UROpedia CANADA

REVIEW

Association of absolute amount of pattern 4 disease on prostate biopsy with oncologic outcomes in intermediate-risk prostate cancer

A systematic review

Melissa Sam Soon[1], Scott C. Morgan[2], Luke T. Lavallée[3], Rodney H. Breau[3], Trevor A. Flood[4], Mark T. Corkum[2]

[1]University of Ottawa, Ottawa, ON, Canada; [2]Division of Radiation Oncology, Department of Radiology, Radiation Oncology and Medical Physics, University of Ottawa and the Ottawa Hospital, Ottawa, ON, Canada; [3]Division of Urology, Department of Surgery, University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, ON, Canada; [4]Department of Anatomical Pathology, University of Ottawa and the Ottawa Hospital, Ottawa, ON, Canada

Cite as: Sam Soon M, Morgan SC, Lavallée LT, et al. Association of absolute amount of pattern 4 disease on prostate biopsy with oncologic outcomes in intermediate-risk prostate cancer: A systematic review. *Can Urol Assoc J* 2025;19(6):211-6. http://dx.doi.org/10.5489/cuaj.8995

Published online February 24, 2025

Appendix available at *cuaj.ca*

ABSTRACT

INTRODUCTION: Managing intermediate-risk prostate cancer is challenging due to the heterogeneity in patient outcomes within this risk category. Evaluating the absolute amount of Gleason pattern 4 disease (GP4) at biopsy using the total linear length of pattern 4 (GP4-TL) or absolute percentage of pattern 4 (APP4) may enhance risk stratification. This review aimed to determine if these absolute measures predict oncologic outcomes in IRPC and to identify optimal prognostic thresholds.

METHODS: A systematic review was conducted following PRISMA guidelines. Studies included were those reporting the absolute amount of GP4 on biopsy and related outcomes in IRPC patients undergoing surgery or radiotherapy. Outcomes included biochemical recurrence, androgen deprivation therapy (ADT)-free survival, distant metastasis, prostate cancer-specific mortality, all-cause mortality, and adverse pathology.

RESULTS: Seven studies with a total of 2523 patients were included. Analysis revealed that APP4 thresholds were highly predictive of biochemical recurrence, ADT-free survival, and distant metastasis. Both APP4 and GP4-TL were superior to relative % GP4 and Gleason grading (4+3 vs. 3+4) in predicting disease progression and mortality.

CONCLUSIONS: The absolute amount of GP4 shows consistent associations with important clinical outcomes and offers an accessible and established method to enhance risk stratification. Further research is needed to define optimal thresholds to guide treatment decisions.

INTRODUCTION

Risk stratification is a core concept in the diagnosis and management of men with prostate cancer. Along with prostate-specific antigen (PSA) and clinical T-stage, the Gleason score obtained from prostate biopsies is integrated into the original D'Amico staging system of low-, intermediate- and high-risk localized prostate cancer.[1,2] National Comprehensive Cancer Network (NCCN) guidelines have since further split these categories into more distinctive subgroups, using biopsy information such as the proportion of positive prostate biopsy cores.[2]

Despite these efforts, clinical outcomes remain heterogeneous for men with intermediate-risk prostate cancer, reflecting different risk profiles within the same risk category. For example, current NCCN guidelines consider a patient with a PSA of 18 and 12/12 biopsy cores of Gleason 4+3 prostate cancer in the same unfavorable intermediate-risk category as a patient with a PSA of 11 and a single core of Gleason 3+4 prostate cancer.

The Gleason score has evolved substantially since its initial inception, with recommendations from the 2014 International Consensus in Chicago recommending the relative percentage of Gleason pattern 4 (GP4) reported on prostate biopsy reports.[3] This may have a major impact on treatment decisions;[4] for example, men with 5% or less of GP4 prostate cancer may now be considered reasonable candidates

for active surveillance despite having intermediate-risk disease.[5]

To enhance prognostication for men with intermediate-risk prostate cancer, it may be beneficial to use measures that quantify the absolute amount of GP4. In this review, we identified two methods for accomplishing this: 1) by measuring the linear length of GP4 in prostate biopsies (GP4-TL); or 2) by calculating the absolute percentage of GP4 (APP4). GP4-TL is obtained with the following equation: GP4-TL (mm) = sum of (cancer length × percentage of GP4 in each cancer-positive core).[6-10] APP4 (%) is calculated as (% of biopsy tissue positive for disease) × (percentage of disease that is pattern 4)/100%.[10-12] See Figure 1 for an example of these calculations.

While no major risk-stratification system incorporates absolute measures of GP4, they can be a practical clinical tool to subdivide patients with intermediate-risk prostate cancer beyond NCCN classification. In this systematic review, we sought to appraise and assess studies that calculated APP4 or GP4-TL on prostate biopsies to determine if clinical outcomes (i.e., biochemical recurrence, androgen deprivation therapy [ADT]-free survival, distant metastasis, prostate cancer-specific mortality, all-cause mortality, and adverse pathology) can be predicted beyond standard risk-classification systems, and if so, what the optimal cut points are.

METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Literature search

A systematic search was conducted in Embase, MEDLINE, and CENTRAL from inception to May 2023. Our search strategy was developed with the assistance of a reference librarian and included keywords such as prostate cancer, prostatectomy, Gleason grade 4, and pattern 4. The search strategy can be viewed in Appendix A (available at *cuaj.ca*). The reference lists of the identified studies were also checked to find additional articles relevant to our research question. Studies were screened in duplicate by two independent reviewers (M.S.S. and M.C.).

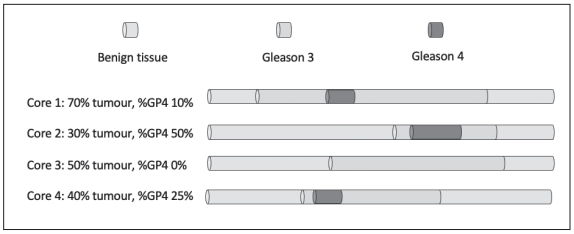

Figure 1. Example case for GP4-TL and APP4 calculations. Core lengths are standardized to 10 mm. GP4-TL is calculated as follows: (7 mm x 0.1) + (3 mm x 0.5) + (5 mm x 0.0) + (4 mm x 0.25)=3.2 mm. APP4 is calculated as follows: global % tissue involved=47.5%, relative pattern 4=16.8; APP04=47.5% x 16.8%/100=8.0%.

Study selection

The inclusion criteria were as follows: studies that evaluated the amount of GP4 on prostate biopsy and reported clinical outcomes; original research published in English; studies involving patients with intermediate-risk localized prostate cancer who underwent surgery or radiotherapy, with or without hormone therapy. We included studies with mixed cohorts of low- and intermediate-risk prostate cancer patients, provided that data for each risk group was reported and analyzed separately. Studies screened at the title and abstract stage were excluded if they did not meet one or more of these inclusion criteria.

Exclusion criteria were studies published in abstract format only, not in English, and not an original article. Studies that measured the volume of GP4 only in radical prostatectomy specimens (but not prostate biopsy samples) were excluded, as they represent a different clinical scenario, and the aim of this review was to evaluate the absolute amount of GP4 as a pre-treatment predictor of outcomes. Reasons for exclusions were recorded at the full-text screening stage.

Data extraction and analysis

Data was extracted by two authors independently (M.S.S. and M.C.) into a standardized collection form. Data abstracted from studies included primary author, year of article publication, study design, country, inclusion and exclusion criteria for study sample, number of patients analyzed, type of biopsy performed, and outcome measures. Patient characteristics included age, followup duration, treatment type, and characteristics if specified (i.e., radiation dose and duration of ADT). Outcomes of interest included biochemical recurrence, ADT-free survival, distant metastasis, prostate cancer-specific mortality, all-cause mortality, and adverse pathology. Measures of effect sizes of APP4 or GP4-TL and associated clinical outcomes were also collected from included studies. Due to the significant heterogeneity among studies, including variability in patient populations, treatment modalities, primary endpoints, and study design, it was not feasible to conduct a meta-analysis. A descriptive summary of the results is provided.

RESULTS

Literature search and study characteristics

The literature search resulted in 2038 articles. Our broad search strategy caught many studies that reported clinical outcomes of radiation and prostatectomy; however, many of these did not report outcomes based on absolute measures of GP4. At the title and abstract stage, 1091 articles were excluded for failing to meet one or more of our inclusion criteria; 53 articles underwent full review and 46 studies were excluded for the following reasons: does not report absolute amount of GP4 (n=36), full text not in English (n=3), review article (n=1), amount GP4 only reported in radical prostatectomy specimen (n=4), and not a full text (n=2). In total, seven studies were included in the final analysis (Figure 2).

Study and patient demographics are provided in Table 1. All studies were retrospective and conducted in the U.S. (n=3), Canada (n=2), Japan (n=2), and Australia/New Zealand (n=1). A total of 2523 patients with intermediate-risk prostate cancer were included in this review, of which 1297 (51%) underwent radical prostatectomy and 1226 (49%) underwent radiotherapy. Of those receiving radiotherapy, 227 (19%) received prostate stereotactic body radiotherapy (SBRT) ± ADT, and 999 (81%) had external beam radiotherapy (EBRT) with high-dose rate (HDR) brachy boost ± ADT. Two articles evaluated APP4, four studies evaluated GP4-TL, and one study evaluated both. Biopsy strategy was reported in 1708 patients (five studies), of which 1240 (73%) were systematic, 431 (25%) were targeted, and 37 (2%) were systematic plus targeted.

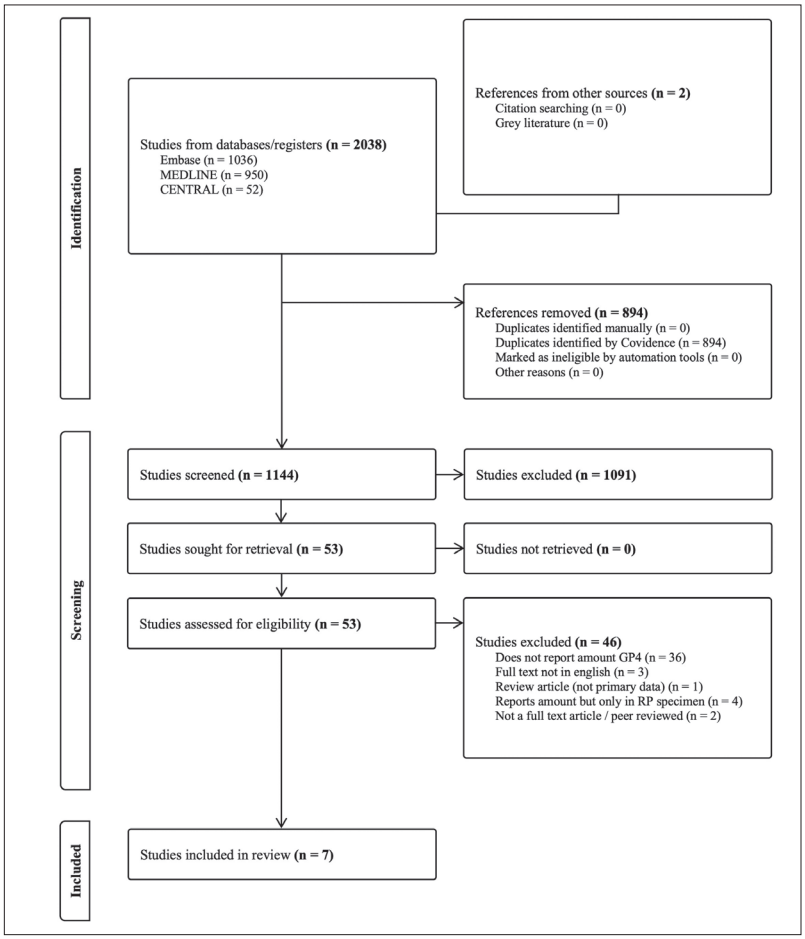

Figure 2. PRISMA diagram.

Outcomes

Biochemical recurrence

Four studies reported outcomes related to biochemical recurrence (BCR), defined as nadir + 2.0 ng/ml[11,12] or as two non-consecutive rises in PSA of ≥0.1 ng/ml starting six weeks post-radical prostatectomy.[7,8] Two studies used multivariable competing risk models to generate optimized APP4 cut points that were significantly predictive of BCR (Table 2). Glicksman et al found that a 5% cut point was significantly associated with BCR four years after SBRT.[12] Of note, 11 (4.9%) patients had ADT use with radiation. Martell et al reported an optimal APP4 threshold of 3.3% for BCR four years after EBRT with HDR brachy boost.[11] Perera et al calculated the risk of BCR after radical prostatectomy alone in mm of GP4-TL; patients with 2 mm of GP4 disease had a risk of 13% of BCR at three years, with 1–2% additional risk per mm increase.[8]

ADT-free survival

One study evaluated ADT-free survival, which consisted of the time from the date of EBRT with HDR brachytherapy boost to the date of any last followup or to the date of ADT initiation for BCR.[11] This study found an APP4 threshold of 6.6% to be highly predictive of ADT-free survival at four years following EBRT with HDR brachy boost.

Distant metastasis and mortality

Three studies investigated outcomes related to metastasis, prostate cancer-specific mortality, and all-cause mortality. Glicksman et al found that APP4 >20% was significantly associated with distant metastasis four years after SBRT.[12] Martell et al yielded a similar threshold of APP4 >17.5% for distant metastasis at four years

Table 1. Study characteristics

Author, year	Country	Study type	Absolute amount GP4	Inclusion criteria	N analyzed	Median age (y) (IQR)	Follow up (IQR)	Biopsy strategy	Treatment	Outcome measure
Dean, 2019	U.S.	R	GP4-TL	GG2 with 12 or more reviewed cores on biopsy	457	61.5 (56– 66)	–	Systematic n=249, targeted n=208	Radical prostatectomy	Adverse pathology (GG3/Gleason 4+3 or higher, extraprostatic extension, seminal vesicle involvement, lymph node metastases)
Martell, 2019	Canada	R	APP4	IRPC patients; sufficient information on biopsy to calculate APP4	411	66 (61–71)	5.2 y (2.9–6.6)	Systematic n=411	HDR brachy boost + EBRT	Biochemical failure (nadir + 2.0 ng/ml) ADT use for biochemical failure Metastatic disease
Sato, 2020	Japan	R	GP4-TL	Gleason 6–7 on biopsy	155 (with GP4 >5% analyzed) (Gleason 6, reference group n=115)	65 (61–69)	5.0 y (3.2–7)	Systematic n=140, MRI targeted n=15	Radical prostatectomy	Adverse pathology (Gleason 4+3 or higher, pT3b, positive lymph nodes) Biochemical recurrence
Delahunt, 2022	Australia New Zealand	R	GP4-TL APP4	IRPC or high-risk prostate cancer; both pattern 3 and 4 on biopsy sample	588	68.5 (63.3–72.9)	10.8 y (9.0–11.9)	–	Radiotherapy (66/70/74 Gy EBRT; HDR brachy boost); 6 or 18 months ADT	Distant progression Prostate cancer specific mortality All-cause mortality
Glicksman, 2022	Canada U.S.	R	APP4	IRPC	227	70 (64–75)	56.5 months (33.5–60.9)	Systematic plus targeted biopsy, number not reported	SBRT (40/5 or 26/2) ± ADT Median duration 4 months; 4.9% used ADT	Biochemical failure (nadir + 2.0 ng/ml) Distant metastasis-free survival
Perera, 2022	U.S.	R	GP4-TL	Gleason 7 prostate cancer, at least 12 cores	457	62 (57–66)	3.0 y (1.7–3.7)*	Systematic n=249, targeted n=208	Radical prostatectomy	Biochemical failure (2 non-consecutive rises in PSA of ≥0.1 ng/ml starting 6 weeks post-RP
Sato, 2023	Japan	R	GP4-TL	IRPC	228	65 (60.75–69)	–	Systematic n=191 Systematic plus targeted biopsy n=37	Radical prostatectomy	Adverse pathology (Gleason 4+3 or higher, pT3b, positive lymph nodes)

*Followup period only among those who did not experience biochemical recurrence. ADT: androgen deprivation therapy; APP4: absolute percentage pattern 4GG: grade group; EBRT: external beam radiotherapy; GP4: Gleason pattern 4; GP4-TL: total linear length of Gleason pattern 4; HDR: high dose rate; IRPC: intermediate-risk prostate cancer; R: retrospective; SBRT: stereotactic body radiation therapy.

after EBRT with HDR brachy boost.[11] In the analysis of Delahunt et al, APP4 was identified as the best prognostic factor for distant progression using the Akaike Information Criteria (AIC) and Harrell's C-index. Their data demonstrated that APP4 had the lowest AIC and highest C-index for distant metastasis, prostate cancer-specific mortality, and all-cause mortality, outperforming Gleason grading (4+3 vs. 3+4), % GP4 (total length GP4/total length malignant tissue), and GP4-TL (Supplementary Table 1; available at *cuaj.ca*).[10]

Table 2. Outcomes stratified by absolute percentage pattern 4 (APP4) cut point

Study, year Outcome	Time point	Optimal cut point	Cumulative incidence below and above cut point
Martell 2019			
BCR	At 4 years	APP4 3.3%	2% vs. 10%
ADT use for BCR		APP4 6.6%	2% vs. 10%
Distant metastasis		APP4 17.5%	0.4% vs. 5.2%
Glicksman 2022			
BCR	At 4 years	APP4 5%	2.3% vs. 23.6%
Distant metastasis		APP4 20%	1% vs. 12.5%

ADT: androgen deprivation therapy; BCR: biochemical recurrence.

Adverse pathology

Three studies evaluated GP4-TL and subsequent frequency of adverse pathology at radical prostatectomy, defined either as Gleason score 4+3=7 or higher, pT3a/b disease, or lymph node metastasis.[7-9] Perera et al estimated a 45% risk of adverse pathology for patients with 2 mm of GP4-TL, with the risk increasing by 5–8% for each additional mm of GP4.[8] Dean et al demonstrated that GP4-TL had the largest increase in the area under the curve on multivariable modeling, improving the model's predictive performance more than other variables tested, including overall % GP4 (GP4 tissue in all cores/total mm of cancer in all cores) and max % GP4 (the single core with the greatest involvement by pattern 4).[9] They also demonstrated that GP4-TL was the most effective measure in predicting adverse pathology on decision curve analysis.

DISCUSSION

This systematic review studied two methods of quantifying the absolute amount of GP4 on biopsy in intermediate-risk prostate cancer patients and found consistent associations between the absolute amount of GP4 and clinically important outcomes. Additionally, there is evidence to suggest that absolute GP4 may serve as a better prognostic factor for survival outcomes compared to relative % GP4 and Gleason 3+4 vs. 4+3. No definitive thresholds for treatment decisions can be recommended based on the current evidence due to the small number of studies evaluating this tool.

The % GP4 represents the proportion of GP4 within the tumor, which is influenced by the amount of GP3. In contrast, absolute measures reflect the percentage or length of GP4 relative to the total biopsied tissue, encompassing both benign and malignant areas. This helps provide a more comprehensive assessment of the potentially aggressive tumor burden within the sampled tissue; for instance, it reduces the risk of underestimating aggressiveness when GP3 predominates in the biopsy but an overall significant amount of GP4 is present across all biopsy cores. Conversely, it reduces the risk of overestimating aggressiveness when GP4 constitutes a large proportion of the tumor within the biopsy core when, in fact, the overall tumor size is small.

Accurate characterization of the Gleason pattern components on biopsy is important because GP3 alone does not appear to be associated with metastasis.[13] A recent editorial by Vickers et al reanalyzed data from two studies included in this review to evaluate whether GP3 is predictive of risk in men with grade groups 2–4.[14] Their multivariable model found that neither the length of GP3 nor the relative proportion of GP4 was predictive of adverse pathology. Additionally, their analysis on the predictive value of PSA showed that while adding the volume of GP3 was statistically significant, it did not substantially improve the R^2 value. This suggests that GP3's predictive value is limited when compared to GP4.

Another recent study demonstrated that a multivariable model incorporating the volume of GP4 or GP5 was a more robust predictor of metastasis after radical prostatectomy (C-index 0.86) than a model incorporating grade groups (C-index 0.74).[15] These results reinforce the findings of this systematic review that suggests that the absolute amount of GP4 may be a better predictor of outcomes in localized cancer.

Incorporating absolute amount of GP4 in practice and management guidelines is feasible and relatively inexpensive. Unlike novel stratification tools, such as genomic risk stratifiers and artificial intelligence biomarkers, which are hindered by high costs and concerns over generalizability,[16,17] absolute amount of GP4 offers an accessible and established method. In various institutions, parameters needed to calculate absolute amount of GP4 are routinely included in biopsy reports. This can be calculated in clinic and used to inform decisions on active surveillance, addition of ADT to radiation, dose escalation with brachytherapy boost, or integration of boost in EBRT.[11]

Magnetic resonance imaging (MRI)-fusion-targeted biopsies are known to increase the detection of clinically significant tumors.[18] Consequently, it raises the question of whether targeted biopsies might oversample GP4 when compared to the traditional systematic biopsy. In the study by Perera et al, involving 208 MRI-targeted and 249 systematic biopsies, the biopsy method did not significantly affect GP4 quantification (all $p>0.063$).[8] Notably, no other studies performed separate analyses

by biopsy type and two studies in this review did not report biopsy strategy. Future research should ensure standardized reporting of biopsy methods and consider separate analyses to assess how biopsy technique may impact the amount of GP4 detected at biopsy.

Limitations

This study is the first to synthesize the available data on absolute amount of GP4, underscoring a promising area for further research; however, our study has some important limitations.

The included studies are heterogeneous in terms of study populations, interventions, outcomes, and methodologies. This variability precluded the possibility of conducting a meta-analysis, thereby limiting the extent of our conclusions. Two of the included studies were conducted by the same author group, resulting in overlapping patient cohorts. While cohorts can skew the perceived amount of evidence supporting the conclusion, we decided to include both studies, as they performed distinct data analyses.[8,9] Another limitation of our systematic review is the absence of a formal risk of bias analysis. Future studies should incorporate risk of bias assessments to evaluate the presence of bias, which may affect the overall validity and generalizability of results.

CONCLUSIONS

The absolute amount of GP4 at biopsy is a practical tool with consistent associations to clinically important outcomes and has the potential to improve risk-stratification models for intermediate-risk prostate cancer patients. Further investigation is needed to establish thresholds that may help guide treatment recommendations. Future studies would benefit from consistently reporting biopsy strategies used in their study sample.

COMPETING INTERESTS: Dr. Lavallée has participated in advisory boards for Knight; and received an unrestricted research grant (paid to his institution) from Tolmar. Dr. Corkum has received grants and/or honoraria from Abbvie, Knight, Tersera, and Tolmar. The remaining authors do not report any competing personal or financial interests related to this work.

ACKNOWLEDGEMENT: The authors would like to thank Risa Shorr for their valuable assistance in conducting the literature search for this systematic review.

REFERENCES

1. D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998;280:969-74. https://doi.org/10.1001/jama.280.11.969
2. National Comprehensive Cancer Network. NCCN guidelines: Prostate cancer version 4. *NCCN* 2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf
3. Chen N, Zhou Q. The evolving Gleason grading system. *Chin J Cancer Res* 2016;28:58-64.
4. Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: Definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol* 2016;40:244-52. https://doi.org/10.1097/PAS.0000000000000530
5. Sauter G, Steurer S, Clauditz TS, et al. Clinical utility of quantitative Gleason grading in prostate biopsies and prostatectomy specimens. *Eur Urol* 2016;69:592-8. https://doi.org/10.1016/j.eururo.2015.10.029
6. Sato S, Kimura T, Onuma H, et al. The highest percentage of Gleason pattern 4 is a predictor in intermediate-risk prostate cancer. *BJUI Compass* 2023;4:234-40. https://doi.org/10.1002/bco2.195
7. Sato S, Kimura T, Onuma H et al. Combination of total length of Gleason pattern 4 and number of Gleason score 3+4=7 cores detects similar outcome group to Gleason score 6 cancers among cases with ≥5% of Gleason pattern 4. *Pathol Int* 2020;70:992-8. https://doi.org/10.1111/pin.13026
8. Perera M, Assel MJ, Benfante NE, et al. Oncologic outcomes of total length Gleason pattern 4 on biopsy in men with grade group 2 prostate cancer. *J Urol* 2022;208:309-16. https://doi.org/10.1097/JU.0000000000002685
9. Dean LW, Assel M, Sjoberg DD et al. Clinical usefulness of total length of Gleason pattern 4 on biopsy in men with grade group 2 prostate cancer. *J Urol* 2019;201:77-82. https://doi.org/10.1016/j.juro.2018.07.062
10. Delahunt B, Steigler A, Atkinson C, et al. Percentage grade 4 tumor predicts outcome for prostate adenocarcinoma in needle biopsies from patients with advanced disease: 10-year data from the TROG 03.04 RADAR trial. *Pathology* 2022;54:49-54. https://doi.org/10.1016/j.pathol.2021.11.004
11. Martell K, Mendez LC, Chung H, et al. Absolute percentage of biopsied tissue positive for Gleason pattern 4 disease (APP4) appears predictive of disease control after high dose rate brachytherapy and external beam radiotherapy in intermediate-risk prostate cancer. *Radiother Oncol* 2019;135:170-7. https://doi.org/10.1016/j.radonc.2019.03.007
12. Glicksman RM, Kishan AU, Quon H, et al. Absolute percentage of pattern 4 disease as a prognostic measure for intermediate-risk prostate cancer treated with stereotactic body radiotherapy. *Clin Oncol* 2022;34:581-8. https://doi.org/10.1016/j.clon.2022.05.002
13. Ross HM, Kryvenko ON, Cowan JE, et al. Do adenocarcinomas of the prostate with Gleason score 6 have the potential to metastasize to lymph nodes? *Am J Surg Pathol* 2012;36:1346-52. https://doi.org/10.1097/PAS.0b013e3182556dcd
14. Vickers AJ, Assel M, Cooperberg MR, et al. Amount of Gleason pattern 3 is not predictive of risk in grade group 2-4 prostate cancer. *Eur Urol* 2024;861-3. https://doi.org/10.1016/j.eururo.2024.01.005
15. Bommelaere T, Villers A, Puech P, et al. Risk estimation of metastatic recurrence after prostatectomy: A model using preoperative magnetic resonance imaging and targeted biopsy. *Eur Urol Open Sci* 2022;41:24-34. https://doi.org/10.1016/j.euros.2022.04.011
16. Gaudreau PO, Stagg J, Soulières D, et al. The present and future of biomarkers in prostate cancer: Proteomics, genomics, and immunology advancements. *Biomark Cancer* 2016;8:15-33. https://doi.org/10.4137/BIC.S31802
17. Spratt DE, Tang S, Sun Y, et al. Artificial intelligence predictive model for hormone therapy use in prostate cancer. *NEJM Evid* 2023;2:EVIDoa2300023. https://doi.org/10.1056/EVIDoa2300023
18. Siddiqui MM, Rais-Bahrami S, Truong H, et al. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer versus systematic 12-core transrectal ultrasound biopsy. *Eur Urol* 2013;64:713-9. https://doi.org/10.1016/j.eururo.2013.05.059

CORRESPONDENCE: Dr. Mark Corkum, Division of Radiation Oncology, Department of Radiology, University of Ottawa and the Ottawa Hospital, Ottawa,ON, Canada; mcorkum@toh.ca

Visit *https://www.cua.org/UROpedia* to complete the questionnaire associated with this article. This program is an Accredited Self-Assessment Program (Section 3) as defined by the Maintenance of Certification Program of RCPSC and approved by the CUA. You may claim a maximum of 1 hour of credit.