not with prior UTUC, who underwent decompression by either stenting (48.3%, n=470) or nephrostomy tube insertion (51.7%, n=503). During a median followup time of 10.9 (IQR 8.7–14.1) years, a UTUC occurred in 55 (5.7%) patients at a median time of 20.0 (3.4–56.4) months. During any time to followup stenting compared to nephrostomy tube insertion was associated with a higher incidence of UTUCs in unadjusted analysis (HR 2.30, 1.31–4.05). The association remained statistically significant (HR 1.85, 1.02–3.36) even after adjusting for assumed confounding variables (CT stage and grade).

Conclusions: Our data supports the hypothesis of retrograde tumor cell seeding in urothelial carcinomas. Although the incidence of UTUC is low, decompression of the upper urinary tract in patients harboring bladder cancer should ideally be achieved by nephrostomy tube insertion. This study is limited by missing information on the laterality of decompression and UTUC incidence.

Acknowledgements: This abstract has been accepted for presentation at the 39th Annual EAU Congress, as well as at the American Urology Association Annual Meeting 2024.