Target prostate biopsies: How best to report in synoptic format?

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Introduction

The implementation and increasingly widespread use of multiparametric magnetic resonance imaging (mpMRI) in prostate cancer patients is changing clinical practice. Traditional systematic transrectal ultrasound (TRUS)-guided biopsy consisting of 10–12 needle cores has been shown to have lower sensitivity than targeted biopsy for the detection of clinically significant cancer,[1] with target biopsies better predicting extraprostatic extension at prostatectomy,[2] detecting anteriorly located tumors,[3] and identifying perineural invasion.[4] Further, target biopsy Gleason scores are less likely to be upgraded at prostatectomy compared with TRUS Gleason scores.[5] The PRECISION trial and the Canadian PRECISE trial, which compared MRI targeted biopsy vs. TRUS biopsy in biopsy-naive men, demonstrated the benefit of MRI targeted biopsy in biopsy-naive patients such that more clinically significant cancers were identified in the MRI targeted arm.[2,6] The ASIST trial also showed a reduction in upgrading at two-year followup biopsies when patients had baseline MRI targeted biopsies.[7]

An MRI targeted biopsies can be either a stand-alone target biopsy consisting of several cores from a single target including multiple targets, or a combination of target and systematic biopsies. Reporting these biopsies in a format that communicates all the relevant information in a concise and accurate manner is crucial. Synoptic reports for prostate biopsies have been in existence in several jurisdictions for many years (International Collaboration Cancer Reporting, Cancer Care Ontario, College of American Pathologists) but the current formats do not account for the evolving change in clinical practice to incorporate prostate target biopsies. The literature to date suggests the optimal method for reporting MRI targeted biopsies is to provide a composite World Health Organization grade (WHO grade)/Gleason score (GS) and cancer extent per target site as opposed to grades/Gleason score for each target core. This method correlates better with both overall tumor volume and extraprostatic extension at prostatectomy.[8] Further, invasive cribriform and intraductal carcinoma (histopathological features associated with adverse clinical outcomes, including biochemical recurrence after prostatectomy and survival), need to be considered in addition to the traditional WHO grade/GS.[9] While most studies have reported that these adverse features are more likely to be present at MRI sites of disease,[10] others have concluded that most cribriform tumors were nonvisible on mpMRI.[11] Given the contradictory reports, there is uncertainty as to whether invasive cribriform and intraductal cancer patterns are visible on MRI or not.

The authors (pathologists, urologists, radiologists, radiation oncologists) propose a comprehensive prostate synoptic biopsy report that can be used for reporting of systematic-only, target-only, or combined target-systematic biopsies (see sample synoptic report below). We have included various data elements based on our experience and practice, which will enable clinicians to derive maximal information to drive patient management. The essential elements of such a synoptic report include both a global WHO grade/GS, taking into account the grade of all biopsy cores, and a composite WHO grade/GS for each separate target component. A variety of additional parameters — presence/absence of cribriform architecture carcinoma (both intraductal carcinoma and cribriform pattern 4), the number of positive sites/cores, total number of sites/cores, perineural invasion, seminal vesicle involvement, periprostatic fat involvement and lymphovascular invasion — are also included as per standard synoptic report format (report template available as an Appendix at *cuaj.ca*).

Synoptic report components

1. Histological type

Several subtypes of prostatic adenocarcinoma (e.g., neuroendocrine, basal/adenoid cystic) do not require a grade/GS, hence the need to specify the histological subtype.

2. Worst WHO grade/GS

The literature shows conflicting results around whether global or worst grade/GS provides better prognostic information, with global WHO grade/GS showing marginal superiority.[12,13] Some clinicians use the "worst" grade/GS, while others prefer the global score.[14] For this reason, we think inclusion of the worst grade/GS by site or core is of relevance.

3. Global WHO grade/GS

We propose inclusion of a global grade to encompass the target and systematic cores in cases where both are performed. Given the preference for global grade assignment in some practices[15] and the use of global scores by some clinicians (and for epidemiological purposes), this is a necessary component of such a synoptic report.

4. Composite WHO grade/GS

The composite WHO grade/GS is of targeted biopsies based on the combined grade of all cores taken from a single MRI focus or TRUS/digital rectal exam (DRE) nodule, considering all cores as originating from a single tumor focus.[16] In a similar manner, a composite score can also be applied in the systematic biopsy setting, where >1 core is sampled from a single site and/or submitted in a single container. Again, the combined/composite WHO grade or GS can be used as opposed to individual GS on a per-core basis. An example is as follows: three biopsies are taken from the right apex. Biopsy core 1 is GS 3+3 in 80% of core, core 2 is GS 3+4 in 40% of core, and core 3 is 4+4 in 5% of core. Thus, a composite score for the three cores from the right apex would 3+4.

5. Adverse prognostic features

Cribriform architecture carcinoma includes intraductal carcinoma and cribriform pattern 4. Both are recognized as adverse morphological features in biopsies[17-19] and their presence should be documented. The ability of MRI to identify these lesions is critical to ensure sampling of these aggressive sub-pathologies; thus, for an individual target, their presence/absence should be recorded. Documentation of whether intraductal carcinoma has been included in grade assignment is also recommended, as some pathologists grade intraductal and others do not.[9,20]

6. Tumor quantitation and extent of carcinoma

Tumor quantitation needs to be reported in several ways for the following reasons: to support data inclusion in nomograms (e.g., the Cancer of the Prostate Risk Assessment [CAPRA], Memorial Sloan-Kettering Cancer Center (MSKCC), European Association of Urology [EAU]) and to determine active surveillance eligibility (some protocols define inclusion by the number of cores containing carcinoma). Firstly, the total number of cores sampled and the number of positive cores should be documented. Likewise, the number of positive sites and total number of sites sampled can be recorded. Thus, for a positive target biopsy, 5/5 cores may be involved but only 1/1 site. For systematic cores, the usual method of core assessment would be employed (consider each site as separate) so that a standard 12-core biopsy with one core per site would still count as 12 cores and 12 sites.

The carcinoma extent within each core needs to be documented for systematic biopsies. This can be done as either mm of carcinoma or as percent core involvement. Additionally, the method by which the tumor has been measured needs to be documented (e.g., considering multiple foci within the core as continuous [each focus is measured individually and the sum is regarded as the amount of core involvement] or discontinuous involvement [intervening benign stroma is included in the estimate of core involvement]). This impacts the overall assessment of tumor volume.[21,22]

For an individual target, an aggregate measurement of carcinoma extent should be provided as either mm of tumor or as a percentage of tissue involved (Fig. 1). This is supported by a previous publication showing aggregate percentage assessment to be superior to individual core assessment[8] in MRI target biopsies.

7. Percent high-grade (pattern 4, 5) carcinoma

For International Society of Urological Pathology (ISUP)/WHO grade 2 and 3 adenocarcinoma, the percentage of pattern 4 should be documented as low-volume pattern 4 (<10%) and could qualify some patients as eligible for active surveillance.[23] For all carcinomas >WHO grade 1/GS6, the percent of high-grade (GG4/5) component needs to be documented, as it has prognostic impact[24] and may be incorporated into algorithms (e.g., absolute percentage pattern 4) that predict for metastatic failure-free survival.[25]

8. Stage-related features

The presence/absence of these features should be documented because of its unfavorable prognostic implications:

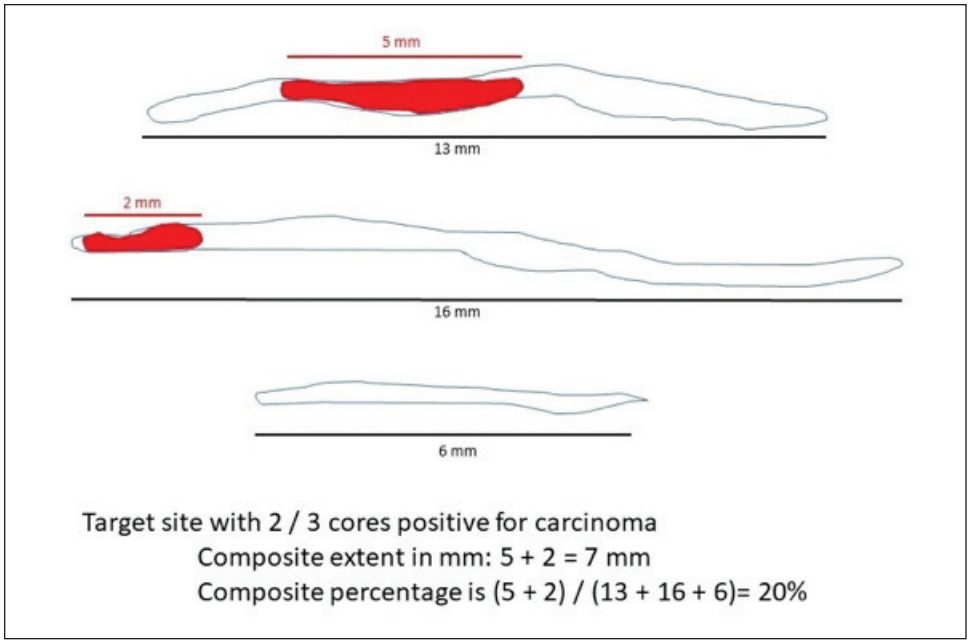

Fig. 1. Diagrammatic representation of composite calculation of Word Health Organization (WHO) grade/Gleason score and tumor volume in a target biopsy.

perineural invasion,[26] periprostatic fat involvement,[27] seminal vesicle invasion, and lymphovascular space invasion.[28]

9. Target specific reporting

The method of target detection — MRI, ultrasound, DRE, or other (e.g., prostate-specific membrane antigen-positron emission tomography [PSMA-PET] scan) — should be specified (Note: For each target, a WHO grade/GS needs to be provided. We term these composite grades/GS to differentiate from the global grade assigned to the entire case [encompasses all targets ± systematic cores]).

10. Other features

The presence of other histological features can be noted in a separate "Additional features" category (e.g., high-grade prostatic intraepithelial neoplasia, atypical small acinar proliferation, adenosis, and inflammation). For target biopsies, it is helpful to document the benign histologies present when the biopsy is negative for carcinoma, as it has been demonstrated that increased stroma, chronic inflammation, and atrophy can be associated with false-positive findings on prostate MRI.[29]

Conclusions

The reporting of prostate biopsies is an evolving field and the advent of mpMRI and other technique-driven target biopsies necessitates a change in practice. We propose a comprehensive synoptic report that can encompass both target and systematic biopsy cores to provide optimal information for patient management. It is not our intention to advise on which elements individual clinicians should use in their management approach. We are advocating for comprehensive, complete synoptic reports including all relevant data to enable clinicians who use any combination of biopsy data to access all the information they require in a single report.

Competing interests: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

References

1. Siddiqui MM, Rais-Bahrami S, Truong H, et al. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer vs. systematic 12-core transrectal ultrasound biopsy. *Eur Urol* 2013;64:713-9. https://doi.org/10.1016/j.eururo.2013.05.059
2. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med* 2018;378:1767-77. https://doi.org/10.1056/NEJMoa1801993
3. Volkin D, Turkbey B, Hoang AN, et al. Multiparametric magnetic resonance imaging (MRI) and subsequent MRI/ultrasonography fusion-guided biopsy increase the detection of anteriorly located prostate cancers. *BJU Int* 2014;114:E43-9. https://doi.org/10.1111/bju.12670
4. Gordetsky JB, Nix JW, Rais-Bahrami S. Perineural invasion in prostate cancer is more frequently detected by multiparametric MRT targeted biopsy compared with standard biopsy. *Am J Surg Pathol* 2016;40:490-4. https://doi.org/10.1097/PAS.0000000000000546
5. Zhao Y, Deng FM, Huang H, et al. Prostate cancers detected by magnetic resonance imaging-targeted biopsies have a higher percentage of Gleason pattern 4 component and are less likely to be upgraded in radical prostatectomies. *Arch Pathol Lab Med* 2019;143:86-91. https://doi.org/10.5858/arpa.2017-0410-OA
6. Klotz L, Chin J, Black PC, et al. Comparison of multiparametric magnetic resonance imaging-targeted biopsy with systematic transrectal ultrasonography biopsy for biopsy-naive men at risk for prostate cancer: A phase 3 randomized clinical trial. *JAMA Oncol* 2021;7:534-42. https://doi.org/10.1001/jamaoncol.2020.7589
7. Klotz L, Pond G, Loblaw A, et al. Randomized study of systematic biopsy vs. magnetic resonance imaging and targeted and systematic biopsy in men on active surveillance (ASIST): 2-year post-biopsy followup. *Eur Urol* 2020;77:311-7. https://doi.org/10.1016/j.eururo.2019.10.007
8. Gordetsky JB, Schultz L, Porter KK, et al. Defining the optimal method for reporting prostate cancer grade and tumor extent on magnetic resonance/ultrasound fusion-targeted biopsies. *Hum Pathol* 2018;76:68-75. https://doi.org/10.1016/j.humpath.2018.03.005
9. van Leenders G, van der Kwast TH, Grignon DJ, et al. The 2019 international society of urological pathology (ISUP) consensus conference on grading of prostatic carcinoma. *Am J Surg Pathol* 2020;44:e87-99. https://doi.org/10.1097/PAS.0000000000001497
10. Prendeville S, Gertner M, Maganti M, et al. Role of magnetic resonance imaging targeted biopsy in detection of prostate cancer harboring adverse pathological features of intraductal carcinoma and invasive cribriform carcinoma. *J Urol* 2018;200:104-13. https://doi.org/10.1016/j.juro.2018.01.081
11. Truong M, Feng C, Hollenberg G, et al. A comprehensive analysis of cribriform morphology on magnetic resonance imaging/ultrasound fusion biopsy correlated with radical prostatectomy specimens. *J Urol* 2018;199:106-13. https://doi.org/10.1016/j.juro.2017.07.037

12. Athanazio D, Gotto G, Shea-Budgell M, et al. Global Gleason grade groups in prostate cancer: Concordance of biopsy and radical prostatectomy grades and predictors of upgrade and downgrade. *Histopathology* 2017;70:1098-106. https://doi.org/10.1111/his.13179
13. Trpkov K, Sangkhamanon S, Yilmaz A, et al. Concordance of "case level" global, highest, and largest volume cancer grade group on needle biopsy vs. grade group on radical prostatectomy. *Am J Surg Pathol* 2018;42:1522-9. https://doi.org/10.1097/PAS.0000000000001137
14. Varma M, Narahari K, Mason M, et al. Contemporary prostate biopsy reporting: Insights from a survey of clinicians' use of pathology data. *J Clin Pathol* 2018;71:874-8. https://doi.org/10.1136/jclinpath-2018-205093
15. Berney DM, Algaba F, Camparo P, et al. The reasons behind variation in Gleason grading of prostatic biopsies: Areas of agreement and misconception among 266 European pathologists. *Histopathology* 2014;64:405-11. https://doi.org/10.1111/his.12284
16. Arias-Stella JA 3rd, Shah AB, Montoya-Cerrillo D, et al. Prostate biopsy and radical prostatectomy Gleason score correlation in heterogenous tumors: Proposal for a composite Gleason score. *Am J Surg Pathol* 2015;39:1213-8. https://doi.org/10.1097/PAS.0000000000000499
17. Downes MR, Xu B, van der Kwast TH. Cribriform architecture prostatic adenocarcinoma in needle biopsies is a strong independent predictor for lymph node metastases in radical prostatectomy. *Eur J Cancer* 2021;148:432-9. https://doi.org/10.1016/j.ejca.2020.09.016
18. Watts K, Li J, Magi-Galluzzi C, et al. Incidence and clinicopathological characteristics of intraductal carcinoma detected in prostate biopsies: A prospective cohort study. *Histopathology* 2013;63:574-9. https://doi.org/10.1111/his.12198
19. Van der Kwast T, Al Daoud N, Collette L, et al. Biopsy diagnosis of intraductal carcinoma is prognostic in intermediate and high-risk prostate cancer patients treated by radiotherapy. *Eur J Cancer* 2012;48:1318-25. https://doi.org/10.1016/j.ejca.2012.02.003
20. Epstein JI, Amin MB, Fine SW, et al. The 2019 genitourinary pathology society (GUPS) white paper on contemporary grading of prostate cancer. *Arch Pathol Lab Med* 2021;145:461-93. https://doi.org/10.5858/arpa.2020-0015-RA
21. Brimo F, Vollmer RT, Corcos J, et al. Prognostic value of various morphometric measurements of tumor extent in prostate needle core tissue. *Histopathology* 2008;53:177-83. https://doi.org/10.1111/j.1365-2559.2008.03087.x
22. Karram S, Trock BJ, Netto GJ, et al. Should intervening benign tissue be included in the measurement of discontinuous foci of cancer on prostate needle biopsy? Correlation with radical prostatectomy findings. *Am J Surg Pathol* 2011;35:1351-5. https://doi.org/10.1097/PAS.0b013e3182217b79
23. Morash C, Tey R, Agbassi C, et al. Active surveillance for the management of localized prostate cancer: Guideline recommendations. *Can Urol Assoc J* 2015;9:171-8. https://doi.org/10.5489/cuaj.2806
24. 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
25. 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
26. Delahunt B, Murray JD, Steigler A, et al. Perineural invasion by prostate adenocarcinoma in needle biopsies predicts bone metastasis: Ten-year data from the TROG 03.04 RADAR trial. *Histopathology* 2020;77:284-92. https://doi.org/10.1111/his.14107
27. Goldberg H, Ramiz AH, Glicksman R, et al. Extraprostatic extension in core biopsies epitomizes high-risk but locally treatable prostate cancer. *Eur Urol Oncol* 2019;2:88-96. https://doi.org/10.1016/j.euo.2018.05.003
28. Saeter T, Vlatkovic L, Waaler G, et al. Combining lymphovascular invasion with reactive stromal grade predicts prostate cancer mortality. *Prostate* 2016;76:1088-94. https://doi.org/10.1002/pros.23192
29. Gordetsky JB, Ullman D, Schultz L, et al. Histological findings associated with false-positive multiparametric magnetic resonance imaging performed for prostate cancer detection. *Hum Pathol* 2019;83:159-65. https://doi.org/10.1016/j.humpath.2018.08.021

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