Poster Session 1: Oncology – Prostate (Part 1)
Sunday, June 30, 2024 • 16:10–17:40

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MP 1.1

Predictors of failed same-day discharge in patients undergoing robot-assisted radical prostatectomy at a Canadian center

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Introduction: Same-day discharge (SDD) after robot-assisted radical prostatectomy (RARP) has been shown to be feasible and safe in centers outside of Canada; however, heterogeneity exists in the inclusion criteria for those offered SDD in published literature. Our objective was to determine patient-specific and intraoperative predictors for failure of SDD for patients undergoing RARP at a Canadian center.

Methods: A retrospective review was conducted of patients undergoing RARP at a Canadian tertiary academic center from May 2021 to May 2023. Multivariate regression analysis determined predictors for non-initiation and failure of SDD (GraphPad Prism, Boston, MA, U.S.).

Results: We identified 387 patients, of whom 201 (51.9 %) were initiated on the SDD pathway. Of those initiated, 104 (51.7 %) were successfully discharged home the same day. Patients who traveled distances >100 km or who had obstructive sleep apnea (OSA) were significantly less likely to be initiated on the SDD pathway (Table 1). No association existed between patient body mass index ≥30 kg/m2, age ≥65, American Anesthesia Society (ASA) score ≥3, or case order on being initiated on the pathway (all p>0.05). Of those initiated on the SDD pathway, cases that were scheduled to be second or later, had an estimated blood loss ≥300 mL, or had a postoperative abdominal drain resulted in an increased likelihood of failing SDD after initiation. Operative time and ASA ≥3 had no significant relationship with failing SDD (all p>0.05).

Conclusions: We found that patients who live a greater distance from the hospital or who have a medical history of OSA are predictive of not being initiated on the SDD pathway. Of those initiated, postoperative abdominal drains, increased intraoperative blood loss, or being the second/third case of the day are more likely to fail SDD. The results of this study inform potential inclusion and exclusion criteria for SDD pathways being developed in Canada.

MP 1.1. Table 1. Predictors of non-initiation and failure of SDD

	Predictors of non-initiation of SDD		Predictors of failed SDD	
	OR (95% CI)	p	OR (95% CI)	p
Preoperative variables				
Age ≥65 (years)	1.35 (0.89–2.06)	0.160	0.70 (0.39–1.27)	0.242
BMI ≥30 (kg/m^2)	1.22 (0.79–1.88)	0.376	0.79 (0.43–1.47)	0.461
ASA ≥3	0.87 (0.51–1.48)	0.597	1.25 (0.59–2.66)	0.564
OSA	**2.18 (1.28–3.72)**	**0.004**	1.51 (0.65–3.51)	0.338
Distance ≥100 km	**3.85 (2.01–7.41)**	**<0.001**	1.58 (0.48–5.25)	0.447
Second case or later	1.32 (0.86–2.01)	0.207	**2.78 (1.52 –5.08)**	**0.001**
Intraoperative variables				
Operative time ≥150 (min)	–	–	2.04 (0.70–5.91)	0.189
Postoperative drain	–	–	**3.22 (1.18–8.75)**	**0.022**
EBL ≥300 (mL)	–	–	**2.33 (1.26–4.29)**	**0.007**

MP 1.2

Integrating stimulated Raman histology and AI for real-time surgical margin assessment during radical prostatectomy

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Introduction: Radical prostatectomy for prostate cancer (PCa) requires clear surgical margins and, when possible, maintaining sexual function. Stimulated Raman histology (SRH), a real-time imaging technique interpretable by artificial intelligence (AI), offers rapid assessment of fresh, unprocessed tissues, potentially improving surgical decision-making and nerve-sparing approaches.[1]

Methods: The IRB-approved study focused on intraoperative surgical margin assessments using SRH and postoperative analysis with a convolutional neural network (CNN). In the study, 22 men underwent robotic-assisted laparoscopic radical prostatectomy, with 121 intraoperative margin assessments using SRH, providing high-resolution images of fresh, unstained samples taken from the surgical bed. Real-time analysis by the surgical team identified cancer in the surgical bed samples, leading to immediate re-resection where PCa was detected. A CNN for prostate biopsy SRH was retrained on 57 margins from 12 patients and tested on 64 margins from 10 participants for margin analysis. The CNN's accuracy, sensitivity, and specificity were compared against final H&E-stained histopathology.

Results: SRH identified cancer in five prostate bed samples from three participants, prompting re-resection for a wider margin. Postoperative CNN analysis, taking 1–2 minutes per scan, accurately differentiated benign and malignant prostate bed samples. Mean CNN tumor probability predictions for benign samples were 0.3% (IQR 0.2–0.45%) and 25.8% (IQR 10–41.8%, p<0.00001) for cancer-bearing samples. The CNN achieved 100% accuracy, sensitivity, and specificity in identifying cancer in margin samples as compared to permanent histologic evaluation of the samples. Moreover, 50% of participants with positive surgical margins on final surgical pathology, were identified intraoperatively using SRH combined with CNN interpretation.

Conclusions: SRH, coupled with AI, provides a promising method for real-time surgical margin assessment in radical prostatectomies, enhancing nerve-sparing surgery accuracy and potentially reducing recurrence risks. Ongoing research is needed to fully establish SRH's oncologic and functional benefits.

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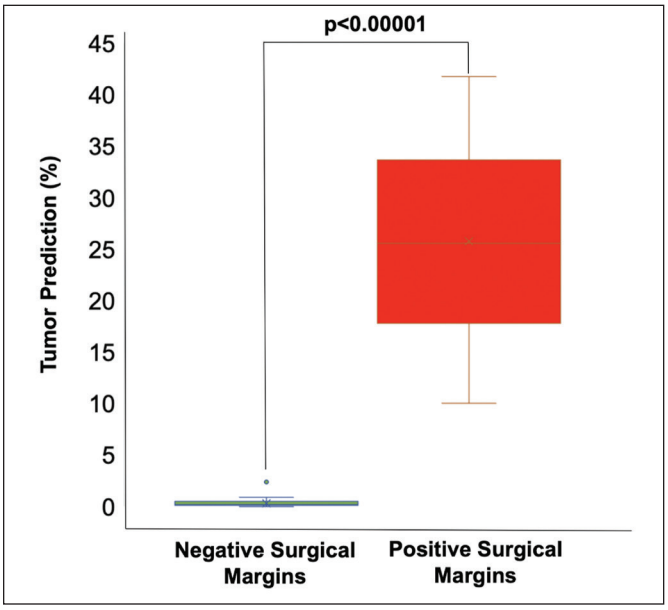
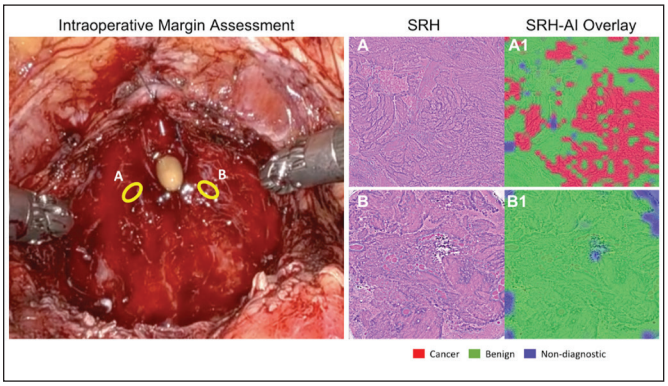
Reference:
1. Mannas MP, Jones D, Deng F-M, et al. Stimulated Raman histology, a novel method to allow for rapid pathologic examination of unprocessed, fresh prostate biopsies. *Prostate* 2023;83:1060-7. https://doi.org/10.1002/pros.24547



MP 1.2. Figure 1. Comparison of tumor prediction in percentages in negatives and positive surgical margins using AI interpreted SRH. The box plot represents the distribution of tumor prediction percentages for surgical margins classified as negative or positive by the AI CNN interpreting SRH. The mean tumor probability for negative surgical margins is markedly lower compared to positive surgical margins, with the red box indicating a substantial increase in tumor prediction percentages for the latter. The significant p-value <0.0001 indicates a statistically meaningful difference between the two groups.



MP 1.2. Figure 2. Intraoperative margin assessment with SRH and AI overlay. This figure represents a participant who underwent a SRH surgical margin assessment during a radical prostatectomy. The left panel shows an intraoperative image of the prostate resection bed with two areas marked A and B, which are areas of interest. For each marked area, there are corresponding SRH images (A, B) and SRH with AI overlays (A1, B1). A1 shows a positive surgical margin with ISUP grade group 2 prostate cancer and perineural invasion, while B1 shows benign peri-prostatic tissue: green=benign, red=tumor, and purple=non-diagnostic areas.

MP 1.3 - WITHDRAWN

MP 1.4

Incidence of second malignancies in prostate cancer patients treated with low-dose-rate brachytherapy and radical prostatectomy at extended followup

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Introduction: Second malignant neoplasia (SMN) is a rare but potentially lethal event after prostate brachytherapy (BT) but data remain scarce on its long-term risk. The primary objective of this study was to estimate the risk of pelvic SMN in patients treated with BT monotherapy compared to radical prostatectomy (RP) (alone or with adjuvant/salvage external bean radiation therapy [EBRT]). Secondary objectives included estimation of the incidence of invasive pelvic SMN, any SMN (pelvic and extrapelvic), and survival from any subsequent malignancy between cohorts.

Methods: We conducted a retrospective review of patients treated with prostate BT monotherapy and RP in British Columbia from 1999–2010. Incidence of pelvic, invasive pelvic, and any second malignancy and death from it were assessed. Cox multivariable analyses were performed, adjusting for initial treatment type, age, adjuvant/salvage EBRT status, and smoking history.

Results: A total of 2378 brachytherapy and 9089 prostatectomy patients were included. The median age was 66 (IQR 61–71) years and 63 (IQR 58–67) years, respectively. Median followup was 14 (IQR 11.5–17.3) years. The absolute risks of pelvic second malignancy at 15 and 20 years were 6.4% and 9.8% after brachytherapy, and 3.2% and 4.2% after prostatectomy, respectively. Time to any second malignancy and time to death from any second malignancy were not significantly different ($p>0.05$). On Cox multivariable analysis, brachytherapy, compared to surgery, was an independent risk factor for pelvic (HR 1.81, 95% CI 1.45–2.26, $p<0.0001$) and invasive pelvic second malignancy (HR 2.13, 95% CI 1.61–2.83, $p<0.0001$). Increased age and smoking were also associated with increased risks ($p<0.05$).

Conclusions: After adjustment for age and smoking status, a significant increased risk of pelvic and invasive pelvic second malignancy in patients treated with brachytherapy compared to radical prostatectomy was noted, even with inclusion of patients who had adjuvant/salvage EBRT.

MP 1.5

Monitoring lethal prostate cancer through genomic alterations in primary tumors and circulating tumor DNA

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Introduction: Prostate cancer (PCa) is a major cause of cancer deaths worldwide. Although curative therapies increase survival, recurrence is inevitable in 25–35% of patients. Markers detecting key modifications are needed to better control disease progression. This study aimed to identify alterations in primary tumors of patients with lethal PCa and shared/exclusive changes in circulating tumor (ct)DNAs.

Methods: Banked fresh frozen prostates (n=25) from radical prostatectomy (RP) cases were processed to identify tumor foci and macro-dissect cores of high cellularity (>75%) for DNA extraction. Serial plasma collections at four timepoints (0/prior RP, 33, 43, and 52 months) from one lethal case were used to isolate cell-free (cf)DNA using the QIAamp Kit, after optimization. Whole genome sequencing (WGS) of tumor and matched germline (blood) DNA, and of cfDNAs was performed at 100x, 40x, and 170x depths, respectively. Sequencing files were processed using an adapted GenPipes DNA-seq pipeline to call mutations in coding regions, copy number variations (CNVs), and fusions.

An in-house Python script was developed to filter alterations and find shared/exclusive modifications.

Results: Already established PCa-CNVs were found in our cases, notably losses in PTEN (72%), NKX3-1 (68%), TP53 (48%), and RB1 (32%), and gains in MYC (40%) and NCOA2 (32%). Also, deletions in 11p15.5 (84%) containing MRPL23, H19 genes and 21q22.3 (80%) harboring tumor suppression gene (SIK1) were discovered. A new genomic loss at 22q11.21 (44%) containing genes involved in PCa cell survival (PRODH) was detected. In the patient whose cfDNAs were sequenced during his entire trajectory, 52 somatic mutations were identified in the tumor, of which 27 were found in ctDNAs. The ctDNA fraction was very low at RP and increased over time. Somatic mutations in PCa-related genes (PRSS3, FOLH1, KMT2C) were differentially detected in tumors vs. ctDNAs. Eight other mutations and CNVs promoting neuroendocrine and stem-like cell phenotypes were only detected in the last ctDNA prior to death, supporting a metastatic origin. Notably, no gain in MYC was found. Mutations in DNA damage response genes (not in BRCA1/2) and PDGFRB were also noticed in germline DNA. Functional analysis of mutated genes studied in this patient revealed an over-representation of cell cycle, DNA repair, and senescence processes.

Conclusions: Our findings pinpoint recurrent and new genomic alterations in patients with severe disease. The ctDNA data support the importance of liquid biopsy to monitor progression. The identification of novel genomic changes in ctDNAs may improve our understanding of lethal PCa and lead to the development of novel tests and more effective treatments.

Acknowledgements: The authors would like to thank the patients who donated samples for this study; the Marathon of Hope Canadian Cancer Network (Health Canada)/Terry Fox Research Institute, CEDARS Cancer Foundation/Royal Victoria Hospital/MUHC Cancer Center, and PROCURE Alliance for financial support. S.R was awarded several studentships, notably from Fonds de Recherche du Québec - Santé. Thanks to the McGill Genome Center Sequencing Core for sequencing services, Dr. Hussein Daoud and Dr. Magalie Celton from Illumina for technical support, and Dr. Ian Watson and his research associate-bioinformatician, Dr. Mathieu Lajoie, for helpful discussion. Bioinformatic analyses were enabled through Calcul Québec (www.calculquebec.ca) and Compute Canada (www.computecanada.ca).

MP 1.6

Temporal validation of SEPERA to inform nerve-sparing strategy during radical prostatectomy and comparison against expert surgeons

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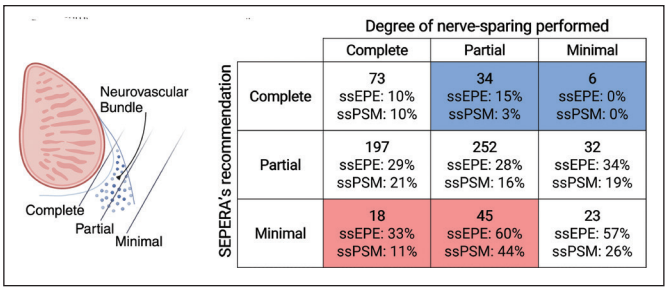
Introduction: Extraprostatic extension is associated with worse oncologic outcomes following radical prostatectomy (RP). Sparing of the neurovascular bundles during RP is a key determinant of functional outcomes, including urinary continence and potency. The degree of nerve-sparing performed is a delicate balance between maximizing functional outcomes while minimizing the risk of positive surgical margins. Thus, accurate prediction of side-specific extraprostatic extension (ssEPE) is essential to inform nerve-sparing strategy.

Methods: We previously developed and validated a machine-learning model, SEPERA (Side-specific Extra-Prostatic Extension Risk Assessment). Temporal validation was performed on 695 patients undergoing RP at University Health Network and Trillium Health Partners from 2020–2022. The SEPERA-predicted risk of ssEPE was used to generate recommendations for the degree of nerve-sparing using thresholds that achieved 95% sensitivity (risk=0.16) and 95% specificity (risk=0.57) on the original dataset. SEPERA recommended strategies of "Complete" (risk<0.16), "Partial" (risk 0.16-0.57), and "Minimal" (risk>0.57) nerve-sparing, which were compared to the actual degree of nerve-sparing performed by surgeons during the study period. The proportion of cases with ssEPE and positive surgical margins (ssPSM) were compared between SEPERA and surgeon-concordant and discordant cases.



MP 1.6. Figure 1. Comparison of pathologic outcomes in cases of SEPERA vs. surgeon-concordant and discordant degrees of nerve-sparing.

Results: ssEPE was found in 467 out of 1390 prostatic lobes (34%). SEPERA performed similarly compared to the original study, with AUROC 0.75 (95% CI 0.73–0.78) and AUPRC 0.63 (95% CI 0.58–0.67). SEPERA's recommendations differed from clinical decisions in 49% of cases (Figure 1). Where SEPERA recommended "Minimal" nerve-sparing but a greater degree of nerve-sparing was performed, 52% of cases had ssEPE and 35% had ssPSM. Conversely, where SEPERA recommended "Complete" nerve-sparing but less was performed, only 13% of cases had ssEPE and 3% had ssPSM.

Conclusions: In both academic and community settings, SEPERA improves current practice and pathologic outcomes by accurately predicting ssEPE. SEPERA can inform nerve-sparing strategy during RP, especially when "Minimal" nerve-sparing is recommended.

Acknowledgements: Lauren Pickel was supported by the T-CAIREM AI in Medicine Summer Student Research Program. Jethro C.C. Kwong was supported by the University of Toronto Surgeon Scientist Training Program.

Reference:

1. https://www.thelancet.com/journals/landig/article/PIIS2589-7500(23)00067-5/fulltext

MP 1.7

Surgeon variability in oncologic and patient-reported outcomes in radical prostatectomy

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Introduction: Radical prostatectomy (RP) requires a balance between complete cancer removal and preserving quality of life. It is logical that closer dissection to the prostate is associated with worse cancer outcomes, but better functional outcomes. We sought to examine variability in oncologic and patient-reported functional outcomes between prostate cancer surgeons.

Methods: A prospective cohort study including eight surgeons and all patients undergoing RP from 2015–2022 was conducted. Patient function was assessed preoperatively and one-year postoperatively using EPIC-32/EPIC-CP validated questionnaires. Cancer outcomes were positive surgical margins (PSM) and disease recurrence (post-op PSA>0.2 ng/ml, receipt of post-op radiation, and/or androgen deprivation). Multivariate logistic regression models were constructed for each outcome using clinically and statistically significant characteristics and were used to calculate observed-to-expected ratios (O/E) for surgeons.

Results: From 2015–2022, 1698 patients were included with mean age of 65 (range 38–81) years. Most patients were continent (98%) and potent (58%) prior to surgery. The majority underwent robotic RP (90%) and nerve spare (NS) (79%). pT3 disease was present in 53% (no statistical difference between surgeons). Following adjustment for baseline variables, statistical differences were observed between surgeons for all outcomes (O/E ranges; NS: 0.48–2.0; PSM: 0.59–1.61; one-year recurrence: 0.79–1.84; one-year continence: 0.68–1.17; one-year potency: 0.45–1.64). Surgeons performing proportionally more NS had better functional outcomes. Counter to our hypothesis, surgeons with better functional outcomes also had better cancer outcomes on multivariate analysis.

Conclusions: We observed large clinical and statistical differences in functional and cancer outcomes between surgeons. Surgeons performing more NS had better functional outcomes, but also better cancer outcomes. These data suggest a need for quality improvement initiatives for prostate cancer surgeons.

MP 1.8

Lymphotropic pattern of PSMA-detected metastases among biochemically recurrent radical prostatectomy patients with cribriform disease

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Introduction: Cribriform morphology portends worse oncologic outcomes and has unique cellular intrinsic pathway alterations and tumor microenvironments that may impact metastatic spread patterns. We aimed to determine whether presence of cribriform morphology in prostatectomy specimens of patients with biochemical recurrence post-radical prostatectomy (RP) is associated with presence of metastasis on PSMA-PET/CT and a distinct pattern of spread.

Methods: We conducted a cross-sectional analysis of all prostate cancer patients with biochemical recurrence post-RP undergoing an 18F-DCFPyL-PET/CT between December 2018 and February 2021 at The Princess Margaret Cancer Centre. Outcomes were the presence of any metastasis in the overall cohort and lymphatic vs. bone/visceral metastases amongst patients with metastatic disease. The associations between intraductal (IDC) and/or invasive cribriform carcinoma (ICC) presence on the RP specimen and study outcomes were evaluated using logistic regression analyses.

Results: The cohort included 176 patients. IDC and ICC were observed in 77 (43.8%) and 80 (45.5%) RP specimens, respectively. The median time from RP to PSMA-PET/CT was 5.0 years. Median serum PSA at PSMA-PET/CT was 1.12 ng/ml. Overall, metastasis was observed in 77 patients, of which 58 were lymphatic-only. On multivariable analysis, the presence of IDC on RP was associated with increased odds of overall metastasis (OR 2.17, 95% CI 1.07–4.45, p=0.033). The presence of ICC on RP was associated with significantly increased odds of lymphatic versus bone/visceral metastases (OR 3.13, 95% CI 1.09–21.7, p=0.004).

Conclusions: The presence of cribriform morphology on RP specimens of patients with biochemical failure post-RP is associated with increased odds of PSMA-PET/CT-detected metastases with a lymphatic-predominant pattern of spread. These findings have implications for the design and evaluation of post-RP salvage therapies.

MP 1.9 - WITHDRAWN

MP 1.10

Screening of metabolic, cardiac, and bone health in prostate cancer patients on androgen deprivation therapy: A population-based assessment of adherence to therapeutic monitoring guidelines

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Introduction: Androgen deprivation therapy (ADT) remains a part of the standard of care for men with advanced prostate cancer. American, Canadian, and European Urologic Associations (AUA/CUA/EUA) suggest regular metabolic monitoring for men on ADT. Surveys of ADT providers have revealed varying adherence to monitoring guidelines. We explored the prevalence and predictors of adherence to monitoring guidelines in this population.

Methods: We conducted a retrospective cohort study using administrative data sources in Ontario, Canada (Institute for Clinical Evaluative Sciences) from 2008–2021. We identified all men receiving ADT for prostate cancer. The primary outcomes were the use of bone density testing, bone health serum testing, lipid testing, and glucose/diabetes testing between six weeks preceding and one year following initiation of ADT. Secondary outcomes included predictors of adherence. Binomial logistic regressions were primarily used to analyze data.

Results: We examined 29 097 patients, of whom 52.8% were prescribed ADT by urologists, 37.9% by radiation oncologists, 2.8% by medical oncologists, and 2.4% by other physicians. Adherence to therapeutic screening guidelines was generally low: only 21.3% of patients received a bone density scan, 41.2% underwent bone health-related serum tests, 51.3% had a lipid profile completed, and 65.9% underwent blood sugar screening. ADT prescription by a medical oncologist was associated with a lower likelihood of undergoing screening tests for plasma glucose (RR 0.78, 95% CI 0.64–0.96, p=0.02), lipids (RR 0.65, 95% CI 0.58–0.80, p≤0.01), and bone density (RR 0.62, 95% CI 0.43–0.89, p=0.009) within a year when compared to prescription by urologists. Increasing patient age was associated with lower adherence to screening guidelines for lipids (RR 0.26, 95% CI 0.12–0.62, p=0.002) and bone health (RR 0.37, 95% CI 0.17–0.83, p=0.016). Trends in adherence to screening guidelines did not significantly change with increased duration of time on ADT.

Conclusions: Adherence to therapeutic screening guidelines for men on ADT was poor across all provider specialities. Increasing age was associated with a significant reduction in likelihood of lipid and bone health screening. Further study is required to identify and address barriers to therapeutic monitoring of men on ADT and reduce treatment associated adverse events.

MP 1.11

Integrating clinical data and FDG-PET/CT imaging with a multi-task machine learning model to predict outcomes in high-grade prostate cancer

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Introduction: We aimed to develop an automated multi-task prognostic model that combines clinical data with radiomics from positron emission tomography (PET) with 18F-fluorodeoxyglucose (FDG) combined with computed tomography (CT), eliminating the need for manual segmentation while providing clinically interpretable results. This is the first study of its kind using radiomics in prostate cancer that describes long-term clinical outcomes.

Methods: The research involved 295 individuals with high-grade prostate cancer (Gleason score ≥8) who underwent radical prostatectomy (RP) and FDG-PET/CT imaging preoperatively at our tertiary care health center. Clinical data (CD), including age, prostate-specific antigen (PSA) level, clinical stage, and Gleason grade, were collected. Six prognostic tasks were defined, including lymph node invasion (LNI), biochemical recurrence (BCR)-free survival (FS), metastasis-free survival (MFS), definitive androgen deprivation therapy (dADT)-FS, castration-resistant prostate cancer (CRPC)-FS, and prostate cancer-specific survival (PCSS). A Bayesian sequential network (BSN), a dynamic prediction model quantifying uncertainty and adapting over time as outcomes from prior tasks unfold, was developed. It was compared with commonly used nomograms (MSKCC and CAPRA-S). Performance metrics on the holdout set were evaluated using the area under the curve of the receiver operator characteristic (AUC-ROC) and the concordance index (C-index).

Results: Median followup was 64.7 (range 29.3–89.6) months. Median age was 66 (48–80) years. Median PSA was 7.4 (1.1–155.3). A total of 230 (88%) and 31 (12%) had clinical T1-T2 and T3a disease, respectively. At RP, 86 (29%) had LNI. At followup, 160 had BCR, 38 had metastases, 72 started dADT, 23 had CRPC, and 11 had PCSS. On the holdout set comprising 45 individuals, the BSN model outperformed nomograms for predicting LNI (AUC 66.3%), MFS (CI 75.3%),

and dADT-FS (CI 69.6%). The nomogram still outperformed our BSN model for predicting BCR-FS (CI=63.5% [MSKCC] vs. 59.2%), CRPC-FS (CI 67.6% [CAPRA-S] vs. 65.6%), and PCSS (CI 87.8% [MSKCC] vs. 78.0%).
Conclusions: We present a fully automated, self-learning, multi-task model that integrates FDG-PET/CT imaging data to predict clinical outcomes while quantifying associated uncertainty. It achieved good predictions with minimal training compared to commonly used nomograms.
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MP 1.12

Causes of death in prostate cancer patients after initial treatment with radical prostatectomy or radiation therapy

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Introduction: We evaluated the causes of death in a cohort of prostate cancer (PCa) patients who underwent radical prostatectomy (RP), external beam radiation therapy (EBRT), or EBRT combined with brachytherapy (BT).
Methods: The study population consisted of 32 772 men who underwent RP, EBRT, or EBRT+BT between 2000 and 2016. A cohort study was constructed using Quebec administrative databases (Med-Echo and RAMQ). Included men were diagnosed and treated for PCa from 2000–2016. Followup ended at the earliest of the following: death, or December 31, 2016. Inverse probability of treatment weighting (IPTW) based on a propensity score was used to control for potential confounding. IPTW-Cox proportional hazards models were used. Four death categories were defined: 1) PCa-specific death; 2) PCa not well-defined death; 3) cardiovascular disease death; and 4) other causes of death.
Results: Compared to RP, the risk increases significantly with EBRT for PC-specific death (HR 3.19, 95% CI 2.85, 3.35), PCa not well-defined death (HR 1.974, 95% CI 1.78, 2.18), cardiovascular disease (HR 1.27, 95% CI 1.27, 1.45), and other causes of death (HR 1.44, 95% CI 1.31, 1.59). For patients receiving EBRT+BT, the risk diminished significantly for PCa-specific death (HR 0.59, 95% CI 0.47, 0.74) and other causes of death (HR 0.74, 95% CI 0.58, 0.95); but not for PCa not well-defined death (HR 0.84, 95% CI 0.66, 1.06) nor cardiovascular disease death (HR 0.81, 95% CI 0.60, 1.08). In the EBRT group, the mortality was higher than in the RP group (59.5 vs. 32.1 within 16 years). Furthermore, most deaths were due to PCa (39.1%), while most patients in the RP group died of other causes, other cancers, or CVD-related (31.6%).
Conclusions: This study found an increased mortality risk in all categories for PCa patients in the EBRT group compared to the RP group. In the EBRT group, most deaths were due to PCa, while in the RP group, most patients died of other causes. The risk of PCa-specific and other causes of death diminished significantly for patients receiving EBRT+BT compared to patients who had undergone RP.

MP 1.13

Accurate risk models with and without magnetic resonance imaging features and digital rectal examination findings to predict clinically significant prostate cancer before prostate biopsy

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Introduction: Most men with prostate cancer (PCa) have low-risk, indolent disease, but men with clinically significant disease (csPCa) are at risk of disease progression and adverse outcomes. Identifying csPCa while avoiding unnecessary biopsies with low-risk PCa is a challenge. The decision to biopsy relies on available clinical data, including magnetic resonance imaging (MRI) and digital rectal exam (DRE) data. This study aimed to create accurate predictive models for csPCa ± MRI and DRE data.
Methods: Optimized ensembles of calibrated random forest models predicting grade group ≥2 used total PSA, free PSA, prior negative biopsy status, and age, with or without DRE and MRI data (prostate volume and PI-RADS score). Risk models were derived (training cohorts n=1257–2191) and validated (validation cohorts n=317–1257) from different clinical sites (Table 1). Models were evaluated by the area under the receiver operating characteristic curve (ROC AUC),

MP 1.13. Table 1. Risk models predicting clinically significant prostate cancer (grade group ≥2) with and without DRE findings and the MRI features prostate volume and PI-RADS score

DRE	MRI (prostate volume & PI-RADS)	Clinical sites	Patient number	ROC AUC	Threshold	Sens	Spe	PPV	NPP	Model label
Training cohort										
No	No	UCLA, UC, JHU	2191	0.80	≥25	94	34	51	89	-DRE/-MRI
Yes	No	UCLA, UC, JHU	2191	0.82	≥25	94	37	52	89	+DRE/-MRI
No	Yes	UCLA, JHU	1626	0.89	≥17	96	45	56	94	-DRE/+MRI
Yes	Yes	UCLA, JHU	1626	0.89	≥17	96	46	56	94	+DRE/+MRI
Validation cohort										
No	No	UA, TUH	1257	0.80	≥25	95	32	52	89	-DRE/-MRI
Yes	No	UA, TUH	1257	0.82	≥25	95	35	54	91	+DRE/-MRI
No	Yes	TUH	317	0.87	≥17	95	45	50	94	-DRE/+MRI
Yes	Yes	TUH	317	0.87	≥17	95	47	51	94	+DRE/+MRI

All models used PSA, free PSA, age, and prior negative biopsy status.

sensitivity, specificity, positive predictive value, and negative predictive value, using thresholds providing approximately 95% sensitivity.

Results: When using a 25% threshold for predicting grade group ≥2 PCa, the model without data on DRE/MRI results had sensitivity and specificity values of 94% and 34%, respectively, in the training cohort, and 95% and 32%, respectively, in the validation cohort. At the same 25% threshold, +DRE -MRI had 3% higher specificity than -DRE -MRI for both the training and validation cohorts. Including MRI features in the models significantly increased the AUC in the validation cohort (AUC 0.80 vs. 0.87). DRE was moderately useful for models without MRI features (AUC 0.80 vs. 0.82) and had a minor value for models with MRI features (AUC 0.87 vs. 0.87; specificity 45% vs. 47%) (Table 1).

Conclusions: The created risk models provide high accuracy and improved specificity for predicting csPCa in a variety of clinical settings. Including MRI features greatly increased model accuracy. Better stratification can maximize detection of high-risk PCa while minimizing harms associated with detecting low-risk PCa and performing unnecessary prostate biopsies.

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MP 1.14

Enhancing urologic function and physical fitness in prostate cancer survivors: Outcomes from a 28-day Prostate Cancer-Patient Empowerment Program (PC-PEP)

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Introduction: Prostate cancer survivors commonly experience urinary, bowel, and erectile dysfunctions post-treatment, which significantly impact their physical and mental health. This study evaluates the effectiveness of a 28-day Prostate Cancer-Patient Empowerment Program (PC-PEP) in improving urologic and physical health outcomes.

Methods: Thirty prostate cancer patients from the Maritimes, Canada, participated in the 28-day PC-PEP feasibility trial. The study measured physical health through anthropometric, aerobic, strength, and flexibility tests, and urologic function using the Expanded Prostate Cancer Index Composite (EPIC), both before and after the intervention. A priori paired t-tests were conducted for EPIC variables and repeated-measures ANOVA was used to assess physical fitness outcomes.

Results: Significant improvements were observed in various EPIC variables post-intervention ($p<0.05$), including bowel subscale bother, $t(29)=-2.11$; sexual subscale bother, $t(20)=6.34$; and hormonal subscale bother, $t(29)=-2.42$. Physical health assessments also showed significant changes ($p<0.05$) in several areas: diastolic blood pressure, $F(1, 29)=4.27$; weight, $F(1, 29)=4.25$; combined grip strength, $F(1, 29)=6.06$; sit-to-stand endurance, $F(1, 29)=11.93$; hamstring flexibility, $F(1, 29)=4.70$; and shoulder flexibility, $F(1, 26)=5.34$.

Conclusions: The study's findings indicate positive trends in improving urologic and physical health outcomes post-PC-PEP by reducing the impact of urologic symptoms and enhancing physical fitness. These results will be instrumental in refining future versions of the PC-PEP, aiming to further augment the well-being of prostate cancer survivors.

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MP 1.14. Table 1. Demographic characteristics for 30 men with a history of PCa from the Maritimes, Canada, who participated in the PC-PEP feasibility trial

Variable	
Age, years, mean (range)	68.93 (56–83)
Ethnicity, n (%)	
White/Caucasian	28 (93%)
Education, n (%)	
University	20 (67%)
Relationship status, n (%)	
In a relationship	30 (100%)
Employment status, n (%)	
Retired or unemployed	21 (70%)
Household income, n (%)	
<$80 000/year	8 (27%)
Time between prostate cancer diagnosis and trial, n (%)	
>25 months	22 (73%)
Treatment modality, n (%)	
Active surveillance	4 (13%)
Radical prostatectomy	14 (47%)
Radiation therapy (beam, brachy or seed) +/- hormone therapy	6 (20%)
Radical prostatectomy, radiation therapy, and hormone therapy	4 (13%)
Androgen deprivation therapy	2 (7%)
Physical activity level, n (%)	
Pre-intervention	
Not very active (<30 min/week) to moderately active (30–150 min/week)	24 (80%)
Post-intervention	
Not very active (<30 min/week) to moderately active (30–150 min/week)	19 (63%)
Support group attendance, n (%)	
Pre-intervention	
Yes	10 (33%)
Post-intervention	
Yes	13 (43%)
Treatment regret, n (%)	
Pre-intervention	
Yes	5 (17%)
Post-intervention	
Yes	3 (10%)
Types of educational information the patient received from the hospital at the time of treatment, n (%)	
Diagnosis	25 (83%)
Available types of treatment	19 (63%)
Best diet	9 (30%)
Best form of exercise	8 (27%)
Impact on relationship with partner/sexual life	14 (47%)
Participants' specific treatment type	13 (43%)
Other side effects/consequences of the treatment received on quality of life	3 (10%)
Self-reported patient satisfaction with regards to the education materials received from the hospital at the time of diagnosis, n (%)	
Not satisfied at all	6 (20%)
Somewhat satisfied	5 (17%)
Neither satisfied nor unsatisfied	10 (33%)
Mostly satisfied	5 (17%)
Extremely satisfied	4 (13%)

MP 1.15

A human-derived 3D model of prostate cancer as a precision medicine tool

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Introduction: Prostate cancer (PCa) ranks among the most prevalent cancers in developed nations, yet treatments for advanced stages offer palliative relief. The existing research models for PCa lack fidelity in replicating crucial aspects of its biology, impeding translational potential to clinical applications. Our project's primary objective was to create a human-derived 3D PCa model using tissue engineering techniques.

Methods: Our methodology involves the cultivation of human prostate fibroblasts through the self-assembly method, creating stroma, and subsequent seeding of prostate epithelial cells on this stroma to mature into an epithelium. Specific cell culture conditions, including testosterone incorporation, replicate the hormone-responsive nature of the prostate. We integrated invasive PCa cell lines and spheroids to analyze invasion dynamics, offering a comprehensive platform for studying the tumor microenvironment. In our process, fibroblasts are initially seeded at confluence in six well plates with a circular paper anchor, held down with a round stainless-steel ingot, and cultured in DMEM medium supplemented with ascorbate to promote collagen deposition over 14 days. Subsequently, these sheets are reseeded with fibroblasts for another 14 days and stacked, aided by rectangular stainless-steel ingots to facilitate stromal layers' fusion. Half of these stromas are cultured using a mixed media, incorporating conditioned media from the DU145 cell line to promote the induction of the fibroblasts into cancer-associated fibroblasts (CAF). Spheroids produced from the LNCAP and DU145 PCa cell lines were deposited onto the stromas. The DU145 line represents invasive PCa cells, while LNCAP denotes a non-invasive cell line.

Results: We successfully created manipulatable stromas formed from prostate fibroblasts and from CAFs. Atomic force microscopy (AFM) was performed on the stromas to measure tissue rigidity, and thus ascertain the presence of CAF in the CAF induced stromas. Spheroids from the DU145 and LNCAP PCa cell lines were deposited on these stromas and their invasion of the tissues was analyzed by atomic force microscopy and by immunofluorescence. These techniques were done to allow better visualization of the spheroid invasion into the stroma and its impact on the neighboring cell's rigidity, mimicking the cancer microenvironment, and the CAFs' induction, leading to a higher rigidity.

Conclusions: This groundbreaking model shows great promise in discovering new treatment targets, which could improve patient outcomes and reduce the economic strain of PCa on healthcare systems. Our work in creating a 3D model of prostate cancer using human cells marks a significant advancement in PCa research.

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MP 1.16

Cost-effectiveness of olaparib vs. rucaparib for patients with metastatic castration-resistant prostate cancer: The Canadian perspective

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Introduction: Through phase 3 clinical trials, olaparib (ola) and rucaparib (ruca), (poly[adenosine diphosphate–ribose] polymerase inhibitors) have demonstrated outcome improvements in metastatic castration-resistant prostate cancer (mCRPC) patients with alterations of BRCA1/2 and having progressed on second-generation androgen-receptor pathway inhibitor (ARPI). While improving outcomes, ruca and ola contribute to the ever-growing economic burden of PCa. Cost-effectiveness analyses are needed to estimate their economic impact. We aimed to evaluate the cost-effectiveness of ola and ruca vs. physician's choice (docetaxel or ARPI) for mCRPC patients with BRCA1/2 mutations in a Canadian healthcare setting.

Methods: Partitioned survival models were created to represent mCRPC disease after progression on ARPI until death or five years. Survival inputs were extracted from PROfound and TRITON3. Ola costs were extracted from the Quebec Health Insurance Board medication list. As ruca is not commercially available in Canada, we hypothesized that it would be priced on par with ola.

Results: Our findings suggest that ruca provides better survival benefits in terms of quality-adjusted life years (QALY) than ola, but at a higher cost (ICER $301 182/QALY). When compared to docetaxel, ola and ruca provided additional 0.07 and 0.24 QALY with additional costs of $78 246 and $129 547, resulting in ICERs of $1 078 005/QALY and $522 504/QALY, respectively. When compared to ARPI, ola and ruca demonstrated clinical benefit and ICERs of $580 158/QALY and $503 417/QALY respectively.

Conclusions: While providing survival benefit to mCRPC patients presenting alterations of BRCA genes, the cost of ola and ruca requires major reductions to be considered cost-effective from the Canadian healthcare perspective.